STEREOSELECTIVE SYNTHESIS OF CYCLOPROPANES WITH QUATERNARY CARBON CENTRES

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STEREOSELECTIVE SYNTHESIS OF CYCLOPROPANES WITH QUATERNARY CARBON CENTRES

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By

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Declaration

The research described in this thesis is, to the best of my knowledge, original, except where due reference is made to other authors and has not been submitted in any part or form for a degree at this or any other university.

Signed_____

Fabrizio Minicone

Abstract

Multi-substituted optically pure cyclopropanes are important motifs present in many agrochemicals, pharmaceuticals and materials employed in manifold applications. Their synthesis is challenging due to both the strained conformation and the need to control both the relative and absolute stereochemistry. This thesis describes an investigation of the scope of the Wadsworth-Emmons cyclopropanation, highlighting it as a potential efficient methodology for diastereoselective and enantiospecific synthesis of these valuable ring systems.

Chapter 1 is an introduction to the cyclopropanation protocols and is split in two subsections. The first is a description of the currently most exploited synthetic pathways to cyclopropanes, with analysis of their substrate scope and critical analysis of their limitations as compared to potential of the Wadsworth-Emmons cyclopropanation (Sections 1.1 to 1.3). The latter section consists of a review on the history and the evolution of this procedure and introduces the preconditions for the development of the project (Sections 1.4 to 1.17).

Chapter 2 describes the results and discussion, introducing the use of novel alkyl-substituted triethyl phosphonoacetates to yield cyclopropyl-esters containing quaternary stereocentres. The high yields and the excellent *trans*-diastereoselectivity values obtained (proved by X-ray crystallography) allowed the proposal of a suggested reaction mechanism, which is supported by the subsequent experiments carried out in the presence of other functional groups, *e.g.* other carbonyls, nitriles, hetero-aromatics, substituted phenyl rings. This study was further extended to examine the effect of fluorine atom, due to its importance in biologically active environments. The study on the stereochemistry of the Wadsworth-Emmons cyclopropanation has been strongly supported by a range of X-ray crystal structures of the cyclopropane products. The chapter ends with an empirical set of guidelines, helpful for the design of successful cyclopropanations.

Chapter 3, describes the experimental methods in full as well as full characterisation of the products obtained. Literature references, noted throughout the thesis, are listed in the final chapter.

Acknowledgements

Firstly, I would like to thank all the people who contributed to the personal and professional support to the project: Dr Bray for applying for the funding and allowing me to undertake this project; EPSRC for financial backing and those who have constructively helped me to achieve this goal. My thanks must also be extended to the Nicky and Siobhán, who have all contributed to making the lab environment a pleasure to work in.

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There are so many other people who I have worked with in the lab, in other research groups, who have made my time here more enjoyable – too many to do justice to on this page and name individually. I would however like to thank Jules, Siobhán, Freda, Tanya, Paolo B, Paolo R, Marco and Greg for their support and friendship over the past years.

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Table of Contents

Abbreviations

Ac	Acetyl
aq	Aqueous
Ar	Aromatic
ASG	Anion Stabilising Group
Boc	*tert*-Butyloxycarbonyl
bp	Boiling point
Bs	4-Bromobenzenesulfonyl
Bz	Benzoyl
cat.	Catalytic
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
de	Diastereomeric Excess
DMAP	4-Dimethylaminopyridine
DME	Dimethoxyethane
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethylsulfoxide
DNA	Deoxyribonucleic Acid
DPPA	Diphenyl phosphoryl azide
dr	Diastereomeric Ratio
Ee	Enantiomeric Excess
equiv	Equivalent
er	Enantiomeric Ratio
EWG	Electron-Withdrawing Group
GABA	γ-Aminobutyric Acid

GC-MS	Gas Chromatography Mass Spectrometry
Hex	Hexyl
HPLC	High Performance Liquid Chromatography
LDA	Lithium diisopropylamine
LHMDS	Lithium hexamethyldisilazide
m-CPBA	*meta*-Chloroperoxybenzoic acid
m/z	Mass to charge ratio
NBS	*N*-Bromosuccinamide
NMR	Nuclear Magnetic Resonance
Nu	Nucleophile
PG	Protecting group
ppm	Part per million
rt	Room temperature
sat	Saturated
TBAB	Tetrabutylammonium Bromide
Tf	Trifluoromethanesulfonyl
TEA	Triethylamine
TFA	Trifluoroacetic acid
TFPAA	Trifluoroperoxyacetic acid
THF	Tetrahydrofuran
TMS	Trimethylsilyl
t_R	Retention time
p-TSA	*para*-toluenesulphonic acid
UV	Ultra Violet

1 INTRODUCTION

1.1 Cyclopropane moiety and current synthetic protocols

Cyclopropanes are the smallest of all the alicyclic rings and show unique geometrical features with respect to the their acyclic homologues. The bond angle between three sp^3 hybridised carbon atoms in a typical alkane is 109.5°, where the C−C electronic bond density is positioned along the inter-nuclear axis. Instead, the cyclopropyl atomic arrangement requires a bond angle of 60°, constituting a noteworthy distortion. According to valence bond theory, this triangular geometry is achieved by enhancing the *p*-character in the *endo*-cyclic bonds. This "bent bond" model reduces the small-angle strain in the molecule, forming an inter-orbital angle of *circa* 102°,[1] where the electronic density is perturbed from the inter-nuclear axis.[2] As this bonding model assigns additional *s*-character to the *exo*-cyclic C−H bonds, these protons show an upfield shift (typically <1 ppm with even <0 ppm being possible) compared to normal alkanes.[3] The sp^2-like nature of the orbitals of this bond is exemplified by the comparison with ethylene, which shows a H−C−H bond angle of 116.5° and a pK_a of 44, as compared to the values for cyclopropane, which possesses a H−C−H bond angle of 116.6° and a pK_a of 46.[4] Other differences are found compared to less strained acyclic alkanes. The cyclopropane bonds are slightly shorter (C−C 1.502 Å; C−H 1.078 Å) than in a regular alkane bond (C−C 1.522 Å; C−H 1.088 Å) (Figure 1).[5]

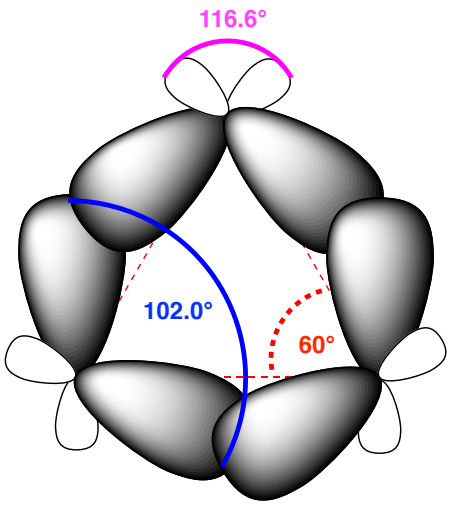
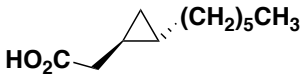
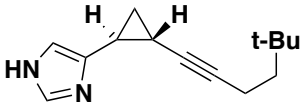


Figure 1 Bond angles in cyclopropane scaffold.

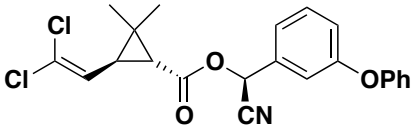
Due to the total strain energy (27.5 kcal/mol), cyclopropanes tend to react to reduce this contribution. For example, cyclopropanes with unsaturation in proximal positions are known to undergo a wide range of transformations in the presence of transition metals such as addition reactions, cycloadditions, cycloisomerisations, cross-coupling and metathesis protocols.[6] As the rigid geometry allows control of the relative stereochemistry between the substituents, this class of compounds may be exploited as precursor molecules in highly challenging syntheses - *i.e.* intermediates in regio- and stereoselective routes to various functionalities.[7] Nevertheless, they often represent the core motif in many natural products, drugs, agrochemicals and food (Figure 2).[8]



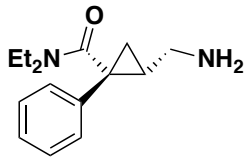
Cascarillic acid
Essential oil used to treat symptons of influenza and respiratory ailments



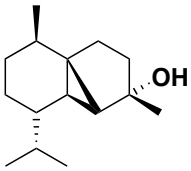
Cipralisant
An extremely potent histamine H_3 antagonist



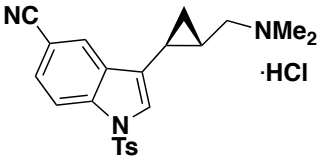
Cypermetrin
An insecticide in many household fly-sprays



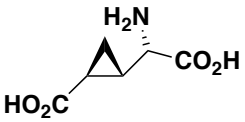
Milnacipran (Ixel)
Approved for fibromyalgia



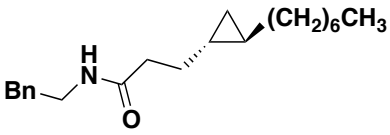
Cubebol
A sesquiterpene used in the food industry



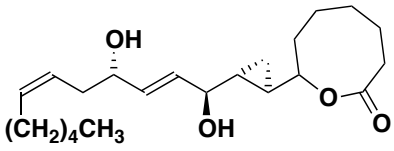
BMS-505130
Selective serotonin reuptake inhibitor



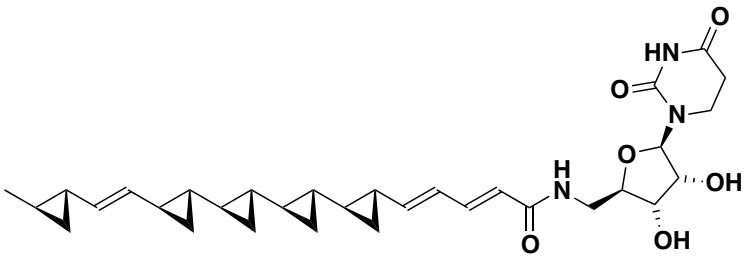
L-CCG-II
Motif present in therapeutic drugs of various neuronal diseases



Grenadamide
Potential cannabinoid receptor binding activity, cytotoxic against tumoral cells



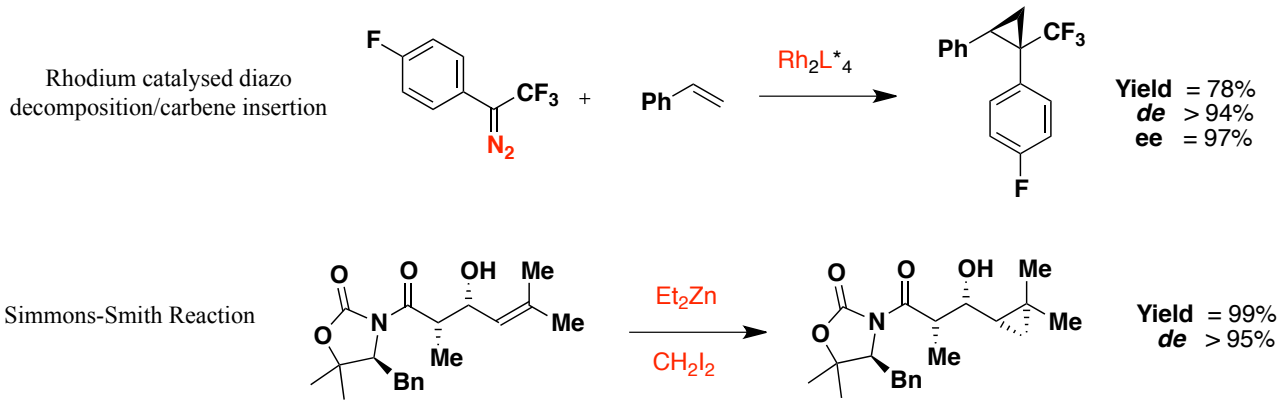
Solandelactone B
Biologically active oxylipin



FR-900848
Nucleoside active against filametous fungi

Figure 2 Important cyclopropane containing molecules.

Two distinct strategies are reported to achieve stereoselective cyclopropanation. The first involves concerted formation of the two C–C bonds, as exemplified by both the Rh-catalysed diazo decomposition/carbene insertion[9] and the Simmons-Smith[9a,10] reaction (Scheme 1). As carbene transfer occurs in a concerted manner, the alkene geometry is normally retained in the product; however the facial selectivity, which determines the enantioselectivity, requires careful control. Furthermore, the use of a prochiral carbene introduces an additional level of complexity where diastereoselectivity must also be considered.

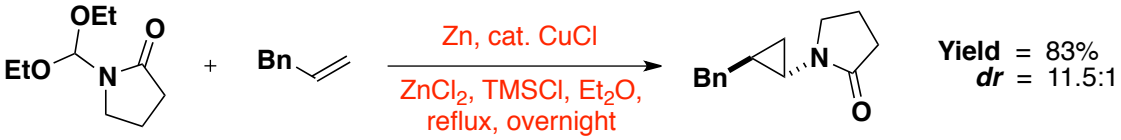


Scheme 1 Concerted formation of two C–C bonds at once, *i.e.* carbene addition to an alkene.

The conversion of olefins *via* transition-metal-catalysed decomposition of diazoalkenes is one of the most widely applied routes to cyclopropane synthesis. The most recent achievements describe highly efficient processes in the presence of catalytic quantities of metals such as Rh(II) or Cu(I), affording excellent enantioselectivity when chiral bidentate ligands are used. A recent review offers greater insight into processes involved.[9a] The relative stereochemistry is determined by the interactions arising during the reaction pathway amongst the substituents installed in the reagents and is therefore more difficult to control. Nevertheless, as with the synthesis of alkenes, it is possible to orientate larger groups *trans* across the ring to give a thermodynamically more stable product. Furthermore, this synthetic protocol is generally restricted to stable diazo compounds bearing electron-withdrawing groups that can stabilize the diazoalkane by both inductive and resonance effects, as unstable substrates are potentially explosive. Finally, the cost of both the metal

and the synthetically challenging chiral ligand alongside laborious substrate dependant optimisation, currently represents major issues to solve.

The Simmons-Smith pathway shows a wider tolerance to a variety of functional groups installed on the olefin. As the methylene transfer occurs in a stereospecific manner, its insertion preserves the relative stereochemistry of the alkene – *i.e.* an (*E*)-olefin is converted to a *trans*-cyclopropane.[11] As the kinetics of the reaction is much faster in the presence of vicinal heteroatoms, this reaction has been broadly investigated for allylic alcohols. Since the alcoholic function additionally promotes *syn*-directed insertion of the methylene group, several enantioselective examples have been described, using either chiral auxiliaries or ligands. In 1994, Charette and co-workers described the application of an amphoteric bifunctional dioxaborolane for the enantioselective cyclopropanation of allylic alcohols.[12] Despite the wide use of this method in the synthesis of natural products,[13] this protocol required super-stoichiometric quantities of the ligand and found its applicability restricted to allylic alcohols only. Other limitations of this method include the pyrophoric nature of the typical reductant (Et_2Zn) and the toxicity of the diiodomethane. Motherwell and co-workers reported a variation of the Simmons-Smith cyclopropanation by replacing the diiodomethane with organozinc carbenoids generated from diethoxymethylamides, allowing for the synthesis of amidocyclopropanes[14a] (Scheme 2).

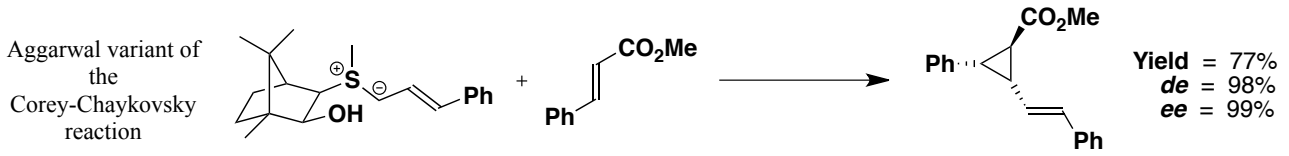


Scheme 2 Motherwell and co-workers variation of the Simmons-Smith cyclopropanation.

These substrates could be further converted to aminoalcohol,[14a] aminoacids[14a] and amines.[14b] Asymmetric syntheses of amido- and aminocyclopropanes were achieved by using chiral organozinc carbenoids.[14b] Additionally, this approach also allowed one-pot cyclopropanation without the need to isolate the diethoxymethylamide derivative.[14] Nevertheless, with respect to the more traditional Simmons-Smith cyclopropanation, the control of the relative stereochemistry is

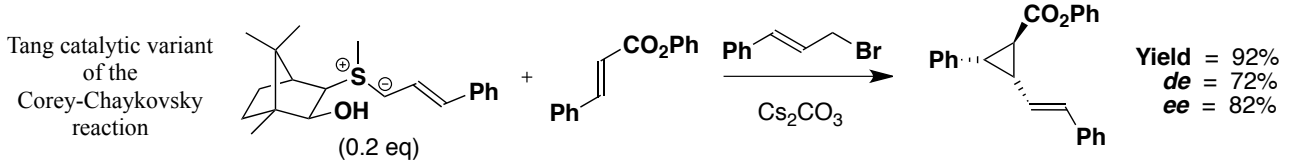
less predictable and may change from substrate to substrate, favouring the *trans*-isomer for mono-substituted olefins and the *cis*-isomer with bulky di-substituted alkenes.

The second strategy, also known as Michael-initiated ring-closure, is a stepwise formation of two C–C bonds. This is exemplified by the Corey-Chaykovsky reaction (Scheme 3).[15]



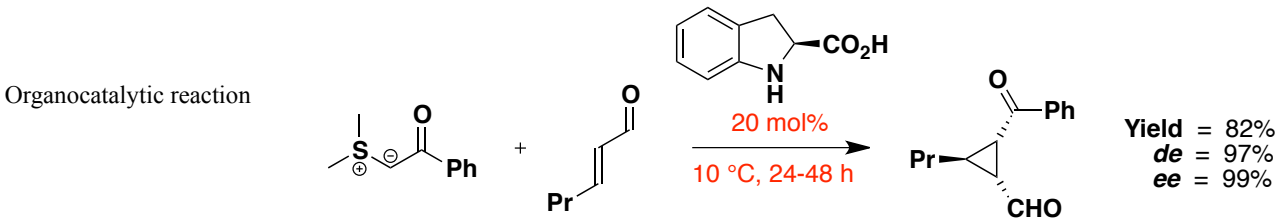
Scheme 3 Stepwise formation of two C−C bonds, *i.e*. addition of an ylide to an electron deficient alkene.

This strategy involves the addition of a sulfur ylide to an olefin bearing an anion-stabilising group, subsequent (non-concerted) displacement of sulfur by the hitherto formed carbanion leads to a cyclopropane. In the Corey-Chaykovsky protocol, the sulfonium ylide may be additionally stabilised by groups such as esters, nitriles or substituted aryl rings. Regardless of the geometry of the reacting partner, this methodology shows a notably *trans*-diastereoselectivity in the product. As this reaction features a stepwise formation of the two C–C bonds, the reaction is non-stereospecific as rotation round the C–C bond of what was the olefin occurs faster than the ring-closure process. High values of enantioselectivity may be achieved using stoichiometric chiral sulfonium ylides, although their cost is often prohibitive and represents a major drawback for application to large-scale processes. Nevertheless, when the sulfonium ylide is generated in the presence of allylic bromides, it may potentially be used in catalytic amounts, as documented by Tang and co-workers[16] (Scheme 4).



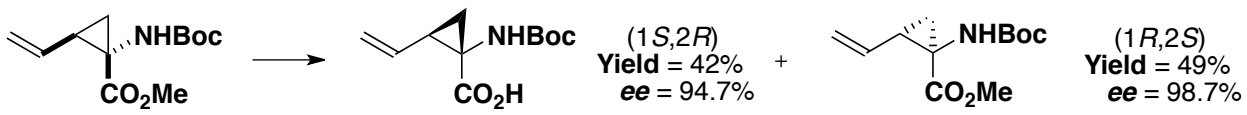
Scheme 4 Catalytic Corey-Chaykovsky cyclopropanation reaction.

The introduction of the relatively cheap proline-based chiral ligand (up to 20 mol%) has made asymmetric routes to cyclopropanes more cost-effective, as witnessed by the organocatalytic reaction (Scheme 5).[17] Unfortunately, although the organocatalytic process may reach high values of stereoselectivity, there are relatively few known examples of application of this reaction. Equally, slow reaction rates render this approach less applicable in an industrial setting.



Scheme 5 Stepwise formation of two C−C bonds: organocatalytic reaction.

Although all of the reactions described may have satisfying degrees of conversion and stereoselectivity, they equally exhibit relevant weaknesses. Indeed, the cost of both metal centres and chiral ligands, together with for example the instability of diazo compounds has made these procedures problematic to handle. Despite the huge industrial demand for synthetic improvements in cyclopropanation procedures, the protocols currently in use rely on enzymatic resolution – obviously limiting the recovery to no more than 50% yield. An example is the scaled-up synthesis of (1*R*,2*S*)-1-amino-2-vinylcyclopropanecarboxylic acid, which is a key motif in BILN 2061, an inhibitor of the hepatitis C virus NS3 protease (Scheme 6).[18] The pathway involved a cyclopropanation reaction on a 12 kg scale to give the *cis*-isomers as racemic mixture. Hydrolytic kinetic resolution of the undesired enantiomer with Alcalase 2.4L required a reaction time of 70 h and a reaction volume of ~35 litres. This left the desired enantiomer in 49% yield with an *ee* ~99%



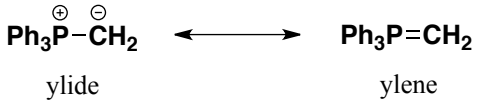
Scheme 6 Enzymatic resolution performed on 12 kg scale.

Clearly, this area of chemistry requires a synthetic methodology able to fulfil the following parameters: absence of metal centres and chiral ligands, tolerance to a wide range of functionalities,

complete control of both the absolute and the relative stereochemistry with reasonable reaction rates. Given these goals, the Wadsworth-Emmons cyclopropanation appeared synthetically intriguing. It is not widely known that the seminal olefination method described by Wadsworth and Emmons also describes the use of phosphonate carbanions reacting with epoxides to give cyclopropane products.[19] Surprisingly, this reaction of extraordinary potential remained largely unstudied.

1.2 Introduction to Wittig reaction

Phosphonium ylides, also known as Wittig reagents, are molecules containing two formal charges of opposite sign. These compounds can be described with two resonance structures named as the ylide and ylene forms respectively (Scheme 7).

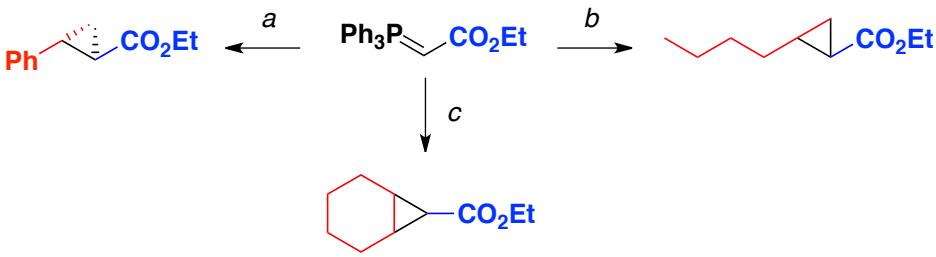


Scheme 7 Ylide and ylene.

Wittig investigated the crucial role of these structures in the formation of new C–C bonds in the mid 1950's. This seminal work reported the use of triphenylphosphoranes and electrophiles such as ketones or aldehydes to generate olefins under basic conditions (Scheme 8).[20]

Scheme 8 General reaction scheme of the Wittig reaction.

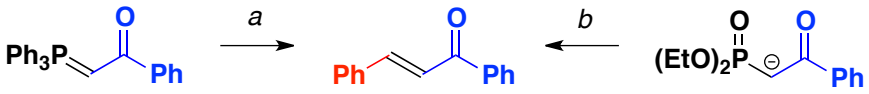
In 1959, Denney and Boskin published the first example of conversion of a mono-substituted epoxide (styrene oxide) to a 1,2-disubstituted cyclopropane.[21a] This process was latter improved in 1962 to include 1,2-disubstituted epoxides (cyclohexene oxide) and enantiopure styrene oxide.[21b] The latter reaction represents one of the earliest recorded asymmetric syntheses of a cyclopropane. This pioneering approach appeared intriguing, although the harsh experimental conditions applied precluded the use of thermally unstable epoxides (Scheme 9).



Scheme 9 Screening over mono-substituted epoxides. Reagents and conditions: (*a*) (−)-styrene oxide, 200 °C, 7 h, 28%; (*b*) (±)-1-octene oxide, 200 °C, 8 h, 46%; (*c*) cyclohexene oxide, 200 °C, 26 h, 56%.

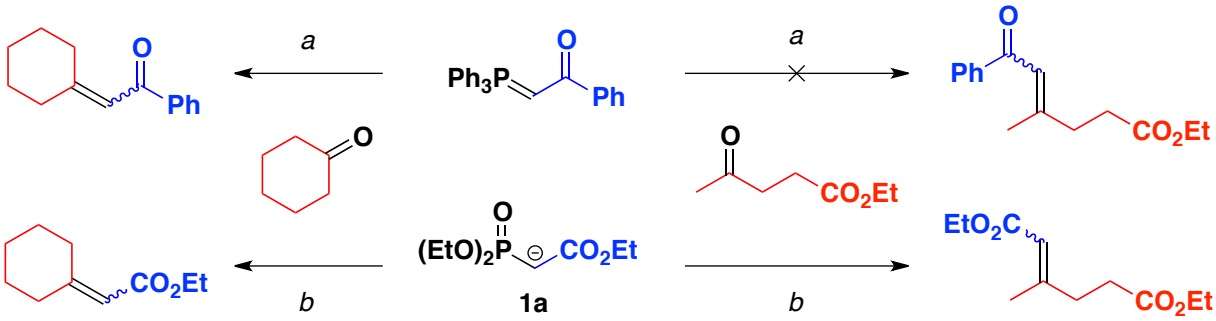
1.3 The Wadsworth-Emmons contribution

This synthetic pathway caught the interest of numerous research groups around the world, whose efforts were aimed towards optimisation of the reaction conditions and to broadening its applications. In 1961, Wadsworth and Emmons released one of the most noteworthy publications in organic chemistry, which is nowadays considered a cornerstone in C−C bond formation.[19] The authors provided further evidence of the success of phosphorous chemistry enabling olefination in the presence of phosphonate anions, occurring at markedly reduced reaction temperatures compared to when using phosphoranylidenes.[22] Their enhanced activity over the traditional "Wittig reagents" was ascribed to the presence of a formal negative charge, which was responsible for increased nucleophilic activity towards the carbonyl. Moreover, the use of lower temperatures widened the functional group tolerance (Scheme 10).



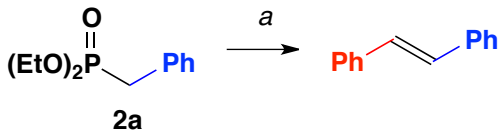
Scheme 10 Phosphoranes and phosphonate anions activity over benzaldehyde. Reagents and conditions: (*a*) **PhCHO**, THF, Δ, 30 h; (*b*) **PhCHO**, THF, rt, "minutes".

The broad versatility of phosphonates as powerful synthetic tools was highlighted by several intruiging examples, where phosphoranylidenes reacted slowly, or not at all.[23] For instance, triethyl phosphonoacetate **1a** proved to have good reactivity with hindered carbonyl compounds. Furthermore, phosphonate anions showed chemoselectivity for ketone groups over ester functionality (Scheme 11).



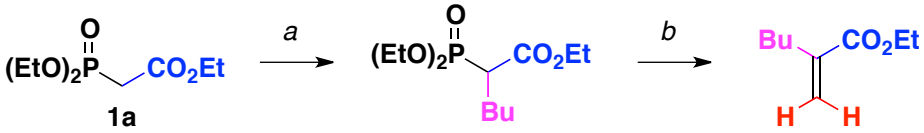
Scheme 11 Differences in the reactivity between phosphonates and phosphoranes. Reagents and conditions: (*a*) THF, Δ, 30 h; (*b*) (*i*) NaH, THF, 25 °C, 1 h; (*ii*) 30 °C, 15 min.

Deprotonation experiments performed on a range of phosphonates highlighted the importance of the presence of an anion stabilizing groups (**ASG**). These groups provide the necessary stabilisation to avoid self-condensation of the phosphonates. Instead, use of borderline **ASGs** such as the benzyl group requires the deprotonation to be performed *in situ* in the presence of the carbonylic compound. This alternative procedure allowed the use of a wider selection of substrates compared to phosphoranes (Scheme 12).[24] As for the "Wittig" reaction, Wadsworth and Emmons reported this procedure to form preferentially the *trans*-diasteroisomer.



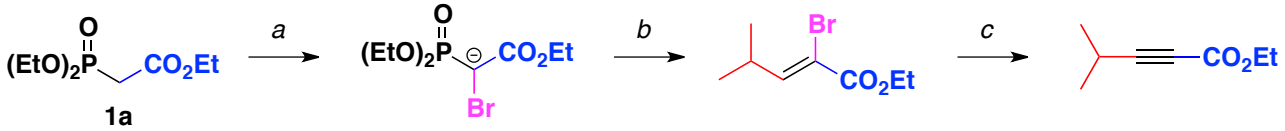
Scheme 12 Role of the **ASG** in the deprotonation step. Reagents and conditions: (*a*) **PhCHO**, NaH, DME, 85 °C, 30 min, 62%.

The phosphonate **1a** could be alkylated on the methylene carbon under basic conditions with alkyl halides. Synthesis of α-alkyl phosphonates could be performed *in situ* with an excess of base before addition of the electrophile (Scheme 13).[25]



Scheme 13 Example of Wadsworth-Emmons olefination with α-alkyl phosphonates. Reagents and conditions: (*a*) NaH, **Bu**Br, DME, 60 °C; (*b*) **CH_2**O, DME, 60 °C, 60%.

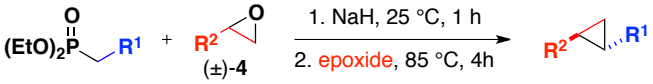
When the acidic proton was substituted by halogens, a halo-substituted olefin was isolated. Such products could be further modified, as exemplified by the conversion to alkynes under strongly basic conditions (Scheme 14).

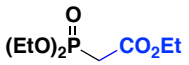
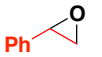
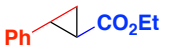
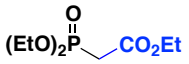
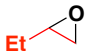
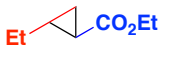
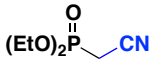
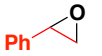


Scheme 14 Example of alkyne formation from α-halophosphonates. Reagents and conditions: (*a*) NaH, **Br_2**, DME, 60 °C; (*b*) *iso*-butyraldehyde, NaH, DME, 60 °C, 60%; (*c*) NaH, DME, 59%.

The breakthrough work of Denney and Boskin prompted Wadsworth and Emmons to examine the activity of phosphonate anions with epoxides (Table 1).

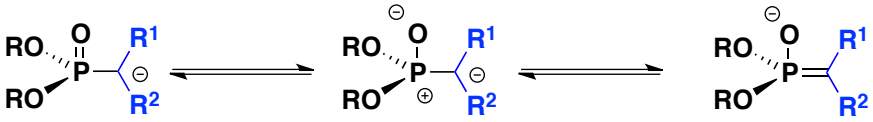
Table 1 First approach to the Wadsworth-Emmons cyclopropanation.



Entry	Phosphonate		Epoxide		Product		Yield[a](%)
1		**1a**		(±)-**4a**		(1*S**,2*S**)-**5a**	42
2		**1a**		(±)-**4b**		(1*S**,2*S**)-**5b**	21
3		**3a**		(±)-**4a**		(1*S**,2*S**)-**6a**	51

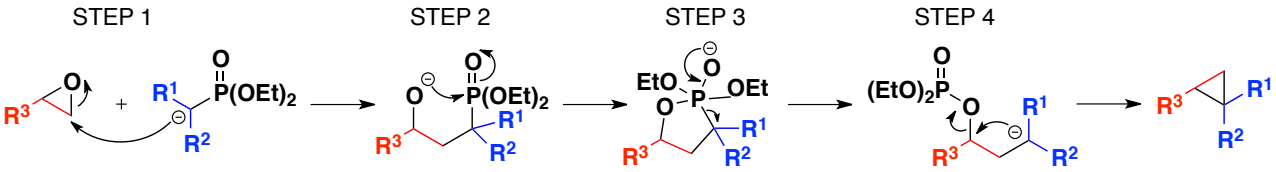
[a]Yields determined on mass recovery by column chromatography

As was the case for the reactions with carbonyl compounds, the experimental conditions required were found to be far milder (115 °C lower) but still afforded broadly comparable yields of cyclopropanes to those carried out with Wittig reagents. Once again, according to the authors, the enhanced activity the phosphonates showed could be rationalised as the consequence of their formal negative charge (Scheme 15).



Scheme 15 Phosphonate anion resonance structure.

The proposed mechanism for the cyclopropanation reaction involves a nucleophilic attack on the epoxide (Step 1), followed by transfer of the phosphonate from carbon to the newly formed alkoxides (Step 2 & 3), before finally (Step 4) 3-*exo*-tet ring-closure *via* an S_N2-like pathway (Scheme 16).

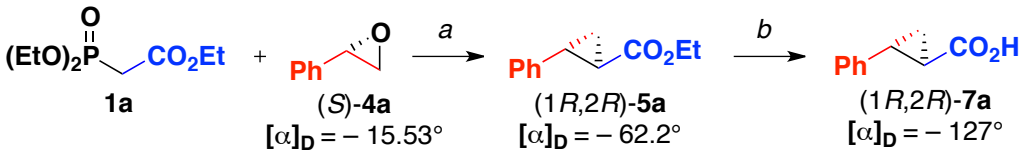


Scheme 16 Wadsworth-Emmons' proposed mechanism.

This newly emerged work on phosphonate anions convinced Denney and Boskin to test their phosphoranes with different epoxides. The experimental evidence collected prompted them to propose a similar mechanism for the cyclopropanation, supported by the retention of optical activity detected in products obtained from enantiopure epoxides.[21b]

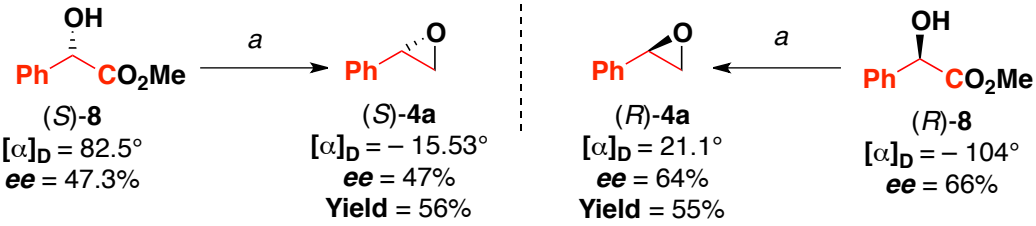
1.4 The Tömösközi study

Tömösközi provided a mechanistic study of the Wadsworth-Emmons reaction by exploring the reactivity of the phosphonate **1a** with (*R*)-styrene oxide (*R*)-**4a**, with the aim of assigning absolute configuration to the *trans*-2-phenylcyclopropane-carboxylic acid **7a** generated (Scheme 17).[26]



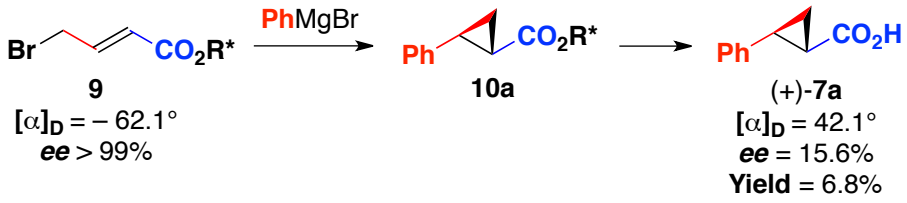
Scheme 17 Wadsworth-Emmons reaction with (*R*)-**4a**. Reaction and conditions: (*a*) NaH, DME, 70 °C, 5 h, 46%; (*b*) THF, H_2O, NaOH, 63%.

The strategy involved the synthesis of the carboxylic acid **7a** *via* two alternative routes with known stereochemical outcome, comparing the sign of the optical rotation of reference compounds with that observed with the product of the Wadsworth-Emmons cyclopropanation reaction. The cyclopropanation was performed on both the enantiomers of the epoxide **4a**, obtained *via* the modified version of the Eliel-Delmonte enantiospecific epoxidation starting from enantioenriched mixtures of both enantiomers of mandelic acid **7** (Scheme 18).[27]



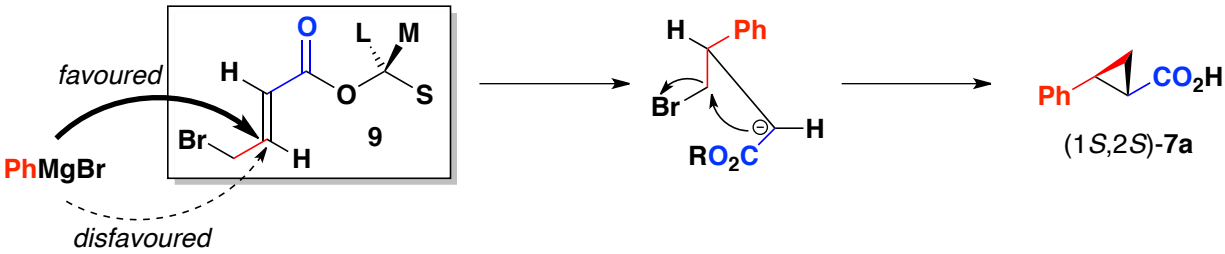
Scheme 18 Enantiospecific synthesis of **4a**. Reagents and conditions: (*a*) (*i*) $LiAlH_4$; (*ii*) BsCl; (*iii*) NaOH.

Reference samples of the two antipodes of acids **7a** were independently synthesized. The dextrorotatory antipode was obtained from the menthyl derived allyl bromide **9** *via* treatment with PhMeBr to give the cyclopropyl ester **10a**, which yielded a cyclopropyl acid with positive optical rotation, later described as (1*S*,2*S*)-**7a** following saponification (Scheme 19).



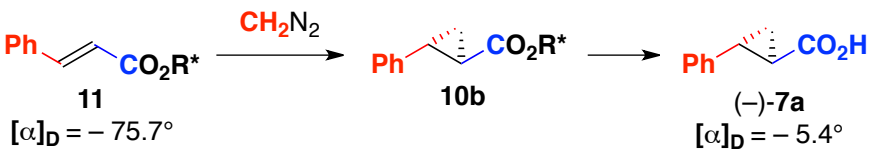
Scheme 19 Route to (1*S*,2*S*)-**7a** induced *via* Grignard addition.

The author assigned the absolute configuration relying on the models from Cram and Prelog[28] widely applied in literature.[29] Indeed, Tömösközi expected the insertion of the Grignard reagent to occur from the less hindered face of the acrylate electrophile, between the small (**S**) and the medium (**M**) group of the chiral auxiliary (top face as drawn below), favouring the formation of the cyclopropyl acid (1*S*,2*S*)-**7a** (Scheme 20).



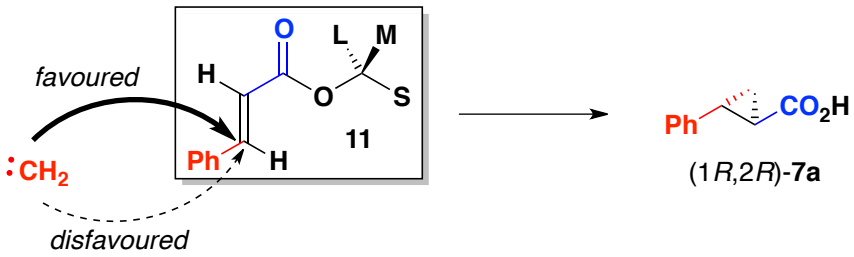
Scheme 20 Suggested facial selectivity for the insertion of the Grignard reagent on the chiral ester **9**.

Nevertheless, due to the distance between the chiral auxiliary and the olefin, such a preference became questionable, as witnessed by the huge loss of optical activity from ester **9** to the acid (+)-**7a**. Conversely, the levorotatory antipode was produced from a photochemically induced insertion of diazomethane, which led to the formation of the cyclopropyl ester **10b**, subsequently converted to acid (1*R*,2*R*)-**7a** upon hydrolysis (Scheme 21). Also in this case, the cyclopropyl acid showed a poor value of optical rotation compared to the same enantiomer isolated by Wadsworth-Emmons cyclopropanation.



Scheme 21 Route to (1*R*,2*R*)-**7a** *via* carbene insertion.

In a similar manner, the carbene insertion to (−)-menthyl cinnamate **11** was expected to occur with the same sense of diastereoselectivity, ultimately producing the enantiomer (1*R*,2*R*)-**7a** (Scheme 22).

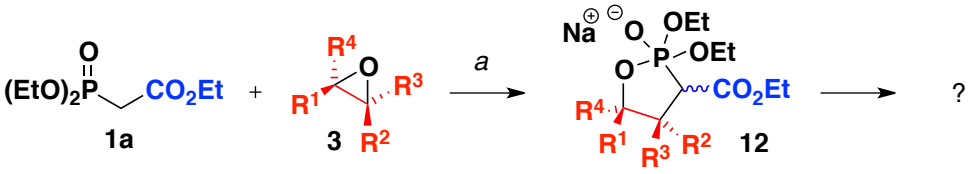


Scheme 22 Suggested facial selectivity for the insertion of the carbene on the chiral ester **11**.

The absolute configuration of cyclopropanes isolated *via* Wadsworth-Emmons reaction was assigned by comparing the sign of the optical rotation to the referenced samples obtained in Schemes 19-22. Despite the poor values of optical rotation displayed by the reference compounds, the assignment proved correct. *In agreement with the proposed mechanism originally suggested for the reaction of phosphoranylidenes with terminal epoxides by Denney and Boskin, inversion of configuration at the stereogenic carbon of the epoxide was observed during the Wadsworth-Emmons cyclopropanation*. Tömösközi ascribed the *trans*-stereoselectivity on the basis of the thermodynamic stability of the products. Further evidence regarding the description of the absolute configuration of di- and tri-substituted cyclopropanes supported this suggested mechanism.[30]

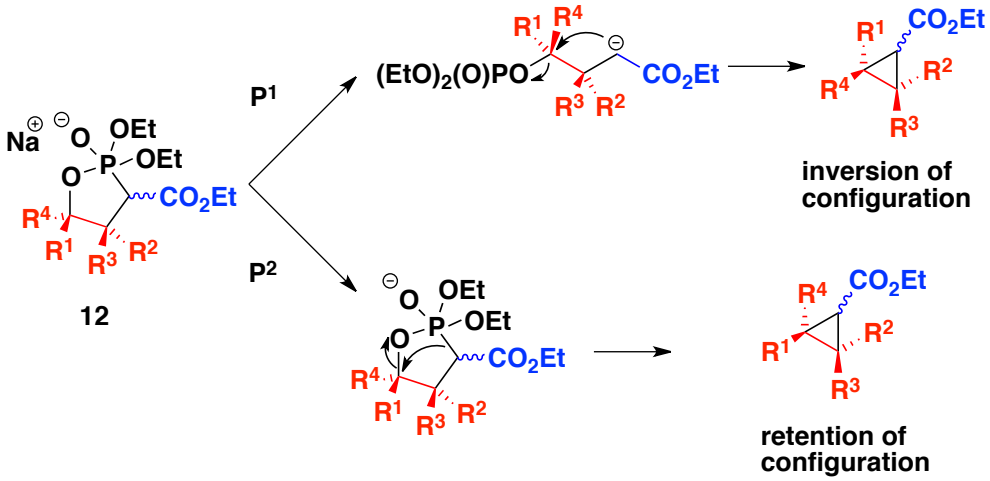
1.5 New mechanistic investigations. The 1970's

Although evidence regarding the conservation of optical purity had been collected, supporting the inversion of configuration at the stereogenic carbon of the epoxide, the low values of optical rotation led Walborski to hypothesise the possibility of a competitive decomposition of the oxaphospholane intermediate **12** with retention of configuration.[30b] Izydore and Ghirardelli aimed to clarify the mechanism by investigating the decomposition of the intermediate **12** (Scheme 23).[31]



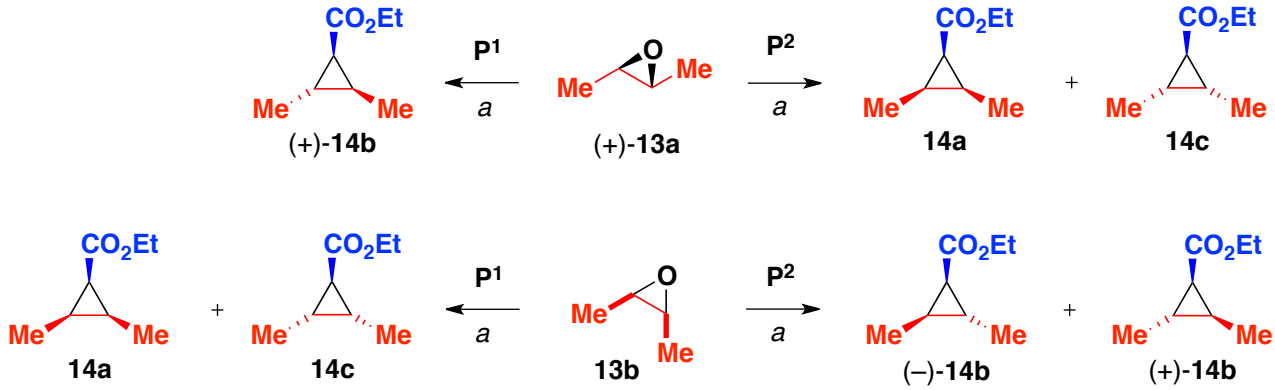
Scheme 23 Unknown decomposition of the oxaphospholane **12**. Reagents and conditions: (*a*) **1a**, NaH, DME, reflux.

Two decomposition pathways were envisaged: the first (as proposed by Denney and Boskin and supported by the evidence from Tömösközi) involved cleavage of the C−P bond with formation of a carbanion (enolate) followed by ring-closing *via* inversion of the configuration at the stereogenic carbon (pathway $\mathbf{P^1}$); the second pathway proceeded *via* a concerted decomposition with retention of configuration at the stereogenic carbon of the epoxide (pathway $\mathbf{P^2}$) (Scheme 24).



Scheme 24 Possible decomposition pathways for diastereoisomeric betaines **12**.

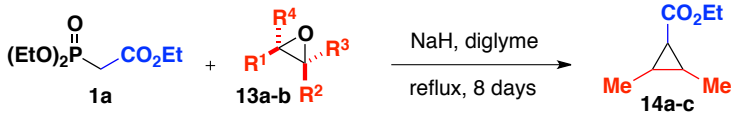
The authors chose to screen two epoxides: (+)-(*2R*,*3R*)-2,3-dimethyloxirane (+)-**13a** and *cis*-2,3-dimethyloxirane **13b** with the phosphonate **1a**. These epoxides were strategically selected, as the product ratio could be directly correlated to the ratio of the two competing pathways $\mathbf{P^1}$ and $\mathbf{P^2}$. The epoxide (+)-**13a** was expected to yield a sole enantiomeric cyclopropane (+)-**14b** *via* pathway $\mathbf{P^1}$ but the two *meso* cyclopropanes **14a** and **14c** *via* pathway $\mathbf{P^2}$. Conversely, these latter two *meso* cyclopropanes would be produced from the *meso* epoxide **13b** only *via* pathway $\mathbf{P^1}$, whilst pathway $\mathbf{P^2}$ was expected to produce **14b** as racemic mixture (Scheme 25).



Scheme 25 Syntheses of tri-substituted cyclopropane **14**. Reagents and conditions: (*a*) **1a**, NaH, DME, reflux, 22 h.

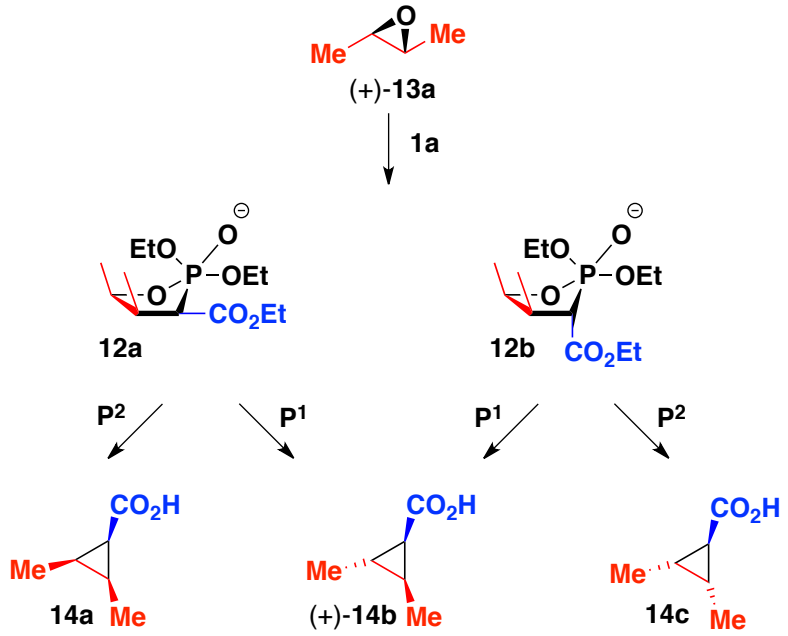
The epoxides **13a** & **b** were separately reacted with the anion of phosphonate **1a** to give the cyclopropanes **14a** & **c** (Table 2). The results confirmed Denney and Boskin's hypothesis of the internal displacement of the phosphate *via* an S_N2-like mechanism ($\mathbf{P^1}$), as the major isomers require the epoxide to undergo an overall even number of inversions (ring-opening and ring-closure).[21]

Table 2 Screening by Izydore and Ghirardelli.



Entry	Epoxide	(+)-**14b**	(±)-**14b**	**14a**	**14c**
1	(+)-**13a**	93%	---	6%	1%
2	**13b**	---	4%	6%	90%

In both reactions, the presence of the minor isomers was ascribed to the difference of both the population of the oxaphospholane rings (**12a** over **12b**) and the probability of the two processes ($\mathbf{P^1}$ over $\mathbf{P^2}$) (Scheme 26).



Scheme 26 Decomposition of oxaphospholane intermediates **12a** and **12b**.

The conversion of the epoxide **13b** gave cyclopropanes **14c** as the major product. Since pathway $\mathbf{P^1}$ also allowed the formation of the cyclopropane **14a**, the authors ascribed the preferential synthesis of the product **14c** as a consequence of steric control, as both the methyl groups lie in *trans*-relationship with respect to the ester functionality.

1.6 First application to total synthesis. The 1980's

With the stereochemical outcome of the Wadsworth-Emmons reaction now secure, this process began to be applied in total synthesis projects. In 1984, Fitzsimmons and Fraser-Reid described the enantiospecific synthesis of (+)-and (−)-chrysanthemum dicarboxylic acids **15** using annulated pyranosides as chiral synthons (Figure 3).[32]

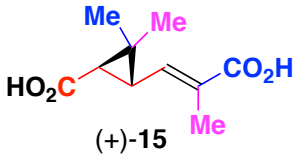
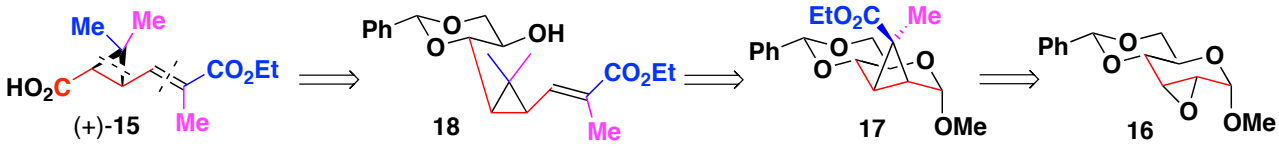


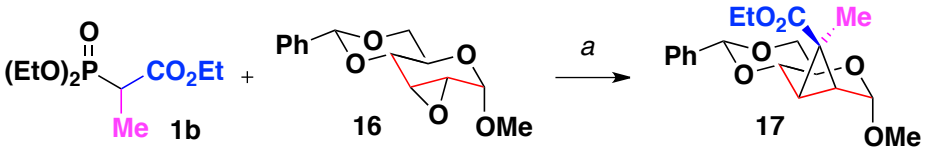
Figure 3 (+)-chrysanthemum dicarboxylic acids (+)-**15**.

The retrosynthetic pathway proposed involved Wadsworth-Emmons reactions to install both the cyclopropane moiety and the olefin scaffold (Scheme 27).



Scheme 27 Retrosynthetic pathway proposed by Fitzsimmons and Fraser-Reid.

Reaction of the phosphonate **1b** with the epoxide **16** gave the desired cyclopropane **17** with a high *dr* (>98:2 by GC-MS). It was suggested that the *exo*-configuration of the ester was enhanced by the electronic repulsion between the lone pair of the pyranosidic oxygen and the π-orbital of the ester carbonyl (Scheme 28).

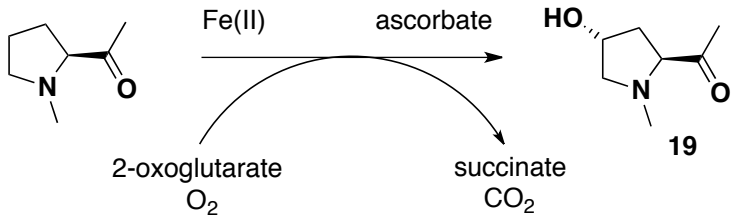


Scheme 28 Wadsworth-Emmons cyclopropanation. Reaction and conditions: (*a*) NaH, 1,4-dioxane, 160 °C, 50%.

This work is relevant for the current research since it clearly demonstrates that substituted phosphonoacetates could participate effectively in the Wadsworth-Emmons cyclopropanation.

1.7 New application to total synthesis

In 1989, Petter reported a further application of the Wadsworth-Emmons cyclopropanation to a total synthesis project.[33] His research involved the use of proline analogues to investigate the kinetics of the reactivity of the enzyme prolyl 4-hydroxylase. This non-heme based iron dioxygenase is responsible for the rate-determining step of the biosynthesis of 1-((*2S,4R*)-4-hydroxy-1-methylpyrrolidin-2-yl)ethanone **19** (Scheme 29).[34] This scaffold is a recurring motif in the protein collagen, stabilising its triple helix *via* inter-chain hydrogen bonds.[35]



Scheme 29 Enzymatic synthesis of **19** in mammalian tissues.

As the enzyme-bound transients for this reaction were unknown at the time, the authors aimed to demonstrate their existence *via* a free-radical clock strategy. The author designed a synthesis to insert a spiro-cyclopropane in position C−5 of proline (Figure 4).[36]

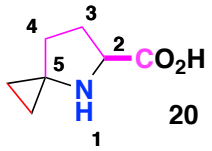
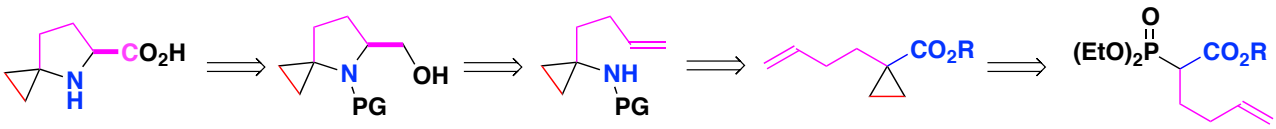


Figure 4 Target inhibitor **20** of the dioxygenase.

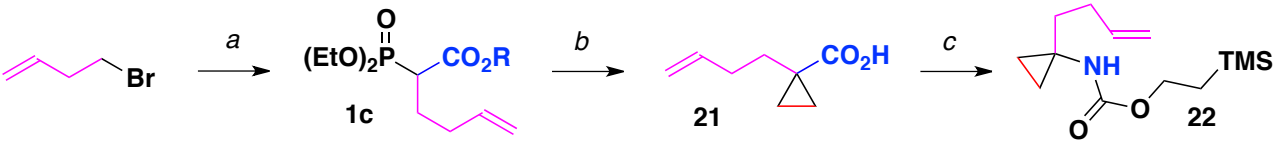
The retrosynthetic pathway included a Wadsworth-Emmons cyclopropanation with a homoallyl-substituted variant of the phosphonate **1a**, which on reaction with oxirane itself would generate a 1,1-disubstituted cyclopropane. Conversion to cyclopropyl amide followed by Curtius rearrangement would introduce the pyrrolidinic nitrogen. Oxidative activation of the olefin followed by 5-*exo*-tet ring-closure would form the pyrrolidine ring and the alcohol thus formed could be converted to the acid found in the proline scaffold (Scheme 30).



Scheme 30 Suggested retrosynthesis.

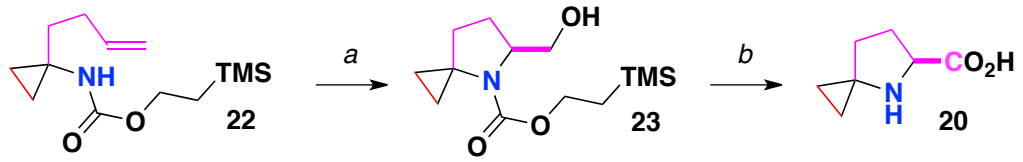
The phosphonate **1c** was obtained by alkylation of **1a** with 4-bromo-1-butene and converted to the geminal di-substituted cyclopropane *via* the Wadsworth-Emmons protocol in the presence of oxirane. *Albeit only with oxirane, this further demonstrated the use of substituted phosphonoacetates in the Wadsworth-Emmons cyclopropanation*.

The insertion of the nitrogen atom was achieved *via* the Shiori variation of the Curtius rearrangement of the acid **21**, producing the carbamate **22** (Scheme 31).



Scheme 31 Wadsworth-Emmons cyclopropanation and Curtius rearrangement. Reactions and conditions: (*a*) **1a**, NaH, 84%; (*b*) (*i*) oxirane, NaH, reflux; (*ii*) KOH, THF, 57%; (*c*) (*i*). DPPA, TEA, PhMe, 80 °C; (*ii*). $TMS(CH_2)_2OH$, 67%.

Use of TFPAA cyclised the carbamate **22** to give the hydroxypyrrolidine **23**, whose formation was favoured over the piperidine isomer. Oxidation of the primary alcohol followed by removal of the protecting group gave 5-cyclopropylproline **20** in 10% yield over six steps (Scheme 32).

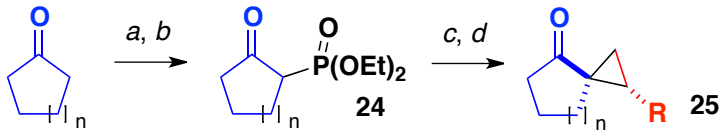


Scheme 32 Ring-closure and oxidation steps. Reactions and conditions: (*a*) TFPAA, 61%; (*b*) (*i*) H^+/CrO_3, acetone, 0 °C, 20 min; (*ii*) *n*-BuN^+F^-, THF, 51%.

Despite the elaboration of the synthetic procedure, no application of 5-cyclopropylproline **20** in the mechanistic study of the biosynthesis of the proline **19** is currently reported in literature.

1.8 Synthesis of spirocyclic ketones

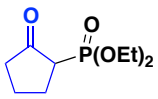
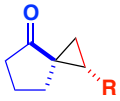
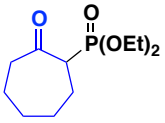
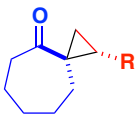
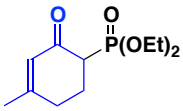
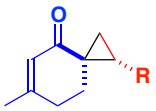
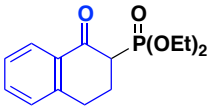
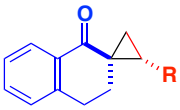
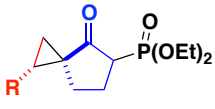
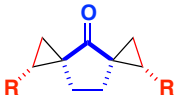
Since its introduction, the Wadsworth-Emmons cyclopropanation reaction was only reported for acyclic phosphonoacetates, no evidence concerning the compatibility of other carbonylic groups was available. In the early 1990's, Wiemer and co-workers developed new synthetic routes to β-keto phosphonates[37] **24** with the aim of assessing their reactivity in the presence of epoxides. This research followed-up from Petter's work for the synthesis of spiro-cyclopropanes and led to an investigation into the synthesis of the spirocyclic ketones **25** (Scheme 33).[38]



Scheme 33 Electrophilic quenching on cyclic ketones. Reagents and conditions (*a*) LDA, diethyl chlorophosphate; (*b*) LDA, H_3O^+; (*c*) NaH, Benzene, 0 °C to rt, 1 h; (*d*) epoxide, 125 °C, 6 h.

The Wadsworth-Emmons cyclopropanation of oxirane, propylene oxide and styrene oxide was examined using a variety of hindered phosphonates (Table 3).

Table 3 Screening over different epoxides.

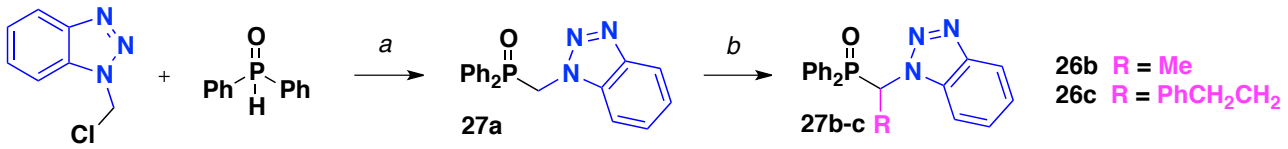
Entry	Phosphonate		Product		R	Yield (%)[a]
1		**24a**		**25a'**	**H**	40
				25a''	**Me**	34
				25a'''	**Ph**	50
2		**24b**		**25b'**	**H**	50
				25b''	**Me**	56
				25b'''	**Ph**	0
3		**24c**		**25c'**	**H**	62
				25c''	**Me**	72
				25c'''	**Ph**	0
4		**24d**		**25d'**	**H**	48
				25d''	**Me**	44
				25d'''	**Ph**	0
5		**24e**		**25e'**	**H**	75
				25e''	**Me**	51
				25e'''	**Ph**	71

[a]Yields calculated on mass recovery.

This work demonstrated the compatibility of the ketone functionality in the Wadsworth-Emmons cyclopropanation, producing multi-substituted cyclopropanes as single isomers, where the carbonyl and the substituent from the epoxide lie in a trans-relationship (as demonstrated by X-ray crystallography). Whilst Fitzsimmons and Fraser-Reid provided a similar conclusion, this work revealed the *trans*-diastereoselectivity of the Wadsworth-Emmons cyclopropanation to be independent from interactions between spectator groups not involved in the process. *Finally, this investigation was the first to highlight limitations of this procedure with regard to the steric hindrance of the nucleophilic phosphonate*.

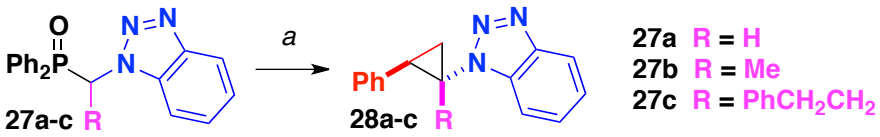
1.9 Synthesis of cyclopropyl benzotriazoles

In 1995, Katritzky and co-workers investigated new routes to novel benzotriazoles due to their importance as agrochemicals[39] and their role as a synthetic tool for further transformations.[40] The increasing attention on cyclopropane synthesis prompted them to investigate the conversion of a suitable phosphonate under the Wadsworth-Emmons cyclopropanation conditions. At the time, the use of phosphonates was limited to carbonylic electron-withdrawing groups; the authors gave this as the reason for assessing the reactivity of benzotriazole-substituted phosphine oxides.[41] Such compounds were produced upon deprotonation of diphenylphosphine oxide and treatment with chloromethylbenzotriazole and further alkylation (Scheme 34).



Scheme 34 Synthesis of benzotriazole phosphonates 26a-f. Reagents and conditions: (*a*) *n*-BuLi, THF, −78 °C, 69%; (*b*) *n*-BuLi, −78 °C, RX, **27b**, 74%; **27c**, 64%.

The phosphine oxides **27a-c** were reacted with (±)-styrene oxide (±)-**4a**. Unsubstituted phosphine oxide **27a** was converted to cyclopropane **28a** in 74% yield in only 2 h in refluxing THF. In contrast, the phosphine oxide **27c** required a longer reaction time and showed a much poorer conversion. The authors suggested that this was due to "pronounced steric effects" (Scheme 35). Cyclopropyl benzotriazoles **28a-c** were isolated as single diastereomers and assigned as the isomers in which the phenyl ring and the benzotriazole have the *trans*-configuration based upon nOe experiments.



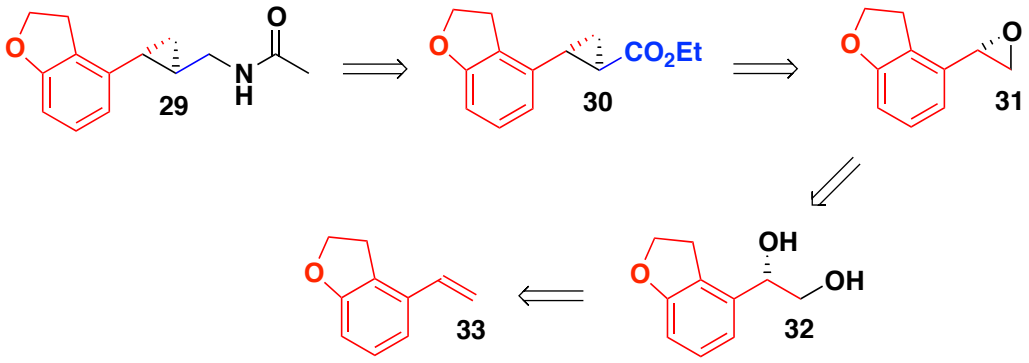
Scheme 35 Synthesis of cyclopropyl benzotriazole **28a-c**. Reagents and conditions: (*a*) (*i*) *n*-BuLi, THF, −78 °C, 1.5 h; (*ii*) (±)-**4a**, Δ; **28a**, 2 h, 74%; **28b**, 6 h, 70%; **28c**, 24 h, 30%.

The phosphine oxide **27a** successfully converted cyclohexene oxide; furthermore, a wide range of tri-substituted cyclopropyl benzotriazoles were accessed upon treatment of **28a** with base and a suitable electrophile, accommodating the **R** group in *cis*-relationship with the **Ph** group.

This work is crucial, as it demonstrated that cyclopropanation reactions of this type were feasible with electron-withdrawing groups other than carbonyls. Additionally, this study showed the compatibility of alkylated phosphine oxides to synthesise tri-substituted cyclopropanes, where the alkyl group lies in cis-relationship with respect to the epoxide substituent, which was in line with Wiemer's observations.

1.10 New applications to medicinal chemistry

In 2002, Singh and co-workers from the Bristol-Myers Squibb process research group described the use of the Wadsworth-Emmons cyclopropanation to synthesize the biologically active melatonergic agent[42] **29.** This in-depth study culminated in the synthesis of cyclopropane **30** on a 14 kg scale.[43] The authors envisaged building the cyclopropyl ester **31** *via* Wadsworth-Emmons cyclopropanation using the phosphonate **1a** and appropriate epoxide **32**. The proposed route to the enantiopure epoxide **31** involved enantiospecific ring-closure of the vicinal diol **32** generated *via* Sharpless asymmetric dihydroxylation from styrene **33 (**Scheme 36).

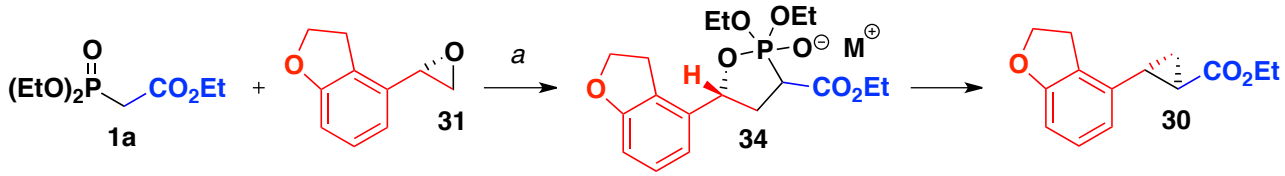


Scheme 36 Retrosynthesis of the melatonergic agent **29**.

The major challenge in this project was the identification of conditions suitable for scale-up of the cyclopropanation reactions. A variety of bases, solvents and temperatures were assessed. These bases included metal hydrides, hydroxides, alkoxides, amides as well as alkyllithiums. Although a wide range of bases gave high yields, particularly when using DME, the authors considered only NaO^{t}Bu for industrial use on safety grounds.

The process was thoroughly analysed by in-process LC-MS/HPLC measurements. This highlighted that no reaction occurred below 50 °C, whereas poor yields were detected above 100 °C. The stability of both the reagents was assessed at 80 °C, proving that the epoxide **31** was stable for extended periods of time; conversely, the desired ester **30** degraded by 10-15% after 24 h. The epoxide **31** and the anion of the phosphonate **1a** were reacted for 12 h at 60 °C. This left ~10%

of an intermediate, which was converted to cyclopropane **30** by raising the reaction temperature of 10 °C. Such intermediate showed the molecular weight matching with that of oxaphospholane **34** (M = H) by LC-MS measurement (Scheme 37). Finally, the optimal concentration to perform the reaction was identified as 1.0 molar. The *de* of the product was >99% as was the *ee* when starting with epoxide of >99% *ee*.

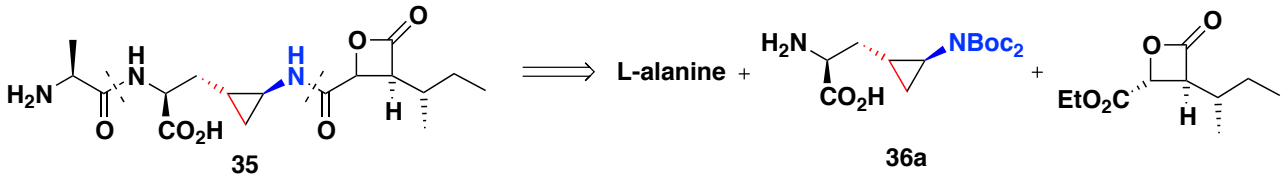


Scheme 37 Synthesis of the cyclopropane **30**. Reagents and conditions: (*a*) (*i*) NaO^{t}Bu, DME, 60 °C, 15 h; 70 °C, 9 h.

This study was important for a number of reasons. 1) It demonstrated that the Wadsworth-Emmons reaction is scalable and amenable to process development. 2) It was the first time that we can consider that the de and ee had been analysed by techniques that we would consider reliable nowadays. 3) It showed that despite a wide solvent screen, that DME as originally used by Wadsworth and Emmons was the optimum solvent. 4) It provided the first experimental evidence of an oxaphospholane as an intermediate in the reaction, although such compound was not isolated and fully characterised by NMR spectroscopy.

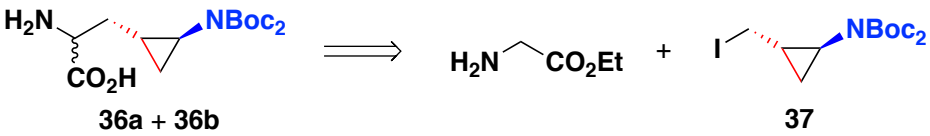
1.11 Synthesis of (+)-belactosin A

In the 2000's, further applications of the Wadsworth-Emmons to the total synthesis of biologically active cyclopropane-containing molecules were reported. One of these regarded the synthesis of (+)-belactosin A[44] **35**, a *Streptomyces* metabolite that mediates cell-cycle progression.[45] The proposed retrosynthetic pathway involved the disconnection of both the amide bonds, producing three subunits (Scheme 38).



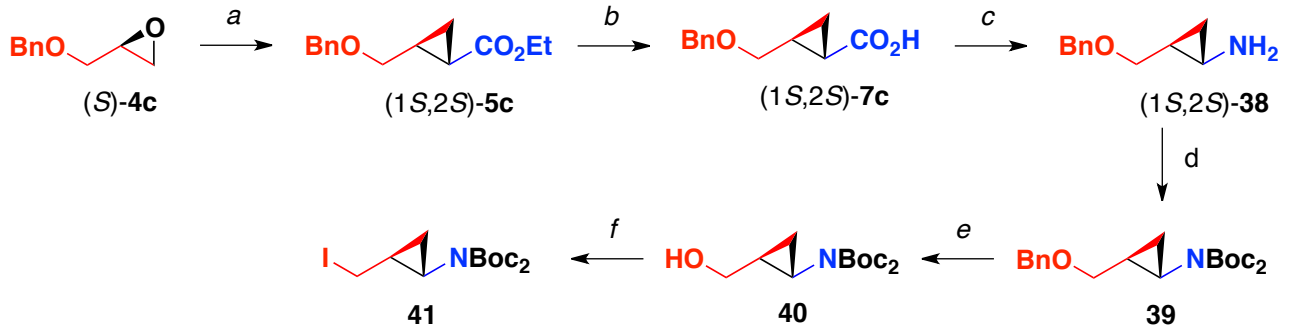
Scheme 38 Retrosynthetic analysis of **(+)**-belactiosin A **35**.

The central motif **36a** featured three stereocentres: two on the cyclopropyl ring as well as that on the amino acid. The first two could be constructed *via* the Wadsworth-Emmons procedure, whereas the latter chiral centre needed to be installed *via* a catalyst controlled-asymmetric alkylation reaction (Scheme 39).



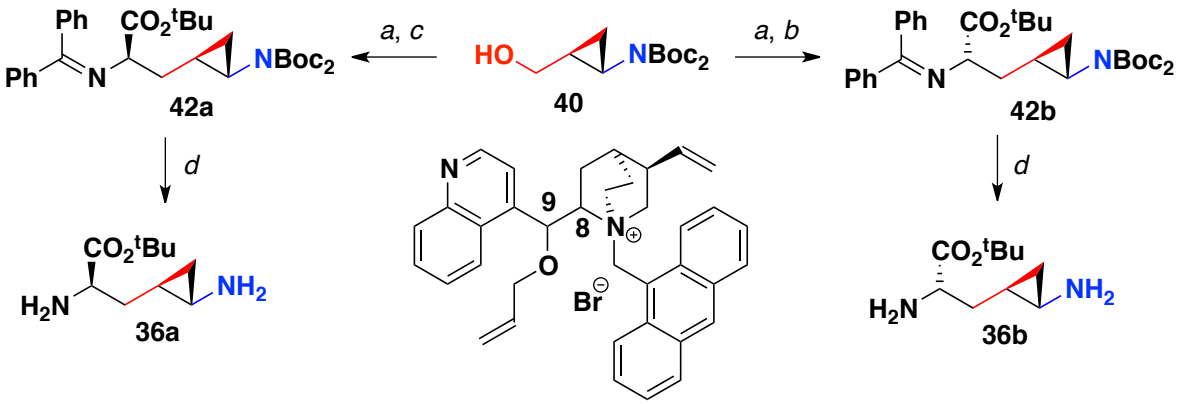
Scheme 39 Inseparable mixtures of epimers **36a** and **36a**.

Application of the Wadsworth-Emmons reaction using the anion of the phosphonate **1a** with (*S*)-benzyl glycidyl ether (*S*)-**4c** gave the cyclopropane (1*S*,2*S*)-**5c**. Hydrolysis to the acid (1*S*,2*S*)-**7c** provided a suitable substrate for the insertion of the free amine *via* Curtius rearrangement. The cyclopropyl amine **38** was protected with two Boc groups, before cleavage of the benzyl ether produced the cyclopropylmethanol **40**, which was then transformed to (iodomethyl)cyclopropane **41** (Scheme 40).



Scheme 40 Synthetic route to the (iodomethyl)cyclopropane **41**. Reagents and conditions: (*a*) **1a**, NaH, PhMe, 110 °C, 14 h, 63%; (*b*) NaOH, EtOH, 96%; (*c*) DPPA, TEA, ^{t}BuOH, 53%; (*d*) Boc_2O, DMAP, MeCN, 95%; (*e*) H_2, Pd/C, cat. AcOH, THF, 98%; (*f*) Bu_4NI, DDQ, PPh_3, $CHCl_3$, rt.

Since the iodide **41** was unstable, it required generation *in situ* in the presence of O'Donnell's glycine and a chiral cinchona alkaloid catalyst. The epimers at the C−2 carbon were produced with excellent stereoselectivity with the two *pseudo*-enantiomeric chiral catalysts *O*-(9)-allyl-*N*-(9-anthracenylmethyl)-cinchonidinium $\mathbf{L^1}$ and cinchonium $\mathbf{L^2}$ bromides.[46] This reaction was further complicated by competition of the solvent DCM as the electrophile. Use of high concentrations of the iodide **41** was required to suppress this (Scheme 41).



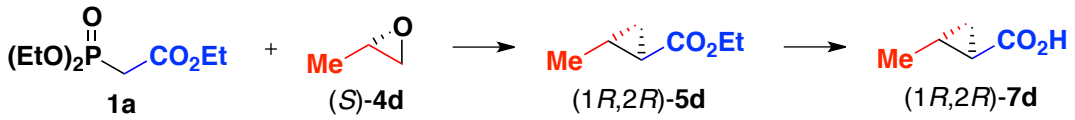
$\mathbf{L^1}$ = 8*S*, 9*R* (cinchonidinium)

$\mathbf{L^2}$ = 8*R*, 9*S* (cinchonium)

Scheme 41 Final steps to the two epimers **36a** and **36b**. Reagents and conditions: (*a*) Bu_4NI, DDQ, PPh_3, $CHCl_3$, rt; (*b*) O'Donnell's glycine (2 eq), $\mathbf{L^1}$ (20 mol%), CsOH H_2O (10 eq), PhMe/DCM (1:1), −40 °C, 66%, 97:3 *dr*; (*c*) O'Donnell's glycine (2 eq), $\mathbf{L^2}$ (20 mol%), CsOH H_2O (10 eq), PhMe/DCM (1:1) −40 °C, 52%, 6:94 *dr*; (*d*) 1.2 M HCl (aq)/THF, rt, 48 h.

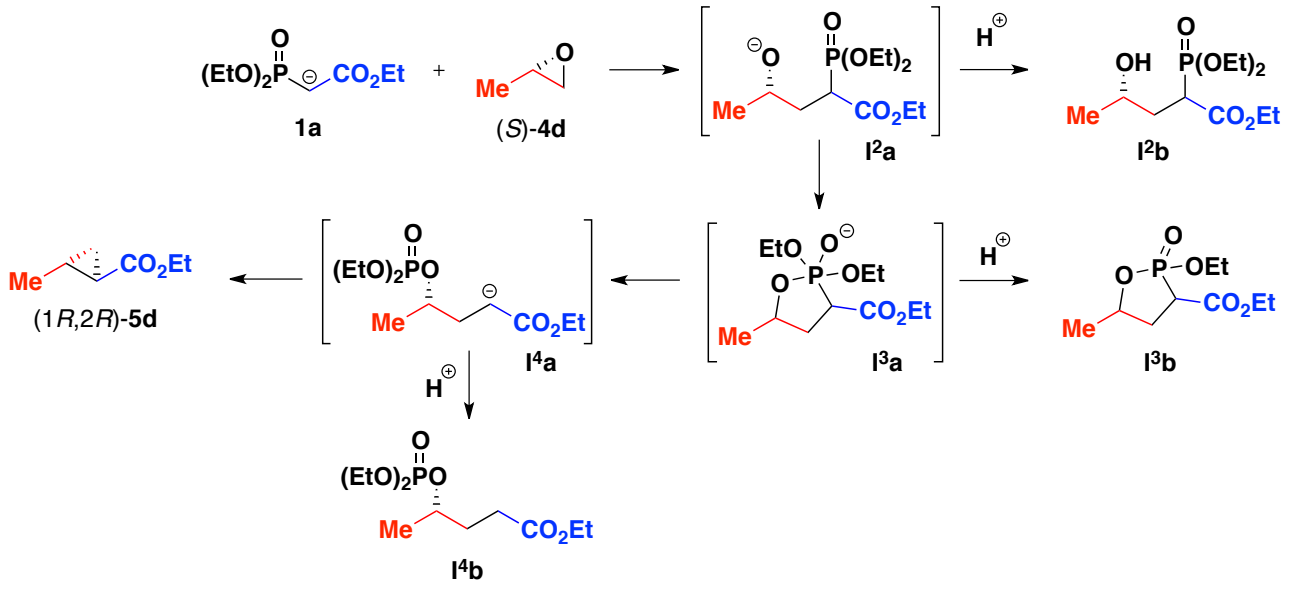
1.12 Latest insights on Wadsworth-Emmons cyclopropanation

In 2007, Merschaert and co-workers from the UCB process research group described a detailed examination on the experimental progress of the Wadsworth-Emmons cyclopropanation reaction starting from (*S*)-propylene oxide (*S*)-**4d** and the anion of the phosphonate **1a** *via in situ* IR spectroscopy. Their aim was the large-scale synthesis of the cyclopropyl acid (1*R*,2*R*)-**7d** (Scheme 42).[47]



Scheme 42 Stereoselective synthesis of (1*R*,2*R*)-2-methylcyclopropanecarboxylic acid (1*R*,2*R*)-**7d**.

The test reactions were run on a 1 mmol scale and were monitored *via in situ* IR spectroscopy. Such technique allowed to study the formation of the phosphonate carbanion in solution and proved crucial for two reasons. First, it demonstrated that the excess of a strong base promoted the polymerisation of the epoxide (*S*)-**4d**; second, it revealed the detrimental effect of TEPA **1a** on the reaction mechanism, as the presence of proton donors protonated the intermediates $\mathbf{I^2a}$, $\mathbf{I^3a}$ and $\mathbf{I^4a}$ to give $\mathbf{I^2b}$, $\mathbf{I^3b}$ and $\mathbf{I^4b}$, hence reducing the final yield (Scheme 43).



Scheme 43 Mechanism of formation of the protonated intermediates in the presence of proton donors.

Interestingly, the excess of TEPA anion appeared compatible with the isolation of the cyclopropyl acid (1*R*,2*R*)-**7d** in high yields.

Several bases were screened such as mineral alkoxides, organic bases, sodium hydride, and alkyl lithiums. The highest values of yield and diastereoselectivity were obtained with hexyl lithium (confirmed throughout the study *via* GC-MS 97% *de* when using HexLi in MeTHF), whereas alkoxides suffered the formation of the protonated intermediates $\mathbf{I}^2$, $\mathbf{I}^3$ and $\mathbf{I}^4$ due to the ability of the conjugated acid to act as a proton donor. Finally, MeTHF was preferred over other ethereal solvents such as diglyme, dioxane and MTBE, although had a marginal effect on the final yield.

Monitoring the process in the initial two hours proved the cyclopropane ring-closure to be the rate-determining step. In fact, the epoxide (*S*)-**4d** was completely converted, mainly to the intermediates $\mathbf{I}^2$**a**, $\mathbf{I}^3$**a** and $\mathbf{I}^4$**a**, with only traces of the final cyclopropyl ester (1*R*,2*R*)-**5d**. As a consequence, this information led the authors to hypothesize the existence of a stable intermediate preceding the formation of the second C−C bond. Additionally, since the highest yield and *trans*-stereoselectivity values were achieved with lithium as a counterion, it appeared that such intermediate had to feature a chelation effect, allowing high diastereoselectivity despite only moderate steric repulsive effects between the methyl group installed on the epoxide moiety and the ester functionality (Figure 5).

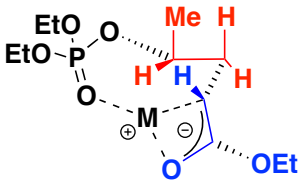


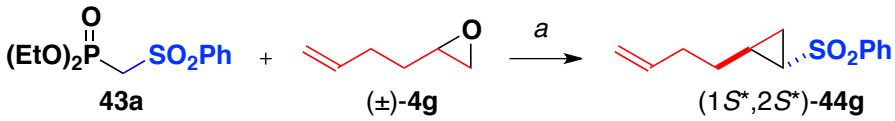
Figure 5 Chelation effect drawn as proposed by Merschaert *et al.* to explain the high diastereoselectivity.

This study was important because it appeared to provide the first direct evidence for the structure of all the intermediates in the Wadsworth-Emmons cyclopropanation. However it should be noted that whilst this is the indication in the paper, no evidence is presented either in the experimental or the supporting information. Finally, despite high diastereoselectivity is achieved in

the presence of lithium as a counterion (98.7% dr), use of sodium (98% dr) or potassium (95% dr) allows comparable results. As all the experiments were run in dipolar aprotic solvents, it appears highly unlikely that metals such sodium and potassium can form stable chelated intermediates in such experimental conditions. Nevertheless, when tert-butoxide was used as a base, the yield of the process dropped from lithium to potassium. This seems to imply that the role of the cation would rather involve the stabilisation of the carbanion, favouring the cyclopropane formation over other reaction pathways. This subject will be discussed in the paragraph 2.2 of the Results and Discussion.

1.13 Route to di-substituted cyclopropyl sulfones

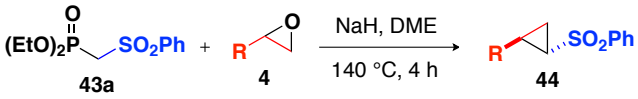
In 2010 Bray and De Faveri[48] reported the first application of the Wadsworth-Emmons protocol to a new class of electron-withdrawing groups – *i.e.* sulfones. The reason of their interest lied in the versatile transformations this structure can undergo. For example, cyclopropyl sulfone chemistry involves several pathways such as alkylation/acylation,[49] conversion to methylene cyclopropanes,[50] formation of π-allyl palladium complexes and reactions with electron deficient alkenes[51] and desulfunylation to give simple cyclopropanes.[52] Once formed, they can also act as synthons for 1,3-dipoles,[53] participate in Julia-type olefinations[54] and be regioselectively cleaved to yield vinylstannanes.[55] Their investigation commenced by improving the conditions of the reaction using two equivalents of phosphonate **43a**, which was examined with the reference epoxide (±)-**4g** (Scheme 44).

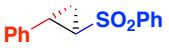
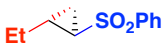
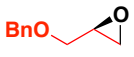
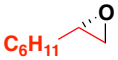
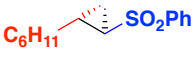
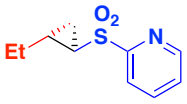


Scheme 44 Synthesis of cyclopropyl sulfone (1*S**,2*S**)-**44g**. Reagents and conditions: (*a*) NaH, DME, 4 h, 140 °C.

Use of sodium hydride was preferable to *n*-BuLi or KH due to solubility issues and formation of by-products; the reaction time was decreased to as little as 4 hours at 140 °C (Table 4). The Wadsworth-Emmons procedure appeared to be compatible with a wide range of epoxides, ranging from simple alkyl substituted to olefin-containing substrates. Isolated cyclopropanes showed excellent *trans*-diastereoselectivity, ranging from *dr* values of 200:1 (Table 4, Entry 1) to 98:2 (Table 4, Entries 2 and 4). Chiral HPLC analysis confirmed preservation of optical purity, suggesting a stereospecific mechanism proceeding *via* inversion of configuration at the epoxide stereocentre. Enantioenriched epoxides (*S*)-**4c** and (*R*)-**4j** were successfully converted into their respective cyclopropanes (1*S*,2*R*)-**44c** and (1*R*,2*R*)-**44j** that were amenable for further synthetic modifications (Table 4, Entries 3 and 5).

Table 4 Cyclopropyl sulfones **44**.[a]



Entry	Epoxide		Product		Yield (%)[b]
1		(*S*)-**4a**		(1*R*,2*S*)-**44a**	86
2		(*S*)-**4b**		(1*R*,2*R*)- **44b**	82
3		(*S*)-**4c**		(1*S*,2*R*)- **44c**	60
4		(*S*)-**4h**		(1*R*,2*R*)- **44h**	85
5		(*R*)-**4j**		(1*R*,2*R*)- **44j**	74
6		(±)-**4k**		(1*S**,2*R**)-**44k**	31
7		(±)-**4l**		(1*S**,2*R**)-**44l**	0
8		(±)-**4m**		(1*S**,6*S**)-**44m**	5
9		(*S*)-**4b**		(1*R*,2*R*)- **44n**	17[c]

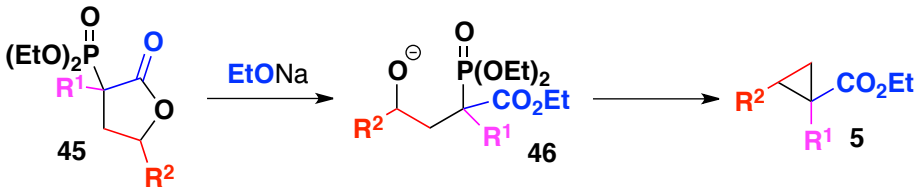
[a]Reactions carried out with 2 eq of **43a**.
[b]Isolated yield following column chromatography.
[c]Diethyl (pyridin-2-yl)sulfonylmethylphosphonate used as reagent.

The effect of the γ-substituent was also examined by screening hindered groups (Table 4, Entries 6-7). The ring-closure process appeared to be retarded by steric bulk, as witnessed by the poorer isolated yields. Epoxide (±)-**4l** failed to convert to cyclopropane (1*S**,2*R**)-**44l**: *in-situ* ^{1}H-NMR measurements showed formation of olefin signals, possibly arising due to neopentyl-like rearrangement (Table 4, Entry 7). The selectivity of the transfer of the phosphorous to the alkoxides with respect to a sulfone prompted the authors to investigate the synthesis of substrates able to undergo subsequent Julia-Kocienski olefination.[56] Phosphonate **43a** was replaced by diethyl (pyridin-2-yl)sulfonylmethylphosphonate, which was reacted (*S*)-**4b**. Surprisingly, the expected product (1*R*,2*R*)-**44n** was isolated with a poor yield (Table 4, Entry 9). This outcome suggested a

potential competitive Julia-Kocienski cyclopropanation, a process that was contemporaneously examined within the group by another PhD student.

1.14 Hypothetic intermediates as novel structurally demanding partners

The demand for configurationally challenging multi-substituted cyclopropanes led to the design of the intermediates normally formed during the Wadsworth-Emmons cyclopropanation *via* alternate stereoselective routes. Krawczyk and co-workers identified phosphonates **45** as suitable cyclopropane precursors, by treating these substrates with ethoxide to induce the subsequent cyclopropanation in accordance with the previously proposed mechanism (Scheme 45).[57]

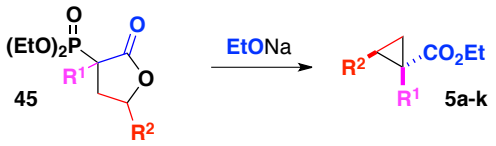


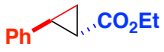
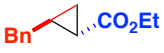
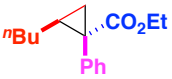
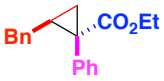
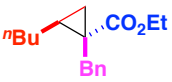
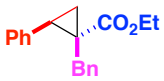
Scheme 45 Krawczyk, Wąsek and Kędzia suggestion.

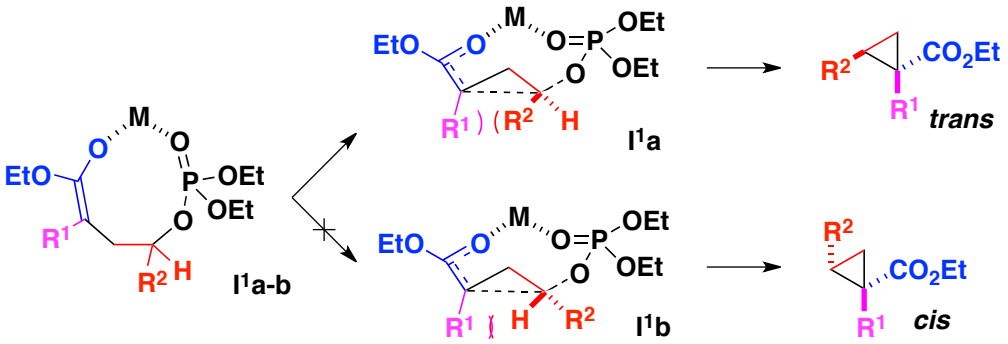
A variety of substituted phosphonates were produced and isolated as mixtures of diastereomers. Without further purification, phosphonates **45** were reacted with ethoxide to induce the corresponding cyclopropanation (Table 5). Cyclopropanes **5a** and **5f-k** were isolated as single isomers, and **5d-e** were produced in excellent diastereoselectivity. Regardless of the level of the substitution and the *de* of the starting phosphonate **45**, the ester group and the $\mathbf{R^2}$ group in the product formed existed in a *trans*-relationship. As phosphonates **45** were produced under non-stereoselective reaction conditions, cyclopropanes **5** were obtained as mixtures of enantiomers.

The origin of the stereoselectivity displayed by the products was ascribed to the formation of two epimeric nine-membered complexes $\mathbf{I^1a}$ **&** $\mathbf{I^1b}$ containing an (*E*)-enolate. Due to the steric transannular interaction arising between $\mathbf{R^1}$ and $\mathbf{R^2}$, the transition state $\mathbf{I^1a}$ would be kinetically favoured, preferring the formation of the *trans*-isomer. Despite the novelty provided, this route only afforded the formation of racemic products, as the syntheses of the lactones **45** lacked any asymmetric induction at the carbon atom undergoing the S_N2 mechanism (Scheme 46).

Table 5 Degradation of **45** to cyclopropanes **5**.



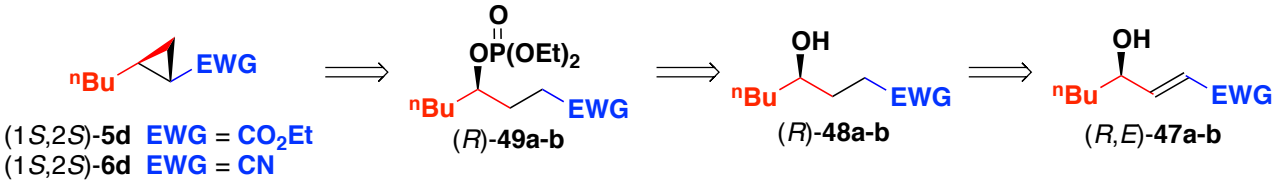
Entry	R^1	R^2	*dr* ratio	Cyclopropane		Yield(%)	*dr* ratio
1	H	Ph	45:55		**5a**	65	>99:1
2	H	^{n}Bu	56:44		**5d**	86	93:7
3	H	Bn	67:33		**5e**	65	93:7
4	Me	^{n}Bu	80:20		**5f**	55	>99:1
5	Me	Bn	80:20		**5g**	53	>99:1
6	Ph	^{n}Bu	90:10		**5h**	58	>99:1
7	Ph	Bn	92:8		**5i**	62	>99:1
8	Bn	^{n}Bu	84:16		**5j**	62	>99:1
9	Bn	Ph	97:3		**5k**	80	>99:1



Scheme 46 Suggested mechanism by Krawczyk, Wąsek and Kędzia.

Given the high diastereocontrol, the authors were prompted to assess the level of enantioselectivity of their variant of the Wadsworth-Emmons cyclopropanation reaction.[58]

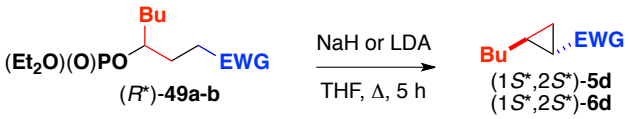
Enantiopure allylic alcohols (*R*,*E*)-**47a-b** were synthesised with both the ester and the nitrile group. Reduction of the double bond to give (*R*)-**48a-b** and protection of the alcohol with diethyl chlorophosphate allowed the synthesis of the cyclopropane precursors (*R*)-**49a-b**, which were converted to cyclopropanes (1*S*,2*S*)-**5d** and (1*S*,2*S*)-**6d** upon treatment with base (Scheme 47).



Scheme 47 Alternative route to enantiopure cyclopropanes.

The optical purity of the phosphonates and the cyclopropanes were assessed by chiral HPLC, demonstrating the preservation of optical activity during the reaction pathway (Table 6). The products were isolated as single diastereomers, whose *trans*-configuration was assigned by ^{1}H and ^{13}C-NMR spectroscopy, in correlation with their previous work.[57b]

Table 6 Enantiospecific cyclopropanation.



Entry	Phosphate		EWG	*ee*%	Product	Yield (%)[a]	*ee*%	Retention of *ee*%
1	(*R*)-**49**	a	CO_2Et	91[b]	(1*S*,2*S*)-**5d**	75	90[b]	98.9
		b	CN	91[b]	(1*S*,2*S*)-**6d**	72	90[b]	98.9
2	(*S*)-**49**	a	CO_2Et	82[b]	(1*R*,2*R*)-**5d**	75	80[b]	97.6
		b	CN	82[b]	(1*R*,2*R*)-**6d**	72	80[b]	97.6

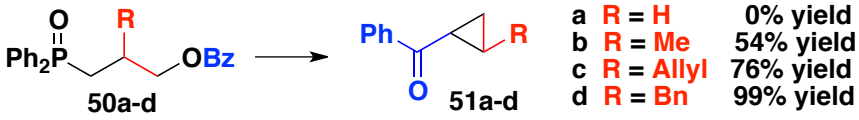
[a]Yields calculated on mass recovery by column chromatography. [b]*ee* calculated by GC.

This investigation described the intrinsic trans-stereoselectivity of the Wadsworth-Emmons cyclopropanation reaction, regardless of the isomeric purity of the starting phosphonates, i.e. mixtures of diastereoisomeric phosphonates produce cyclopropanes where the anion-stabilising group and the vicinal substituent lies in a trans-relationship. The cis-isomer is usually not found in the reaction mixture, or is only detected in trace amounts. It also demonstrated that the Wadsworth-

Emmons protocol retains the optical purity when enantioenriched starting materials are used, in agreement with the hypothesis of a stereospecific 3-exo-tet ring-closure occurring via S_N2-like mechanism. The authors suggested that such stereoselectivity arises from the kinetic decomposition of nine-membered ring intermediate where the transannular steric interactions are reduced. This is in contrast with the chelated model proposed by Merschaert (Figure 5, Page 32), where chelation is responsible for the high level of stereoselectivity even in the presence of moderate repulsive steric effects.

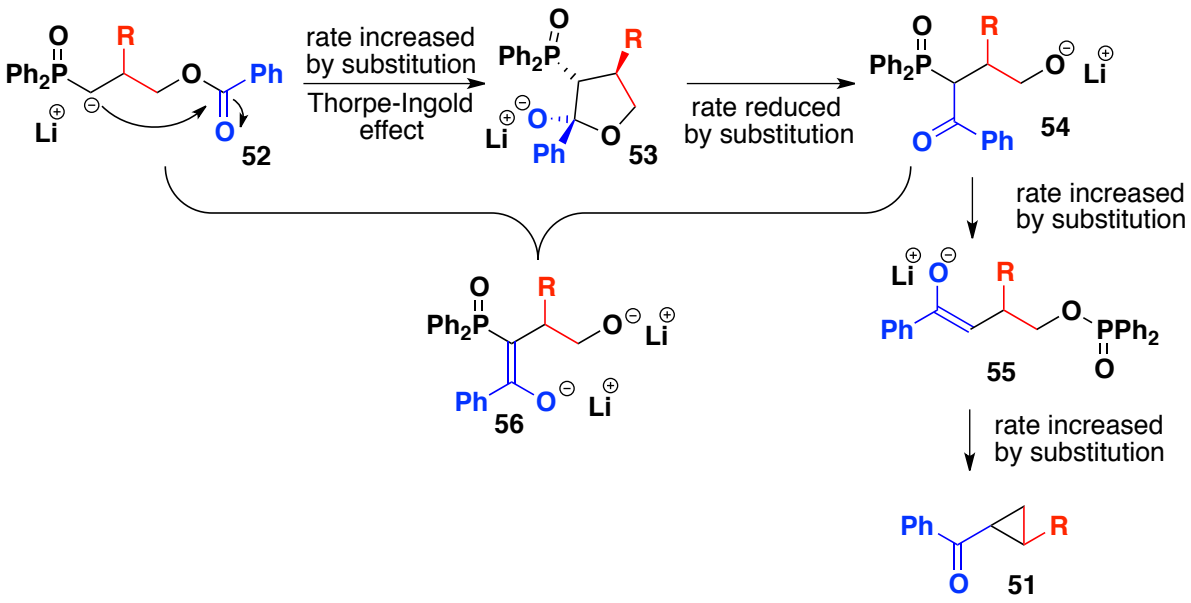
1.15 Role of the β–substituent in the cyclopropanation reaction

Warren and co-workers investigated the role of the β-substituent in the cascade cyclopropanation, whilst keeping both the α- and γ-positions unsubstituted.[59] Alkyl chains with increasing hindrance were screened. Substituted racemic phosphine oxides produced only the *trans*-cyclopropane, improving yields as the bulk of the substituent was increased. Only the unsubstituted phosphine oxide failed to give the corresponding cyclopropane (Scheme 48).



Scheme 48 Racemic cascade cyclopropanation with β-substituted phosphine oxides.

This outcome was explained as a consequence of the Thorpe-Ingold effect. The formation of the 5-membered ring **53b-d** is supported by the size of the substituent at the β-position. Although the rate of ring-opening process is reduced with the hindrance in **54b-d**, the cascade reaction to the cyclopropane **51b-d** is actually supported, yielding only the as *trans*-isomers (Scheme 49). Conversely, when the compound **54a** is formed, a high concentration of the phosphine oxide **52a** is still present, deprotonating the species **54a** to the di-anionic inactive enolate **56**.



Scheme 49 Effect of the β-substituent in the cascade cyclopropanation.

This study is important as it describes the effect of the β-substituent during the cascade reaction, favouring the formation of the new C−C bond between nearby carbon atoms. It also suggests that lack of β-substitution may also restrict the range of electron-withdrawing groups active in the Wadsworth-Emmons cyclopropanation reaction, as the intermediate undergoing the 3-exo-tet ring-closure could potentially be deprotonated by previous intermediates in the reaction pathway.

1.16 State of the art at the beginning of the current work

The Wadsworth-Emmons reaction is an important and highly stereoselective reaction to afford cyclopropane motifs in high yields. At the beginning of this project, in late 2009, several investigations had already been instigated that led to a greater insight into this reaction. The following summarises the work that had already been completed and published in the peer reviewed literature:

1. Enantioselectivity is preserved when enantiopure starting materials are used.[21b,26,43,44,47,48,57b]
2. When using a simple unsubstituted phosphonoacetate with a terminal epoxide, *trans*-cyclopropanes products are obtained.[19,26,43,44,47,48]
3. Alkyl substituted phosphonoacetates do react with epoxides; however this had only been explored in a small number of cases, using very specific phosphonates or epoxides.[33,33,38,41]
4. If the intermediates of the Wadsworth-Emmons reaction are generated independently as a mixture of diastereomers, then only a single diastereomer of the cyclopropane product is produced.[57a]
5. Only a small number of alternate anion-stabilizing groups had been employed: nitrile (Wadsworth-Emmons),[19] ketones (Wiemer),[38] benzotriazole (Katritzky),[41] sulfones (Bray).[48]
6. There was a single report (Katritzky)[41] of a substituted anion-stabilizing group other than an ester reacting to give a tri-substituted cyclopropane in high yields and *dr*.

1.17 Aim of the current work

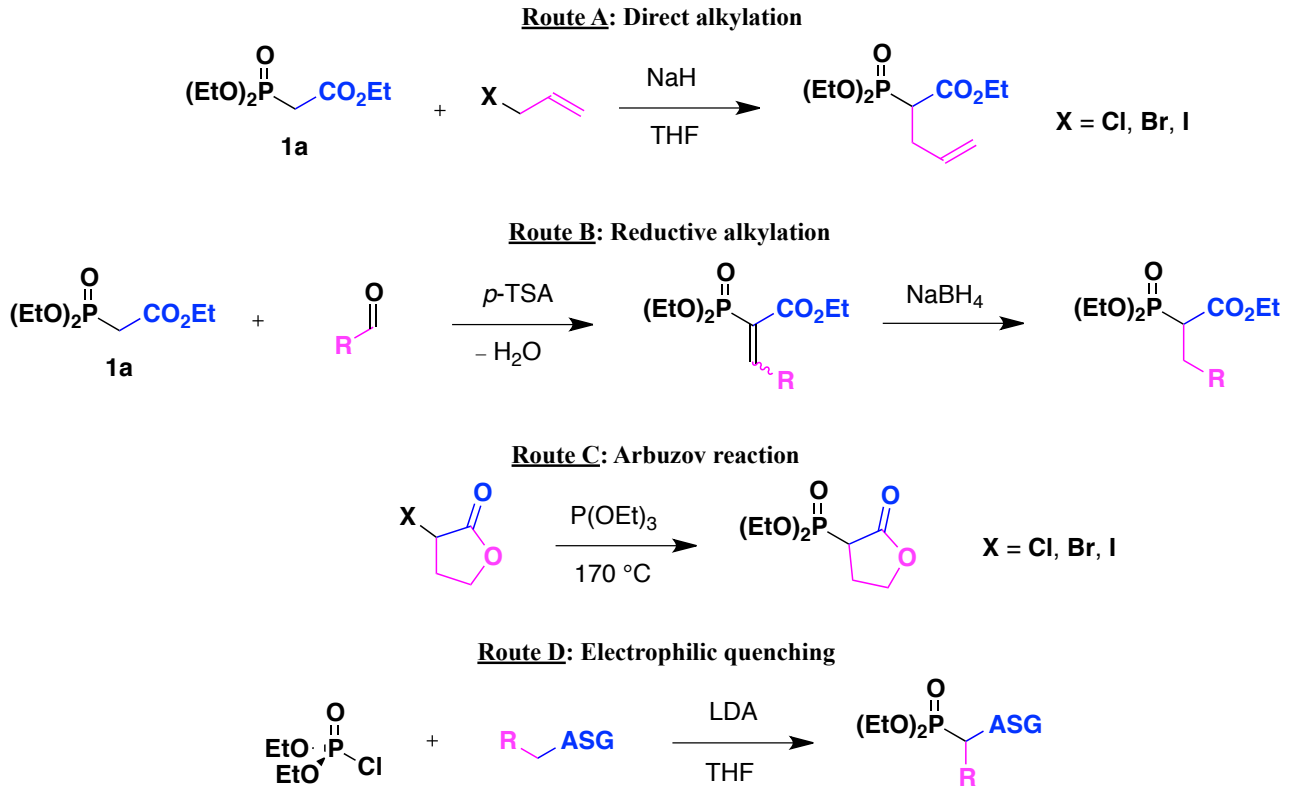
The aim of this project was to investigate the Wadsworth-Emmons reaction, according to the following *modus operandi*:

1. Systemic production of a library of novel phosphonate molecules for use in Wadsworth-Emmons reactions.
2. Investigation of the scope and limitations of the Wadsworth-Emmons reaction in tolerating a variety of additional alkyl substituents on triethyl phosphonoacetate.
3. Investigation of the scope and limitation of a broad range of unsubstituted phosphonates bearing alternative Anion Stabilising Groups.
4. Investigation of the scope and limitation of a broad range of substituted phosphonates bearing alternative Anion Stabilizing Groups.

2 RESULTS AND DISCUSSION

2.1 Synthesis of phosphonates

The work of Wadsworth and Emmons contribution over 60 years ago has now led to the inspiration of this work, as we felt the full scope of this important cyclopropanation reaction had not been fully explored. The first task was to examine the use of alkyl-substituted derivatives of Horner's reagent **1a**, in order to develop a reproducible, regio- and stereoselective route to quaternary cyclopropyl esters. Nevertheless, before approaching the cyclopropanation, we needed to first explore the possible routes to access the required phosphonates. Review of the literature highlighted four potentially viable pathways (Scheme 50).



Scheme 50 Approaches to the synthesis of phosphonates.

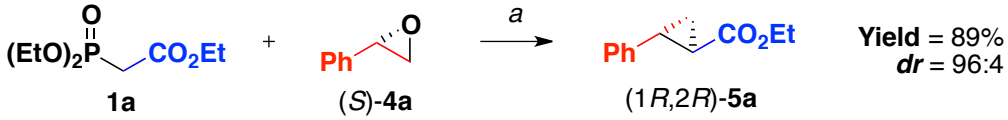
In cases where the unsubstituted phosphonate precursors were commercially available, two of the above pathways were feasible: the first involved direct alkylation, representing the most straightforward strategy and was possible when the precursor alkyl halide was available (**Route A**).[60] In some instances, formation of the dialkylated by-products made purification by flash

chromatography problematic, and use of reduced pressure distillation was only successful in cases where the alkyl groups featured a high molecular weight. The formation of the disubstituted by-product could be avoided *via* the reductive alkylation pathway (**Route B**).[61] This two-step protocol involved condensation of the phosphonate with an aldehyde and subsequent reduction of the double bond, *e.g*. with $NaBH_4$.

In cases where the required phosphonate precursors were not commercially available, two further synthetic strategies were useful. The first alternative route consisted of the Arbuzov reaction (**Route C**) and involved the use of triethyl phosphite (or diethyl phosphite and a Lewis acid) and a suitable alkyl halide.[62] Unreacted starting materials were removed by distillation under reduced pressure to give a single product. However there were major drawbacks in this approach - di- and tri-alkyl phosphites are incredibly toxic and their use (for this reason) is tightly regulated by the Organization for the Prohibition of Chemical Weapons. Furthermore, the scope of this route to afford the required phosphonate was limited in **Route C**, as the reaction did not proceed in the presence of electron-rich heteroatoms (*e.g*. those containing nitrogen and sulfur). This was due to the ethyl halide that evolved during the course of the process, further reacting to form quaternary salts. When the Arbuzov reaction failed, installation of the phosphonate could be achieved with an electrophilic source of phosphorous such as diethyl chlorophosphate (**Route D**).[63] This strategy required deprotonation of the precursor, *i.e*. only carbanions stabilised by electron withdrawing groups proved successful. This procedure allowed isolation of the target phosphonate upon purification by flash chromatography.

2.2 Cyclopropyl esters

The first approach to the cyclopropanation began by optimising the experimental conditions to reproduce the original work reported by Wadsworth and Emmons.[19] In keeping with this work, epoxide (*S*)-**4a** was used. The presence of the aromatic ring appeared an important initial feature to incorporate in our first approach, due to its potential to support the sp^3-carbon efficient S_N2-like nucleophilic substitution during the cyclopropane ring-closure. The experimental conditions were taken from the work reported previously in the group[48] and modified initially solely in terms of reaction times. Under these conditions, cyclopropane (1*R*,2*R*)-**5a** was recovered following flash chromatography in more than double the yield compared to the original paper. The GC-MS analysis performed on the crude mixture indicated two peaks with the expected *m/z* ratio of **5a**, and revealed the diastereoselectivity to be 96:4 *dr* (Scheme 51).



Scheme 51 Route to cyclopropane (1*R*,2*R*)-**5a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

It was fortunate that despite this reaction having been performed previously by a variety of groups, that it was possible to obtain crystals of suitable quality for X-ray crystallographic analysis. This supported the *trans*-selectivity of this reaction (Figure 6).

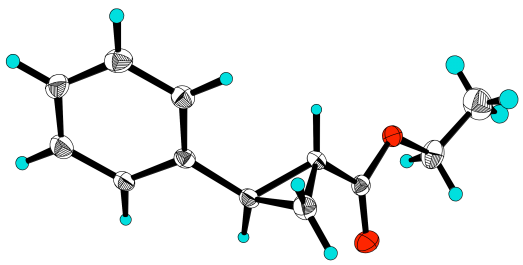
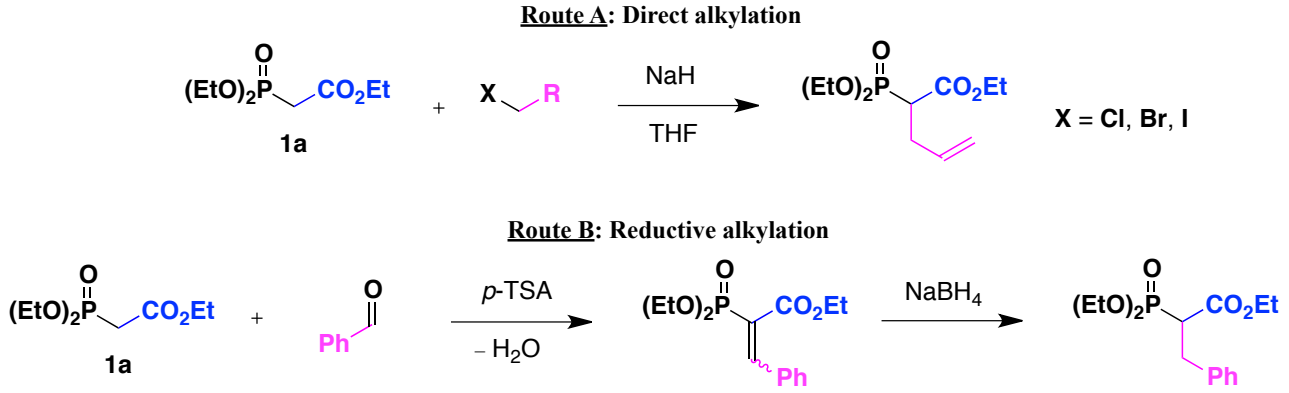


Figure 6 Crystal structure of cyclopropane (1*R*,2*R*)-**5a**.

The stereochemical outcome was in agreement with the work described in the literature and prompted us to investigate the compatibility of the Wadsworth-Emmons protocol with substituted

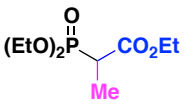
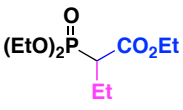
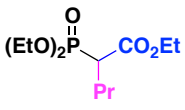
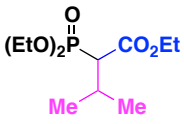
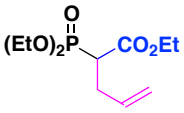
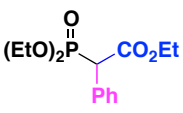
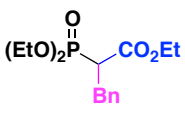
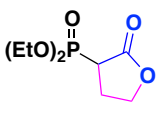
derivatives of **1a**. Horner's reagent **1a** was modified by insertion of alkyl/aryl groups at the C−2 position *via* both **Route A** and **Route B** (Scheme 52).



Scheme 52 Synthesis of phosphonates *via* both **ROUTE A** and **ROUTE B**.

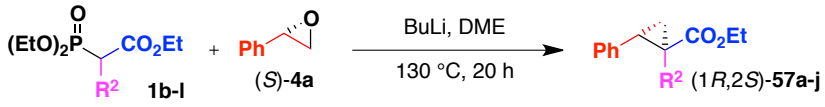
The acidity of the phosphonate **1a** was reported in DMSO (pK_a 18.6)[64] offering a key reference value to predict its reactivity. However, none of the substituted homologous phosphonates were described in the literature. Therefore, in lieu of a classification of the reactivity based on pK_a values, it was agreed to build an empirical reactivity scale with regard to the NMR spectroscopy. Our assessment of the compatibility of phosphonates **1** was then referred to the resonance values of both the acidic proton as well as the ^{31}P NMR as compared to those of the phosphonate **1a** (^{1}H = δ 2.97 ppm, ^{31}P = δ 19.7 ppm) (Table 7).

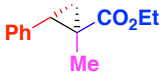
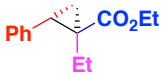
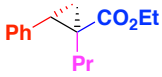
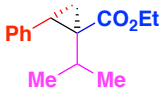
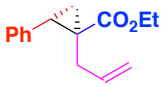
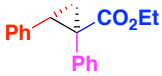
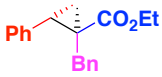
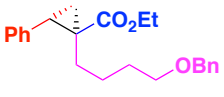
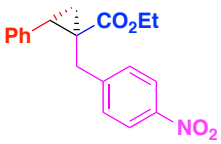
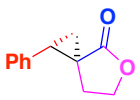
Table 7 List of homologous phosphonate **1** and relative resonance values.

				
	1b	**1d**	**1e**	**1f**
^{1}H NMR	2.91	2.87	3.10-2.89	2.73
^{31}P NMR	23.4	22.1	23.1	22.1
				
	1g	**1h**	**1i**	**1l**
^{1}H NMR	3.01	3.57-3.51	3.32-3.14	3.23-2.45
^{31}P NMR	22.2	19.4	22.0	21.1

This approach suggested that alkyl chains produce a downfield effect on the ^{31}P nucleus, which becomes apparent in the ^{1}H NMR with the increasing hindrance. The presence of an aromatic ring may enhance this effect in the proton spectroscopy, which becomes more enhanced when the substitution contributes to the resonance structures. Phosphonates **1b-l** were treated under the Wadsworth-Emmons cyclopropanation conditions and the resulting were produced in high yields and excellent stereoselectivity (Table 8).

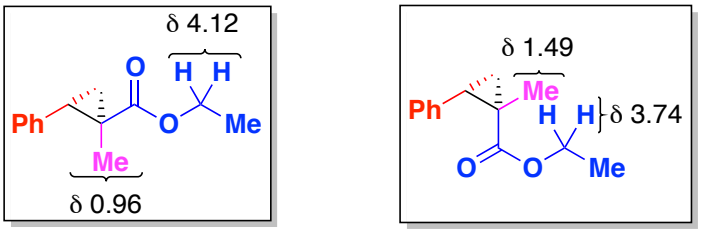
Table 8 Wadsworth-Emmons cyclopropanation of derivatives (1*R*,2*S*)-**57a-j**.[a]



Entry	R^2	Phosphonate	Cyclopropane		Yield[b](%)	*dr* ratio[c]
1	Me	**1b**		(1*R*,2*S*)-**57a**	95	>99:1
2	Et	**1d**		(1*R*,2*S*)-**57b**	97	>99:1
3	Pr	**1e**		(1*R*,2*S*)-**57c**	93	98:2
4	^{i}Pr	**1f**		(1*R*,2*S*)-**57d**	0	---
5	Allyl	**1g**		(1*R*,2*S*)-**57e**	86	98:2
6	Ph	**1h**		(1*R*,2*S*)-**57f**	0	---
7	Bn	**1i**		(1*R*,2*S*)-**57g**	91	93:7
8	$(CH_2)_4OBn$	**1j**		(1*R*,2*S*)-**57h**	76	>99:1
9	(*p*-NO_2)Bn	**1k**		(1*R*,2*S*)-**57i**	0	---
10	$(CH_2)_2OH$	**1l**		(1*R*,2*S*)-**57j**	0	---

[a]Reactions carried out with 2 eq of phosphonate. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS. [d]Enaniomeric excess 99% determined by chiral HPLC.

The cyclopropanes **57a-j** were all obtained as oils. For the known compounds (1*R*,2*R*)-**57a-c** the *trans*-relationship between the phenyl ring and the ester was assigned on the basis of the resonance of the methylene of the ethyl ester functionality. Fox and co-workers have provided a detailed description of the shifts observed for these signals in the ^{1}H NMR. Where such a *trans*-relationship exists, a normal resonance at ~δ 4.10 is observed. Whereas when a *cis*-relationship exists, a distinct upfield chemical shift occurs due to the anisotropic effect of the proximal phenyl ring.[65] Similar dichotomal shifts are reported for the methyl or methylene of the alkyl substituents (Figure 7).

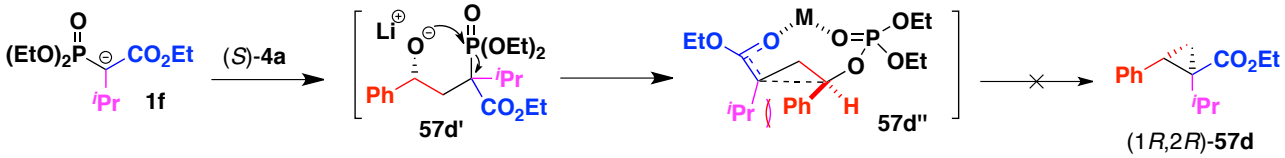


(1*R*,2*S*)-**57a** (1*R*,2*S*)-**57b**

Figure 7 Chemical shifts for methyl and methylene groups in (1*R*,2*S*)-**57a-b**.

These general trends allowed for ready assignment of the stereochemical arrangement of the remaining cyclopropanes. The stereochemical trend remained unchanged throughout the screening, although yields dropped marginally as the bulkiness of the alkyl group increased. The presence of small alkyl chains proved compatible with the reaction conditions (Table 8, Entries 1-3). It is interesting to compare entries 3 & 4, homologues of the propyl chain. This clearly showcases the impact of sterics on the reaction. Cyclopropane (1*R*,2*R*)-**57c** was isolated in excellent yield and *dr*, whereas phosphonate **1f** was not converted to the expected cyclopropane (1*R*,2*R*)-**57d**, despite the starting materials being consumed. Analysis of the crude reaction mixture for this latter reaction revealed the formation of several by-products (by GC-MS), with ^{31}P NMR spectroscopy indicating the presence of multiple phosphorous environments. Finally, the ^{1}H NMR contained signals in the characteristic double bond area. These observations may be explained if we consider the Krawczyk model for selectivity (Scheme 46, Page 38). This would require the alkyl substituent (**^{i}Pr**) to be

placed proximal to the phenyl ring in the ring-closure step. This steric clash would retard the nucleophilic attack, allowing for the competition of alternate eliminative pathways (Scheme 53).



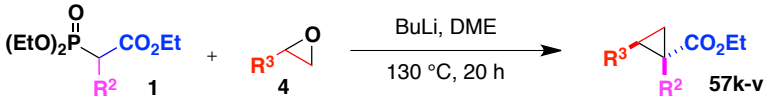
Scheme 53 Suggested steric clash during the elimination of the phosphate.

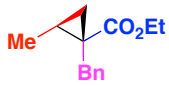
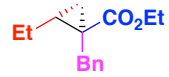
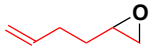
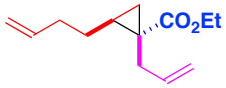
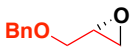
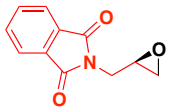
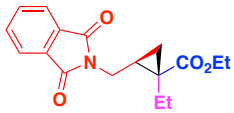
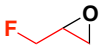
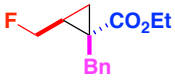
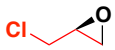
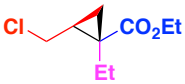
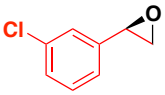
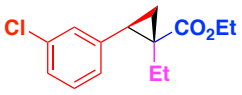
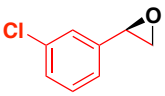
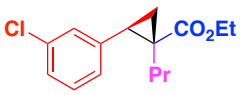
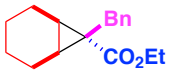
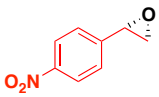
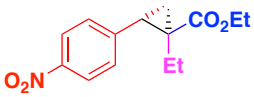
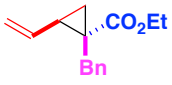
The importance of the role of the substituent on the C−2 carbon of the phosphonate prompted us to test another set of homologous $\mathbf{R^2}$ groups such as a phenyl ring or benzyl group (Table 8, Entries 6-7). As expected, the phosphonate **1h** failed to convert styrene oxide to the cyclopropane (1*R*,2*R*)-**57f**, with several side-products being detected by NMR spectroscopy. Satisfyingly however the benzyl substituted phosphonate **1i** led to the (1*R*,2*R*)-**57g** in quantitative yield, although with the poorest diastereoselectivity yet observed. This "partial loss" of diastereoselectivity suggested that we should also investigate any potential loss of enantioselectivity. Cyclopropane (1*R*,2*R*)-**57g** was isolated as a single diastereomer and analysed by chiral HPLC, with an enantiomeric excess equal to 98% *ee*. Since this value matched with that of the sample of (*S*)-styrene oxide (*S*)-**4a** used in the screening, it confirmed that the introduction of a quaternary carbon centre on cyclopropyl esters is compatible with the retention of optical purity of the epoxide moiety, in line with the literature.[21b,26,43,44,47,48,57b]

Following this, we moved on to investigating the role of the substituents $\mathbf{R^3}$ on the epoxide functionality. Since some of the epoxides used are highly volatile and lack chromophores, we opted to perform the screening against a UV-visible phosphonate with a very high molecular weight such as **1i**. When bulky and UV-active epoxides were handled, the size of $\mathbf{R^2}$ group was reduced so as not to affect the ring-closure mechanism. The broad compatibility with steric hindrance of the $\mathbf{R^2}$ group could be extended to the $\mathbf{R^3}$ scaffolds linked to the epoxide structure (Table 9). Small alkyl chains showed satisfying reactivity (Table 9, Entries 1-3). Epoxides (*R*)-**4d**, (*S*)-**4b** and (±)-**4g** were

respectively converted to cyclopropanes (1*R*,2*S*)-**57k**, (1*S*,2*R*)-**57l** and (1*S**,2*S**)-**57m** with high yields and excellent diastereoselectivity. The lower yields may be connected to the high volatility of either the starting epoxide or the sweet smelling ester products.

Table 9 Investigation of the role of the R^3 group on cyclopropanes **57k-v**.[a]



Entry	R^2	Epoxide		bp(°C)	Cyclopropane		Yield[b](%)	*dr* ratio[c]
1	Bn		(*R*)-**4d**	34		(1*R*,2*S*)-**57k**	75	>99:1
2	Bn		(*S*)-**4b**	63		(1*S*,2*R*)-**57l**	76	98:2
3	Allyl		(±)-**4g**	121		(1*S**,2*S**)-**57m**	86	>99:1
4	Me		(*R*)-**4c**	257		(1*S*,2*R*)-**57n**	78	>99:1
5	Et		(*R*)-**4h**	---		(1*R*,2*S*)-**57o**	57	99:1
6	Bn		(±)-**4j**	86		(1*R**,2*S**)-**57p**	75	>99:1
7	Bn		(*S*)-**4k**	117		(1*R*,2*S*)-**57q**	0	---
8	Et		(*R*)-**4l**	---		(1*R*,2*R*)-**57r**	73	98:2
9	Pr		(*R*)-**4l**	---		(1*R*,2*R*)-**57s**	46	99:1
10	Bn		**4m**	130		**57t**	0	---
11	Et		(*R*)-**4n**	---		(1*S*,2*S*)-**57u**	0	---
12	Bn		(±)-**4o**	66		(1*S**,2*R**)-**57v**	0	---

[a]Reactions carried out with 2 eq of phosphonate. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS.

Our screening also involved the compatibility of heteroatoms such as oxygen and nitrogen on the epoxide moiety (Table 9, Entries 4-5): The epoxide (*R*)-**4c** was successfully converted to cyclopropane (1*S*,2*R*)-**57n** (Table 9, Entry 4). Potentially appealing further modifications may include the cleavage of the Bn−O bond to provide a cyclopropyl methyl alcohol form. This substrate has been indeed investigated as an intermediate in routes to cyclopropyl carbocyclic nucleosides containing quaternary stereogenic centres.[66] Finally, chlorination of the alcohol may also lead to the isolation of a potential enantiopure electrophile.

The phthalimide moiety gave a significantly lower yield than expected under our reaction conditions (Table 9, Entry 5): this outcome could be rationalized as a consequence of lower solubility of the solid epoxide in DME. Enantiospecific synthesis of (1*R*,2*S*)-**57o** is noteworthy, as unusual derivatives of γ-aminobutyric analogues with restricted rotation are reported to be highly active in GABA receptor binding studies.[67] Both the cyclopropanes (1*S*,2*R*)-**57n** and (1*R*,2*S*)-**57o** were obtained with excellent diastereoselectivity.

Compatibility of electron-withdrawing $\mathbf{R^3}$ groups was verified with both aliphatic and aromatic epoxides. Epifluorohydrin (±)-**4j** produced the corresponding cyclopropane (1*R**,2*S**)-**57p** with a yield comparable to other epoxides with a similarly low boiling point (Table 9, Entry 6), whilst epichlorohydrin (*S*)-**4k** (Table 9, Entry 7) failed to react as desired. This may be the result of competition between the two electrophilic sites in the ring-opening step. In fact, the chlorine inductive effect may activate the adjacent carbon atom towards nucleophilic addition, generating a competition with the methylene carbon of the epoxide. Despite the fluorine being the element with the highest electronegativity, the very high dissociation energy of the C−F bond prevents this bond from cleavage.

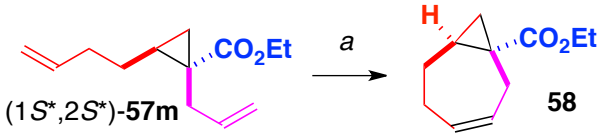
The compatibility of the chlorine atom on aromatic rings was investigated (Table 9, Entries 8-9). The epoxide (*R*)-**4l** was screened with phosphonates **1d** and **1e** to assess the reactivity with respect to the increasing size of the $\mathbf{R^2}$ chain. Phosphonate **1d** was transformed to (1*R*,2*R*)-**57r**

as expected, whereas the insertion of a methylene group in the phosphonate **1e** seemed to be connected to a drop in yield. As no internal standard was employed in the assessment of the conversion to cyclopropane, no statement can be made, as this drop in yield could be the simple consequence of a different solubility in ether of the two cyclopropanes. Nevertheless, it appeared interesting that the GC-MS analysis of the crude mixture did not detect the presence of unreacted epoxide (*R*)-**4l**, whilst it displayed four peaks with the expected *m/z* ratio. This observation seemed to suggest the formation of the elimination product, as already discussed for the phosphonate **1f** in Scheme 53 (Page 51). Conversely, no elimination product was observed for the cyclopropane (1*R*,2*R*)-**57r**. Finally, the steric bulk seemed not to influence the *trans*-selectivity, excellent for both the cyclopropyl esters.

Electrophiles with higher hindrance appeared to prevent the ring-closure step, as observed using (±)-cyclohexene oxide **4m** (Table 9, Entry 10). Highly electron-withdrawing epoxides did not form the desired product, producing an un-identifiable mixture of compounds (Table 9, Entries 11). Moreover, no sign of the desired product was observed by either ^{1}H NMR or GC-MS, so these functionalities were not considered any further in the course of our study. Finally, (±)-vinyl oxirane (±)-**4o** failed to produce the expected cyclopropane (1*S**,2*R**)-**57v**, possibly due to a competition between two electrophilic centres similar in fashion to that discussed in Entries 8-9. The crude mixture highlighted a distribution of products in the crude mixture, showing a lack of chemoselectivity.

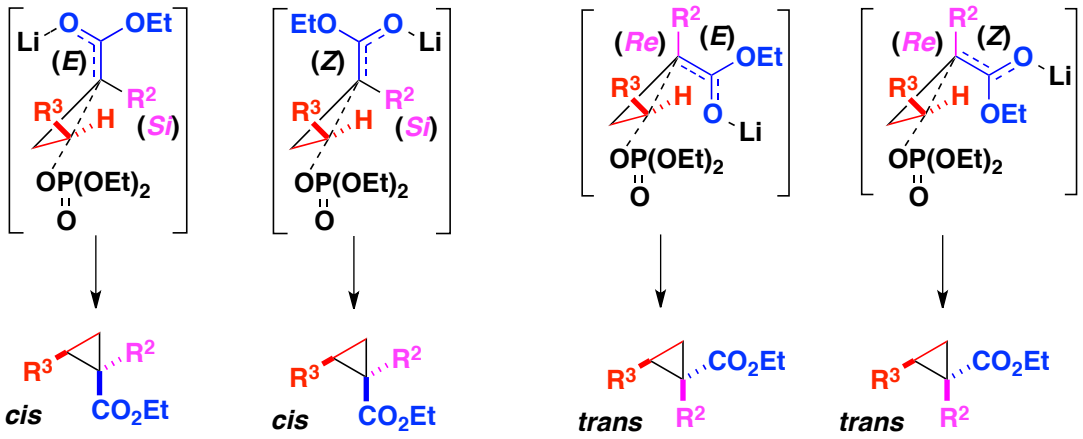
In order to widen the scope of the Wadsworth-Emmons procedure, we decided to investigate potential manipulations of the cyclopropanes obtained. The cyclopropane (1*S**,2*S**)-**56m** appeared an interesting substrate due to the potential synthetic modifications such as metathesis or oxidative processes. This compound, upon treatment with Grubbs' 1st generation catalyst (5 mol%), afforded the product of the ring-closing metathesis reaction **58**. Given the small size of the newly generated ring, this result seemed to suggest a *cis*-relationship between the $\mathbf{R^2}$ and $\mathbf{R^3}$ substituents. This test

also represented an interesting application of the present synthetic route to enantiopure medium-sized rings bearing cyclopropanes (Scheme 54).



Scheme 54 Metathesis reaction. Reagents and conditions: (*a*) Grubbs' 1st catalyst (5 mol%), DCM, 12 h, 56%.

In conclusion, Horner reagent's **1a** and its derivatives proved compatible with the Wadsworth-Emmons cyclopropanation, ring-opening terminal epoxides **4** to form the first C−C bond. The ring-closure step appeared to proceed smoothly for unencumbered phosphonates, whereas the more hindered homologues **1h** and **1i** failed to convert to the relative cyclopropanes. The Wadsworth-Emmons cyclopropanation showed an excellent *trans*-stereoselectivity, regardless of the size of the substituents. This suggested to us that the reasons of such a stereochemical course are ascribable to factors other than simple steric interactions. Indeed, the proposed mechanism would involve an S_N2-like mechanism performed by the ester enolate. Although said enolate could perform the attack from both faces, only the ring-closure promoted by the ***Re***-face would produce the *trans*-cyclopropane, independently from the descriptor of configuration of the enolate (Scheme 55).



Scheme 55 Suggested mechanism for the ring-closure process.

Nevertheless, this arrangement would necessarily bring the two groups R^2 and R^3 in *cis*-relationship, generating steric repulsion. Hence, the high diastereoselective elimination of diethyl phosphate would require a strong compensation of such a repulsive steric interaction by an additional energetic parameter.

This result would appear in agreement with the recent findings reported by Merschaert[47], whose model describes high *trans*-diastereoselectivity as a consequence of a stable chelated intermediate, regardless of the steric hindrance (Figure 5, Page 32). However, comparable values of *trans*-diastereoselectivity were achieved when the Wadsworth-Emmons cyclopropanation was applied to produce cyclopropyl sulfones in the presence of NaH in DME.[48] Given the lower charge density of sodium as compared to lithium, hence the lower chelating power, the formation of said stable chelated intermediate seems unlikely, especially in a dipolar aprotic solvent such as DME, where polar species are better solvated.

Finally, an interesting feature has been observed in the crystal structure of cyclopropane (1*R*,2*R*)-**5a** (Figure 6, Page 48): the carbonyl and the proton of the cyclopropyl-methine lie in eclipsed conformation. This trend has been observed for all the other crystal structures acquired throughout the project and would appear to indicate a potential electronic interaction between the heteroatom and the proton. Such an interaction could represent the additional energetic contribution that favours the nucleophilic attack of ***Re***-face despite the steric repulsion between the groups R^2 and R^3. If this were the case, the role of the cation would simply involve the stabilisation of the carbanion according to the hard-soft theory. The negative charge on the ester group would be better stabilised by a hard cation as lithium, whereas a softer cation as sodium would be more indicated to balance the negative charge on a softer group as the sulfone. In fact, Bray and De Faveri reported the synthesis of cyclopropyl sulfones in the presence of NaH, as BuLi led to the formation of by-products.[48]

The formation of the olefin would possibly result from the combination of two factors: an obstructed nucleophilicity of the carbanion and a substantial activation of the electrophilic site, favoured by the presence of EWG scaffolds. These conditions could lead to a loss of chemoselectivity, with the enolate following the alternative reaction pathway described in Scheme 53 (Page 52).

In conclusion, this first approach to the Wadsworth and Emmons synthetic methodology showed incredible results when performed in the presence of ***1a*** *and its analogues. Broad tolerance to various epoxides was also displayed, with the only restriction being the use of strongly electron-withdrawing groups and scaffolds with reduced flexibility. The volatility of the electrophilic partner is potentially responsible for the reduced conversion rate, since the population of the epoxide in solution may drastically decrease under the designed reaction conditions. This first approach to this cyclopropanation has pleasingly been published*[68] *and subsequently applied to the total synthesis of natural products,*[69] *thus demonstrating the useful contribution to the many methods available for the synthesis of the cyclopropanes.*

2.3 Cyclopropyl nitriles

Extending this work, our attention was then focused on further expansion of the scope of this reaction by modifying the **ASG**. Wadsworth and Emmons alluded to the use of phosphonate nitriles **3a** in the cyclopropanation reaction and this seemed like the logical place to initiate this area of investigation.

As discussed in the previous section, the majority of the phosphonates treated in this study lacked of a full detailed characterisation involving the pK_a value. Nevertheless, Bordwell described the acidity of diethyl (cyanomethyl)phosphonate **3a** in DMSO to be 16.4,[64] higher than the reference **1a**, suggesting that the nitrile function provides a better stability to the negative charge with regard to an ester. Given our interest to define an experimental reactivity scale based on the key NMR spectroscopic peaks previously decribed (acidic proton and ^{31}P) we decided to extend the comparison to the chemical shift values (Figure 8). Interestingly, if the methylene signals appeared similar, phosphorous resonance of the phosphonate **3a** appeared sensibly shielded compared to the reference **1a**.

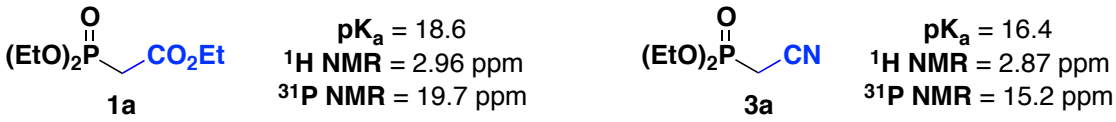
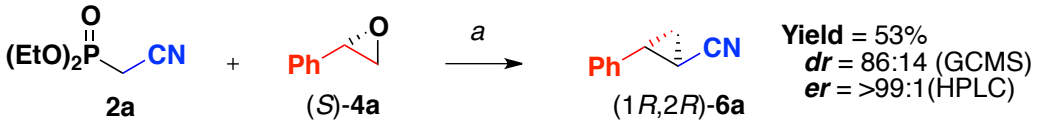


Figure 8 Comparison between phosphonates **1a** and **3a**.

We began our study on the nitrile functionality by reproducing the reaction reported by Wadsworth and Emmons, *i.e.* monitoring the activity of **3a** with epoxide (*S*)-**4a**. The cyclopropane (1*R*,2*R*)-**6a** was isolated with the same yield as reported by Wadsworth-Emmons (Table 1, Entry 2, Page 12). However, GC-MS analysis revealed that the diastereoselectivity was no longer as high, since the *dr* value dropped to 86:14 *trans*:*cis* compared to 96:4 for the corresponding cyclopropane (1*R*,2*R*)-**5a**. The enantiomeric ratio of the trans isomer was determined by chiral HPLC that again confirmed the enantiospecific nature of the reaction mechanism (Scheme 56).



Scheme 56 Synthesis of cyclopropane (1*R*,2*R*)-**6a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

Once again, the major diastereomer could be crystallised (although only from a racemic sample) and analysis by X-ray crystallography gave unequivocal evidence for the *trans*-configuration (Figure 9).

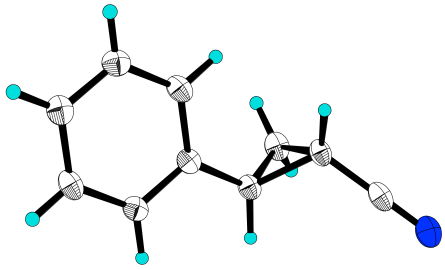
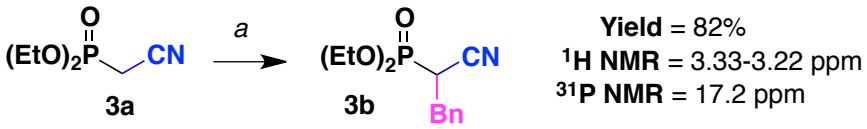


Figure 9 Crystal structure of cyclopropane (1*R*,2*R*)-**6a**.

The GC-MS analysis of the reaction mixture showed the presence of unreacted phosphonate **3a**, suggesting a slower ring-opening process. This observation could be connected to a reduced nucleophilic nature of this substrate as compared to the phosphonate **1a**. Furthermore, the phosphonate **3a** undergoes alternative synthetic processes, as witnessed by the range of environments in the ^{31}P NMR spectroscopy.

As mentioned in the introduction, the diastereoselectivity of the Wadsworth-Emmons cyclopropanation is strictly connected to the formation of the second C−C bond.[57a] According to the results discussed in the previous paragraph, the lower *dr* value observed in the formation of (1*R*,2*R*)-**6a** with respect to the homologue (1*R*,2*R*)-**5a** could be connected to the reduced ability of the nitrile group to develop interactions with the substituents installed on the epoxide. As described by the crystal structure, the digonal geometry of the **ASG** group reduces both the steric repulsion with the **R^3** group and weakens the potential interactions with the cyclopropyl-methine proton due to the longer distance with the heteroatom. The low molecular weight of this compound, coupled with its poor UV-visibility at 254 nm, led us to abandoning this investigation and that of other di-

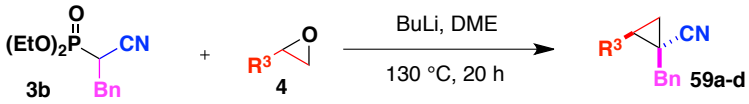
substituted nitrile-containing cyclopropanes. However, since the synthesis of such enantiopure substrates makes cyclopropyl nitriles attractive compounds for isolation of enantiopure imines and amines upon reduction, we decided to insert an **R^2** group on the phosphonate **3a**, with the hope to convert these to cyclopropanes containing a quaternary carbon stereocentre. The **Bn** scaffold was installed *via* direct alkylation to obtain the phosphonate **3b** in good yield (Scheme 57). In line with the evidence collected, the introduction of an alkyl substituent caused a downfield effect in both the ^{1}H and ^{31}P NMRs. However, the comparison with the homologous phosphonate **1i** (^{1}H = δ 3.32-3.14 ppm, ^{31}P = δ 22.0 ppm) showed that both the target nuclei resonated upfield.

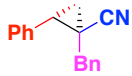
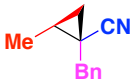
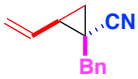
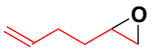
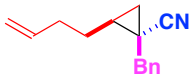


Scheme 57 Synthesis of the phosphonate **3b**. Reagents and conditions: (*a*) NaH, **Bn**Br.

The phosphonate **3b** was reacted with a selected range of epoxides, including (*S*)-styrene oxide (*S*)-**4a**, (*R*)-propylene oxide (*R*)-**4d**, (±)-vinyl oxirane (±)-**4o** and (±)-1,2-epoxy-5-hexene (±)-**4g** (Table 10).

Table 10 Cyclopropyl nitriles with quaternary carbon centres **59a-d**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*S*,2*S*)-**59a**	35[d]	86:14
2		(*R*)-**4d**		(1*S*,2*R*)-**59b**	71	1.92:1
3		(±)-**4o**		(1*R**,2*R**)-**59c**	26	2.13:1
4		(±)-**4g**		(1*R**,2*S**)-**59d**	63	3:1

[a]Reactions carried out with 1 eq of phosphonate. [b]Percentage isolated yield of the major diastereomer following column chromatography. [c]Diastereomeric ratio determined by GC-MS. [d]Percentage isolated yield of the major diastereomer following column chromatography.

The conversion of (*S*)-**4a** to (1*S*,2*S*)-**59a** appeared to occur smoothly, as GC-MS analysis of the crude reaction mixture showed neither traces of by-products nor of unreacted starting materials; nevertheless, the product was isolated with a disappointing yield upon flash chromatography (Table 10, Entry 1). The envisaged lower nucleophilicity of the nitrile as **ASG** group in the Wadsworth-Emmons cyclopropanation appeared to be further retarded by the insertion of a benzyl scaffold. This poor reactivity probably favoured the decomposition of the phosphonate **3b** into water-soluble by-products, removed *via* acidic work-up. Unexpectedly, the cyclopropane (1*S*,2*S*)-**59a** was produced with the same *dr* ratio as the homologue (1*R*,2*R*)-**6a** (Scheme 56, Page 60) regardless of the presence of the group $\mathbf{R^2}$. This observation combined with those for the ester analogues suggests it is the nature of the **anion stabilising group** and the epoxide substituent $\mathbf{R^3}$ that is the dominant factor in controlling the diastereoselectivity. Chiral HPLC analysis of the major diastereomer (1*S*,2*S*)-**59a** met with expectation, revealing a reassuring 99:1 *er*. Furthermore, it was isolated as a crystalline solid and unequivocally assigned the *trans*-configuration (with respect to the phenyl ring and the nitrile) by X-ray crystallographic analysis (Figure 10).

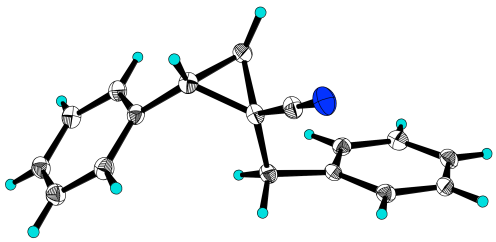


Figure 10 Crystal structure for nitrile (1*S*,2*S*)-**59a**.

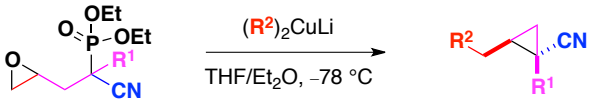
Epoxide (*R*)-**4d** was converted to the cyclopropane (1*S*,2*R*)-**59b** with a good yield, although with a reduced stereoselectivity (Table 10, Entry 2). The reduced steric hindrance of the $\mathbf{R^2}$ group appears to promote the ring-opening process, making the electrophilic carbon of the epoxide more accessible to the phosphonate carbanion. Conversely, the product was obtained with a poorer diastereoselectivity (66:34 *dr*) compared to the cyclopropane (1*S*,2*S*)-**59a**. This observation shows once more that the stereoselectivity of the Wadsworth-Emmons cyclopropanation is driven by a system of complex interactions, as opposed to just simple steric repulsions. The diastereoselectivity

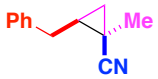
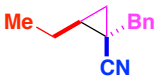
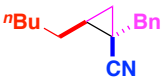
values become even poorer compared to that assigned for the homologous cyclopropyl-ester (1*R*,2*S*)-**57k** (*dr* ratio >99:1) and seems to suggest that the geometry of the **ASG** group is a key aspect in the definition of the relative stereochemistry of the final product, in agreement with a potential electronic interaction with the cyclopropyl-methine proton. On the other hand, the ability of such a proton to build electronic interactions with the flanking **ASG** group might be affected by the $\mathbf{R^2}$ group, offering an explanation as to why the cyclopropyl-nitriles (1*S*,2*S*)-**59a** and (1*S*,2*R*)-**59b** were produced with different stereoselectivity in the presence of the same **ASG** group.

At the time, by analogy with the work with the ester homologues and with the backing of our X-ray crystal structures, the stereochemistry between the methyl group and the nitrile was tentatively assigned by analogy as *trans*. A similar analysis was used for compounds (1*R**,2*R**)-**59c** and (1*R**,2*S**)-**59d** (Table 10, Entries 3-4). Apart from (1*S*,2*S*)-**59a**, all the cyclopropyl nitriles were isolated as mixtures of diastereomers upon flash chromatography and could not be characterised as single isomers by NMR spectroscopy. On account of the relatively poor stereoselectivity, no further effort was injected in to attempting to resolve the stereochemical issue unequivocally.

Serendipitously, in late 2012, Sokolsky and Smith published their work on the Anion Relay Chemistry (ARC) of phosphonate derivatives, where a set of cyclopropanes were isolated and characterised by NMR spectroscopy (Table 11).[70] The cyclopropanes **59e-h** were produced as a mixture of diastereomers, subsequently separated by MPLC to be fully characterised as single diastereomers by NMR spectroscopy. Within each set of diastereomers, the cyclopropyl-methine protons were assigned by comparing the most divergent resonances amongst the cyclopropyl-protons. Therefore, a 1D-nOe experiment was performed on the minor diastereomer only, which allowed the authors to identify the major diastereomers as the ones in which the group $\mathbf{R^1}$ and $\mathbf{R^2}$ are *cis* to one another. This appeared to be in agreement with the current work, until we noticed the assignment regarding the cyclopropyl nitrile **59f**, whose structure is very similar to (1*S*,2*R*)-**59b**.

Table 11 Cyclopropyl nitriles obtained *via* Anion Relay Chemistry (ARC).[70]



Entry	R^1	R^2	Cyclopropane	Yield (%)[a]	*dr* ratio[b]
1	Me	Ph	 (1*S**,2*S**)-**59e**	61	7.7:1
2	Bn	Me	 (1*R**,2*S**)-**59f**	89	4:1
3	Bn	^{n}Bu	 (1*R**,2*S**)-**59g**	87	1.7:1
4	Bn	Ph	 (1*R**,2*S**)-**59h**	81	7.5:1

[a]Percentage isolated yield following flash column chromatography. [c]Diastereomeric ratio determined by MPLC.

Surprisingly, these authors assigned the stereochemistry of the minor diastereomer of **59b** on the basis of the cyclopropyl-methine that had a resonance at δ 0.70 (exactly where our major diastereomer shows a peak). This resonance was found to have an nOe enhancement with the benzylic methylene protons, but sadly no percentage was given though the spectra are included as supporting information (Figure 11).

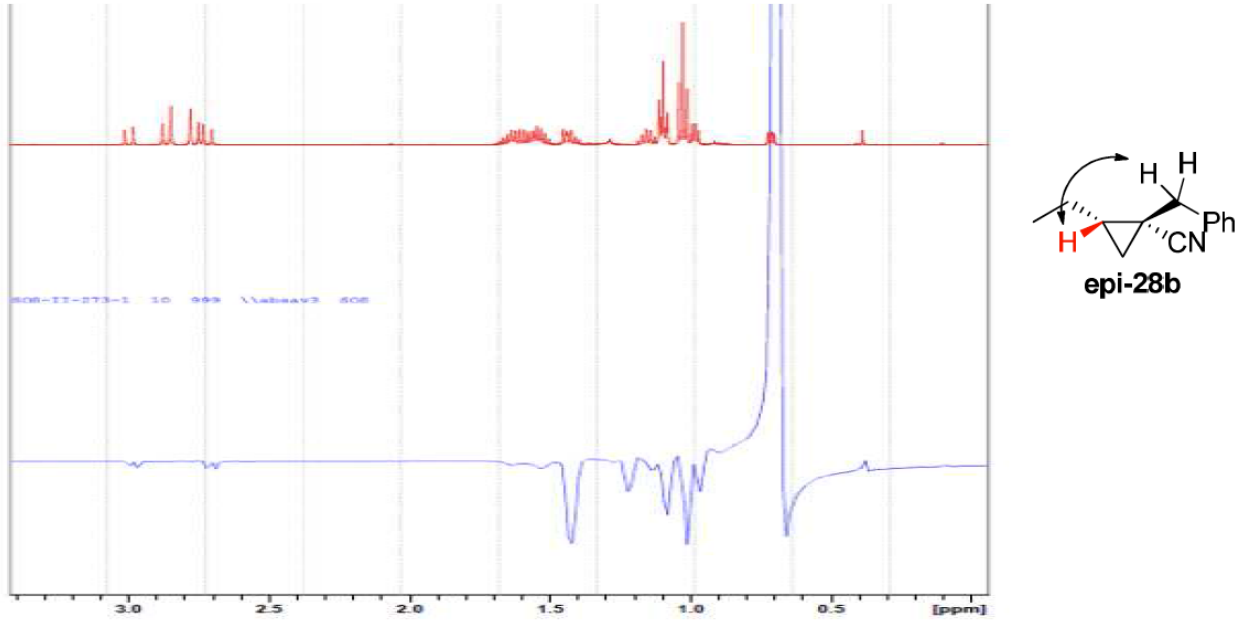


Figure 11 1D-nOe experiment for cyclopropane (1*S*,2*R*)-**59f** (named epi-28b in the original paper).

On inspection, the enhancement appears to be very weak. Furthermore, they did not assign the methine of the major isomer and hence they did not do a similar analysis to look for the difference in nOe enhancements. Therefore, whilst this sheds some doubt on the true stereochemical relationship more work will be needed to enable unequivocal assignment.

However, our assignment of the NMR spectra of the mixture of diastereomers of cyclopropane **59b** suggests a different interpretation The COSY experiment clearly shows that the set of peaks at δ 1.7 ppm, δ 1.5 ppm, δ 1.3 ppm and δ 0.7 ppm belong to the same compound, *i.e.* the major isomer (Figure 12). In detail, the signal at δ 1.7 ppm shows no definite splitting pattern, hence it is called a multiplet. Both the signals at δ 1.5 ppm and δ 0.7 ppm show a typical shape of a doublet of doublets, whereas the peak at δ 1.3 ppm is a doublet and is assigned to the methyl group. Interestingly, the peak of the methyl group only couples with the signal at δ 1.7 ppm, which can only be the cyclopropyl-methine proton.

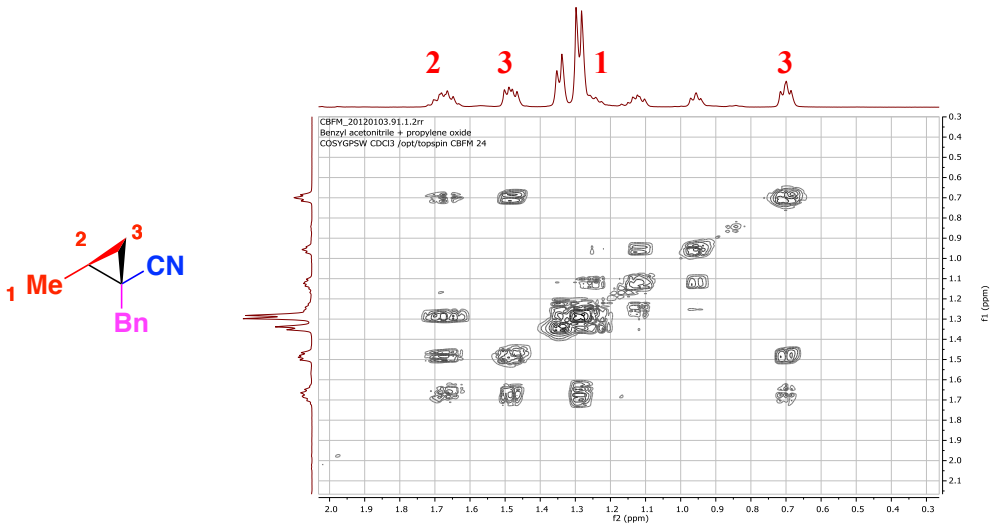


Figure 12 COSY experiment for cyclopropane (1*S*,2*R*)-**59b**.

Such assignment is supported by the HSQC spectrum, which displays that the two protons at δ 0.7 and δ 1.5 ppm are connected to the same carbon atom, *i.e.* the cyclopropyl-methylene (Figure 13). Unfortunately, due to the presence of the minor diastereomer, no unequivocal information could be provided by DEPT experiment.

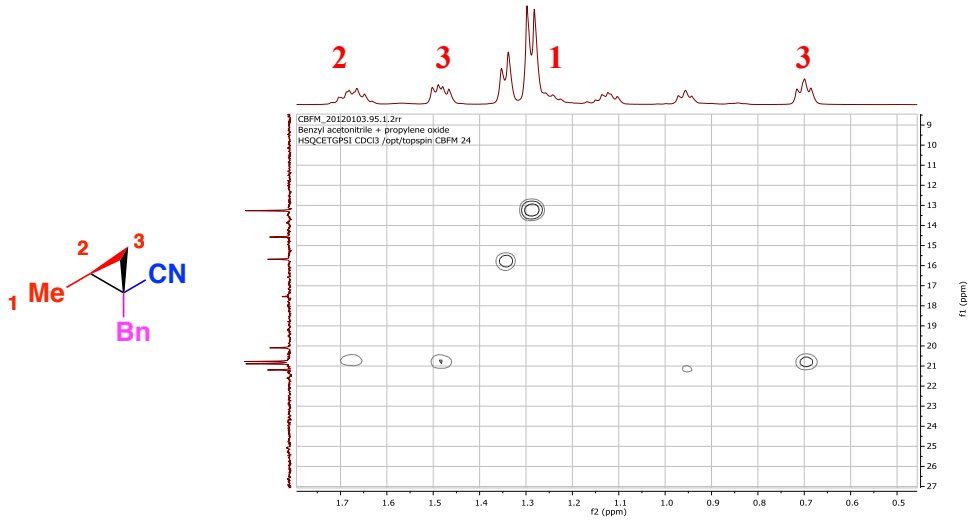
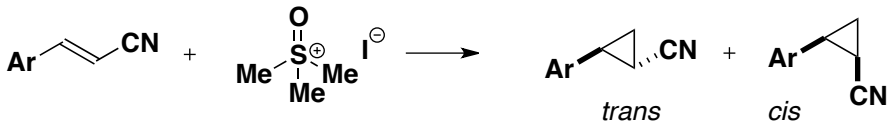


Figure 13 HSQC experiment for cyclopropane (1*S*,2*R*)-**59b**.

In 2002, Wang and co-workers investigated the enantioselective enzymatic hydrolysis of both *cis*- and *trans*-cyclopropyl nitriles to give cyclopropyl amides and acids.[71] Such racemic diastereomers were produced by reacting substituted cinnamonitriles with trimethylsolfoxonium iodide (Figure 58).



Scheme 58 Synthesis of both epimers of cyclopropyl-nitriles.

Within each set of diastereomers, both the epimers were isolated and characterised as single diastereomers. Specifically, both the diastereomers of the cyclopropyl-nitrile **6a** were described by NMR spectroscopy: the authors reported that the resonances of the cyclopropyl-methine protons for *cis*-isomer showed a chemical shift of δ 2.55, as compared to the more downfield resonance of the homologous group on the *trans*-epimer (δ 2.66) (Figure 14).

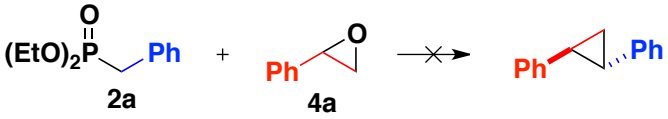
Figure 14 Assignment of the cyclopropyl-methine proton resonances for both the *trans*- and the *cis*- **6a**.

This observation suggested that groups in *cis*-relationship with the nitrile function are mildly deshielded due to the anisotropic effect generated by the triple bond. Moreover, our evidence seems to suggest that the insertion of the benzyl group (R^1) on the quaternary centre of the cyclopropane (1*S*,2*S*)-**59a** produces an additional deshielding effect of the cyclopropyl methine. Said assignment led us to suggest the *trans*-configuration between the **ASG** and the R^2 group for the major diastereomers of the products listed in Table 9, Entries 2-4, in contrast with the conclusions reported by Sokolsky and Smith.

*In conclusion, this screening of the nitrile function as an **ASG** in the Wadsworth-Emmons cyclopropanation is in agreement with the hypothesis, i.e. that the favoured diastereomer is the one which arranges the **ASG** and the R^2 group in trans-relationship as a consequence of the interactions arising in the reaction pathway. The drop of the dr values observed in Table 9 support the correlation amongst: a) the geometry of the **ASG**; b) the ability of the cyclopropyl-methine proton to interact with the **ASG** during the ring-closure step; c) the diastereoselectivity of the final product.* It should be noted that, once again, it did not appear in either this work or that of Sokolsky and Smith, that sterics govern the ring-closure process since if this had been the case, the very small size of the nitrile would likely have resulted in a reversal of selectivity, which was not seen.

2.4 Cyclopropyl Amides

In their seminal work, Wadsworth and Emmons reported that a third phosphonate, *i.e.* diethyl benzyl phosphonate **2a**, failed to convert styrene oxide **4a** to the relative cyclopropane (Scheme 59).[19]

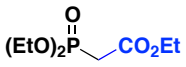
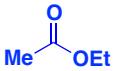
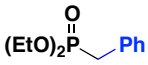
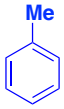
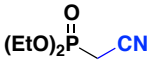


Scheme 59 Cyclopropanation reaction of the phosphonate **2a**.

As previously mentioned in Section 1.3, the carbanion of the phosphonate **2a** is unstable and undergoes a competing polymerisation reaction. Despite its conversion to olefin is feasible by forming the phosphonate carbanion in the presence of the carbonylic species, this is no longer possible when the electrophile is an epoxide. The authors ascribed this poor reactivity as the consequence of the lower ability of the phenyl ring to stabilise the negative charge of the phosphonate carbanion.

Almost thirty years later, Bordwell supported this speculation by determining the pK_a values for the phosphonate **1-3a**, showing a huge gap between the acidity values of phosphonate **1&3a** and **2a** (Table 12).[64] Since this table suggested the first limitation in the range of compatible substrates with the Wadsworth-Emmons cyclopropanation procedure, we decided to assess its limits by testing another phosphonate with higher pK_a value.

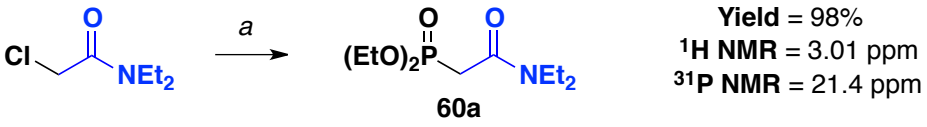
Table 12 Acidity values for phosphonates **1-3a** and their precursors.

Entry	Phosphonate		pK_a	Precursor	pK_a
1		**1a**	18.6[64]		29.5[72]
2		**2a**	27.6[64]		43[73]
3		**3a**	16.4[64]		31.3[74]

In order to perform the future screenings, a new reference was required. Indeed, due to the little information available in the literature about the pK_a of phosphonates, the reference **1a** could no longer be used. Nevertheless, as many of the ideal precursors were instead fully described in the literature, it was agreed to select the new **ASGs** on the basis of the acidity to the precursors of **1-3a**, *i.e.* ethyl acetate (pK_a 29.5),[72] **2a** (pK_a 43)[73] and **3a** (31.3)[74], with the aim of narrowing this empirical working range.

According to the Bordwell's acidity table, secondary amides appeared a potential target for our screening. This choice was made for three reasons: *a*) its pK_a matches the range of values of our interest (35)[64]; *b*) despite a lower acidity with respect to ethyl acetate, this **ASG** still owns a trigonal geometry, which we deemed crucial for the diastereoselectivity of the final product; *c*) direct synthesis of cyclopropyl amides is of great interest, due to their various pharmacological implications as antimalarial agents[75] and conformationally constrained DNA-mimics.[76]

The target phosphonate **60a** was produced in quantitative yield *via* **Route C**[77] and purified by distillation under reduced pressure. The proton resonance appeared comparable to that of the phosphonate **1a** (^{1}H NMR 2.96 ppm, ^{31}P NMR 19.7 ppm), whilst the ^{31}P signal peak displayed a deshielded signal (Scheme 60).

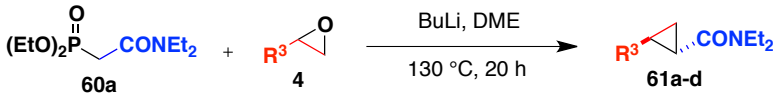


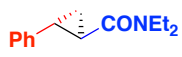
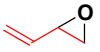
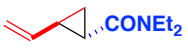
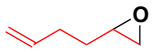
Scheme 60 Synthesis of the phosphonate **60a** *via* **Route C**. Reagents and conditions: (*a*) $P(OEt)_3$, 170 °C, 3 h.

The phosphonate **60a** was then treated under the standard conditions with the usual reference epoxides used with phosphonate **3b**, producing cyclopropyl amides with good to high yield and excellent stereoselectivity (Table 13). Epoxide (*S*)-**4a** was successfully converted to cyclopropane (1*R*,2*R*)-**61a** in high yield (Table 13, Entry 1). The crude reaction mixture looked very clean as judged by GC-MS analysis and suggested an excellent diastereoselectivity. This compound was purified by flash column chromatography and was initially assigned the

trans-configuration *via* spectroscopic correlation of the cyclopropyl-hydrogens to those of the cyclopropane (1*R*,2*R*)-**5a**. This assignment was then supported by the comparison with the cyclopropanes made by Concellon and co-workers *via* Sm-mediated insertion of CH_2I_2 into a α,β-unsaturated amides.[78] Similar conclusions may be drawn for other reactions listed in Table 13, where the reduced conversion may be ascribed to the lower boiling points of the epoxides **4**. Finally, the *dr* values appeared comparable with those detected for esters **57**, in agreement with our hypothesis that relates the trigonal geometry of the ASG group with higher values of *trans*-stereoselectivity, regardless of the different acidity of the phosphonate precursors **1a** and **60a** (ethyl acetate and diethyl amide).

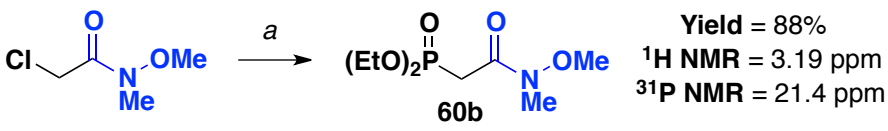
Table 13 Cyclopropyl amides **61a-d**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*R*,2*R*)-**61a**	88	>99:1
2		(*R*)-**4d**		(1*S*,2*S*)-**61b**	68	>99:1
3		(±)-**4o**		(1*S**,2*R**)-**61c**	72	>99:1
4		(±)-**4g**		(1*S**,2*S**)-**61d**	73	>99:1

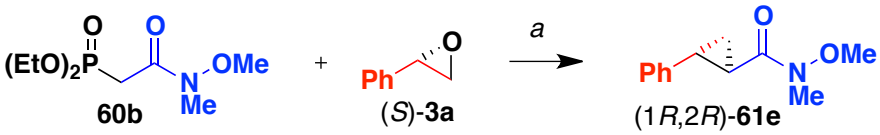
[a]Reactions carried out with 1 eq of phosphonate.. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS.

Given the success of the amide group, we were intrigued by the potential compatibility of the derivative Weinreb amide. The phosphonate **60b,** obtained *via* **Route C**[79] featured resonance values comparable to phosphonate **60a** (^{1}H NMR 3.01 ppm, ^{31}P NMR 21.4 ppm) (Scheme 61).



Scheme 61 Synthesis of the phosphonate **60b**. Reagents and conditions: (*a*) $P(OEt)_3$, 170 °C, 3 h.

The phosphonate **60b** was treated under the standard condition for the cyclopropanation, yielding the expected cyclopropane but with a poor conversion (Scheme 62).



Scheme 62 Testing the phosphonate with the Weinreb amide **60b**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 17%

This output might be the consequence of the introduction of an additional oxygen atom in the **ASG**. The advantageous application of the Weinreb amide in the synthesis of carbonylic compounds relies on the chelation of the two oxygen atoms by the cation, preventing undesired multiple substitutions of the organometallic species. Such chelation may be responsible for the presence of alternative reaction pathways. The GC-MS analysis of the crude mixture revealed the absence of the starting phosphonate **60b**. Nevertheless, the ^{31}P NMR showed formation of various phosphorous-containing by-products that were not analysed any further.

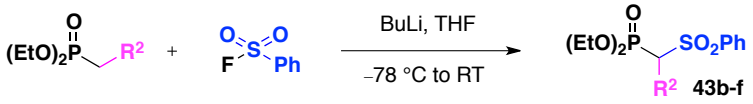
2.5 Cyclopropanes containing sulfur

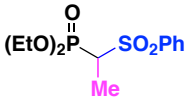
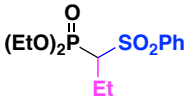
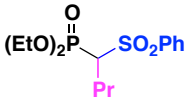
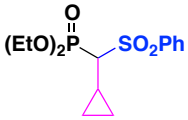
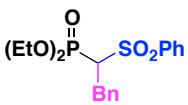
These first positive results prompted us to study other functional groups to broaden the scope of the Wadsworth-Emmons cyclopropanation reaction. As this research group reported the compatibility of the phenyl sulfone phosphonate **43a** with the Wadsworth-Emmons protocol (Table 4, Page 35), we decided to approach further this **ASG** by introducing a quaternary carbon centre.

The precursor of the phosphonate **43a** features a pK_a of 29,[74] very close to the reference ethyl acetate (pK_a 29.5).[72] Despite the insertion of a methylene carbon seemed to reduce the acidity (pK_a 31),[80] this **ASG** still fitted in the range of promising values defined by ethyl acetate (29.5)[72] and acetonitrile (31.3)[74].

The phosphonates **43b-f** were obtained by a modification of **Route D**, trapping the carbanion of alkylphosphonates with benzenesulfonyl fluoride (Table 14). [81]

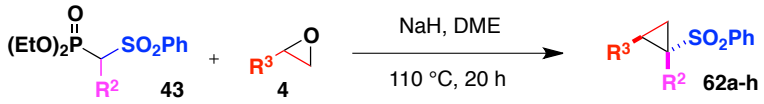
Table 14 Investigation of the role of the R^2 group on chemical shifts.



Entry	Phosphonate		Yield (%)	^{1}H NMR	^{31}P NMR
1		**43b**	67	3.59	16.5
2		**43c**	33	3.40	16.2
3		**43d**	44	3.47	16.5
4		**43e**	38	2.76	15.5
5		**43f**	39	3.82	15.5

The chemical shifts of the acidic protons and the ^{31}P nuclei appeared in line with those of the phosphonate **3b** (^{1}H NMR 2.87 ppm, ^{31}P NMR 15.2 ppm). Noeworthily, the introduction of the cyclopropane shielded the resonance of the acidic proton (Table 14, Entry 4). The significant drop in yield observed with the increasing hindrance of the R^2 group appeared to suggest a retarded nucleophilicity in the cyclopropanation reaction.

Table 15 Cyclopropyl sulfones with quaternary carbon centres **62a-h**.[a]



Entry	R^2	Epoxide		Product		Yield[b](%)	*dr* ratio[c]
1	Me	**43b**	(*S*)-**4a**		(1*S*,2*R*)-**62a**	91	96:4
2	Me	**43b**	(*R*)-**4d**		(1*S*,2*S*)-**62b**	71	>99:1
3	Me	**43b**	(*R*)-**4o**		(1*S*,2*R*)-**62c**	46	99:1
4	Me	**43b**	(±)-**4g**		(1*S**,2*S**)-**62d**	74	>99:1
5	Et	**43c**	(*S*)-**4a**		**62e'**	62	---
6	Pr	**43d**	(*S*)-**4a**		(1*R*,2*S*)-**62f**	22	>99:1
7	Cyc	**43e**	(*S*)-**4a**		(1*S*,2*S*)-**62g**	19	>99:1
8	Bn	**43f**	(*S*)-**4a**		**62h'**	51	---

[a]Reactions carried out with 2 eq of phosphonates. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS.

We first assessed the compatibility of the smallest phosphonate **43b** with the elected range of epoxides **4** (Table 15, Entries 1-4). Once the compatibility was demonstrated, we moved on to screen the other phosphonates **43c-f** with epoxide (*S*)-**4a** (Table 14, Entries 5-8). In line with the previous work, the cyclopropanation reactions were carried out in the presence of NaH as a base,

due to solubility issues arising with lithium as counter ion and the lower yields detected upon mass recovery.[48] Finally, the temperature was reduced to 110 °C compared to the standard conditions during the previous applications.

The phosphonate **43b** was smoothly converted to cyclopropane (1*S*,2*R*)-**62a** with an excellent yield (Table 15, Entry 1). GC-MS analysis showed the presence of traces of a minor diastereomer (96:4 *dr*). The major cyclopropane (1*S*,2*R*)-**62a** was isolated as a crystalline solid after flash column chromatography and assigned the *trans*-configuration by X-ray crystallographic analysis (Figure 15). Chiral HPLC analysis revealed an enantiomeric ratio of 98:2, in line with previous results.

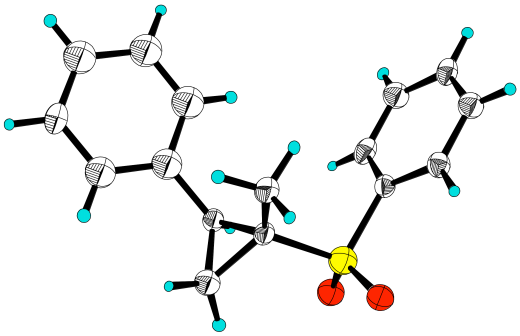


Figure 15 Crystal structure for cyclopropane (1*S*,2*R*)-**62a**.

The cyclopropane (1*S*,2*S*)-**62b** was isolated with a lower yield (Table 15, Entry 2). GC-MS analysis of the crude reaction mixture revealed a *dr* of >99:1, but also showed the presence of an impurity with a different *m/z* ratio. The product was purified as a crystalline solid and assigned the *trans*-configuration by X-ray crystallographic analysis (Figure 16).

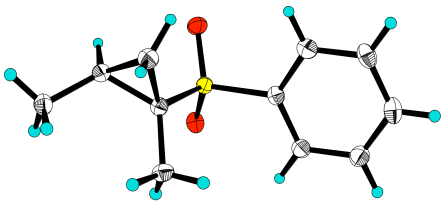


Figure 16 Crystal structure for cyclopropane (1*S*,2*S*)-**62b**.

The epoxide (*R*)-**4o** was transformed to cyclopropane (1*S*,2*R*)-**62c** with excellent diastereoselectivity (99:1 *dr*), albeit with a poorer yield (46%) (Table 15, Entry 3). The GC-MS

analysis of the crude reaction mixture showed a lack of the excess starting phosphonate **43b**, suggesting a potential decomposition to water-soluble products. Since the cyclopropane (1*S*,2*R*)-**62c** was isolated as oil, the *trans*-configuration was assigned by spectroscopic correlation of the cyclopropyl-protons with the homologue (1*S*,2*R*)-**62a & b**.

The epoxide (±)-**4g** was converted to sulfone (1*S**,2*S**)-**62d** with good yield and excellent diastereoselectivity (Table 15, Entry 4). Nevertheless, the GC-MS highlighted the same impurity observed for Entry 2, attributing its origin to the decomposition of the phosphonate **43b**.

Our attention then was turned towards the elongation of the R^2 alkyl chain. The presence of a hindered group on the C−2 position appeared to have a dramatic effect on the ring-closure mechanism (Table 15, Entry 5). In fact, the peak with the expected *m/z* ratio detected in the GC-MS of the crude reaction mixture showed the typical signal of the unsaturation by ^{1}H NMR. The major compound was purified by flash column chromatography to give the elimination product **62e'** (Figure 17).

62e'

Figure 17 Olefin **62e'** obtained with phosphonate **43c.**

This result suggests that the hindrance of the R^2 group affects the formation of both C−C bonds. Specifically, it retards the nucleophilic attack to ring-open the epoxide, as witnessed by the poorer yield in which the olefin **62e'** was isolated with respect to the mass recovery of the cyclopropane (1*S*,2*R*)-**62a**. On the other hand, it prevents the formation of the second C−C bond, as no cyclopropane was observed in the GC-MS of the crude reaction mixture, favouring the elimination of the phosphate group leading *via* E1cb mechanism.

The addition of the methylene group on the chain helped the isolation of the cyclopropane (1*R*,2*S*)-**62f**, although with a poor yield (Table 15, Entry 6). Surprisingly, the unreacted

phosphonate **43b** was observed in the GC-MS of the crude mixture, excluding potential decomposition pathways. The cyclopropane (1*R*,2*S*)-**62f** was isolated as a crystalline solid with *trans*-configuration (Figure 18).

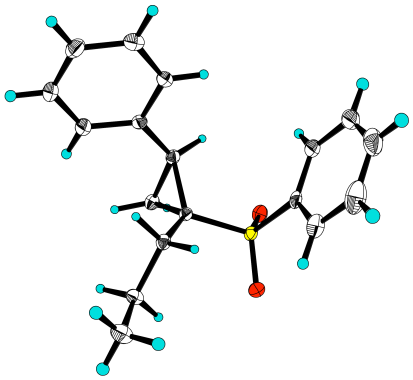


Figure 18 Crystal structure for clopropane (1*R*,2*S*)-**62f**.

The increased hindrance of the alkyl chain seemed to influence the course of the reaction as expected, since the cyclopropane (1*S*,2*S*)-**62g** was isolated in a lower yield (Table 15, Entry 7). The excellent diastereoselectivity remained unchanged and the relative stereochemistry was proven by X-ray crystallography (Figure 19).

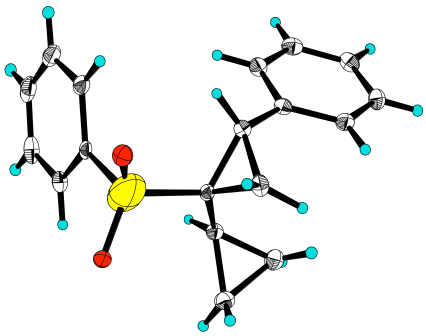
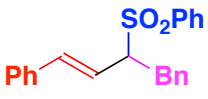


Figure 19 Crystal structure for cyclopropane (1*S*,2*S*)-**62g**.

Finally, the phosphonate **43f** only produced the elimination product **62h'**, as already discussed for the phosphonate **43c (**Figure 20).



62h'

Figure 20 Elimination product **62h'**.

While we were conducting this research, Sigma-Aldrich® commercialised the phosphonate **43g**, also known as the McCarthy's reagent. Although the acidity of its precursor (pK_a 28.5)[64] was reported to be close to the reference ethyl acetate (pK_a 29.5),[72] the ^{1}H and ^{31}P resonance values appeared notably different with respect to phosphonate **1a** (Figure 21).

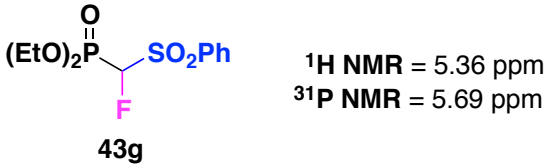
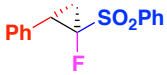
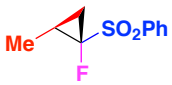
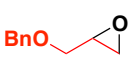
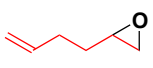
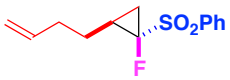


Figure 21 McCarthy's reagent **43g**.

Due to the expense of this phosphonate, we reduced the reagent ratio to one-to-one. As under the standard reaction conditions the phosphonate **43g** seemed to decompose, we assessed a range of temperatures to preserve its reactivity. Our screen suggested that performing the reaction at 90 °C maximised the yields of the cyclopropanation, reducing the competitive decomposition of both of the starting materials (Table 16).

Table 16 Screening of McCarthy's reagent **43g**.[a]

Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*S*,2*R*)-**62i**[c]	42	96:4
2		(*R*)-**4d**		(1*S*,2*S*)-**62j**	43	79:21
3		(±)-**4o**		(1*S**,2*R**)-**62k**	42	98:2
4		(±)-**4c**		(1*S**,2*R**)-**62l**	16	93:7
5		(±)-**4g**		(1*S**,2*S**)-**62m**	37	94:6

[a]Reactions carried out with phosphonate (1 eq) at 90 °C in DME for 20 h. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS. [c]Enantioselective ratio (99:1) determined by HPLC.

The epoxide (*S*)-**4a** was converted to fluorocyclopropane (1*S*,2*R*)-**62i** with a poor yield but with high diastereoselectivity (Table 16, Entry 1). The absence of starting material in the GC-MS of the crude mixture suggested decomposition to water-soluble by-products. The product (1*S*,2*R*)-**62i** was isolated as a crystalline solid following flash chromatography and assigned the *trans*-configuration by X-ray crystallography (Figure 22). Chiral HPLC analysis confirmed the retention of optical purity (99:1 *er*).

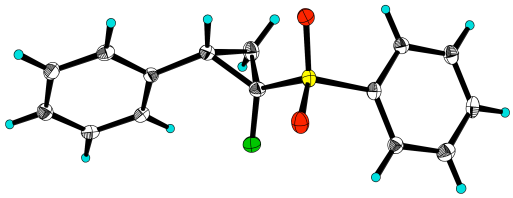


Figure 22 Crystal structure for fluorocyclopropane (1*S*,2*R*)-**62i**.

The epoxide (*R*)-**4d** was converted to fluorocyclopropane (1*S*,2*S*)-**62j** in a comparable yield to (1*S*,2*R*)-**62i** (Table 16, Entry 2). The GC-MS analysis of the crude reaction mixture suggested that the cyclopropanation reaction suffered the competing decomposition of the phosphonate **43g**. Moreover, a lower *dr* ratio with respect to cyclopropane (1*S*,2*S*)-**62b** was observed. The crystalline solid product was assigned the *trans*-configuration by X-ray (Figure 22).

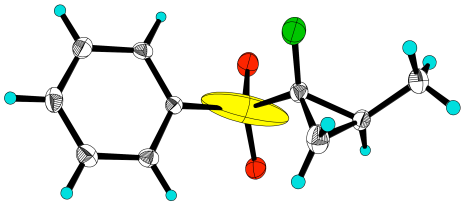


Figure 22 Crystal structure for fluorocyclopropane (1*S*,2*S*)-**62j**.

The reaction with epoxide (±)-**4o** showed moderate yield and excellent diastereoselectivity, in line with previous screening with other phosphonates (Table 16, Entry 3). The fluorocyclopropane (1*S**,2*R**)-**62k** was isolated as a crystal, endorsing the *trans*-stereoselectivity of the process (Figure 23).

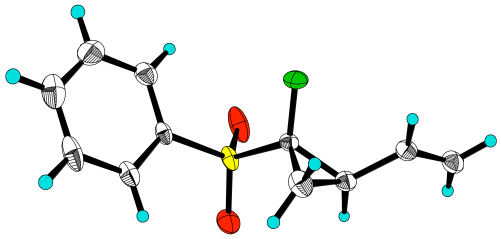


Figure 23 Crystal structure for fluorocyclopropane (1*S**,2*R**)-**62k**.

The epoxide (±)-**4c** reacted poorly, suffering decomposition of the starting materials and cyclising with reduced diastereoselectivity (Table 16, Entry 4). The fluorocyclopropane (1*S**,2*R**)-**62l** was purified as a crystalline solid and analysed by X-ray, assigning the *trans*-configuration (Figure 24).

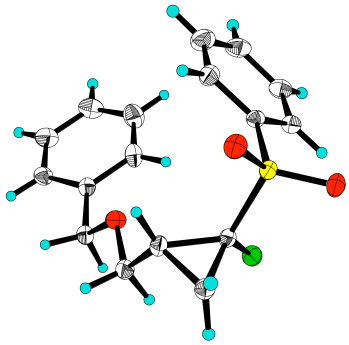


Figure 24 X-ray for fluorocyclopropane (1*S**,2*R**)-**62l**.

The fluorocyclopropane (1*S**,2*S**)-**62m** was isolated with a similar efficiency to cyclopropanes **62i-k** (Table 16, Entry 5). The configuration of the major isomer was assigned by spectroscopic correlation with cyclopropanes **62i-k.**

In conclusion, the phosphonosulfones **43a-h** confirmed to be valid **ASG** groups in the cyclopropanation reaction, show compatibility with the formation of quaternary carbon centres. The insertion of an alkyl chain leaves the stereoselectivity untouched, in line with our previous experimental evidence. With respect to the reference ethyl acetate, sulfones display a tetrahedral geometry, which may allow the building of stronger interactions with the cyclopropyl-methine proton during the reaction mechanism. Such geometry is responsible for a conflicting effect: on one side it provides excellent *trans*-diastereoselectivy in the products, as witnessed throughout the

screening performed with the phosphonate **43a-h**. On the other hand, the bulkier geometry of the **ASG** group seems to suffer the hindrance of the R^2 group, which significantly decreases the nucleophilicity. Despite the sterics, the ring-opening process is not completely prevented: in fact, the isolation of the elimination products **62e'&h'** suggests that the formation of the first C−C bond is still accessible, unlike the ring closure, which leads to the elimination of the phosphate leaving group *via* E1cb process.

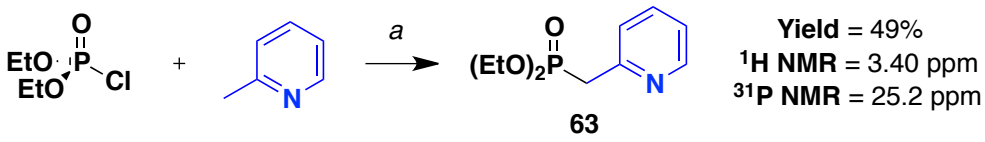
Instead, the insertion of a fluorine atom as R^2 group appears to provoke an effect on the reactivity of the phosphonate **43g**. Indeed, this substrate is more prone to decomposition, converting the epoxide with a lower efficiency. The *trans*-stereoselectivity is still high, but the *cis*-isomer can be formed in higher yield in the presence of smaller epoxides, suggesting that the fluorine atom can develop interactions with the cyclopropyl-methine proton as well.

To date, these rections represent the first example of direct insertion of a fluorine atom on a cyclopropane using the Wadsworth-Emmons process.

2.6 Cyclopropanes containing quinoline

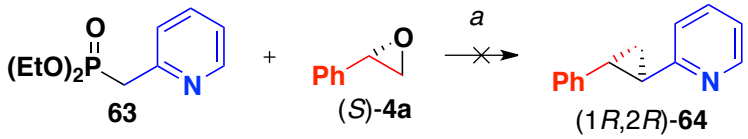
The excellent results obtained in the first part of our investigation on the Wadsworth-Emmons cyclopropanation made it a promising tool to apply to total synthesis projects. Given the great relevance of heteroaromatic groups usually involved, it seemed appropriate to investigate the compatibility of a selected range of heteroaromatic **ASG** groups to the protocol.

Within this wide family, the first structure that we approached was pyridine and its derivatives. We began our study focusing on 2-picoline, whose acidity value is not reported in the literature, but it is routinely lithiated using LDA. The synthesis of the phosphonate **63** was initially attempted *via* Arbuzov reaction (**Route C**), but the formation of black slurries of quaternary ammonium salts made this strategy inapplicable. The target product was instead obtained in moderate yield *via* electrophilic quenching (**ROUTE D**).[82] The resonance of the acidic proton fitted the values of phosphonates active in the Wadsworth-Emmons procedure, although the ^{31}P NMR revealed an unusually deshielded signal (Scheme 63).



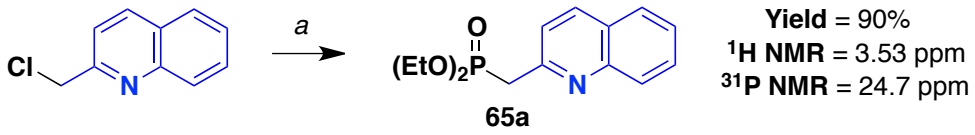
Scheme 63 Route to phosphonate **63**. Reagents and conditions: (*a*) LDA, THF, −78 °C

The phosphonate **63** was reacted with the epoxide (*S*)-**4a** under the standard conditions. GC-MS analysis showed a distribution of products, none of which had the expected *m/z* ratio. The crude reaction mixture failed to show the expected cyclopropane signals in the NMR spectra. This outcome could be potentially related to failure of the Arbuzov reaction on account of the competitive reactivity of the nitrogen atom (Scheme 64).



Scheme 64 Synthesis of cyclopropane (1*R*,2*R*)-**64**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 0%.

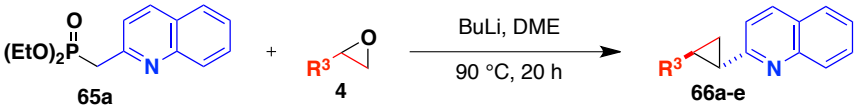
We envisaged that the insertion of a fused ring would have provided additional stability to the **ASG** group, preventing alternative reactions promoted by the lone pair. Therefore, the next substrate we screened was 2-methylquinoline, whose acidity value is only reported for the conjugate acid $(N-H)^+$ in water (pK_a 5.7)[83] so no expectation could be established *a priori*. Encouragingly, the required phosphonate **65a** could be synthesised *via* an Arbuzov reaction (**Route C**); furthermore, isolation by distillation under reduced pressure suggested an increased level of stability.[84] The chemical shift of the acidic protons appeared promising, whereas the phosphorous resonance appeared critically different from the reference **1a** (Scheme 65).

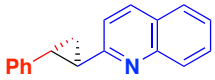
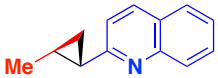
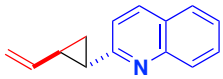
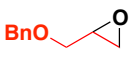
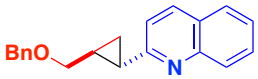
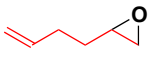
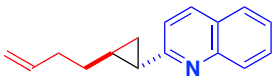


Scheme 65 Synthesis of phosphonate **65a**. Reagents and conditions: (*a*) $P(OEt)_3$, 170 °C, 3 h.

The phosphonate **65a** was treated under the standard reaction conditions in the presence of styrene oxide (*S*)-**4a** (Table 17, Entry 1).

Table 17 Screening of the phosphonate **65a**.



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*R*,2*R*)-**66a**[a,e]	80	97:3
2		(*R*)-**4d**		(1*S*,2*S*)-**66b**[d]	49	87:13
3		(±)-**4o**		(1*S**,2*R**)-**66c**[d]	18	>99:1
4		(±)-**4c**		(1*S**,2*S**)-**66d**[d]	30	82:18
5		(±)-**4g**		(1*S**,2*S**)-**66e**[d]	49	92:8

[a]Reactions carried out with 2 eq of phosphonate at 130 °C in DME for 20 h. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS. [d]Reactions carried out with 1 eq of phosphonate. [e]Enantiomeric ratio (99:1) determined by HPLC.

GC-MS analysis revealed the presence of traces of unreacted starting materials. Nevertheless, the product (1*R*,2*R*)-**66a** was isolated in good yield and with a very high diastereoselectivity. The major isomer was purified by flash chromatography, whose relative configuration was assigned *trans*- on the basis of the comparison with the ^{1}H NMR and crystallographic data reported by Deng and Yao on the same compound.[85] Finally, chiral HPLC confirmed the retention of optical purity, since the epoxide of 98% *ee* was converted to cyclopropane with 98% *ee*.

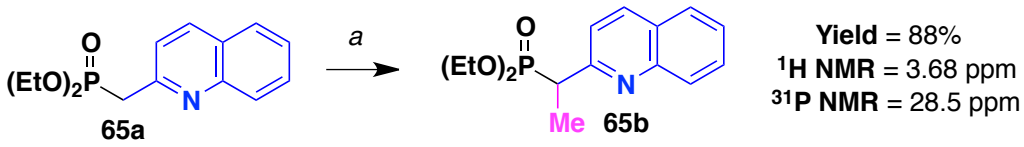
Unexpectedly, reactions in entries 2-5 displayed decomposition of the starting materials. This outcome prompted us to investigate the effect of a range of temperatures on the compatibility of the reactants. As was previously found for the fluorosulfone phosphonate **43g**, a balance of reactivity and stability could be achieved at a temperature of 90 °C (Table 17, Entries 2-5). Under these conditions, the cyclopropane (1*S*,2*S*)-**66b** was isolated as a mixture of diastereomers with an almost halved yield (49%) compared to (1*R*,2*R*)-**66a** (80%) (Table 17, Entry 2). GC-MS analysis showed a trace amount of the phosphonate **64a** in the crude mixture, suggesting significant decomposition to water-soluble by-products. The poorer stereoselectivity with respect to that of the cyclopropane (1*R*,2*R*)-**66a** suggests lower interactions of the **ASG** group with the cyclopropyl-methine proton, as already observed in the conversion of the epoxide (*R*)-**4d** to the fluorocyclopropane (1*S*,2*S*)-**62j** (79:21 *dr*).

Epoxide (±)-**4o** was poorly converted to cyclopropyl quinoline (1*S**,2*S**)-**66c** (18%) (Table 17, Entry 3). A major impurity was detected by GC-MS analysis, possibly due to the competition between the two electrophilic sites in epoxide (±)-**4o**. Nevertheless, the product was isolated with an excellent *trans*-diastereoselectivity, in agreement with the previous observations.

The conversion of the epoxide (±)-**4c** to (1*S**,2*S**)-**66d** was poor due to the decomposition of the starting materials (Table 17, Entry 4). Surprisingly, the cyclopropane (1*S**,2*S**)-**66d** was obtained with the lowest stereoselectivity in the screening on the phosphonate **65a**.

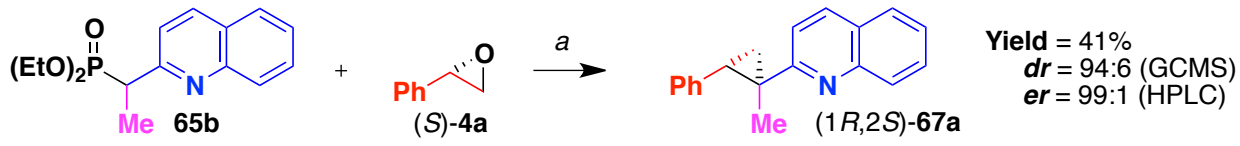
The epoxide (±)-**4g** showed a higher yield (49%), still affected by the competitive decomposition of the phosphonate **65a** (Table 17, Entry 5). Nevertheless, the GC-MS analysis of the crude reaction mixture showed an improved diastereoselectivity (92:8 *dr*).

Once the compatibility of this **ASG** was proved, our study was then dedicated to the installation of a quaternary carbon centre. In agreement with our *modus operandi*, we began our investigation with the methyl group. This scaffold was introduced *via* **Route A** with an excellent yield, causing a marked deshielding effect for both the acidic proton and the phosphorous nuclei in the NMR spectra (Scheme 66).



Scheme 66 Alkylation of phosphonate **65a** to yield **65b**. Reagents and conditions: (*a*) NaH, MeI, THF, 0 °C.

The phosphonate **65b** was converted to the cyclopropane (1*R*,2*S*)-**67a** with poor yield, but high diastereoselectivity (Scheme 67). The GC-MS of the crude mixture showed a substantial lack of reactivity, as both the starting materials were detected. This is in contrast with the chemistry of the phosphonate **65a**, prone to competitive decomposition under the reaction conditions. Finally, the cyclopropane (1*R*,2*S*)-**67a** was analysed by chiral HPLC, proving the retention of optical purity (98% *ee*).



Scheme 67 Cyclopropanation to yield (1*R*,2*S*)-**67a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 90 °C.

The *trans*-configuration between the two aromatic rings was assigned by X-ray crystallography, supporting the attribution by spectroscopic correlation for the homologues **66a-e** (Figure 25).

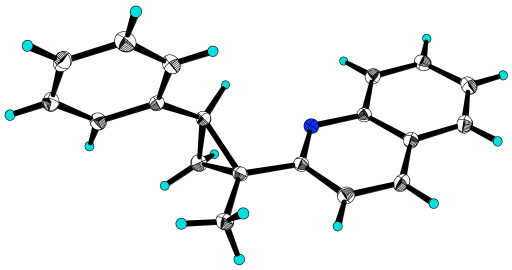
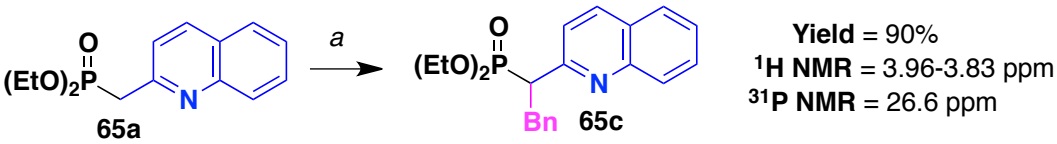


Figure 25 X-ray of cyclopropane (1*R*,2*S*)-**67a**.

The next $\mathbf{R^2}$ group screened was the benzyl, inserted *via* **Route A**. The alkylation reaction formed traces of the di-substituted product, which was removed by flash chromatography. Both the resonance values of the phosphonate **65c** appeared far from those of the reference **1a** (Scheme 68).

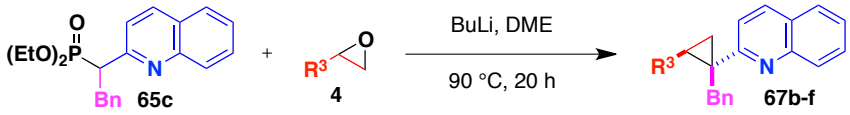


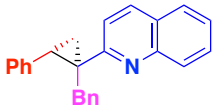
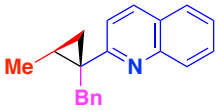
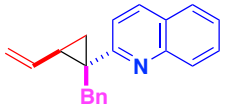
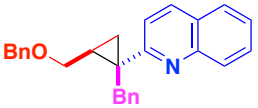
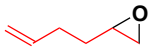
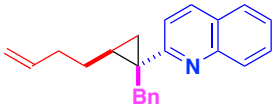
Scheme 68 Benzylation of the phosphonate **65a** to yield **65c**. Reagents and conditions: (*a*) NaH, **Bn**Br, THF, 0 °C.

The phosphonate **65c** was reacted with the usual set of epoxides **4** under the modified reaction conditions. Compared to the series **66a-e**, the cyclopropanes **67b-f** were isolated with higher yields, but with reduced diastereoselectivity values (Table 18). The *trans*-configuration between the original epoxide substituent and the quinoline was proven by X-ray crystallography, which further supported the assignment already made on the basis of the spectroscopic correlation.

The epoxide (*S*)-**4**a was converted to the cyclopropane (1*S*,2*S*)-**67b** with a good yield and with a consistent *dr* ratio compared to the methyl substituted homologue **67a** (Table 18, Entry 1). The fluctuating yield in the series again suggests that sterics play an important role in this process. The major isomer (1*S*,2*S*)-**67b** was purified *via* flash column chromatography and isolated as a crystalline solid that could be analysed by X-ray crystallography (Figure 26). Finally, chiral HPLC analysis (98% *ee*) yet again revealed the stereospecific nature of this reaction.

Table 18 Screening of the phosphonate **65c**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*S*,2*S*)-**67b**[d]	72	94:6
2		(*R*)-**4d**		(1*R*,2*S*)-**67c**	83	78:22
3		(±)-**4o**		(1*R**,2*R**)-**67d**	18	90:10
4		(±)-**4c**		(1*R**,2*S**)-**67e**	57	77:23
5		(±)-**4g**		(1*R**,2*S**)-**67f**	56	78:22

[a]Reactions carried out with 1 eq of phosphonate. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS. [d]Enantiomeric ratio (99:1) determined by HPLC.

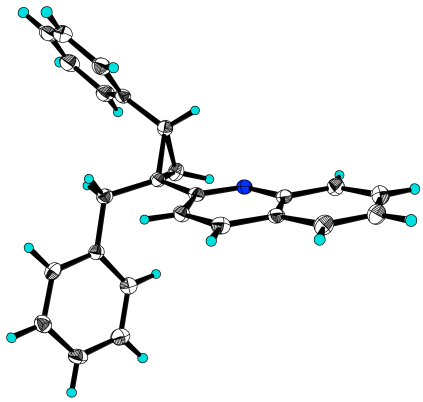


Figure 26 Crystal structure for the cyclopropane (1*S*,2*S*)-**67b**.

The epoxide (*R*)-**4d** showed an increased reactivity as witnessed by the higher isolated yield of the cyclopropane (1*R*,2*S*)-**65c** (Table 18, Entry 2). This result appeared to suggest that the relief of the steric interaction favoured the ring-opening step. However, as had been observed previously, this had a knock-on effect in terms of partial loss of diastereoselectivity.

The competition between the electrophilic sites within the epoxide (±)-**4o** was detected also during the synthesis of the cyclopropane (1*R**,2*R**)-**67d** (Table 18, Entry 3), isolated with the same yield as the di-substituted homologue (1*S**,2*S**)-**67c**. Nevertheless, the product was isolated with the high diastereoselectivity typical of the vinyl group.

The cyclopropane (1*R**,2*S**)-**67e** showed an improved yield compared to its homologue (1*S**,2*S**)-**67d**, although a fair amount of phosphonate **65c** was found in the reaction mixture (Table 18, Entry 4). Conversely, no traces of the unreacted epoxide (±)-**4c** were found, suggesting that its decomposition determined the moderate yield of the process. The cyclopropane (1*R**,2*S**)-**67e** was isolated as a crystalline solid, with which we could once again unequivocally determine the stereochemistry (Figure 27).

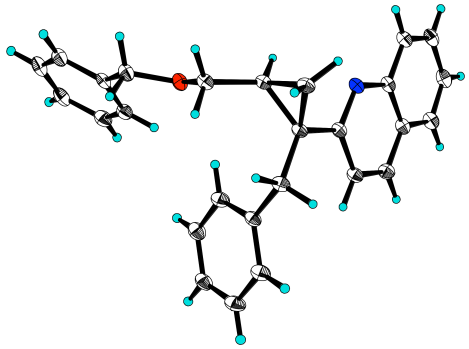
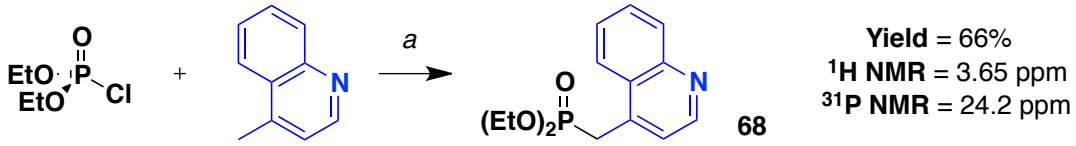


Figure 27 Crystal structure for the cyclopropane (1*R**,2*S**)-**67e**.

The phosphonate **65c** reacted with epoxide (±)-**4g** with slightly improved yield (Table 18, Entry 5), although with lower stereoselectivity with respect to the homologue (1*S**,2*S**)-**67e**. Nevertheless, the *dr* ratio is in agreement with the values observed for those epoxides lacking unsaturations in the α-position.

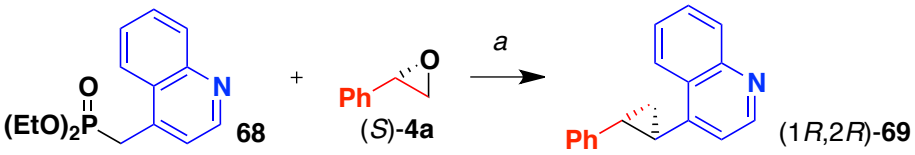
In conclusion, 2-methylquinoline proved compatible with the Wadsworth-Emmons reaction, although it showed a retarded nucleophilicity due to a lack of steric encumbrance of the phosphonate. The stereoselectivity was reduced, suggesting a reduced ability of the quinoline to interact with the cyclopropyl-methine proton in the reaction pathway, allowing the formation of some of the cis-isomer.

These results prompted us to investigate the reactivity of the isomeric substrate 4-methylquinoline, whose pK_a was reported as 27.5[86] in THF. Its conjugated acid $N{-}H^+$ in water was reported to have a pK_a of 5.67,[87] very similar to the isomeric 2-methylquinoline. The phosphonate **68** was produced according to **Route D** but only with a moderate yield (Scheme 69).



Scheme 69 Synthesis of the phosphonate **68**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

The phosphonate **68** was reacted with (*S*)-**4a** under the modified reaction conditions, producing only traces of the cyclopropane (1*R*,2*R*)-**69**. GC-MS analysis showed a distribution of products difficult to purify, the sign of an uncontrolled reactivity (Scheme 70).

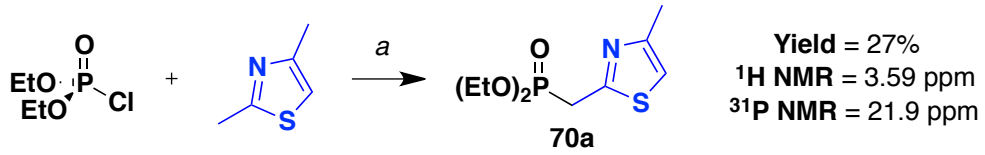


Scheme 70 Route to cyclopropane (1*R*,2*R*)-**69**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 90 °C, 11%.

This stark contrast in reactivity served to demonstrate the importance of the proximal co-ordinating N-heteroatom in the Wadsworth-Emmons reaction. As the position occupied by the heteroatom seemed to affect dramatically the reactivity, we decided to quit our investigation on this substrate and to focus on different **ASG** groups.

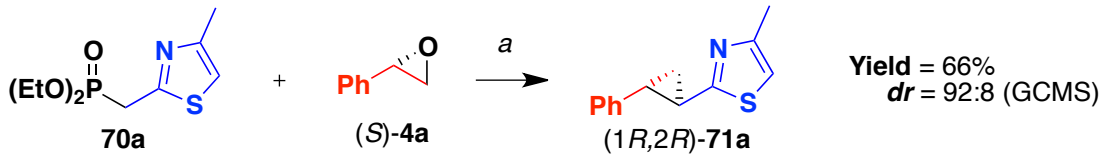
2.7 Cyclopropanes containing thiazole and benzothiazole

The next substrate selected was 2,4-dimethylthiazole, due to its reported pK_a of 30.3[64] close to that of ethyl acetate (pK_a 29.5).[72] The synthesis of the phosphonate **70a** was achieved *via* **Route D** albeit with a poor yield. This product showed encouraging resonance values for both the acidic proton and the phosphorous nucleus similar to those of the phosphonate **1a** (Scheme 71).



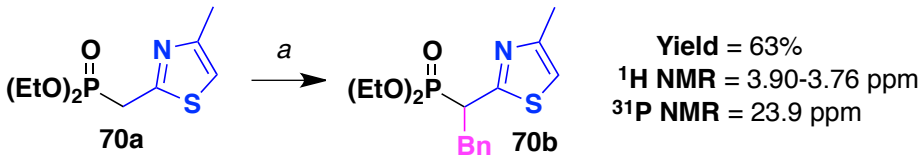
Scheme 71 Synthesis of phosphonate **70a**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

The anion of phosphonate **70a** reacted with styrene oxide (*S*)-**4a** at 90 °C to yield the cyclopropane (1*R*,2*R*)-**71a** in 66% yield. GC-MS analysis identified the presence of the unreacted phosphonate **70a**, whereas only traces (<5%) of the epoxide (*S*)-**4a** were present in the crude reaction mixture. The preference for *trans*-selectivity was initially assigned by spectroscopic correlation to the reference (1*R*,2*R*)-**5a** (Scheme 72).



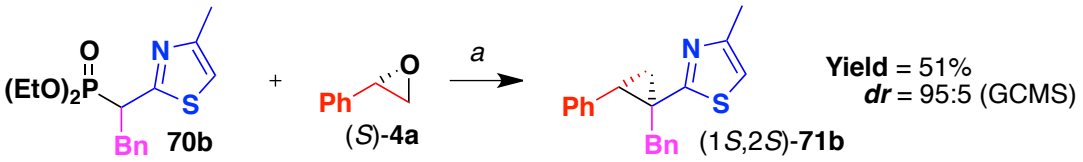
Scheme 72 Synthesis of the cyclopropane (1*R*,2*R*)-**71a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 90 °C.

The phosphonate **70a** was benzylated *via* **Route A** to produce the phosphonate **70b** with moderate yield. As for the precursor **70a**, the product **70b** also displayed promising values in terms of chemical shifts (Scheme 73).



Scheme 73 Benzylation of the phosphonate **70a** to yield **70b**. Reagents and conditions: (*a*) NaH, BnBr, THF, 0 °C.

The conversion of the epoxide (*S*)-**4a** under the standard conditions yielded the cyclopropane (1*S*,2*S*)-**71b** with a moderate yield, lower than its homologue (1*R*,2*R*)-**71a**. This is ascribable to the increased hindrance provided by the R^2 group, responsible for the reduced nucleophilicity. GC-MS analysis highlighted the absence of unreacted starting materials, potentially decomposed to water-soluble by-products (Scheme 74). The cyclopropane (1*S*,2*S*)-**71b** was isolated as a crystalline solid, whose analysis by X-ray crystallography confirmed the *trans*-relationship between the phenyl ring and the thiazole (Figure 28).



Scheme 74 Synthesis of the cyclopropane (1*S*,2*S*)-**71b**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

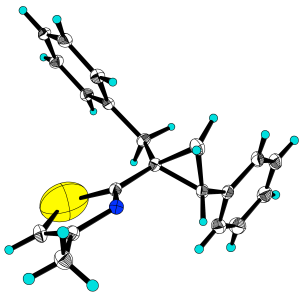
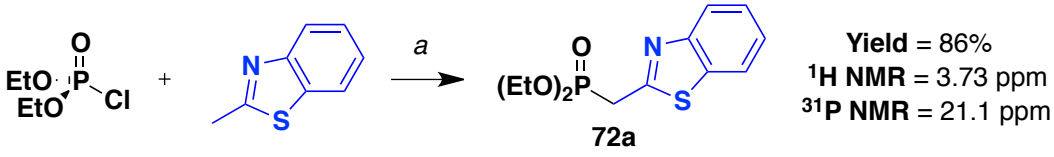


Figure 28 Crystal structure of the cyclopropane (1*S*,2*S*)-**71b**.

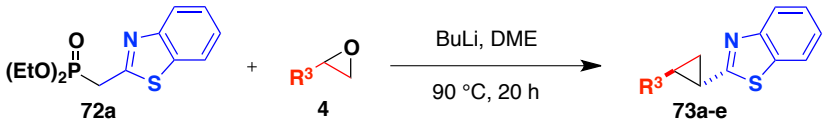
Since the introduction of the fused ring appeared strategically necessary for the compatibility of the quinoline substrate to the Wadsworth-Emmons cyclopropanation, we decided to assess the extent of such an effect on the benzothiazole scaffold. No information was available on the acidity of this ASG, though its lithiation with LDA is reported. The synthesis of the phosphonate **72a** by application of **Route D** occurred with very high yield.[88] The values of the chemical shifts appeared in agreement with those of related active phosphonates (Scheme 75).

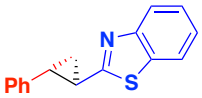
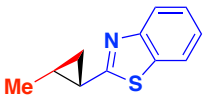
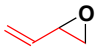
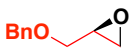
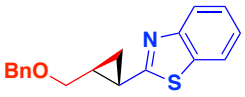
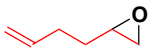
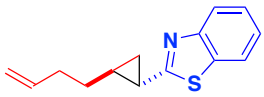


Scheme 75 Route to phosphonate **72a**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

Styrene oxide (*S*)-**4a** was reacted with the phosphonate **72a** yielding the cyclopropane (1*R*,2*R*)-**73a** with good yield (Table 19, Entry 1). GC-MS analysis revealed the absence of both starting materials in the crude reaction mixture, suggesting a competing decomposition to water-soluble by-products. The diastereoselectivity appeared comparable to the value observed for the cyclopropane (1*R*,2*R*)-**71a** and the *trans*-configuration was initially assigned by spectroscopic correlation. The chiral HPLC analysis (98% *ee*) confirmed the retention of optical purity of the epoxide (98% *ee*).

Table 19 Screening of the phosphonate **72a**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*R*,2*R*)-**73a**[d]	78	93:7
2		(*R*)-**4d**		(1*S*,2*S*)-**73b**	62	96:4
3		(±)-**4o**		(1*S**,2*R**)-**73c**	33	98:2
4		(*S*)-**4c**		(1*S*,2*S*)-**73d**	53	85:15
5		(±)-**4g**		(1*S**,2*S**)-**73e**	66	86:14

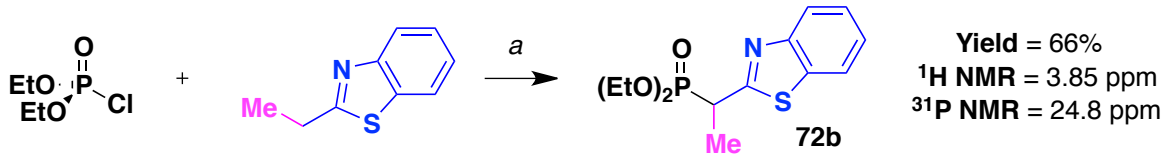
[a]Reactions carried out with 2 eq of phosphonate. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS. [d]Enantiomeric ratio (99:1) determined by chiral HPLC.

The cyclopropane (1*R*,2*R*)-**73b** was obtained with a good yield and excellent diastereoselectivity (Table 19, Entry 2). GC-MS analysis revealed a distribution of products, amongst which a consistent quantity of unreacted phosphonate **72a** was identified. The *trans*-configuration was again initially assigned by spectroscopic correlation.

The conversion of the epoxide (±)-**4o** to the cyclopropane (1*S**,2*R**)-**73c** was poor. A large peak in the GC-MS trace indicated a number of high-molecular weight products. A variety of alternative synthetic pathways, potentially connected to the competition between the electrophilic sites inside the epoxide (±)-**4o** can be envisaged. As usual, there was a striking preference for a *trans*-configuration.

Epoxides (*S*)-**4c** and (±)-**4g** reacted to give the expected cyclopropane products with only reasonable yield and *dr*. Overall it appeared that the benzothiazole phosphonate **72a** and quinoline-based homologue **65a** performed better in the Wadsworth-Emmons cyclopropanation reaction. This may be on account of their higher nucleophilicity than the thiazole-containing phosphonate **70a**. Given the diastereoselectivity values observed, comparable with epoxide (*S*)-**4a** and fluctuating with other epoxides **4**, it seems that the phosphonate **72a** develops stronger interactions during the reaction pathway as compared to the phosphonate **65a**. This appears in line with our hypothesis of the *trans*-stereoselectivity being a consequence of *a*) the geometry of the **ASG** group and *b*) number and position of heteroatoms on it.

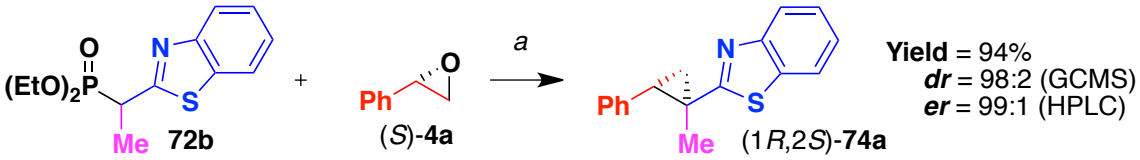
This investigation was extended to involve the modification of the phosphonate **72a** to insert a quaternary carbon centre. In order to avoid the formation of the di-alkylated product, we followed **Route D** with a different source of the **ASG** (Scheme 76). The spectroscopic effect due to the presence of the methyl group was comparable to that observed for **65b**, although less significant in the ^{31}P NMR (^{1}H NMR = δ 3.69; ^{31}P NMR = δ 21.9).



Scheme 76 Route to the phosphonate **72b**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

The phosphonate **72b** was reacted with the epoxide (*S*)-**4a** to yield the cyclopropane (1*R*,2*S*)-**74a** with very high yield and extremely high stereoselectivity. GC-MS analysis of the crude

mixture was clean, detecting only traces of impurities, whereas the chiral HPLC analysis confirmed the retention of optical purity (98% *ee*) (Scheme 77). The product (1*R*,2*S*)-**74a** was isolated as a crystalline solid and assigned the *trans*-configuration by X-ray crystallography (Figure 29).



Scheme 77 Screening the route to cyclopropane (1*R*,2*S*)-**74a**. Reagents and conditions: (*a*) BuLi, DME; 20 h, 130 °C.

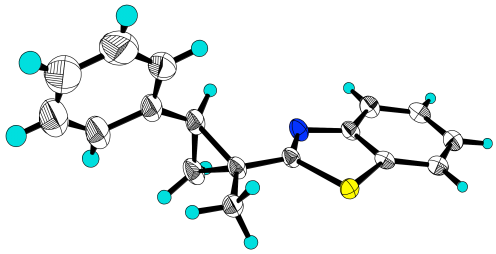
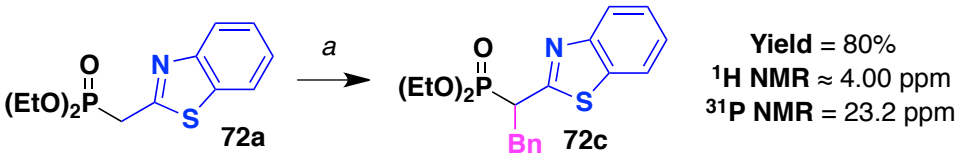


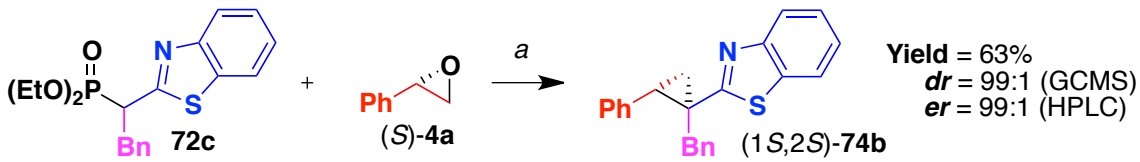
Figure 29 X-ray of the to cyclopropane (1*R*,2*S*)-**74a**.

The next target was represented by the benzylation of the phosphonate **72a**, obtained *via* **Route A**. This R^2 group generated a deshielding effect on the resonance of the acidic hydrogen, whereas ^{31}P NMR was in line with the range of values previously observed (Scheme 78).



Scheme 78 Benzylation to produce the phosphonate **72c**. Reagents and conditions: (*a*) NaH, **Bn**Br, THF, 0 °C.

The enhanced hindrance of the phosphonate **72c** affected the conversion of the epoxide (*S*)-**4a**, as the GC-MS trace of the crude reaction mixture showed both unreacted starting materials and an impurity (Scheme 79).



Scheme 79 Synthesis of the cyclopropane (1*S*,2*S*)-**74b**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

Nevertheless, the cyclopropane (1*S*,2*S*)-**74b** was produced with excellent diastereoselectivity and retention of enantiopurity (98% *ee*).

The racemic product was isolated as a crystalline solid and characterised by X-ray crystallographic analysis as the isomer with the phenyl ring and the benzothiazole *trans* to one another (Figure 30).

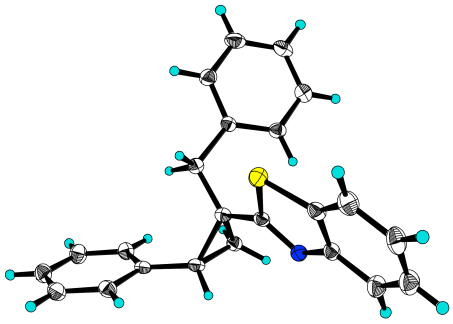
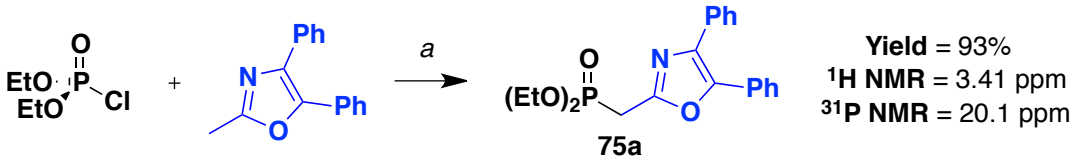


Figure 30 Crystal structure of the cyclopropane (1*S*,2*S*)-**74b**.

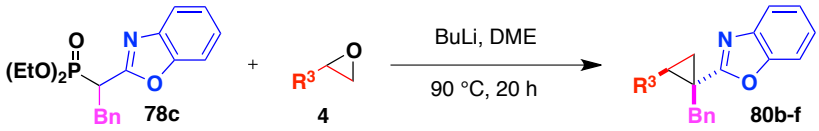
2.8 Cyclopropanes containing oxazole and benzoxazole

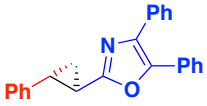
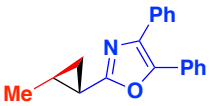
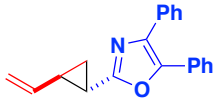
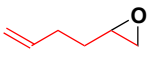
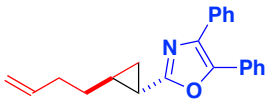
At this stage, we were intrigued to tune the electronic properties of the last two **ASGs** groups by replacing the sulfur atoms with oxygen. Therefore, we reproduced the last screening with the homologous phosphonates containing oxazoles and benzoxazoles. The phosphonate **75a** was obtained *via* **Route D** with an excellent yield (Scheme 80). This excellent yield was in contrast with that of the homologue phosphonate **70a** (29%) and suggested an improved nucleophilicity. Since the values of both the resonances of the ^{1}H and ^{31}P nuclei appeared compatible to those already investigated, the phosphonate **75a** was screened with the elected epoxides **4** (Table 20).



Scheme 80 Synthesis of phosphonate **75a**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

Table 20 Screening of the phosphonate **75a**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*R*,2*R*)-**76a**	60	98:2
2		(*R*)-**4d**		(1*S*,2*S*)-**76b**	54	88:12
3		(±)-**4o**		(1*S**,2*R**)-**76c**	16	>99:1
4		(±)-**4g**		(1*S**,2*S**)-**76d**	49	95:5

[a]Reactions carried out with 1 eq of phosphonate. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS.

The cyclopropane (1*R*,2*R*)-**76a** was isolated with a comparable yield to the cyclopropane (1*R*,2*R*)-**71a** (66%), although with an improved selectivity (Table 20, Entry 1). Some unreacted phosphonate **75a** was detected in the crude mixture, as a consequence of the huge hindrance retarding the nucleophilicity. Furthermore, no unreacted epoxide (*S*)-**4a** was observed *via* the GC-MS analysis, suggesting a competitive reaction pathway. The *trans*-configuration was again initially assigned by spectroscopic correlation with the library of cyclopropanes obtained. The epoxide (*R*)-**4d** was converted to the cyclopropane (1*S*,2*S*)-**76b** with a similar yield to cyclopropane (1*R*,2*R*)-**76a** (Table 20, Entry 2). No unreacted phosphonate **75a** was shown by the GC-MS analysis of the crude reaction mixture, suggesting decomposition to water-soluble by-products. The *dr* ratio slightly dropped with respect to Entry 1, in line with the previous results. The *trans*-configuration was assigned by analogy as for cyclopropane (1*R*,2*R*)-**76a**. The epoxide (±)-**4o** produced the cyclopropane (1*S**,2*R**)-**76c** with a poor yield and the typical excellent diastereoselectivity (Table 20, Entry 3). The absence of unreacted phosphonate **75a** and the presence of a major impurity in the crude mixture matched the trend observed with this epoxide throughout the investigation. The cyclopropane (1*S**,2*S**)-**76d** was isolated with a modest yield and excellent diastereoselectivity, in agreement with the previous entries. The GC-MS analysis showed a lack of both unreacted phosphonate **75a** and elimination products. The cyclopropane (1*S**,2*S**)-**76d** was isolated as a solid, whose *trans*-configuration was assigned by X-ray crystallography, further supporting the spectroscopic correlation for cyclopropanes **76a-c** (Figure 31).

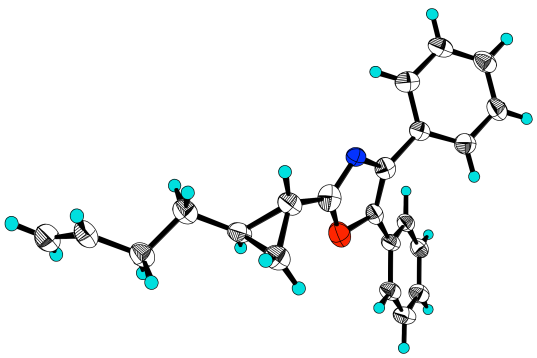
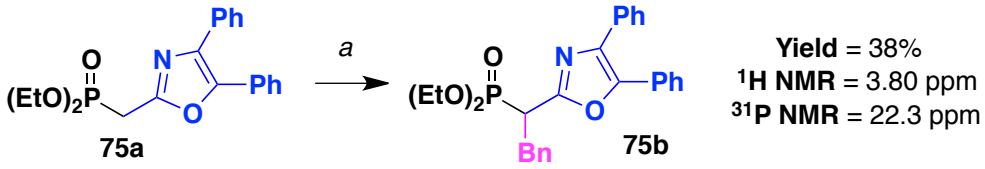


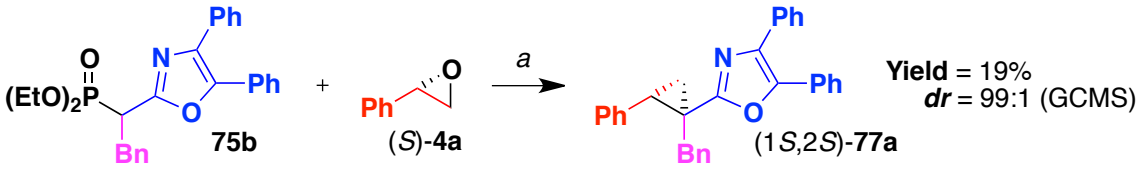
Figure 31 Crystal structure for the cyclopropane (1*S**,2*S**)-**76d**.

This work was continued with the assessment following the insertion of a benzyl substituent. The phosphonate **75b** was obtained *via* **Route A**. The poor yield highlighted the steric issues of this phosphonate **75b**, potentially retarding its later nucleophilicity (Scheme 81).



Scheme 81 Alkylation of the phosphonate **75a** to yield **75b**. Reagents and conditions: (*a*) NaH, **Bn**Br, THF, 0 °C.

As expected, the phosphonate **75b** converted the epoxide (*S*)-**4a** to the cyclopropane (1*S*,2*S*)-**77a** with a poor yield, although with excellent stereocontrol. The presence of unreacted starting materials in the crude mixture was detected as well as elimination products (GC-MS), making it difficult to purify by flash column chromatography due to their reduced polarity (Scheme 82).



Scheme 82 Cyclopropanation reaction to produce (1*S*,2*S*)-**77a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

The *trans*-configuration was assigned by X-ray crystallography (Figure 32).

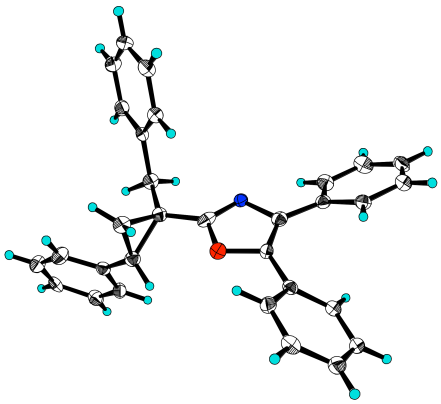
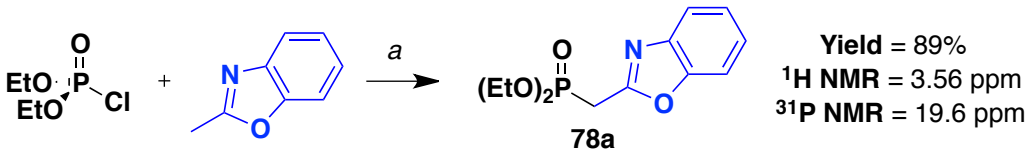


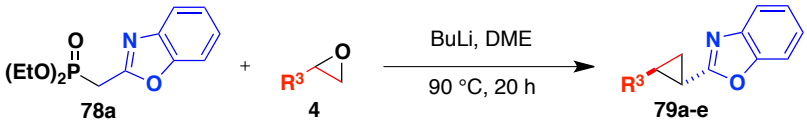
Figure 32 X-ray for the cyclopropane (1*S*,2*S*)-**77a**.

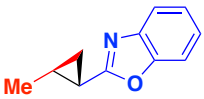
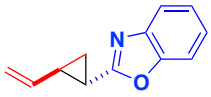
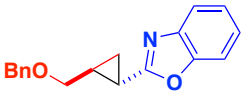
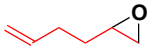
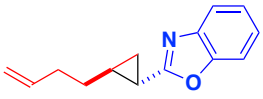
Given the low isolated yield of the cyclopropane (1*S*,2*S*)-**77a**, we decided not to verify the reactivity with other epoxides **4**, moving our attention to the study of the benzoxazole scaffold. The synthetic route to the phosphonate **78a** was adopted from the homologue benzothiazole and occurred *via* **Route D**,[89] with a similar yield to the homologue **72a** (86%). Although no information about the acidity was available in literature, the spectroscopy data was in line with the experimental range of active phosphonates (Scheme 83).



Scheme 83 Synthesis of phosphonate **78a**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

Table 21 Screening of the phosphonate **78a**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*R*,2*R*)-**79a**	86	89:11
2		(*R*)-**4d**		(1*S*,2*S*)-**79b**	59	87:13
3		(±)-**4o**		(1*S**,2*R**)-**79c**	51	95:5
4		(±)-**4c**		(1*S**,2*S**)-**79d**	56	97:3
5		(±)-**4g**		(1*S**,2*S**)-**79e**	67	97:3

[a]Reactions carried out with phosphonate (1 eq) at 90 °C in DME for 20 h. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS.

The phosphonate **78a** was screened with the usual epoxides **4** (Table 21). The cyclopropane (1*R*,2*R*)-**79a** was produced with a higher yield compared to the cyclopropane (1*R*,2*R*)-**73a** (78%)

although with a lower selectivity. The GC-MS analysis showed traces of unreacted phosphonate **78a**, whereas the epoxide (*S*)-**4a** appeared completely consumed. The insertion of the fused ring increased the nucleophilicity, although it reduced the selectivity, as witnessed by the parameters relative to the cyclopropane (1*R*,2*R*)-**76a** (60% yield, 98:2 *trans*:*cis*). Unexpectedly, a reduced enantiomeric excess value (94% *ee*) was observed by chiral HPLC analysis. Nevertheless, to date this example represented the only value lower than 96% *ee*. The racemic product (1*R*,2*R*)-**79a** was isolated as a crystalline solid, confirming the *trans*-configuration (Figure 33).

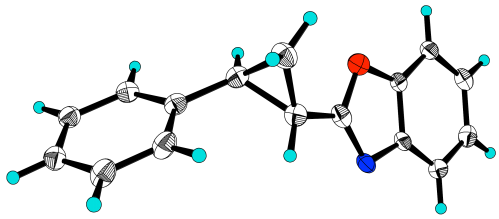
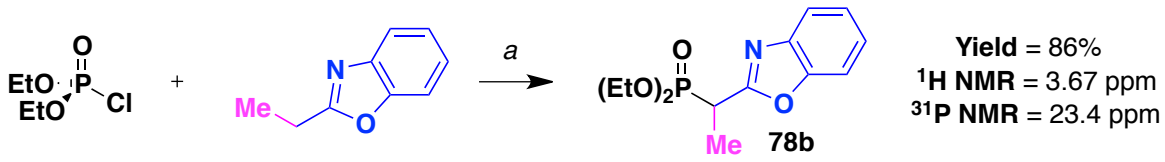


Figure 33 X-ray for cyclopropane (1*R*,2*R*)-**79a**.

The epoxide (*R*)-**4d** was converted to cyclopropane (1*S*,2*S*)-**79b** with a moderate yield (Table 21, Entry 2). Surprisingly, the diastereoselectivity was in line with the result in Entry 1. No traces of unreacted phosphonate were observed by GC-MS, suggesting a potential decomposition pathway. The *trans*-configuration was assigned by spectroscopic correlation to the cyclopropane (1*R*,2*R*)-**79a**. The cyclopropane (1*S**,2*R**)-**79c** was produced with a moderate yield, as witnessed by the mass recovery but with the expected excellent stereoselectivity (Table 21, Entry 3). The competition between the electrophilic sites of the epoxide seemed to be restrained with respect to the cyclopropane (1*S**,2*R**)-**73c**. Once again, the *trans*-configuration was confirmed by spectroscopic correlation. The phosphonate **78a** provided moderate yields with more flexible epoxides (±)-**4c** and (±)-**4g** (Table 21, Entries 4-5). This trend showed an improved stereoselectivity with respect to cyclopropanes **73d-e** (Table 19, Entries 4-5, Page 91).

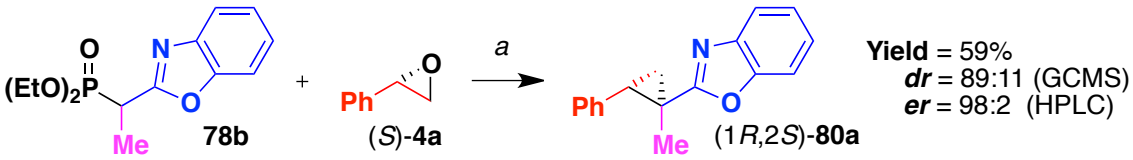
In conclusion, the benzoxazole reactivity displayed a similar reactivity to the homologous benzothiazoles, with the latter providing a higher diastereoselectivity in the presence of more rigid epoxides. In both cases, the introduction of the fused ring improved the nucleophilicity.

Our investigation carried on by introducing a methyl group on the phosphonate **78a**. In analogy with the homologue **72b** (Scheme 76, Page 92), the reaction was performed *via* **Route D**, displaying an improved reactivity with respect to the benzothiazole (Scheme 84).



Scheme 84 Synthesis of phosphonate **78b**. Reagents and conditions: (*a*) LDA, THF, −78 °C.

The phosphonate **78b** converted styrene oxide (*S*)-**4a** to cyclopropane (1*R*,2*R*)-**80a** with a moderate yield and selectivity compared to the excellent values of the cyclopropane (1*R*,2*S*)-**74a** (94% yield, 98:2 *dr*). The GC-MS of the crude mixture showed the presence of a distribution of compounds, including both the starting materials. Chiral HPLC analysis described a lower enantiomeric excess value (96% *ee*), in line with the homologue cyclopropane (1*R*,2*R*)-**79a** (Scheme 85).



Scheme 85 Synthesis of the cyclopropane (1*R*,2*S*)-**80a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

The cyclopropane (1*R*,2*S*)-**80a** was isolated as a crystalline solid upon flash column chromatography, which proved the *trans*-configuration by X-ray crystallography (Figure 34).

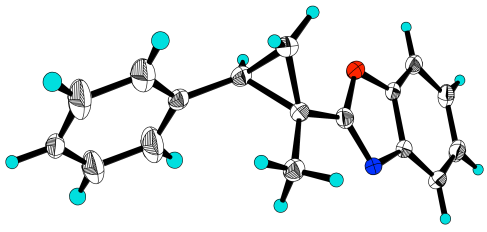
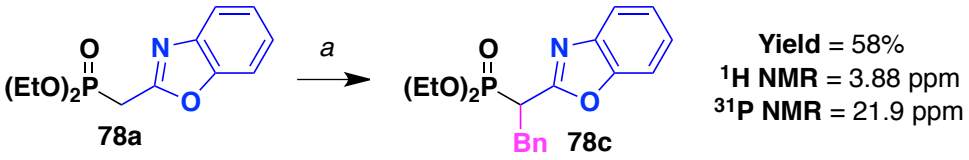


Figure 34 Crystal structure for the cyclopropane (1*R*,2*S*)-**80a**.

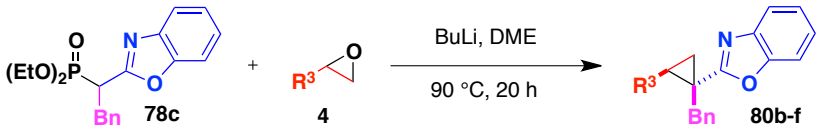
As previously described for the phosphonate **72a**, the benzoxazole phosphonate **78a** was alkylated with benzyl bromide according to **Route A**. The phosphonate **78a** showed a retarded

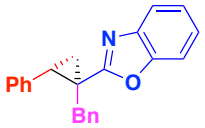
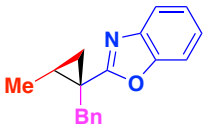
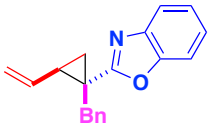
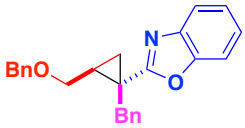
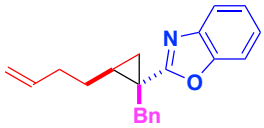
nucleophilicity compared to the benzothiazole-based phosphonate **72a**. The substituent shifted the resonances of both nuclei downfield, still within the range of active phosphonates (Scheme 86).



Scheme 86 Benzylation of phosphonate **78c**. Reagents and conditions: (*a*) NaH, **Bn**Br, THF, 0 °C.

Table 22 Screening of the phosphonate **78c**.[a]



Entry	Epoxide		Cyclopropane		Yield[b](%)	*dr* ratio[c]
1		(*S*)-**4a**		(1*S*,2*S*)-**80b**	36	89:11
2		(*R*)-**4d**		(1*R*,2*S*)-**80c**	58	91:9
3		(±)-**4o**		(1*R**,2*R**)-**80d**	21	93:7
4		(±)-**4c**		(1*R**,2*S**)-**80e**	49	93:7
5		(±)-**4g**		(1*R**,2*S**)-**80f**	50	94:6

[a]Reactions carried out with 1 eq of phosphonate. [b]Percentage isolated yield following column chromatography. [c]Diastereomeric ratio determined by GC-MS.

As envisaged by the yield of the benzylation reaction, the retarded nucleophilicity affected the cyclopropanation process, as the cyclopropane (1*S*,2*S*)-**80b** was obtained with a poor yield (Table 22, Entry 1). Unreacted starting materials and side-products were detected by GC-MS. The selectivity appeared not to suffer from the increased bulkiness, as the *dr* ratio remained unchanged

in all the benzoxazole-based phosphonates reacting with the epoxide (*S*)-**4a**. The product (1*S*,2*S*)-**80b** was isolated as a crystalline solid and assigned the *trans*-configuration by X-ray analysis (Figure 35).

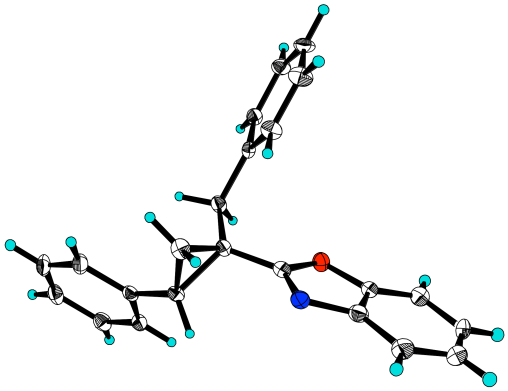


Figure 35 X-ray for cyclopropane (1*S*,2*S*)-**80b**.

The impact of steric bulk on the reactivity was confirmed by the synthesis of the cyclopropane (1*R*,2*S*)-**80c**, isolated with a higher yield than with (*S*)-**4a** (Table 22, Entry 2). GC-MS analysis revealed a higher selectivity, assigning the *trans*-configuration to the major isomer by spectroscopic correlation. The epoxide (±)-**4o** was converted to cyclopropane (1*R**,2*R**)-**80d** with a poor yield. The GC-MS showed a distribution of products, in agreement with the typical pattern observed with this epoxide (Table 20, Entry 3). The ring-closure happened with a high stereoselectivity, assigning the *trans*-configuration by spectroscopic correlation. Finally, the cyclopropanes **80e-f** were isolated in moderate yields and high diastereoselectivity (Table 22, Entries 4-5).

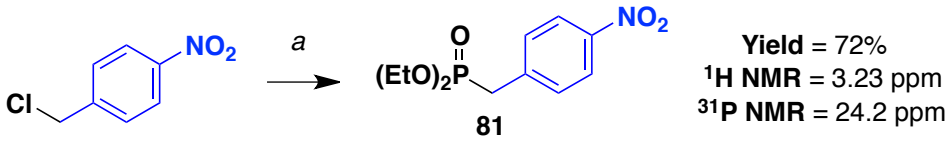
*In conclusion, hetero-aromatic **ASGs** proved to be compatible with the Wadsworth-Emmons protocol, although with fluctuating yields, as competitive decomposition of both the starting materials may occur under the reaction conditions. Due to the lack of information about the acidity of many phosphonates tested in this study, these **ASGs** have been selected according to the pK_a value of the reference **ASG** group (ethyl acetate, i.e. the precursor of the reference phosphonate **1a**). As sometimes this data was missing, both the resonance values of the acidic*

proton and ^{31}P nucleus of the phosphonates were used to draft a general classification of the active substrates. Nevertheless, our results showed that there is no direct correlation between the compatibility to the cyclopropanation conditions and a range of chemical shift values. However, this appears to be strictly connected to the presence and the position occupied by heteroatoms, as it influences both the nucleophilicity and the stereoelectronic effects in the reaction pathway. The trans-stereoselectivity of the Wadsworth-Emmons cyclopropanation was confirmed, although to different extent depending on the epoxide used. Finally, other hetero-aromatic ***ASGs*** *were tested without success, such as oxazoline, imidazole, benzimidazole, triazole and tetrazoles, but they did not give any of the desired products.*

2.9 Aromatic rings as Anion Stabilising Groups

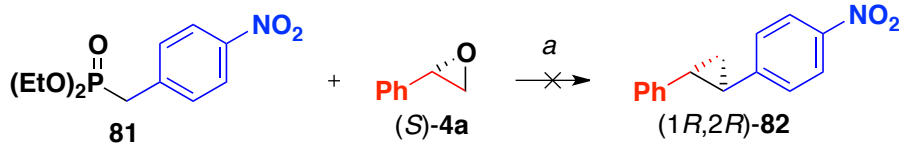
In light of the encouraging results observed in the presence of heteroaromatic **ASG** groups, it appeared interesting to assess the compatibility of heteroatom-substituted benzyl groups to the Wadsworth-Emmons protocol. Furthermore, this investigation would have provided additional support to our hypothesis regarding the influence of heteroatoms in the reaction pathway in relation to their position.

Since strong EWGs proved unreactive when installed as R^2 and R^3 groups, our first approached focused on the *p*-nitrobenzyl scaffold. This **ASG** was reported to be more acidic (pK_a 20.4) than that of ethyl acetate (pK_a 29.5),[72] suggesting a poor reactivity in the cyclopropanation process. The phosphonate **81** was synthesized *via* **Route C** in a good yield, as the EWG character complied with the Arbuzov protocol.[90] The chemical shift values appeared promising, since they were quite similar to other active phosphonates (Scheme 87).



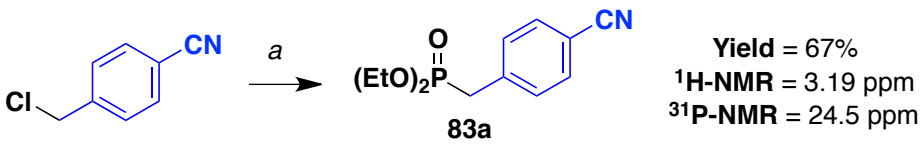
Scheme 87 Synthesis of the phosphonate **81**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h, 170 °C.

The phosphonate **81** failed to convert the styrene oxide (*S*)-**4a**, to the desired product, instead forming a thick slurry during the addition of the base. The GC-MS analysis of the crude mixture showed the formation of several by-products, amongst which none showed the desired *m/z* ratio. As a consequence, the use of such strongly electron-withdrawing groups in the Wadsworth-Emmons cyclopropanation was abandoned (Scheme 88).



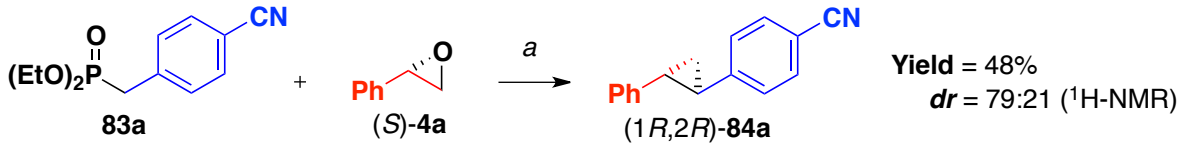
Scheme 88 Synthesis of the cyclopropane (1*R*,2*R*)-**82**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 0%.

We then moved to investigate the nitrile function, positioned in both *para*- and *ortho*-positions. The first reported to have a pK_a of 30.8,[73] an intermediate value in the range between ethyl acetate (pK_a 29.5)[72] and ethyl phenylsulfone (pK_a 31).[80] The phosphonate **83a** was isolated in moderate yield by application of **Route C**,[91] showing interesting resonance values for both the nuclei (Scheme 89).



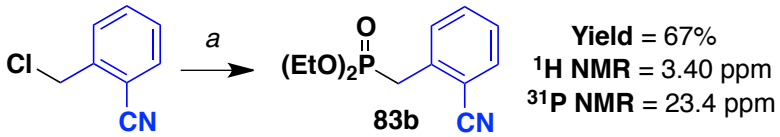
Scheme 89 Synthesis of the phosphonate **83a**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h, 170 °C.

The phosphonate **83a** was converted to the cyclopropane (1*R*,2*R*)-**84a** with an average yield of 48% (Scheme 90). GC-MS analysis revealed the presence of a distribution of products and a significantly lower *trans*-selectivity, as had already been observed for acetonitrile (Table 10, Page 61).



Scheme 90 Route to cyclopropanes (1*R*,2*R*)-**84a**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

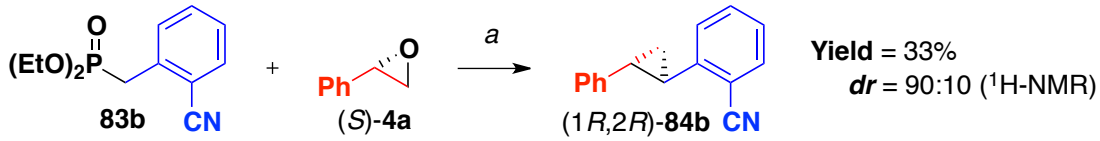
The synthesis of the phosphonate **83b** occurred *via* **Route A**[92] with the same yield as for the isomer **83a**. The *ortho*-substituted product **83b** showed a more deshielded peak for the acidic protons, still fitting the range of active phosphonates (Scheme 91).



Scheme 91 Synthesis of the phosphonate **83b**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h 170 °C.

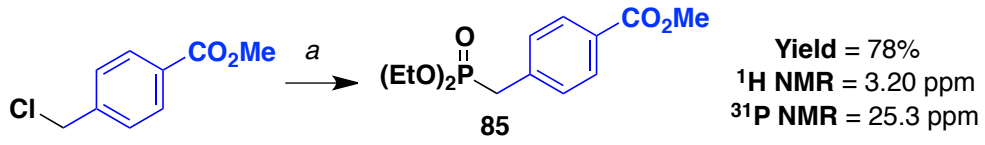
The cyclopropane (1*R*,2*R*)-**84b** was produced with a lower yield than the isomer (1*R*,2*R*)-**84a**, but with a much higher *trans*-selectivity. These values show the dual effect of the

nitrile function on the aryl ring: the first involves the steric effect, retarding the nucleophilicity, (effect on the conversion), whereas the second involves the electronic effect in the reaction pathway, due to the closer position of the **ASG** to the cyclopropyl-methine proton of the **R^3** group (effect on the stereoselectivity) (Scheme 92).



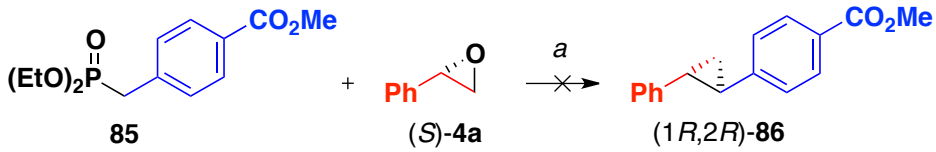
Scheme 92 Cyclopropanation to produce the product (1*R*,2*R*)-**84b**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C.

The investigation was repeated with an ester moiety installed in the *para*-position. The phosphonate **85** was produced again *via* **Route C** with a high yield.[93] Both the ^{1}H and the ^{31}P NMR resonance values appeared compatible to the Wadsworth-Emmons cyclopropanation (Scheme 93).



Scheme 93 Arbuzov reaction to produce the phosphonate **85**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h 170 °C

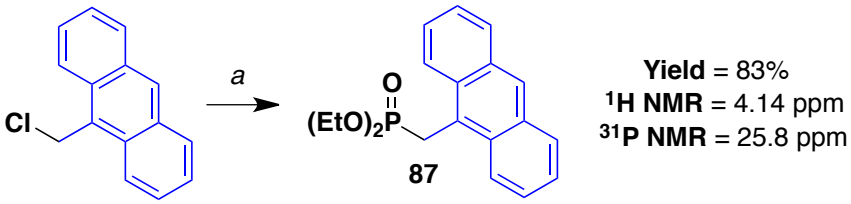
The phosphonate **85** failed to convert the epoxide (*S*)-**4a** to the cyclopropane (1*R*,2*R*)-**86**, forming instead a distribution of products difficult to identify (Scheme 94).



Scheme 94 Wadsworth-Emmons cyclopropanation with phosphonate (1*R*,2*R*)-**86** Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 0%.

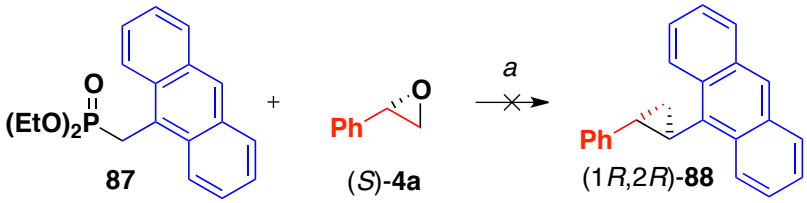
The final approach dealt with the assessment of the reactivity of aromatic rings without any heteroatoms. As mentioned in the paragraph 2.3, Wadsworth and Emmons proved that when toluene was employed as **ASG** group, it failed to convert the epoxide **4a** to the relative cyclopropane.[19] Given our success in the previous investigations, when the installation of a fused ring appeared to improve the reactivity of our heteroaromatic substrates, we decided to study the

reactivity of 9-methylanthracene. This **ASG** group showed an acidity value (pK_a 31.1)[94] close to the experimentally observed reference ethyl acetate (pK_a 29.5)[72] and was converted to phosphonate **87** *via* **Route C** in high yield (Scheme 95).[95]



Scheme 95 Arbuzov reaction to produce the phosphonate **87**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h 170 °C.

The phosphonate **87** failed to produce the desired cyclopropane, showing uncontrolled reactivity. Several by-products were observed in the crude mixture, together with unreacted phosphonate **87**. Interestingly, the two peaks with the expected *m/z* ratio observed in GC-MS featured the presence of double bonds (^{1}H NMR). The formation of the elimination products suggested that the phosphonate **87** is nucleophilic enough to form the new C−C bond, but potentially too hindered to perform the S_N2-like ring-closure, favouring instead an E1cb-like process (Scheme 96).



Scheme 96 Route to produce the cyclopropane (1*R*,2*R*)-**88**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 0%.

In conclusion, this study confirmed the relevance of the position occupied by heteroatoms in the reaction pathway for both the reactivity and the selectivity of the Wadsworth-Emmons cyclopropanation. Installation of a substituent in the ortho-position increases steric encumbrance of the carbanion, retarding the ring-closure step. On the other hand, it can enhance the electronic interactions with the cyclopropyl-methine proton in the reaction pathway, increasing the

stereoselectivity. Finally, the use of strong electron-withdrawing groups (e.g. NO_2) is not compatible with the Wadsworth-Emmons cyclopropanation reaction.

2.10 Fluorinated Anion Stabilising Groups

Our first approach to fluorinated ASGs dealt with the reactivity of McCarthy's reagents **43g** (Figure 21, Page 77), whose compatibility with the Wadsworth-Emmons cyclopropanation was partially affected by competitive decomposition of both the starting materials. It was decided to carry on this research on fluorinated phosphonates by assessing the reactivity of the homologue phosphonate **1m**. The ^{1}H NMR resonance of the acidic proton appeared compatible to the value detected for the phosphonate **43g**, whereas the phosphorous peak appeared downfield (Figure 36).

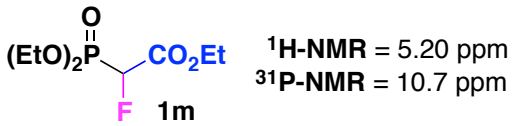
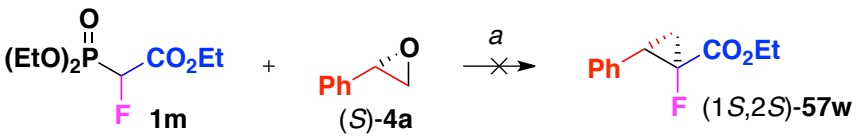


Figure 36 Resonance values of phosphonate **1m**.

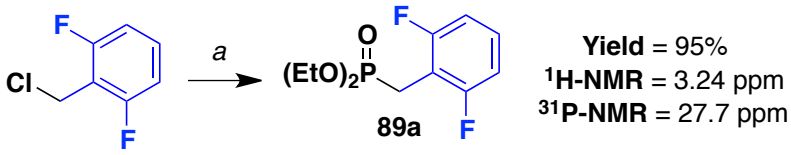
The cyclopropanation reaction was tested with styrene oxide (*S*)-**4a**, yielding a distribution of products. In the GC-MS analysis of the reaction mixture there were four peaks with the expected *m/z* ratio. Due to the formation of a precipitate under deprotonation at room temperature, the addition of the base was repeated at −78 °C. The reaction mixture remained opaque at room temperature; however warming up the reaction caused the same precipitation effect, irrespective of the presence of the electrophile (*S*)-**4a**. No suitable eluent was found to purify the traces of the product **57w**, so no characterisation could be performed satisfactorily (Scheme 97).



Scheme 97 Cyclopropanation reaction with the phosphonate **1m**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, traces.

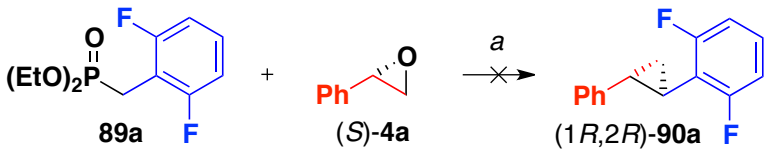
Since the use of other bases such as NaH or MeMgBr failed to produce any change, the investigation with the phosphonate **1m** was abandoned. We then moved on to the phosphonate **89a**, prepared *via* **Route C** in an excellent yield.[96] The resonance values appeared compatible with the

chemical shifts of the experimental library of active phosphonates, although the ^{31}P NMR seemed very deshielded (Scheme 98).



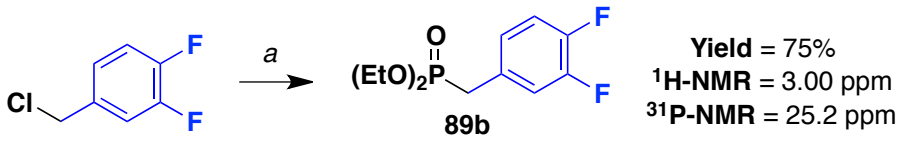
Scheme 98 Route to the fluorinate phosphonate **89a**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h 170 °C.

The phosphonate **89a** was reacted with styrene oxide (*S*)-**4a** with a range of different bases such as *n*-BuLi, MeMgBr and NaH. Decomposition of both the starting materials was found by GC-MS analysis. Lowering the reaction temperature allowed formation of traces of the desired product (as judged by ^{1}H NMR spectroscopy). The crude mixture could not be purified by flash column chromatography, so the research on this substrate was interrupted (Scheme 99).



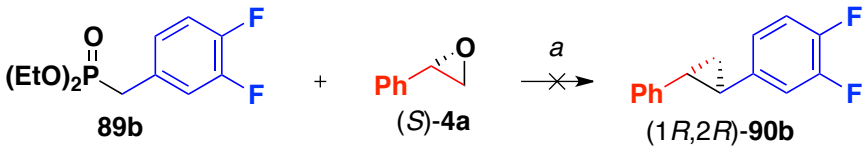
Scheme 99 Cyclopropanation to produce the cyclopropane (1*R*,2*R*)-**90a**. Reagents and conditions: (*a*) BuLi or NaH or MeMgBr, DME, 20 h, 130 °C, traces.

The isomeric phosphonate **89b** was obtained *via* application of **Route C** with a good yield,[97] showing interesting resonance values for both the ^{1}H and ^{31}P (Scheme 100).



Scheme 100 Arbuzov reaction to produce **89b**. Reagents and conditions: (*a*) $P(OEt)_3$, 3 h 170 °C.

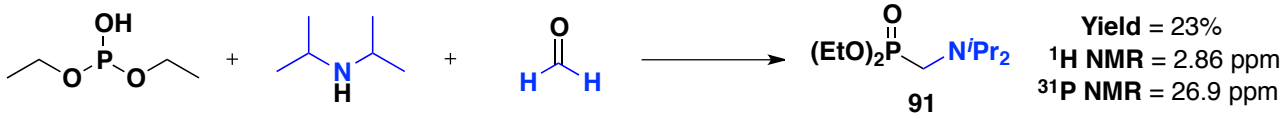
Treatment of the phosphonate **89b** in the presence of the epoxide (*S*)-**4a** failed to produce the desired cyclopropane, instead forming a distribution of products (Scheme 101). Furthermore, tri- and tetra-fluorinated phosphonates failed to deliver desired cyclopropanes in a satisfactorily yield. Due to this sequence of failed reactions, we decided to quit our study on fluorine chemistry applied to the Wadsworth-Emmons cyclopropanation.



Scheme 101 Failed synthesis of the fluorinated cyclopropane (1*R*,2*R*)-**90b**. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 0%.

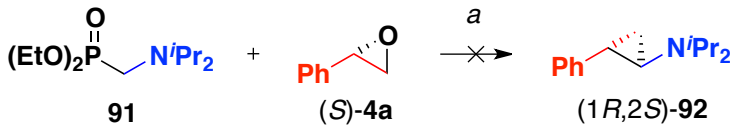
2.11 Cyclopropyl amines

Our final efforts were focused on the challenging insertion of the amine functionality on cyclopropanes. The phosphonate **91** was easily synthesised at room temperature according to a known procedure (Scheme 102).[98]



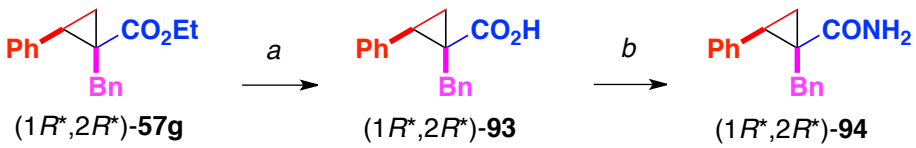
Scheme 102 Synthesis of the phosphonate **91**.

The phosphonate **91** was screened with the epoxide (*S*)-**4a**. No reactivity was observed, as both starting materials were found in the crude mixture by GC-MS analysis (Scheme 103).



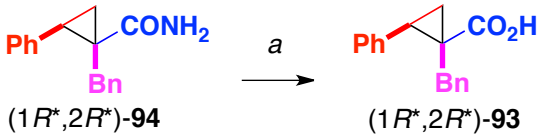
Scheme 103 Failed cyclopropanation reaction. Reagents and conditions: (*a*) BuLi, DME, 20 h, 130 °C, 0%.

Given the apparent impossibility of installing the amine functionality directly, we were prompted to investigate two alternative routes to rearrange the acid into the desired substrate. The two pathways involved the Hoffman and the Curtius rearrangement.[99] Both reactions are reported for the synthesis of cyclopropyl amines on tertiary carbon centres, but no examples are reported for quaternary carbon centres homologues. The ester from which we chose to study the Hoffman rearrangement was the cyclopropane (1*R**,2*R**)-**57g**. This substrate was easily hydrolysed into the acid (1*R**,2*R**)-**93**, then activated with thionyl chloride and treated with ammonia to yield the primary amide (1*R**,2*R**)-**94** (Scheme 104).



Scheme 104 Route to the cyclopropyl amide (1*R**,2*R**)-**94**. Reagents and conditions: (*a*) LiOH, H_2O, THF, 100 °C, (*b*) (*i*) $SOCl_2$; (*ii*) NH_3/H_2O, 85%.

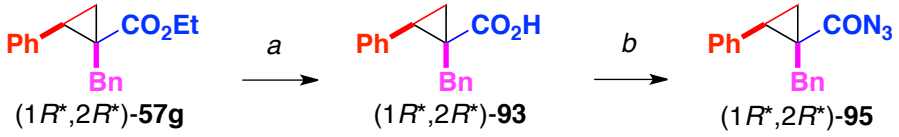
The cyclopropane (1*R**,2*R**)-**94** was treated in water with sodium hydroxide and bleach to promote the migration of the cyclopropane moiety. Upon acidic work-up, both the GC-MS analysis and the ^{1}H NMR spectroscopy of the crude reaction mixture showed the presence of the acid (1*R**,2*R**)-**93** only (Scheme 105).



(1*R**,2*R**)-**94** (1*R**,2*R**)-**93**

Scheme 105 Failed Hoffmann rearrangement. Reagents and conditions: (*a*) NaOCl, NaOH.

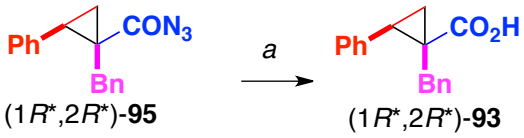
Following this, we attempted the Curtius rearrangement, keeping the same reference substrate (1*R**,2*R**)-**57g**. The azide scaffold was introduced upon hydrolysis to form the acid (1*R**,2*R**)-**93**. Treatment with thionyl chloride and a Lewis acid in the presence of sodium azide produced the cyclopropyl azide (1*R**,2*R**)-**95** (Scheme 106).



(1*R**,2*R**)-**57g** (1*R**,2*R**)-**93** (1*R**,2*R**)-**95**

Scheme 106 Insertion of the azide group to produce the species (1*R**,2*R**)-**95**. Reagents and conditions: (*a*) LiOH, H_2O, THF, 100 °C, (*b*) (*i*) $SOCl_2$; (*ii*) NaN_3, TBAB, $ZnCl_2$.

The azide (1*R**,2*R**)-**95** was treated under acidic conditions, forming the acid (1*R**,2*R**)-**93** as a single product in the reaction mixture (GC-MS and ^{1}H NMR) (Scheme 107).



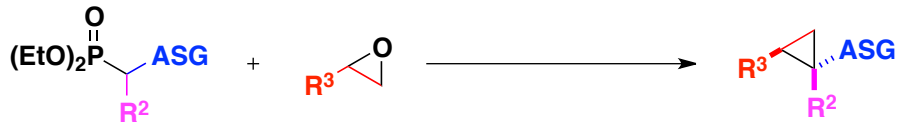
(1*R**,2*R**)-**95** (1*R**,2*R**)-**93**

Scheme 107 Failed Curtius rearrangement. Reagents and conditions: (*a*) HCl, H_2O.

The lack of migration observed in both the attempts is possibly ascribable to strain and reduced flexibility faced by the migrating group. Given the lack of reactivity, we decided to abandon the research on quaternary cyclopropyl amines.

2.12 Conclusions

The Wadsworth-Emmons protocol proved to be an excellent procedure to synthesise cyclopropanes bearing tertiary and quaternary carbon centres with almost complete control of both the absolute and the relative stereochemistry. Our investigation confirmed the excellent compatibility of the ester group to the protocol, which was extended to a range of other functional groups to design cyclopropanes difficulty synthesised *via* alternative routes. In the majority of the cases, a strong preference for the formation of the stereoisomer where the substituent of the phosphonate (**ASG**) and the group originally on the epoxide ($\mathbf{R^3}$) are in *trans*-relationship to one another was observed, regardless of the presence of the additional substituent ($\mathbf{R^2}$) on the phosphonate moiety (Scheme 108).

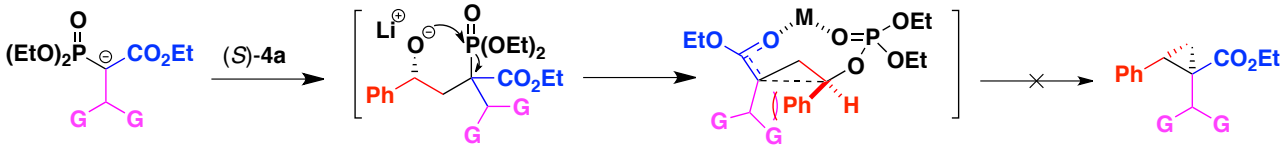


Scheme 108 General scheme for the Wadsworth-Emmons cyclopropanation reaction.

A wide tolerance with respect to the functional groups was found. Our experimental evidence suggested that the **ASG** group might be any function where at least one β-position with respect to the carbanion is occupied by an electron rich heteroatom, although the best results have been obtained when both the β-positions are filled by heteroatoms. Highest values of yield and diastereoselectivity were achieved when the geometry of the **ASG** group was trigonal; on the other hand, tetrahedral groups proved to suffer the steric hindrance when the size of the $\mathbf{R^2}$ was increased, though leaving the stereoselectivity untouched. Use of digonal groups seemed to drop the stereoselectivity, unless aromatic $\mathbf{R^3}$ groups are used.

The phosphonate substituent $\mathbf{R^2}$ was usually an alkyl chain with the size ranging from a methyl to a benzyl group. This moiety tolerated the presence olefins and heteroatoms, not in proximal positions to the carbanion. When this group became a fluorine atom, competitive

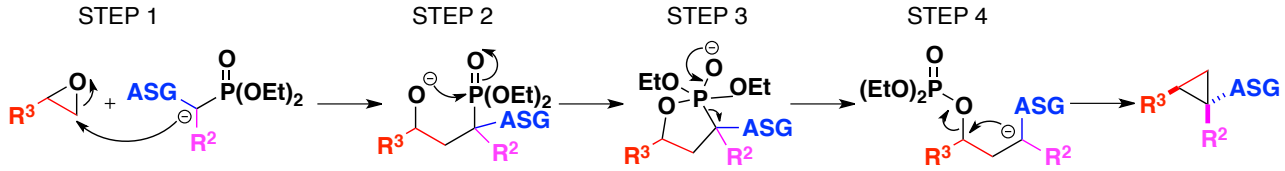
decomposition of the fluorosulfone phosphonate was hypothesised to justify the loss in yield. Eventually, this group required a methylene carbon adjacent to the carbanion: when this position was replaced by tertiary or quaternary carbon, the reaction failed to produce the cyclopropane, favouring instead the formation of by-products (Scheme 109).



Scheme 109 Steric interactions causing the formation of by-products

The substituent **R^3** proved to be very tolerant to different groups, such as aromatic and aliphatic groups. Presence of double bonds and heteroatoms proved compatible with the cyclopropanation protocol; nevertheless, the presence of electron-withdrawing groups appeared detrimental, as they might generate an electrophilic site. In particular, halogens (fluorine apart) and vinyl group appeared to divert the nucleophilic attack of the phosphonate carbanion, preventing the ring-opening step. In general, use of strong EWG groups proved unsuccessful on all the three positions explored.

The mechanism of the reaction is suggested to go through four steps, as highlighted in Scheme 110.



Scheme 110 Suggested mechanism of the Wadsworth-Emmons cyclopropanation reaction.

The stepwise formation of the two C−C bonds is suggested to proceed *via* two critical steps. First, the nucleophilic attack of the phosphonate carbanion on the less substituted carbon of the terminal epoxide; second, the 3-*exo*-tet ring-closure performed by the **ASG** *via* an S_N2-like mechanism. In order to rationalise these steps, we referred the reactivity of the phosphonates on the

basis of their pK_a values (where known), as compared to that of the most reactive triethyl phosphonoacetate **1a** (18.6).[64] When this was not possible due to the little information available in the literature, we referred the reactivity of the phosphonates to their precursors, using ethyl acetate (29.5)[72] as the new reference. At the same time, we approached the definition of an empirical scale of reactivity of the phosphonates, based on the NMR spectroscopy of the acidic proton (^{1}H NMR) and the phosphorous nucleus (^{31}P NMR). At the end of our study, we can claim that:

1. The Wadsworth-Emmons cyclopropanation is accessible to a wide range of phosphonates, with a preference for those **ASG** group showing trigonal or tetrahedral geometry and with heteroatoms in the β-positions with respect to the carbanion
2. The presence of heteroatoms in this position seems to favour the formation of the cyclopropanes in high yield and with excellent *trans*-diastereoselectivity
3. Phosphonates whose precursors show a pK_a value in the range between 28 and 35 appeared to convert the epoxides with higher yields
4. Excessive steric hindrance on both the phosphonate and the epoxide may retard the nucleophilicity and the formation of the new C−C bonds, leading to the formation of by-products. Nevertheless, it seems not to affect the excellent *trans*-diastereoselectivity
5. The empirical scale of reactivity based on the NMR spectroscopy failed to provide general guidelines in terms of activity
6. The reactions appeared to be more efficient in DME as a solvent
7. The role of the cation seems to be restricted to the simple stabilisation of the carbanion, as the evidence suggests that no chelated intermediate is involved in the reaction pathway. The choice of the cation should be made according to the electronic nature of the **ASG** and the hard-soft acid-base theory
8. The design of novel phosphonates was broadly achieved by application of the Arbuzov reaction (**Route C**), allows a straightforward purification by distillation under reduced

pressure. Alternatively, when the substrate featured the presence of an electron rich heteroatom, the phosphonate could be generated *via* electrophilic quenching of the carbanion (**Route D**). Introduction of alkyl chains on the phosphonates was achieved *via* direct (**Route A**) or reductive alkylation (**Route B**).

In conclusion, this study has extended the potential of the Wadsworth-Emmons cyclopropanation procedure, allowing the synthesis of products under convenient experimental conditions with respect to other currently used protocols, *i.e*. without using pyrophoric species such as diethyl zinc, irritant species such as diiodomethane or expensive transition metals such as rhodium or chiral sulfonium ylides. This reaction can potentially be applied in the total synthesis of natural products, given the compatibility with heteroaromatic anion stabilising groups, as well as being used as a synthetic tool due to the control of the stereoselectivity. Given the manifold strategies to ring-open the cyclopropane ring, this investigation makes stereochemically-challenging targets more accessible and future insights on the Wadsworth-Emmons cyclopropanation more appealing in the synthetic organic chemistry landscape.

3 EXPERIMENTAL

3.1 Experimental Procedures and Analytical Data:

All reactions were carried out under an atmosphere of argon. All glassware was either oven or flame-dried prior to use as required. All the solvents utilised were purchased "anhydrous" commercially or dried using a MBraun solvent purification system. ^{1}H NMR spectra were recorded on Brüker AV400 and AMX400 (400 MHz ^{1}H, 100 MHz ^{13}C, 162 MHz ^{31}P, 376 MHz ^{19}F) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to the respective solvent resonance as the internal standard ($CDCl_3$, δ 7.26 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (brs), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet of doublets (td), doublet of triplets (dt), doublet of quartets (dq), multiplet (m),], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.23 ppm). NMR data were collected at 25 ºC. Infrared spectra were recorded directly as neat liquids on a Brüker Tensor 37 FTIR machine fitted with a PIKE MIRacle ATR accessory. Analytical thin-layer chromatography (TLC) was performed using silica gel plates (0.25 mm thickness) precoated with a fluorescent indicator. Visualization was accomplished by irradiation with an UV lamp and/or staining with $KMnO_4$, or *p*-anisaldehyde (PAA) solutions. Flash chromatography was performed using Kieselgel 60 (40-63 μm) or with a Varian Superflash automated purification system. Petrol refers to the fraction boiling between 40 - 60 ºC. Residual solvent was removed using a static oil pump (< 1 mbar). Melting points (m.p.) were obtained using a Griffin & George MFB-590-010T melting point apparatus. Optical rotations were obtained on Jasco P1010 digital polarimeter and reported as $[\alpha]^{T}_{\lambda}$ = Specific O. R. (concentration, solvent). High Resolution Mass Spectrometry (HRMS) measurements were performed by EPSRC National Mass Service (Swansea) using a high-resolution double focusing mass spectrometer (Finnigan MAT 95 XP). GC-MS determinations of diastereoselective ratios were performed on a 6890N/MS5973 Agilent Technologies Ltd Cheshire UK using an Agilent HP-5MS column

(30.0 m × 320 μm × 0.25 μm, 40 - 300 °C, 20 °C/min). HPLC determinations of enantiopurity were performed on an 1100 Series HPLC Agilent Technologies Ltd Cheshire UK instrument using Daicel™ Chiralpak® columns (IA, IB, IC, ID, 25 °C).

3.2 General Procedures

Phosphonates **1g**, **3b**, **65b-c**, **70b**, **72c**, **75b** and **78c** were prepared according to a modified procedure reported by Janecki and co-workers:[60]

Route A: To a solution of diethyl alkylphosphonate (9.10 mmol, 1.0 equiv) in THF (100.0 mL) at 0 °C, NaH (240 mg, 10.0 mmol, 1.0 equiv) was added portionwise and the mixture was stirred at 0 °C for 2 h. Alkyl halide (10.0 mmol, 1.0 equiv) was added in one portion and the solution was stirred at 0 °C for 8 h. The solvent was evaporated at reduced pressure and the residue was washed with a saturated aqueous solution of NH_4Cl (8.0 mL) and extracted three times with Et_2O (3 × 20.0 mL). The organic layers were combined, dried with $MgSO_4$ filtered and the solvent was removed at reduced pressure. The crude oil was purified by flash column chromatography (SiO_2, 30 - 50% EtOAc in Petrol) to give the desired product.

Phosphonate **1i'** was prepared according to a modified procedure reported by Patai and co-workers:[61]

Route B: To triethylphoshonoacetate (13.6 g, 62.0 mmol, 1.0 equiv) in toluene (25.0 mL) at 25 °C, benzaldehyde (7.0 mL, 70.0 mmol, 1.13 equiv), piperidine (0.2 mL, 2.0 mmol, 0.03 equiv) and acetic acid (57 μL, 1.0 mmol, 0.02 equiv) were added. The reaction was heated at 100 °C for 50 hours using the Dean-Stark condenser. The reaction was washed with a saturated solution of $Na_2S_2O_5$ and extracted three times with Et_2O (3 × 30.0 mL) to remove the excess of the benzaldehyde. The organic layers were combined, dried with $MgSO_4$ and the solvent was evaporated *in vacuo*. The crude oil was distilled under reduced pressure to give the desired product.

Phosphonates **60a**, **43d'** and **65a** were prepared according to a modified procedure of the Arbuzov[100] reaction.

Route C: To triethylphosphite (9.69 g, 58.3 mmol, 14.6 equiv), the alkyl halide (4.00 mmol, 1.0 equiv) was added in one portion. The reaction was heated to 170 °C for 3 h. The reaction was cooled down and the mixture was distilled at reduced pressure or purified by column chromatography to give the desired product.

Phosphonates **70a**, **72a-b**, **75a**, and **80a-b** were prepared according to a modified procedure reported by Jackson and co-workers.[101]

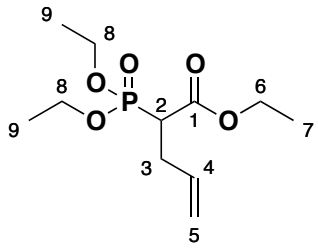
Route D: To a solution of freshly prepared lithium diisopropylamide (2.5 M; 10.0 mL, 25.00 mmol, 2.5 equiv) in THF (50.0 mL) at –78 °C, 2-methylheterocycle (10.0 mmol, 1.0 equiv) was added in one portion and left stirring for 2 h. Diethyl chlorophosphate (1.45 mL, 10.00 mmol, 1.0 equiv) was added in one portion and left stirring overnight. The reaction was allowed to warm up gently at -20 °C, then up to room temperature before saturated aqueous solution of NH_4Cl (8 mL) was added. The reaction was extracted three times with EtOAc (3 × 20 mL). The organic layers were combined and washed once with saturated aqueous solution of NaCl. The organic layer was dried ($MgSO_4$), filtered and the solvent was removed at reduced pressure. The crude oil was loaded onto 5 mL of silica and purified by flash column chromatography (SiO_2, 50% EtOAc in Petrol) to give the desired product.

Representative procedure for the cyclopropanation:

Route E: To a solution of phosphonate (1.00 mmol, 1.0 equiv) in DME (3.0 mL) at 25 °C was added *n*-butyllithium (2.5 M; 0.41 mL, 1.02 mmol, 1.02 equiv) dropwise over 5 min. The epoxide (1.00 mmol, 1.0 equiv) was added in one portion. The reaction was heated to 130 °C for 20 h. The reaction was cooled before a saturated aqueous solution of NH_4Cl (8 mL) was added. The reaction was extracted three times with Et_2O (3 × 20 mL). The organic layers were combined and washed with a saturated solution of NaCl. The organic layer was dried ($MgSO_4$), filtered and the solvent

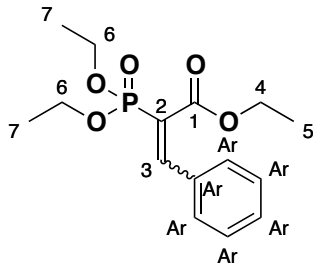
was removed at reduced pressure. The residue was loaded onto 5 mL of silica and purified by flash column chromatography (SiO_2, 2-20% Et_2O in Petrol) to give the desired compound.

Ethyl 2-(diethoxyphosphoryl)pent-4-enoate **1g**



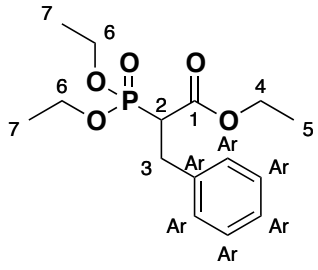
Prepared according to **Route A** from triethyl phosphonoacetate (4.49 g, 20.0 mmol, 1.0 equiv). Distillation under reduced pressure (130 °C, 0.1 mmHg) afforded the title compound **1g** as a colourless oil (4.17 g, 79%); **IR** (cm^{-1}) 1734, 1328, 1018; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.82-5.69 (m, 1H, H−4), 5.11 (d, *J* = 16.8 Hz, 1H, H−5), 5.00 (d, *J* = 10.4 Hz, 1H, H−5') 4.25-4.10 (m, 6H, H−6 and H−8), 3.01 (ddd, *J* = 22.3, 11.1 and 3.7 Hz, 1H, H−2), 2.77-2.64 (m, 1H, H−3), 2.64-2.63 (m, 1H, H−3'), 1.33 (t, *J* = 7.2 Hz, 6H, H−9), 1.27 (t, *J* = 7.2 Hz, 3H, H−7); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.8 (d, *J* = 4.5 Hz, C−1), 134.8 (d, *J* = 16.4 Hz, C-4), 117.3 (C-5), 63.0 (d, *J* = 6.4 Hz, (C-8), 62.9 (d, *J* = 7.0 Hz, C-8), 61.5 (C-6), 45.6 (d, *J* = 130.7 Hz, C−2), 31.1 (d, *J* = 4.5 Hz, C−3), 16.5 (d, *J* = 2.6 Hz, C−9), 16.5 (d, *J* = 3.0 Hz, C−9), 14.3 (C-7); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 22.2; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{11}H_{22}O_5P$ requires 265.1199; found, 265.1195; **GC-MS** (40-300 °C, 20 °C/min): t_R = 7.767 min.

Ethyl 2-(diethoxyphosphoryl)-3-phenylacrylate **1i'**



Prepared according to **Route B** from triethyl phosphonoacetate (13.6 g, 62.0 mmol, 1.0 equiv). Distillation under reduced pressure (130 °C, 0.1 mmHg) afforded the title compound **1i'** as a clear oil (17.29 g, 89%); **IR** (cm^{-1}) 1721, 1615, 1451, 1372, 1292, 1253, 1216, 1203, 1166, 1045, 1015; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 21.1 Hz, 1H, H-3), 7.44-7.33 (m, 5H, H-Ar), 4.27 (q, *J* = 7.1 Hz, 2H, H-5), 4.24-4.13 (m, 4H, H-6), 1.37 (t, *J* = 7.1 Hz, 6H, H-7), 1.37 (t, *J* = 7.1 Hz, 3H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.4 (d, *J* = 12.6 Hz, C-1), 148.2 (d, *J* = 6.4 Hz, C-3), 133.7 (d, *J* = 20.2 Hz, C-Ar), 130.4 (C-Ar), 129.2 (C-Ar), 128.6 (C-Ar), 124.7 (d, *J* = 178.8 Hz, C-2), 62.7 (d, *J* = 5.2 Hz, C-6), 61.7 (C-4), 36.4 (d, *J* = 6.7 Hz, (C-7), 13.9 (C-5); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 14.0; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{22}O_5P$ requires 313.1199; found, 313.1196; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 87%) = 10.445 min, t_R (minor, 13%) = 10.483 min.

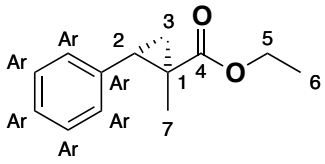
Ethyl 2-(diethoxyphosphoryl)-3-phenylpropanoate **1i**[102]



To a solution of ethyl 2-(diethoxyphosphoryl)-3-phenylacrylate (1.5 g, 4.31 mmol) in EtOH (10.0 mL) at 0 °C, $NaBH_4$ (115 mg, 4.31 mmol) was added slowly over 20 min. The reaction was

stirred at 0 °C for 1 h and at 25 °C for 2 h. The solvent was evaporated *in vacuo* and the residue was washed with water and extracted three times with Et_2O (3 × 20.0 mL). The organic layers were combined, dried with $MgSO_4$ and the solvent was evaporated *in vacuo*. The crude oil was distilled under reduced pressure (130 °C, < 0.1 mmHg) to give the title compound **1i** as a colourless oil (1.15 g, 85%); **IR** (cm^{-1}) 1734, 1256, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30-7.16 (m, 5H, H-Ar), 4.42-4.13 (m, 4H, H-6), 4.13-4.05 (m, 2H, H-4), 3.31-3.14 (m, 3H, H-2 and H-3), 1.35 (t, *J* = 7.1 Hz, 6H, H-7), 1.14 (t, *J* = 7.1 Hz, 3H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.6 (C-1), 138.7 (d, *J* = 15.9 Hz, C-Ar), 128.9 (d, *J* = 47.4 Hz, C-Ar), 128.7 (d, *J* = 11.0 Hz, C-Ar), 126.8 (C-Ar), 63.1 (d, *J* = 6.6 Hz, C-6), 62.9 (d, *J* = 6.7 Hz, C-6), 61.5 (C-4), 47.9 (d, *J* = 129.1 Hz, C-2), 33.0 (d, *J* = 4.3 Hz, C-3), 16.6 (d, *J* = 3.4 Hz, C-7), 16.5 (d, *J* = 3.5 Hz, C-7), 14.2 (C-5); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 22.0; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{24}O_5P$ requires 315.1356; found, 315.1355; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.121 min.

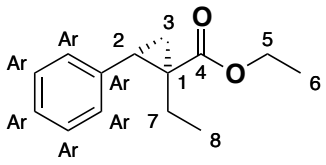
(1*R*,2*S*)-Ethyl 1-methyl-2-phenyl-cyclopropanecarboxylate (1*R*,2*S*)-**57a**



Prepared according to **Route E** from triethyl 2-phosphonopropionate (476 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the title compound (1*R*,2*S*)-**57a** as a colourless oil (195 mg, 95%); **$[\alpha]^{25}_D$** = +142.0° (c = 1.7, Me_2CO); **IR** (cm^{-1}) 1714, 1454, 1381, 1311, 1240, 1151, 1026; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26-7.08 (m, 5H, H-Ar), 4.10 (q, *J* = 7.1 Hz, 2H, H-5), 2.73 (dd, *J* = 9.2, 7.0 Hz, 1H, H-2), 1.61 (dd, *J* = 9.2, 4.5 Hz, 1H, H-3), 1.21 (t, *J* = 7.1 Hz, 3H, H-6), 1.08 (dd, *J* = 7.0, 4.5 Hz, 1H, H-3'), 0.91 (s, 3H, H-7); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.6 (C-4), 137.0 (C-Ar), 129.3 (C-Ar), 128.1 (C-Ar), 126.6 (C-Ar), 60.7 (C-5), 31.6 (C-2), 25.1 (C-1), 19.9

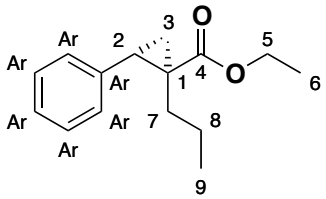
(C-3), 14.5 (C-7), 14.2 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{17}O_2$ requires 205.1223; found, 205.1223; **GC-MS** (40-300 °C, 20 °C/min): t_R = 7.667 min.

(1*R*,2*S*)-Ethyl 1-ethyl-2-phenylcyclopropanecarboxylate (1*R*,2*S*)-**57b**



Prepared according to **Route E** from triethyl 2-phosphobutyrate (505 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the title compound (1*R*,2*S*)-**57b** as a colourless oil (211 mg, 97%); **[α]$^{25}_D$** = −107.8° (c = 1.07, Me_2CO); **IR** (cm^{-1}) 1715, 1451, 1379, 1275, 1209, 1152, 1105, 1050, 1028; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24-7.09 (m, 5H, H-Ar), 4.18-4.04 (m, 2H, H-5), 2.73 (dd, *J* = 9.2, 7.0 Hz, 1H, H-2), 1.61-1.51 (m, 2H, H-3 and H-7), 1.22 (t, *J* = 7.1 Hz, 3H, H-6), 1.08 (dd, *J* = 7.0, 4.5 Hz, 1H, H-3'), 0.91 (m, 4H, H-8 and H-7'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.9 (C-4), 137.1 (C-Ar), 129.3 (C-Ar), 128.1 (C-Ar), 126.6 (C-Ar), 60.6 (C-5), 32.3 (C-2), 31.4 (C-1), 21.8 (C-7), 17.8 (C-3), 14.3 (C-6), 11.7 (C-8); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{19}O_2$ requires 219.1380; found, 219.1380; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.036 min.

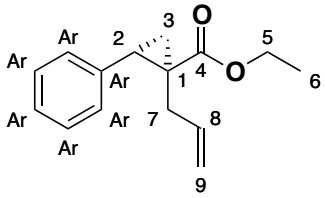
(1*R*,2*S*)-Ethyl 2-phenyl-1-propylcyclopropanecarboxylate (1*R*,2*S*)-**57c**



Prepared according to **Route E** from triethyl 2-phosphonopentanoate (534 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**57c** as a colourless oil (216 mg,

93%); **[α]$^{25}_{D}$** = −113.6° (c = 1.41, Me_2CO); **IR** (cm^{-1}) 1713, 1453, 1381, 1291, 1224, 1205, 1151, 1071, 1025; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25-7.09 (m, 5H, H-Ar), 4.17-4.04 (m, 2H, H-5), 2.67 (dd, *J* = 9.6, 7.2 Hz, 1H, H-2), 1.61 (dd, *J* = 9.6, 4.5 Hz, 1H, H-3), 1.57-1.48 (m, 1H, H-7), 1.34-1.18 (m, 2H, H-8), 1.21 (t, *J* = 7.4 Hz, 3H, H-6), 1.10 (dd, *J* = 7.2, 4.5 Hz, 1H, H-3'), 0.76-0.68 (m, 1H, H-7'), 0.66 (t, *J* = 7.4 Hz, 3H, H-9); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.0 (C-4), 137.1 (C-Ar), 129.2 (C-Ar), 128.1 (C-Ar), 126.6 (C-Ar), 60.6 (C-5), 32.0 (C-2), 30.6 (C-4), 30.4 (C-7), 20.7 (C-8), 17.9 (C-3), 14.2 (C-6), 14.2 (C-9); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{21}O_2$ requires 233.1536; found, 233.1538; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 8.202 min, t_R (major, 98%) = 8.418 min.

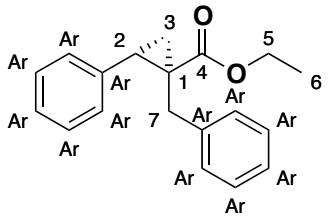
(1*R*,2*S*)-Ethyl 1-allyl-2-phenylcyclopropanecarboxylate (1*R*,2*S*)-**57e**



Prepared according to **Route E** from 2-allyl triethylphosphonoacetate (530 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**57e** as a colourless oil (198 mg, 86%); **[α]$^{25}_{D}$** = −65.0° (c = 1.86, Me_2CO); **IR** (cm^{-1}) 1716, 1304, 1219, 1203, 1151; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25-7.10 (m, 5H, H-Ar), 5.75-5.63 (m, 1H, H-8), 4.85-4.74 (m, 2H, H-9), 4.17-4.04 (m, 2H, H-5), 2.77 (dd, *J* = 8.7, 7.2 Hz, 1H, H-2), 2.36 (dd, *J* = 15.4, 7.2 Hz, 1H, H-7), 1.65 (ddd, *J* = 8.7, 4.8 and 1.2 Hz, 1H, H-3), 1.49 (dd, *J* = 15.4, 7.3 and 1.2 Hz, 1H, H-7'), 1.21 (t, *J* = 7.1 Hz, 3H, H-6), 1.16 (dd, *J* = 7.3, 4.8 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.5 (C-4), 136.7 (C-8), 135.9 (C-Ar), 129.3 (C-Ar), 128.2 (C-Ar), 126.8 (C-Ar), 115.7 (C-9), 60.7 (C-5), 32.5 (C-7), 32.0 (C-2), 29.5 (C-1), 17.7 (C-3), 14.2 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd

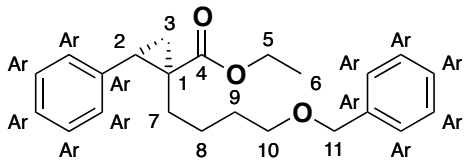
for $C_{15}H_{19}O_2$ requires 231.1380; found, 231.1382; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 8.164 min, t_R (major, 98%) = 8.437 min.

(1*S*,2*S*)-Ethyl 1-benzyl-2-phenylcyclopropanecarboxylate (1*S*,2*S*)-**57g**



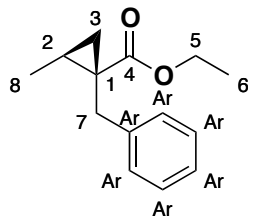
Prepared according to **Route E** from 2-benzyltriethylphosphonoacetate (630 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**57g** as a colourless oil (275 mg, 98%); $[\alpha]^{25}_D = -16.5°$ (c = 1.09, Me_2CO); **IR** (cm^{-1}) 1714, 1496, 1453, 1380, 1301, 1194, 1135, 1095, 1027; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40-7.14 (m, 10H, H-Ar), 4.24-4.08 (m, 2H, H-5), 3.23 (d, *J* = 15.4 Hz, 1H, H-7), 2.89 (dd, *J* = 7.6, 6.3 Hz, 1H, H-2), 2.03 (d, *J* = 15.4 Hz, 1H, H-7'), 1.93 (dd, *J* = 6.3, 4.9 Hz, 1H, H-3), 1.45 (dd, *J* = 7.6, 4.9 Hz, 1H, H-3'), 1.21 (t, *J* = 7.1 Hz, 3H, H-6); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.6 (C-4), 140.4 (C-Ar), 136.7 (C-Ar), 129.3 (C-Ar), 128.7 (C-Ar), 128.4 (C-Ar), 128.0 (C-Ar), 127.0 (C-Ar), 125.9 (C-Ar), 60.9 (C-5), 33.5 (C-7), 32.7 (C-2), 30.9 (C-1), 17.9 (C-3), 14.1 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{19}H_{21}O_2$ requires 281.1536; found, 281.1532; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 7%) = 10.734 min, t_R (major, 93%) = 10.874 min. **HPLC** (IC, 1% THF in Hexane, 1 mL/min): t_R (major, 99%) = 18.242 min, t_R (minor, 1%) = 24.968 min.

(1*R*,2*S*)-ethyl 1-(4-(benzyloxy)butyl)-2-phenylcyclopropanecarboxylate (1*R*,2*S*)-**57h**



Prepared according to **Route E** from ethyl 6-(benzyloxy)-2-(diethoxyphosphoryl)hexanoate (774 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**57h** as a yellow oil (268 mg, 76%); $[\alpha]^{25}_{D} = -43.3°$ (c = 2.54, Me_2CO); **IR** (cm^{-1}) 1715, 1183, 1149, 1101; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.14 (m, 10H, H-Ar), 4.41 (s, 2H, H-11), 4.22-4.08 (m, 2H, H-5), 3.35-3.28 (m, 2H, H-10), 2.76 (t, *J* = 8.7 Hz, 1H, H-2), 1.69-1.64 (m, 1H, H-3), 1.64-1.57 (m, 1H, H-7), 1.47-1.34 (m, 4H, H-8 and H-9), 1.27 (t, *J* = 7.3 Hz, 3H, H-6), 1.18 (dd, *J* = 7.1, 4.7 Hz, 1H, H-3'), 0.91-0.82 (m, 1H, H-7'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.0 (C-4), 138.9 (C-Ar), 137.2 (C-Ar), 129.4 (C-Ar), 128.5 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 126.8 (C-Ar), 72.9 (C-11), 70.5 (C-10), 60.8 (C-5), 32.2 (C-2), 30.6 (C-1), 29.9 (C-7), 28.5 (C-8), 24.3 (C-9), 18.1 (C-3), 14.4 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{23}H_{29}O_3$ requires 370.2377; found, 370.2376; **GC-MS** (40-300 °C, 20 °C/min): t_R = 12.973 min.

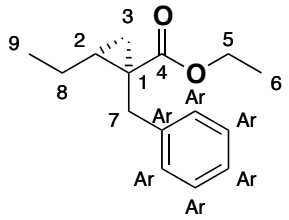
(1*R*,2*S*)-Ethyl 1-benzyl-2-methylcyclopropanecarboxylate (1*R*,2*S*)-**57k**



Prepared according to **Route E** from 2-benzyltriethylphosphonoacetate (630 mg, 2.00 mmol, 2.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**57k** as a colourless oil (172 mg,

79%) after column chromatography (10% Et_2O/Petrol); **[α]$^{25}_D$** = +10.1° (c = 0.61, Me_2CO); **IR** (cm^{-1}) 1715, 1497, 1455, 1381, 1303, 1195, 1136, 1097, 1029; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23-7.08 (m, 5H, H-Ar), 4.01-3.84 (m, 2H, H-5), 3.14 (d, *J* = 15.1 Hz, 1H, H-7), 2.71 (d, *J* = 15.1 Hz, 1H H-7'), 1.60-1.51 (m, 1H, H-2), 1.43 (dd, *J* = 9.1, 4.1 Hz, 1H, H-3), 1.13 (d, *J* = 6.6 Hz, 3H, H-8), 1.04 (t, *J* = 7.1 Hz, 3H, H-6), 0.48 (dd, *J* = 6.6, 4.1 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.0 (C-4), 140.7 (C-Ar), 128.5 (C-Ar), 128.1 (C-Ar), 125.7 (C-Ar), 60.5 (C-5), 33.4 (C-7), 27.7 (C-1), 22.3 (C-3), 21.9 (C-2), 14.1 (C-8), 14.1 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{19}O_2$ requires 219.1380; found, 219.1377; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.056 min.

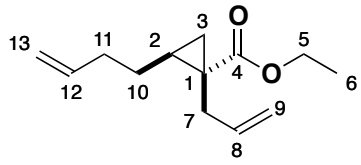
(1*S*,2*R*)-Ethyl 1-benzyl-2-ethylcyclopropanecarboxylate (1*S*,2*R*)-**57l**



Prepared according to **Route E** from 2-benzyltriethylphosphonoacetate (630 mg, 2.00 mmol, 2.0 equiv) and (*S*)-1,2-epoxybutane (87 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*R*)-**57i** as a colourless oil (177 mg, 76%); **[α]$^{25}_D$** = −3.24° (c = 0.50, Me_2CO); **IR** (cm^{-1}) 1730, 1600, 1493, 1453, 1261, 1229, 1208, 1178, 1156, 1074, 1029; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20-7.05 (m, 5H, H-Ar), 4.01-3.90 (m, 2H, H-5), 3.25 (d, *J* = 15.3 Hz, 1H, H-7), 2.59 (d, *J* = 15.3 Hz, 1H, H-7'), 1.55-1.36 (m, 3H, H-2, H-3 and H-8), 1.35-1.25 (m, 1H, H-8'), 1.04 (t, *J* = 7.1 Hz, 3H, H-6), 0.96 (t, *J* = 7.1 Hz, 3H, H-9), 0.52-0.48 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.4 (C-4), 140.8 (C-Ar), 128.6 (C-Ar), 128.1 (C-Ar), 125.8 (C-Ar), 60.5 (C-5), 33.4 (C-7), 29.8 (C-2), 28.1 (C-1), 22.8 (C-8), 21.0 (C-3), 14.1 (C-6), 13.9 (C-9); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{21}O_2$ requires 233.1536; found,

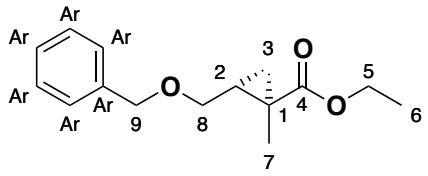
233.1534; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 8.253 min, t_R (major, 98%) = 8.482 min.

(1*S**,2*S**)-Ethyl 1-allyl-2-(but-3-enyl)cyclopropanecarboxylate (1*S**,2*S**)-**57m**



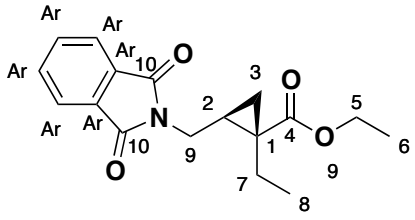
Prepared according to **Route E** from 2-allyl triethylphosphonoacetate (530 mg, 2.00 mmol, 2.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**57m** as a colourless oil (179 mg, 86%); **IR** (cm^{-1}) 1718, 1307, 1209, 1157; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.91-5.69 (m, 2H, H-8 and H-12), 5.02- 4.85 (m, 4H, H-9 and H-13), 4.03 (qd, *J* = 7.1, 1.7 Hz, 2H, H-5), 2.48 (dd, *J* = 15.4, 6.2 Hz, 1H, H-7), 2.15-2.03 (m, 3H, H-7' and H-11), 1.62-1.50 (m, 1H, H-10), 1.47-1.37 (m, 1H, H-2), 1.36-1.27 (m, 2H, H-3 and H-10'), 1.16 (t, *J* = 7.1 Hz, 3H, H-6), 0.36 (dd, *J* = 6.7, 4.1 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.2 (C-4), 138.1 (C-8), 136.6 (C-12), 115.6 (C-9), 114.9 (C-13), 60.5 (C-5), 33.7 (C-11), 32.7 (C-7), 28.6 (C-10), 27.2 (C-2), 26.9 (C-1), 20.8 (C-3), 14.0 (C-6); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{21}O_2$ requires 209.1536; found, 209.1530; **GC-MS** (40-300 °C, 20 °C/min): t_R = 6.783 min.

(1*R*,2*R*)-Ethyl 2-(benzyloxymethyl)-1-methylcyclopropanecarboxylate (1*R*,2*R*)-**57n**



Prepared according to **Route E** from triethyl 2-phosphonopropionate (476 mg, 2.00 mmol, 2.0 equiv) and (*R*)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*R*)-**57n** as a colourless oil (194 mg, 78%); $[\alpha]^{25}_{D} = -60.6°$ (c = 1.74, Me_2CO); **IR** (cm^{-1}) 1717, 1456, 1369, 1323, 1308, 1279, 1178, 1153, 1078, 1030; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 4H, H-Ar), 7.32-7.26 (m, 1H, H-Ar), 4.55 (d, *J* = 12.2 Hz, 1H, H-9), 4.51 (d, *J* = 12.2 Hz, 1H, H-9'), 4.09 (dq, *J* = 7.1, 1.8 Hz, 2H, H-5), 3.65 (dd, *J* = 10.6, 5.8 Hz, 1H, H-8), 3.37 (dd, *J* = 10.6, 8.6 Hz, 1H, H-8'), 1.86 (m, 1H, H-2), 1.40 (dd, *J* = 9.3, 4.3 Hz, 1H, H-3), 1.31 (s, 3H, H-7), 1.24 (t, *J* = 7.1 Hz, 3H, H-6), 0.54 (dd, *J* = 6.3, 4.3 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.6 (C-4), 138.2 (C-Ar), 128.4 (C-Ar), 127.7 (C-Ar), 127.7 (C-Ar), 72.8 (C-9), 69.4 (C-8), 60.7 (C-5), 25.8 (C-2), 22.8 (C-1), 20.5 (C-3), 14.2 (C-6), 13.9 (C-7); **HRMS-CI** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{21}O_3$ requires 249.1485; found, 249.1485; **GC-MS** (40-300 °C, 20 °C/min): t_R = 9.468 min.

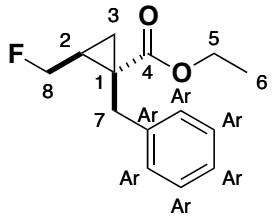
(1*S*,2*S*)-Ethyl 2-((1,3-dioxoisoindolin-2-yl)methyl)-1-ethylcyclopropanecarboxylate (1*S*,2*S*)-**57o**



Prepared according to **Route E** from triethyl 2-phosphobutyrate (505 mg, 2.00 mmol, 2.0 equiv) and (*R*)-*N*-(2,3-epoxypropyl)phthalamide (203 mg, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**57o** as a colourless

oil (172 mg, 57%); $[\alpha]^{25}_{D}$ = +60.6° (c = 0.85, Me_2CO); **IR** (cm^{-1}) 1774, 1708, 1468, 1435, 1389, 1368, 1329, 1305, 1246, 1158, 1115, 1089, 1037; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 5.4 Hz, 2H, H-Ar), 7.65 (dd, *J* = 5.4, 3.0 Hz, 2H, H-Ar), 4.01 (q, *J* = 7.2 Hz, 2H, H-5), 3.90 (dd, *J* = 14.1, 5.8 Hz, 1H, H-9), 3.50 (dd, *J* = 14.1, 9.2 Hz, 1H, H-9'), 1.92-1.82 (m, 1H, H-2), 1.81-1.72 (m, 1H, H-7), 1.69-1.59 (m, 1H, H-7'), 1.25 (dd, *J* = 9.2, 4.4 Hz, 1H, H-3), 1.14 (t, *J* = 7.2 Hz, 3H, H-6), 1.00 (t, *J* = 7.3 Hz, 3H, H-8), 0.65 (dd, *J* = 6.5, 4.4 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.3 (C-4), 168.2 (C-10), 134.0 (C-Ar), 132.1 (C-Ar), 123.3 (C-Ar), 60.6 (C-5), 37.5 (C-9), 29.4 (C-1), 25.4 (C-2), 22.0 (C-9), 19.7 (C-3), 14.2 (C-6), 12.5 (C-8); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{17}H_{20}NO_4$ requires 302.1387; found, 302.1390; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 1%) = 11.504 min, t_R (major, 99%) = 11.771 min.

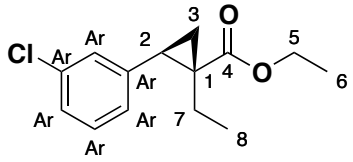
(1*R**,2*S**)-Ethyl 1-benzyl-2-(fluoromethyl)cyclopropanecarboxylate (1*R**,2*S**)-**57p**



Prepared according to **Route E** from 2-benzyltriethylphosphonoacetate (630 mg, 2.00 mmol, 2.0 equiv) and (±)-epifluorohydrin (71 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R**,2*S**)-**57o** as a colourless oil (177 mg, 75%); **IR** (cm^{-1}) 1718, 1454, 1412, 1369, 1305, 1247, 1206, 1170, 1136, 1055; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23-7.07 (m, 5H, H-Ar), 4.61 (ddd, *J* = 48.0, 10.4 and 5.7 Hz, 1H, H-8), 4.32 (ddd, *J* = 48.0, 10.4 and 9.0 Hz, 1H, H-8'), 4.07-3.94 (m, 2H, H-5), 3.30 (d, *J* = 15.9 Hz, 1H, H-7), 2.75 (d, *J* = 15.9 Hz, 1H, H-7'), 2.03-1.93 (m, 1H, H-2), 1.58-1.51 (m, 1H, H-3), 1.06 (t, *J* = 7.1 Hz, 3H, H-6), 0.84-0.76 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.9 (C-4), 139.8 (C-Ar), 128.5 (C-Ar), 128.2 (C-Ar), 126.1 (C-Ar), 82.7 (d, *J* = 16.4 Hz, C-8), 61.0 (C-5), 33.3 (C-7), 28.4

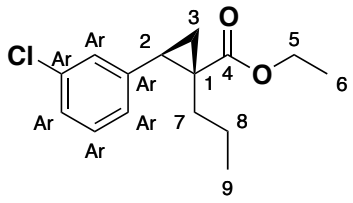
(d, J = 3.4 Hz, C-1) 26.1 (d, J = 24.2 Hz, C-2), 18.1 (d, J = 8.8 Hz, C-3), 14.0 (C-6); **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ calcd for $C_{14}H_{21}FNO_2$ requires 254.1551; found, 254.1553; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.437 min.

(1*S*,2*R*)-Ethyl 2-(3-chlorophenyl)-1-ethylcyclopropanecarboxylate (1*S*,2*R*)-**57r**



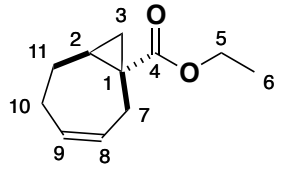
Prepared according to **Route E** from triethyl 2-phosphobutyrate (505 mg, 2.00 mmol, 2.0 equiv) and (*R*)-3-chlorostyrene oxide (127 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*R*)-**57r** as a colourless oil (185 mg, 73%); $[\alpha]^{25}_D$ = +99.0° (c = 1.39, Me_2CO); **IR** (cm^{-1}) 1716, 1313, 1241, 1154; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28-7.20 (m, 3H, H-Ar), 7.17-7.08 (m, 1H, H-Ar), 4.28-4.15 (m, 2H, H-5), 2.80 (dd, J = 8.7, 7.2 Hz, 1H, H-2), 1.71-1.61 (m, 2H, H-3 and H-7), 1.32 (t, J = 7.1 Hz, 3H, H-6), 1.16 (dd, J = 7.0, 1.8 Hz, 1H, H-3'), 0.98-0.86 (m, 4H, H-8 and H-7'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.5 (C-4), 139.4 (C-Ar), 134.1 (C-Ar), 129.4 (C-Ar), 129.3 (C-Ar), 127.6 (C-Ar), 126.9 (C-Ar), 60.8 (C-5), 31.7 (C-2), 31.5 (C-1), 21.9 (C-7), 17.9 (C-3), 14.3 (C-6), 11.7 (C-8); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{18}{}^{35}ClO_2$ requires 253.0990; found, 253.0986; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 8.704 min, t_R (major, 98%) = 9.061 min.

(1*S*,2*R*)-Ethyl 2-(3-chlorophenyl)-1-methylcyclopropanecarboxylate (1*S*,2*R*)-**57s**



Prepared according to **Route E** from triethyl 2-phosphonopentanoate (534 mg, 2.00 mmol, 2.0 equiv) and (*R*)-3-chlorostyrene oxide (127 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*R*)-**57s** as a colourless oil (123 mg, 46; $[\alpha]^{25}_D$ = +81.6° (c = 1.50, Me_2CO); **IR** (cm^{-1}) 1715, 1598, 1570, 1479, 1464, 1445, 1376, 1292, 1224, 1206, 1152, 1095, 1071, 1052, 1029; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 5.6, 5.6 Hz, 3H, H-Ar), 7.01-6.94 (m, 2H, H-Ar), 4.16-4.01 (m, 2H, H-5), 2.62 (dd, *J* = 7.8, 7.8 Hz, 1H, H-2), 1.61 (dd, *J* = 9.2, 4.5 Hz, 1H, H-3), 1.57-1.46 (m, 1H, H-7), 1.33-1.21 (m, 2H, H-8), 1.19 (t, *J* = 7.1 Hz, 3H, H-6), 1.06 (dd, *J* = 7.8, 4.8 Hz, 1H, H-3'), 0.69 (m, 1H, H-7), 0.73-0.65 (t, *J* = 7.1 Hz, 3H, H-9); ^{13}**C NMR** (100 MHz, $CDCl_3$) δ 174.5 (C-4), 139.4 (C-Ar), 134.0 (C-Ar), 129.3 (C-Ar), 127.5 (C-Ar), 126.9 (C-Ar), 60.7 (C-5), 31.4 (C-2), 31.2 (C-1), 30.8 (C-7), 30.5 (C-8), 20.7 (C-3), 17.9 (C-6), 14.2 (C-9); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{20}ClO_2$ requires 267.1151; found, 267.1149; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 1%) = 9.169 min, t_R (major, 99%) = 9.341 min.

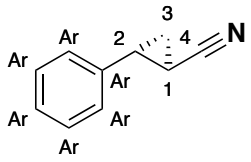
(1*R**,7*S**)-Ethyl bicyclo[5.1.0]oct-3-ene-1-carboxylate **58**



To a solution of ethyl 1-allyl-2-(but-3-enyl)cyclopropanecarboxylate (392 mg, 1.59 mmol) in CH_2Cl_2 (15.0 mL) at 25 °C was added Grubb's 1st generation catalyst (5 mol%, 66 mg, 0.08 mmol)

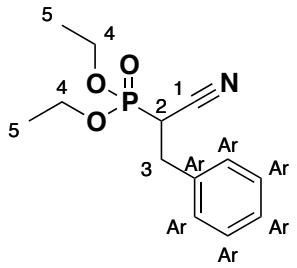
in one portion. The reaction was heated to 40 °C for 12 h. The reaction was cooled and the residue was loaded onto 5 mL of silica and purified by flash column chromatography (SiO_2, 100% Petrol) to give the *title compound* **58** as a colourless oil (161 mg, 56%): **IR** (cm^{-1}) 1715, 1447, 1305, 1194, 1153, 1037; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.67-5.57 (m, 1H), 5.42-5.34 (m, 1H), 4.02 (q, *J* = 7.1 Hz, 2H, H-5), 2.79 (dd, *J* = 16.2, 8.1 Hz, 1H, H-7), 2.28-2.20 (m, 2H, H-10) 1.99 (m, 2H, H-11), 1.59-1.46 (m, 2H, H-2 and H-7'), 1.32 (dd, *J* = 7.9, 3.9 Hz, 1H, H-3), 1.15 (t, *J* = 7.1 Hz, 3H, H-6), 0.67 (dd, *J* = 5.1, 3.8 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.8 (C-4), 129.6 (C-8), 127.1 (C-9), 60.4 (C-5), 30.9 (C-10), 30.9 (C-1), 28.0 (C-11), 27.9 (C-7), 26.2 (C-2), 24.7 (C-3), 14.2 (C-6); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{11}H_{17}O_2$ requires 181.1229; found, 181.1230.

(1*R*,2*R*)-2-phenylcyclopropanecarbonitrile (1*R*,2*R*)-**6a**



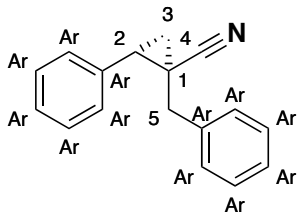
Prepared according to **Route E** from diethyl cyanomethylphosphonate (354 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 3% Et_2O in Petrol) afforded the title compound (1*R*,2*R*)-**6a** as a white solid (76 mg, 53%); **m.p.**: 74-81 °C; **$[\alpha]^{25}_D$** = -203.8° (c = 0.25, $CHCl_3$); **IR** (cm^{-1}) 2237, 1605, 1500, 1461, 1077, 1056, 1033; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.23 (m, 3H, H-Ar), 7.13-7.09 (m, 2H, H-Ar), 2.67-2.60 (m, 1H, H-2), 1.65-1.60 (m, 1H, H-3), 1.58-1.53 (m, 1H, H-1), 1.49-1.42 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.7 (C-4), 128.9 (C-Ar), 127.5 (C-Ar), 126.5 (C-Ar), 121.2 (C-Ar), 25.0 (C-2), 15.4 (C-3), 6.8 (C-1); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{10}H_{10}N$ requires 144.0808; found, 144.0805; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 86%) = 6.650 min, t_R (minor, 14%) = 6.929 min; **HPLC** (IC, 1% THF in Hexane, 1 mL/min): t_R = 54.057 min.

Diethyl (1-cyano-2-phenylethyl)phosphonate **3b**



Prepared according to **Route A** from diethyl (cyanomethyl)phosphonate (1.77 g, 10.0 mmol). Flash column chromatography (SiO_2, 30% EtOAc in Petrol) afforded the title compound **3b** as a colourless oil (2.19 mg, 82%); **IR** (cm^{-1}) 2245, 1500, 1480, 1459, 1448, 1396, 1373, 1259, 1165, 1100, 1013; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H, H−Ar), 4.31-4.19 (m, 4H, H−4), 3.33-3.22 (m, 1H, H−2), 3.18-3.00 (m, 2H, H−3), 1.39 (t, *J* = 7.1 Hz, 3H, H−5), 1.37 (t, *J* = 7.1 Hz, 3H, H−5'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.4 (d, *J* = 13.4 Hz, C-4), 129.0 (C-Ar), 129.0 (C-Ar), 127.8 (C-Ar), 116.0 (d, *J* = 9.0 Hz, C-Ar), 64.4 (d, *J* = 7.1 Hz, C-4), 64.0 (d, *J* = 7.0 Hz, C-4), 33.2 (d, *J* = 3.8 Hz, C-3), 32.8 (d, *J* = 140.8 Hz, C-2), 16.5 (d, *J* = 2.4 Hz, C-5), 16.5 (d, *J* = 2.6 Hz, C-5); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 17.2; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{19}O_3NP$ requires 268.1097; found, 268.1092; **GC-MS** (40-300 °C, 20 °C/min): t_R = 9.713 min.

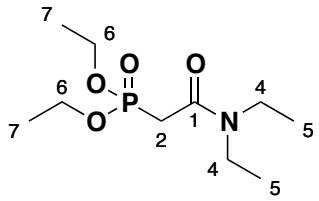
(1*S*,2*S*)-1-Benzyl-2-phenylcyclopropanecarbonitrile (1*S*,2*S*)-**59a**



Prepared according to **Route E** from diethyl (1-cyano-2-phenylethyl)phosphonate (267 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 3% Et_2O in Petrol) afforded the title compound (1*S*,2*S*)-**59a** as a white solid (81 mg, 35%); **m.p.**: 78-83 °C; **$[\alpha]^{25}_D$** = −65.9° (c = 0.65, $CHCl_3$); **IR** (cm^{-1}) 2232, 1602, 1498,

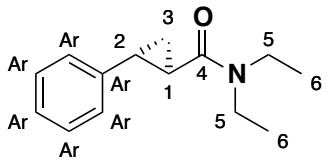
1496, 1455, 1449, 1434, 1377, 1092, 1076, 1062, 1034, 1030. 1005; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 3H, H-Ar), 7.30-7.21 (m, 5H, H-Ar), 7.11-7.07 (m, 2H, H-Ar), 2.97 (dd, *J* = 9.3, 7.9 Hz, 1H, H-2), 2.74 (d, *J* = 15.1 Hz, 1H, H-5), 2.22 (d, *J* = 15.1 Hz, 1H, H-5'), 1.74 (ddd, *J* = 9.3, 5.9 Hz, 1H, H-3), 1.52 (dd, *J* = 7.9, 5.9 Hz, 1H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.2 (C-Ar), 134.2 (C-4), 129.4 (C-Ar), 128.9 (C-Ar), 128.8 (C-Ar), 128.7 (C-Ar), 127.9 (C-Ar), 127.2 (C-Ar), 123.7 (C-Ar), 35.6 (C-5), 30.8 (C-2), 17.4 (C-3), 17.4 (C-1); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{17}H_{16}N$ requires 234.1277; found, 234.1272; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 86%) = 10.339 minutes, t_R (minor, 14%) = 10.537 minutes; **HPLC** (IC, 3% THF in Hexane, 1 mL/min): t_R (minor, 1%) = 19.762 min, t_R (major, 99%) = 21.128 min.

Diethyl 2-(diethylamino)-2-oxoethylphosphonate **60a**



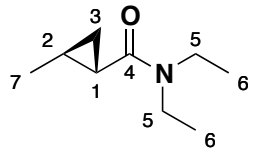
Prepared according to **Route C** from 2-chloro-*N*,*N*-diethylacetamide (599 mg, 4.00 mmol, 1.0 equiv). Distillation at reduced pressure (100 °C, < 0.1 mmHg) afforded the title compound **60a** as a colourless oil (980 mg, 98%); **IR** (cm^{-1}) 1638, 1434, 1383, 1365, 1285, 1285, 1251, 1164, 1098, 1051, 1022; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.24-4.07 (m, 4H, H-6), 3.49-3.33 (m, 4H, H-4), 3.01 (d, *J* = 22.1 Hz, 2H, H-2), 1.34 (t, *J* = 7.0 Hz, 6H, H-7), 1.20 (t, *J* = 7.1 Hz, 3H, H-5), 1.13 (t, *J* = 7.1 Hz, 3H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.0 (d, *J* = 5.8 Hz, C-1), 62.6 (d, *J* = 6.3 Hz, C-6), 43.1 (C-4), 40.5 (C-4), 33.5 (d, *J* = 134.6 Hz, C-2), 16.4 (d, *J* = 6.5 Hz, C-7), 14.2 (C-5), 13.0 (C-5); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 21.4; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{10}H_{23}NO_4P$ requires 252.1359; found, 252.1360; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.447 min.

(1*R*,2*R*)-*N*,*N*-Diethyl-2-phenylcyclopropanecarboxamide (1*R*,2*R*)-**61a**



Prepared according to **Route E** from diethyl 2-(diethylamino)-2-oxoethylphosphonate (252 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the title compound (1*R*,2*R*)-**61a** as a colourless oil (151 mg, 88%); $[\alpha]^{25}_D$ = -191.8° (c = 0.72, Me_2CO); **IR** (cm^{-1}) 1628, 1483, 1461, 1428, 1255, 1140; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 7.4, 7.4 Hz, 2H, H-Ar), 7.18 (dd, *J* = 7.4, 7.4 Hz, 1H, H-Ar), 7.12 (d, *J* = 7.4 Hz, 2H, H-Ar), 3.49- 3.35 (m, 4H, H-5), 2.51-2.44 (m, 1H, H-2), 1.96-1.88 (m, 1H, H-1), 1.68-1.62 (m, 1H, H-3), 1.28-1.22 (m, 1H, H-3), 1.18 (t, *J* = 7.1 Hz, 3H, H-6), 1.13 (t, *J* = 7.1 Hz, 3H, H-6); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.1 (C-4), 141.4 (C-Ar), 128.6 (C-Ar), 126.3 (C-Ar), 42.3 (C-5), 41.1 (C-5), 25.6 (C-2), 23.4 (C-1), 16.3 (C-3), 15.0 (C-6), 13.4 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{20}NO$ requires 218.1539; found, 218.1540; **GC-MS** (40-300 °C, 20 °C/min): t_R = 9.232 min.

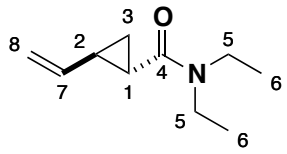
(1*S*,2*S*)-*N*,*N*-Diethyl-2-methylcyclopropanecarboxamide (1*S*,2*S*)-**61b**



Prepared according to **Route E** from diethyl 2-(diethylamino)-2-oxoethylphosphonate (252 mg, 1.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the title compound (1*S*,2*S*)-**61b** as a colourless oil (106 mg, 68%); $[\alpha]^{25}_D$ = +438.3° (c = 0.66, $CHCl_3$); **IR** (cm^{-1}) 1627, 1483, 1452, 1427, 1379, 1362, 1254, 1224, 1142, 1074, 1038; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.52-3.40 (m, 2H, H-5),

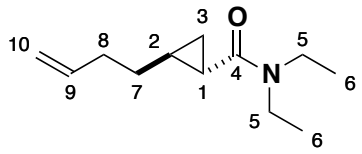
3.40-3.29 (m, 2H, H-5), 1.39-1.27 (m, 2H, H-2 and H-1), 1.22 (t, J = 7.1 Hz, 3H, H-7), 1.18-1.13 (m, 1H, H-3), 1.12-1.06 (m, 6H, H-6), 0.56-0.50 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.4 (C-4), 42.2 (C-5), 40.9 (C-5), 20.3 (C-2), 18.2 (C-6), 16.1 (C-3), 15.9 (C-1), 15.0 (C-7), 13.4 (C-6); **HRMS-CI** (*m/z*) $[M + H]^+$ calcd for $C_9H_{18}NO$ requires 156.1383; found, 156.1383; **GC-MS** (40-300 °C, 20 °C/min): t_R = 5.644 min.

(1*S**,2*R**)-*N*,*N*-Diethyl-2-vinylcyclopropanecarboxamide (1*S**,2*R**)-**61c**



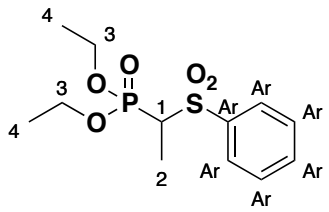
Prepared according to **Route E** from diethyl 2-(diethylamino)-2-oxoethylphosphonate (252 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**61c** as a colourless oil (120 mg, 72; **IR** (cm^{-1}) 1628, 1483, 1460, 1428, 1379, 1363, 1253, 1223, 1140, 1096, 1075; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.51-5.42 (m, 1H, H-7), 5.15 (dd, J = 17.1, 1.4 Hz, 1H, H-8), 4.96 (dd, J = 10.3, 1.4 Hz, 1H, H-8'), 3.50-3.32 (m, 4H, H-5), 2.00-1.92 (m, 1H, H-2), 1.73-1.67 (m, 1H, H-1), 1.46-1.41 (m, 1H, H-3), 1.22 (t, J = 7.2 Hz, 3H, H-6), 1.11 (t, J = 7.2 Hz, 3H, H-6), 0.91-0.85 (m, 1H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.1 (C-4), 139.4 (C-7), 114.2 (C-8), 42.3 (C-5), 41.1 (C-5), 25.0 (C-2), 21.0 (C-1), 15.0 (C-6), 14.9 (C-3), 13.4 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{10}H_{18}NO$ requires 168.1383; found, 168.1380; **GC-MS** (40-300 °C, 20 °C/min): t_R = 6.255 min.

(1*S**,2*R**)-2-(But-3-en-1-yl)-*N*,*N*-Diethylcyclopropanecarboxamide (1*S**,2*R**)-**61d**



Prepared according to **Route E** from diethyl 2-(diethylamino)-2-oxoethylphosphonate (252 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**61d** as a colourless oil (142 mg, 73%); **IR** (cm^{-1}) 1629, 1482, 1453, 1427, 1378, 1362, 1256, 1224, 1141, 1096, 1074, 1040; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.90-5.78 (m, 1H, H-9), 5.02 (dd, *J* = 17.2, 1.4 Hz, 1H, H-10), 4.95 (dd, *J* = 10.0, 1.4 Hz, 1H, H-10'), 3.46 (q, *J* = 7.1 Hz, 2H, H-5), 3.38 (q, *J* = 7.1 Hz, 2H, H-5), 2.22-2.11 (m, 2H, H-7), 1.54-1.32 (m, 4H, H-1, H-2 and H-8), 1.24 (t, *J* = 7.1 Hz, 3H, H-6), 1.20-1.15 (m, 1H, H-3), 1.11 (t, *J* = 7.1 Hz, 3H, H-6), 0.62-0.56 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.3, 138.5, 114.8, 42.2, 41.0, 33.7, 33.1, 21.6, 19.1, 15.0, 14.9, 13.4; **HRMS-ESI** (*m/z*) $[M + H]^+$ $C_{12}H_{22}NO$ requires 196.1696; found, 196.1694; **GC-MS** (40-300 °C, 20 °C/min): t_R = 7.445 min.

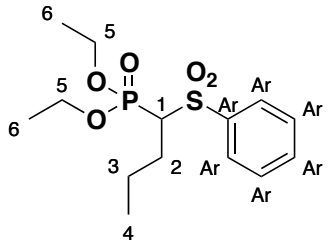
Diethyl (1-(phenylsulfonyl)ethyl)phosphonate **43b**



Prepared according to **Route D** (modified version) from diethyl ethylphosphonate (2.07 g, 12.48 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 60% EtOAc in Petrol) afforded the title compound **43b** as a colourless oil (2.55 g, 67%); **IR** (cm^{-1}) 1447, 1310, 1256, 1205, 1149, 1086, 1016; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 2H, H-Ar), 7.66 (dd, *J* = 8.1,

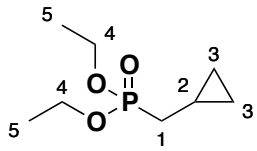
8.1 Hz, 1H, H-Ar), 7.56 (dd, *J* = 8.1, 8.1 Hz, 2H, H-Ar), 4.22-4.08 (m, 4H, H-3), 3.59 (dq, *J* = 19.0, 7.4 Hz, 1H, H-1), 1.58 (dd, *J* = 15.7, 7.4 Hz, 3H, H-2), 1.29 (t, *J* = 7.1 Hz, 6H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.4 (C-Ar), 134.1 (C-Ar), 129.5 (C-Ar), 129.0 (C-Ar), 63.4 (t, *J* = 6.7 Hz, C-3), 58.6 (d, *J* = 138.9 Hz, C-1), 16.4 (d, *J* = 6.7 Hz, C-6), 11.3 (d, *J* = 4.2 Hz, (C-2); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 16.5; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{12}H_{20}O_5PS$ requires 307.0764; found, 307.0773; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.782 min.

Diethyl (1-(phenylsulfonyl)butyl)phosphonate **43d**



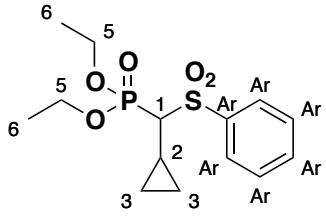
Prepared according to **Route D** (modified version) from diethyl butylphosphonate (1.94 g, 10.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 100% EtOAc) afforded the title compound **43d** as a colourless oil (1.47 g, 44%); **IR** (cm^{-1}) 1447, 1309, 1251, 1149, 1018; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.4 Hz, 2H, H-Ar), 7.66 (dd, *J* = 7.4, 7.4 Hz, 1H, H-Ar), 7.56 (dd, *J* = 7.4, 7.4 Hz, 2H, H-Ar), 4.20-4.07 (m, 4H, H-5), 3.47 (dt, *J* = 19.3, 5.4 Hz, 1H, H-1), 2.15-1.91 (m, 2H, H-2), 1.70-1.47 (m, 2H, H-3), 1.31-1.25 (m, 6H, H-6), 0.88 (t, *J* = 7.2 Hz, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.2 (C-Ar), 133.8 (C-Ar), 129.3 (C-Ar), 128.8 (C-Ar), 63.4 (d, *J* = 137.9 Hz, C-1), 63.2 (d, *J* = 6.7 Hz, C-5), 63.1 (d, *J* = 7.1 Hz, C-5), 28.0 (d, *J* = 3.2 Hz, C-2), 21.7 (d, *J* = 5.1 Hz, C-3), 16.2 (d, *J* = 6.3 Hz, C-6), 13.6 (C-4); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 16.5; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{24}O_5PS$ requires 335.1077; found, 335.1071; **GC-MS** (40-300 °C, 20 °C/min): t_R = 11.202 min.

Diethyl (cyclopropylmethyl)phosphonate **43d'**



Prepared according to **Route C** from (bromomethyl)cyclopropane (540 mg, 4.00 mmol, 1.0 equiv). Flash column chromatography (SiO2, 100% EtOAc) afforded the title compound **43d'** as a colourless oil (870 mg, 45%); **IR** (cm^{-1}) 1393, 1257, 1163, 1097, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.18-4.03 (m, 4H, H-4), 1.67 (dd, *J* = 17.7, 7.4 Hz, 2H, H-1), 1.31 (t, *J* = 7.0 Hz, 6H, H-5), 0.98-0.86 (m, 1H, H-2), 0.60-0.53 (m, 2H, H-3), 0.22-0.17 (m, 2H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 61.5 (d, *J* = 6.6 Hz, C-4), 30.9 (d, *J* = 140.3 Hz, C-1), 16.5 (d, *J* = 6.0 Hz, C-5), 5.2 (d, *J* = 10.0 Hz, C-3), 4.3 (d, *J* = 5.1 Hz, C-2); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 30.8 **HRMS-EI** (*m/z*) $[M - H]^+$ calcd for $C_8H_{16}O_3P$ requires 191.0835; found, 191.0835.

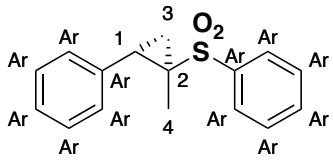
Diethyl (cyclopropyl(phenylsulfonyl)methyl)phosphonate **43e**



Prepared according to **Route D** (modified version) from (cyclopropylmethyl)phosphonate (870 mg, 4.53 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 100% EtOAc) afforded the *title compound* **43e** as a white solid (572 mg, 38%); **m.p.**: 94-100 °C; **IR** (cm^{-1}) 1453, 1308, 1251, 1187, 1148, 1086, 1033, 1008; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04-7.98 (m, 2H, H-Ar), 7.68-7.61 (m, 1H, H-Ar), 7.55 (dd, *J* = 7.2, 7.2 Hz, 2H, H-Ar), 4.32-4.15 (m, 4H, H-5), 2.76 (dd, *J* = 19.2, 11.2 Hz, 1H, H-1), 1.37-1.30 (m, 6H, H-6), 1.07-0.96 (m, 1H, H-3), 0.82-0.71 (m, 1H, H-3), 0.60-0.43 (m, 2H, H-2 and H-3), 0.30-0.21 (m, 1H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$)

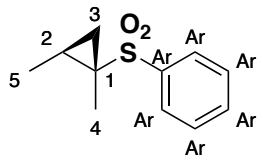
δ 139.1 (C-Ar), 134.0 (C-Ar), 129.7 (C-Ar), 128.9 (C-Ar), 69.1 (d, *J* = 140.2 Hz, C-1), 63.7 (d, *J* = 6.9 Hz, C-5), 63.3 (d, *J* = 6.3 Hz, C-5), 16.5 (d, *J* = 6.1 Hz, C-6), 8.3 (d, *J* = 2.9 Hz, C-2), 6.9 (d, *J* = 12.5 Hz, C-3), 6.1 (C-3); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 15.5; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{22}O_5PS$ requires 333.0920; found, 333.0922; **GC-MS** (40-300 °C, 20 °C/min): t_R = 11.533 min.

((1*S*,2*R*)-2-Methyl-2-(phenylsulfonyl)cyclopropyl)benzene (1*S*,2*R*)-**62a**



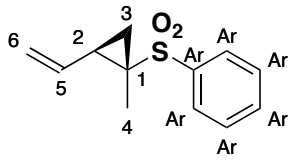
Prepared according to **Route E** from diethyl (1-(phenylsulfonyl)ethyl)phosphonate (614 mg, 2.00 mmol, 2.0 equiv), sodium hydride (48 mg, 2.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S*,2*R*)-**62a** as a white solid (250 mg, 91%); **m.p.**: 120-122 °C; **$[\alpha]^{25}_D$** = −47.1° (c = 0.92, $CHCl_3$); **IR** (cm^{-1}) 1606, 1603, 1602, 1474, 1445, 1313, 1307, 1201, 1168, 1159, 1146, 1104, 1094, 1072, 1063, 1039, 1005; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98-7.94 (m, 2H, H-Ar), 7.70 (m, 1H, H-Ar), 7.62 (dd, *J* = 7.8, 7.8 Hz, 1H, H-Ar), 7.31-7.21 (m, 3H, H-Ar), 7.08-7.03 (m, 2H, H-Ar), 3.24 (dd, *J* = 9.9, 7.1 Hz, 1H, H-1), 2.05 (dd, *J* = 9.9, 5.7 Hz, 1H, H-3), 1.30 (dd, *J* = 7.1, 5.7 Hz, 1H, H-3'), 1.03 (s, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.4 (C-Ar), 135.0 (C-Ar), 133.6 (C-Ar), 129.3 (C-Ar), 129.0 (C-Ar), 129.0 (C-Ar), 128.6 (C-Ar), 127.3 (C-Ar), 43.0 (C-2), 27.7 (C-1), 16.5 (C-3), 13.9 (C-4); **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ calcd for $C_{16}H_{20}O_2NS$ requires 290.1209; found, 290.1212; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 96%) = 11.371 min, t_R (major, 4%) = 11.568 min; **HPLC** (IB, 10% THF in Hexane, 1 mL/min): t_R (major, 98%) = 12.221 min, t_R (minor, 2%) = 14.854 min.

(((1*S*,2*S*)-1,2-Dimethylcyclopropyl)sulfonyl)benzene (1*S*,2*S*)-**62b**



Prepared according to **Route E** from diethyl (1-(phenylsulfonyl)ethyl)phosphonate (614 mg, 2.00 mmol, 2.0 equiv), sodium hydride (48 mg, 2.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**62b** as a white solid (150 mg, 71%); **m.p.**: 48-52 °C; **[α]$^{25}_D$** = +30.5° (c = 1.25, $CHCl_3$); **IR** (cm^{-1}) 1445, 1298, 1281, 1136,0 1100, 1083, 1045, 1023; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.2 Hz, 2H, H-Ar), 7.63 (ddd, *J* = 7.2, 7.2 Hz, 1H, H-Ar), 7.55 (dd, *J* = 7.2, 7.2 Hz, 2H, H-Ar), 2.03-1.93 (m, 1H, H-2), 1.70 (dd, *J* = 10.0, 5.2 Hz, 1H, H-3), 1.30 (s, 3H, H-4), 1.11 (d, *J* = 6.6 Hz, 3H, H-5), 0.47 (dd, *J* = 6.6, 5.2 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.0 (C-Ar), 133.3 (C-Ar), 129.2 (C-Ar), 128.8 (C-Ar), 40.9 (C-1), 19.7 (C-3), 17.3 (C-2), 13.0 (C-5), 12.9 (C-4); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{11}H_{15}O_2S$ requires 211.0787; found, 211.0788; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.730 min.

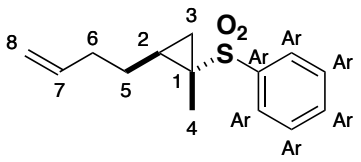
(((1*S*,2*R*)-1-Methyl-2-vinylcyclopropyl)sulfonyl)benzene (1*S*,2*R*)-**62c**



Prepared according to **Route E** from diethyl (1-(phenylsulfonyl)ethyl)phosphonate (614 mg, 2.00 mmol, 2.0 equiv), sodium hydride (48 mg, 2.00 mmol, 1.0 equiv) and (*R*)-2-vinyloxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S*,2*R*)-**62c** as a white solid (102 mg, 46%); **m.p.**: 58-64 °C; **[α]$^{25}_D$** = +7.88° (c = 0.97, $CHCl_3$); **IR** (cm^{-1}) 1446, 1298, 1277, 1213, 1190, 1137, 1072, 1023; **^{1}H NMR**

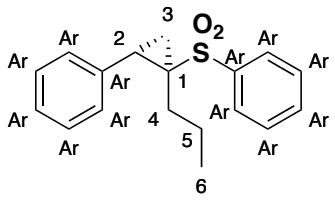
(400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 2H, H-Ar), 7.65 (dd, *J* = 7.8, 7.2 Hz, 1H, H-Ar), 7.56 (dd, *J* = 7.8, 7.2 Hz, 2H, H-Ar), 5.56-5.46 (m, 1H, H-5), 5.25 (d, *J* = 17.0 Hz, 1H, H-6), 5.18 (d, *J* = 10.2 Hz, 1H, H-6'), 2.67-2.59 (m, 1H, H-2), 1.85 (dd, *J* = 9.8, 6.1 Hz, 1H, H-3), 1.28 (s, 3H, H-4), 0.88 (t, *J* = 6.1 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.5 (C-Ar), 133.5 (C-Ar), 133.1 (C-Ar), 129.2 (C-Ar), 128.8 (C-5), 119.3 (C-6), 42.5 (C-1), 26.1 (C-2), 18.2 (C-3), 13.7 (C-4); **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ calcd for $C_{12}H_{18}O_2NS$ requires 240.1053; found, 240.1054; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 1%) = 9.042 min, t_R (major, 99%) = 9.099 min.

(1*S**,2*S**)-((2-(But-3-en-1-yl)-1-Methylcyclopropyl)sulfonyl)benzene (1*S**,2*S**)-**62d**



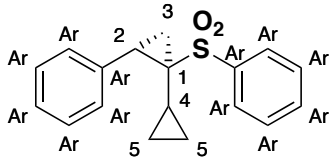
Prepared according to **Route E** from diethyl (1-(phenylsulfonyl)ethyl)phosphonate (614 mg, 2.00 mmol, 2.0 equiv), sodium hydride (48 mg, 2.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**62d** as a colourless oil (185 mg, 74%); **IR** (cm^{-1}) 1446, 1301, 1285, 1139, 1083; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.5 Hz, 2H, H-Ar), 7.64 (dd, *J* = 7.5, 7.5 Hz, 1H, H-Ar), 7.55 (dd, *J* = 7.5, 7.5 Hz, 1H, H-Ar), 5.84-5.70 (m, 1H, H-7), 5.00 (dd, *J* = 17.0, 1.6 Hz, 1H, H-8), 4.96 (dd, *J* = 10.0, 1.6 Hz, 1H, H-8'), 2.16-1.99 (m, 2H, H-6), 1.96-1.87 (m, 1H, H-2), 1.70 (dd, *J* = 9.9, 5.2 Hz, 1H, H-3), 1.52-1.37 (m, 2H, H-5), 1.31 (s, 3H, H-4), 0.52 (dd, *J* = 6.4, 5.2 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.7 (C-Ar), 137.6 (C-Ar), 133.4 (C-Ar), 129.1 (C-Ar), 128.9 (C-7), 115.4 (C-7), 41.1 (C-1), 33.4 (C-6), 27.9 (C-5), 22.6 (C-2), 18.6 (C-3), 13.2 (C-4); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{19}O_2S$ requires 251.1100; found, 251.1105; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.144 min.

(((1*R*,2*S*)-2-Phenyl-1-propylcyclopropyl)sulfonyl)benzene (1*R*,2*S*)-**62f**



Prepared according to **Route E** from diethyl (1-(phenylsulfonyl)butyl)phosphonate (668 mg, 2.00 mmol, 2.0 equiv), sodium hydride (48 mg, 2.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**62f** as a white solid (65 mg, 22%); **m.p.**: 106-118 °C; $[\alpha]^{25}_D = -16.3°$ (c = 0.59, $CHCl_3$); **IR** (cm^{-1}) 1497, 1446, 1301, 1256, 1180, 1138, 1081, 1032; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00-7.93 (m, 2H, H-Ar), 7.69 (dd, *J* = 7.8, 7.8 Hz, 1H, H-Ar), 7.61 (dd, *J* = 7.8, 7.8 Hz, 2H, H-Ar), 7.29-7.19 (m, 3H, H-Ar), 7.05-6.97 (m, 2H, H-Ar), 3.22 (dd, *J* = 10.1, 7.3 Hz, 1H, H-2), 2.07 (dd, *J* = 10.1, 6.0 Hz, 1H, H-3), 1.52-1.43 (m, 4H, H-3', H-4 and H-5), 0.95-0.84 (m, 1H, H-4'), 0.60 (t, *J* = 7.3 Hz, 3H, H-6); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.1 (C-Ar), 135.0 (C-Ar), 133.6 (C-Ar), 129.3 (C-Ar), 129.0 (C-Ar), 128.9 (C-Ar), 128.6 (C-Ar), 127.4 (C-Ar), 47.4 (C-1), 29.2 (C-3), 28.9 (C-2), 20.4 (C-4), 14.7 (C-5), 14.2 (C-6); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{20}O_2S$ requires 300.1179; found, 300.1176; **GC-MS** (40-300 °C, 20 °C/min): t_R = 12.051 min.

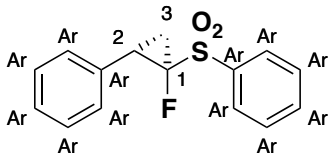
(1*S*,2*S*)-2-Phenyl-1-(phenylsulfonyl)-1,1'-bi(cyclopropane) (1*S*,2*S*)-**62g**



Prepared according to **Route E** from diethyl cyclopropyl(phenylsulfonyl)methyl)phosphonate (664 mg, 2.00 mmol, 2.0 equiv), sodium hydride (48 mg, 2.00 mmol, 1.0 equiv) and (*S*)-styrene

oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 100% CH_2Cl_2) afforded the *title compound* (1*S*,2*S*)-**62g** a white solid (56 mg, 19%); **m.p.**: 128-136 °C; $[\alpha]^{25}_D$ = -59.4° (c = 0.56, $CHCl_3$); **IR** (cm^{-1}) 1584, 1499, 1447, 1426, 1373, 1297, 1159, 1133, 1096, 1076, 1032; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.2 Hz, 2H, H-Ar), 8.02 (dd, *J* = 7.4, 7.4 Hz, 1H, H-Ar), 7.94 (dd, *J* = 7.4, 7.4 Hz, 2H, H-Ar), 7.63-7.55 (m, 3H, H-Ar), 7.48 (d, *J* = 7.2 Hz, 2H, H-Ar), 3.69 (dd, *J* = 9.9, 6.5 Hz, 1H, H-2), 2.18 (dd, *J* = 9.9, 6.5 Hz, 1H, H-3), 1.53 (d, *J* = 6.5, 6.5 Hz, 1H, H-3'), 1.13-1.04 (m, 1H, H-4), 0.77-0.68 (m, 1H, H-5), 0.49-0.41 (m, 1H, H-5), 0.34-0.25 (m, 1H, H-5), 0.15-0.07 (m, 1H, H-5); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.1 (C-Ar), 135.0 (C-Ar), 133.5 (C-Ar), 129.3 (C-Ar), 129.1 (C-Ar), 129.0 (C-Ar), 128.3 (C-Ar), 127.0 (C-Ar), 48.8 (C-1), 28.6 (C-2), 12.3 (C-3), 8.0 (C-4), 5.0 (C-5), 4.9 (C-5); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{19}O_2S$ requires 299.1100; found, 299.1102; **GC-MS** (40-300 °C, 20 °C/min): t_R = 12.388 min.

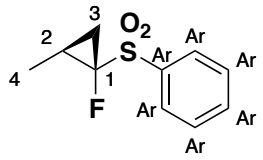
((1*S*,2*R*)-2-Fluoro-2-(phenylsulfonyl)cyclopropyl)benzene (1*S*,2*R*)-**62i**



Prepared according to **Route E** from (fluoro(phenylsulfonyl)methyl)phosphonate (310 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*R*)-**62i** as a white solid (116 mg, 42%); **m.p.**: 60-68 °C; $[\alpha]^{25}_D$ = –33.8° (c = 0.68, $CHCl_3$); **IR** (cm^{-1}) 1602, 1583, 1499, 1475, 1458, 1445, 1424, 1409, 1376, 1326, 1309, 1272, 1203, 1190, 1145, 1075, 1102, 1047, 1023; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 2H, H-Ar), 7.73 (dd, *J* = 7.8, 7.8 Hz, 1H, H-Ar), 7.62 (dd, *J* = 7.8, 7.8 Hz, 2H, H-Ar), 7.27 (d, *J* = 7.4 Hz, 3H, H-Ar), 7.08 (d, *J* = 7.4 Hz, 2H, H-Ar), 3.21 (m, 1H, H-2), 2.19 (ddd, *J* = 18.3, 10.5 and 8.1, 1H, H-3), 1.81 (ddd,

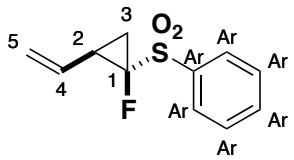
J = 18.3, 17.5 and 8.1 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.8 (C-Ar), 134.6 (C-Ar), 131.9 (d, J = 2.3 Hz, C-Ar), 129.6 (C-Ar), 129.2 (C-Ar), 128.8 (C-Ar), 128.7 (C-Ar), 127.9 (C-Ar), 91.2 (d, J = 226.9 Hz, C-1), 27.4 (d, J = 9.7 Hz, C-2), 16.1 (d, J = 9.0 Hz, C-3); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –201.2; **HRMS-ASAP** (*m/z*) $[M + NH_4]^+$ calcd for $C_{15}H_{17}O_2NFS$ requires 294.0959; found, 294.0964; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 4%) = 10.747 min, t_R (major, 96%) = 11.007 min; **HPLC** (IA, 2% MeOH in Hexane, 1 mL/min): t_R (minor, 1%) = 15.626 min, t_R (major, 99%) = 17.725 min.

(((1*S*,2*S*)-1-Fluoro-2-methylcyclopropyl)sulfonyl)benzene (1*S*,2*S*)-**62j**



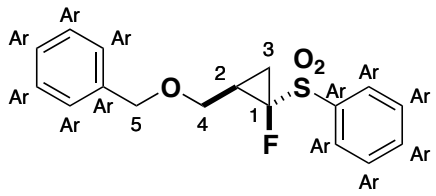
Prepared according to **Route E** from (fluoro(phenylsulfonyl)methyl)phosphonate (310 mg, 1.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**62j** as a yellow solid (91 mg, 43%); **m.p.**: 35-40 °C; **$[\alpha]^{25}_D$** = +26.7° (c = 1.14, $CHCl_3$); **IR** (cm^{-1}) 1584, 1467, 1447, 1394, 1324, 1312, 1289, 1262, 1203, 1145, 1114, 1083, 1050, 1024, 1007; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.8 Hz, 2H, H-Ar), 7.71 (dd, J = 7.8, 7.8 Hz, 1H, H-Ar), 7.60 (dd, J = 6.9, 6.9 Hz, 2H, H-Ar), 2.08-1.95 (m, 1H, H-2), 1.77 (dd, J = 18.6, 8.1 Hz, 1H, H-3), 1.20 (d, J = 6.3 Hz, 3H, H-4), 1.02 (ddd, J = 18.1, 15.5 and 8.1 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.2 (C-Ar), 134.4 (C-Ar), 129.4 (C-Ar), 129.0 (C-Ar), 92.3 (d, J = 226.7 Hz, C-1), 17.8 (d, J = 8.4 Hz, C-3), 17.7 (d, J = 9.5 Hz, C-2), 11.2 (d, J = 7.0 Hz, C-4); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –206.2; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{10}H_{12}FO_2S$ requires 215.0537; found, 215.0536; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 79%) = 7.817 min, t_R (minor, 21%) = 8.139 min.

(1*S**,2*R**)-((1-Fluoro-2-vinylcyclopropyl)sulfonyl)benzene (1*S**,2*R**)-**62k**



Prepared according to **Route E** from (fluoro(phenylsulfonyl)methyl)phosphonate (310 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**62k** as a white solid (96 mg, 42%); **m.p.**: 54-56 °C; **IR** (cm^{-1}) 1636, 1585, 1478, 1446, 1419, 1324, 1307, 1264, 1204, 1176, 1144, 1088, 1065, 1046, 1018; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 2H, H-Ar), 7.71 (dd, *J* = 7.4, 7.4 Hz, 1H, H-Ar), 7.60 (dd, *J* = 7.7, 7.7 Hz, 2H, H-Ar), 5.53-5.42 (m, 1H, H-4), 5.32 (d, *J* = 16.8 Hz, 1H, H-5), 5.21 (d, *J* = 10.2 Hz, 1H, H-5'), 2.68 (m, 1H, H-2), 1.97 (ddd, *J* = 18.1, 10.5 and 8.0 Hz, 1H, H-3), 1.41 (ddd, *J* = 19.4, 15.9 and 8.0 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.8 (C-Ar), 134.6 (C-Ar), 130.0 (d, *J* = 6.3 Hz, C-4), 129.5 (C-Ar), 129.1 (C-Ar), 119.7 (C-5), 91.7 (d, *J* = 269.2 Hz, H-1), 26.5 (d, *J* = 9.1 Hz, (C-2), 17.2 (d, *J* = 9.3 Hz, C-3); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -201.6; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{11}H_{12}FO_2S$ requires 227.0537; found, 227.0536; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 98%) = 8.240 min, t_R (minor, 2%) = 8.755 min.

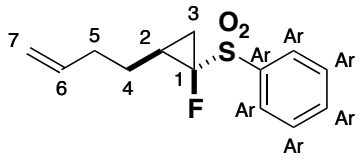
(1*S**,2*R**)-((2-((Benzyloxy)methyl)-1-fluorocyclopropyl)sulfonyl)benzene (1*S**,2*R**)-**62l**



Prepared according to **Route E** from (fluoro(phenylsulfonyl)methyl)phosphonate (310 mg, 1.00 mmol, 1.0 equiv) and (±)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column

chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**62l** as a white solid (51 mg, 16%); **m.p.**: 35-42 °C; **IR** (cm^{-1}) 1636, 1585, 1478, 1446, 1419, 1324, 1307, 1264, 1204, 1176, 1144, 1088, 1065, 1046, 1018; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.9 Hz, 2H, H-Ar), 7.69 (dd, *J* = 7.9, 7.9 Hz, 1H, H-Ar), 7.57 (dd, *J* = 7.9, 7.9 Hz, 2H, H-Ar), 7.33-7.24 (m, 3H, H-Ar), 7.17 (d, *J* = 6.5 Hz, 2H, H-Ar), 4.37 (d, *J* = 11.9 Hz, 1H, H-5), 4.33 (d, *J* = 11.9 Hz, 1H, H-4), 3.78 (dd, *J* = 11.0, 5.5 Hz, 1H, H-4'), 3.23 (dd, *J* = 7.6, 7.6 Hz, 1H, H-2), 2.36-2.24 (m, 1H, H-3), 1.90 (dd, *J* = 17.0, 8.1 Hz, 1H, H-3'), 1.27 (ddd, *J* = 19.1, 16.0 and 8.1 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.9 (C-Ar), 136.8 (C-Ar), 134.5 (C-Ar), 129.4 (C-Ar), 129.2 (C-Ar), 128.5 (C-Ar), 127.8 (C-Ar), 127.6 (C-Ar), 91.6 (d, *J* = 268.5 Hz, C-1), 72.4 (C-5), 66.0 (d, *J* = 6.5 Hz, C-4), 23.0 (d, *J* = 9.6 Hz, C-2), 14.5 (d, *J* = 9.5 Hz, C-3); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –203.5; **HRMS-ESI** (*m/z*) $[M + NH_4]^+$ calcd for $C_{17}H_{21}O_3NFS$ requires 338.1221; found, 338.1224; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 7%) = 12.133 min, t_R (major, 93%) = 12.242 min.

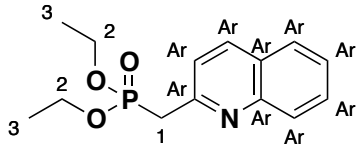
(1*S**,2*S**)-((2-(But-3-en-1-yl)-1-fluorocyclopropyl)sulfonyl)benzene (1*S**,2*S**)-**62m**



Prepared according to **Route E** from (fluoro(phenylsulfonyl)methyl)phosphonate (310 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**62m** as a colourless oil (94 mg, 37%); **IR** (cm^{-1}) 1641, 1585, 1479, 1448, 1382, 1328, 1311, 1265, 1224, 1190, 1147, 1087, 1039, 1023; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 2H, H-Ar), 7.71 (dd, *J* = 7.7, 7.7 Hz, 1H, H-Ar), 7.60 (dd, *J* = 7.7, 7.7 Hz, 2H, H-Ar), 5.77-5.66 (m, 1H, H-6), 4.96 (d, *J* = 17.9 Hz, 1H, H-7), 4.95 (d, *J* = 9.2 Hz, 1H, H-7'), 2.06-1.98 (m, 2H, H-5), 1.98-1.89 (m, 1H, H-2), 1.84-1.75 (m, 1H, H-3), 1.72-1.61 (m, 1H, H-4), 1.53-1.42 (m, 1H, H-4'), 1.10 (ddd,

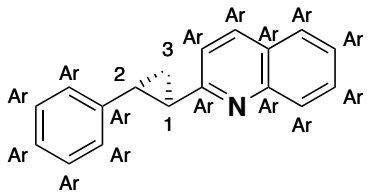
J = 18.6, 15.6 and 7.7 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.1 (C-6), 137.1 (C-Ar), 134.4 (C-Ar), 129.4 (C-Ar), 129.1 (C-Ar), 115.7 (C-7), 92.4 (d, *J* = 266.7 Hz, C-1), 33.0 (C-5), 26.0 (d, *J* = 5.1 Hz, C-4), 22.7 (d, *J* = 9.6 Hz, C-2), 16.7 (d, *J* = 8.8 Hz, C-3); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –205.4; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{16}FO_2S$ requires 255.0850; found, 255.0849; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 6%) = 9.271 min, t_R (major, 94%) = 9.353 min.

Diethyl quinolin-2-ylmethylphosphonate **65a**



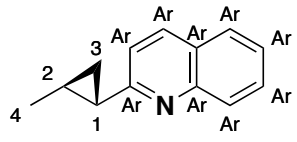
Prepared according to **Route C** from 2-(chloromethyl)quinoline hydrochloride (856.4 mg, 4.00 mmol, 1.0 equiv). Distillation at reduced pressure (100 °C, < 0.1 mmHg) afforded the title compound **65a** as a clear oil a (980 mg, 98%); **IR** (cm^{-1}) 1504, 1251, 1050, 1021; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.6 Hz, 1H, H-Ar), 7.97 (d, *J* = 8.6 Hz, 1H, H-Ar), 7.73 (d, *J* = 8.2 Hz, 1H, H-Ar), 7.63 (dd, *J* = 8.2, 8.2 Hz, 1H, H-Ar), 7.45 (dd, *J* = 8.2, 8.2 Hz, 2H, H-Ar), 4.14-4.04 (m, 4H, H-2), 3.53 (d, *J* = 22.0 Hz, 2H, H-1), 1.19 (t, *J* = 7.3 Hz, 6H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.4 (d, *J* = 8.1 Hz, C-Ar), 148.2 (d, *J* = 2.3 Hz, C-Ar), 136.6 (d, *J* = 1.8 Hz, C-Ar), 129.7 (C-Ar), 129.1 (C-Ar), 127.7 (C-Ar), 127.1 (d, *J* = 2.1 Hz, C-Ar), 126.4 (d, *J* = 1.1 Hz, C-Ar), 122.4 (d, *J* = 3.1 Hz, C-Ar), 62.4 (d, *J* = 6.5 Hz, C-2), 37.8 (d, *J* = 133.9 Hz, C-1), 16.5 (d, *J* = 6.0 Hz, C-3); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 24.7; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{19}NO_3P$ requires 280.1097; found, 280.1098; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.808 min.

2-((1*R*,2*R*)-2-Phenylcyclopropyl)quinoline (1*R*,2*R*)-**66a**



Prepared according to **Route E** from diethyl quinolin-2-ylmethylphosphonate (279 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the title compound (1*R*,2*R*)-**66a** as a clear oil (196 mg, 80%); $[\alpha]^{25}_{D} = -701.5°$ (c = 1.49, Me_2CO); **IR** (cm^{-1}) 1599, 1502, 1196; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.4, 8.4 Hz, 2H, H-Ar), 7.75 (d, *J* = 8.0 Hz, 1H, H-Ar) 7.66 (dd, *J* = 8.4, 8.4 Hz, 1H, H-Ar), 7.44 (dd, *J* = 8.0, 8.0 Hz, 1H, H-Ar), 7.29 (dd, *J* = 8.4, 8.4 Hz, 3H, H-Ar), 7.19 (dd, *J* = 8.4, 8.4 Hz, 3H, H-Ar), 2.69-2.63 (m, 1H, H-2), 2.50-2.44 (m, 1H, H-1), 2.00-1.94 (m, 1H, H-3), 1.59-1.53 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.8 (C-Ar), 148.3 (C-Ar), 142.4 (C-Ar), 135.9 (C-Ar), 129.5 (C-Ar), 129.0 (C-Ar), 128.6 (C-Ar), 127.7 (C-Ar), 127.0 (C-Ar), 126.1 (C-Ar), 126.0 (C-Ar), 125.4 (C-Ar), 120.6 (C-Ar), 30.4 (C-1), 29.2 (C-2), 19.5 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{16}N$ requires 246.1277; found, 246.1278; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 97%) = 10.641 min, t_R (minor, 3%) = 11.825 min; **HPLC** (IA, 1% THF in Hexane, 1 mL/min): t_R (major, 99%) = 16.058 min, t_R (minor, 1%) = 26.731 min.

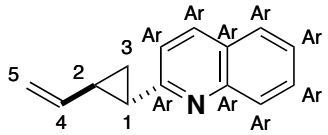
2-((1*S*,2*S*)-2-Methylcyclopropyl)quinoline (1*S*,2*S*)-**66b**



Prepared according to **Route E** from diethyl quinolin-2-ylmethylphosphonate (279 mg, 1.00 mmol, 1.0 equiv) and (*R*)-Propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**66b** as a colourless oil (90 mg, 49%);

IR (cm^{-1}) 1618, 1600, 1561, 1503, 1440, 1425, 1215, 1180, 1141, 1117, 1077, 1060, 1033; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 1H, H-Ar), 7.86 (d, *J* = 8.4 Hz, 1H, H-Ar), 7.63 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.54 (dd, *J* = 8.0, 1.4 Hz, 1H, H-Ar), 7.32 (dd, *J* = 8.0, 1.4 Hz, 1H, H-Ar), 7.30 (d, *J* = 8.4 Hz, 1H, H-Ar), 1.89-1.82 (m, 1H, H-1), 1.49-1.38 (m, 1H, H-2), 1.30-1.23 (m, 1H, H-3), 1.17 (d, *J* = 5.9 Hz, 3H, H-4), 0.84-0.77 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.5 (C-Ar), 148.2 (C-Ar), 135.8 (C-Ar), 129.3 (C-Ar), 128.8 (C-Ar), 127.5 (C-Ar), 126.8 (C-Ar), 125.2 (C-Ar), 119.5 (C-Ar), 22.7 (C-1), 19.2 (C-2), 18.9 (C-4), 18.8 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{16}N$ requires 184.1121; found, 184.1124; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 13%) = 8.147 min, t_R (major, 87%) = 8.207 min.

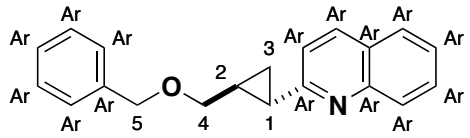
2-((1*S**,2*R**)-2-Vinylcyclopropyl)quinoline (1*S**,2*R**)-**66c**



Prepared according to **Route E** from diethyl quinolin-2-ylmethylphosphonate (279 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**66c** as a brown oil (35 mg, 18%). Major diastereomer: **IR** (cm^{-1}) 1635, 1617, 1599, 1504, 1425, 1210, 1173; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.6 Hz, 1H, H-Ar), 7.96 (d, *J* = 8.6 Hz, 1H, H-Ar), 7.74 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.64 (dd, *J* = 8.3, 1.3 Hz, 1H, H-Ar), 7.43 (dd, *J* = 8.0, 1.3 Hz, 1H, H-Ar), 7.23 (d, *J* = 8.3 Hz, 1H, H-Ar), 5.67-5.57 (m, 1H, H-4), 5.17 (dd, *J* = 17.0, 1.1 Hz, 1H, H-5), 4.98 (dd, *J* = 10.3, 1.1 Hz, 1H, H-5'), 2.28-2.22 (m, 1H, H-1), 2.22-2.15 (m, 1H, H-2), 1.74-1.67 (m, 1H, H-3), 1.27-1.19 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.8 (C-Ar), 148.3 (C-4), 140.3 (C-Ar), 135.9 (C-Ar), 129.5 (C-Ar), 129.0 (C-Ar), 127.6 (C-Ar), 126.9 (C-Ar), 125.4 (C-Ar), 120.3

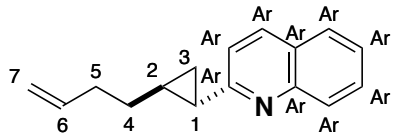
(C-Ar), 113.4 (C-5), 28.4 (C-1), 27.7 (C-2), 17.8 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{16}N$ requires 196.1121; found, 196.1122; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.843 min.

2-((1*S**,2*S**)-2-((Benzyloxy)methyl)cyclopropyl)quinoline (1*S**,2*S**)-**66d**



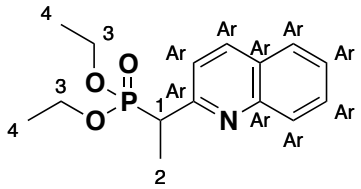
Prepared according to **Route E** from diethyl quinolin-2-ylmethylphosphonate (279 mg, 1.00 mmol, 1.0 equiv) and (±)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 20% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**66d** as a yellow oil (88 mg, 30%). Major diastereomer: **IR** (cm^{-1}) 1617, 1600, 1561, 1504, 1453, 1425, 1361, 1203, 1176, 1139, 1073, 1028; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.6 Hz, 1H, H-Ar), 7.97 (d, *J* = 8.6 Hz, 1H, H-Ar), 7.74 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.65 (dd, *J* = 8.0, 1.3 Hz, 1H, H-Ar), 7.43 (dd, *J* = 8.0, 1.3 Hz, 1H, H-Ar), 7.39-7.31 (m, 4H, H-Ar), 7.30-7.27 (m, 1H, H-Ar), 7.20 (d, *J* = 8.5 Hz, 1H, H-Ar), 4.58 (s, 2H, H-5), 3.58 (dd, *J* = 6.6, 3.1 Hz, 2H, H-4), 2.22-2.14 (m, 1H, H-1), 2.00-1.90 (m, 1H, H-2), 1.50-1.43 (m, 1H, H-3), 1.13-1.06 (m, 1H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3 (C-Ar), 138.7 (C-Ar), 129.5 (C-Ar), 128.5 (C-Ar), 128.2 (C-Ar), 127.8 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.9 (C-Ar), 125.4 (C-Ar), 119.9 (C-Ar), 73.1 (C-4), 72.7 (C-5), 24.1 (C-1), 23.8 (C-2), 15.4 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{20}NO$ requires 290.1539; found, 290.1546; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 18%) = 12.253 min, t_R (major, 82%) = 12.746 min.

2-((1*S**,2*S**)-2-(But-3-en-1-yl)cyclopropyl)quinoline (1*S**,2*S**)-**66e**



Prepared according to **Route E** from diethyl quinolin-2-ylmethylphosphonate (279 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv); Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**66e** as a yellow oil (110 mg, 49%). Major diastereomer: **IR** (cm^{-1}) 1618, 1601, 1562, 1504, 1446, 1178; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.3, 8.3 Hz, 2H, H-Ar), 7.73 (d, *J* = 8.3 Hz, 1H, H-Ar), 7.64 (dd, *J* = 6.9, 1.2 Hz, 1H, H-Ar), 7.42 (dd, *J* = 6.9, 1.2 Hz, 1H, H-Ar), 7.14 (d, *J* = 8.3 Hz, 1H, H-Ar), 5.94-5.83 (m, 1H, H-6), 5.02 (dd, *J* = 17.1, 1.7 Hz, 1H, H-7), 4.96 (dd, *J* = 10.2, 1.7 Hz, 1H, H-7'), 2.26-2.21 (m, 2H, H-5), 2.04-1.97 (m, 1H, H-1), 1.67-1.57 (m, 1H, H-4), 1.56-1.47 (m, 2H, H-2 and H-4'), 1.43-1.34 (m, 1H H-3), 0.98-0.91 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.4 (C-Ar), 138.7 (C-6), 135.9 (C-Ar), 129.4 (C-Ar), 128.8 (C-Ar), 127.6 (C-Ar), 126.8 (C-Ar), 125.2 (C-Ar), 119.6 (C-Ar), 114.7 (C-7), 33.8 (C-4), 33.8 (C-5), 26.1 (C-1), 24.8 (C-2), 17.5 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{16}H_{18}N$ requires 224.1434; found, 224.1438; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 8%) = 9.484 min, t_R (major, 92%) = 9.747 min.

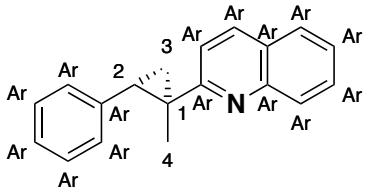
Diethyl (1-(quinolin-2-yl)ethyl)phosphonate **65b**



Prepared according to **Route A** from diethyl quinolin-2-ylmethylphosphonate (2.53 g, 9.10 mmol). Flash column chromatography (SiO_2, 30% EtOAc in Petrol) afforded the *title compound* **65b** as a yellow oil (2.35 g, 88%); **IR** (cm^{-1}) 1601, 1505, 1248, 1054, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$)

δ 8.12 (d, *J* = 8.7 Hz, 1H, H-Ar), 8.05 (d, *J* = 8.4 Hz, 1H, H-Ar), 7.80 (d, *J* = 7.9 Hz, 1H, H-Ar), 7.69 (ddd, *J* = 8.4, 7.1 and 1.4 Hz, 1H, H-Ar), 7.60 (dd, *J* = 8.7, 1.4 Hz, 1H, H-Ar); 7.51 (dd, *J* = 7.9, 7.1 Hz, 1H, H-Ar), 4.19-3.88 (m, 4H, H-3), 3.68 (dq, *J* = 22.7, 7.4 Hz, 1H, H-1), 1.72 (dd, *J* = 18.3, 7.4 Hz, 3H, H-2), 1.29 (t, *J* = 7.1 Hz, 3H, H-4), 1.16 (t, *J* = 7.1 Hz, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.7 (d, *J* = 5.2 Hz, C-Ar), 148.0 (d, *J* = 1.4 Hz, C-Ar), 136.5 (d, *J* = 1.5 Hz, C-Ar), 129.6 (C-Ar), 129.3 (C-Ar), 127.7 (C-Ar), 127.3 (d, *J* = 1.8 Hz, C-Ar), 126.4 (C-Ar), 121.2 (d, *J* = 5.2 Hz, C-Ar), 62.4 (d, *J* = 4.1 Hz, C-3), 62.4 (d, *J* = 3.9 Hz, C-3), 42.3 (d, *J* = 134.3 Hz, (C-1), 16.6 (d, *J* = 5.6 Hz, (C-4), 16.4 (d, *J* = 5.9 Hz, (C-4), 14.9 (d, *J* = 5.6 Hz, (C-2); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 28.5; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{21}NO_3P$ requires 294.1254; found, 294.1254; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.846 min.

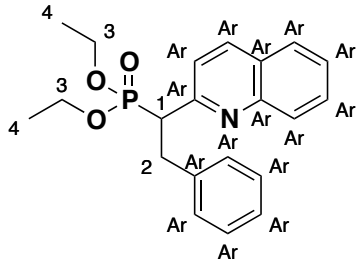
2-((1*R*,2*S*)-1-Methyl-2-phenylcyclopropyl)quinoline (1*R*,2*S*)-**67a**



Prepared according to **Route E** from diethyl (1-(quinolin-2-yl)ethyl)phosphonate (293 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 3% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**67a** as a white solid (106 mg, 41%); **m.p.**: 106-111 °C; **$[\alpha]^{25}_D$** = –447.3° (c = 0.73, $CHCl_3$); **IR** (cm^{-1}) 1598, 1499, 1451, 1425, 1317, 1140, 1043, 1030, 1017; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.5 Hz, 1H, H-Ar), 8.02 (d, *J* = 8.5 Hz, 1H, H-Ar), 7.78 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.67 (dd, *J* = 8.5, 6.9 Hz, 1H, H-Ar), 7.52 (d, *J* = 8.5 Hz, 1H), 7.46 (dd, *J* = 8.1, 6.9 Hz, 1H, H-Ar), 7.36 - 7.20 (m, 5H, H-Ar), 2.90 (dd, *J* = 8.9, 6.9 Hz, 1H, H-2), 2.1 (dd, *J* = 8.9, 4.5 Hz, 1H, H-3), 1.40 (dd, *J* = 6.9, 4.5 Hz, 1H, H-3'), 1.33 (s, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.3 (C-Ar), 148.0 (C-Ar), 139.1 (C-Ar),

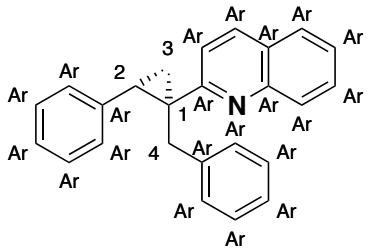
136.0 (C-Ar), 129.5 (C-Ar), 129.4 (C-Ar), 129.2 (C-Ar), 128.2 (C-Ar), 127.5 (C-Ar), 126.6 (C-Ar), 126.3 (C-Ar), 125.5 (C-Ar), 118.6 (C-Ar), 34.1, 28.2, 21.1, 17.8; **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{19}H_{18}N$ requires 260.1434; found, 260.1432; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 6%) = 10.706 min, t_R (major, 94%) = 11.666 min; **HPLC** (IA, 1% THF in Hexane, 1 mL/min): t_R (major, 99%) = 7.696 min, t_R (minor, 1%) = 17.221 min.

Diethyl (2-phenyl-1-(quinolin-2-yl)ethyl)phosphonate **65c**



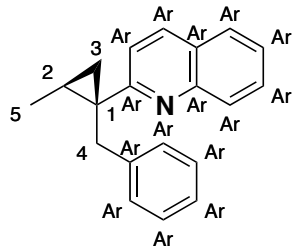
Prepared according to **Route A** from diethyl quinolin-2-ylmethylphosphonate (1.09 g, 3.89 mmol). Flash column chromatography (SiO_2, 30% EtOAc in Petrol) afforded the *title compound* **65c** as a yellow oil (1.29 g, 90%); **IR** (cm^{-1}) 1599, 1503, 1245, 1050, 1022; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.7 Hz, 2H, H-Ar), 7.76 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.67 (ddd, *J* = 8.1, 7.5 and 7.5 Hz, 1H, H-Ar), 7.50 (d, *J* = 7.5 Hz, 1H, H-Ar), 7.46 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.12-7.08 (m, 4H, H-Ar), 7.08-7.02 (m, 1H, H-Ar), 4.19-3.83 (m, 4H, H-3), 3.96-3.83 (m, 1H, H-1), 3.70-3.59 (m, 1H, H-2), 3.57-3.48 (m, 1H, H-2'), 1.27 (t, *J* = 7.1 Hz, 3H, H-4), 1.15 (t, *J* = 7.1 Hz, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.6 (d, *J* = 6.3 Hz, C-Ar), 148.0 (d, *J* = 2.1 Hz, C-Ar), 139.4 (C-Ar), 139.3 (C-Ar), 136.3 (d, *J* = 1.2 Hz, C-Ar), 129.5 (C-Ar), 129.3 (C-Ar), 129.0 (C-Ar), 127.7 (C-Ar), 127.7 (d, *J* = 2.0 Hz, C-Ar), 127.2 (d, *J* = 4.1 Hz, C-Ar), 126.3 (d, *J* = 4.1 Hz, C-Ar), 122.2 (d, *J* = 3.7 Hz, C-Ar), 62.6 (d, *J* = 6.7 Hz, C-3), 62.5 (d, *J* = 6.8 Hz, C-3), 49.8 (d, *J* = 131.9 Hz, C-1), 35.0 (d, *J* = 3.6 Hz, C-2), 16.5 (d, *J* = 6.0 Hz, C-4), 16.4 (d, *J* = 6.0 Hz, C-4); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 26.6; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{21}H_{25}NO_3P$ requires 370.1567; found, 370.1567; **GC-MS** (40-300 °C, 20 °C/min): t_R = 13.215 min.

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)quinoline (1*S*,2*S*)-**67b**



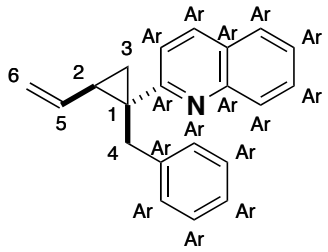
Prepared according to **Route E** from diethyl (2-phenyl-1-(quinolin-2-yl)ethyl)phosphonate (370 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 2% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**67b** as a white solid (243 mg, 72%); **m.p.**: 116-122 °C; **[α]$^{25}_{D}$ =** –208.0° (c = 1.98, $CHCl_3$); **IR** (cm^{-1}) 1619, 1598, 1495, 1425, 1448, 1319, 1302, 1187, 1154, 1136, 1082, 1045, 1035; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.94 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.72 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.66 (dd, *J* = 7.0, 7.0 Hz, 1H, H-Ar), 7.45 (dd, *J* = 7.0, 7.0 Hz, 1H, H-Ar), 7.38-7.31 (m, 5H, H-Ar), 7.29-7.23 (m, 2H, H-Ar), 7.11 (d, *J* = 4.2 Hz, 1H, H-Ar), 7.09-7.03 (m, 1H, H-Ar), 3.47 (d, *J* = 16.6, 1H, H-4), 2.84 (t, *J* = 8.7 Hz, 1H, H-2), 2.55 (d, *J* = 16.6 Hz, 1H, H-4'), 2.48-2.42 (m, 1H, H-3), 1.69-1.64 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.8 (C-Ar), 148.1 (C-Ar), 140.2 (C-Ar), 138.7 (C-Ar), 135.7 (C-Ar), 129.4 (C-Ar), 129.3 (C-Ar), 129.3 (C-Ar), 128.9 (C-Ar), 128.4 (C-Ar), 128.2 (C-Ar), 127.5 (C-Ar), 126.5 (C-Ar), 125.8 (C-Ar), 125.6 (C-Ar), 119.7 (C-Ar), 36.3 (C-2), 34.8 (C-4), 32.9 (C-1), 19.1 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{25}H_{22}N$ requires 336.1747; found, 336.1750; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 6%) = 13.412 min, t_R (major, 94%) = 13.978 min; **HPLC** (IA, 3% THF in Hexane, 1 mL/min): t_R (major, 99%) = 6.823 min, t_R (minor, 1%) = 9.283 min.

2-((1*R*,2*S*)-1-Benzyl-2-methylcyclopropyl)quinoline (1*R*,2*S*)-**67c**



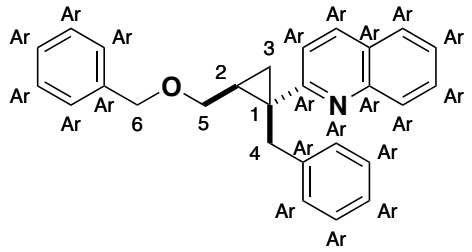
Prepared according to **Route E** from diethyl (2-phenyl-1-(quinolin-2-yl)ethyl)phosphonate (370 mg, 1.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μl, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 3% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**67c** as a yellow oil (228 mg, 83%). Major diastereomer: **IR** (cm^{-1}) 1618, 1598, 1558, 1502, 1453, 1426, 1314, 1141, 1114, 1096, 1075, 1030; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.5 Hz, 1H, H-Ar), 7.87 (d, *J* = 8.5 Hz, 1H, H-Ar), 7.69 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.64 (dd, *J* = 8.1, 8.1 Hz, 1H, H-Ar), 7.42 (dd, *J* = 7.5, 7.5 Hz, 1H, H-Ar), 7.28-7.22 (m, 3H, H-Ar), 7.18 (dd, *J* = 7.5, 7.5 Hz, 2H, H-Ar), 7.19 (dd, *J* = 7.5, 7.5 Hz, 1H, H-Ar), 3.54 (d, *J* = 16.5 Hz, 1H, H-4), 3.31 (d, *J* = 16.5 Hz, 1H, H-4'), 1.81 (s, 2H, H-2 and H-3), 1.37 (b, 3H, H-5), 0.78 (s, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.9 (C-Ar), 148.0 (C-Ar), 140.6 (C-Ar), 135.4 (C-Ar), 129.2 (C-Ar), 129.1 (C-Ar), 129.0 (C-Ar), 128.2 (C-Ar), 127.4 (C-Ar), 126.4 (C-Ar), 125.8 (C-Ar), 125.4 (C-Ar), 119.8 (C-Ar), 36.3 (C-4), 29.9 (C-1), 23.9 (C-3), 22.9 (C-2), 14.8 (C-5); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{16}N$ requires 274.1590; found, 274.1591; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 22%) = 11.251 min, t_R (major, 78%) = 11.574 min.

2-((1*R**,2*R**)-1-Benzyl-2-vinylcyclopropyl)quinoline (1*R**,2*R**)-**67d**



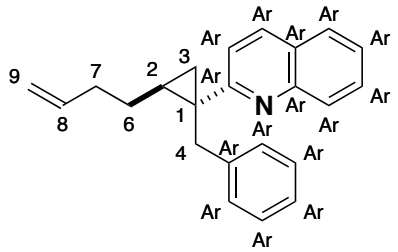
Prepared according to **Route E** from diethyl (2-phenyl-1-(quinolin-2-yl)ethyl)phosphonate (370 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 3% Et_2O in Petrol) afforded the *title compound* (1*R**,2*R**)-**67d** as a yellow oil (40 mg, 18%). Major diastereomer: **IR** (cm^{-1}) 1633, 1618, 1598, 1558, 1502, 1453, 1426, 1309, 1189, 1138, 1113, 1076, 1031; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.9 Hz, 1H, H-Ar), 7.8 (d, *J* = 8.9 Hz, H-Ar), 7.71 (dd, *J* = 8.9, 8.9 Hz, 1H, H-Ar), 7.65 (dd, *J* = 7.3, 7.3 Hz, 1H, H-Ar), 7.43 (dd, *J* = 7.3, 7.3 Hz, 1H, H-Ar), 7.26 (dd, *J* = 8.9, 8.9 Hz, 3H, H-Ar), 7.18 (dd, *J* = 7.3, 7.3 Hz, 1H, H-Ar), 7.11 (dd, *J* = 7.3, 7.3 Hz, 1H, H-Ar), 6.03-5.90 (m, 1H, H-5), 5.29 (d, *J* = 16.9 Hz, 1H, H-6), 5.19 (d, *J* = 10.3 Hz, 1H, H-6'), 3.55 (d, *J* = 16.6 Hz, 1H, H-4), 3.27 (d, *J* = 16.6 Hz, 1H, H-4'), 2.45 (dd, *J* = 15.7, 8.7 Hz, 1H, H-2), 2.11 (dd, *J* = 8.7, 4.1 Hz, 1H, H-3), 1.24 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.4 (C-Ar), 148.0 (C-Ar), 140.1 (C-Ar), 137.2 (C-5), 135.6 (C-Ar), 129.2 (C-Ar), 129.2 (C-Ar), 129.0 (C-Ar), 128.3 (C-Ar), 127.4 (C-Ar), 126.5 (C-Ar), 125.9 (C-Ar), 125.6 (C-Ar), 119.8 (C-Ar), 116.6 (C-6), 36.6 (C-4), 32.4 (C-1), 32.4 (C-2), 22.2 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{21}H_{20}N$ requires 286.1590; found, 286.1593; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 10%) = 11.905 min, t_R (major, 90%) = 12.687 min.

2-((1*R**,2*S**)-1-Benzyl-2-((benzyloxy)methyl)cyclopropyl)quinoline (1*R**,2*S**)-**67e**



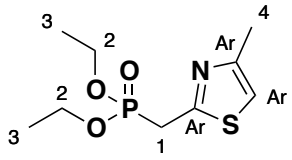
Prepared according to **Route E** from diethyl (2-phenyl-1-(quinolin-2-yl)ethyl)phosphonate (370 mg, 1.00 mmol, 1.0 equiv) and (±)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R**,2*S**)-**67e** as a white solid (215 mg, 57%); **m.p.**: 61-70 °C; **IR** (cm^{-1}) 1600, 1502, 1453, 1426, 1265, 1165, 1092, 1075, 1028; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.89 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.69 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.64 (dd, *J* = 7.0, 1.4 Hz, 1H, H-Ar), 7.43 (dd, *J* = 7.0, 1.4 Hz, 1H, H-Ar), 7.40-7.33 (m, 4H, H-Ar), 7.33 - 7.27 (m, 2H, H-Ar), 7.23 (d, *J* = 8.0 Hz, 2H, H-Ar), 7.16 (dd, *J* = 8.0, 8.0 Hz, 2H, H-Ar), 7.10 (dd, *J* = 7.0, 7.0 Hz, 1H, H-Ar), 4.63 (d, *J* = 12.0 Hz, 1H, H-6), 4.57 (d, *J* = 12.0 Hz, 1H, H-6'), 3.83 (dd, *J* = 10.6, 6.1 Hz, 2H, H-5), 3.75 (dd, *J* = 10.6, 8.7 Hz, 1H), 3.67 (d, *J* = 16.5 Hz, 1H, H-4), 3.22 (d, *J* = 16.5 Hz, 1H, H-4'), 2.10-2.01 (m, 1H, H-2), 1.97 (dd, *J* = 8.7, 4.1 Hz, 1H, H-3), 1.02 (dd, *J* = 6.1, 4.1 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.7 (C-Ar), 148.0 (C-Ar), 140.2 (C-Ar), 138.7 (C-Ar), 135.6 (C-Ar), 129.2 (C-Ar), 129.2 (C-Ar), 129.0 (C-Ar), 128.6 (C-Ar), 128.5 (C-Ar), 128.2 (C-Ar), 127.9 (C-Ar), 127.9 (C-Ar), 127.7 (C-Ar), 127.4 (C-Ar), 126.5 (C-Ar), 125.9 (C-Ar), 125.6 (C-Ar), 119.9 (C-Ar), 72.9 (C-6), 70.3 (C-5), 36.4 (C-4), 30.3 (C-1), 27.8 (C-2), 20.1 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{27}H_{26}NO$ requires 380.2009; found, 380.2010; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 23%) = 14.530 min, t_R (major, 77%) = 15.057 min.

2-((1*R**,2*S**)-1-Benzyl-2-(but-3-en-1-yl)cyclopropyl)quinoline (1*R**,2*S**)-**67f**



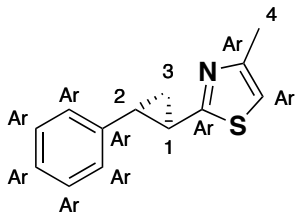
Prepared according to **Route E** from diethyl (2-phenyl-1-(quinolin-2-yl)ethyl)phosphonate (370 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 3% Et_2O in Petrol) afforded the *title compound* (1*R**,2*S**)-**67f** as a yellow oil (176 mg, 56%); **IR** (cm^{-1}) 1619, 1599, 1559, 1502, 1453, 1426, 1141, 1030; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.8 (d, *J* = 8.7 Hz, 1H, H-Ar), 7.69 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.64 (dd, *J* = 7.5, 1.4 Hz, 1H, H-Ar), 7.42 (dd, *J* = 8.1, 1.4 Hz, 1H, H-Ar), 7.24 (dd, *J* = 8.7, 8.7 Hz, 3H, H-Ar), 7.16 (dd, *J* = 7.5, 7.5 Hz, 2H, H-Ar), 7.09 (dd, *J* = 7.5, 7.5 Hz, 1H, H-Ar), 5.99-5.86 (m, 1H, H-8), 5.06 (dd, *J* = 17.1, 1.8 Hz, 1H, H-9), 4.98 (dd, *J* = 10.2, 1.8 Hz, 1H, H-9'), 3.64 (d, *J* = 16.7 Hz, 1H, H-4), 3.21 (d, *J* = 16.7 Hz, 1H, H-4'), 2.30 (dd, *J* = 14.5, 7.1 Hz, 2H, H-7), 1.96-1.85 (m, 2H, H-3 and H-6), 1.64-1.53 (m, 2H, H-2 and H-6'), 0.83 (dd, *J* = 5.9, 4.1 Hz, 1H H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.7 (C-Ar), 148.0 (C-Ar), 140.5 (C-Ar), 138.8 (C-8), 135.5 (C-Ar), 129.2 (C-Ar), 129.1 (C-Ar), 129.0 (C-Ar), 128.2 (C-Ar), 127.4 (C-Ar), 126.4 (C-Ar), 125.8 (C-Ar), 125.4 (C-Ar), 119.7 (C-Ar), 114.8 (C-9), 36.6 (C-4), 34.2 (C-7), 30.3 (C-1), 29.7 (C-6), 28.9 (C-2), 22.2 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{23}H_{24}N$ requires 314.1903; found, 314.1906; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 22%) = 12.211 min, t_R (major, 78%) = 12.576 min.

Diethyl ((4-methylthiazol-2-yl)methyl)phosphonate **70a**



Prepared according to **Route D** from 2,4-dimethylthiazole (1.13 g, 10.0 mmol, 1.0 equiv). Flash column chromatography afforded the *title compound* **70a** as a yellow oil (667 mg, 27%); **IR** (cm^{-1}) 1532, 1443, 1392, 1251, 1200, 1163, 1091, 1048, 1019; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.82 (s, 1H, H-Ar), 4.16-4.08 (m, 4H, H-2), 3.59 (d, J = 21.3 Hz, 2H, H-1), 2.42 (s, 3H, H-4), 1.30 (t, J = 7.0 Hz, 6H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.3 (d, J = 9.3 Hz, C-Ar), 152.6 (d, J = 2.4 Hz, C-Ar), 114.5 (d, J = 3.0 Hz, C-Ar), 62.8 (d, J = 6.6 Hz, C-2), 32.3 (d, J = 139.0 Hz, C-1), 17.1 (C-4), 16.5 (d, J= 6.3 Hz, C-3); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 21.9; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_9H_{17}NO_3PS$ requires 250.0661; found, 250.0661; **GC-MS** (40-300 °C, 20 °C/min): t_R = 8.723 min.

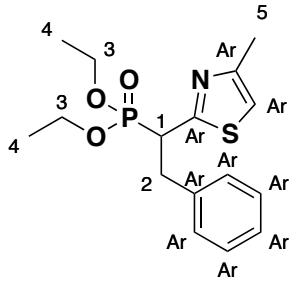
4-Methyl-2-((1*R*,2*R*)-2-phenylcyclopropyl)thiazole (1*R*,2*R*)-**71a**



Prepared according to **Route E** from diethyl ((4-methylthiazol-2-yl)methyl)phosphonate (249 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*R*,2*R*)-**71a** as a yellow oil (142 mg, 66%); **$[\alpha]^{25}_D$** = -341.0° (c = 0.63, Me_2CO); **IR** (cm^{-1}) 1677, 1527, 1498, 1458, 1438, 1385, 1304, 1183, 1141, 1100, 1074, 1033, 1016; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (dd, J = 7.8, 7.8 Hz, 2H, H-Ar), 7.21 (dd, J = 7.8, 7.8 Hz, 1H, H-Ar), 7.15 (d, J = 7.8 Hz, 2H, H-Ar),

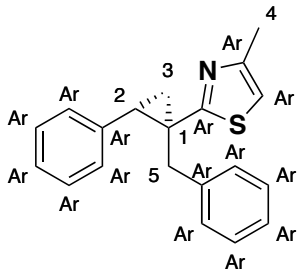
6.65 (d, J = 0.9 Hz, 1H, H-Ar), 2.60-2.49 (m, 2H, H-2), 2.41 (d, J = 0.9 Hz, 3H, H-4), 1.80-1.73 (m, 1H, H-3), 1.60-1.54 (m, 1H, H-3'), 0.91-0.82 (m, 1H, H-1); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.2 (C-Ar), 152.4 (C-Ar), 141.1 (C-Ar), 128.6 (C-Ar), 126.3 (C-Ar), 126.1 (C-Ar), 111.2 (C-Ar), 29.3 (C-2), 25.9 (C-3), 19.8 (C-4), 17.3 (C-1); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{14}N_{13}S$ requires 216.0840; found, 216.0840; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 8%) = 8.603 min, t_R (major, 92%) = 9.194 min.

Diethyl (1-(5-methylthiazol-2-yl)-2-phenylethyl)phosphonate **70b**



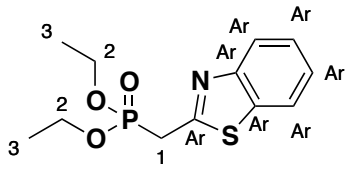
Prepared according to **Route A** from diethyl ((4-methylthiazol-2-yl)methyl)phosphonate (821 mg, 3.21 mmol). Flash column chromatography (SiO_2, 50% EtOAc in Petrol) afforded the *title compound* **70b** as a yellow oil (706 mg, 63%); **IR** (cm^{-1}) 1250, 1049, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22-7.09 (m, 5H, H-Ar), 6.76 (s, 1H, H-Ar), 4.08-3.86 (m, 4H, H-3), 3.90-3.76 (m, 1H, H-1), 3.55-3.46 (m, 1H, H-2), 3.39-3.28 (m, 1H, H-2'), 2.38 (s, 3H, H-5), 1.29 (t, J = 7.0 Hz, 3H, H-4), 1.23 (t, J = 7.0 Hz, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.3 (d, J = 7.9 Hz, C-Ar), 152.4 (d, J = 2.7 Hz, C-Ar), 138.4 (d, J = 15.0 Hz, C-Ar), 128.9 (C-Ar), 128.5 (C-Ar), 126.6 (C-Ar), 114.1 (C-Ar), 62.9 (d, J = 7.1 Hz, C-3), 62.8 (d, J = 6.7 Hz, C-3), 45.6 (d, J = 137.8 Hz, C-1), 36.5 (d, J = 2.8 Hz, C-2), 17.2 (C-5), 16.5 (d, J = 6.4 Hz, C-4), 16.4 (d, J = 6.8 Hz, C-4); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 23.9; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{16}H_{23}NO_3PS$ requires 340.1141; found, 340.1141; **GC-MS** (40-300 °C, 20 °C/min): t_R = 11.427 min.

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)-5-methylthiazole (1*S*,2*S*)-**71b**



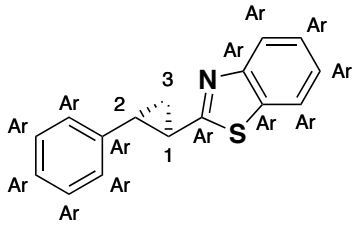
Prepared according to **Route E** from diethyl (1-(5-methylthiazol-2-yl)-2-phenylethyl)phosphonate (340 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**71b** as a yellow solid (156 mg, 51%); **m.p.**: 106-110 °C, **IR** (cm^{-1}) 1603, 1525, 1496, 1476, 1450, 1374, 1293, 1100, 1060, 1032; $[\alpha]^{25}_{D} = -33.9°$ (c = 1.40, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H, H-Ar), 7.19-7.14 (m, 2H, H-Ar), 7.14-7.10 (m, 3H, H-Ar), 6.63 (d, *J* = 1.0 Hz, 1H, H-Ar), 3.28 (d, *J* = 16.4 Hz, 1H, H-5), 2.80 (dd, *J* = 9.0, 7.2 Hz, 1H, H-2), 2.45 (d, *J* = 16.4 Hz, 1H, H-5'), 2.40 (d, *J* = 1.0 Hz, 3H, H-4), 2.14 (ddd, *J* = 9.0, 5.3 and 1.4 Hz, 1H, H-3), 1.69 (dd, *J* = 7.2, 5.3 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.3 (C-Ar), 152.2 (C-Ar), 139.5 (C-Ar), 137.6 (C-Ar), 129.3 (C-Ar), 129.0 (C-Ar), 128.5 (C-Ar), 128.2 (C-Ar), 126.8 (C-Ar), 126.1 (C-Ar), 112.0 (C-Ar), 37.3 (C-5), 35.5 (C-2), 31.2 (C-1), 20.0 (C-4), 17.4 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{20}NS$ requires 306.1311; found, 306.1314; **GC-MS** analysis (40-300 °C, 20 °C/min): t_R (minor, 5%) = 11.612 min, t_R (major, 95%) = 12.006 min.

Diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate **72a**



Prepared according to **Route D** from 2-methylbenzo[*d*]thiazole (1.49 g, 10.0 mmol, 1.0 equiv). Flash column chromatography afforded the title compound **72a** as a yellow oil (2.45 g, 86%); **IR** (cm^{-1}) 2981, 2907, 1685, 1593, 1559, 1511, 1478, 1457, 1436, 1392, 1368, 1313, 1195, 1162, 1126, 1093, 1046, 1019; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.85 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.47 (dd, *J* = 8.1, 7.2 Hz, 1H, H-Ar), 7.38 (t, *J* = 8.1, 7.2 Hz, 1H, H-Ar), 4.20-4.10 (m, 4H, H-2), 3.73 (d, *J* = 21.6 Hz, 2H, H-1), 1.31 (t, *J* = 7.1 Hz, 6H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2 (d, *J* = 9.3 Hz, C-Ar), 153.0 (d, *J* = 2.4 Hz, C-Ar), 136.1 (C-Ar), 126.2 (C-Ar), 125.3 (C-Ar), 123.0 (C-Ar), 121.6 (C-Ar), 63.0 (d, *J* = 6.7 Hz, C-2), 33.3 (d, *J* = 140.4 Hz, C-1), 16.5 (d, *J* = 6.0 Hz, C-3); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 21.1; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{12}H_{17}NO_3PS$ requires 286.0665; found: 286.0665; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.814 min.

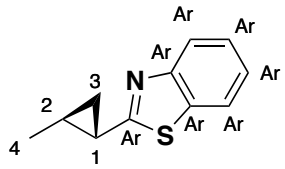
2-((1*R*,2*R*)-2-Phenylcyclopropyl)benzo[*d*]thiazole (1*R*,2*R*)-**73a**



Prepared according to **Route E** from diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (570 mg, 2.00 mmol, 2.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*R*)-**73a** as a yellow oil (196 mg, 78%); **[α]$^{25}_{D}$** = -550.2° (c = 1.23, Me_2CO); **IR** (cm^{-1}) 1516, 1500, 1458, 1440, 1107,

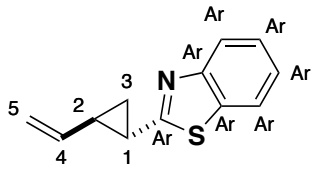
1062, 1033; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 1H, H-Ar), 7.74 (d, *J* = 8.3 Hz, 1H, H-Ar), 7.38 (dd, *J* = 7.9, 7.9 Hz, 1H, H-Ar), 7.29-7.22 (m, 3H, H-Ar), 7.20-7.09 (m, 3H, H-Ar), 2.72-2.66 (m, 1H, H-2), 2.57-2.51 (m, 1H, H-1), 1.99-1.86 (m, 1H, H-3), 1.67-1.60 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.3 (C-Ar), 153.5 (C-Ar), 140.6 (C-Ar), 134.4 (C-Ar), 128.6 (C-Ar), 126.5 (C-Ar), 126.1 (C-Ar), 124.5 (C-Ar), 122.3 (C-Ar), 121.5 (C-Ar), 30.1 (C-2), 26.6 (C-1), 20.2 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{16}H_{13}NS$ requires 252.0840; found, 252.0840; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 7%) = 10.931 min, t_R (major, 93%) = 11.593 min; **HPLC** (IB, 2% THF in Hexane, 1 mL/min): t_R (major, 99%) = 17.686 min, t_R (minor, 1%) = 25.684 min.

2-((1*S*,2*S*)-2-Methylcyclopropyl)benzo[*d*]thiazole (1*S*,2*S*)-**73b**



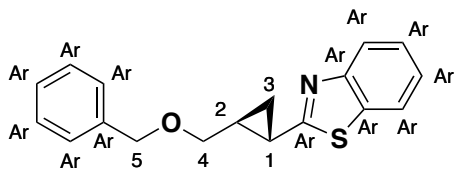
Prepared according to **Route E** from diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (570 mg, 2.00 mmol, 2.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**73b** as a colourless oil (118 mg, 62%); **IR** (cm^{-1}) 1517, 1456, 1438, 1243, 1205, 1111, 1083, 1063, 1037, 1015; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.78 (d, *J* = 8.0 Hz, 1H, H-Ar), 7.41 (dd, *J* = 8.0, 8.0 Hz, 1H, H-Ar), 7.29 (dd, *J* = 7.5, 7.5 Hz, 1H, H-Ar), 2.13-2.07 (m, 1H, H-2), 1.63-1.53 (m, 1H, H-1), 1.42-1.36 (m, 1H, H-3), 1.26 (d, *J* = 6.0 Hz, 3H, H-4), 1.10-1.01 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.5 (C-Ar), 153.6 (C-Ar), 134.3 (C-Ar), 126.0 (C-Ar), 124.3 (C-Ar), 122.1 (C-Ar), 121.4 (C-Ar), 23.8 (C-2), 20.9 (C-1), 20.2 (C-3), 18.7 (C-4); **HRMS-EI** (*m/z*) $[M - H]^+$ calcd for $C_{11}H_{10}NS$ requires 188.0528; found, 188.0524; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 4%) = 8.215 min, t_R (major, 96%) = 8.259 min.

2-((1*S**,2*R**)-2-(2-Vinylcyclopropyl)benzo[*d*]thiazole (1*S**,2*R**)-**73c**



Prepared according to **Route E** from diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (570 mg, 2.00 mmol, 2.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**73c** as a colourless oil (66 mg, 33%); **IR** (cm^{-1}) 1636, 1515, 1437, 1456, 1312, 1281, 1244, 1202, 1109, 1059, 1014; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 1H, H-Ar), 7.79 (d, *J* = 8.2 Hz, 1H, H-Ar), 7.42 (dd, *J* = 8.2, 1.0 Hz, 1H, H-Ar) 7.31 (dd, *J* = 8.2, 1.0 Hz, 1H, H-Ar), 5.63-5.52 (m, 1H, H-4), 5.21 (d, *J* = 17.0 Hz, 1H, H-5), 5.04 (d, *J* = 10.4 Hz, 1H, H-5'), 2.42-2.35 (m, 1H, H-2), 2.29 - 2.21 (m, 1H, H-1), 1.69 (ddd, *J* = 10.2, 5.7 and 5.7 Hz, 1H, H-3), 1.69 (ddd, *J* = 11.1, 5.7 and 5.7 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.5 (C-Ar), 153.5 (C-Ar), 138.6 (C-4), 134.4 (C-Ar), 126.1 (C-Ar), 124.5 (C-Ar), 122.3 (C-Ar), 121.5 (C-Ar), 114.7 (C-5), 29.3 (C-1), 24.3 (C-2), 18.9 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{12}H_{11}NS$ requires 202.0685; found, 202.0689; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 8.736 min, t_R (major, 98%) = 8.787 min.

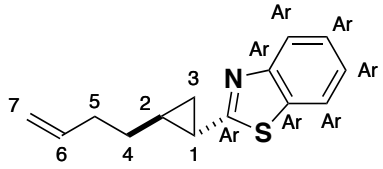
2-((1*S*,2*S*)-2-((Benzyloxy)methyl)cyclopropyl)benzo[*d*]thiazole (1*S*,2*S*)-**73d**



Prepared according to **Route E** from diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (570 mg, 2.00 mmol, 2.0 equiv) and (*S*)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**73d** as a colourless

oil (156 mg, 53%); $[\alpha]^{25}_{D}$ = +112.8° (c = 1.44, $CHCl_3$); **IR** (cm^{-1}) 1518, 1454, 1438, 1360, 1311, 1244, 1200, 1110, 1075, 1028, 1015; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 1H, H-Ar), 7.79 (d, *J* = 8.3 Hz, 1H, H-Ar), 7.42 (dd, *J* = 7.4, 7.4 Hz, 1H, H-Ar), 7.35 (d, *J* = 7.4 Hz, 4H, H-Ar), 7.33-7.27 (m, 2H, H-Ar), 4.57 (s, 2H, H-5), 3.61-3.52 (m, 2H, H-4), 2.38-2.32 (m, 1H, H-2), 2.01-1.91 (m, 1H, H-1), 1.51-1.43 (m, 1H, H-3), 1.27-1.20 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.2 (C-Ar), 153.5 (C-Ar), 138.4 (C-Ar), 134.4 (C-Ar), 128.6 (C-Ar), 127.8 (C-Ar), 126.1 (C-Ar), 124.5 (C-Ar), 122.3 (C-Ar), 121.5 (C-Ar), 72.8 (C-5), 72.0 (C-4), 25.2 (C-2), 20.8 (C-1), 16.3 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{18}NOS$ requires 296.1104; found, 296.1105; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 15%) = 12.305 min, t_R (major, 85%) = 12.782 min.

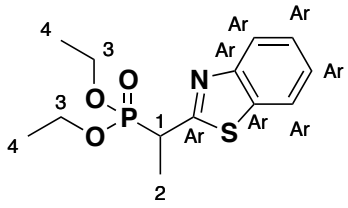
2-((1*S**,2*S**)-2-(But-3-en-1-yl)cyclopropyl)benzo[*d*]thiazole (1*S**,2*S**)-**73e**



Prepared according to **Route E** from diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (570 mg, 2.00 mmol, 2.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**73e** as a yellow oil (147 mg, 66%); **IR** (cm^{-1}) 1640, 1517, 1438, 1311, 1279, 1244, 1113, 1062, 1014; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.2 Hz, 1H, H-Ar), 7.78 (d, *J* = 8.2 Hz, 1H, H-Ar), 7.41 (dd, *J* = 7.3, 1.3 Hz, 1H, H-Ar), 7.29 (dd, *J* = 7.3, 1.3 Hz, 1H, H-Ar), 5.92-5.80 (m, 1H, H-6), 5.03 (ddd, *J* = 17.1, 3.5 and 1.6 Hz, 1H, H-7), 4.99-4.96 (m, 1H, H-7'), 2.24 (dd, *J* = 14.1, 7.2 Hz, 2H, H-5), 2.17-2.12 (m, 1H, H-2), 1.63-1.48 (m, 3H, H-1 and H-4), 1.45-1.39 (m, 1H, H-3), 1.08 (dt, *J* = 10.2, 5.0 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.3 (C-Ar), 153.6 (C-Ar), 138.2 (C-6), 134.2 (C-Ar), 134.3 (C-Ar), 126.0 (C-Ar), 124.4 (C-Ar), 122.2 (C-Ar), 121.5 (C-Ar), 115.2

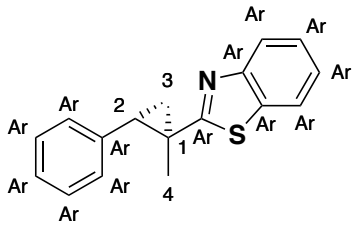
(C-7), 33.5 (C-4), 33.5 (C-5), 26.2 (C-1), 22.8 (C-2), 18.9 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{14}H_{16}NS$ requires 230.0998; found, 230.1001; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 14%) = 9.582 min, t_R (major, 86%) = 9.830 min.

Diethyl (1-(benzo[*d*]thiazol-2-yl)ethyl)phosphonate **72b**



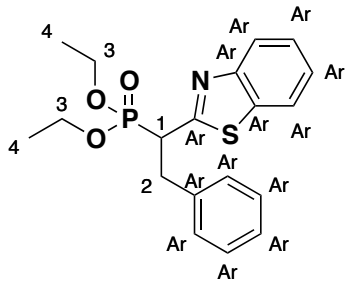
Prepared according to **Route D** from from 2-ethylbenzo[*d*]thiazole (2.04 g, 12.50 mmol, 1.0 equiv). Distillation at reduced pressure (207 °C, < 0.1 mmHg) afforded the title compound **72b** as a yellow oil (2.24 g, 66%); **IR** (cm^{-1}) 1507, 1455, 1438, 1253, 1162, 1097, 1049, 1014; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.86 (dd, *J* = 8.1, 7.3 Hz, 1H, H-Ar), 7.46 (dd, *J* = 8.1, 7.3 Hz, 1H, H-Ar), 7.37 (dd, *J* = 8.1, 7.3 Hz, 1H, H-Ar), 4.20-4.08 (m, 4H, H-3), 3.85 (dq, *J* = 22.8, 7.3 Hz, 1H, H-1), 1.77 (dd, *J* = 17.4, 7.3 Hz, 3H, H-2), 1.31 (t, *J* = 7.3 Hz, 3H, H-4); 1.27 (t, *J* = 7.3 Hz, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.0 (d, *J* = 7.6 Hz, C-Ar), 152.7 (d, *J* = 2.0 Hz, C-Ar), 135.5 (C-Ar), 126.0 (C-Ar), 125.1 (C-Ar), 123.0 (C-Ar), 121.5 (C-Ar), 62.9 (d, *J* = 7.3 Hz, C-3), 62.7 (d, *J* = 7.1 Hz, C-3), 38.8 (d, *J* = 140.3 Hz, C-1), 16.4 (d, *J* = 2.5 Hz, C-4), 16.4 (d, *J* = 2.4 Hz, C-4), 15.5 (d, *J* = 5.5 Hz, C-2); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 24.8; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{19}NO_3PS$ requires 300.0818; found, 300.0818; **GC-MS** (40-300 °C, 20 °C/min): t_R = 10.808 min.

2-((1*R*,2*S*)-1-Methyl-2-phenylcyclopropyl)benzo[*d*]thiazole (1*R*,2*S*)-**74a**



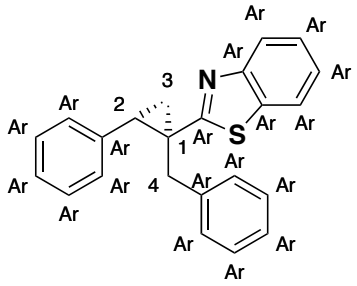
Prepared according to **Route E** from diethyl ((1-(benzo[*d*]thiazol-2-yl)ethyl)phosphonate (299 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**74a** as a white solid (249 mg, 94%); **m.p.**: 62-67 °C; $[\alpha]^{25}_{D} = -368.5°$ (c = 1.77, $CHCl_3$); **IR** (cm^{-1}) 1601, 1496, 1447, 1436, 1383, 1312, 1286, 1271, 1257, 1241, 1200, 1131, 1107, 1078, 1047, 1027, 1015; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 1H, H-Ar), 7.84 (d, *J* = 7.8 Hz, 1H, H-Ar), 7.45 (dd, *J* = 8.2, 1.3 Hz, 1H, H-Ar), 7.33 (dd, *J* = 7.8, 7.8 Hz, 3H, H-Ar), 7.28-7.23 (m, 3H, H-Ar), 3.02 (dd, *J* = 9.2, 7.3 Hz, 1H, H-2), 2.45 (dd, *J* = 9.2, 5.0 Hz, 1H, H-3), 1.58 (dd, *J* = 7.3, 5.0 Hz, 1H, H-3'), 1.36 (s, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.3 (C-Ar), 153.6 (C-Ar), 137.4 (C-Ar), 134.8 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 126.8 (C-Ar), 126.1 (C-Ar), 124.4 (C-Ar), 122.4 (C-Ar), 121.5 (C-Ar), 35.8 (C-2), 27.0 (C-1), 23.0 (C-3), 18.1 (C-4); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{17}H_{16}NS$ requires 266.0998; found, 266.0993; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 10.798 min, t_R (major, 98%) = 11.637 min; **HPLC** (IB, 1% THF in Hexane, 1 mL/min): t_R (major, 99%) = 13.670 min, t_R (minor, 1%) = 27.087 min.

Diethyl (1-(benzo[*d*]thiazol-2-yl)-2-phenylethyl)phosphonate **72c**



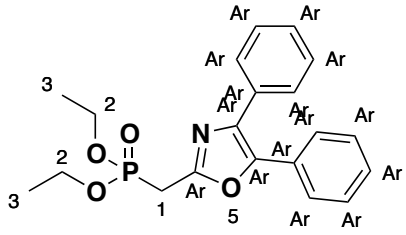
Prepared according to **Route A** from diethyl (benzo[*d*]thiazol-2-ylmethyl)phosphonate (1.87 g, 6.56 mmol). Flash column chromatography (SiO_2, 50% EtOAc in Petrol) afforded the *title compound* **72c** as a yellow oil (1.97 g, 80%); **IR** (cm^{-1}) 1736, 1437, 1243, 1162, 1099, 1047, 1020; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H), 7.44 (dd, J = 8.2, 7.9 Hz, 1H), 7.35 (dd, J = 7.9, 7.9 Hz, 1H), 7.22-7.08 (m, 5H), 4.23-3.96 (m, 5H), 3.64-3.43 (m, 2H), 1.31 (d, J = 7.1 Hz, 3H), 1.24 (d, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.2 (d, J = 7.9 Hz, C-Ar), 152.9 (d, J = 2.3 Hz, C-Ar), 138.2 (d, J = 14.8 Hz, C-Ar), 135.6 (d, J = 1.1 Hz, C-Ar), 128.9 (C-Ar), 128.6 (C-Ar), 126.8 (C-Ar), 126.0 (C-Ar), 125.1 (C-Ar), 123.2 (C-Ar), 121.6 (C-Ar), 63.1 (d, J = 7.0 Hz, C-3), 63.1 (d, J = 6.7 Hz, C-3), 45.5 (d, J = 137.3 Hz, C-1), 36.2 (d, J = 3.1 Hz, C-2), 16.5 (d, J = 5.7 Hz, C-4), 16.5 (d, J = 5.6 Hz, C-4); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 23.2; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{19}H_{23}NO_3PS$ requires 376.1134; found, 376.1134; **GC-MS** (40-300 °C, 20 °C/min): t_R = 13.092 min.

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)benzo[*d*]thiazole (1*S*,2*S*)-**74b**



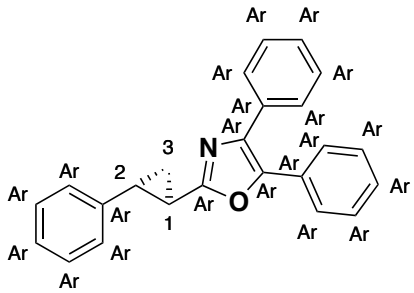
Prepared according to **Route E** from diethyl (1-(benzo[*d*]thiazol-2-yl)-2-phenylethyl)phosphonate (375 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**74b** a white solid (214 mg, 63%); **m.p.**: 130-136 °C; $[\alpha]^{25}_{D} = -154.9°$ (c = 2.03, $CHCl_3$); **IR** (cm^{-1}) 1599, 1496, 1454, 1437, 1378,9, 1290, 1241, 1169, 1108, 1079, 1041, 1004; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H, H-Ar), 7.43 (dd, *J* = 7.3, 1.2 Hz, 1H, H-Ar), 7.39-7.33 (m, 2H, H-Ar), 7.33-7.27 (m, 4H, H-Ar), 7.21-7.14 (m, 4H, H-Ar), 7.14-7.08 (m, 1H, H-Ar), 3.42 (d, *J* = 16.7 Hz, 1H, H-4), 2.94 (dd, *J* = 8.7, 8.7 Hz, 1H, H-2), 2.51 (d, *J* = 16.7 Hz, 1H, H-4'), 2.37 (dd, *J* = 8.7, 5.4 Hz, 1H, H-3), 1.81 (dd, *J* = 7.3, 5.4 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.8 (C-Ar), 153.4 (C-Ar), 139.3 (C-Ar), 137.1 (C-Ar), 135.2 (C-Ar), 129.3 (C-Ar), 128.9 (C-Ar), 128.6 (C-Ar), 128.4 (C-Ar), 127.1 (C-Ar), 126.3 (C-Ar), 126.0 (C-Ar), 124.5 (C-Ar), 122.5 (C-Ar), 121.6 (C-Ar), 37.0 (C-4), 36.4 (C-2), 31.9 (C-1), 20.5 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{23}H_{20}NS$ requires 342.1311; found, 342.1314; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 99%) = 13.791 min, t_R (major, 1%) = 14.351 min; **HPLC** (ID, 2% THF in Hexane, 1 mL/min): t_R = 7.299 min.

Diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate **75a**



Prepared according to **Route D** from 2-methyl-4,5-diphenyloxazole (2.35 g, 10.0 mmol, 1.0 equiv). Flash column chromatography afforded the title compound **75a** as a yellow oil (3.45 g, 93%); **IR** (cm^{-1}) 1568, 1503, 1444, 1392, 1368, 1257, 1217, 1162, 1097, 1051, 1021; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.3, 1.8 Hz, 2H, H-Ar), 7.58 (dd, *J* = 8.3, 1.8 Hz, 2H, H-Ar), 7.40-7.29 (m, 6H, H-Ar), 4.30-4.13 (m, 4H, H-2), 3.41 (d, *J* = 21.4 Hz, 2H, H-1), 1.35 (t, *J* = 7.1 Hz, 6H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.1 (d, *J* = 10.6 Hz, C-Ar), 146.5 (d, *J* = 2.7 Hz, C-Ar), 135.8 (d, *J* = 2.0 Hz, C-Ar), 132.4 (C-Ar), 128.9 (C-Ar), 128.8 (C-Ar), 128.8 (C-Ar), 128.7 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 126.7 (C-Ar), 63.0 (d, *J* = 6.4 Hz, C-2), 27.6 (d, *J* = 141.4 Hz, (C-1), 16.5 (d, *J* = 6.1 Hz, C-3); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 20.1; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{23}O_4NP$ requires 372.1359; found, 372.1360; **GC-MS** (40-300 °C, 20 °C/min): t_R = 13.451 min.

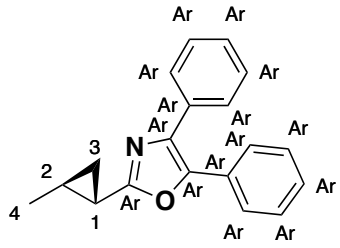
4,5-Diphenyl-2-((1*R*,2*R*)-2-phenylcyclopropyl)oxazole (1*R*,2*R*)-**76a**



Prepared according to **Route E** from diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate (371 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash

column chromatography (SiO_2, 2% Et_2O in Petrol) afforded the *title compound* (1*R*,2*R*)-**76a** as a colourless oil (203 mg, 60%); **IR** (cm^{-1}) 1604, 1578, 1570, 1500, 1460, 1444, 1409, 1364, 1348, 1304, 1285, 1221, 1205, 1178, 1157, 1138, 1115, 1071, 1058, 1026, 1001; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 2H, H-Ar), 7.48 (d, *J* = 7.7 Hz, 2H, H-Ar), 7.30-7.18 (m, 8H, H-Ar), 7.15-7.06 (m, 3H, H-Ar), 2.63-2.56 (m, 1H, H-2), 2.36-2.30 (m, 1H, H-1), 1.79-1.71 (m, 1H, H-3), 1.49-1.42 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.5 (C-Ar), 144.7 (C-Ar), 140.4 (C-Ar), 135.4 (C-Ar), 132.7 (C-Ar), 129.1 (C-Ar), 128.7 (C-Ar), 128.6 (C-Ar), 128.6 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 128.0 (C-Ar), 126.5 (C-Ar), 126.4 (C-Ar), 126.2 (C-Ar), 26.6 (C-2), 20.2 (C-1), 17.2 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{24}H_{20}ON$ requires 338.1539; found, 338.1542; **$[\alpha]^{25}_D$** = -326.0° (c = 1.18, $CHCl_3$); **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 2%) = 13.495 min, t_R (major, 98%) = 14.258 min.

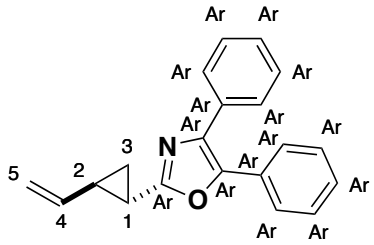
2-((1*S*,2*S*)-2-Methylcyclopropyl)-4,5-diphenyloxazole (1*S*,2*S*)-**76b**



Prepared according to **Route E** from diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate (371 mg, 1.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 2% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**76b** as a yellow oil (148 mg, 54%); **IR** (cm^{-1}) 1659, 1502, 1485, 1444, 1207, 1069, 1026; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57-7.50 (m, 2H, H-Ar), 7.48-7.41 (m, 2H, H-Ar), 7.27-7.11 (m, 6H, H-Ar), 1.76-1.70 (m, 1H, H-2), 1.49-1.39 (m, 1H, H-1), 1.28-1.21 (m, 1H, H-3), 1.10 (d, *J* = 6.0 Hz, 3H, H-4), 0.79-0.72 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.7 (C-Ar), 144.4 (C-Ar), 135.3 (C-Ar), 132.8 (C-Ar), 129.3 (C-Ar), 128.6 (C-Ar), 128.2 (C-Ar), 128.0 (C-Ar), 128.0 (C-Ar), 126.4

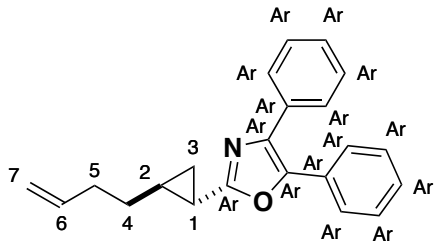
(C-Ar), 126.4 (C-Ar), 18.4 (C-4), 17.2 (C-2), 17.1 (C-1), 16.5 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{19}H_{18}NO$ requires 276.1383; found, 276.1381; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 12%) = 11.453 min, t_R (major, 88%) = 11.542 min.

4,5-Diphenyl-2-((1*S**,2*R**)-2-vinylcyclopropyl)oxazole (1*S**,2*R**)-**76c**



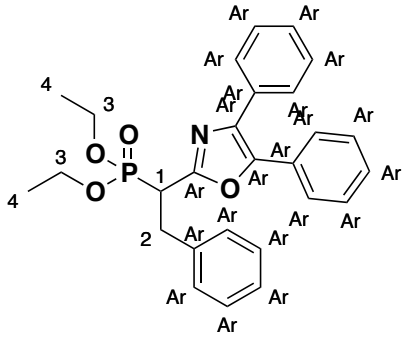
Prepared according to **Route E** from diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate (371 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 2% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**76c** as a yellow oil (47 mg, 16%); **IR** (cm^{-1}) 1604, 1580, 1570, 1502, 1485, 1448, 1444, 1210, 1177, 1157, 1101, 1071, 1058, 1025, 1001; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.9 Hz, 2H, H-Ar), 7.48 (d, *J* = 7.9 Hz, 2H, H-Ar), 7.31-7.15 (m, 6H, H-Ar), 5.52-5.41 (m, 1H, H-4), 5.13 (d, *J* = 17.0 Hz, 1H, H-5), 5.13 (d, *J* = 10.3 Hz, 1H, H-5'), 2.16-2.07 (m, 2H, H-1 and H-2), 1.57-1.50 (m, 1H, H-3), 1.21-1.10 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.5 (C-Ar), 144.7 (C-Ar), 138.5 (C-Ar), 132.7 (C-Ar), 129.2 (C-Ar), 128.7 (C-Ar), 128.7 (C-Ar), 128.7 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 128.0 (C-Ar), 126.5 (C-Ar), 114.6 (C-Ar), 25.9 (C-1), 18.0 (C-2), 15.7 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{20}H_{18}NO$ requires 288.1383; found, 288.1376; **GC-MS** (40-300 °C, 20 °C/min): t_R = 11.955 min.

2-((1*S**,2*S**)-2-(But-3-en-1-yl)cyclopropyl)-4,5-diphenyloxazole (1*S**,2*S**)-**76d**



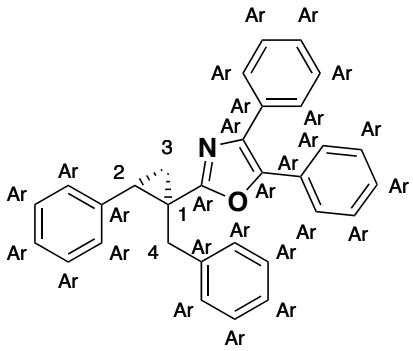
Prepared according to **Route E** from diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate (371 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 2% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**76d** as a yellow solid (154 mg, 49%); **m.p.**: 35-38 °C; **IR** (cm^{-1}) 1640, 1603, 1580, 1569, 1502, 1444, 1415, 1365, 1225, 1199, 1071, 1057, 1024, 1015; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.3 Hz, 2H, H-Ar), 7.54 (d, *J* = 8.3 Hz, 2H, H-Ar), 7.39-7.28 (m, 6H, H-Ar), 5.93-5.81 (m, 1H, H-6), 5.05 (dd, *J* = 17.1, 1.7 Hz, H-7), 4.98 (d, *J* = 10.2 Hz, 1H, H-7'), 2.28-2.19 (m, 2H, H-5), 1.93-1.87 (m, 1H, H-1), 1.65-1.51 (m, 2H, H-4), 1.50-1.41 (m, 1H, H-2), 1.40-1.33 (m, 1H, H-3), 0.95 - 0.89 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.7 (C-Ar), 144.5 (C-Ar), 138.3 (C-6), 138.3 (C-Ar), 129.4 (C-Ar), 128.7 (C-Ar), 128.7 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 128.1 (C-Ar), 126.4 (C-Ar), 115.1 (C-7), 33.5 (C-5), 33.2 (C-4), 22.5 (C-2), 16.2 (C-1), 15.4 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{22}H_{22}NO$ requires 316.1696; found, 316.1687; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 5%) = 12.356 min, t_R (major, 95%) = 12.661 min.

Diethyl (1-(4,5-diphenyloxazol-2-yl)-2-phenylethyl)phosphonate **75b**



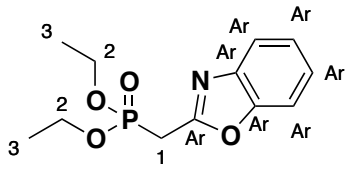
Prepared according to **Route A** from diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate (1.18 g, 3.18 mmol). Flash column chromatography (SiO_2, 50% EtOAc in Petrol) afforded the *title compound* **75b** as a yellow oil (545 mg, 38%); **IR** (cm^{-1}) 1739, 1607, 1566, 1502, 1447, 1393, 1374, 1255, 1164, 1098, 1051, 1024; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.7 Hz, 2H, H-Ar), 7.53 (d, *J* = 7.7 Hz, 2H, H-Ar), 7.38-7.29 (m, 6H, H-Ar), 7.25-7.15 (m, 5H, H-Ar), 4.26-4.08 (m, 4H, H-3), 3.80 (ddd, *J* = 22.7, 10.8 and 4.6 Hz, 1H, H-1), 3.58-3.42 (m, 2H, H-2), 1.36-1.28 (m, 6H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.3 (C-Ar), 158.1 (d, *J* = 9.0 Hz, C-Ar), 146.1 (d, *J* = 2.8 Hz, C-Ar), 138.6 (d, *J* = 14.4 Hz, C-Ar), 135.7 (d, *J* = 2.3 Hz, C-Ar), 132.5 (C-Ar), 129.0 (C-Ar), 128.9 (C-Ar), 128.7 (C-Ar), 128.6 (d, *J* = 3.0 Hz, C-Ar), 128.2 (C-Ar), 128.1 (C-Ar), 126.9 (C-Ar), 126.7 (C-Ar), 63.1 (d, *J* = 7.1 Hz, C-3), 63.0 (d, *J* = 7.5 Hz, C-3), 41.6 (d, *J* = 137.9 Hz, C-1), 34.02 (d, *J* = 3.2 Hz, C-2), 16.6 (d, *J* = 5.8 Hz, C-4); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 22.3; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{27}H_{29}NO_4P$ requires 462.1826; found, 462**.**1827; **GC-MS** (40-300 °C, 20 °C/min): t_R = 15.297 min.

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)-4,5-diphenyloxazole (1*S*,2*S*)-**77a**



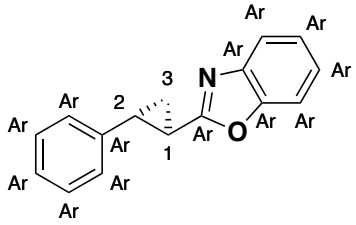
Prepared according to **Route E** from diethyl ((4,5-diphenyloxazol-2-yl)methyl)phosphonate (371 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 2% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**77a** as a white solid (81 mg, 19%); **m.p.**: 140-146 °C; $[\alpha]^{25}_{D}$ = –132.8° (c = 0.64, $CHCl_3$); **IR** (cm^{-1}) 1602, 1564, 1495, 1444, 1421, 1218, 1201, 1181, 1155, 1126, 1091, 1073, 1057, 1026; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68-7.63 (m, 2H, H-Ar), 7.55-7.49 (m, 2H, H-Ar), 7.41-7.28 (m, 9H, H-Ar), 7.28-7.25 (m, 3H, H-Ar), 7.24-7.20 (m, 3H, H-Ar), 7.20-7.11 (m, 1H, H-Ar), 3.50 (d, *J* = 15.5 Hz, 1H, H-4), 2.99-2.91 (m, 1H, H-2), 2.31 (d, *J* = 15.5 Hz, 1H, H-4'), 2.15-2.07 (m, 1H, H-3), 1.70-1.64 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0 (C-Ar), 165.9 (C-Ar), 140.1 (C-Ar), 137.0 (C-Ar), 135.5 (C-Ar), 132.9 (C-Ar), 129.4 (C-Ar), 129.4 (C-Ar), 129.1 (C-Ar), 128.7 (C-Ar), 128.7 (C-Ar), 128.5 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 128.1 (C-Ar), 127.0 (C-Ar), 126.5 (C-Ar), 126.2 (C-Ar), 34.6 (C-4), 33.5 (C-1), 27.3 (C-2), 17.8 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{31}H_{26}NO$ requires 428.2009; found, 428.2010; **GC-MS** (40-300 °C, 20 °C/min): t_R (major, 99%) = 16.116 min, t_R (minor, 1%) = 16.899 min.

Diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate **78a**



Prepared according to **Route D** from 2-methylbenzo[*d*]oxazole (1.33 g, 10.00 mmol, 1.0 equiv). Flash column chromatography afforded the title compound **78a** as a yellow oil (2.49 g, 89%); **IR** (cm^{-1}) 1613, 1569, 1455, 1240, 1017; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73-7.67 (m, 1H, H-Ar), 7.55-7.49 (m, 1H, H-Ar), 7.36-7.29 (m, 2H, H-Ar), 4.26-4.12 (m, 4H, H-2), 3.56 (d, *J* = 21.9 Hz, 2H, H-1), 1.33 (t, *J* = 7.2 Hz, 6H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 158.8 (d, *J* = 10.3 Hz, C-Ar), 151.3 (C-Ar), 141.5 (d, *J* = 2.0 Hz, C-Ar), 125.2 (C-Ar), 124.6 (C-Ar), 120.1 (C-Ar), 110.7 (C-Ar), 63.1 (d, *J* = 6.5 Hz, C-2), 28.2 (d, *J* = 139.0 Hz, C-1), 16.5 (d, *J* = 6.1 Hz, C-3); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 19.6; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{12}H_{17}NO_4P$ requires 270.0890; found, 270.0890; **GC-MS** (40-300 °C, 20 °C/min): t_R = 9.872 min.

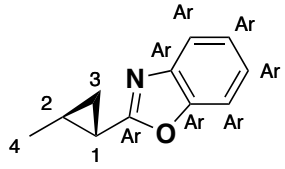
2-((1*R*,2*R*)-2-Phenylcyclopropyl)benzo[*d*]oxazole (1*R*,2*R*)-**79a**



Prepared according to **Route E** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (286 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*R*,2*R*)-**79a** as a white solid (203 mg, 86%); **m.p.**: 37-43 °C; **$[\alpha]^{25}_D$** = –425.0° (c = 1.18, $CHCl_3$); **IR** (cm^{-1}) 1615, 1568, 1497, 1455, 1220, 1152; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 6.9 Hz, 1H, H-Ar), 7.46 (d, *J* = 7.9 Hz, 1H, H-Ar), 7.35-7.16 (m, 6H, H-Ar), 7.19 (d, *J* = 7.9 Hz, 2H, H-Ar), 2.81-2.74 (m, 1H, H-2),

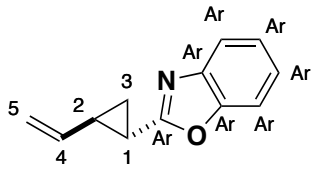
2.49-2.44 (m, 1H, H-1), 1.95-1.88 (m, 1H, H-3), 1.68-1.62 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.4 (C-Ar), 150.7 (C-Ar), 140.7 (C-Ar), 140.1 (C-Ar), 128.7 (C-Ar), 126.8 (C-Ar), 126.3 (C-Ar), 124.4 (C-Ar), 124.3 (C-Ar), 119.3 (C-Ar), 110.3 (C-Ar), 27.6 (C-2), 20.5 (C-1), 17.8 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{16}H_{14}NO$ requires 236.1070; found, 236.1071; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 11%) = 9.951 min, t_R (major, 89%) = 10.677 min; **HPLC** (ID, 5% THF in Hexane, 0.4 mL/min): t_R (minor, 3%) = 18.397 min, t_R (major, 97%) = 19.769 min.

2-((1*S*,2*S*)-2-Methylcyclopropyl)benzo[*d*]oxazole (1*S*,2*S*)-**79b**



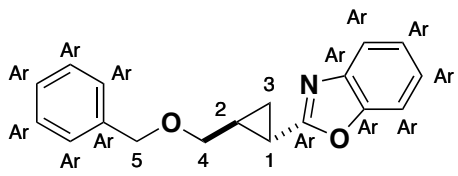
Prepared according to **Route E** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (286 mg, 1.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**79b** as a yellow oil (103 mg, 59%). Major diastereomer: **IR** (cm^{-1}) 1616, 1570, 1455, 1287, 1243, 1222, 1173, 1152, 1081, 1042, 1003; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 6.9, 1.6 Hz, 1H, H-Ar), 7.41 (dd, *J* = 6.9, 1.6 Hz, 1H, H-Ar), 7.30-7.20 (m, 2H, H-Ar), 1.93-1.86 (m, 1H, H-1), 1.69-1.58 (m, 1H, H-2), 1.49-1.41 (m, 1H, H-3), 1.24 (d, *J* = 6.0 Hz, 3H, H-4), 1.00-0.93 (m, 1H, H-2); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.7 (C-Ar), 150.6 (C-Ar), 141.9 (C-Ar), 124.2 (C-Ar), 124.0 (C-Ar), 119.1 (C-Ar), 110.1 (C-Ar), 18.4 (C-1), 18.3 (C-2), 17.5 (C-4), 17.5 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{11}H_{12}NO$ requires 174.0919; found, 174.0913; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 13%) = 7.031 min, t_R (major, 87%) = 7.101 min.

2-((1*S**,2*R**)-2-Vinylcyclopropyl)benzo[*d*]oxazole (1*S**,2*R**)-**79c**



Prepared according to **Route E** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (286 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S**,2*R**)-**79c** as a yellow oil (94 mg, 51%). Major diastereomer: **IR** (cm^{-1}) 1638, 1616, 1569, 1455, 1397, 1288, 1243, 1222, 1204, 1173, 1153,1099, 1077, 1050, 1003; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62-7.59 (m, 1H, H-Ar), 7.45-7.40 (m, 1H, H-Ar), 7.31-7.22 (m, 2H, H-Ar), 5.60-5.50 (m, 1H, H-4), 5.22 (d, *J* = 17.0 Hz, 1H, H-5), 5.03 (d, *J* = 10.2 Hz, 1H, H-5'), 2.31-2.17 (m, 2H, H-1 and H-2), 1.71-1.64 (m, 1H, H-3), 1.33-1.25 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.3 (C-Ar), 150.7 (C-Ar), 141.8 (C-Ar), 138.1 (C-4), 124.3, (C-Ar), 124.2 (C-Ar), 119.3 (C-Ar), 115.2 (C-Ar), 110.2 (C-Ar), 26.8 (C-1), 18.3 (C-2), 16.4 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{12}H_{12}NO$ requires 186.0919; found, 186.0913; **GC-MS** analysis (40-300 °C, 20 °C/min): t_R (minor, 5%) = 7.680 min, t_R (major, 95%) = 7.718 min.

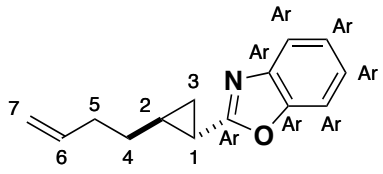
2-((1*S**,2*S**)-2-((Benzyloxy)methyl)cyclopropyl)benzo[*d*]oxazole (1*S**,2*S**)-**79d**



Prepared according to **Route E** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (286 mg, 1.00 mmol, 1.0 equiv) and (±)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**79d** as a yellow

oil (158 mg, 56%); **IR** (cm^{-1}) 1616, 1570, 1454, 1362, 1242, 1152, 1076, 1028, 1003; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63-7.57 (m, 1H, H-Ar), 7.45-7.40 (m, 1H, H-Ar), 7.35 (d, *J* = 4.4 Hz, 4H, H-Ar), 7.32-7.22 (m, 3H, H-Ar), 4.57 (s, 2H, H-5), 3.60 (dd, *J* = 10.4, 5.9 Hz, 1H, H-4), 3.50 (dd, *J* = 10.4, 5.9 Hz, 1H, H-4'), 2.21-2.13 (m, 1H, H-2), 2.04-1.95 (m, 1H, H-1), 1.53-1.46 (m, 1H, H-3), 1.23-1.14 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.7 (C-Ar), 150.7 (C-Ar), 141.8 (C-Ar), 138.3 (C-Ar), 128.6 (C-Ar), 127.8 (C-Ar), 127.8 (C-Ar), 124.3 (C-Ar), 124.2 (C-Ar), 119.2 (C-Ar), 110.2 (C-Ar), 72.9 (C-5), 71.7 (C-4), 22.7 (C-1), 14.8 (C-2), 13.8 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{18}NO_2$ requires 280.1338; found, 280.1332; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 3%) = 11.491 min, t_R (major, 97%) = 11.917 min.

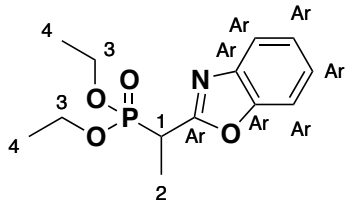
2-((1*S**,2*S**)-2-(But-3-en-1-yl)cyclopropyl)benzo[*d*]oxazole (1*S**,2*S**)-**79e**



Prepared according to **Route E** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (286 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S**,2*S**)-**79e** as a yellow oil (143 mg, 67%); **IR** (cm^{-1}) 1616, 1570, 1455, 1242, 1152, 1075; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61-7.57 (m, 1H, H-Ar), 7.43-7.39 (m, 1H, H-Ar), 7.29-7.21 (m, 2H, H-Ar), 5.91-5.69 (m, 1H, H-6), 5.03 (d, *J* = 17.1, 1.7 Hz, 1H, H-7), 4.98 (d, *J* = 10.2 Hz, 1H, H-7'), 2.27-2.19 (m, 2H, H-5), 1.98-1.92 (m, 1H, H-1), 1.69-1.59 (m, 1H, H-2), 1.58-1.48 (m, 2H, H-4), 1.48-1.42 (m, 1H, H-3), 1.04-0.97 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.5 (C-Ar), 150.6 (C-Ar), 141.9 (C-Ar), 138.1 (C-6), 124.2 (C-Ar), 124.0 (C-Ar), 119.1 (C-Ar), 115.2 (C-Ar), 110.1 (C-7), 33.4 (C-5), 33.2 (C-4), 23.5 (C-2), 16.5 (C-1), 16.3 (C-3); **HRMS-ASAP** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{18}N$ requires

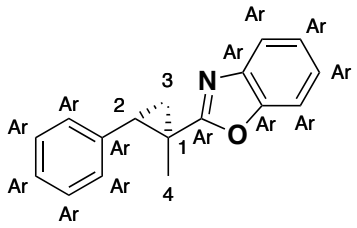
214.1232; found, 214.1226; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 3%) = 8.526 min, t_R (major, 97%) = 8.787 min.

Diethyl (1-(benzo[*d*]oxazol-2-yl)ethyl)phosphonate **78b**



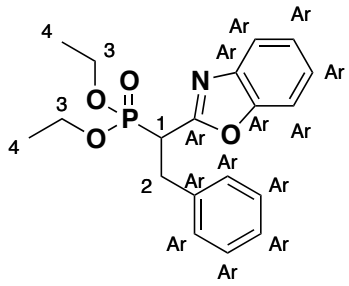
Prepared according to **Route D** from 2-ethylbenzo[*d*]oxazole (1.47 g, 10.00 mmol, 1.0 equiv). Flash column chromatography afforded *the title compound* **78b** as a yellow oil (2.42 g, 86%); **IR** (cm^{-1}) 2985, 2946, 2907, 1613, 1564, 1477, 1456, 1393, 1369, 1259, 1242, 1164, 1147, 1097, 1018; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 - 7.68 (m, 1H), 7.55 - 7.49 (m, 1H), 7.35-7.29 (m, 2H), 4.25 - 4.09 (m, 4H), 3.67 (dq, *J* = 23.7, 7.3 Hz, 1H), 1.77 (dd, *J* = 17.3, 7.3 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.5 (d, *J* = 8.8 Hz), 151.1, 141.4 (d, *J* = 1.7 Hz), 125.1, 124.5, 120.1, 110.7, 63.1 (d, *J* = 6.8 Hz), 63.1 (d, *J* = 6.4 Hz), 34.0 (d, *J* = 139.8 Hz), 16.6 (d, *J* = 5.7 Hz), 13.1 (d, *J* = 5.6 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 23.4; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{13}H_{19}NO_4P$ requires 284.1046; found, 284.1043; **GC-MS** (40 - 300 °C, 20 °C/min): t_R = 9.993 min.

2-((1*R*,2*S*)-1-Methyl-2-phenylcyclopropyl)benzo[*d*]oxazole (1*R*,2*S*)-**80a**



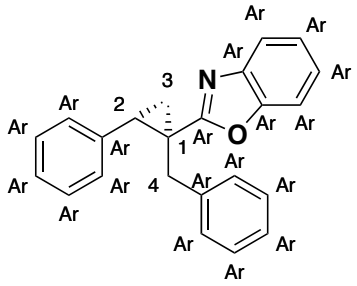
Prepared according to **Route E** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (283 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 5% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**80a** as a white solid (147 mg, 59%); **m.p.**: 35-41 °C; $[\alpha]^{25}_{D} = -344.6°$ (c = 1.44, $CHCl_3$); **IR** (cm^{-1}) 1613, 1562, 1498, 1455, 1285, 1242, 1130, 1093, 1045, 1002; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.2, 1.5 Hz, 1H, H-Ar), 7.47 (d, *J* = 7.2, 1.5 Hz, 1H, H-Ar), 7.36-7.28 (m, 3H, H-Ar), 7.28-7.22 (m, 2H, H-Ar), 3.04 (dd, *J* = 9.2, 7.5 Hz, 1H, H-2), 2.00 (dd, *J* = 9.2, 5.1 Hz, 1H, H-3), 1.50 (dd, *J* = 7.5, 5.1 Hz, 1H, H-3'), 1.35 (s, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.5 (C-Ar), 150.7 (C-Ar), 141.8 (C-Ar), 136.6 (C-Ar), 129.3 (C-Ar), 128.3 (C-Ar), 126.9 (C-Ar), 124.2 (C-Ar), 124.1 (C-Ar), 119.2 (C-Ar), 110.1 (C-Ar), 32.7 (C-2), 21.7 (C-1), 20.5 (C-3), 15.6 (C-4); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{17}H_{16}NO$ requires 250.1226; found, 250.1228; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 11%) = 9.745 min, t_R (major, 89%) = 10.719 min; **HPLC** (IC, 2% THF in Hexane, 1 mL/min): t_R (major, 98%) = 9.512 min, t_R (minor, 2%) = 11.851 min.

Diethyl (1-(benzo[*d*]oxazol-2-yl)-2-phenylethyl)phosphonate **78c**



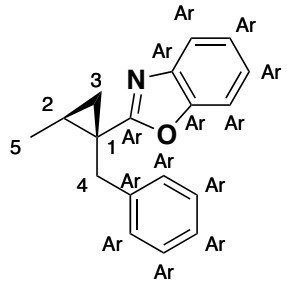
Prepared according to **Route A** from diethyl (benzo[*d*]oxazol-2-ylmethyl)phosphonate (1.74 g, 6.46 mmol). Flash column chromatography (SiO_2, 50% EtOAc in Petrol) afforded the *title compound* **78c** as a yellow oil (1.34 mg, 58%); **IR** (cm^{-1}) 1737, 1611, 1564, 1454, 1241, 1165, 1097, 1048, 1019; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70-7.64 (m, 1H, H-Ar), 7.51-7.45 (m, 1H, H-Ar), 7.33-7.27 (m, 2H, H-Ar), 7.22-7.08 (m, 5H, H-Ar), 4.23-4.05 (m, 4H. H-3), 3.88 (ddd, *J* = 23.0, 10.9 and 3.5 Hz, 1H, H-1), 3.63-3.45 (m, 2H, H-2), 1.31 (t, *J* = 7.2 Hz, 3H, H-4), 1.27 (t, *J* = 7.2 Hz, 3H, H-4); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.3 (C-Ar), 161.9 (d, *J* = 8.8 Hz, C-Ar), 151.0 (C-Ar), 141.3 (d, *J* = 2.1 Hz, C-Ar), 138.3 (d, *J* = 14.8 Hz, C-Ar), 128.7 (d, *J* = 2.0 Hz, C-Ar), 126.9 (C-Ar), 125.0 (C-Ar), 124.4 (C-Ar), 120.1 (C-Ar), 110.7 (C-Ar), 63.2 (d, *J* = 6.8 Hz, C-3), 42.1 (d, *J* = 136.4 Hz, C-1), 33.9 (d, *J* = 3.5 Hz, C-2), 16.5 (d, *J* = 5.9 Hz, C-4); **^{31}P NMR** (162 MHz, $CDCl_3$) δ 21.9; **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{19}H_{23}NO_4P$ requires 360.1375; found, 360.1366; **GC-MS** (40-300 °C, 20 °C/min): t_R = 12.309 min.

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)benzo[*d*]oxazole (1*S*,2*S*)-**80b**



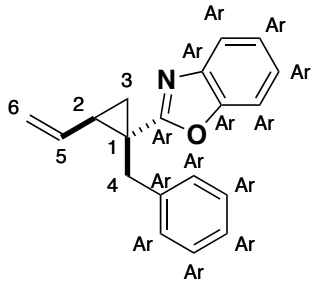
Prepared according to **Route E** from diethyl (1-(benzo[*d*]oxazol-2-yl)-2-phenylethyl)phosphonate (461 mg, 1.00 mmol, 1.0 equiv) and (*S*)-styrene oxide (114 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*S*,2*S*)-**80b** a white solid (118 mg, 36%); **m.p.**: 96-106 °C; $[\alpha]^{25}_{D}$ = –193.8° (c = 1.99, $CHCl_3$); **IR** (cm^{-1}) 1610, 1562, 1454, 1496, 1454, 1243, 1175, 1128, 1084, 1058, 1032, 1002; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 6.1, 2.3 Hz, 1H, H-Ar), 7.50-7.43 (m, 1H, H-Ar), 7.36 (dd, *J* = 7.2, 7.2 Hz, 2H, H-Ar), 7.33-7.26 (m, 5H, H-Ar), 7.17 (d, *J* = 4.2 Hz, 4H, H-Ar), 7.14-7.07 (m, 1H, H-Ar), 3.60 (d, *J* = 15.9 Hz, 1H, H-4), 2.97 (t, *J* = 7.7 Hz, 1H, H-2), 2.31 (d, *J* = 15.9 Hz, 1H, H-4'), 2.26-2.19 (m, 1H, H-3), 1.70 (dd, *J* = 7.7, 5.7 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.5 (C-Ar), 169.8 (C-Ar), 150.9 (C-Ar), 141.9 (C-Ar), 139.6 (C-Ar), 136.5 (C-Ar), 129.5 (C-Ar), 128.8 (C-Ar), 128.6 (C-Ar), 128.3 (C-Ar), 127.2 (C-Ar), 126.2 (C-Ar), 124.3 (C-Ar), 119.5 (C-Ar), 110.4 (C-Ar), 34.4 (C-4), 34.3 (C-2), 27.3 (C-1), 18.2 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{23}H_{20}NO$ requires 326.1539; found, 326.1542; **GC-MS** analysis (40-300 °C, 20 °C/min): t_R (minor, 11%) = 12.591 min, t_R (major, 89%) = 13.145 min; **HPLC** (IC, 3% THF in Hexane, 1 mL/min): t_R (minor, 1%) = 6.830 min, t_R (major, 99%) = 9.183 min.

2-((1*R*,2*S*)-1-Benzyl-2-methylcyclopropyl)benzo[*d*]oxazole (1*R*,2*S*)-**80c**



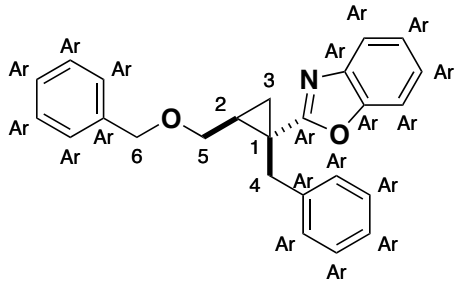
Prepared according to **Route E** from diethyl (1-(benzo[*d*]oxazol-2-yl)-2-phenylethyl)phosphonate (461 mg, 1.00 mmol, 1.0 equiv) and (*R*)-propylene oxide (70 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R*,2*S*)-**80c** as a yellow oil (152 mg, 58%); **IR** (cm^{-1}) 1612, 1560, 1496, 1455, 1243, 1137, 1121, 1098, 1078, 1031, 1003; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66-7.62 (m, 1H, H-Ar), 7.45-7.41 (m, 1H, H-Ar), 7.36-7.23 (m, 6H, H-Ar), 7.18 (dd, *J* = 7.3, 7.3 Hz, 1H, H-Ar), 3.61 (d, *J* = 16.1 Hz, 1H, H-4), 3.21 (d, *J* = 16.1 Hz, 1H, H-4'), 1.93-1.78 (m, 2H, H-2 and H-3), 1.36 (d, *J* = 6.2 Hz, 3H, H-5), 0.88 (dd, *J* = 6.2, 4.5 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.7 (C-Ar), 150.8 (C-Ar), 141.9 (C-Ar), 139.9 (C-Ar), 128.8 (C-Ar), 128.4 (C-Ar), 126.1 (C-Ar), 124.1 (C-Ar), 124.0 (C-Ar), 119.3 (C-Ar), 110.1 (C-Ar), 34.3 (C-4), 24.1 (C-2), 23.1 (C-1), 22.9 (C-3), 14.3 (C-5); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{18}NO$ requires 264.1383; found, 264.1386; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 9%) = 10.435 min, t_R (major, 91%) = 10.810 min.

2-((1*R**,2*R**)-1-Benzyl-2-vinylcyclopropyl)benzo[*d*]oxazole (1*R**,2*R**)-**80d**



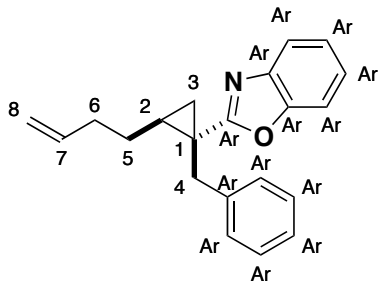
Prepared according to **Route E** from diethyl (1-(benzo[*d*]oxazol-2-yl)-2-phenylethyl)phosphonate (461 mg, 1.00 mmol, 1.0 equiv) and (±)-vinyl oxirane (81 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R**,2*R**)-**80d** as a yellow oil (58 mg, 21%); **IR** (cm^{-1}) 1612, 1561, 1496, 1473, 1454, 1242, 1122, 1100, 1078, 1031, 1002; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63-7.59 (m, 1H, H-Ar), 7.43-7.39 (m, 1H, H-Ar), 7.35-7.18 (m, 6H, H-Ar), 7.14 (dd, *J* = 7.4, 7.4 Hz, 1H, H-Ar), 5.90-5.78 (m, 1H, H-5), 5.30 (d, *J* = 17.0 Hz, 1H, H-6), 5.24 (d, *J* = 10.3 Hz, 1H, H-6'), 3.61 (d, *J* = 15.9 Hz, 1H, H-4), 3.05 (d, *J* = 15.9 Hz, 1H, H-4'), 2.45 (dd, *J* = 8.9, 7.6 Hz, 1H, H-2), 1.98 (dd, *J* = 8.9, 5.3 Hz, 1H, H-3), 1.28 (dd, *J* = 7.6, 5.3 Hz, 1H, H-3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.8 (C-Ar), 141.8 (C-Ar), 139.5 (C-5), 135.0 (C-Ar), 128.9 (C-Ar), 128.4 (C-Ar), 126.3 (C-Ar), 124.2 (C-Ar), 119.5 (C-Ar), 118.3 (C-Ar), 110.3 (C-6), 34.5 (C-4), 32.0 (C-2), 26.7 (C-1), 20.7 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{12}H_{12}NO$ requires 276.1383; found, 276.1387; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 7%) = 11.166 min, t_R (major, 93%) = 11.707 min.

2-((1*R**,2*S**)-1-Benzyl-2-((benzyloxy)methyl)cyclopropyl)benzo[*d*]oxazole (1*R**,2*S**)-**80e**



Prepared according to **Route E** from diethyl (1-(benzo[*d*]oxazol-2-yl)-2-phenylethyl)phosphonate (461 mg, 1.00 mmol, 1.0 equiv) and (±)-benzyl glycidyl ether (153 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R**,2*S**)-**80e** as a yellow oil (182 mg, 49%); **IR** (cm^{-1}1612, 1562, 1496, 1455, 1243, 1162, 1101, 1077, 1028, 1002; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64-7.57 (m, 1H, H-Ar), 7.42-7.38 (m, 1H, H-Ar), 7.35 (d, *J* = 4.3 Hz, 4H, H-Ar), 7.31-7.17 (m, 7H, H-Ar), 7.14 (dd, *J* = 7.1, 7.1 Hz, 1H, H-Ar), 4.58 (d, *J* = 12.0 Hz, 1H, H-6), 4.53 (d, *J* = 12.0 Hz, 1H, H-6'), 3.80 (dd, *J* = 10.8, 5.6 Hz, 1H, H-5), 3.75 (d, *J* = 16.0 Hz, 1H, H-4), 3.60 (dd, *J* = 10.8, 8.2 Hz, 1H, H-5'), 3.04 (d, *J* = 16.0 Hz, 1H, H-4), 2.15-2.04 (m, 1H, H-2), 1.86 (dd, *J* = 8.2, 5.6 Hz, 1H, H-3), 1.08 (dd, *J* = 6.7, 5.6 Hz, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.8 (C-Ar), 150.9, (C-Ar), 141.8 (C-Ar), 139.6 (C-Ar), 138.3 (C-Ar), 128.8 (C-Ar), 128.6 (C-Ar), 128.4 (C-Ar), 128.0 (C-Ar), 127.9 (C-Ar), 124.2 (C-Ar), 124.2 (C-Ar), 110.3 (C-Ar), 73.0 (C-6), 69.2 (C-5), 34.2, (C-4) 28.1 (C-2), 24.6 (C-1), 19.2 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{18}H_{18}NO_2$ requires 370.1802; found, 370.1805; **GC-MS** (40-300 °C, 20 °C/min): t_R (minor, 7%) = 13.813 min, t_R (major, 93%) = 14.297 min.

2-((1*R**,2*S**)-1-Benzyl-2-(but-3-en-1-yl)cyclopropyl)benzo[*d*]oxazole (1*R**,2*S**)-**80f**



Prepared according to **Route E** from diethyl (1-(benzo[*d*]oxazol-2-yl)-2-phenylethyl)phosphonate (461 mg, 1.00 mmol, 1.0 equiv) and (±)-1,2-epoxy-5-hexene (113 μL, 1.00 mmol, 1.0 equiv). Flash column chromatography (SiO_2, 10% Et_2O in Petrol) afforded the *title compound* (1*R**,2*S**)-**80f** as a colourless oil; **IR** (cm^{-1}) 1612, 1561, 1496, 1455, 1242, 1122, 1031, 1002; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62-7.58 (m, 1H, H-Ar), 7.42-7.38 (m, 1H, H-Ar), 7.32-7.18 (m, 6H, H-Ar), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H, H-Ar), 5.94-5.81 (m, 1H, H-7), 5.05 (dd, *J* = 17.1, 1.7 Hz, 1H, H-8), 4.99 (dd, *J* = 10.2, 1.7 Hz, 1H, H-8'), 3.67 (d, *J* = 16.0 Hz, 1H, H-4), 3.07 (d, *J* = 16.0 Hz, 1H, H-4'), 2.29-2.21 (m, 2H, H-6), 1.87-1.78 (m, 2H, H-2 and H-3), 1.78-1.68 (m, 1H, H-5), 1.60-1.50 (m, 1H, H-5), 0.96-0.84 (m, 1H, H-3'); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.6 (C-Ar), 150.8 (C-Ar), 141.8 (C-Ar), 139.8 (C-Ar), 138.1 (C-7), 128.8 (C-Ar), 128.4 (C-Ar), 126.2 (C-Ar), 124.1 (C-Ar), 124.1 (C-Ar), 119.4 (C-Ar), 115.3 (C-8), 110.2 (C-Ar), 34.5 (C-4), 33.7 (C-6), 29.2 (C-2), 28.9 (C-5), 24.4 (C-1), 21.7 (C-3); **HRMS-ESI** (*m/z*) $[M + H]^+$ calcd for $C_{15}H_{18}N$ requires 304.1696; found, 304.1699; **GC-MS** (40 - 300 °C, 20 °C/min): t_R (minor, 6%) = 11.421 min, t_R (major, 94%) = 11.853 min.

4 CRYSTALLOGRAPHYC DATA

(1*R*,2*R*)-Ethyl 2-phenylcyclopropanecarboxylate 5a

Crystal data

$C_{12}H_{14}O_2$	
M_r = 190.23	D_x = 1.224 Mg m^{-3}
Orthorhombic, *Pca*2$_1$	Melting point: 37 °C
Hall symbol: ?	radiation, λ = 0.71073 Å
a = 6.7594 (14) Å	Cell parameters from 3334 reflections
b = 7.5434 (16) Å	θ = 2.7–28.3°
c = 20.239 (4) Å	μ = 0.08 mm^{-1}
V = 1032.0 (4) Å^3	*T* = 100 K
Z = 4	Block, translucent colourless
F(000) = 408	0.35 × 0.15 × 0.05 mm

Data collection

diffractometer	2039 independent reflections
Radiation source:	1949 reflections with $I > 2\sigma(I)$
	R_{int} = 0.047
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.3°, θ_{min} = 2.0°
	h = −4→9
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	*k* = −10→9
T_{min} = 0.68, T_{max} = 1.00	*l* = −27→22
5035 measured reflections	

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.065$
$wR(F^2) = 0.177$
$S = 1.00$
2039 reflections
128 parameters
1 restraint
constraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.4698 (6)	1.3785 (5)	0.2093 (2)	0.0460 (9)
H1B	0.4047	1.4535	0.2424	0.069*
H1C	0.4442	1.426	0.1651	0.069*
H1A	0.6127	1.3771	0.2176	0.069*
C2	0.3914 (4)	1.1966 (5)	0.21389 (16)	0.0308 (7)
H2B	0.2504	1.1949	0.2006	0.037*

H2A	0.4659	1.1173	0.1839	0.037*
C3	0.4075 (3)	0.9600 (4)	0.29070 (13)	0.0168 (5)
C4	0.4275 (3)	0.9161 (3)	0.36159 (12)	0.0154 (5)
H4	0.4411	1.0174	0.3931	0.018*
C5	0.3162 (3)	0.7528 (3)	0.38588 (13)	0.0169 (5)
H5	0.2397	0.6873	0.3514	0.02*
C6	0.5350 (4)	0.7468 (3)	0.37857 (16)	0.0226 (5)
H6A	0.5899	0.6761	0.3416	0.027*
H6B	0.6155	0.7454	0.4194	0.027*
C7	0.2248 (3)	0.7554 (3)	0.45330 (13)	0.0163 (5)
C8	0.0495 (4)	0.6626 (3)	0.46390 (13)	0.0183 (5)
H8	−0.0114	0.6019	0.4281	0.022*
C9	−0.0376 (4)	0.6575 (4)	0.52621 (15)	0.0252 (6)
H9	−0.1567	0.593	0.5329	0.03*
C10	0.0498 (4)	0.7467 (4)	0.57863 (14)	0.0247 (6)
H10	−0.0087	0.7433	0.6213	0.03*
C11	0.2225 (4)	0.8404 (4)	0.56817 (14)	0.0251 (6)
H11	0.2821	0.9022	0.6039	0.03*
C12	0.3100 (4)	0.8455 (4)	0.50630 (13)	0.0197 (5)
H12	0.4287	0.9108	0.4999	0.024*
O1	0.4113 (2)	1.1360 (3)	0.28169 (10)	0.0198 (4)
O2	0.3913 (3)	0.8532 (3)	0.24673 (12)	0.0274 (5)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.052 (2)	0.0345 (19)	0.052 (2)	0.0057 (15)	0.0050 (18)	0.0212 (17)
C2	0.0325 (13)	0.0391 (17)	0.0208 (14)	0.0007 (12)	0.0025 (10)	0.0133 (13)
C3	0.0133 (9)	0.0181 (12)	0.0190 (11)	0.0000 (7)	0.0016 (7)	0.0005 (9)

C4	0.0170 (9)	0.0117 (10)	0.0173 (12)	−0.0024 (7)	−0.0002 (7)	0.0019 (8)
C5	0.0173 (10)	0.0127 (10)	0.0207 (12)	−0.0014 (7)	0.0012 (8)	−0.0002 (8)
C6	0.0201 (11)	0.0190 (12)	0.0287 (13)	0.0034 (8)	0.0047 (10)	0.0053 (10)
C7	0.0165 (10)	0.0132 (10)	0.0193 (12)	0.0026 (7)	−0.0010 (8)	0.0001 (9)
C8	0.0211 (10)	0.0137 (10)	0.0201 (12)	−0.0023 (8)	−0.0020 (9)	0.0001 (9)
C9	0.0274 (12)	0.0183 (12)	0.0299 (16)	−0.0004 (9)	0.0054 (10)	0.0022 (11)
C10	0.0362 (14)	0.0209 (13)	0.0171 (13)	0.0066 (10)	0.0049 (10)	0.0054 (10)
C11	0.0318 (13)	0.0231 (13)	0.0204 (13)	0.0034 (9)	−0.0091 (10)	−0.0018 (11)
C12	0.0193 (10)	0.0198 (12)	0.0199 (13)	−0.0021 (8)	−0.0049 (8)	0.0005 (10)
O1	0.0232 (8)	0.0181 (9)	0.0181 (10)	0.0005 (6)	0.0023 (7)	0.0049 (7)
O2	0.0373 (10)	0.0270 (11)	0.0178 (9)	−0.0043 (8)	0.0037 (8)	−0.0047 (8)

Geometric parameters (Å, °)

C1—C2	1.474 (6)	C5—H5	1.0
C1—H1B	0.98	C6—H6A	0.99
C1—H1C	0.98	C6—H6B	0.99
C1—H1A	0.98	C7—C8	1.393 (3)
C2—O1	1.453 (3)	C7—C12	1.395 (3)
C2—H2B	0.99	C8—C9	1.392 (4)
C2—H2A	0.99	C8—H8	0.95
C3—O2	1.206 (4)	C9—C10	1.388 (4)
C3—O1	1.340 (3)	C9—H9	0.95
C3—C4	1.479 (4)	C10—C11	1.381 (4)
C4—C6	1.509 (3)	C10—H10	0.95
C4—C5	1.525 (3)	C11—C12	1.385 (4)
C4—H4	1.0	C11—H11	0.95
C5—C6	1.487 (3)	C12—H12	0.95
C5—C7	1.498 (3)		

C2—C1—H1B	109.5	C4—C5—H5	115.4
C2—C1—H1C	109.5	C5—C6—C4	61.17 (15)
H1B—C1—H1C	109.5	C5—C6—H6A	117.7
C2—C1—H1A	109.5	C4—C6—H6A	117.7
H1B—C1—H1A	109.5	C5—C6—H6B	117.7
H1C—C1—H1A	109.5	C4—C6—H6B	117.7
O1—C2—C1	108.6 (3)	H6A—C6—H6B	114.8
O1—C2—H2B	110.0	C8—C7—C12	118.6 (2)
C1—C2—H2B	110.0	C8—C7—C5	119.0 (2)
O1—C2—H2A	110.0	C12—C7—C5	122.4 (2)
C1—C2—H2A	110.0	C9—C8—C7	120.9 (2)
H2B—C2—H2A	108.4	C9—C8—H8	119.6
O2—C3—O1	124.3 (3)	C7—C8—H8	119.6
O2—C3—C4	125.1 (3)	C10—C9—C8	119.9 (2)
O1—C3—C4	110.6 (2)	C10—C9—H9	120.0
C3—C4—C6	117.0 (2)	C8—C9—H9	120.0
C3—C4—C5	116.7 (2)	C11—C10—C9	119.4 (3)
C6—C4—C5	58.70 (16)	C11—C10—H10	120.3
C3—C4—H4	117.2	C9—C10—H10	120.3
C6—C4—H4	117.2	C10—C11—C12	120.9 (3)
C5—C4—H4	117.2	C10—C11—H11	119.5
C6—C5—C7	120.1 (2)	C12—C11—H11	119.5
C6—C5—C4	60.13 (15)	C11—C12—C7	120.3 (2)
C7—C5—C4	119.1 (2)	C11—C12—H12	119.8
C6—C5—H5	115.4	C7—C12—H12	119.8
C7—C5—H5	115.4	C3—O1—C2	116.0 (2)
O2—C3—C4—C6	32.4 (3)	C4—C5—C7—C12	−34.0 (3)
O1—C3—C4—C6	−147.1 (2)	C12—C7—C8—C9	−0.9 (4)

O2—C3—C4—C5	−34.2 (3)	C5—C7—C8—C9	178.3 (2)
O1—C3—C4—C5	146.3 (2)	C7—C8—C9—C10	0.4 (4)
C3—C4—C5—C6	106.9 (3)	C8—C9—C10—C11	0.2 (4)
C3—C4—C5—C7	−143.2 (2)	C9—C10—C11—C12	−0.4 (4)
C6—C4—C5—C7	110.0 (3)	C10—C11—C12—C7	−0.1 (4)
C7—C5—C6—C4	−108.4 (2)	C8—C7—C12—C11	0.8 (4)
C3—C4—C6—C5	−106.2 (2)	C5—C7—C12—C11	−178.4 (2)
C6—C5—C7—C8	−142.8 (2)	O2—C3—O1—C2	0.9 (3)
C4—C5—C7—C8	146.8 (2)	C4—C3—O1—C2	−179.55 (19)
C6—C5—C7—C12	36.3 (3)	C1—C2—O1—C3	−159.5 (3)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Data collection: Bruker Instrument Service v2012.6.0.0; cell refinement: *SAINT* V8.18C (Bruker AXS Inc., 2011); data reduction: *SAINT* V8.18C (Bruker AXS Inc., 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

(1*R*,2*R*)-2-Phenylcyclopropanecarbonitrile 6a

Crystal data

$C_{10}H_9N$	
M_r = 143.18	D_x = 1.205 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 74-81 °C
Hall symbol: ?	radiation, λ = 0.71073 Å
a = 6.225 (3) Å	Cell parameters from 527 reflections
b = 7.555 (4) Å	θ = 3.5–24.9°
c = 16.776 (7) Å	μ = 0.07 mm^{-1}
V = 789.0 (6) Å^3	*T* = 108 K
Z = 4	Shard, translucent colourless
F(000) = 304	0.50 × 0.14 × 0.06 mm

Data collection

diffractometer	1898 independent reflections
Radiation source:	1317 reflections with $I > 2\sigma(I)$
	R_{int} = 0.053
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.2°, θ_{min} = 3.0°
	h = −7→8
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	*k* = −8→9
T_{min} = 0.79, T_{max} = 1.00	*l* = −22→21
3742 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.051$	$w = 1/[\sigma^2(F_o^2) + (0.0384P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.103$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.01$	$\Delta\rho_{max} = 0.17$ e Å^{-3}
1898 reflections	$\Delta\rho_{min} = -0.21$ e Å^{-3}
100 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: −9 (6)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	−0.2229 (4)	0.4388 (3)	0.04419 (11)	0.0245 (5)
C2	−0.0132 (4)	0.4555 (3)	0.07986 (10)	0.0220 (5)
H2	0.0835	0.3503	0.0755	0.026*
C3	0.0065 (4)	0.5662 (3)	0.15649 (10)	0.0217 (5)

H3	−0.1298	0.6233	0.1748	0.026*
C4	0.0946 (4)	0.6356 (3)	0.07881 (11)	0.0268 (5)
H4A	0.2526	0.639	0.0724	0.032*
H4B	0.0168	0.7343	0.0528	0.032*
C5	0.1539 (3)	0.5085 (3)	0.22149 (11)	0.0197 (5)
C6	0.1022 (4)	0.5475 (3)	0.30040 (10)	0.0210 (5)
H6	−0.0327	0.5999	0.3124	0.025*
C7	0.2447 (4)	0.5109 (3)	0.36157 (11)	0.0245 (5)
H7	0.208	0.5399	0.415	0.029*
C8	0.4419 (4)	0.4317 (3)	0.34500 (11)	0.0260 (5)
H8	0.5413	0.4086	0.3867	0.031*
C9	0.4913 (4)	0.3872 (3)	0.26730 (11)	0.0254 (5)
H9	0.6238	0.3301	0.2559	0.031*
C10	0.3499 (4)	0.4248 (3)	0.20587 (11)	0.0233 (5)
H10	0.3862	0.3935	0.1527	0.028*
N1	−0.3906 (3)	0.4264 (3)	0.01569 (10)	0.0308 (5)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0400 (15)	0.0115 (11)	0.0219 (10)	0.0014 (11)	0.0017 (9)	−0.0005 (9)
C2	0.0308 (13)	0.0160 (11)	0.0192 (9)	−0.0001 (10)	−0.0028 (9)	−0.0019 (8)
C3	0.0273 (12)	0.0148 (10)	0.0229 (9)	0.0005 (11)	−0.0007 (9)	−0.0026 (9)
C4	0.0364 (15)	0.0178 (11)	0.0263 (10)	−0.0042 (11)	−0.0020 (10)	0.0032 (9)
C5	0.0254 (13)	0.0093 (9)	0.0244 (9)	−0.0021 (9)	0.0005 (8)	−0.0002 (8)
C6	0.0253 (12)	0.0123 (11)	0.0254 (9)	−0.0011 (10)	0.0030 (8)	−0.0029 (9)
C7	0.0366 (14)	0.0163 (11)	0.0207 (10)	−0.0029 (11)	0.0015 (9)	−0.0020 (8)
C8	0.0329 (13)	0.0182 (11)	0.0267 (10)	0.0003 (11)	−0.0038 (9)	0.0017 (10)
C9	0.0279 (13)	0.0174 (11)	0.0309 (11)	0.0025 (11)	0.0021 (9)	0.0008 (9)

C10	0.0331 (14)	0.0121 (10)	0.0247 (10)	0.0027 (10)	0.0029 (9)	−0.0018 (9)
N1	0.0417 (13)	0.0205 (11)	0.0302 (9)	0.0020 (10)	−0.0068 (9)	−0.0006 (8)

Geometric parameters (Å, °)

C1—N1	1.152 (3)	C5—C10	1.399 (3)
C1—C2	1.442 (3)	C6—C7	1.384 (3)
C2—C4	1.517 (3)	C6—H6	0.95
C2—C3	1.539 (3)	C7—C8	1.394 (3)
C2—H2	1.0	C7—H7	0.95
C3—C5	1.491 (3)	C8—C9	1.381 (3)
C3—C4	1.508 (3)	C8—H8	0.95
C3—H3	1.0	C9—C10	1.385 (3)
C4—H4A	0.99	C9—H9	0.95
C4—H4B	0.99	C10—H10	0.95
C5—C6	1.394 (3)		

N1—C1—C2	179.7 (3)	C6—C5—C10	118.36 (18)
C1—C2—C4	118.29 (19)	C6—C5—C3	119.39 (19)
C1—C2—C3	117.80 (19)	C10—C5—C3	122.15 (17)
C4—C2—C3	59.13 (13)	C7—C6—C5	120.9 (2)
C1—C2—H2	116.5	C7—C6—H6	119.5
C4—C2—H2	116.5	C5—C6—H6	119.5
C3—C2—H2	116.5	C6—C7—C8	120.16 (18)
C5—C3—C4	120.7 (2)	C6—C7—H7	119.9
C5—C3—C2	120.09 (18)	C8—C7—H7	119.9
C4—C3—C2	59.73 (13)	C9—C8—C7	119.3 (2)
C5—C3—H3	115.1	C9—C8—H8	120.4
C4—C3—H3	115.1	C7—C8—H8	120.4

C2—C3—H3	115.1	C8—C9—C10	120.7 (2)
C3—C4—C2	61.14 (13)	C8—C9—H9	119.6
C3—C4—H4A	117.7	C10—C9—H9	119.6
C2—C4—H4A	117.7	C9—C10—C5	120.52 (18)
C3—C4—H4B	117.7	C9—C10—H10	119.7
C2—C4—H4B	117.7	C5—C10—H10	119.7
H4A—C4—H4B	114.8		
N1—C1—C2—C4	−20 (30)	C2—C3—C5—C10	35.1 (3)
N1—C1—C2—C3	50 (30)	C10—C5—C6—C7	2.5 (3)
C1—C2—C3—C5	141.9 (2)	C3—C5—C6—C7	−173.8 (2)
C4—C2—C3—C5	−110.1 (2)	C5—C6—C7—C8	−0.9 (3)
C1—C2—C3—C4	−108.0 (2)	C6—C7—C8—C9	−1.3 (3)
C5—C3—C4—C2	109.2 (2)	C7—C8—C9—C10	1.8 (3)
C1—C2—C4—C3	107.2 (2)	C8—C9—C10—C5	−0.1 (3)
C4—C3—C5—C6	140.8 (2)	C6—C5—C10—C9	−2.0 (3)
C2—C3—C5—C6	−148.68 (19)	C3—C5—C10—C9	174.2 (2)
C4—C3—C5—C10	−35.4 (3)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2012.6.0.0; cell refinement: *SAINT* V8.18C (Bruker AXS Inc., 2011); data reduction: *SAINT* V8.18C (Bruker AXS Inc., 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

(1*S*,2*S*)-1-Benzyl-2-phenylcyclopropanecarbonitrile 59a

Crystal data

$C_{17}H_{15}N$	
M_r = 233.30	D_x = 1.212 Mg m^{-3}
Orthorhombic, *Aba*2	Melting point: 73-81 °C
Hall symbol: ?	radiation, λ = 1.54178 Å
a = 19.9490 (13) Å	Cell parameters from 9897 reflections
b = 17.0062 (12) Å	θ = 5.2–63.7°
c = 7.5354 (5) Å	μ = 0.54 mm^{-1}
V = 2556.4 (3) Å^3	*T* = 100 K
Z = 8	Needle, translucent colourless
F(000) = 992	0.35 × 0.05 × 0.05 mm

Data collection

diffractometer	1892 independent reflections
Radiation source:	1878 reflections with $I > 2\sigma(I)$
	R_{int} = 0.032
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 63.7°, θ_{min} = 5.2°
	h = −23→23
Absorption correction: multi-scan *SADABS* V2012/1 (Bruker AXS Inc.)	*k* = −19→17
T_{min} = 0.84, T_{max} = 0.97	*l* = −8→6
11616 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.024$	$w = 1/[\sigma^2(F_o^2) + (0.0324P)^2 + 0.8577P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.059$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.05$	$\Delta\rho_{max} = 0.09$ e Å^{-3}
1892 reflections	$\Delta\rho_{min} = -0.13$ e Å^{-3}
163 parameters	Extinction correction: none
1 restraint	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.0 (6)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.26197 (5)	0.79658 (6)	0.91922 (17)	0.0256 (3)
C1	0.29177 (6)	1.10170 (7)	1.16120 (19)	0.0216 (3)
H1	0.2643	1.1424	1.208	0.026*
C2	0.33485 (6)	1.11700 (7)	1.0206 (2)	0.0216 (3)

H15	0.3374	1.1685	0.9722	0.026*
C3	0.37424 (6)	1.05723 (7)	0.95064 (19)	0.0185 (3)
H3	0.4038	1.0683	0.855	0.022*
C4	0.37083 (5)	0.98136 (7)	1.01913 (18)	0.0160 (3)
C5	0.40819 (5)	0.91459 (6)	0.92999 (19)	0.0172 (3)
H14	0.4227	0.8761	1.0208	0.021*
H6	0.4488	0.9355	0.8709	0.021*
C6	0.36402 (5)	0.87361 (7)	0.79331 (19)	0.0166 (3)
C7	0.39351 (6)	0.83965 (7)	0.62245 (18)	0.0180 (3)
H7	0.37	0.7918	0.5772	0.022*
C8	0.46747 (6)	0.84012 (7)	0.59094 (17)	0.0168 (3)
C9	0.49608 (6)	0.89099 (7)	0.46823 (18)	0.0185 (3)
H11	0.4685	0.9275	0.4068	0.022*
C10	0.56455 (6)	0.88902 (7)	0.4343 (2)	0.0213 (3)
H8	0.5835	0.9239	0.3497	0.026*
C11	0.60510 (6)	0.83613 (7)	0.5240 (2)	0.0213 (3)
H2	0.6519	0.8349	0.5013	0.026*
C12	0.32810 (5)	0.96691 (7)	1.16192 (18)	0.0175 (3)
H5	0.3257	0.9156	1.2112	0.021*
C13	0.28904 (6)	1.02663 (7)	1.23274 (18)	0.0202 (3)
H4	0.2603	1.0161	1.3305	0.024*
C14	0.57714 (6)	0.78498 (7)	0.64682 (19)	0.0214 (3)
H10	0.6049	0.7486	0.708	0.026*
C15	0.50872 (6)	0.78672 (7)	0.68071 (19)	0.0201 (3)
H9	0.4899	0.7516	0.765	0.024*
C16	0.35266 (6)	0.91333 (7)	0.61532 (19)	0.0190 (3)
H12	0.3073	0.91	0.5627	0.023*
H13	0.3765	0.9634	0.5924	0.023*

C17	0.30713 (6)	0.83078 (7)	0.86495 (18)	0.0186 (3)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0196 (5)	0.0242 (5)	0.0330 (7)	−0.0010 (4)	0.0071 (5)	−0.0019 (5)
C1	0.0158 (6)	0.0244 (6)	0.0244 (8)	0.0024 (5)	−0.0052 (5)	−0.0093 (6)
C2	0.0221 (6)	0.0169 (6)	0.0259 (8)	−0.0011 (5)	−0.0071 (6)	−0.0020 (6)
C3	0.0172 (5)	0.0206 (6)	0.0178 (7)	−0.0039 (4)	−0.0024 (5)	−0.0019 (5)
C4	0.0107 (5)	0.0201 (6)	0.0172 (7)	−0.0009 (4)	−0.0031 (5)	−0.0017 (5)
C5	0.0130 (5)	0.0192 (6)	0.0194 (7)	−0.0003 (4)	0.0008 (5)	−0.0001 (5)
C6	0.0143 (5)	0.0153 (6)	0.0203 (7)	0.0009 (4)	0.0022 (5)	−0.0009 (5)
C7	0.0175 (6)	0.0170 (6)	0.0194 (8)	−0.0030 (4)	0.0031 (5)	−0.0033 (5)
C8	0.0176 (6)	0.0150 (6)	0.0176 (7)	−0.0005 (4)	0.0017 (5)	−0.0059 (5)
C9	0.0194 (6)	0.0155 (6)	0.0207 (7)	−0.0001 (4)	0.0023 (5)	−0.0018 (5)
C10	0.0208 (6)	0.0194 (6)	0.0238 (8)	−0.0046 (5)	0.0063 (6)	−0.0031 (6)
C11	0.0156 (6)	0.0224 (6)	0.0259 (8)	−0.0020 (4)	0.0023 (6)	−0.0065 (6)
C12	0.0150 (5)	0.0192 (6)	0.0184 (7)	−0.0022 (4)	−0.0030 (5)	0.0005 (6)
C13	0.0135 (5)	0.0287 (7)	0.0184 (7)	−0.0025 (5)	−0.0009 (5)	−0.0060 (5)
C14	0.0206 (6)	0.0205 (6)	0.0232 (8)	0.0024 (5)	−0.0016 (5)	−0.0049 (6)
C15	0.0228 (6)	0.0168 (6)	0.0208 (7)	−0.0005 (5)	0.0033 (6)	−0.0018 (5)
C16	0.0151 (5)	0.0217 (6)	0.0200 (7)	−0.0005 (5)	−0.0001 (6)	−0.0017 (5)
C17	0.0163 (6)	0.0174 (6)	0.0220 (7)	0.0021 (5)	0.0013 (5)	−0.0039 (5)

Geometric parameters (Å, °)

N1—C17	1.1477 (17)	C7—H7	1.0
C1—C13	1.3869 (19)	C8—C9	1.3889 (18)
C1—C2	1.389 (2)	C8—C15	1.3998 (18)
C1—H1	0.95	C9—C10	1.3902 (17)

C2—C3	1.3887 (17)	C9—H11	0.95
C2—H15	0.95	C10—C11	1.3853 (18)
C3—C4	1.3913 (17)	C10—H8	0.95
C3—H3	0.95	C11—C14	1.387 (2)
C4—C12	1.3946 (18)	C11—H2	0.95
C4—C5	1.5153 (16)	C12—C13	1.3868 (17)
C5—C6	1.5242 (18)	C12—H5	0.95
C5—H14	0.99	C13—H4	0.95
C5—H6	0.99	C14—C15	1.3890 (17)
C6—C17	1.4525 (18)	C14—H10	0.95
C6—C16	1.5187 (19)	C15—H9	0.95
C6—C7	1.5289 (18)	C16—H12	0.99
C7—C8	1.4944 (16)	C16—H13	0.99
C7—C16	1.4957 (17)		
C13—C1—C2	119.55 (11)	C9—C8—C7	120.99 (11)
C13—C1—H1	120.2	C15—C8—C7	120.00 (11)
C2—C1—H1	120.2	C8—C9—C10	120.74 (11)
C1—C2—C3	120.18 (12)	C8—C9—H11	119.6
C1—C2—H15	119.9	C10—C9—H11	119.6
C3—C2—H15	119.9	C11—C10—C9	119.99 (12)
C2—C3—C4	120.68 (12)	C11—C10—H8	120.0
C2—C3—H3	119.7	C9—C10—H8	120.0
C4—C3—H3	119.7	C10—C11—C14	119.85 (11)
C3—C4—C12	118.65 (11)	C10—C11—H2	120.1
C3—C4—C5	120.43 (11)	C14—C11—H2	120.1
C12—C4—C5	120.71 (10)	C13—C12—C4	120.75 (11)
C4—C5—C6	110.96 (9)	C13—C12—H5	119.6
C4—C5—H14	109.4	C4—C12—H5	119.6

C6—C5—H14	109.4	C12—C13—C1	120.16 (12)
C4—C5—H6	109.4	C12—C13—H4	119.9
C6—C5—H6	109.4	C1—C13—H4	119.9
H14—C5—H6	108.0	C11—C14—C15	120.28 (12)
C17—C6—C16	115.77 (11)	C11—C14—H10	119.9
C17—C6—C5	115.46 (12)	C15—C14—H10	119.9
C16—C6—C5	118.66 (10)	C14—C15—C8	120.18 (12)
C17—C6—C7	115.10 (10)	C14—C15—H9	119.9
C16—C6—C7	58.78 (8)	C8—C15—H9	119.9
C5—C6—C7	121.29 (10)	C7—C16—C6	60.95 (8)
C8—C7—C16	121.84 (10)	C7—C16—H12	117.7
C8—C7—C6	120.78 (10)	C6—C16—H12	117.7
C16—C7—C6	60.27 (8)	C7—C16—H13	117.7
C8—C7—H7	114.5	C6—C16—H13	117.7
C16—C7—H7	114.5	H12—C16—H13	114.8
C6—C7—H7	114.5	N1—C17—C6	179.04 (15)
C9—C8—C15	118.96 (11)		
C13—C1—C2—C3	0.89 (19)	C15—C8—C9—C10	0.14 (19)
C1—C2—C3—C4	0.44 (19)	C7—C8—C9—C10	−177.42 (12)
C2—C3—C4—C12	−1.33 (18)	C8—C9—C10—C11	−0.28 (19)
C2—C3—C4—C5	173.41 (11)	C9—C10—C11—C14	0.3 (2)
C3—C4—C5—C6	−91.46 (13)	C3—C4—C12—C13	0.91 (17)
C12—C4—C5—C6	83.18 (14)	C5—C4—C12—C13	−173.82 (11)
C4—C5—C6—C17	−67.18 (13)	C4—C12—C13—C1	0.40 (17)
C4—C5—C6—C16	76.82 (14)	C2—C1—C13—C12	−1.30 (18)
C4—C5—C6—C7	145.78 (11)	C10—C11—C14—C15	−0.19 (19)
C17—C6—C7—C8	−142.35 (12)	C11—C14—C15—C8	0.05 (19)
C16—C6—C7—C8	111.53 (13)	C9—C8—C15—C14	−0.03 (18)

C5—C6—C7—C8	4.80 (17)	C7—C8—C15—C14	177.56 (11)
C17—C6—C7—C16	106.12 (12)	C8—C7—C16—C6	−109.81 (13)
C5—C6—C7—C16	−106.74 (12)	C17—C6—C16—C7	−104.96 (11)
C16—C7—C8—C9	−35.42 (18)	C5—C6—C16—C7	111.15 (11)
C6—C7—C8—C9	−107.38 (14)	C16—C6—C17—N1	38 (8)
C16—C7—C8—C15	147.05 (13)	C5—C6—C17—N1	−180 (100)
C6—C7—C8—C15	75.08 (15)	C7—C6—C17—N1	−28 (8)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Data collection: Bruker Instrument Service v2012.12.0.3; cell refinement: *SAINT* V8.27B (Bruker AXS Inc., 2012); data reduction: *SAINT* V8.27B (Bruker AXS Inc., 2012); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008)

((1*S*,2*R*)-2-Methyl-2-(phenylsulfonyl)cyclopropyl)benzene 62a

Crystal data

$C_{16}H_{16}O_2S$	
M_r = 272.35	D_x = 1.290 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 120-122 °C
Hall symbol: P 2ac 2ab	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 8.1715 (3) Å	Cell parameters from 5950 reflections
b = 10.0740 (2) Å	θ = 2.9–27.5°
c = 17.0385 (6) Å	μ = 0.23 mm^{-1}
V = 1402.60 (8) Å^3	T = 120 K
Z = 4	Block, colourless
F(000) = 576	0.20 × 0.12 × 0.07 mm

Data collection

Bruker-Nonius Roper CCD camera on κ-goniostat diffractometer	3138 independent reflections
Radiation source: Bruker-Nonius FR591 rotating anode	2771 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.047
Detector resolution: 9.091 pixels mm^{-1}	θ_{max} = 27.5°, θ_{min} = 3.1°
φ & ω scans	h = −9→10
Absorption correction: multi-scan *SADABS* 2007/2 (Sheldrick, G.M., 2007)	k = −13→11
T_{min} = 0.956, T_{max} = 0.984	l = −22→18
8435 measured reflections	

Refinements

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.044$	$w = 1/[\sigma^2(F_o^2) + (0.0114P)^2 + 1.0748P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.099$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.03$	$\Delta\rho_{max} = 0.21$ e Å^{-3}
3138 reflections	$\Delta\rho_{min} = -0.36$ e Å^{-3}
173 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.14 (10)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even lar

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.6493 (3)	1.1748 (2)	0.87435 (14)	0.0228 (5)
C2	0.7204 (3)	1.2548 (2)	0.80639 (14)	0.0233 (5)
H2	0.7692	1.1999	0.7634	0.028*
C3	0.5381 (3)	1.2402 (3)	0.81539 (18)	0.0343 (7)
H3A	0.4802	1.1822	0.7776	0.041*

H3B	0.4754	1.3190	0.8327	0.041*
C4	0.6575 (4)	1.2253 (2)	0.95795 (15)	0.0318 (6)
H4A	0.5691	1.1852	0.9888	0.048*
H4B	0.6455	1.3220	0.9582	0.048*
H4C	0.7633	1.2012	0.9810	0.048*
C5	0.8077 (3)	1.3818 (2)	0.82220 (14)	0.0215 (5)
C6	0.7324 (3)	1.5040 (3)	0.81203 (12)	0.0245 (5)
H6	0.6209	1.5076	0.7963	0.029*
C7	0.8183 (4)	1.6215 (2)	0.82469 (15)	0.0278 (6)
H7	0.7657	1.7046	0.8169	0.033*
C8	0.9795 (3)	1.6176 (2)	0.84841 (15)	0.0283 (6)
H8	1.0373	1.6977	0.8582	0.034*
C9	1.0573 (3)	1.4954 (3)	0.85791 (14)	0.0293 (5)
H9	1.1688	1.4923	0.8736	0.035*
C10	0.9727 (3)	1.3791 (2)	0.84451 (15)	0.0259 (6)
H10	1.0269	1.2963	0.8505	0.031*
C11	0.8593 (3)	0.9631 (2)	0.90546 (13)	0.0201 (5)
C12	0.8672 (3)	0.9056 (2)	0.97983 (14)	0.0221 (5)
H12	0.7700	0.8851	1.0079	0.027*
C13	1.0198 (3)	0.8787 (2)	1.01210 (15)	0.0270 (5)
H13	1.0275	0.8378	1.0622	0.032*
C14	1.1607 (3)	0.9114 (2)	0.97139 (14)	0.0249 (5)
H14	1.2647	0.8952	0.9944	0.030*
C15	1.1512 (3)	0.9677 (2)	0.89706 (14)	0.0231 (5)
H15	1.2486	0.9886	0.8692	0.028*
C16	0.9999 (2)	0.9935 (2)	0.86349 (13)	0.0204 (4)
H16	0.9926	1.0314	0.8126	0.024*
O1	0.6662 (2)	0.96700 (15)	0.78307 (10)	0.0298 (4)

O2	0.5428 (2)	0.94003 (17)	0.91473 (12)	0.0346 (5)
S1	0.66505 (7)	1.00007 (6)	0.86534 (3)	0.02295 (14)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0183 (11)	0.0165 (10)	0.0337 (13)	0.0005 (10)	0.0013 (10)	0.0025 (9)
C2	0.0272 (12)	0.0194 (11)	0.0233 (13)	−0.0004 (10)	−0.0051 (10)	0.0006 (9)
C3	0.0280 (13)	0.0214 (12)	0.0534 (19)	0.0000 (11)	−0.0186 (13)	0.0035 (12)
C4	0.0408 (15)	0.0228 (11)	0.0319 (14)	0.0023 (13)	0.0104 (13)	0.0007 (10)
C5	0.0265 (13)	0.0188 (10)	0.0191 (12)	−0.0013 (10)	−0.0024 (10)	0.0016 (9)
C6	0.0287 (11)	0.0235 (11)	0.0213 (11)	−0.0002 (12)	0.0014 (9)	0.0020 (12)
C7	0.0367 (16)	0.0187 (10)	0.0281 (13)	0.0015 (12)	0.0040 (12)	−0.0010 (10)
C8	0.0413 (16)	0.0202 (11)	0.0235 (13)	−0.0100 (12)	0.0039 (12)	−0.0042 (10)
C9	0.0307 (12)	0.0302 (12)	0.0269 (12)	−0.0016 (13)	−0.0051 (10)	−0.0007 (13)
C10	0.0286 (14)	0.0219 (12)	0.0272 (14)	0.0006 (11)	−0.0050 (11)	0.0029 (11)
C11	0.0182 (11)	0.0132 (10)	0.0289 (12)	0.0009 (9)	−0.0047 (9)	0.0000 (8)
C12	0.0210 (12)	0.0167 (11)	0.0286 (12)	−0.0012 (9)	0.0028 (10)	−0.0004 (9)
C13	0.0329 (14)	0.0225 (12)	0.0256 (13)	−0.0005 (11)	−0.0041 (11)	0.0030 (10)
C14	0.0212 (11)	0.0203 (11)	0.0333 (13)	0.0031 (10)	−0.0069 (11)	−0.0023 (9)
C15	0.0172 (10)	0.0225 (12)	0.0295 (12)	0.0019 (10)	0.0003 (10)	−0.0015 (9)
C16	0.0195 (10)	0.0192 (10)	0.0226 (11)	−0.0022 (11)	−0.0005 (8)	0.0002 (12)
O1	0.0284 (9)	0.0231 (8)	0.0380 (10)	0.0006 (8)	−0.0141 (8)	−0.0044 (7)
O2	0.0183 (8)	0.0241 (9)	0.0613 (13)	−0.0030 (8)	0.0010 (9)	0.0081 (9)
S1	0.0156 (2)	0.0156 (2)	0.0376 (3)	−0.0010 (3)	−0.0049 (2)	0.0019 (3)

Geometric parameters (Å, °)

C1—C3	1.506 (3)	C8—H8	0.9500
C1—C4	1.514 (3)	C9—C10	1.380 (4)
C1—C2	1.526 (3)	C9—H9	0.9500

C1—S1	1.772 (2)	C10—H10	0.9500
C2—C5	1.490 (3)	C11—C16	1.387 (3)
C2—C3	1.504 (4)	C11—C12	1.395 (3)
C2—H2	1.0000	C11—S1	1.768 (2)
C3—H3A	0.9900	C12—C13	1.389 (3)
C3—H3B	0.9900	C12—H12	0.9500
C4—H4A	0.9800	C13—C14	1.384 (4)
C4—H4B	0.9800	C13—H13	0.9500
C4—H4C	0.9800	C14—C15	1.390 (3)
C5—C6	1.387 (3)	C14—H14	0.9500
C5—C10	1.401 (4)	C15—C16	1.387 (3)
C6—C7	1.394 (3)	C15—H15	0.9500
C6—H6	0.9500	C16—H16	0.9500
C7—C8	1.378 (4)	O1—S1	1.4409 (18)
C7—H7	0.9500	O2—S1	1.4396 (19)
C8—C9	1.395 (4)		
C3—C1—C4	120.5 (2)	C7—C8—C9	119.7 (2)
C3—C1—C2	59.50 (17)	C7—C8—H8	120.2
C4—C1—C2	121.3 (2)	C9—C8—H8	120.2
C3—C1—S1	114.88 (17)	C10—C9—C8	120.1 (2)
C4—C1—S1	114.32 (16)	C10—C9—H9	119.9
C2—C1—S1	115.55 (17)	C8—C9—H9	119.9
C5—C2—C3	122.7 (2)	C9—C10—C5	120.7 (2)
C5—C2—C1	119.9 (2)	C9—C10—H10	119.6
C3—C2—C1	59.60 (17)	C5—C10—H10	119.6
C5—C2—H2	114.6	C16—C11—C12	121.4 (2)
C3—C2—H2	114.6	C16—C11—S1	119.85 (17)
C1—C2—H2	114.6	C12—C11—S1	118.73 (18)

C2—C3—C1	60.90 (16)	C13—C12—C11	118.8 (2)
C2—C3—H3A	117.7	C13—C12—H12	120.6
C1—C3—H3A	117.7	C11—C12—H12	120.6
C2—C3—H3B	117.7	C14—C13—C12	120.1 (2)
C1—C3—H3B	117.7	C14—C13—H13	119.9
H3A—C3—H3B	114.8	C12—C13—H13	119.9
C1—C4—H4A	109.5	C13—C14—C15	120.5 (2)
C1—C4—H4B	109.5	C13—C14—H14	119.7
H4A—C4—H4B	109.5	C15—C14—H14	119.7
C1—C4—H4C	109.5	C16—C15—C14	120.1 (2)
H4A—C4—H4C	109.5	C16—C15—H15	119.9
H4B—C4—H4C	109.5	C14—C15—H15	119.9
C6—C5—C10	118.6 (2)	C11—C16—C15	119.0 (2)
C6—C5—C2	121.8 (2)	C11—C16—H16	120.5
C10—C5—C2	119.6 (2)	C15—C16—H16	120.5
C5—C6—C7	120.7 (2)	O2—S1—O1	118.43 (12)
C5—C6—H6	119.6	O2—S1—C11	107.99 (11)
C7—C6—H6	119.6	O1—S1—C11	108.76 (11)
C8—C7—C6	120.2 (2)	O2—S1—C1	108.44 (11)
C8—C7—H7	119.9	O1—S1—C1	108.33 (11)
C6—C7—H7	119.9	C11—S1—C1	103.95 (11)
C3—C1—C2—C5	112.6 (3)	C11—C12—C13—C14	1.3 (3)
C4—C1—C2—C5	3.3 (3)	C12—C13—C14—C15	−1.9 (4)
S1—C1—C2—C5	−142.37 (19)	C13—C14—C15—C16	1.0 (3)
C4—C1—C2—C3	−109.3 (3)	C12—C11—C16—C15	−1.0 (3)
S1—C1—C2—C3	105.0 (2)	S1—C11—C16—C15	177.91 (18)
C5—C2—C3—C1	−108.1 (3)	C14—C15—C16—C11	0.5 (3)
C4—C1—C3—C2	110.7 (3)	C16—C11—S1—O2	171.13 (18)

S1—C1—C3—C2	−106.2 (2)	C12—C11—S1—O2	−9.9 (2)
C3—C2—C5—C6	−29.2 (4)	C16—C11—S1—O1	41.4 (2)
C1—C2—C5—C6	−100.3 (3)	C12—C11—S1—O1	−139.65 (17)
C3—C2—C5—C10	153.8 (2)	C16—C11—S1—C1	−73.8 (2)
C1—C2—C5—C10	82.7 (3)	C12—C11—S1—C1	105.10 (18)
C10—C5—C6—C7	−0.8 (3)	C3—C1—S1—O2	−91.5 (2)
C2—C5—C6—C7	−177.8 (2)	C4—C1—S1—O2	54.0 (2)
C5—C6—C7—C8	−0.7 (3)	C2—C1—S1—O2	−157.97 (17)
C6—C7—C8—C9	1.5 (4)	C3—C1—S1—O1	38.3 (2)
C7—C8—C9—C10	−0.8 (4)	C4—C1—S1—O1	−176.29 (18)
C8—C9—C10—C5	−0.8 (4)	C2—C1—S1—O1	−28.2 (2)
C6—C5—C10—C9	1.5 (4)	C3—C1—S1—C11	153.82 (19)
C2—C5—C10—C9	178.6 (2)	C4—C1—S1—C11	−60.7 (2)
C16—C11—C12—C13	0.1 (3)	C2—C1—S1—C11	87.30 (19)
S1—C11—C12—C13	−178.81 (18)		

All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

Data collection: *COLLECT* (Hooft, R.W.W., 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) & *COLLECT* (Hooft, R.W.W., 1998); data reduction: *DENZO* (Otwinowski & Minor, 1997) & *COLLECT* (Hooft, R.W.W., 1998); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* publication routines (Farrugia, 1999).

(((1*S*,2*S*)-1,2-Dimethylcyclopropyl)sulfonyl)benzene 62b

Crystal data

$C_{11}H_{14}O_2S$	
M_r = 210.28	D_x = 1.335 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 48-52 °C
Hall symbol:	radiation, λ = 1.54178 Å
a = 6.2243 (1) Å	Cell parameters from 9302 reflections
b = 7.5312 (1) Å	θ = 4.0–66.7°
c = 22.3180 (4) Å	μ = 2.51 mm^{-1}
V = 1046.19 (3) Å^3	T = 100 K
Z = 4	Block, translucent colourless
F(000) = 448	0.25 × 0.20 × 0.07 mm

Data collection

diffractometer	1758 independent reflections
Radiation source: ?	1755 reflections with $I > 2\sigma(I)$
	R_{int} = 0.033
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 67.3°, θ_{min} = 4.0°
	h = −7→7
Absorption correction: multi-scan SADABS V2008/1 (Bruker AXS)	k = −6→8
T_{min} = 0.62, T_{max} = 0.84	l = −26→24
9173 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.023$	$w = 1/[\sigma^2(F_o^2) + (0.038P)^2 + 0.2651P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.064$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.05$	$\Delta\rho_{max} = 0.30$ e Å^{-3}
1758 reflections	$\Delta\rho_{min} = -0.23$ e Å^{-3}
130 parameters	Extinction correction: SHELXL
0 restraints	Extinction coefficient: 0.0073 (6)
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.078 (18)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.3216 (2)	0.0640 (2)	0.92440 (6)	0.0170 (3)
C2	0.4489 (2)	−0.1046 (2)	0.91502 (7)	0.0208 (3)
H2B	0.3702	−0.2187	0.9164	0.025*
H2A	0.5698	−0.101	0.8862	0.025*

C3	0.4731 (2)	−0.0025 (2)	0.97275 (7)	0.0187 (3)
H3	0.6102	0.0659	0.9765	0.022*
C4	0.0800 (2)	0.0620 (2)	0.93244 (7)	0.0219 (3)
H4A	0.0105	0.0526	0.8932	0.033*
H4B	0.0342	0.172	0.9521	0.033*
H4C	0.0389	−0.0399	0.9572	0.033*
C5	0.3848 (3)	−0.0731 (2)	1.03095 (6)	0.0219 (3)
H5B	0.27	−0.1585	1.0226	0.033*
H5A	0.3272	0.0254	1.0547	0.033*
H5C	0.4999	−0.1319	1.0534	0.033*
C6	0.3113 (2)	0.2333 (2)	0.81173 (6)	0.0173 (3)
C7	0.4336 (3)	0.1521 (2)	0.76745 (7)	0.0212 (3)
H7	0.5697	0.102	0.7768	0.025*
C8	0.3541 (3)	0.1453 (2)	0.70949 (7)	0.0247 (4)
H8	0.4364	0.091	0.6787	0.03*
C9	0.1541 (3)	0.2179 (2)	0.69643 (7)	0.0257 (4)
H9	0.0999	0.2123	0.6567	0.031*
C10	0.0333 (3)	0.2982 (2)	0.74099 (7)	0.0247 (4)
H10	−0.1028	0.3482	0.7317	0.03*
C11	0.1112 (3)	0.3059 (2)	0.79942 (7)	0.0206 (3)
H11	0.0289	0.3598	0.8303	0.025*
O1	0.32689 (18)	0.40882 (14)	0.91199 (5)	0.0215 (3)
O2	0.64743 (16)	0.23905 (15)	0.88028 (4)	0.0230 (2)
S1	0.41731 (5)	0.25191 (4)	0.885209 (14)	0.01636 (13)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0178 (7)	0.0158 (7)	0.0175 (7)	−0.0009 (6)	−0.0009 (6)	0.0012 (6)

C2	0.0221 (8)	0.0179 (7)	0.0223 (7)	0.0032 (6)	0.0021 (6)	−0.0005 (6)
C3	0.0179 (7)	0.0191 (8)	0.0192 (7)	0.0022 (6)	−0.0001 (6)	0.0009 (6)
C4	0.0166 (7)	0.0208 (8)	0.0281 (8)	−0.0010 (7)	0.0005 (6)	0.0029 (6)
C5	0.0249 (8)	0.0216 (8)	0.0193 (7)	0.0022 (7)	0.0004 (6)	0.0030 (6)
C6	0.0204 (7)	0.0145 (7)	0.0170 (6)	−0.0020 (7)	0.0013 (5)	0.0020 (6)
C7	0.0234 (8)	0.0163 (7)	0.0238 (7)	0.0019 (7)	0.0050 (7)	0.0030 (6)
C8	0.0363 (9)	0.0186 (7)	0.0192 (7)	0.0004 (7)	0.0080 (7)	−0.0010 (6)
C9	0.0376 (9)	0.0202 (8)	0.0194 (7)	−0.0047 (7)	−0.0046 (7)	0.0013 (6)
C10	0.0236 (8)	0.0264 (9)	0.0241 (8)	−0.0004 (7)	−0.0033 (7)	0.0038 (6)
C11	0.0211 (8)	0.0206 (7)	0.0202 (7)	0.0011 (6)	0.0021 (6)	0.0008 (6)
O1	0.0282 (6)	0.0169 (5)	0.0194 (5)	−0.0011 (5)	0.0000 (5)	−0.0017 (4)
O2	0.0173 (5)	0.0265 (6)	0.0253 (5)	−0.0036 (5)	−0.0015 (4)	0.0036 (6)
S1	0.01619 (19)	0.0161 (2)	0.01676 (19)	−0.00152 (16)	−0.00046 (11)	0.00060 (16)

Geometric parameters (Å, °)

C1—C2	1.511 (2)	C6—C11	1.388 (2)
C1—C4	1.515 (2)	C6—C7	1.389 (2)
C1—C3	1.518 (2)	C6—S1	1.7731 (14)
C1—S1	1.7673 (15)	C7—C8	1.386 (2)
C2—C3	1.508 (2)	C7—H7	0.95
C2—H2B	0.99	C8—C9	1.391 (2)
C2—H2A	0.99	C8—H8	0.95
C3—C5	1.507 (2)	C9—C10	1.386 (2)
C3—H3	1.0	C9—H9	0.95
C4—H4A	0.98	C10—C11	1.392 (2)
C4—H4B	0.98	C10—H10	0.95
C4—H4C	0.98	C11—H11	0.95
C5—H5B	0.98	O1—S1	1.4389 (11)

C5—H5A	0.98	O2—S1	1.4398 (11)
C5—H5C	0.98		
C2—C1—C4	121.93 (13)	C3—C5—H5C	109.5
C2—C1—C3	59.72 (10)	H5B—C5—H5C	109.5
C4—C1—C3	121.97 (13)	H5A—C5—H5C	109.5
C2—C1—S1	115.32 (11)	C11—C6—C7	121.62 (13)
C4—C1—S1	113.64 (11)	C11—C6—S1	119.08 (11)
C3—C1—S1	113.99 (11)	C7—C6—S1	119.26 (11)
C3—C2—C1	60.36 (10)	C8—C7—C6	118.99 (15)
C3—C2—H2B	117.7	C8—C7—H7	120.5
C1—C2—H2B	117.7	C6—C7—H7	120.5
C3—C2—H2A	117.7	C7—C8—C9	120.05 (14)
C1—C2—H2A	117.7	C7—C8—H8	120.0
H2B—C2—H2A	114.9	C9—C8—H8	120.0
C5—C3—C2	121.33 (14)	C10—C9—C8	120.46 (15)
C5—C3—C1	120.15 (13)	C10—C9—H9	119.8
C2—C3—C1	59.92 (10)	C8—C9—H9	119.8
C5—C3—H3	114.8	C9—C10—C11	120.07 (15)
C2—C3—H3	114.8	C9—C10—H10	120.0
C1—C3—H3	114.8	C11—C10—H10	120.0
C1—C4—H4A	109.5	C6—C11—C10	118.79 (14)
C1—C4—H4B	109.5	C6—C11—H11	120.6
H4A—C4—H4B	109.5	C10—C11—H11	120.6
C1—C4—H4C	109.5	O1—S1—O2	118.43 (7)
H4A—C4—H4C	109.5	O1—S1—C1	108.69 (6)
H4B—C4—H4C	109.5	O2—S1—C1	108.61 (7)
C3—C5—H5B	109.5	O1—S1—C6	107.66 (7)
C3—C5—H5A	109.5	O2—S1—C6	107.10 (6)

H5B—C5—H5A	109.5	C1—S1—C6	105.62 (7)
C4—C1—C2—C3	−111.01 (16)	C2—C1—S1—O1	−162.27 (11)
S1—C1—C2—C3	104.15 (12)	C4—C1—S1—O1	49.98 (12)
C1—C2—C3—C5	109.09 (16)	C3—C1—S1—O1	−95.85 (11)
C2—C1—C3—C5	−111.00 (17)	C2—C1—S1—O2	−32.16 (13)
C4—C1—C3—C5	−0.1 (2)	C4—C1—S1—O2	−179.91 (11)
S1—C1—C3—C5	142.61 (13)	C3—C1—S1—O2	34.26 (13)
C4—C1—C3—C2	110.94 (17)	C2—C1—S1—C6	82.45 (12)
S1—C1—C3—C2	−106.39 (12)	C4—C1—S1—C6	−65.30 (12)
C11—C6—C7—C8	0.7 (2)	C3—C1—S1—C6	148.86 (11)
S1—C6—C7—C8	−177.04 (12)	C11—C6—S1—O1	−27.34 (14)
C6—C7—C8—C9	−0.5 (2)	C7—C6—S1—O1	150.43 (12)
C7—C8—C9—C10	0.4 (2)	C11—C6—S1—O2	−155.71 (12)
C8—C9—C10—C11	−0.4 (2)	C7—C6—S1—O2	22.06 (14)
C7—C6—C11—C10	−0.7 (2)	C11—C6—S1—C1	88.65 (13)
S1—C6—C11—C10	177.01 (12)	C7—C6—S1—C1	−93.58 (13)
C9—C10—C11—C6	0.6 (2)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2011.6.0.0; cell refinement: *SAINT* V7.68A (Bruker AXS, 2009); data reduction: *SAINT* V7.68A (Bruker AXS, 2009); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008)

(((1*R*,2*S*)-2-Phenyl-1-propylcyclopropyl)sulfonyl)benzene 62f

Crystal data

$C_{18}H_{20}O_2S$	?
M_r = 300.40	D_x = 1.286 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 106-118 °C
Hall symbol:	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 8.5152 (11) Å	Cell parameters from 2250 reflections
b = 10.1406 (15) Å	θ = 2.3–25.1°
c = 17.970 (3) Å	μ = 0.21 mm^{-1}
V = 1551.7 (4) Å^3	T = 100 K
Z = 4	Needle, colourless
F(000) = 640	0.50 × 0.10 × 0.09 mm

Data collection

Bruker APEX-II CCD diffractometer	2760 independent reflections
Radiation source: sealed tube	2470 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.043
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 25.2°, θ_{min} = 2.3°
φ and ω scans	h = −10→10
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	k = −12→12
T_{min} = 0.90, T_{max} = 0.98	l = −21→21
9014 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.033	$w = 1/[\sigma^2(F_o^2) + (0.0316P)^2 + 0.1485P]$

	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.071$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.04$	$\Delta\rho_{max} = 0.16$ e Å^{-3}
2760 reflections	$\Delta\rho_{min} = -0.26$ e Å^{-3}
191 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.05 (7)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.0575 (2)	0.6690 (2)	0.39339 (12)	0.0143 (5)
H1A	0.0963	0.7609	0.3962	0.017*
H1B	0.0898	0.6235	0.4397	0.017*
C2	−0.1219 (2)	0.6711 (2)	0.38949 (12)	0.0177 (5)
H2A	−0.1556	0.7337	0.3504	0.021*
H2B	−0.1606	0.5824	0.3757	0.021*
C3	−0.1933 (3)	0.7116 (2)	0.46328 (13)	0.0260 (6)
H3A	−0.1625	0.6482	0.5018	0.039*

H3B	−0.308	0.713	0.4589	0.039*
H3C	−0.1555	0.7996	0.4769	0.039*
C4	0.1341 (2)	0.60164 (18)	0.32812 (11)	0.0123 (4)
C5	0.2623 (2)	0.6668 (2)	0.28093 (12)	0.0141 (5)
H5	0.3445	0.6046	0.2622	0.017*
C6	0.1019 (2)	0.6442 (2)	0.24927 (12)	0.0160 (5)
H6A	0.0903	0.5744	0.2112	0.019*
H6B	0.0339	0.7223	0.2418	0.019*
C7	0.3226 (2)	0.7985 (2)	0.30237 (12)	0.0145 (5)
C8	0.2412 (2)	0.9149 (2)	0.28998 (13)	0.0222 (5)
H8	0.1423	0.9122	0.2656	0.027*
C9	0.3017 (3)	1.0348 (2)	0.31256 (14)	0.0267 (6)
H9	0.2439	1.1136	0.3041	0.032*
C10	0.4458 (3)	1.0403 (2)	0.34740 (14)	0.0235 (5)
H10	0.4869	1.1227	0.3634	0.028*
C11	0.5299 (2)	0.9265 (2)	0.35885 (12)	0.0221 (5)
H11	0.6298	0.9303	0.3823	0.027*
C12	0.4697 (2)	0.8068 (2)	0.33638 (13)	0.0185 (5)
H12	0.5291	0.7287	0.3442	0.022*
C13	0.3201 (2)	0.4132 (2)	0.40200 (12)	0.0163 (5)
C14	0.2924 (3)	0.4032 (2)	0.47753 (13)	0.0249 (5)
H14	0.1882	0.4063	0.4964	0.03*
C15	0.4185 (3)	0.3889 (3)	0.52509 (15)	0.0383 (7)
H15	0.4015	0.3811	0.5772	0.046*
C16	0.5702 (3)	0.3858 (2)	0.49682 (17)	0.0374 (7)
H16	0.6568	0.3774	0.5298	0.045*
C17	0.5961 (3)	0.3946 (2)	0.42142 (16)	0.0326 (6)
H17	0.7001	0.3908	0.4025	0.039*

C18	0.4706 (2)	0.4092 (2)	0.37319 (13)	0.0220 (5)
H18	0.4876	0.4164	0.3211	0.026*
O1	0.02286 (16)	0.37736 (14)	0.37687 (8)	0.0194 (4)
O2	0.20510 (17)	0.37319 (15)	0.27018 (8)	0.0184 (4)
S1	0.15945 (6)	0.42969 (5)	0.34038 (3)	0.01341 (13)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0153 (10)	0.0123 (11)	0.0152 (11)	−0.0004 (9)	−0.0021 (9)	−0.0009 (9)
C2	0.0138 (11)	0.0206 (13)	0.0188 (12)	0.0003 (9)	0.0006 (9)	−0.0001 (10)
C3	0.0197 (12)	0.0337 (14)	0.0245 (14)	0.0044 (10)	0.0036 (10)	−0.0011 (11)
C4	0.0122 (9)	0.0112 (11)	0.0135 (11)	−0.0022 (8)	−0.0013 (9)	0.0016 (8)
C5	0.0153 (10)	0.0139 (12)	0.0130 (11)	0.0013 (9)	0.0034 (9)	0.0024 (9)
C6	0.0186 (10)	0.0148 (12)	0.0147 (11)	−0.0009 (9)	−0.0015 (9)	0.0016 (10)
C7	0.0140 (10)	0.0154 (11)	0.0141 (12)	−0.0017 (9)	0.0035 (9)	0.0020 (9)
C8	0.0182 (10)	0.0168 (12)	0.0315 (13)	−0.0002 (10)	−0.0031 (10)	0.0014 (11)
C9	0.0234 (12)	0.0153 (12)	0.0412 (16)	0.0036 (10)	0.0009 (11)	0.0025 (10)
C10	0.0270 (11)	0.0168 (13)	0.0269 (14)	−0.0060 (10)	0.0078 (11)	−0.0012 (11)
C11	0.0182 (10)	0.0258 (12)	0.0223 (12)	−0.0043 (11)	−0.0002 (9)	0.0006 (11)
C12	0.0143 (10)	0.0170 (11)	0.0242 (13)	0.0012 (9)	0.0008 (11)	0.0000 (11)
C13	0.0201 (10)	0.0083 (10)	0.0204 (11)	0.0014 (9)	−0.0065 (9)	0.0024 (9)
C14	0.0335 (12)	0.0190 (13)	0.0220 (13)	0.0051 (10)	−0.0060 (11)	0.0001 (10)
C15	0.0619 (18)	0.0279 (16)	0.0251 (14)	0.0119 (13)	−0.0188 (14)	−0.0001 (12)
C16	0.0384 (15)	0.0214 (15)	0.0523 (19)	0.0040 (11)	−0.0291 (14)	0.0002 (13)
C17	0.0230 (12)	0.0192 (14)	0.0557 (18)	−0.0007 (10)	−0.0085 (12)	0.0076 (13)
C18	0.0212 (11)	0.0142 (13)	0.0307 (13)	−0.0016 (10)	−0.0033 (10)	0.0050 (10)
O1	0.0173 (7)	0.0162 (8)	0.0248 (9)	−0.0040 (6)	0.0012 (7)	0.0030 (7)
O2	0.0234 (8)	0.0149 (8)	0.0168 (8)	0.0003 (6)	−0.0016 (6)	−0.0036 (6)

S1	0.0145 (2)	0.0110 (2)	0.0148 (2)	−0.0013 (2)	−0.0013 (2)	−0.0004 (2)

Geometric parameters (Å, °)

C1—C4	1.506 (3)	C9—C10	1.379 (3)
C1—C2	1.529 (3)	C9—H9	0.95
C1—H1A	0.99	C10—C11	1.374 (3)
C1—H1B	0.99	C10—H10	0.95
C2—C3	1.515 (3)	C11—C12	1.378 (3)
C2—H2A	0.99	C11—H11	0.95
C2—H2B	0.99	C12—H12	0.95
C3—H3A	0.98	C13—C14	1.381 (3)
C3—H3B	0.98	C13—C18	1.382 (3)
C3—H3C	0.98	C13—S1	1.768 (2)
C4—C6	1.506 (3)	C14—C15	1.380 (3)
C4—C5	1.532 (3)	C14—H14	0.95
C4—S1	1.7708 (19)	C15—C16	1.389 (4)
C5—C7	1.482 (3)	C15—H15	0.95
C5—C6	1.497 (3)	C16—C17	1.376 (4)
C5—H5	1.0	C16—H16	0.95
C6—H6A	0.99	C17—C18	1.384 (3)
C6—H6B	0.99	C17—H17	0.95
C7—C8	1.387 (3)	C18—H18	0.95
C7—C12	1.396 (3)	O1—S1	1.4368 (15)
C8—C9	1.381 (3)	O2—S1	1.4390 (15)
C8—H8	0.95		
C4—C1—C2	113.76 (17)	C9—C8—C7	121.05 (19)
C4—C1—H1A	108.8	C9—C8—H8	119.5
C2—C1—H1A	108.8	C7—C8—H8	119.5

C4—C1—H1B	108.8	C10—C9—C8	120.1 (2)
C2—C1—H1B	108.8	C10—C9—H9	120.0
H1A—C1—H1B	107.7	C8—C9—H9	120.0
C3—C2—C1	111.37 (18)	C11—C10—C9	119.8 (2)
C3—C2—H2A	109.4	C11—C10—H10	120.1
C1—C2—H2A	109.4	C9—C10—H10	120.1
C3—C2—H2B	109.4	C10—C11—C12	120.16 (19)
C1—C2—H2B	109.4	C10—C11—H11	119.9
H2A—C2—H2B	108.0	C12—C11—H11	119.9
C2—C3—H3A	109.5	C11—C12—C7	121.00 (19)
C2—C3—H3B	109.5	C11—C12—H12	119.5
H3A—C3—H3B	109.5	C7—C12—H12	119.5
C2—C3—H3C	109.5	C14—C13—C18	121.6 (2)
H3A—C3—H3C	109.5	C14—C13—S1	119.34 (17)
H3B—C3—H3C	109.5	C18—C13—S1	119.04 (17)
C1—C4—C6	121.61 (17)	C15—C14—C13	118.9 (2)
C1—C4—C5	122.95 (17)	C15—C14—H14	120.6
C6—C4—C5	59.03 (13)	C13—C14—H14	120.6
C1—C4—S1	113.75 (14)	C14—C15—C16	120.0 (3)
C6—C4—S1	114.94 (14)	C14—C15—H15	120.0
C5—C4—S1	113.97 (14)	C16—C15—H15	120.0
C7—C5—C6	123.53 (19)	C17—C16—C15	120.5 (2)
C7—C5—C4	119.44 (18)	C17—C16—H16	119.7
C6—C5—C4	59.62 (13)	C15—C16—H16	119.7
C7—C5—H5	114.4	C16—C17—C18	120.0 (2)
C6—C5—H5	114.4	C16—C17—H17	120.0
C4—C5—H5	114.4	C18—C17—H17	120.0
C5—C6—C4	61.36 (13)	C13—C18—C17	119.0 (2)

C5—C6—H6A	117.6	C13—C18—H18	120.5
C4—C6—H6A	117.6	C17—C18—H18	120.5
C5—C6—H6B	117.6	O1—S1—O2	118.15 (9)
C4—C6—H6B	117.6	O1—S1—C13	107.79 (9)
H6A—C6—H6B	114.7	O2—S1—C13	107.59 (9)
C8—C7—C12	117.86 (19)	O1—S1—C4	108.76 (9)
C8—C7—C5	123.53 (19)	O2—S1—C4	108.42 (9)
C12—C7—C5	118.61 (18)	C13—S1—C4	105.41 (9)
C4—C1—C2—C3	167.26 (18)	C18—C13—C14—C15	−0.1 (3)
C2—C1—C4—C6	55.7 (3)	S1—C13—C14—C15	179.28 (18)
C2—C1—C4—C5	126.9 (2)	C13—C14—C15—C16	0.6 (4)
C2—C1—C4—S1	−88.6 (2)	C14—C15—C16—C17	−1.1 (4)
C1—C4—C5—C7	4.0 (3)	C15—C16—C17—C18	1.2 (4)
C6—C4—C5—C7	113.9 (2)	C14—C13—C18—C17	0.2 (3)
S1—C4—C5—C7	−140.41 (16)	S1—C13—C18—C17	−179.21 (18)
C1—C4—C5—C6	−109.8 (2)	C16—C17—C18—C13	−0.7 (3)
S1—C4—C5—C6	105.74 (16)	C14—C13—S1—O1	−23.1 (2)
C7—C5—C6—C4	−107.2 (2)	C18—C13—S1—O1	156.28 (16)
C1—C4—C6—C5	112.1 (2)	C14—C13—S1—O2	−151.53 (17)
S1—C4—C6—C5	−104.09 (16)	C18—C13—S1—O2	27.86 (19)
C6—C5—C7—C8	−5.1 (3)	C14—C13—S1—C4	92.93 (19)
C4—C5—C7—C8	−76.3 (3)	C18—C13—S1—C4	−87.69 (17)
C6—C5—C7—C12	175.4 (2)	C1—C4—S1—O1	39.60 (16)
C4—C5—C7—C12	104.2 (2)	C6—C4—S1—O1	−107.12 (15)
C12—C7—C8—C9	−1.9 (3)	C5—C4—S1—O1	−172.63 (14)
C5—C7—C8—C9	178.6 (2)	C1—C4—S1—O2	169.26 (13)
C7—C8—C9—C10	0.6 (4)	C6—C4—S1—O2	22.55 (17)
C8—C9—C10—C11	0.7 (4)	C5—C4—S1—O2	−42.97 (16)

C9—C10—C11—C12	−0.8 (3)	C1—C4—S1—C13	−75.76 (15)
C10—C11—C12—C7	−0.5 (3)	C6—C4—S1—C13	137.52 (15)
C8—C7—C12—C11	1.8 (3)	C5—C4—S1—C13	72.00 (16)
C5—C7—C12—C11	−178.6 (2)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

(((1*S*,2*S*)-2-Phenyl-[1,1'-bi(cyclopropan)]-1-yl)sulfonyl)benzene 62g

Crystal data

$C_{18}H_{18}O_2S$	
M_r = 298.38	D_x = 1.348 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 128-136 °C
Hall symbol:	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 8.2682 (9) Å	Cell parameters from 3770 reflections
b = 10.3472 (11) Å	θ = 2.7–25.1°
c = 17.1808 (17) Å	μ = 0.22 mm^{-1}
V = 1469.9 (3) Å^3	T = 100 K
Z = 4	Shard, colourless
F(000) = 632	0.24 × 0.17 × 0.14 mm

Data collection

Bruker APEX-II CCD diffractometer	2596 independent reflections
Radiation source: sealed tube	2469 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.024
Detector resolution: 8.333 pixels mm^{-1}	θ_{max} = 25.2°, θ_{min} = 2.3°
φ and ω scans	h = −9→9
Absorption correction: multi-scan SADABS-2008/1 - Bruker AXS area detector scaling and absorption correction	k = −12→12
T_{min} = 0.95, T_{max} = 0.97	l = −20→20
8492 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.025	$w = 1/[\sigma^2(F_o^2) + (0.0334P)^2 + 0.3404P]$

	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.062$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.02$	$\Delta\rho_{max} = 0.23$ e Å^{-3}
2596 reflections	$\Delta\rho_{min} = -0.26$ e Å^{-3}
190 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.01 (6)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2490 (2)	0.79942 (17)	0.21034 (9)	0.0146 (4)
H1	0.3265	0.8556	0.2395	0.018*
C2	0.0758 (2)	0.81595 (18)	0.23445 (10)	0.0173 (4)
H2B	0.0527	0.8758	0.278	0.021*
H2A	0.0047	0.7391	0.2321	0.021*
C3	0.13107 (18)	0.87391 (15)	0.15853 (10)	0.0128 (4)
C4	0.0748 (2)	0.82569 (17)	0.08136 (10)	0.0153 (4)
H4	0.1487	0.8456	0.0369	0.018*

C5	−0.0218 (2)	0.70307 (18)	0.07248 (11)	0.0234 (4)
H5A	−0.0028	0.65	0.0254	0.028*
H5B	−0.0469	0.6533	0.1202	0.028*
C6	−0.1028 (2)	0.83139 (18)	0.06213 (11)	0.0203 (4)
H6B	−0.1778	0.8606	0.1034	0.024*
H6A	−0.1337	0.8573	0.0087	0.024*
C7	0.3188 (2)	0.67413 (16)	0.18473 (9)	0.0148 (4)
C8	0.4716 (2)	0.67423 (17)	0.14983 (9)	0.0181 (4)
H8	0.5263	0.7537	0.1414	0.022*
C9	0.5437 (2)	0.55904 (18)	0.12742 (9)	0.0201 (4)
H9	0.6473	0.5603	0.1035	0.024*
C10	0.4665 (2)	0.44329 (18)	0.13955 (9)	0.0204 (4)
H10	0.516	0.3647	0.1237	0.025*
C11	0.3158 (2)	0.44191 (18)	0.17506 (10)	0.0216 (4)
H13	0.262	0.362	0.1838	0.026*
C12	0.2435 (2)	0.55630 (17)	0.19782 (10)	0.0181 (4)
H12	0.141	0.5542	0.2227	0.022*
C13	0.3308 (2)	1.07363 (14)	0.10411 (9)	0.0139 (3)
C14	0.3130 (2)	1.10304 (16)	0.02599 (10)	0.0184 (4)
H14	0.2087	1.107	0.0029	0.022*
C15	0.4505 (3)	1.12668 (17)	−0.01803 (11)	0.0262 (5)
H15	0.441	1.1478	−0.0716	0.031*
C16	0.6011 (2)	1.11951 (18)	0.01618 (13)	0.0280 (5)
H16	0.6949	1.1338	−0.0146	0.034*
C17	0.6178 (2)	1.09193 (18)	0.09434 (12)	0.0247 (4)
H17	0.7222	1.0889	0.1173	0.03*
C18	0.4815 (2)	1.06865 (16)	0.13920 (10)	0.0182 (4)
H18	0.4913	1.0496	0.1931	0.022*

O1	0.02157 (14)	1.10457 (11)	0.12309 (7)	0.0173 (3)
O2	0.19413 (14)	1.08080 (11)	0.23978 (6)	0.0175 (3)
S1	0.15727 (5)	1.04409 (4)	0.16088 (2)	0.01219 (10)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0149 (9)	0.0138 (9)	0.0152 (8)	0.0002 (7)	−0.0014 (7)	0.0017 (7)
C2	0.0193 (10)	0.0140 (8)	0.0185 (8)	0.0012 (7)	0.0055 (7)	0.0035 (7)
C3	0.0110 (9)	0.0100 (8)	0.0172 (8)	0.0004 (6)	0.0030 (7)	0.0008 (7)
C4	0.0143 (9)	0.0148 (9)	0.0170 (8)	0.0003 (7)	0.0001 (7)	0.0001 (7)
C5	0.0233 (10)	0.0179 (9)	0.0291 (9)	−0.0042 (8)	−0.0070 (8)	−0.0028 (8)
C6	0.0173 (9)	0.0192 (10)	0.0244 (9)	−0.0008 (8)	−0.0047 (7)	−0.0023 (8)
C7	0.0150 (9)	0.0159 (8)	0.0133 (8)	0.0018 (8)	−0.0026 (6)	0.0007 (6)
C8	0.0187 (9)	0.0169 (8)	0.0186 (8)	0.0011 (8)	−0.0002 (7)	0.0014 (7)
C9	0.0178 (8)	0.0263 (10)	0.0162 (7)	0.0045 (9)	−0.0003 (7)	−0.0010 (8)
C10	0.0245 (9)	0.0190 (9)	0.0179 (8)	0.0092 (9)	−0.0028 (7)	−0.0032 (7)
C11	0.0237 (10)	0.0139 (8)	0.0272 (9)	−0.0018 (8)	−0.0022 (8)	0.0003 (8)
C12	0.0140 (8)	0.0173 (9)	0.0229 (8)	0.0027 (8)	−0.0005 (7)	0.0015 (8)
C13	0.0143 (8)	0.0069 (8)	0.0206 (8)	−0.0010 (7)	0.0045 (7)	−0.0016 (6)
C14	0.0227 (10)	0.0123 (8)	0.0202 (9)	−0.0001 (8)	0.0033 (7)	−0.0008 (7)
C15	0.0411 (13)	0.0135 (9)	0.0239 (10)	−0.0048 (9)	0.0138 (9)	−0.0011 (8)
C16	0.0262 (11)	0.0139 (10)	0.0439 (12)	−0.0045 (8)	0.0206 (9)	−0.0059 (9)
C17	0.0163 (10)	0.0155 (9)	0.0424 (11)	−0.0025 (7)	0.0051 (8)	−0.0061 (8)
C18	0.0163 (9)	0.0124 (8)	0.0259 (9)	−0.0003 (7)	−0.0003 (7)	−0.0030 (7)
O1	0.0122 (6)	0.0136 (6)	0.0261 (6)	0.0022 (5)	−0.0003 (5)	0.0002 (5)
O2	0.0184 (7)	0.0161 (6)	0.0179 (6)	0.0009 (5)	0.0024 (5)	−0.0037 (5)
S1	0.01121 (19)	0.01005 (18)	0.01530 (18)	0.00058 (17)	0.00130 (16)	−0.00107 (17)

Geometric parameters (Å, °)

C1—C7	1.486 (2)	C9—C10	1.373 (3)
C1—C2	1.500 (2)	C9—H9	0.95
C1—C3	1.529 (2)	C10—C11	1.388 (3)
C1—H1	1.0	C10—H10	0.95
C2—C3	1.507 (2)	C11—C12	1.382 (2)
C2—H2B	0.99	C11—H13	0.95
C2—H2A	0.99	C12—H12	0.95
C3—C4	1.491 (2)	C13—C18	1.385 (2)
C3—S1	1.7746 (16)	C13—C14	1.384 (2)
C4—C6	1.506 (2)	C13—S1	1.7613 (17)
C4—C5	1.507 (3)	C14—C15	1.387 (3)
C4—H4	1.0	C14—H14	0.95
C5—C6	1.498 (3)	C15—C16	1.379 (3)
C5—H5A	0.99	C15—H15	0.95
C5—H5B	0.99	C16—C17	1.380 (3)
C6—H6B	0.99	C16—H16	0.95
C6—H6A	0.99	C17—C18	1.386 (3)
C7—C12	1.387 (2)	C17—H17	0.95
C7—C8	1.398 (2)	C18—H18	0.95
C8—C9	1.387 (2)	O1—S1	1.4394 (12)
C8—H8	0.95	O2—S1	1.4404 (12)
C7—C1—C2	123.51 (15)	C9—C8—C7	120.45 (16)
C7—C1—C3	121.02 (14)	C9—C8—H8	119.8
C2—C1—C3	59.64 (10)	C7—C8—H8	119.8
C7—C1—H1	114.0	C10—C9—C8	120.50 (16)
C2—C1—H1	114.0	C10—C9—H9	119.7
C3—C1—H1	114.0	C8—C9—H9	119.7

C1—C2—C3	61.12 (11)	C9—C10—C11	119.55 (17)
C1—C2—H2B	117.7	C9—C10—H10	120.2
C3—C2—H2B	117.7	C11—C10—H10	120.2
C1—C2—H2A	117.7	C12—C11—C10	120.25 (17)
C3—C2—H2A	117.7	C12—C11—H13	119.9
H2B—C2—H2A	114.8	C10—C11—H13	119.9
C4—C3—C2	122.82 (14)	C11—C12—C7	120.83 (16)
C4—C3—C1	123.23 (14)	C11—C12—H12	119.6
C2—C3—C1	59.24 (11)	C7—C12—H12	119.6
C4—C3—S1	112.98 (12)	C18—C13—C14	121.70 (16)
C2—C3—S1	114.35 (12)	C18—C13—S1	119.02 (12)
C1—C3—S1	114.16 (12)	C14—C13—S1	119.28 (14)
C3—C4—C6	119.09 (15)	C15—C14—C13	118.73 (17)
C3—C4—C5	122.49 (15)	C15—C14—H14	120.6
C6—C4—C5	59.61 (12)	C13—C14—H14	120.6
C3—C4—H4	114.8	C16—C15—C14	119.88 (17)
C6—C4—H4	114.8	C16—C15—H15	120.1
C5—C4—H4	114.8	C14—C15—H15	120.1
C6—C5—C4	60.17 (12)	C15—C16—C17	121.08 (18)
C6—C5—H5A	117.8	C15—C16—H16	119.5
C4—C5—H5A	117.8	C17—C16—H16	119.5
C6—C5—H5B	117.8	C16—C17—C18	119.72 (18)
C4—C5—H5B	117.8	C16—C17—H17	120.1
H5A—C5—H5B	114.9	C18—C17—H17	120.1
C5—C6—C4	60.21 (12)	C13—C18—C17	118.87 (16)
C5—C6—H6B	117.7	C13—C18—H18	120.6
C4—C6—H6B	117.7	C17—C18—H18	120.6
C5—C6—H6A	117.7	O2—S1—O1	118.34 (7)

C4—C6—H6A	117.7	O2—S1—C13	107.64 (8)
H6B—C6—H6A	114.9	O1—S1—C13	108.03 (7)
C12—C7—C8	118.40 (15)	O2—S1—C3	107.99 (7)
C12—C7—C1	122.98 (15)	O1—S1—C3	109.03 (7)
C8—C7—C1	118.51 (15)	C13—S1—C3	105.01 (7)
C7—C1—C2—C3	−109.17 (17)	C8—C7—C12—C11	−1.7 (2)
C1—C2—C3—C4	112.02 (17)	C1—C7—C12—C11	−177.92 (16)
C1—C2—C3—S1	−104.68 (14)	C18—C13—C14—C15	0.7 (2)
C7—C1—C3—C4	1.9 (2)	S1—C13—C14—C15	179.71 (13)
C2—C1—C3—C4	−111.36 (17)	C13—C14—C15—C16	0.6 (3)
C7—C1—C3—C2	113.22 (18)	C14—C15—C16—C17	−1.5 (3)
C7—C1—C3—S1	−141.77 (14)	C15—C16—C17—C18	1.2 (3)
C2—C1—C3—S1	105.01 (14)	C14—C13—C18—C17	−1.0 (2)
C2—C3—C4—C6	61.2 (2)	S1—C13—C18—C17	179.98 (14)
C1—C3—C4—C6	133.47 (17)	C16—C17—C18—C13	0.0 (3)
S1—C3—C4—C6	−82.52 (18)	C18—C13—S1—O2	27.80 (14)
C2—C3—C4—C5	−9.4 (2)	C14—C13—S1—O2	−151.26 (13)
C1—C3—C4—C5	62.9 (2)	C18—C13—S1—O1	156.66 (12)
S1—C3—C4—C5	−153.13 (14)	C14—C13—S1—O1	−22.40 (15)
C3—C4—C5—C6	107.14 (18)	C18—C13—S1—C3	−87.09 (13)
C3—C4—C6—C5	−112.73 (18)	C14—C13—S1—C3	93.85 (14)
C2—C1—C7—C12	−15.7 (2)	C4—C3—S1—O2	173.80 (11)
C3—C1—C7—C12	−87.66 (19)	C2—C3—S1—O2	26.86 (14)
C2—C1—C7—C8	168.10 (15)	C1—C3—S1—O2	−38.80 (13)
C3—C1—C7—C8	96.1 (2)	C4—C3—S1—O1	44.01 (13)
C12—C7—C8—C9	1.4 (2)	C2—C3—S1—O1	−102.94 (13)
C1—C7—C8—C9	177.82 (15)	C1—C3—S1—O1	−168.59 (11)
C7—C8—C9—C10	−0.3 (2)	C4—C3—S1—C13	−71.56 (13)

C8—C9—C10—C11	−0.5 (2)	C2—C3—S1—C13	141.50 (12)
C9—C10—C11—C12	0.2 (3)	C1—C3—S1—C13	75.84 (13)
C10—C11—C12—C7	0.9 (3)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

((1*S*,2*R*)-2-Fluoro-2-(phenylsulfonyl)cyclopropyl)benzene 62i

Crystal data

$C_{15}H_{13}FO_2S$	
M_r = 276.31	D_x = 1.452 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 60-68 °C
Hall symbol:	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 7.4989 (13) Å	Cell parameters from 1593 reflections
b = 11.401 (2) Å	θ = 3.1–24.9°
c = 14.784 (3) Å	μ = 0.26 mm^{-1}
V = 1264.0 (4) Å^3	T = 100 K
Z = 4	Block, colourless
F(000) = 576	0.80 × 0.50 × 0.18 mm

Data collection

Bruker APEX-II CCD diffractometer	2242 independent reflections
Radiation source: sealed tube	1952 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.047
Detector resolution: 8.333 pixels mm^{-1}	θ_{max} = 25.2°, θ_{min} = 2.3°
φ and ω scans	h = −8→8
Absorption correction: multi-scan *SADABS2008*/1 - Bruker AXS area detector scaling and absorption correction	k = −13→13
T_{min} = 0.82, T_{max} = 0.95	l = −17→17
7241 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.035	$w = 1/[\sigma^2(F_o^2) + (0.0434P)^2]$

	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.079$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.00$	$\Delta\rho_{max} = 0.18$ e Å^{-3}
2242 reflections	$\Delta\rho_{min} = -0.30$ e Å^{-3}
172 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: −0.02 (9)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.1743 (3)	0.6412 (2)	0.08526 (17)	0.0137 (6)
C2	0.2193 (3)	0.5311 (2)	0.05361 (17)	0.0160 (6)
H2	0.2662	0.4732	0.0933	0.019*
C3	0.1942 (3)	0.5070 (2)	−0.03770 (18)	0.0205 (6)
H3	0.2233	0.4316	−0.0608	0.025*
C4	0.1272 (3)	0.5921 (2)	−0.09499 (18)	0.0192 (6)
H4	0.1104	0.575	−0.1573	0.023*
C5	0.0845 (3)	0.7022 (2)	−0.06182 (18)	0.0186 (6)
H5	0.0406	0.7609	−0.1017	0.022*

C6	0.1056 (3)	0.7271 (2)	0.02911 (17)	0.0154 (6)
H6	0.0736	0.8017	0.0526	0.018*
C7	0.0230 (3)	0.6331 (2)	0.26029 (18)	0.0160 (6)
C8	−0.0385 (3)	0.7077 (2)	0.33835 (17)	0.0158 (6)
H8	0.0258	0.7842	0.3433	0.019*
C9	−0.1485 (3)	0.6957 (2)	0.25275 (17)	0.0201 (6)
H9A	−0.2593	0.6487	0.2559	0.024*
H9B	−0.1542	0.7642	0.2116	0.024*
C10	−0.0900 (3)	0.6565 (2)	0.42779 (17)	0.0144 (6)
C11	−0.0306 (3)	0.7140 (2)	0.50487 (18)	0.0167 (6)
H11	0.0411	0.7822	0.499	0.02*
C12	−0.0744 (3)	0.6734 (2)	0.58987 (17)	0.0186 (6)
H12	−0.0344	0.7143	0.642	0.022*
C13	−0.1768 (3)	0.5729 (2)	0.59938 (18)	0.0178 (6)
H13	−0.2063	0.5441	0.6578	0.021*
C14	−0.2352 (4)	0.5151 (2)	0.52287 (17)	0.0176 (6)
H14	−0.3049	0.446	0.5291	0.021*
C15	−0.1941 (3)	0.5562 (2)	0.43725 (18)	0.0163 (6)
H15	−0.2368	0.5161	0.3852	0.02*
F1	0.0193 (2)	0.51363 (13)	0.26839 (10)	0.0211 (4)
O1	0.2212 (2)	0.80291 (14)	0.20660 (11)	0.0194 (4)
O2	0.3628 (2)	0.60920 (16)	0.23155 (12)	0.0197 (4)
S1	0.21542 (8)	0.67769 (6)	0.19934 (4)	0.01525 (16)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0091 (13)	0.0183 (14)	0.0136 (13)	−0.0015 (10)	0.0021 (10)	−0.0001 (11)
C2	0.0148 (12)	0.0169 (14)	0.0164 (13)	0.0003 (12)	0.0018 (12)	0.0019 (11)

C3	0.0169 (14)	0.0200 (15)	0.0245 (16)	−0.0014 (12)	0.0050 (12)	−0.0045 (12)
C4	0.0151 (13)	0.0286 (16)	0.0138 (14)	−0.0057 (12)	0.0045 (12)	−0.0030 (12)
C5	0.0157 (12)	0.0232 (15)	0.0169 (13)	−0.0006 (11)	0.0015 (11)	0.0041 (12)
C6	0.0139 (12)	0.0160 (14)	0.0162 (13)	−0.0006 (11)	0.0015 (11)	0.0000 (11)
C7	0.0173 (13)	0.0139 (14)	0.0169 (14)	−0.0029 (11)	−0.0007 (12)	−0.0007 (11)
C8	0.0170 (13)	0.0145 (14)	0.0159 (13)	0.0011 (11)	−0.0008 (11)	0.0017 (11)
C9	0.0180 (12)	0.0258 (15)	0.0165 (14)	0.0013 (12)	−0.0023 (11)	0.0030 (12)
C10	0.0148 (12)	0.0139 (13)	0.0145 (13)	0.0028 (11)	0.0022 (11)	0.0011 (11)
C11	0.0146 (12)	0.0152 (15)	0.0202 (14)	0.0003 (11)	0.0010 (11)	−0.0030 (12)
C12	0.0201 (13)	0.0187 (14)	0.0170 (14)	0.0037 (13)	−0.0011 (11)	−0.0044 (13)
C13	0.0168 (14)	0.0190 (14)	0.0177 (14)	0.0011 (12)	0.0039 (11)	0.0024 (12)
C14	0.0166 (13)	0.0128 (13)	0.0234 (15)	0.0017 (11)	0.0025 (12)	−0.0008 (11)
C15	0.0171 (13)	0.0152 (13)	0.0168 (14)	0.0012 (12)	0.0018 (12)	−0.0056 (11)
F1	0.0278 (8)	0.0147 (8)	0.0206 (9)	−0.0034 (7)	0.0043 (7)	−0.0025 (7)
O1	0.0266 (9)	0.0156 (9)	0.0158 (9)	−0.0050 (8)	0.0016 (9)	−0.0014 (8)
O2	0.0169 (9)	0.0263 (10)	0.0158 (9)	0.0032 (8)	−0.0026 (8)	0.0032 (8)
S1	0.0166 (3)	0.0174 (3)	0.0117 (3)	−0.0014 (3)	0.0002 (3)	0.0003 (3)

Geometric parameters (Å, °)

C1—C2	1.382 (3)	C8—C9	1.517 (3)
C1—C6	1.383 (3)	C8—H8	1.0
C1—S1	1.764 (3)	C9—H9A	0.99
C2—C3	1.390 (4)	C9—H9B	0.99
C2—H2	0.95	C10—C11	1.388 (4)
C3—C4	1.383 (4)	C10—C15	1.391 (3)
C3—H3	0.95	C11—C12	1.379 (4)
C4—C5	1.385 (4)	C11—H11	0.95
C4—H4	0.95	C12—C13	1.386 (4)

C5—C6	1.383 (4)	C12—H12	0.95
C5—H5	0.95	C13—C14	1.380 (4)
C6—H6	0.95	C13—H13	0.95
C7—F1	1.367 (3)	C14—C15	1.384 (4)
C7—C9	1.475 (4)	C14—H14	0.95
C7—C8	1.506 (4)	C15—H15	0.95
C7—S1	1.776 (3)	O1—S1	1.4323 (17)
C8—C10	1.496 (3)	O2—S1	1.4348 (18)
C2—C1—C6	122.1 (2)	C7—C9—C8	60.42 (17)
C2—C1—S1	119.69 (19)	C7—C9—H9A	117.7
C6—C1—S1	118.16 (19)	C8—C9—H9A	117.7
C1—C2—C3	118.4 (2)	C7—C9—H9B	117.7
C1—C2—H2	120.8	C8—C9—H9B	117.7
C3—C2—H2	120.8	H9A—C9—H9B	114.8
C4—C3—C2	120.3 (3)	C11—C10—C15	119.0 (2)
C4—C3—H3	119.8	C11—C10—C8	117.3 (2)
C2—C3—H3	119.8	C15—C10—C8	123.7 (2)
C3—C4—C5	120.2 (3)	C12—C11—C10	120.9 (2)
C3—C4—H4	119.9	C12—C11—H11	119.6
C5—C4—H4	119.9	C10—C11—H11	119.6
C6—C5—C4	120.2 (3)	C11—C12—C13	120.1 (3)
C6—C5—H5	119.9	C11—C12—H12	119.9
C4—C5—H5	119.9	C13—C12—H12	119.9
C5—C6—C1	118.8 (2)	C14—C13—C12	119.1 (2)
C5—C6—H6	120.6	C14—C13—H13	120.4
C1—C6—H6	120.6	C12—C13—H13	120.4
F1—C7—C9	118.1 (2)	C13—C14—C15	121.1 (2)
F1—C7—C8	119.3 (2)	C13—C14—H14	119.4

C9—C7—C8	61.15 (17)	C15—C14—H14	119.4
F1—C7—S1	110.25 (17)	C14—C15—C10	119.7 (2)
C9—C7—S1	122.10 (19)	C14—C15—H15	120.2
C8—C7—S1	118.43 (18)	C10—C15—H15	120.2
C10—C8—C7	122.4 (2)	O1—S1—O2	119.63 (12)
C10—C8—C9	124.2 (2)	O1—S1—C1	108.19 (11)
C7—C8—C9	58.43 (17)	O2—S1—C1	108.88 (11)
C10—C8—H8	113.6	O1—S1—C7	105.77 (11)
C7—C8—H8	113.6	O2—S1—C7	107.57 (11)
C9—C8—H8	113.6	C1—S1—C7	105.98 (12)
C6—C1—C2—C3	0.0 (4)	C10—C11—C12—C13	1.0 (4)
S1—C1—C2—C3	–176.56 (19)	C11—C12—C13—C14	–0.6 (4)
C1—C2—C3—C4	0.5 (4)	C12—C13—C14—C15	–0.3 (4)
C2—C3—C4—C5	0.0 (4)	C13—C14—C15—C10	0.9 (4)
C3—C4—C5—C6	–1.1 (4)	C11—C10—C15—C14	–0.5 (4)
C4—C5—C6—C1	1.7 (4)	C8—C10—C15—C14	–180.0 (2)
C2—C1—C6—C5	–1.1 (4)	C2—C1—S1—O1	158.7 (2)
S1—C1—C6—C5	175.50 (19)	C6—C1—S1—O1	–18.0 (2)
F1—C7—C8—C10	5.1 (4)	C2—C1—S1—O2	27.3 (2)
C9—C7—C8—C10	113.1 (3)	C6—C1—S1—O2	–149.47 (18)
S1—C7—C8—C10	–133.9 (2)	C2—C1—S1—C7	–88.2 (2)
F1—C7—C8—C9	–107.9 (3)	C6—C1—S1—C7	95.1 (2)
S1—C7—C8—C9	113.1 (2)	F1—C7—S1—O1	–171.37 (17)
F1—C7—C9—C8	109.8 (3)	C9—C7—S1—O1	43.1 (2)
S1—C7—C9—C8	–107.2 (2)	C8—C7—S1—O1	–29.0 (2)
C10—C8—C9—C7	–110.1 (3)	F1—C7—S1—O2	–42.4 (2)
C7—C8—C10—C11	137.4 (3)	C9—C7—S1—O2	172.0 (2)
C9—C8—C10—C11	–151.2 (2)	C8—C7—S1—O2	100.0 (2)

C7—C8—C10—C15	–43.2 (4)	F1—C7—S1—C1	73.91 (19)
C9—C8—C10—C15	28.2 (4)	C9—C7—S1—C1	–71.6 (2)
C15—C10—C11—C12	–0.4 (4)	C8—C7—S1—C1	–143.7 (2)
C8—C10—C11—C12	179.1 (2)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2011.12.3.0; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

((1*R*,2*S*)-2-Fluoro-2-(phenylsulfonyl)cyclopropyl)benzene 62j

Crystal data

$C_{10}H_{11}FO_2S$	
M_r = 214.25	D_x = 1.427 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 35-40 °C
Hall symbol: ?	? radiation, λ = 0.71073 Å
a = 5.9831 (3) Å	Cell parameters from 2384 reflections
b = 7.2799 (4) Å	θ = 2.9–28.2°
c = 22.8905 (13) Å	μ = 0.31 mm^{-1}
V = 997.03 (9) Å^3	T = 100 K
Z = 4	Block, translucent colourless
F(000) = 448	0.35 × 0.15 × 0.05 mm

Data collection

diffractometer	2378 independent reflections
Radiation source:	2200 reflections with $I > 2\sigma(I)$
	R_{int} = 0.020
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.2°, θ_{min} = 1.8°
	h = −7→7
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS)	k = −9→9
T_{min} = 0.89, T_{max} = 0.98	l = −30→21
5478 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)]$ = 0.028	$w = 1/[\sigma^2(F_o^2) + (0.0334P)^2 + 0.1383P]$

	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.066$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.05$	$\Delta\varrho_{max} = 0.27$ e Å^{-3}
2378 reflections	$\Delta\varrho_{min} = -0.20$ e Å^{-3}
128 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
? constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: –0.04 (7)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.1913 (3)	0.5929 (2)	–0.01675 (8)	0.0266 (4)
H1A	0.0457	0.566	–0.0344	0.04*
H1B	0.3025	0.611	–0.0476	0.04*
H1C	0.1802	0.7048	0.0069	0.04*
C2	0.2613 (3)	0.4343 (2)	0.02157 (7)	0.0200 (3)
H2	0.264	0.3115	0.002	0.024*
C3	0.1951 (3)	0.4323 (2)	0.08434 (7)	0.0201 (3)
C4	0.4331 (3)	0.4611 (3)	0.06892 (8)	0.0309 (4)
H4A	0.5389	0.3594	0.0766	0.037*

H4B	0.4961	0.5858	0.0742	0.037*
C5	0.1897 (2)	0.2442 (2)	0.19132 (6)	0.0154 (3)
C6	0.3994 (3)	0.1795 (2)	0.20726 (7)	0.0192 (3)
H6	0.4995	0.1324	0.1788	0.023*
C7	0.4591 (3)	0.1855 (2)	0.26586 (7)	0.0237 (4)
H7	0.6015	0.1416	0.2778	0.028*
C8	0.3116 (3)	0.2553 (2)	0.30693 (7)	0.0242 (3)
H8	0.3535	0.2585	0.3469	0.029*
C9	0.1038 (3)	0.3205 (2)	0.29030 (7)	0.0230 (3)
H9	0.0043	0.3684	0.3188	0.028*
C10	0.0404 (3)	0.3162 (2)	0.23204 (7)	0.0185 (3)
H10	–0.1015	0.3612	0.2202	0.022*
F1	0.0760 (2)	0.57764 (13)	0.10590 (4)	0.0424 (3)
O1	0.2271 (2)	0.08060 (16)	0.09059 (5)	0.0258 (3)
O2	–0.13568 (17)	0.22284 (18)	0.11645 (5)	0.0300 (3)
S1	0.10448 (6)	0.22632 (5)	0.117724 (16)	0.01766 (9)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0291 (9)	0.0292 (9)	0.0215 (9)	–0.0001 (8)	–0.0048 (7)	0.0035 (7)
C2	0.0199 (8)	0.0239 (8)	0.0162 (8)	–0.0006 (6)	0.0016 (6)	0.0006 (7)
C3	0.0274 (9)	0.0170 (8)	0.0159 (8)	0.0022 (6)	0.0017 (7)	–0.0020 (6)
C4	0.0255 (10)	0.0404 (10)	0.0266 (9)	–0.0111 (8)	–0.0067 (7)	0.0120 (8)
C5	0.0163 (7)	0.0135 (7)	0.0163 (7)	–0.0021 (6)	0.0008 (5)	0.0014 (6)
C6	0.0168 (7)	0.0179 (7)	0.0228 (8)	0.0003 (7)	0.0032 (6)	0.0030 (6)
C7	0.0206 (8)	0.0242 (9)	0.0262 (8)	–0.0013 (6)	–0.0044 (6)	0.0084 (7)
C8	0.0366 (9)	0.0186 (8)	0.0175 (7)	–0.0033 (7)	–0.0036 (6)	0.0036 (7)
C9	0.0335 (9)	0.0152 (7)	0.0204 (8)	0.0015 (7)	0.0079 (7)	0.0009 (6)

C10	0.0184 (8)	0.0140 (7)	0.0230 (8)	0.0029 (5)	0.0035 (6)	0.0028 (6)
F1	0.0743 (9)	0.0229 (5)	0.0299 (6)	0.0168 (6)	0.0213 (6)	0.0023 (4)
O1	0.0345 (8)	0.0205 (6)	0.0223 (6)	0.0018 (5)	0.0013 (5)	–0.0048 (5)
O2	0.0176 (6)	0.0472 (7)	0.0252 (6)	–0.0045 (5)	–0.0030 (5)	0.0046 (7)
S1	0.01668 (17)	0.01899 (16)	0.01731 (17)	–0.00099 (14)	–0.00012 (15)	0.00049 (15)

Geometric parameters (Å, °)

C1—C2	1.510 (2)	C5—C10	1.393 (2)
C1—H1A	0.98	C5—S1	1.7648 (15)
C1—H1B	0.98	C6—C7	1.389 (2)
C1—H1C	0.98	C6—H6	0.95
C2—C3	1.491 (2)	C7—C8	1.386 (2)
C2—C4	1.507 (2)	C7—H7	0.95
C2—H2	1.0	C8—C9	1.384 (3)
C3—F1	1.3682 (18)	C8—H8	0.95
C3—C4	1.482 (2)	C9—C10	1.387 (2)
C3—S1	1.7680 (17)	C9—H9	0.95
C4—H4A	0.99	C10—H10	0.95
C4—H4B	0.99	O1—S1	1.4317 (12)
C5—C6	1.389 (2)	O2—S1	1.4374 (11)
C2—C1—H1A	109.5	C6—C5—C10	122.04 (14)
C2—C1—H1B	109.5	C6—C5—S1	119.14 (11)
H1A—C1—H1B	109.5	C10—C5—S1	118.77 (11)
C2—C1—H1C	109.5	C7—C6—C5	118.41 (14)
H1A—C1—H1C	109.5	C7—C6—H6	120.8
H1B—C1—H1C	109.5	C5—C6—H6	120.8
C3—C2—C4	59.27 (11)	C8—C7—C6	120.18 (15)
C3—C2—C1	119.59 (15)	C8—C7—H7	119.9

C4—C2—C1	120.54 (15)	C6—C7—H7	119.9
C3—C2—H2	115.3	C9—C8—C7	120.73 (15)
C4—C2—H2	115.3	C9—C8—H8	119.6
C1—C2—H2	115.3	C7—C8—H8	119.6
F1—C3—C4	118.49 (15)	C8—C9—C10	120.14 (15)
F1—C3—C2	118.59 (13)	C8—C9—H9	119.9
C4—C3—C2	60.91 (11)	C10—C9—H9	119.9
F1—C3—S1	109.89 (11)	C9—C10—C5	118.49 (15)
C4—C3—S1	121.19 (12)	C9—C10—H10	120.8
C2—C3—S1	120.42 (11)	C5—C10—H10	120.8
C3—C4—C2	59.83 (11)	O1—S1—O2	119.37 (8)
C3—C4—H4A	117.8	O1—S1—C5	108.70 (7)
C2—C4—H4A	117.8	O2—S1—C5	108.02 (7)
C3—C4—H4B	117.8	O1—S1—C3	106.48 (7)
C2—C4—H4B	117.8	O2—S1—C3	108.23 (8)
H4A—C4—H4B	114.9	C5—S1—C3	105.16 (7)
C4—C2—C3—F1	108.57 (18)	C6—C5—S1—O1	23.94 (14)
C1—C2—C3—F1	−1.4 (2)	C10—C5—S1—O1	−153.53 (12)
C1—C2—C3—C4	−110.01 (18)	C6—C5—S1—O2	154.83 (12)
C4—C2—C3—S1	−111.13 (16)	C10—C5—S1—O2	−22.63 (14)
C1—C2—C3—S1	138.85 (14)	C6—C5—S1—C3	−89.76 (13)
F1—C3—C4—C2	−108.73 (16)	C10—C5—S1—C3	92.77 (13)
S1—C3—C4—C2	109.91 (14)	F1—C3—S1—O1	176.72 (12)
C1—C2—C4—C3	108.44 (18)	C4—C3—S1—O1	−38.98 (15)
C10—C5—C6—C7	0.8 (2)	C2—C3—S1—O1	33.34 (16)
S1—C5—C6—C7	−176.57 (12)	F1—C3—S1—O2	47.23 (14)
C5—C6—C7—C8	−0.2 (2)	C4—C3—S1—O2	−168.47 (13)
C6—C7—C8—C9	−0.2 (2)	C2—C3—S1—O2	−96.15 (14)

C7—C8—C9—C10	0.2 (2)	F1—C3—S1—C5	−68.03 (13)
C8—C9—C10—C5	0.4 (2)	C4—C3—S1—C5	76.27 (15)
C6—C5—C10—C9	−0.9 (2)	C2—C3—S1—C5	148.59 (13)
S1—C5—C10—C9	176.52 (11)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2011.12.3.0; cell refinement: *SAINT* V7.68A (Bruker AXS, 2009); data reduction: *SAINT* V7.68A (Bruker AXS, 2009); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

(((1*S**,2*R**)-1-Fluoro-2-vinylcyclopropyl)sulfonyl)benzene 62k

Crystal data

$C_{11}H_{11}FO_2S$	
M_r = 226.26	D_x = 1.414 Mg m^{-3}
Monoclinic, *C*2/*c*	Melting point: 54-56 °C
Hall symbol:	Mo *K*α radiation, λ = 0.71073 Å
a = 22.4293 (12) Å	Cell parameters from 4794 reflections
b = 7.9254 (6) Å	θ = 2.8–28.2°
c = 13.4400 (6) Å	μ = 0.29 mm^{-1}
β = 117.145 (2)°	*T* = 100 K
V = 2126.0 (2) Å^3	Block, translucent colourless
Z = 8	0.20 × 0.10 × 0.04 mm
F(000) = 944	

Data collection

Bruker APEX-II CCD diffractometer	2637 independent reflections
Radiation source: sealed tube	2152 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.039
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.3°, θ_{min} = 2.0°
φ and ω scans	*h* = −29→29
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS)	*k* = −5→10
T_{min} = 0.95, T_{max} = 0.99	*l* = −17→17
18643 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.034$	H-atom parameters constrained
$wR(F^2) = 0.092$	$w = 1/[\sigma^2(F_o^2) + (0.0525P)^2 + 1.8039P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.98$	$(\Delta/\sigma)_{max} = 0.001$
2637 reflections	$\Delta\varrho_{max} = 0.37$ e Å^{-3}
136 parameters	$\Delta\varrho_{min} = -0.26$ e Å^{-3}
0 restraints	Extinction correction: none
constraints	Extinction coefficient: ?
Primary atom site location: structure-invariant direct methods	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.32079 (8)	0.4919 (2)	0.28176 (13)	0.0257 (3)
H1A	0.2823	0.4653	0.214	0.031*
H1B	0.3398	0.4093	0.339	0.031*
C2	0.34795 (7)	0.6438 (2)	0.29642 (12)	0.0214 (3)
H2	0.3864	0.6664	0.3651	0.026*
C3	0.32209 (7)	0.78132 (19)	0.21226 (12)	0.0202 (3)

H3	0.2775	0.7618	0.1464	0.024*
C4	0.37178 (7)	0.88253 (18)	0.19131 (11)	0.0158 (3)
C5	0.33929 (8)	0.9646 (2)	0.25217 (14)	0.0252 (3)
H5A	0.3052	1.0522	0.2124	0.03*
H5B	0.3667	0.9845	0.3333	0.03*
C6	0.39724 (7)	1.13859 (17)	0.07368 (11)	0.0176 (3)
C7	0.46245 (8)	1.1310 (2)	0.08652 (13)	0.0252 (3)
H7	0.4823	1.026	0.0844	0.03*
C8	0.49773 (9)	1.2809 (3)	0.10248 (14)	0.0345 (4)
H8	0.5422	1.2792	0.1113	0.041*
C9	0.46815 (10)	1.4328 (2)	0.10555 (14)	0.0357 (4)
H9	0.4925	1.5349	0.1163	0.043*
C10	0.40330 (10)	1.4377 (2)	0.09313 (14)	0.0321 (4)
H10	0.3836	1.5426	0.0958	0.039*
C11	0.36726 (8)	1.29014 (19)	0.07694 (12)	0.0229 (3)
H11	0.3228	1.2924	0.0682	0.028*
F1	0.43812 (4)	0.84040 (13)	0.24870 (7)	0.0269 (2)
O1	0.28143 (6)	0.98761 (16)	0.00137 (10)	0.0330 (3)
O2	0.37695 (7)	0.82775 (14)	0.00366 (10)	0.0355 (3)
S1	0.351834 (19)	0.95017 (4)	0.05358 (3)	0.01991 (11)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0245 (8)	0.0287 (8)	0.0230 (8)	−0.0014 (6)	0.0102 (6)	0.0053 (6)
C2	0.0195 (7)	0.0284 (8)	0.0158 (6)	−0.0012 (6)	0.0077 (5)	0.0025 (6)
C3	0.0185 (7)	0.0236 (7)	0.0188 (7)	−0.0029 (6)	0.0088 (5)	−0.0010 (6)
C4	0.0145 (6)	0.0195 (6)	0.0126 (6)	−0.0006 (5)	0.0055 (5)	−0.0001 (5)
C5	0.0339 (8)	0.0243 (7)	0.0256 (8)	0.0013 (7)	0.0206 (7)	−0.0021 (6)
C6	0.0252 (7)	0.0141 (6)	0.0124 (6)	−0.0011 (5)	0.0077 (5)	0.0010 (5)

C7	0.0275 (8)	0.0296 (8)	0.0196 (7)	0.0050 (6)	0.0116 (6)	0.0069 (6)
C8	0.0281 (8)	0.0487 (11)	0.0237 (8)	−0.0104 (8)	0.0092 (7)	0.0083 (8)
C9	0.0520 (11)	0.0309 (9)	0.0201 (8)	−0.0200 (8)	0.0128 (8)	0.0000 (7)
C10	0.0577 (12)	0.0150 (7)	0.0240 (8)	−0.0031 (7)	0.0189 (8)	−0.0012 (6)
C11	0.0312 (8)	0.0176 (7)	0.0203 (7)	0.0024 (6)	0.0119 (6)	0.0013 (6)
F1	0.0157 (4)	0.0371 (5)	0.0253 (5)	0.0020 (4)	0.0072 (4)	0.0097 (4)
O1	0.0262 (6)	0.0320 (6)	0.0237 (6)	−0.0074 (5)	−0.0034 (5)	0.0069 (5)
O2	0.0751 (9)	0.0160 (5)	0.0279 (6)	−0.0016 (6)	0.0343 (6)	−0.0025 (5)
S1	0.0303 (2)	0.01431 (17)	0.01258 (17)	−0.00298 (14)	0.00754 (14)	−0.00020 (12)

Geometric parameters (Å, °)

C1—C2	1.323 (2)	C6—C7	1.394 (2)
C1—H1A	0.95	C6—S1	1.7576 (14)
C1—H1B	0.95	C7—C8	1.389 (2)
C2—C3	1.485 (2)	C7—H7	0.95
C2—H2	0.95	C8—C9	1.385 (3)
C3—C4	1.500 (2)	C8—H8	0.95
C3—C5	1.535 (2)	C9—C10	1.387 (3)
C3—H3	1.0	C9—H9	0.95
C4—F1	1.3686 (16)	C10—C11	1.381 (2)
C4—C5	1.472 (2)	C10—H10	0.95
C4—S1	1.7771 (14)	C11—H11	0.95
C5—H5A	0.99	O1—S1	1.4364 (13)
C5—H5B	0.99	O2—S1	1.4330 (12)
C6—C11	1.387 (2)		
C2—C1—H1A	120.0	C11—C6—C7	121.99 (14)
C2—C1—H1B	120.0	C11—C6—S1	119.04 (12)
H1A—C1—H1B	120.0	C7—C6—S1	118.97 (11)

C1—C2—C3	124.15 (14)	C8—C7—C6	118.32 (16)
C1—C2—H2	117.9	C8—C7—H7	120.8
C3—C2—H2	117.9	C6—C7—H7	120.8
C2—C3—C4	118.03 (12)	C9—C8—C7	120.10 (16)
C2—C3—C5	118.66 (13)	C9—C8—H8	120.0
C4—C3—C5	58.00 (9)	C7—C8—H8	120.0
C2—C3—H3	116.5	C10—C9—C8	120.72 (16)
C4—C3—H3	116.5	C10—C9—H9	119.6
C5—C3—H3	116.5	C8—C9—H9	119.6
F1—C4—C5	118.76 (12)	C9—C10—C11	120.13 (16)
F1—C4—C3	118.26 (12)	C9—C10—H10	119.9
C5—C4—C3	62.18 (10)	C11—C10—H10	119.9
F1—C4—S1	110.67 (9)	C10—C11—C6	118.74 (15)
C5—C4—S1	119.50 (11)	C10—C11—H11	120.6
C3—C4—S1	120.08 (10)	C6—C11—H11	120.6
C4—C5—C3	59.82 (9)	O2—S1—O1	119.37 (8)
C4—C5—H5A	117.8	O2—S1—C6	108.86 (7)
C3—C5—H5A	117.8	O1—S1—C6	109.29 (7)
C4—C5—H5B	117.8	O2—S1—C4	108.52 (7)
C3—C5—H5B	117.8	O1—S1—C4	105.63 (7)
H5A—C5—H5B	114.9	C6—S1—C4	104.08 (6)
C1—C2—C3—C4	−136.03 (16)	S1—C6—C11—C10	179.79 (12)
C1—C2—C3—C5	157.12 (15)	C11—C6—S1—O2	154.06 (12)
C2—C3—C4—F1	1.58 (19)	C7—C6—S1—O2	−26.32 (14)
C5—C3—C4—F1	109.52 (14)	C11—C6—S1—O1	22.10 (14)
C2—C3—C4—C5	−107.94 (15)	C7—C6—S1—O1	−158.29 (12)
C2—C3—C4—S1	142.32 (12)	C11—C6—S1—C4	−90.37 (12)
C5—C3—C4—S1	−109.74 (13)	C7—C6—S1—C4	89.25 (12)

F1—C4—C5—C3	−108.73 (14)	F1—C4—S1—O2	49.86 (12)
S1—C4—C5—C3	110.64 (12)	C5—C4—S1—O2	−166.60 (12)
C2—C3—C5—C4	106.85 (15)	C3—C4—S1—O2	−93.57 (13)
C11—C6—C7—C8	−0.3 (2)	F1—C4—S1—O1	178.98 (10)
S1—C6—C7—C8	−179.91 (12)	C5—C4—S1—O1	−37.49 (13)
C6—C7—C8—C9	0.1 (2)	C3—C4—S1—O1	35.54 (13)
C7—C8—C9—C10	0.2 (3)	F1—C4—S1—C6	−65.95 (11)
C8—C9—C10—C11	−0.3 (3)	C5—C4—S1—C6	77.59 (13)
C9—C10—C11—C6	0.1 (2)	C3—C4—S1—C6	150.62 (11)
C7—C6—C11—C10	0.2 (2)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2011.12.3.0; cell refinement: *SAINT* V7.68A (Bruker AXS, 2009); data reduction: *SAINT* V7.68A (Bruker AXS, 2009); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

(((1*S**,2*R**)-2-((Benzyloxy)methyl)-1-fluorocyclopropyl)sulfonyl)benzene 62l

Crystal data

$C_{34}H_{34}F_2O_6S_2$	$F(000) = 336$
$M_r = 640.73$	
Triclinic, $P\overline{1}$	$D_x = 1.361$ Mg m^{-3}
Hall symbol:	Melting point: 35-42 °C
$a = 6.0384$ (4) Å	radiation, $\lambda = 0.71073$ Å
$b = 7.8085$ (5) Å	Cell parameters from 9249 reflections
$c = 16.6089$ (10) Å	$\theta = 2.5–28.3°$
$\alpha = 93.413$ (1)°	$\mu = 0.23$ mm^{-1}
$\beta = 90.500$ (1)°	$T = 100$ K
$\gamma = 90.255$ (1)°	Plate, translucent colourless
$V = 781.70$ (9) Å^3	0.45 × 0.40 × 0.14 mm
$Z = 1$	

Data collection

diffractometer	5729 independent reflections
Radiation source:	5578 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.014$
Detector resolution: 8.3333 pixels mm^{-1}	$\theta_{max} = 28.3°$, $\theta_{min} = 2.5°$
	$h = -8 \rightarrow 8$
Absorption correction: multi-scan *SADABS* V2012/1 (Bruker AXS Inc.)	$k = -6 \rightarrow 10$
$T_{min} = 0.90$, $T_{max} = 0.97$	$l = -22 \rightarrow 22$
13310 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites

Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.027$	$w = 1/[\sigma^2(F_o^2) + (0.050P)^2 + 0.1353P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.074$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.02$	$\Delta\rho_{max} = 0.47$ e Å^{-3}
5729 reflections	$\Delta\rho_{min} = -0.19$ e Å^{-3}
397 parameters	Extinction correction: none
3 restraints	Extinction coefficient: ?
? constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.06 (4)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.93961 (5)	0.73730 (5)	−0.15774 (2)	0.01685 (9)
S2	1.04742 (5)	−0.72495 (5)	0.15891 (2)	0.01594 (9)
F1	0.91634 (16)	1.05579 (14)	−0.10777 (6)	0.0217 (2)
F2	1.07256 (15)	−0.41590 (14)	0.11212 (6)	0.0210 (2)
O1	1.4108 (2)	1.14253 (18)	−0.16738 (7)	0.0218 (3)
O2	1.0885 (2)	0.59688 (18)	−0.14704 (8)	0.0232 (3)

O3	0.7090 (2)	0.71609 (19)	−0.13977 (8)	0.0239 (3)
O4	0.5725 (2)	−0.31880 (17)	0.16978 (7)	0.0208 (3)
O5	1.27759 (19)	−0.75108 (19)	0.13985 (8)	0.0227 (3)
O6	0.8962 (2)	−0.86723 (18)	0.14742 (8)	0.0226 (3)
C1	1.0100 (4)	0.9279 (3)	−0.40706 (11)	0.0290 (4)
H1	1.0256	0.9694	−0.4593	0.035*
C2	1.1730 (3)	0.8244 (3)	−0.37704 (11)	0.0274 (4)
H3	1.2984	0.7946	−0.4089	0.033*
C3	1.1533 (3)	0.7640 (3)	−0.30002 (11)	0.0221 (4)
H17	1.2654	0.6949	−0.2782	0.027*
C4	0.9641 (3)	0.8079 (2)	−0.25591 (9)	0.0180 (3)
C5	1.0425 (3)	0.9135 (2)	−0.09687 (9)	0.0165 (3)
C6	1.2857 (3)	0.9367 (2)	−0.08228 (10)	0.0187 (3)
H4	1.3819	0.8423	−0.1052	0.022*
C7	1.3784 (3)	1.1135 (3)	−0.08448 (10)	0.0211 (3)
H12	1.2741	1.1985	−0.0599	0.025*
H11	1.5208	1.123	−0.0545	0.025*
C8	1.5104 (3)	1.3042 (2)	−0.17893 (10)	0.0194 (3)
H5	1.6679	1.3031	−0.1619	0.023*
H6	1.4339	1.3953	−0.146	0.023*
C9	1.4930 (3)	1.3391 (2)	−0.26711 (10)	0.0178 (3)
C10	1.3011 (3)	1.2962 (3)	−0.31105 (11)	0.0222 (4)
H10	1.1831	1.2393	−0.286	0.027*
C11	1.2812 (3)	1.3361 (3)	−0.39117 (11)	0.0269 (4)
H9	1.1506	1.3051	−0.4209	0.032*
C12	1.4521 (3)	1.4212 (3)	−0.42791 (11)	0.0284 (4)
H2	1.4374	1.4503	−0.4824	0.034*
C13	1.6443 (3)	1.4634 (3)	−0.38457 (12)	0.0293 (4)

H8	1.7614	1.5218	−0.4094	0.035*
C14	1.6655 (3)	1.4205 (3)	−0.30513 (11)	0.0239 (4)
H7	1.7991	1.4469	−0.2763	0.029*
C15	1.1323 (3)	0.8893 (3)	−0.01428 (10)	0.0213 (4)
H14	1.1398	0.771	0.0038	0.026*
H13	1.1002	0.9789	0.0287	0.026*
C16	0.7983 (3)	0.9108 (3)	−0.28554 (10)	0.0224 (4)
H15	0.6708	0.9386	−0.2544	0.027*
C17	0.8236 (3)	0.9720 (3)	−0.36182 (11)	0.0286 (4)
H16	0.7137	1.0438	−0.3831	0.034*
C18	0.9965 (4)	−0.4931 (3)	0.41331 (11)	0.0296 (4)
H18	0.9861	−0.4451	0.4671	0.035*
C19	1.1766 (3)	−0.4513 (3)	0.36620 (11)	0.0261 (4)
H34	1.2867	−0.3733	0.3873	0.031*
C20	1.1942 (3)	−0.5245 (3)	0.28818 (10)	0.0205 (3)
H20	1.318	−0.4997	0.2559	0.025*
C21	1.0273 (3)	−0.6349 (2)	0.25809 (9)	0.0169 (3)
C22	0.9455 (3)	−0.5611 (2)	0.09961 (9)	0.0156 (3)
C23	0.7033 (3)	−0.5427 (2)	0.08404 (10)	0.0182 (3)
H23	0.6062	−0.6325	0.106	0.022*
C24	0.6107 (3)	−0.3652 (3)	0.08718 (10)	0.0205 (3)
H30	0.7171	−0.2846	0.0644	0.025*
H31	0.4706	−0.3628	0.0559	0.025*
C25	0.4738 (3)	−0.1546 (2)	0.18205 (10)	0.0187 (3)
H29	0.3203	−0.1578	0.1605	0.022*
H24	0.5589	−0.0687	0.1534	0.022*
C26	0.4727 (3)	−0.1064 (2)	0.27064 (10)	0.0190 (3)
C27	0.2959 (3)	−0.0164 (3)	0.30558 (11)	0.0233 (4)

H25	0.1709	0.0083	0.2732	0.028*
C28	0.2986 (4)	0.0377 (3)	0.38658 (12)	0.0305 (4)
H28	0.1787	0.1025	0.4089	0.037*
C29	0.4769 (4)	−0.0029 (3)	0.43507 (12)	0.0327 (5)
H19	0.4797	0.0333	0.4907	0.039*
C30	0.8576 (3)	−0.6044 (3)	0.01671 (10)	0.0205 (3)
H22	0.8502	−0.727	−0.0021	0.025*
H21	0.8912	−0.5245	−0.0257	0.025*
C31	0.6503 (3)	−0.0967 (3)	0.40152 (13)	0.0343 (5)
H27	0.7706	−0.1275	0.4349	0.041*
C32	0.6516 (3)	−0.1465 (3)	0.32007 (12)	0.0275 (4)
H26	0.7741	−0.2081	0.2977	0.033*
C33	0.8447 (3)	−0.6763 (3)	0.30436 (11)	0.0228 (4)
H32	0.7321	−0.7518	0.2831	0.027*
C34	0.8334 (3)	−0.6033 (3)	0.38274 (12)	0.0313 (5)
H33	0.7114	−0.6297	0.4156	0.038*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.01664 (18)	0.0149 (2)	0.01913 (18)	0.00120 (14)	0.00419 (13)	0.00147 (15)
S2	0.01527 (17)	0.0145 (2)	0.01822 (17)	−0.00011 (14)	0.00414 (13)	0.00131 (14)
F1	0.0203 (5)	0.0188 (6)	0.0256 (5)	0.0091 (4)	−0.0022 (4)	−0.0014 (4)
F2	0.0199 (5)	0.0191 (6)	0.0244 (5)	−0.0073 (4)	−0.0027 (4)	0.0048 (4)
O1	0.0257 (6)	0.0193 (7)	0.0201 (6)	−0.0050 (5)	0.0029 (5)	0.0005 (5)
O2	0.0254 (6)	0.0172 (7)	0.0275 (6)	0.0052 (5)	0.0053 (5)	0.0046 (5)
O3	0.0181 (6)	0.0249 (8)	0.0288 (7)	−0.0026 (5)	0.0059 (5)	0.0008 (5)
O4	0.0246 (6)	0.0186 (7)	0.0194 (6)	0.0047 (5)	0.0037 (5)	0.0018 (5)
O5	0.0171 (6)	0.0244 (7)	0.0267 (6)	0.0026 (5)	0.0067 (5)	0.0021 (5)

O6	0.0231 (6)	0.0153 (7)	0.0290 (6)	−0.0045 (5)	0.0038 (5)	−0.0003 (5)
C1	0.0433 (11)	0.0263 (11)	0.0172 (8)	−0.0105 (9)	−0.0029 (7)	0.0002 (7)
C2	0.0355 (10)	0.0244 (10)	0.0219 (8)	−0.0044 (8)	0.0087 (7)	−0.0034 (7)
C3	0.0247 (8)	0.0181 (10)	0.0233 (8)	0.0001 (7)	0.0062 (6)	−0.0010 (7)
C4	0.0211 (8)	0.0171 (9)	0.0157 (7)	−0.0016 (6)	0.0013 (6)	−0.0003 (6)
C5	0.0161 (7)	0.0167 (8)	0.0167 (7)	0.0037 (6)	0.0016 (5)	0.0013 (6)
C6	0.0148 (7)	0.0206 (9)	0.0209 (7)	0.0025 (6)	0.0017 (6)	0.0032 (7)
C7	0.0187 (7)	0.0253 (10)	0.0192 (7)	−0.0031 (7)	0.0004 (6)	0.0011 (7)
C8	0.0187 (8)	0.0161 (9)	0.0232 (8)	−0.0003 (7)	−0.0016 (6)	0.0008 (7)
C9	0.0174 (7)	0.0125 (8)	0.0232 (8)	0.0023 (6)	0.0016 (6)	−0.0009 (6)
C10	0.0198 (8)	0.0211 (9)	0.0259 (8)	−0.0004 (7)	−0.0006 (6)	0.0023 (7)
C11	0.0289 (9)	0.0244 (10)	0.0269 (9)	0.0042 (8)	−0.0053 (7)	−0.0016 (7)
C12	0.0378 (10)	0.0269 (11)	0.0205 (8)	0.0070 (9)	0.0037 (7)	0.0007 (7)
C13	0.0292 (9)	0.0291 (11)	0.0300 (9)	−0.0004 (8)	0.0122 (7)	0.0034 (8)
C14	0.0186 (8)	0.0233 (10)	0.0293 (9)	−0.0016 (7)	0.0029 (6)	−0.0032 (7)
C15	0.0196 (7)	0.0276 (10)	0.0171 (7)	0.0003 (7)	0.0001 (6)	0.0061 (7)
C16	0.0213 (8)	0.0229 (10)	0.0226 (8)	−0.0011 (7)	−0.0039 (6)	−0.0021 (7)
C17	0.0327 (9)	0.0277 (11)	0.0251 (9)	−0.0029 (8)	−0.0105 (7)	0.0019 (8)
C18	0.0420 (11)	0.0298 (11)	0.0172 (8)	0.0058 (9)	0.0043 (7)	0.0025 (7)
C19	0.0329 (9)	0.0238 (10)	0.0217 (8)	−0.0007 (8)	−0.0035 (7)	0.0028 (7)
C20	0.0221 (8)	0.0204 (9)	0.0195 (7)	0.0002 (7)	−0.0001 (6)	0.0062 (7)
C21	0.0190 (7)	0.0156 (8)	0.0163 (7)	0.0018 (6)	0.0027 (6)	0.0031 (6)
C22	0.0139 (7)	0.0158 (8)	0.0173 (7)	−0.0025 (6)	0.0012 (5)	0.0017 (6)
C23	0.0142 (7)	0.0205 (9)	0.0198 (7)	−0.0015 (6)	0.0013 (5)	−0.0004 (6)
C24	0.0181 (7)	0.0236 (10)	0.0197 (7)	0.0034 (7)	0.0014 (6)	0.0015 (7)
C25	0.0181 (7)	0.0139 (9)	0.0241 (8)	0.0001 (6)	−0.0012 (6)	0.0027 (7)
C26	0.0181 (7)	0.0145 (8)	0.0242 (8)	−0.0032 (6)	−0.0009 (6)	0.0014 (6)
C27	0.0255 (8)	0.0206 (9)	0.0244 (8)	0.0058 (7)	0.0012 (6)	0.0060 (7)

C28	0.0394 (11)	0.0252 (11)	0.0272 (9)	0.0101 (9)	0.0058 (8)	0.0027 (8)
C29	0.0461 (12)	0.0264 (11)	0.0248 (9)	−0.0002 (9)	−0.0032 (8)	−0.0040 (8)
C30	0.0189 (7)	0.0248 (10)	0.0172 (7)	0.0003 (7)	0.0003 (6)	−0.0034 (6)
C31	0.0309 (10)	0.0377 (13)	0.0335 (10)	0.0017 (9)	−0.0136 (8)	−0.0036 (9)
C32	0.0199 (8)	0.0283 (11)	0.0336 (10)	0.0009 (8)	−0.0073 (7)	−0.0034 (8)
C33	0.0216 (8)	0.0223 (10)	0.0249 (8)	0.0006 (7)	0.0068 (6)	0.0038 (7)
C34	0.0349 (10)	0.0334 (12)	0.0264 (9)	0.0059 (9)	0.0140 (7)	0.0058 (8)

Geometric parameters (Å, °)

S1—O3	1.4374 (12)	C13—H8	0.95
S1—O2	1.4391 (13)	C14—H7	0.95
S1—C4	1.7593 (16)	C15—H14	0.99
S1—C5	1.7652 (19)	C15—H13	0.99
S2—O6	1.4377 (14)	C16—C17	1.390 (3)
S2—O5	1.4409 (12)	C16—H15	0.95
S2—C21	1.7577 (17)	C17—H16	0.95
S2—C22	1.7700 (17)	C18—C34	1.379 (3)
F1—C5	1.3703 (18)	C18—C19	1.394 (3)
F2—C22	1.370 (2)	C18—H18	0.95
O1—C8	1.420 (2)	C19—C20	1.390 (3)
O1—C7	1.4237 (19)	C19—H34	0.95
O4—C24	1.419 (2)	C20—C21	1.393 (3)
O4—C25	1.421 (2)	C20—H20	0.95
C1—C2	1.384 (3)	C21—C33	1.397 (2)
C1—C17	1.392 (3)	C22—C30	1.491 (2)
C1—H1	0.95	C22—C23	1.492 (2)
C2—C3	1.396 (3)	C23—C24	1.495 (3)
C2—H3	0.95	C23—C30	1.520 (2)

C3—C4	1.396 (2)	C23—H23	1.0
C3—H17	0.95	C24—H30	0.99
C4—C16	1.391 (2)	C24—H31	0.99
C5—C15	1.493 (2)	C25—C26	1.497 (2)
C5—C6	1.495 (2)	C25—H29	0.99
C6—C7	1.490 (3)	C25—H24	0.99
C6—C15	1.528 (2)	C26—C27	1.393 (2)
C6—H4	1.0	C26—C32	1.399 (2)
C7—H12	0.99	C27—C28	1.386 (3)
C7—H11	0.99	C27—H25	0.95
C8—C9	1.508 (2)	C28—C29	1.388 (3)
C8—H5	0.99	C28—H28	0.95
C8—H6	0.99	C29—C31	1.383 (3)
C9—C10	1.392 (2)	C29—H19	0.95
C9—C14	1.394 (2)	C30—H22	0.99
C10—C11	1.389 (2)	C30—H21	0.99
C10—H10	0.95	C31—C32	1.385 (3)
C11—C12	1.390 (3)	C31—H27	0.95
C11—H9	0.95	C32—H26	0.95
C12—C13	1.388 (3)	C33—C34	1.392 (3)
C12—H2	0.95	C33—H32	0.95
C13—C14	1.385 (3)	C34—H33	0.95
O3—S1—O2	118.97 (8)	H14—C15—H13	115.0
O3—S1—C4	109.07 (8)	C17—C16—C4	118.40 (17)
O2—S1—C4	109.93 (8)	C17—C16—H15	120.8
O3—S1—C5	108.05 (8)	C4—C16—H15	120.8
O2—S1—C5	106.70 (8)	C16—C17—C1	119.97 (18)
C4—S1—C5	102.88 (8)	C16—C17—H16	120.0

O6—S2—O5	118.84 (8)	C1—C17—H16	120.0
O6—S2—C21	109.73 (8)	C34—C18—C19	120.70 (18)
O5—S2—C21	109.02 (8)	C34—C18—H18	119.7
O6—S2—C22	106.66 (8)	C19—C18—H18	119.7
O5—S2—C22	108.05 (7)	C20—C19—C18	119.6 (2)
C21—S2—C22	103.41 (8)	C20—C19—H34	120.2
C8—O1—C7	112.68 (14)	C18—C19—H34	120.2
C24—O4—C25	112.82 (13)	C19—C20—C21	118.93 (16)
C2—C1—C17	121.00 (17)	C19—C20—H20	120.5
C2—C1—H1	119.5	C21—C20—H20	120.5
C17—C1—H1	119.5	C20—C21—C33	122.02 (16)
C1—C2—C3	120.11 (17)	C20—C21—S2	118.94 (12)
C1—C2—H3	119.9	C33—C21—S2	119.04 (14)
C3—C2—H3	119.9	F2—C22—C30	118.21 (14)
C2—C3—C4	118.06 (17)	F2—C22—C23	118.83 (15)
C2—C3—H17	121.0	C30—C22—C23	61.25 (11)
C4—C3—H17	121.0	F2—C22—S2	110.04 (10)
C16—C4—C3	122.43 (16)	C30—C22—S2	120.15 (13)
C16—C4—S1	118.82 (13)	C23—C22—S2	121.02 (12)
C3—C4—S1	118.70 (13)	C22—C23—C24	117.59 (16)
F1—C5—C15	117.88 (14)	C22—C23—C30	59.33 (10)
F1—C5—C6	118.52 (15)	C24—C23—C30	120.89 (15)
C15—C5—C6	61.51 (11)	C22—C23—H23	115.7
F1—C5—S1	110.05 (11)	C24—C23—H23	115.7
C15—C5—S1	120.77 (13)	C30—C23—H23	115.7
C6—C5—S1	120.84 (12)	O4—C24—C23	106.34 (13)
C7—C6—C5	117.67 (15)	O4—C24—H30	110.5
C7—C6—C15	120.72 (16)	C23—C24—H30	110.5

C5—C6—C15	59.20 (10)	O4—C24—H31	110.5
C7—C6—H4	115.8	C23—C24—H31	110.5
C5—C6—H4	115.8	H30—C24—H31	108.7
C15—C6—H4	115.8	O4—C25—C26	108.58 (13)
O1—C7—C6	106.18 (14)	O4—C25—H29	110.0
O1—C7—H12	110.5	C26—C25—H29	110.0
C6—C7—H12	110.5	O4—C25—H24	110.0
O1—C7—H11	110.5	C26—C25—H24	110.0
C6—C7—H11	110.5	H29—C25—H24	108.4
H12—C7—H11	108.7	C27—C26—C32	118.28 (17)
O1—C8—C9	108.57 (14)	C27—C26—C25	120.76 (15)
O1—C8—H5	110.0	C32—C26—C25	120.94 (16)
C9—C8—H5	110.0	C28—C27—C26	121.34 (17)
O1—C8—H6	110.0	C28—C27—H25	119.3
C9—C8—H6	110.0	C26—C27—H25	119.3
H5—C8—H6	108.4	C29—C28—C27	119.85 (18)
C10—C9—C14	118.93 (16)	C29—C28—H28	120.1
C10—C9—C8	120.56 (15)	C27—C28—H28	120.1
C14—C9—C8	120.47 (16)	C31—C29—C28	119.27 (18)
C9—C10—C11	120.46 (17)	C31—C29—H19	120.4
C9—C10—H10	119.8	C28—C29—H19	120.4
C11—C10—H10	119.8	C22—C30—C23	59.42 (10)
C10—C11—C12	120.14 (18)	C22—C30—H22	117.8
C10—C11—H9	119.9	C23—C30—H22	117.8
C12—C11—H9	119.9	C22—C30—H21	117.8
C13—C12—C11	119.68 (17)	C23—C30—H21	117.8
C13—C12—H2	120.2	H22—C30—H21	115.0
C11—C12—H2	120.2	C29—C31—C32	121.09 (18)

C12—C13—C14	120.08 (18)	C29—C31—H27	119.5
C12—C13—H8	120.0	C32—C31—H27	119.5
C14—C13—H8	120.0	C31—C32—C26	120.11 (18)
C13—C14—C9	120.68 (17)	C31—C32—H26	119.9
C13—C14—H7	119.7	C26—C32—H26	119.9
C9—C14—H7	119.7	C34—C33—C21	117.77 (18)
C5—C15—C6	59.28 (10)	C34—C33—H32	121.1
C5—C15—H14	117.8	C21—C33—H32	121.1
C6—C15—H14	117.8	C18—C34—C33	120.95 (18)
C5—C15—H13	117.8	C18—C34—H33	119.5
C6—C15—H13	117.8	C33—C34—H33	119.5
C17—C1—C2—C3	−0.6 (3)	C34—C18—C19—C20	−1.4 (3)
C1—C2—C3—C4	1.3 (3)	C18—C19—C20—C21	1.7 (3)
C2—C3—C4—C16	−0.9 (3)	C19—C20—C21—C33	−1.1 (3)
C2—C3—C4—S1	−178.45 (16)	C19—C20—C21—S2	179.06 (14)
O3—S1—C4—C16	31.57 (18)	O6—S2—C21—C20	164.38 (13)
O2—S1—C4—C16	163.67 (15)	O5—S2—C21—C20	32.65 (16)
C5—S1—C4—C16	−82.97 (16)	C22—S2—C21—C20	−82.13 (14)
O3—S1—C4—C3	−150.82 (15)	O6—S2—C21—C33	−15.50 (16)
O2—S1—C4—C3	−18.72 (17)	O5—S2—C21—C33	−147.24 (14)
C5—S1—C4—C3	94.64 (16)	C22—S2—C21—C33	97.98 (15)
O3—S1—C5—F1	−54.69 (12)	O6—S2—C22—F2	175.55 (10)
O2—S1—C5—F1	176.29 (10)	O5—S2—C22—F2	−55.62 (13)
C4—S1—C5—F1	60.59 (12)	C21—S2—C22—F2	59.85 (12)
O3—S1—C5—C15	88.13 (14)	O6—S2—C22—C30	−41.93 (14)
O2—S1—C5—C15	−40.89 (15)	O5—S2—C22—C30	86.90 (13)
C4—S1—C5—C15	−156.59 (13)	C21—S2—C22—C30	−157.62 (12)
O3—S1—C5—C6	161.21 (13)	O6—S2—C22—C23	30.63 (16)

O2—S1—C5—C6	32.19 (15)	O5—S2—C22—C23	159.46 (13)
C4—S1—C5—C6	−83.51 (14)	C21—S2—C22—C23	−85.06 (15)
F1—C5—C6—C7	−2.9 (2)	F2—C22—C23—C24	−3.0 (2)
C15—C5—C6—C7	−111.04 (17)	C30—C22—C23—C24	−111.32 (17)
S1—C5—C6—C7	138.23 (14)	S2—C22—C23—C24	138.90 (14)
F1—C5—C6—C15	108.10 (17)	F2—C22—C23—C30	108.27 (16)
S1—C5—C6—C15	−110.73 (15)	S2—C22—C23—C30	−109.79 (16)
C8—O1—C7—C6	−176.88 (13)	C25—O4—C24—C23	−177.20 (14)
C5—C6—C7—O1	−81.95 (17)	C22—C23—C24—O4	−82.72 (17)
C15—C6—C7—O1	−150.79 (14)	C30—C23—C24—O4	−151.74 (15)
C7—O1—C8—C9	−167.99 (13)	C24—O4—C25—C26	−171.36 (13)
O1—C8—C9—C10	39.9 (2)	O4—C25—C26—C27	−143.36 (18)
O1—C8—C9—C14	−142.53 (17)	O4—C25—C26—C32	38.3 (2)
C14—C9—C10—C11	−0.8 (3)	C32—C26—C27—C28	2.2 (3)
C8—C9—C10—C11	176.81 (17)	C25—C26—C27—C28	−176.18 (19)
C9—C10—C11—C12	−0.8 (3)	C26—C27—C28—C29	−2.3 (3)
C10—C11—C12—C13	1.1 (3)	C27—C28—C29—C31	0.3 (3)
C11—C12—C13—C14	0.1 (3)	F2—C22—C30—C23	−109.26 (17)
C12—C13—C14—C9	−1.8 (3)	S2—C22—C30—C23	111.17 (15)
C10—C9—C14—C13	2.1 (3)	C24—C23—C30—C22	105.82 (18)
C8—C9—C14—C13	−175.55 (17)	C28—C29—C31—C32	1.8 (4)
F1—C5—C15—C6	−109.12 (18)	C29—C31—C32—C26	−1.8 (4)
S1—C5—C15—C6	110.84 (15)	C27—C26—C32—C31	−0.1 (3)
C7—C6—C15—C5	105.94 (17)	C25—C26—C32—C31	178.2 (2)
C3—C4—C16—C17	−0.2 (3)	C20—C21—C33—C34	0.0 (3)
S1—C4—C16—C17	177.32 (15)	S2—C21—C33—C34	179.89 (15)
C4—C16—C17—C1	0.9 (3)	C19—C18—C34—C33	0.3 (3)
C2—C1—C17—C16	−0.5 (3)	C21—C33—C34—C18	0.3 (3)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2012.12.0.3; cell refinement: *SAINT* V8.27B (Bruker AXS Inc., 2012); data reduction: *SAINT* V8.27B (Bruker AXS Inc., 2012); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008);

2-((1*R*,2*S*)-1-Methyl-2-phenylcyclopropyl)quinoline 67a

Crystal data

$C_{19}H_{17}N$	?
M_r = 259.34	D_x = 1.260 Mg m^{-3}
Monoclinic, $P2_1/n$	Melting point: 106-111 °C
Hall symbol: ?	? radiation, λ = 0.71073 Å
a = 12.2590 (8) Å	Cell parameters from 7256 reflections
b = 5.4626 (4) Å	θ = 3.3–28.3°
c = 20.4676 (13) Å	μ = 0.07 mm^{-1}
β = 93.912 (2)°	T = 100 K
V = 1367.44 (16) Å^3	Block, translucent colourless
Z = 4	0.32 × 0.30 × 0.10 mm
F(000) = 552	

Data collection

diffractometer	3382 independent reflections
Radiation source: ?	3000 reflections with $I > 2\sigma(I)$
	R_{int} = 0.014
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.3°, θ_{min} = 1.9°
	h = −16→16
Absorption correction: multi-scan SADABS V2008/1 (Bruker AXS Inc.)	k = −7→5
T_{min} = 0.94, T_{max} = 0.99	l = −26→27
12684 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.041$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.114$	$w = 1/[\sigma^2(F_o^2) + (0.0585P)^2 + 0.6935P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} < 0.001$
3382 reflections	$\Delta\varrho_{max} = 0.38$ e Å^{-3}
182 parameters	$\Delta\varrho_{min} = -0.22$ e Å^{-3}
0 restraints	Extinction correction: none
? constraints	Extinction coefficient: ?
Primary atom site location: structure-invariant direct methods	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.34133 (9)	0.8405 (2)	−0.02408 (5)	0.0190 (2)
H1	0.3828	0.9648	−0.0433	0.023*
C2	0.39113 (9)	0.6853 (2)	0.02118 (5)	0.0183 (2)
H2	0.4672	0.7008	0.0326	0.022*
C3	0.32981 (8)	0.5013 (2)	0.05111 (5)	0.0148 (2)
C4	0.21603 (8)	0.47906 (19)	0.03365 (5)	0.0133 (2)
C5	0.16695 (9)	0.6398 (2)	−0.01430 (5)	0.0161 (2)

H5	0.0913	0.6251	−0.0271	0.019*
C6	0.22848 (9)	0.8166 (2)	−0.04231 (5)	0.0182 (2)
H6	0.1949	0.9239	−0.0742	0.022*
C7	0.37588 (8)	0.3372 (2)	0.09883 (5)	0.0173 (2)
H7	0.4519	0.3426	0.1113	0.021*
C8	0.31027 (8)	0.1708 (2)	0.12685 (5)	0.0161 (2)
H8	0.3406	0.0586	0.1586	0.019*
C9	0.19633 (8)	0.16626 (19)	0.10831 (5)	0.0130 (2)
C10	0.12186 (8)	−0.00089 (19)	0.14232 (5)	0.0132 (2)
C11	0.01878 (8)	−0.0867 (2)	0.10407 (5)	0.0163 (2)
H11A	0.0089	−0.0405	0.0573	0.02*
H11B	−0.0098	−0.2507	0.1145	0.02*
C12	0.00927 (8)	0.11188 (19)	0.15386 (5)	0.0135 (2)
H12	−0.0013	0.2779	0.1338	0.016*
C13	0.17279 (9)	−0.1729 (2)	0.19343 (5)	0.0174 (2)
H13C	0.2244	−0.2818	0.1732	0.026*
H13B	0.1154	−0.2707	0.2119	0.026*
H13A	0.2117	−0.078	0.2283	0.026*
C14	−0.04339 (8)	0.08551 (19)	0.21709 (5)	0.0132 (2)
C15	−0.11218 (8)	−0.1077 (2)	0.23115 (5)	0.0170 (2)
H15	−0.1242	−0.2369	0.2004	0.02*
C16	−0.16372 (9)	−0.1133 (2)	0.29009 (6)	0.0194 (2)
H16	−0.2104	−0.2462	0.299	0.023*
C17	−0.14706 (9)	0.0736 (2)	0.33547 (5)	0.0187 (2)
H17	−0.1824	0.0699	0.3754	0.022*
C18	−0.07818 (9)	0.2667 (2)	0.32201 (5)	0.0199 (2)
H18	−0.0662	0.3957	0.3528	0.024*
C19	−0.02683 (9)	0.2712 (2)	0.26348 (5)	0.0180 (2)

H19	0.0205	0.4034	0.2549	0.022*
N1	0.15102 (7)	0.31345 (17)	0.06268 (4)	0.01375 (19)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0229 (5)	0.0167 (5)	0.0182 (5)	−0.0045 (4)	0.0068 (4)	−0.0005 (4)
C2	0.0165 (5)	0.0199 (5)	0.0189 (5)	−0.0037 (4)	0.0036 (4)	−0.0028 (4)
C3	0.0144 (5)	0.0156 (5)	0.0147 (5)	−0.0011 (4)	0.0029 (4)	−0.0029 (4)
C4	0.0142 (5)	0.0131 (5)	0.0130 (4)	0.0007 (4)	0.0033 (3)	−0.0019 (4)
C5	0.0157 (5)	0.0172 (5)	0.0156 (5)	0.0012 (4)	0.0027 (4)	0.0006 (4)
C6	0.0225 (5)	0.0167 (5)	0.0157 (5)	0.0016 (4)	0.0041 (4)	0.0020 (4)
C7	0.0129 (4)	0.0200 (5)	0.0187 (5)	0.0000 (4)	0.0001 (4)	−0.0017 (4)
C8	0.0155 (5)	0.0174 (5)	0.0152 (5)	0.0022 (4)	0.0001 (4)	0.0012 (4)
C9	0.0143 (4)	0.0124 (5)	0.0125 (4)	0.0006 (4)	0.0020 (3)	−0.0017 (4)
C10	0.0137 (4)	0.0117 (5)	0.0143 (4)	0.0006 (4)	0.0012 (3)	0.0007 (4)
C11	0.0168 (5)	0.0163 (5)	0.0157 (5)	−0.0021 (4)	0.0006 (4)	−0.0014 (4)
C12	0.0130 (4)	0.0127 (5)	0.0149 (5)	−0.0002 (4)	0.0016 (3)	0.0010 (4)
C13	0.0177 (5)	0.0152 (5)	0.0193 (5)	0.0015 (4)	0.0011 (4)	0.0046 (4)
C14	0.0111 (4)	0.0131 (5)	0.0156 (5)	0.0014 (4)	0.0010 (3)	0.0024 (4)
C15	0.0159 (5)	0.0146 (5)	0.0207 (5)	−0.0015 (4)	0.0016 (4)	0.0002 (4)
C16	0.0151 (5)	0.0179 (5)	0.0257 (6)	−0.0019 (4)	0.0046 (4)	0.0059 (4)
C17	0.0162 (5)	0.0220 (6)	0.0184 (5)	0.0038 (4)	0.0045 (4)	0.0058 (4)
C18	0.0247 (5)	0.0180 (5)	0.0171 (5)	0.0000 (4)	0.0025 (4)	−0.0009 (4)
C19	0.0203 (5)	0.0148 (5)	0.0190 (5)	−0.0041 (4)	0.0029 (4)	0.0012 (4)
N1	0.0141 (4)	0.0134 (4)	0.0139 (4)	0.0001 (3)	0.0019 (3)	0.0001 (3)

Geometric parameters (Å, °)

	1.3683 (16)	C10—C12	1.5443 (14)
C1—C6	1.4141 (16)	C11—C12	1.4985 (15)

C1—H1	0.95	C11—H11A	0.99
C2—C3	1.4187 (15)	C11—H11B	0.99
C2—H2	0.95	C12—C14	1.4921 (13)
C3—C7	1.4149 (15)	C12—H12	1.0
C3—C4	1.4213 (14)	C13—H13C	0.98
C4—N1	1.3679 (13)	C13—H13B	0.98
C4—C5	1.4198 (14)	C13—H13A	0.98
C5—C6	1.3746 (15)	C14—C15	1.3933 (14)
C5—H5	0.95	C14—C19	1.3948 (15)
C6—H6	0.95	C15—C16	1.3998 (15)
C7—C8	1.3655 (15)	C15—H15	0.95
C7—H7	0.95	C16—C17	1.3862 (17)
C8—C9	1.4225 (14)	C16—H16	0.95
C8—H8	0.95	C17—C18	1.3904 (16)
C9—N1	1.3252 (13)	C17—H17	0.95
C9—C10	1.4962 (14)	C18—C19	1.3910 (15)
C10—C13	1.5095 (14)	C18—H18	0.95
C10—C11	1.5146 (14)	C19—H19	0.95
C2—C1—C6	120.32 (10)	C10—C11—H11A	117.6
C2—C1—H1	119.8	C12—C11—H11B	117.6
C6—C1—H1	119.8	C10—C11—H11B	117.6
C1—C2—C3	120.40 (10)	H11A—C11—H11B	114.7
C1—C2—H2	119.8	C14—C12—C11	125.33 (9)
C3—C2—H2	119.8	C14—C12—C10	122.57 (9)
C7—C3—C2	123.27 (10)	C11—C12—C10	59.68 (7)
C7—C3—C4	117.26 (9)	C14—C12—H12	113.0
C2—C3—C4	119.46 (10)	C11—C12—H12	113.0
N1—C4—C5	118.51 (9)	C10—C12—H12	113.0

N1—C4—C3	122.56 (9)	C10—C13—H13C	109.5
C5—C4—C3	118.89 (9)	C10—C13—H13B	109.5
C6—C5—C4	120.27 (10)	H13C—C13—H13B	109.5
C6—C5—H5	119.9	C10—C13—H13A	109.5
C4—C5—H5	119.9	H13C—C13—H13A	109.5
C5—C6—C1	120.63 (10)	H13B—C13—H13A	109.5
C5—C6—H6	119.7	C15—C14—C19	118.20 (10)
C1—C6—H6	119.7	C15—C14—C12	123.78 (10)
C8—C7—C3	119.53 (10)	C19—C14—C12	117.95 (9)
C8—C7—H7	120.2	C14—C15—C16	120.64 (10)
C3—C7—H7	120.2	C14—C15—H15	119.7
C7—C8—C9	119.69 (10)	C16—C15—H15	119.7
C7—C8—H8	120.2	C17—C16—C15	120.45 (10)
C9—C8—H8	120.2	C17—C16—H16	119.8
N1—C9—C8	122.29 (9)	C15—C16—H16	119.8
N1—C9—C10	117.28 (9)	C16—C17—C18	119.33 (10)
C8—C9—C10	120.38 (9)	C16—C17—H17	120.3
C9—C10—C13	117.76 (9)	C18—C17—H17	120.3
C9—C10—C11	117.55 (9)	C17—C18—C19	120.04 (11)
C13—C10—C11	117.16 (9)	C17—C18—H18	120.0
C9—C10—C12	114.07 (9)	C19—C18—H18	120.0
C13—C10—C12	118.30 (8)	C18—C19—C14	121.33 (10)
C11—C10—C12	58.66 (7)	C18—C19—H19	119.3
C12—C11—C10	61.66 (7)	C14—C19—H19	119.3
C12—C11—H11A	117.6	C9—N1—C4	118.61 (9)
C6—C1—C2—C3	−1.03 (17)	C13—C10—C11—C12	108.15 (10)
C1—C2—C3—C7	−179.16 (10)	C10—C11—C12—C14	−110.48 (11)
C1—C2—C3—C4	0.10 (16)	C9—C10—C12—C14	−136.35 (10)

C7—C3—C4—N1	2.35 (15)	C13—C10—C12—C14	8.72 (15)
C2—C3—C4—N1	−176.95 (9)	C11—C10—C12—C14	114.92 (11)
C7—C3—C4—C5	−179.70 (9)	C9—C10—C12—C11	108.73 (10)
C2—C3—C4—C5	1.00 (15)	C13—C10—C12—C11	−106.20 (11)
N1—C4—C5—C6	176.85 (10)	C11—C12—C14—C15	−15.52 (16)
C3—C4—C5—C6	−1.19 (15)	C10—C12—C14—C15	−89.18 (13)
C4—C5—C6—C1	0.27 (16)	C11—C12—C14—C19	167.65 (10)
C2—C1—C6—C5	0.85 (17)	C10—C12—C14—C19	94.00 (12)
C2—C3—C7—C8	177.77 (10)	C19—C14—C15—C16	0.49 (15)
C4—C3—C7—C8	−1.49 (15)	C12—C14—C15—C16	−176.32 (10)
C3—C7—C8—C9	−0.71 (16)	C14—C15—C16—C17	−0.01 (17)
C7—C8—C9—N1	2.36 (16)	C15—C16—C17—C18	−0.27 (17)
C7—C8—C9—C10	−175.07 (10)	C16—C17—C18—C19	0.06 (17)
N1—C9—C10—C13	178.81 (9)	C17—C18—C19—C14	0.45 (17)
C8—C9—C10—C13	−3.63 (14)	C15—C14—C19—C18	−0.71 (16)
N1—C9—C10—C11	29.90 (13)	C12—C14—C19—C18	176.29 (10)
C8—C9—C10—C11	−152.54 (10)	C8—C9—N1—C4	−1.56 (15)
N1—C9—C10—C12	−35.92 (13)	C10—C9—N1—C4	175.95 (9)
C8—C9—C10—C12	141.63 (10)	C5—C4—N1—C9	−178.78 (9)
C9—C10—C11—C12	−102.76 (10)	C3—C4—N1—C9	−0.83 (15)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2012.6.0.0; cell refinement: *SAINT* V8.18C (Bruker AXS Inc., 2011); data reduction:

SAINT V8.18C (Bruker AXS Inc., 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008);

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)quinoline 67b

Crystal data

$C_{25}H_{21}N$	
M_r = 335.43	D_x = 1.234 Mg m^{-3}
Monoclinic, $P2_1$	Melting point: ? K
Hall symbol: ?	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 6.0245 (6) Å	Cell parameters from 1129 reflections
b = 17.4083 (14) Å	θ = 2.6–24.2°
c = 8.6107 (6) Å	μ = 0.07 mm^{-1}
β = 91.372 (1)°	T = 100 K
V = 902.80 (13) Å^3	Shard, colourless
Z = 2	0.25 × 0.11 × 0.04 mm
F(000) = 356	

Data collection

Bruker APEX-II CCD diffractometer	3851 independent reflections
Radiation source: sealed tube	2834 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.037
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 27.1°, θ_{min} = 2.3°
φ and ω scans	h = −7→7
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	k = −22→21
T_{min} = 0.98, T_{max} = 1.00	l = −11→11
6882 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.048$	$w = 1/[\sigma^2(F_o^2) + (0.0386P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.095$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.00$	$\Delta\rho_{max} = 0.17$ e Å^{-3}
3851 reflections	$\Delta\rho_{min} = -0.21$ e Å^{-3}
235 parameters	Extinction correction: none
1 restraint	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0 (4)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.8303 (4)	0.41712 (13)	0.5904 (2)	0.0175 (5)
C2	0.6323 (4)	0.37735 (13)	0.5493 (2)	0.0187 (5)
H12	0.5195	0.4022	0.4888	0.022*
C3	0.6041 (4)	0.30348 (13)	0.5967 (2)	0.0205 (5)
H3	0.4727	0.2762	0.5683	0.025*
C4	0.7718 (4)	0.26764 (14)	0.6884 (2)	0.0178 (5)

C5	0.9661 (4)	0.31040 (13)	0.7226 (2)	0.0183 (5)
C6	1.1374 (4)	0.27692 (14)	0.8149 (2)	0.0215 (5)
H6	1.2683	0.3053	0.8393	0.026*
C7	1.1142 (4)	0.20336 (15)	0.8693 (2)	0.0260 (6)
H7	1.2308	0.1808	0.9298	0.031*
C8	0.9191 (4)	0.16076 (14)	0.8364 (3)	0.0272 (6)
H8	0.9043	0.1102	0.8761	0.033*
C9	0.7522 (4)	0.19218 (15)	0.7477 (2)	0.0237 (5)
H9	0.6216	0.1632	0.7255	0.028*
C10	0.8587 (4)	0.50043 (13)	0.5499 (2)	0.0168 (5)
C11	0.9236 (4)	0.55186 (13)	0.6893 (3)	0.0196 (5)
H11	0.949	0.523	0.7887	0.024*
C12	1.0893 (4)	0.53421 (13)	0.5676 (3)	0.0225 (5)
H12A	1.2124	0.4988	0.5958	0.027*
H12B	1.1297	0.5762	0.4959	0.027*
C13	0.8185 (4)	0.62885 (13)	0.7098 (2)	0.0200 (5)
C14	0.6111 (4)	0.63422 (15)	0.7754 (3)	0.0258 (6)
H14	0.5344	0.5887	0.8027	0.031*
C15	0.5133 (4)	0.70558 (16)	0.8020 (3)	0.0313 (6)
H15	0.3711	0.7085	0.847	0.038*
C16	0.6241 (5)	0.77191 (16)	0.7624 (3)	0.0334 (7)
H16	0.5591	0.8206	0.7812	0.04*
C17	0.8293 (5)	0.76725 (16)	0.6956 (3)	0.0337 (7)
H17	0.9049	0.813	0.6681	0.04*
C18	0.9266 (4)	0.69648 (15)	0.6682 (3)	0.0272 (6)
H18	1.0673	0.694	0.6209	0.033*
C19	0.7016 (4)	0.53540 (13)	0.4303 (2)	0.0196 (5)
H19A	0.7478	0.5892	0.4125	0.024*

H19B	0.5513	0.5368	0.4742	0.024*
C20	0.6864 (4)	0.49502 (13)	0.2744 (2)	0.0177 (5)
C21	0.8622 (4)	0.45459 (14)	0.2133 (2)	0.0216 (5)
H21	0.9988	0.4518	0.2704	0.026*
C22	0.8424 (4)	0.41806 (14)	0.0703 (3)	0.0255 (6)
H22	0.964	0.3899	0.0313	0.031*
C23	0.6457 (4)	0.42266 (14)	−0.0153 (3)	0.0233 (6)
H23	0.6328	0.3982	−0.1137	0.028*
C24	0.4674 (4)	0.46299 (14)	0.0425 (2)	0.0225 (6)
H24	0.332	0.4664	−0.0159	0.027*
C25	0.4886 (4)	0.49831 (14)	0.1866 (2)	0.0207 (5)
H25	0.3656	0.5254	0.2266	0.025*
N1	0.9938 (3)	0.38487 (11)	0.6727 (2)	0.0180 (4)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0208 (13)	0.0184 (12)	0.0134 (10)	0.0009 (11)	0.0030 (9)	−0.0017 (10)
C2	0.0193 (13)	0.0208 (13)	0.0161 (11)	0.0015 (11)	0.0007 (9)	−0.0005 (10)
C3	0.0222 (13)	0.0204 (14)	0.0190 (12)	−0.0033 (11)	0.0011 (10)	−0.0036 (10)
C4	0.0228 (13)	0.0151 (12)	0.0155 (10)	−0.0016 (11)	0.0010 (9)	−0.0043 (10)
C5	0.0240 (13)	0.0161 (13)	0.0150 (11)	0.0035 (10)	0.0042 (10)	−0.0035 (10)
C6	0.0200 (12)	0.0209 (14)	0.0235 (12)	−0.0002 (11)	−0.0002 (10)	−0.0035 (10)
C7	0.0299 (14)	0.0239 (14)	0.0238 (12)	0.0051 (13)	−0.0055 (10)	0.0016 (11)
C8	0.0390 (17)	0.0167 (14)	0.0257 (13)	−0.0019 (12)	−0.0023 (12)	0.0015 (11)
C9	0.0282 (14)	0.0166 (13)	0.0262 (12)	−0.0052 (12)	−0.0010 (10)	−0.0014 (10)
C10	0.0192 (12)	0.0143 (12)	0.0167 (11)	−0.0011 (11)	−0.0003 (9)	−0.0003 (10)
C11	0.0194 (13)	0.0186 (13)	0.0207 (11)	0.0002 (11)	−0.0015 (9)	0.0003 (10)
C12	0.0208 (12)	0.0190 (13)	0.0279 (13)	−0.0011 (11)	0.0030 (10)	0.0035 (11)

C13	0.0276 (14)	0.0154 (12)	0.0167 (11)	−0.0018 (11)	−0.0050 (10)	−0.0033 (10)
C14	0.0301 (15)	0.0250 (15)	0.0222 (12)	−0.0023 (12)	−0.0019 (11)	−0.0024 (10)
C15	0.0376 (16)	0.0326 (17)	0.0236 (12)	0.0107 (14)	−0.0038 (11)	−0.0066 (13)
C16	0.057 (2)	0.0235 (16)	0.0188 (13)	0.0144 (15)	−0.0143 (13)	−0.0040 (11)
C17	0.057 (2)	0.0184 (14)	0.0256 (13)	−0.0060 (14)	−0.0080 (13)	−0.0012 (11)
C18	0.0354 (15)	0.0215 (14)	0.0245 (12)	−0.0052 (13)	−0.0003 (11)	−0.0026 (12)
C19	0.0228 (13)	0.0169 (13)	0.0192 (11)	0.0008 (11)	0.0028 (10)	−0.0019 (10)
C20	0.0222 (12)	0.0135 (12)	0.0174 (11)	−0.0016 (11)	0.0025 (9)	0.0015 (9)
C21	0.0211 (13)	0.0213 (13)	0.0224 (12)	−0.0026 (11)	0.0018 (10)	0.0000 (10)
C22	0.0282 (14)	0.0240 (14)	0.0247 (12)	0.0008 (12)	0.0068 (11)	−0.0044 (11)
C23	0.0325 (15)	0.0208 (14)	0.0169 (11)	−0.0059 (12)	0.0042 (11)	−0.0013 (10)
C24	0.0255 (14)	0.0208 (13)	0.0210 (12)	−0.0023 (11)	−0.0035 (10)	0.0036 (10)
C25	0.0214 (13)	0.0156 (13)	0.0253 (12)	0.0018 (11)	0.0038 (10)	−0.0003 (11)
N1	0.0210 (11)	0.0169 (11)	0.0162 (9)	0.0012 (9)	0.0011 (8)	−0.0018 (8)

Geometric parameters (Å, °)

C1—N1	1.324 (3)	C13—C14	1.387 (3)
C1—C2	1.417 (3)	C13—C18	1.396 (3)
C1—C10	1.502 (3)	C14—C15	1.396 (4)
C2—C3	1.361 (3)	C14—H14	0.95
C2—H12	0.95	C15—C16	1.381 (4)
C3—C4	1.412 (3)	C15—H15	0.95
C3—H3	0.95	C16—C17	1.378 (4)
C4—C5	1.412 (3)	C16—H16	0.95
C4—C9	1.415 (3)	C17—C18	1.387 (4)
C5—N1	1.377 (3)	C17—H17	0.95
C5—C6	1.413 (3)	C18—H18	0.95
C6—C7	1.372 (3)	C19—C20	1.516 (3)
C6—H6	0.95	C19—H19A	0.99

C7—C8	1.412 (3)	C19—H19B	0.99
C7—H7	0.95	C20—C21	1.385 (3)
C8—C9	1.363 (3)	C20—C25	1.396 (3)
C8—H8	0.95	C21—C22	1.388 (3)
C9—H9	0.95	C21—H21	0.95
C10—C19	1.511 (3)	C22—C23	1.383 (3)
C10—C12	1.513 (3)	C22—H22	0.95
C10—C11	1.540 (3)	C23—C24	1.386 (3)
C11—C13	1.495 (3)	C23—H23	0.95
C11—C12	1.497 (3)	C24—C25	1.388 (3)
C11—H11	1.0	C24—H24	0.95
C12—H12A	0.99	C25—H25	0.95
C12—H12B	0.99		
N1—C1—C2	122.5 (2)	H12A—C12—H12B	114.7
N1—C1—C10	116.5 (2)	C14—C13—C18	118.6 (2)
C2—C1—C10	120.9 (2)	C14—C13—C11	119.8 (2)
C3—C2—C1	119.8 (2)	C18—C13—C11	121.6 (2)
C3—C2—H12	120.1	C13—C14—C15	121.0 (2)
C1—C2—H12	120.1	C13—C14—H14	119.5
C2—C3—C4	119.5 (2)	C15—C14—H14	119.5
C2—C3—H3	120.3	C16—C15—C14	119.7 (2)
C4—C3—H3	120.3	C16—C15—H15	120.2
C3—C4—C5	117.5 (2)	C14—C15—H15	120.2
C3—C4—C9	123.2 (2)	C17—C16—C15	119.8 (3)
C5—C4—C9	119.3 (2)	C17—C16—H16	120.1
N1—C5—C4	122.5 (2)	C15—C16—H16	120.1
N1—C5—C6	118.1 (2)	C16—C17—C18	120.7 (3)
C4—C5—C6	119.4 (2)	C16—C17—H17	119.7

C7—C6—C5	119.8 (2)	C18—C17—H17	119.7
C7—C6—H6	120.1	C17—C18—C13	120.2 (2)
C5—C6—H6	120.1	C17—C18—H18	119.9
C6—C7—C8	120.9 (2)	C13—C18—H18	119.9
C6—C7—H7	119.6	C10—C19—C20	116.16 (19)
C8—C7—H7	119.6	C10—C19—H19A	108.2
C9—C8—C7	120.1 (2)	C20—C19—H19A	108.2
C9—C8—H8	120.0	C10—C19—H19B	108.2
C7—C8—H8	120.0	C20—C19—H19B	108.2
C8—C9—C4	120.5 (2)	H19A—C19—H19B	107.4
C8—C9—H9	119.7	C21—C20—C25	117.75 (19)
C4—C9—H9	119.7	C21—C20—C19	122.7 (2)
C1—C10—C19	118.33 (19)	C25—C20—C19	119.5 (2)
C1—C10—C12	117.5 (2)	C20—C21—C22	121.3 (2)
C19—C10—C12	118.07 (19)	C20—C21—H21	119.4
C1—C10—C11	114.10 (17)	C22—C21—H21	119.4
C19—C10—C11	116.15 (19)	C23—C22—C21	120.1 (2)
C12—C10—C11	58.70 (14)	C23—C22—H22	120.0
C13—C11—C12	123.9 (2)	C21—C22—H22	120.0
C13—C11—C10	120.83 (19)	C22—C23—C24	120.0 (2)
C12—C11—C10	59.72 (14)	C22—C23—H23	120.0
C13—C11—H11	113.9	C24—C23—H23	120.0
C12—C11—H11	113.9	C23—C24—C25	119.3 (2)
C10—C11—H11	113.9	C23—C24—H24	120.3
C11—C12—C10	61.58 (15)	C25—C24—H24	120.3
C11—C12—H12A	117.6	C24—C25—C20	121.6 (2)
C10—C12—H12A	117.6	C24—C25—H25	119.2
C11—C12—H12B	117.6	C20—C25—H25	119.2

C10—C12—H12B	117.6	C1—N1—C5	118.1 (2)
N1—C1—C2—C3	1.0 (3)	C12—C11—C13—C14	153.5 (2)
C10—C1—C2—C3	−175.4 (2)	C10—C11—C13—C14	81.3 (3)
C1—C2—C3—C4	0.9 (3)	C12—C11—C13—C18	−28.3 (3)
C2—C3—C4—C5	−1.9 (3)	C10—C11—C13—C18	−100.4 (3)
C2—C3—C4—C9	177.4 (2)	C18—C13—C14—C15	−1.1 (3)
C3—C4—C5—N1	1.2 (3)	C11—C13—C14—C15	177.2 (2)
C9—C4—C5—N1	−178.1 (2)	C13—C14—C15—C16	0.0 (3)
C3—C4—C5—C6	179.6 (2)	C14—C15—C16—C17	0.6 (3)
C9—C4—C5—C6	0.2 (3)	C15—C16—C17—C18	−0.3 (4)
N1—C5—C6—C7	178.8 (2)	C16—C17—C18—C13	−0.8 (4)
C4—C5—C6—C7	0.5 (3)	C14—C13—C18—C17	1.4 (3)
C5—C6—C7—C8	−1.1 (3)	C11—C13—C18—C17	−176.8 (2)
C6—C7—C8—C9	1.0 (4)	C1—C10—C19—C20	−54.7 (3)
C7—C8—C9—C4	−0.3 (3)	C12—C10—C19—C20	97.1 (2)
C3—C4—C9—C8	−179.6 (2)	C11—C10—C19—C20	163.87 (19)
C5—C4—C9—C8	−0.3 (3)	C10—C19—C20—C21	−29.6 (3)
N1—C1—C10—C19	167.75 (19)	C10—C19—C20—C25	150.7 (2)
C2—C1—C10—C19	−15.7 (3)	C25—C20—C21—C22	−0.5 (3)
N1—C1—C10—C12	15.8 (3)	C19—C20—C21—C22	179.8 (2)
C2—C1—C10—C12	−167.65 (19)	C20—C21—C22—C23	1.1 (4)
N1—C1—C10—C11	−50.1 (3)	C21—C22—C23—C24	−0.8 (4)
C2—C1—C10—C11	126.5 (2)	C22—C23—C24—C25	−0.1 (3)
C1—C10—C11—C13	−137.5 (2)	C23—C24—C25—C20	0.8 (3)
C19—C10—C11—C13	5.5 (3)	C21—C20—C25—C24	−0.5 (3)
C12—C10—C11—C13	113.8 (2)	C19—C20—C25—C24	179.3 (2)
C1—C10—C11—C12	108.6 (2)	C2—C1—N1—C5	−1.6 (3)
C19—C10—C11—C12	−108.4 (2)	C10—C1—N1—C5	174.89 (18)

C13—C11—C12—C10	−108.8 (2)	C4—C5—N1—C1	0.5 (3)
C1—C10—C12—C11	−102.9 (2)	C6—C5—N1—C1	−177.82 (19)
C19—C10—C12—C11	105.1 (2)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

2-((1*R**,2*S**)-1-Benzyl-2-((benzyloxy)methyl)cyclopropyl)quinoline 67e

Crystal data

$C_{27}H_{25}NO$	$F(000) = 404$
$M_r = 379.48$	
Triclinic, $P\bar{1}$	$D_x = 1.268$ Mg m^{-3}
Hall symbol: ?	Melting point: 61-70 °C
$a = 5.1897$ (4) Å	? radiation, $\lambda = 0.71073$ Å
$b = 14.1552$ (11) Å	Cell parameters from 8676 reflections
$c = 14.8377$ (12) Å	$\theta = 2.5–28.4°$
$\alpha = 68.757$ (2)°	$\mu = 0.08$ mm^{-1}
$\beta = 80.782$ (2)°	$T = 100$ K
$\gamma = 79.656$ (2)°	Block, lustrous colourless
$V = 994.03$ (14) Å^3	0.32 × 0.20 × 0.07 mm
$Z = 2$	

Data collection

diffractometer	4839 independent reflections
Radiation source: ?	4201 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.018$
Detector resolution: 8.3333 pixels mm^{-1}	$\theta_{max} = 28.4°$, $\theta_{min} = 1.5°$
	$h = -6 \rightarrow 6$
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	$k = -18 \rightarrow 18$
$T_{min} = 0.89$, $T_{max} = 0.99$	$l = -19 \rightarrow 19$
16811 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map

Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.040$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.112$	$w = 1/[\sigma^2(F_o^2) + (0.061P)^2 + 0.3768P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.00$	$(\Delta/\sigma)_{max} < 0.001$
4839 reflections	$\Delta\rho_{max} = 0.37$ e Å^{-3}
262 parameters	$\Delta\rho_{min} = -0.20$ e Å^{-3}
0 restraints	Extinction correction: none
constraints	Extinction coefficient: ?
Primary atom site location: structure-invariant direct methods	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.02762 (14)	0.21749 (5)	0.37607 (5)	0.01709 (16)
N1	0.22595 (17)	−0.09257 (6)	0.31423 (6)	0.01517 (18)
C1	0.5177 (2)	0.51988 (9)	0.27776 (9)	0.0265 (3)
H1	0.6346	0.5697	0.2478	0.032*
C2	0.4787 (2)	0.45575 (9)	0.23047 (9)	0.0254 (2)
H25	0.5713	0.4611	0.1685	0.03*
C3	0.3044 (2)	0.38357 (8)	0.27343 (8)	0.0204 (2)
H3	0.2783	0.3402	0.2404	0.025*

C4	0.1678 (2)	0.37457 (8)	0.36479 (8)	0.0174 (2)
C5	−0.0320 (2)	0.30093 (8)	0.41096 (8)	0.0182 (2)
H21	−0.031	0.2752	0.4825	0.022*
H22	−0.2102	0.3367	0.3954	0.022*
C6	−0.17960 (19)	0.15431 (8)	0.40763 (7)	0.0156 (2)
H4	−0.3373	0.1909	0.3739	0.019*
H5	−0.2283	0.137	0.4785	0.019*
C7	−0.08130 (19)	0.05862 (7)	0.38404 (7)	0.01393 (19)
H6	0.1021	0.0291	0.4007	0.017*
C8	−0.15295 (19)	0.03605 (7)	0.29801 (7)	0.01374 (19)
C9	0.06402 (19)	−0.02467 (7)	0.25397 (7)	0.01424 (19)
C10	0.43280 (19)	−0.14764 (8)	0.27761 (7)	0.0154 (2)
C11	0.4820 (2)	−0.13497 (8)	0.17702 (8)	0.0167 (2)
C12	0.7077 (2)	−0.19208 (8)	0.14414 (8)	0.0203 (2)
H9	0.7422	−0.1842	0.0771	0.024*
C13	0.8756 (2)	−0.25839 (9)	0.20860 (9)	0.0220 (2)
H2	1.0276	−0.2953	0.1859	0.026*
C14	0.8238 (2)	−0.27215 (8)	0.30881 (9)	0.0214 (2)
H7	0.9405	−0.3188	0.353	0.026*
C15	0.6069 (2)	−0.21883 (8)	0.34298 (8)	0.0188 (2)
H8	0.573	−0.2296	0.4106	0.023*
C16	0.3000 (2)	−0.06448 (8)	0.11517 (8)	0.0183 (2)
H10	0.3208	−0.0552	0.0478	0.022*
C17	0.0936 (2)	−0.00959 (8)	0.15253 (7)	0.0170 (2)
H11	−0.0285	0.038	0.1113	0.02*
C18	−0.25720 (19)	−0.02078 (8)	0.40245 (7)	0.0156 (2)
H12	−0.4461	−0.0042	0.4227	0.019*
H13	−0.1836	−0.0933	0.4323	0.019*

C19	−0.36041 (19)	0.10687 (8)	0.23420 (7)	0.0161 (2)
H14	−0.4984	0.1339	0.2763	0.019*
H20	−0.4439	0.0649	0.2093	0.019*
C20	−0.27604 (19)	0.19749 (8)	0.14769 (7)	0.0157 (2)
C21	−0.0876 (2)	0.25499 (8)	0.15036 (8)	0.0203 (2)
H19	0.0007	0.2358	0.207	0.024*
C22	−0.0277 (2)	0.34081 (9)	0.07020 (8)	0.0229 (2)
H18	0.1011	0.3794	0.0728	0.028*
C23	−0.1547 (2)	0.37004 (9)	−0.01315 (8)	0.0231 (2)
H17	−0.1141	0.4286	−0.0673	0.028*
C24	−0.3418 (2)	0.31281 (9)	−0.01661 (8)	0.0247 (2)
H16	−0.4296	0.3321	−0.0733	0.03*
C25	−0.4004 (2)	0.22716 (9)	0.06318 (8)	0.0206 (2)
H15	−0.5276	0.1882	0.06	0.025*
C26	0.2123 (2)	0.43828 (8)	0.41200 (8)	0.0222 (2)
H23	0.1231	0.4321	0.4746	0.027*
C27	0.3851 (2)	0.51085 (9)	0.36901 (10)	0.0259 (2)
H24	0.4123	0.554	0.402	0.031*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0169 (3)	0.0153 (3)	0.0205 (4)	−0.0030 (3)	0.0026 (3)	−0.0093 (3)
N1	0.0141 (4)	0.0146 (4)	0.0170 (4)	−0.0026 (3)	0.0003 (3)	−0.0062 (3)
C1	0.0258 (6)	0.0165 (5)	0.0341 (6)	−0.0053 (4)	−0.0073 (5)	−0.0022 (5)
C2	0.0268 (6)	0.0224 (6)	0.0231 (5)	−0.0049 (4)	−0.0019 (4)	−0.0029 (4)
C3	0.0235 (5)	0.0184 (5)	0.0198 (5)	−0.0028 (4)	−0.0039 (4)	−0.0062 (4)
C4	0.0179 (5)	0.0129 (4)	0.0203 (5)	0.0020 (4)	−0.0047 (4)	−0.0051 (4)
C5	0.0189 (5)	0.0161 (5)	0.0207 (5)	0.0000 (4)	0.0001 (4)	−0.0094 (4)

C6	0.0140 (4)	0.0162 (5)	0.0167 (4)	−0.0021 (4)	0.0005 (4)	−0.0065 (4)
C7	0.0126 (4)	0.0150 (4)	0.0138 (4)	−0.0015 (3)	−0.0008 (3)	−0.0048 (4)
C8	0.0129 (4)	0.0144 (4)	0.0131 (4)	−0.0027 (3)	−0.0002 (3)	−0.0039 (4)
C9	0.0136 (4)	0.0142 (4)	0.0157 (4)	−0.0051 (3)	0.0007 (3)	−0.0055 (4)
C10	0.0141 (4)	0.0144 (5)	0.0195 (5)	−0.0036 (3)	0.0006 (4)	−0.0080 (4)
C11	0.0162 (5)	0.0169 (5)	0.0198 (5)	−0.0056 (4)	0.0017 (4)	−0.0096 (4)
C12	0.0192 (5)	0.0212 (5)	0.0231 (5)	−0.0052 (4)	0.0042 (4)	−0.0122 (4)
C13	0.0175 (5)	0.0202 (5)	0.0313 (6)	−0.0026 (4)	0.0035 (4)	−0.0149 (4)
C14	0.0190 (5)	0.0174 (5)	0.0286 (6)	0.0002 (4)	−0.0037 (4)	−0.0096 (4)
C15	0.0193 (5)	0.0171 (5)	0.0211 (5)	−0.0021 (4)	−0.0013 (4)	−0.0083 (4)
C16	0.0201 (5)	0.0208 (5)	0.0161 (5)	−0.0064 (4)	0.0013 (4)	−0.0083 (4)
C17	0.0179 (5)	0.0175 (5)	0.0160 (5)	−0.0039 (4)	−0.0016 (4)	−0.0057 (4)
C18	0.0140 (4)	0.0172 (5)	0.0140 (4)	−0.0035 (4)	0.0007 (3)	−0.0037 (4)
C19	0.0130 (4)	0.0185 (5)	0.0157 (4)	−0.0021 (4)	−0.0015 (3)	−0.0045 (4)
C20	0.0141 (4)	0.0159 (5)	0.0155 (4)	0.0009 (3)	0.0002 (4)	−0.0055 (4)
C21	0.0215 (5)	0.0217 (5)	0.0169 (5)	−0.0041 (4)	−0.0033 (4)	−0.0046 (4)
C22	0.0250 (5)	0.0205 (5)	0.0228 (5)	−0.0064 (4)	0.0007 (4)	−0.0067 (4)
C23	0.0271 (6)	0.0186 (5)	0.0178 (5)	−0.0012 (4)	0.0020 (4)	−0.0022 (4)
C24	0.0260 (6)	0.0272 (6)	0.0166 (5)	−0.0003 (4)	−0.0044 (4)	−0.0029 (4)
C25	0.0192 (5)	0.0229 (5)	0.0187 (5)	−0.0025 (4)	−0.0031 (4)	−0.0057 (4)
C26	0.0239 (5)	0.0184 (5)	0.0261 (5)	0.0019 (4)	−0.0036 (4)	−0.0114 (4)
C27	0.0278 (6)	0.0164 (5)	0.0373 (6)	0.0005 (4)	−0.0101 (5)	−0.0124 (5)

Geometric parameters (Å, °)

O1—C5	1.4211 (12)	C12—C13	1.3703 (16)
O1—C6	1.4339 (12)	C12—H9	0.95
N1—C9	1.3257 (13)	C13—C14	1.4150 (16)
N1—C10	1.3692 (13)	C13—H2	0.95
C1—C27	1.3895 (18)	C14—C15	1.3723 (15)

C1—C2	1.3896 (18)	C14—H7	0.95
C1—H1	0.95	C15—H8	0.95
C2—C3	1.3942 (16)	C16—C17	1.3715 (14)
C2—H25	0.95	C16—H10	0.95
C3—C4	1.3986 (15)	C17—H11	0.95
C3—H3	0.95	C18—H12	0.99
C4—C26	1.3935 (15)	C18—H13	0.99
C4—C5	1.5081 (15)	C19—C20	1.5210 (14)
C5—H21	0.99	C19—H14	0.99
C5—H22	0.99	C19—H20	0.99
C6—C7	1.5020 (14)	C20—C21	1.3935 (15)
C6—H4	0.99	C20—C25	1.3948 (15)
C6—H5	0.99	C21—C22	1.3989 (15)
C7—C18	1.4957 (14)	C21—H19	0.95
C7—C8	1.5362 (14)	C22—C23	1.3884 (16)
C7—H6	1.0	C22—H18	0.95
C8—C9	1.5025 (13)	C23—C24	1.3891 (17)
C8—C19	1.5204 (13)	C23—H17	0.95
C8—C18	1.5251 (13)	C24—C25	1.3932 (15)
C9—C17	1.4281 (14)	C24—H16	0.95
C10—C15	1.4204 (14)	C25—H15	0.95
C10—C11	1.4232 (14)	C26—C27	1.3927 (17)
C11—C16	1.4162 (15)	C26—H23	0.95
C11—C12	1.4237 (14)	C27—H24	0.95
C5—O1—C6	111.27 (7)	C12—C13—H2	119.8
C9—N1—C10	119.00 (9)	C14—C13—H2	119.8
C27—C1—C2	119.73 (11)	C15—C14—C13	120.78 (10)
C27—C1—H1	120.1	C15—C14—H7	119.6

C2—C1—H1	120.1	C13—C14—H7	119.6
C1—C2—C3	120.36 (11)	C14—C15—C10	120.22 (10)
C1—C2—H25	119.8	C14—C15—H8	119.9
C3—C2—H25	119.8	C10—C15—H8	119.9
C2—C3—C4	120.38 (11)	C17—C16—C11	119.97 (10)
C2—C3—H3	119.8	C17—C16—H10	120.0
C4—C3—H3	119.8	C11—C16—H10	120.0
C26—C4—C3	118.58 (10)	C16—C17—C9	119.40 (10)
C26—C4—C5	119.74 (10)	C16—C17—H11	120.3
C3—C4—C5	121.64 (10)	C9—C17—H11	120.3
O1—C5—C4	110.20 (8)	C7—C18—C8	61.13 (6)
O1—C5—H21	109.6	C7—C18—H12	117.7
C4—C5—H21	109.6	C8—C18—H12	117.7
O1—C5—H22	109.6	C7—C18—H13	117.7
C4—C5—H22	109.6	C8—C18—H13	117.7
H21—C5—H22	108.1	H12—C18—H13	114.8
O1—C6—C7	107.86 (8)	C8—C19—C20	118.67 (8)
O1—C6—H4	110.1	C8—C19—H14	107.6
C7—C6—H4	110.1	C20—C19—H14	107.6
O1—C6—H5	110.1	C8—C19—H20	107.6
C7—C6—H5	110.1	C20—C19—H20	107.6
H4—C6—H5	108.4	H14—C19—H20	107.1
C18—C7—C6	121.15 (8)	C21—C20—C25	118.38 (10)
C18—C7—C8	60.38 (6)	C21—C20—C19	122.92 (9)
C6—C7—C8	125.34 (9)	C25—C20—C19	118.64 (9)
C18—C7—H6	113.3	C20—C21—C22	120.40 (10)
C6—C7—H6	113.3	C20—C21—H19	119.8
C8—C7—H6	113.3	C22—C21—H19	119.8

C9—C8—C19	118.41 (8)	C23—C22—C21	120.63 (11)
C9—C8—C18	114.93 (8)	C23—C22—H18	119.7
C19—C8—C18	114.98 (8)	C21—C22—H18	119.7
C9—C8—C7	114.71 (8)	C24—C23—C22	119.33 (10)
C19—C8—C7	121.08 (8)	C24—C23—H17	120.3
C18—C8—C7	58.50 (6)	C22—C23—H17	120.3
N1—C9—C17	122.01 (9)	C23—C24—C25	119.94 (10)
N1—C9—C8	116.43 (9)	C23—C24—H16	120.0
C17—C9—C8	121.56 (9)	C25—C24—H16	120.0
N1—C10—C15	118.24 (9)	C24—C25—C20	121.32 (11)
N1—C10—C11	122.65 (9)	C24—C25—H15	119.3
C15—C10—C11	119.10 (9)	C20—C25—H15	119.3
C16—C11—C10	116.90 (9)	C27—C26—C4	121.15 (11)
C16—C11—C12	123.90 (10)	C27—C26—H23	119.4
C10—C11—C12	119.20 (10)	C4—C26—H23	119.4
C13—C12—C11	120.37 (10)	C1—C27—C26	119.79 (11)
C13—C12—H9	119.8	C1—C27—H24	120.1
C11—C12—H9	119.8	C26—C27—H24	120.1
C12—C13—C14	120.31 (10)		
C27—C1—C2—C3	0.98 (18)	C11—C12—C13—C14	1.13 (16)
C1—C2—C3—C4	−0.30 (17)	C12—C13—C14—C15	−0.65 (16)
C2—C3—C4—C26	−0.74 (16)	C13—C14—C15—C10	−0.94 (16)
C2—C3—C4—C5	176.91 (10)	N1—C10—C15—C14	−176.92 (9)
C6—O1—C5—C4	−171.51 (8)	C11—C10—C15—C14	2.00 (15)
C26—C4—C5—O1	−155.60 (9)	C10—C11—C16—C17	2.30 (15)
C3—C4—C5—O1	26.77 (14)	C12—C11—C16—C17	−177.31 (10)
C5—O1—C6—C7	−169.65 (8)	C11—C16—C17—C9	−0.31 (15)
O1—C6—C7—C18	−176.26 (8)	N1—C9—C17—C16	−2.02 (15)

O1—C6—C7—C8	−102.48 (10)	C8—C9—C17—C16	177.86 (9)
C18—C7—C8—C9	−105.20 (9)	C6—C7—C18—C8	115.71 (10)
C6—C7—C8—C9	145.76 (9)	C9—C8—C18—C7	104.82 (9)
C18—C7—C8—C19	102.06 (10)	C19—C8—C18—C7	−112.49 (9)
C6—C7—C8—C19	−6.98 (14)	C9—C8—C19—C20	−64.42 (12)
C6—C7—C8—C18	−109.04 (10)	C18—C8—C19—C20	154.25 (9)
C10—N1—C9—C17	2.10 (14)	C7—C8—C19—C20	87.35 (11)
C10—N1—C9—C8	−177.78 (8)	C8—C19—C20—C21	−38.08 (14)
C19—C8—C9—N1	−173.75 (9)	C8—C19—C20—C25	144.68 (10)
C18—C8—C9—N1	−32.40 (12)	C25—C20—C21—C22	0.59 (16)
C7—C8—C9—N1	32.73 (12)	C19—C20—C21—C22	−176.66 (10)
C19—C8—C9—C17	6.37 (14)	C20—C21—C22—C23	−0.01 (17)
C18—C8—C9—C17	147.71 (9)	C21—C22—C23—C24	−0.35 (17)
C7—C8—C9—C17	−147.15 (9)	C22—C23—C24—C25	0.11 (17)
C9—N1—C10—C15	178.96 (9)	C23—C24—C25—C20	0.49 (17)
C9—N1—C10—C11	0.08 (15)	C21—C20—C25—C24	−0.83 (16)
N1—C10—C11—C16	−2.27 (15)	C19—C20—C25—C24	176.53 (10)
C15—C10—C11—C16	178.86 (9)	C3—C4—C26—C27	1.12 (16)
N1—C10—C11—C12	177.35 (9)	C5—C4—C26—C27	−176.58 (10)
C15—C10—C11—C12	−1.52 (14)	C2—C1—C27—C26	−0.60 (18)
C16—C11—C12—C13	179.56 (10)	C4—C26—C27—C1	−0.46 (17)
C10—C11—C12—C13	−0.03 (15)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument

Service v2012.6.0.0; cell refinement: *SAINT* V8.18C (Bruker AXS Inc., 2011); data reduction: *SAINT* V8.18C (Bruker AXS Inc., 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008);

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)-4-methylthiazole 71b

Crystal data

$C_{20}H_{19}NS$	
M_r = 305.42	D_x = 1.257 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 106-110 °C
Hall symbol: ?	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 8.7941 (4) Å	Cell parameters from 5744 reflections
b = 11.7103 (5) Å	θ = 2.2–28.3°
c = 15.6716 (7) Å	μ = 0.20 mm^{-1}
V = 1613.89 (12) Å^3	T = 100 K
Z = 4	Block, translucent colourless
F(000) = 648	0.36 × 0.34 × 0.20 mm

Data collection

Bruker APEX-II CCD diffractometer	3759 independent reflections
Radiation source: sealed tube	3620 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.014
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.3°, θ_{min} = 2.2°
φ and ω scans	h = −11→10
Absorption correction: multi-scan *SADABS* V2012/1 (Bruker AXS Inc.)	k = −6→15
T_{min} = 0.86, T_{max} = 0.96	l = −11→20
8308 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.028	$w = 1/[\sigma^2(F_o^2) + (0.0407P)^2 + 0.3702P]$

	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.072$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.00$	$\Delta\rho_{max} = 0.24$ e Å^{-3}
3759 reflections	$\Delta\rho_{min} = -0.17$ e Å^{-3}
200 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
? constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: −0.06 (5)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.55723 (13)	0.31444 (9)	0.81556 (8)	0.0140 (2)
C2	0.66287 (15)	0.39446 (10)	0.93000 (8)	0.0170 (2)
C3	0.61281 (16)	0.29686 (11)	0.96726 (8)	0.0212 (3)
H3	0.6268	0.2777	1.0256	0.025*
C4	0.74599 (17)	0.48908 (12)	0.97387 (9)	0.0237 (3)
H4A	0.7626	0.4687	1.0338	0.036*
H4B	0.6856	0.5593	0.9707	0.036*
H4C	0.8443	0.5013	0.9458	0.036*
C5	0.51546 (14)	0.29564 (9)	0.72501 (7)	0.0140 (2)

C6	0.64874 (14)	0.30606 (10)	0.66117 (8)	0.0163 (2)
H6	0.7478	0.3287	0.6875	0.02*
C7	0.52825 (16)	0.39639 (10)	0.66460 (8)	0.0194 (3)
H7A	0.4554	0.4003	0.6165	0.023*
H7B	0.5563	0.4713	0.6893	0.023*
C8	0.66220 (14)	0.22024 (11)	0.59083 (8)	0.0175 (2)
C9	0.74694 (16)	0.12154 (12)	0.60551 (9)	0.0247 (3)
H9	0.7991	0.1126	0.6582	0.03*
C10	0.75620 (19)	0.03607 (14)	0.54421 (10)	0.0307 (3)
H10	0.8137	−0.031	0.5554	0.037*
C11	0.68183 (18)	0.04846 (14)	0.46686 (9)	0.0289 (3)
H11	0.6872	−0.0102	0.4251	0.035*
C12	0.59952 (17)	0.14718 (14)	0.45076 (9)	0.0268 (3)
H12	0.5497	0.1566	0.3974	0.032*
C13	0.58966 (16)	0.23213 (12)	0.51220 (9)	0.0219 (3)
H13	0.5327	0.2993	0.5006	0.026*
C14	0.39904 (14)	0.20422 (10)	0.70600 (8)	0.0159 (2)
H14B	0.4426	0.1296	0.7229	0.019*
H14A	0.3829	0.2021	0.6435	0.019*
C15	0.24535 (14)	0.21626 (10)	0.74854 (7)	0.0144 (2)
C16	0.15785 (15)	0.11830 (10)	0.76089 (8)	0.0167 (2)
H16	0.1975	0.046	0.7447	0.02*
C17	0.01361 (15)	0.12488 (11)	0.79651 (8)	0.0199 (3)
H17	−0.0445	0.0573	0.8046	0.024*
C18	−0.04615 (14)	0.23026 (12)	0.82042 (8)	0.0207 (3)
H18	−0.1448	0.235	0.8448	0.025*
C19	0.03972 (15)	0.32809 (11)	0.80830 (8)	0.0198 (3)
H19	−0.0009	0.4003	0.824	0.024*

C20	0.18523 (16)	0.32155 (11)	0.77322 (8)	0.0181 (3)
H20	0.2437	0.3891	0.7661	0.022*
N1	0.63098 (12)	0.40358 (8)	0.84363 (7)	0.0148 (2)
S1	0.52052 (4)	0.21282 (3)	0.89369 (2)	0.02175 (8)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0139 (6)	0.0135 (5)	0.0145 (5)	0.0007 (4)	0.0034 (4)	0.0019 (4)
C2	0.0172 (6)	0.0183 (5)	0.0156 (6)	0.0036 (5)	0.0013 (5)	−0.0031 (5)
C3	0.0262 (7)	0.0233 (6)	0.0141 (6)	0.0004 (5)	0.0007 (5)	0.0004 (5)
C4	0.0277 (7)	0.0228 (6)	0.0205 (7)	0.0005 (5)	−0.0035 (6)	−0.0069 (5)
C5	0.0147 (6)	0.0123 (5)	0.0151 (5)	−0.0015 (4)	0.0020 (4)	−0.0001 (4)
C6	0.0167 (6)	0.0179 (5)	0.0142 (6)	−0.0056 (4)	0.0009 (5)	0.0015 (4)
C7	0.0263 (7)	0.0141 (5)	0.0176 (6)	−0.0016 (5)	−0.0026 (5)	0.0019 (4)
C8	0.0161 (6)	0.0211 (5)	0.0153 (6)	−0.0054 (5)	0.0041 (4)	0.0003 (5)
C9	0.0247 (7)	0.0305 (7)	0.0187 (6)	0.0055 (5)	−0.0020 (6)	−0.0028 (6)
C10	0.0314 (8)	0.0334 (8)	0.0272 (7)	0.0087 (6)	−0.0016 (6)	−0.0074 (6)
C11	0.0271 (8)	0.0378 (8)	0.0217 (7)	−0.0018 (6)	0.0033 (6)	−0.0127 (6)
C12	0.0249 (7)	0.0402 (8)	0.0152 (6)	−0.0057 (6)	−0.0009 (5)	−0.0020 (6)
C13	0.0226 (7)	0.0258 (7)	0.0171 (6)	−0.0034 (5)	0.0006 (5)	0.0029 (5)
C14	0.0139 (6)	0.0148 (5)	0.0191 (6)	−0.0029 (4)	0.0024 (5)	−0.0032 (5)
C15	0.0138 (5)	0.0169 (5)	0.0124 (5)	0.0013 (5)	−0.0012 (4)	−0.0010 (5)
C16	0.0156 (6)	0.0170 (5)	0.0175 (6)	0.0010 (5)	−0.0002 (5)	−0.0032 (5)
C17	0.0157 (6)	0.0231 (6)	0.0210 (6)	−0.0030 (5)	0.0009 (5)	−0.0006 (5)
C18	0.0135 (6)	0.0329 (7)	0.0157 (6)	0.0045 (5)	0.0010 (5)	−0.0013 (5)
C19	0.0208 (6)	0.0209 (5)	0.0179 (6)	0.0083 (5)	−0.0013 (5)	−0.0016 (5)
C20	0.0204 (6)	0.0154 (5)	0.0186 (6)	0.0018 (5)	0.0002 (5)	−0.0009 (5)
N1	0.0162 (5)	0.0125 (4)	0.0156 (5)	0.0001 (4)	0.0011 (4)	−0.0010 (4)

S1	0.02842 (17)	0.01875 (13)	0.01807 (15)	−0.00726 (13)	0.00144 (13)	0.00496 (12)

Geometric parameters (Å, °)

C1—N1	1.3053 (15)	C9—H9	0.95
C1—C5	1.4824 (16)	C10—C11	1.385 (2)
C1—S1	1.7377 (12)	C10—H10	0.95
C2—C3	1.3568 (18)	C11—C12	1.387 (2)
C2—N1	1.3864 (17)	C11—H11	0.95
C2—C4	1.4949 (18)	C12—C13	1.387 (2)
C3—S1	1.7195 (14)	C12—H12	0.95
C3—H3	0.95	C13—H13	0.95
C4—H4A	0.98	C14—C15	1.5137 (16)
C4—H4B	0.98	C14—H14B	0.99
C4—H4C	0.98	C14—H14A	0.99
C5—C14	1.5110 (16)	C15—C16	1.3949 (17)
C5—C7	1.5167 (15)	C15—C20	1.3962 (16)
C5—C6	1.5457 (16)	C16—C17	1.3879 (18)
C6—C8	1.4963 (17)	C16—H16	0.95
C6—C7	1.4981 (18)	C17—C18	1.3926 (18)
C6—H6	1.0	C17—H17	0.95
C7—H7A	0.99	C18—C19	1.3852 (19)
C7—H7B	0.99	C18—H18	0.95
C8—C9	1.3943 (18)	C19—C20	1.3948 (19)
C8—C13	1.3946 (18)	C19—H19	0.95
C9—C10	1.390 (2)	C20—H20	0.95
N1—C1—C5	124.36 (10)	C11—C10—C9	120.12 (14)
N1—C1—S1	113.74 (9)	C11—C10—H10	119.9
C5—C1—S1	121.80 (8)	C9—C10—H10	119.9
C3—C2—N1	114.80 (11)	C10—C11—C12	119.54 (13)

C3—C2—C4	125.81 (12)	C10—C11—H11	120.2
N1—C2—C4	119.39 (11)	C12—C11—H11	120.2
C2—C3—S1	110.28 (10)	C11—C12—C13	120.26 (13)
C2—C3—H3	124.9	C11—C12—H12	119.9
S1—C3—H3	124.9	C13—C12—H12	119.9
C2—C4—H4A	109.5	C12—C13—C8	120.88 (13)
C2—C4—H4B	109.5	C12—C13—H13	119.6
H4A—C4—H4B	109.5	C8—C13—H13	119.6
C2—C4—H4C	109.5	C5—C14—C15	116.89 (10)
H4A—C4—H4C	109.5	C5—C14—H14B	108.1
H4B—C4—H4C	109.5	C15—C14—H14B	108.1
C1—C5—C14	117.50 (10)	C5—C14—H14A	108.1
C1—C5—C7	117.62 (10)	C15—C14—H14A	108.1
C14—C5—C7	118.58 (10)	H14B—C14—H14A	107.3
C1—C5—C6	114.84 (10)	C16—C15—C20	118.62 (11)
C14—C5—C6	116.24 (10)	C16—C15—C14	118.50 (11)
C7—C5—C6	58.57 (8)	C20—C15—C14	122.85 (11)
C8—C6—C7	123.82 (11)	C17—C16—C15	120.95 (12)
C8—C6—C5	118.93 (10)	C17—C16—H16	119.5
C7—C6—C5	59.75 (8)	C15—C16—H16	119.5
C8—C6—H6	114.4	C16—C17—C18	120.15 (12)
C7—C6—H6	114.4	C16—C17—H17	119.9
C5—C6—H6	114.4	C18—C17—H17	119.9
C6—C7—C5	61.68 (8)	C19—C18—C17	119.35 (12)
C6—C7—H7A	117.6	C19—C18—H18	120.3
C5—C7—H7A	117.6	C17—C18—H18	120.3
C6—C7—H7B	117.6	C18—C19—C20	120.59 (12)
C5—C7—H7B	117.6	C18—C19—H19	119.7

H7A—C7—H7B	114.7	C20—C19—H19	119.7
C9—C8—C13	118.22 (12)	C19—C20—C15	120.33 (12)
C9—C8—C6	118.52 (11)	C19—C20—H20	119.8
C13—C8—C6	123.21 (12)	C15—C20—H20	119.8
C10—C9—C8	120.96 (13)	C1—N1—C2	111.58 (10)
C10—C9—H9	119.5	C3—S1—C1	89.59 (6)
C8—C9—H9	119.5		
N1—C2—C3—S1	−0.70 (15)	C10—C11—C12—C13	−1.0 (2)
C4—C2—C3—S1	179.05 (11)	C11—C12—C13—C8	0.2 (2)
N1—C1—C5—C14	−165.57 (11)	C9—C8—C13—C12	1.03 (19)
S1—C1—C5—C14	18.36 (15)	C6—C8—C13—C12	−176.62 (12)
N1—C1—C5—C7	−13.79 (18)	C1—C5—C14—C15	57.67 (15)
S1—C1—C5—C7	170.13 (9)	C7—C5—C14—C15	−93.83 (14)
N1—C1—C5—C6	52.23 (16)	C6—C5—C14—C15	−160.65 (10)
S1—C1—C5—C6	−123.85 (10)	C5—C14—C15—C16	−155.53 (11)
C1—C5—C6—C8	137.14 (11)	C5—C14—C15—C20	26.77 (17)
C14—C5—C6—C8	−5.56 (16)	C20—C15—C16—C17	0.34 (19)
C7—C5—C6—C8	−114.45 (13)	C14—C15—C16—C17	−177.46 (12)
C1—C5—C6—C7	−108.41 (11)	C15—C16—C17—C18	0.1 (2)
C14—C5—C6—C7	108.89 (12)	C16—C17—C18—C19	0.0 (2)
C8—C6—C7—C5	106.46 (12)	C17—C18—C19—C20	−0.6 (2)
C1—C5—C7—C6	103.64 (12)	C18—C19—C20—C15	1.0 (2)
C14—C5—C7—C6	−104.90 (12)	C16—C15—C20—C19	−0.91 (19)
C7—C6—C8—C9	−161.34 (12)	C14—C15—C20—C19	176.78 (12)
C5—C6—C8—C9	−90.15 (15)	C5—C1—N1—C2	−176.00 (11)
C7—C6—C8—C13	16.31 (18)	S1—C1—N1—C2	0.36 (13)
C5—C6—C8—C13	87.49 (15)	C3—C2—N1—C1	0.22 (16)
C13—C8—C9—C10	−1.4 (2)	C4—C2—N1—C1	−179.54 (11)

C6—C8—C9—C10	176.36 (13)	C2—C3—S1—C1	0.73 (11)
C8—C9—C10—C11	0.6 (2)	N1—C1—S1—C3	−0.64 (10)
C9—C10—C11—C12	0.7 (2)	C5—C1—S1—C3	175.83 (10)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2012.12.0.3; cell refinement: *SAINT* V8.27B (Bruker AXS Inc., 2012); data reduction: *SAINT* V8.27B (Bruker AXS Inc., 2012); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

2-((1*R*,2*S*)-1-Methyl-2-phenylcyclopropyl)benzo[*d*]thiazole 74a

Crystal data

$C_{17}H_{16}NS$	$F(000) = 282$
$M_r = 266.37$	
	$D_x = 1.296$ Mg m^{-3}
Hall symbol: ?	Melting point: 62-67 °C
$a = 7.3594$ (9) Å	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$b = 5.3452$ (6) Å	Cell parameters from ? reflections
$c = 17.683$ (2) Å	$\theta = ?°$
$\alpha = 90°$	$\mu = 0.22$ mm^{-1}
$\beta = 101.065$ (3)°	$T = 100$ K
$\gamma = 90°$	
$V = 682.69$ (14) Å^3	0.20 × 0.10 × 0.08 mm
$Z = 2$	

Data collection

diffractometer	$R_{int} = 0.037$
Radiation source: fine-focus sealed tube	$\theta_{max} = 27.1°$, $\theta_{min} = 2.4°$
graphite	$h = -9 \rightarrow 9$
	$k = -6 \rightarrow 5$
5863 measured reflections	$l = -22 \rightarrow 22$
2722 independent reflections	Standard reflections: ?
2221 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.045$	$w = 1/[\sigma^2(F_o^2) + (0.0532P)^2 + 0.0269P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.103$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.02$	$\Delta\rho_{max} = 0.29$ e Å^{-3}
2722 reflections	$\Delta\rho_{min} = -0.25$ e Å^{-3}
173 parameters	Extinction correction: none
1 restraint	Extinction coefficient: ?
? constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: −0.05 (10)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.35969 (8)	0.87403 (13)	0.71379 (3)	0.02323 (16)
N1	0.0362 (3)	1.0591 (5)	0.65623 (14)	0.0303 (6)
C1	0.4480 (4)	1.4021 (7)	0.56088 (14)	0.0276 (6)
H1	0.5434	1.4777	0.5394	0.033*
C2	0.4921 (4)	1.2156 (6)	0.61526 (15)	0.0253 (6)
H2	0.6162	1.1607	0.6315	0.030*

C3	0.3484 (4)	1.1109 (5)	0.64539 (15)	0.0225 (6)
C4	0.1186 (3)	0.8928 (7)	0.70434 (13)	0.0243 (6)
C5	0.0223 (4)	0.7163 (6)	0.74724 (17)	0.0288 (7)
C6	−0.1583 (3)	0.8111 (6)	0.76883 (19)	0.0369 (8)
H6	−0.1918	0.9866	0.7521	0.044*
C7	−0.2063 (4)	0.7413 (7)	0.8442 (2)	0.0443 (10)
C8	−0.1464 (4)	0.8904 (9)	0.9077 (2)	0.0512 (9)
H8	−0.0738	1.0342	0.9027	0.061*
C9	−0.1896 (6)	0.8352 (9)	0.9786 (3)	0.0770 (16)
H9	−0.1479	0.9420	1.0214	0.092*
C10	−0.2918 (7)	0.6282 (10)	0.9874 (4)	0.087 (2)
H10	−0.3191	0.5886	1.0364	0.104*
C11	0.2662 (4)	1.4810 (6)	0.53705 (16)	0.0306 (7)
H11	0.2395	1.6085	0.4991	0.037*
C12	0.1231 (3)	1.3785 (8)	0.56726 (15)	0.0322 (6)
H12	−0.0002	1.4372	0.5513	0.039*
C13	0.1633 (4)	1.1870 (6)	0.62168 (16)	0.0255 (6)
C14	−0.1661 (4)	0.6303 (6)	0.7043 (2)	0.0429 (9)
H14A	−0.2088	0.6936	0.6512	0.052*
H14B	−0.2038	0.4564	0.7128	0.052*
C15	−0.3562 (5)	0.4746 (10)	0.9240 (4)	0.0845 (19)
H15	−0.4283	0.3309	0.9297	0.101*
C16	−0.3150 (4)	0.5318 (8)	0.8532 (3)	0.0618 (13)
H16	−0.3607	0.4284	0.8100	0.074*
C17	0.1416 (4)	0.5322 (6)	0.80033 (16)	0.0296 (7)
H17A	0.2171	0.4353	0.7708	0.044*
H17B	0.0621	0.4186	0.8229	0.044*
H17C	0.2228	0.6239	0.8415	0.044*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0204 (3)	0.0243 (3)	0.0239 (3)	−0.0002 (4)	0.0015 (2)	0.0037 (4)
N1	0.0238 (12)	0.0258 (14)	0.0366 (14)	−0.0074 (11)	−0.0062 (10)	0.0099 (11)
C1	0.0333 (13)	0.0285 (18)	0.0218 (13)	−0.0065 (15)	0.0074 (10)	−0.0014 (14)
C2	0.0303 (14)	0.0255 (17)	0.0200 (14)	−0.0002 (13)	0.0042 (11)	−0.0025 (12)
C3	0.0281 (14)	0.0195 (16)	0.0178 (13)	−0.0004 (11)	−0.0006 (10)	−0.0007 (10)
C4	0.0201 (11)	0.0212 (15)	0.0286 (13)	−0.0056 (14)	−0.0030 (10)	0.0023 (15)
C5	0.0175 (13)	0.0227 (16)	0.0422 (18)	−0.0035 (12)	−0.0040 (12)	0.0108 (13)
C6	0.0140 (13)	0.030 (2)	0.065 (2)	0.0001 (11)	0.0022 (13)	0.0204 (15)
C7	0.0187 (14)	0.034 (2)	0.084 (3)	0.0088 (14)	0.0199 (16)	0.028 (2)
C8	0.0517 (19)	0.036 (2)	0.078 (2)	0.013 (2)	0.0431 (18)	0.022 (2)
C9	0.101 (3)	0.054 (3)	0.099 (3)	0.040 (3)	0.076 (3)	0.037 (3)
C10	0.083 (3)	0.065 (4)	0.140 (5)	0.047 (3)	0.090 (4)	0.058 (3)
C11	0.0402 (17)	0.0253 (16)	0.0231 (14)	−0.0029 (13)	−0.0020 (13)	0.0047 (12)
C12	0.0276 (13)	0.0297 (16)	0.0337 (14)	−0.0016 (17)	−0.0082 (10)	0.0081 (18)
C13	0.0252 (14)	0.0207 (16)	0.0280 (15)	−0.0048 (12)	−0.0015 (11)	−0.0008 (12)
C14	0.0229 (15)	0.031 (2)	0.066 (2)	−0.0123 (13)	−0.0118 (15)	0.0148 (16)
C15	0.041 (2)	0.058 (3)	0.172 (5)	0.027 (2)	0.066 (3)	0.070 (4)
C16	0.0232 (16)	0.044 (2)	0.121 (4)	0.0090 (16)	0.0221 (19)	0.046 (2)
C17	0.0211 (13)	0.0265 (17)	0.0407 (18)	0.0027 (12)	0.0042 (13)	0.0123 (13)

Geometric parameters (Å, °)

S1—C3	1.742 (3)	C8—C9	1.383 (5)
S1—C4	1.753 (2)	C8—H8	0.9500
N1—C4	1.298 (4)	C9—C10	1.364 (7)
N1—C13	1.391 (4)	C9—H9	0.9500
C1—C2	1.380 (4)	C10—C15	1.397 (7)
C1—C11	1.389 (4)	C10—H10	0.9500

C1—H1	0.9500	C11—C12	1.382 (4)
C2—C3	1.390 (4)	C11—H11	0.9500
C2—H2	0.9500	C12—C13	1.397 (4)
C3—C13	1.406 (4)	C12—H12	0.9500
C4—C5	1.475 (4)	C14—H14A	0.9900
C5—C17	1.518 (4)	C14—H14B	0.9900
C5—C14	1.519 (4)	C15—C16	1.379 (6)
C5—C6	1.538 (4)	C15—H15	0.9500
C6—C14	1.488 (5)	C16—H16	0.9500
C6—C7	1.490 (5)	C17—H17A	0.9800
C6—H6	1.0000	C17—H17B	0.9800
C7—C8	1.379 (5)	C17—H17C	0.9800
C7—C16	1.403 (5)		
C3—S1—C4	88.84 (14)	C10—C9—H9	119.9
C4—N1—C13	110.8 (2)	C8—C9—H9	119.9
C2—C1—C11	121.0 (3)	C9—C10—C15	119.7 (5)
C2—C1—H1	119.5	C9—C10—H10	120.2
C11—C1—H1	119.5	C15—C10—H10	120.2
C1—C2—C3	117.6 (3)	C12—C11—C1	121.6 (3)
C1—C2—H2	121.2	C12—C11—H11	119.2
C3—C2—H2	121.2	C1—C11—H11	119.2
C2—C3—C13	122.3 (3)	C11—C12—C13	118.7 (3)
C2—C3—S1	128.4 (2)	C11—C12—H12	120.6
C13—C3—S1	109.4 (2)	C13—C12—H12	120.6
N1—C4—C5	124.4 (2)	N1—C13—C12	126.2 (2)
N1—C4—S1	116.0 (2)	N1—C13—C3	114.9 (2)
C5—C4—S1	119.5 (2)	C12—C13—C3	118.8 (3)
C4—C5—C17	117.0 (2)	C6—C14—C5	61.5 (2)

C4—C5—C14	114.8 (2)	C6—C14—H14A	117.6
C17—C5—C14	118.5 (3)	C5—C14—H14A	117.6
C4—C5—C6	116.1 (2)	C6—C14—H14B	117.6
C17—C5—C6	119.0 (2)	C5—C14—H14B	117.6
C14—C5—C6	58.3 (2)	H14A—C14—H14B	114.7
C14—C6—C7	122.8 (3)	C16—C15—C10	119.9 (4)
C14—C6—C5	60.2 (2)	C16—C15—H15	120.0
C7—C6—C5	120.2 (2)	C10—C15—H15	120.0
C14—C6—H6	114.3	C15—C16—C7	120.6 (5)
C7—C6—H6	114.3	C15—C16—H16	119.7
C5—C6—H6	114.3	C7—C16—H16	119.7
C8—C7—C16	118.0 (4)	C5—C17—H17A	109.5
C8—C7—C6	119.4 (3)	C5—C17—H17B	109.5
C16—C7—C6	122.6 (4)	H17A—C17—H17B	109.5
C7—C8—C9	121.5 (4)	C5—C17—H17C	109.5
C7—C8—H8	119.3	H17A—C17—H17C	109.5
C9—C8—H8	119.3	H17B—C17—H17C	109.5
C10—C9—C8	120.3 (5)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)benzo[*d*]thiazole 74b

Crystal data

$C_{23}H_{19}NS$	?
M_r = 341.45	D_x = 1.293 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 130-136 °C
Hall symbol: ?	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 5.5209 (11) Å	Cell parameters from 1603 reflections
b = 17.432 (3) Å	θ = 2.6–22.1°
c = 18.220 (3) Å	μ = 0.19 mm^{-1}
V = 1753.5 (6) Å^3	T = 100 K
Z = 4	Needle, colourless
F(000) = 720	0.25 × 0.05 × 0.05 mm

Data collection

Bruker APEX-II CCD diffractometer	3140 independent reflections
Radiation source: sealed tube	2548 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.059
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 25.3°, θ_{min} = 2.2°
φ and ω scans	h = −6→6
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	k = −20→20
T_{min} = 0.95, T_{max} = 0.99	l = −21→21
10186 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.039$	$w = 1/[\sigma^2(F_o^2) + (0.0297P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.076$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.01$	$\Delta\rho_{max} = 0.18$ e Å^{-3}
3140 reflections	$\Delta\rho_{min} = -0.22$ e Å^{-3}
226 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: −0.05 (8)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.8471 (4)	0.93954 (13)	0.72469 (12)	0.0173 (5)
C2	0.7566 (5)	0.88501 (14)	0.61844 (12)	0.0194 (6)
C3	0.6321 (5)	0.83823 (14)	0.56954 (12)	0.0279 (6)
H3	0.4898	0.8117	0.5843	0.034*
C4	0.7202 (5)	0.83131 (16)	0.49918 (14)	0.0315 (7)

H4	0.6378	0.7993	0.4651	0.038*
C5	0.9270 (5)	0.87004 (15)	0.47699 (12)	0.0301 (7)
H5	0.9824	0.8644	0.4279	0.036*
C6	1.0540 (5)	0.91662 (15)	0.52466 (12)	0.0279 (6)
H6	1.1954	0.9432	0.5093	0.034*
C7	0.9668 (4)	0.92315 (14)	0.59608 (12)	0.0205 (6)
C8	0.8366 (4)	0.95776 (13)	0.80384 (12)	0.0186 (6)
C9	0.8246 (4)	0.88560 (14)	0.85394 (12)	0.0193 (6)
H9	0.8173	0.8363	0.826	0.023*
C10	0.6064 (4)	0.93532 (13)	0.84316 (12)	0.0188 (5)
H10A	0.5543	0.9676	0.885	0.023*
H10B	0.4722	0.9145	0.8131	0.023*
C11	0.9628 (4)	0.88003 (13)	0.92350 (12)	0.0186 (6)
C12	1.1662 (4)	0.83268 (14)	0.92520 (13)	0.0230 (6)
H12	1.2102	0.8049	0.8823	0.028*
C13	1.3058 (5)	0.82516 (15)	0.98800 (13)	0.0281 (6)
H13	1.4455	0.7933	0.9878	0.034*
C14	1.2401 (5)	0.86441 (15)	1.05101 (13)	0.0281 (7)
H14	1.3348	0.8596	1.0943	0.034*
C15	1.0368 (5)	0.91049 (15)	1.05077 (13)	0.0284 (7)
H15	0.9912	0.9371	1.0941	0.034*
C16	0.8986 (5)	0.91822 (14)	0.98763 (12)	0.0235 (6)
H16	0.7586	0.9499	0.9882	0.028*
C17	0.9688 (4)	1.02849 (13)	0.82834 (13)	0.0196 (5)
H17A	1.138	1.0257	0.8105	0.023*
H17B	0.9736	1.0292	0.8827	0.023*
C18	0.8572 (4)	1.10263 (13)	0.80169 (12)	0.0170 (5)
C19	0.9714 (4)	1.17176 (14)	0.81807 (12)	0.0238 (6)

H19	1.1217	1.1713	0.8434	0.029*
C20	0.8699 (5)	1.24062 (15)	0.79811 (13)	0.0300 (7)
H20	0.9488	1.2872	0.8109	0.036*
C21	0.6527 (5)	1.24288 (15)	0.75941 (12)	0.0271 (6)
H21	0.5822	1.2905	0.7458	0.033*
C22	0.5422 (5)	1.17488 (14)	0.74125 (12)	0.0251 (6)
H22	0.3948	1.1755	0.7144	0.03*
C23	0.6433 (4)	1.10558 (14)	0.76163 (11)	0.0210 (6)
H23	0.5652	1.0592	0.748	0.025*
N1	0.6932 (4)	0.89573 (11)	0.69201 (10)	0.0194 (5)
S1	1.08592 (12)	0.97320 (4)	0.67029 (3)	0.02330 (16)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0180 (13)	0.0136 (12)	0.0203 (11)	0.0031 (10)	−0.0006 (10)	0.0035 (11)
C2	0.0238 (15)	0.0183 (13)	0.0159 (11)	0.0053 (11)	−0.0020 (10)	−0.0018 (12)
C3	0.0313 (17)	0.0303 (15)	0.0222 (12)	0.0006 (13)	−0.0056 (12)	−0.0025 (12)
C4	0.0371 (18)	0.0341 (17)	0.0232 (13)	0.0075 (14)	−0.0056 (12)	−0.0044 (14)
C5	0.0337 (17)	0.0395 (17)	0.0171 (12)	0.0123 (15)	0.0001 (13)	0.0002 (12)
C6	0.0286 (16)	0.0320 (16)	0.0232 (12)	0.0075 (13)	0.0027 (12)	0.0036 (13)
C7	0.0229 (15)	0.0177 (13)	0.0210 (12)	0.0080 (11)	−0.0010 (11)	0.0027 (11)
C8	0.0199 (13)	0.0154 (13)	0.0203 (11)	0.0010 (10)	0.0006 (10)	0.0013 (11)
C9	0.0232 (14)	0.0128 (13)	0.0218 (12)	−0.0006 (11)	0.0010 (11)	0.0014 (11)
C10	0.0202 (13)	0.0182 (12)	0.0182 (11)	0.0000 (11)	0.0007 (11)	0.0018 (10)
C11	0.0207 (14)	0.0125 (12)	0.0225 (12)	−0.0014 (11)	0.0020 (10)	0.0030 (11)
C12	0.0241 (15)	0.0226 (14)	0.0222 (12)	−0.0017 (12)	0.0040 (11)	0.0067 (12)
C13	0.0250 (16)	0.0248 (15)	0.0345 (15)	0.0003 (12)	−0.0016 (12)	0.0094 (13)
C14	0.0297 (17)	0.0315 (16)	0.0231 (13)	−0.0058 (13)	−0.0064 (12)	0.0081 (13)

C15	0.0298 (17)	0.0325 (16)	0.0228 (13)	−0.0007 (13)	−0.0017 (11)	−0.0030 (12)
C16	0.0219 (14)	0.0247 (14)	0.0238 (12)	0.0023 (12)	−0.0019 (12)	0.0012 (11)
C17	0.0188 (13)	0.0193 (12)	0.0206 (11)	−0.0018 (11)	−0.0009 (10)	0.0023 (13)
C18	0.0197 (14)	0.0177 (13)	0.0136 (10)	0.0006 (10)	0.0042 (10)	0.0012 (10)
C19	0.0265 (15)	0.0232 (13)	0.0217 (13)	−0.0056 (11)	−0.0014 (10)	−0.0014 (12)
C20	0.0425 (19)	0.0186 (14)	0.0289 (12)	−0.0043 (13)	0.0024 (13)	−0.0010 (12)
C21	0.0372 (18)	0.0203 (14)	0.0237 (12)	0.0066 (13)	0.0077 (12)	0.0045 (12)
C22	0.0258 (15)	0.0264 (14)	0.0232 (13)	0.0064 (12)	0.0024 (11)	0.0010 (13)
C23	0.0265 (15)	0.0178 (13)	0.0188 (11)	−0.0017 (11)	0.0040 (11)	−0.0029 (11)
N1	0.0218 (12)	0.0179 (11)	0.0184 (10)	−0.0004 (9)	−0.0015 (8)	−0.0003 (9)
S1	0.0231 (3)	0.0264 (3)	0.0204 (3)	−0.0039 (3)	0.0023 (3)	0.0002 (3)

Geometric parameters (Å, °)

C1—N1	1.288 (3)	C11—C12	1.394 (3)
C1—C8	1.478 (3)	C12—C13	1.386 (3)
C1—S1	1.751 (2)	C12—H12	0.95
C2—C3	1.390 (3)	C13—C14	1.385 (3)
C2—N1	1.398 (3)	C13—H13	0.95
C2—C7	1.398 (3)	C14—C15	1.380 (4)
C3—C4	1.377 (3)	C14—H14	0.95
C3—H3	0.95	C15—C16	1.387 (3)
C4—C5	1.386 (4)	C15—H15	0.95
C4—H4	0.95	C16—H16	0.95
C5—C6	1.380 (4)	C17—C18	1.512 (3)
C5—H5	0.95	C17—H17A	0.99
C6—C7	1.392 (3)	C17—H17B	0.99
C6—H6	0.95	C18—C23	1.389 (3)
C7—S1	1.738 (2)	C18—C19	1.392 (3)
C8—C17	1.501 (3)	C19—C20	1.373 (3)

C8—C10	1.511 (3)	C19—H19	0.95
C8—C9	1.556 (3)	C20—C21	1.392 (4)
C9—C11	1.483 (3)	C20—H20	0.95
C9—C10	1.497 (3)	C21—C22	1.374 (3)
C9—H9	1.0	C21—H21	0.95
C10—H10A	0.99	C22—C23	1.381 (3)
C10—H10B	0.99	C22—H22	0.95
C11—C16	1.391 (3)	C23—H23	0.95
N1—C1—C8	123.5 (2)	C13—C12—C11	121.5 (2)
N1—C1—S1	115.70 (17)	C13—C12—H12	119.3
C8—C1—S1	120.66 (18)	C11—C12—H12	119.3
C3—C2—N1	124.7 (2)	C14—C13—C12	119.5 (2)
C3—C2—C7	120.2 (2)	C14—C13—H13	120.3
N1—C2—C7	115.1 (2)	C12—C13—H13	120.3
C4—C3—C2	118.3 (3)	C15—C14—C13	119.9 (2)
C4—C3—H3	120.9	C15—C14—H14	120.1
C2—C3—H3	120.9	C13—C14—H14	120.1
C3—C4—C5	121.3 (3)	C14—C15—C16	120.4 (2)
C3—C4—H4	119.3	C14—C15—H15	119.8
C5—C4—H4	119.3	C16—C15—H15	119.8
C6—C5—C4	121.4 (2)	C15—C16—C11	120.7 (2)
C6—C5—H5	119.3	C15—C16—H16	119.7
C4—C5—H5	119.3	C11—C16—H16	119.7
C5—C6—C7	117.4 (3)	C8—C17—C18	114.13 (19)
C5—C6—H6	121.3	C8—C17—H17A	108.7
C7—C6—H6	121.3	C18—C17—H17A	108.7
C6—C7—C2	121.4 (2)	C8—C17—H17B	108.7
C6—C7—S1	129.6 (2)	C18—C17—H17B	108.7

C2—C7—S1	109.03 (17)	H17A—C17—H17B	107.6
C1—C8—C17	116.6 (2)	C23—C18—C19	117.7 (2)
C1—C8—C10	116.1 (2)	C23—C18—C17	123.1 (2)
C17—C8—C10	118.74 (19)	C19—C18—C17	119.1 (2)
C1—C8—C9	113.62 (19)	C20—C19—C18	121.0 (2)
C17—C8—C9	120.69 (19)	C20—C19—H19	119.5
C10—C8—C9	58.43 (14)	C18—C19—H19	119.5
C11—C9—C10	124.3 (2)	C19—C20—C21	120.7 (3)
C11—C9—C8	122.2 (2)	C19—C20—H20	119.7
C10—C9—C8	59.28 (15)	C21—C20—H20	119.7
C11—C9—H9	113.5	C22—C21—C20	118.7 (3)
C10—C9—H9	113.5	C22—C21—H21	120.7
C8—C9—H9	113.5	C20—C21—H21	120.7
C9—C10—C8	62.28 (16)	C21—C22—C23	120.7 (2)
C9—C10—H10A	117.5	C21—C22—H22	119.7
C8—C10—H10A	117.5	C23—C22—H22	119.7
C9—C10—H10B	117.5	C22—C23—C18	121.1 (2)
C8—C10—H10B	117.5	C22—C23—H23	119.4
H10A—C10—H10B	114.6	C18—C23—H23	119.4
C16—C11—C12	118.1 (2)	C1—N1—C2	110.9 (2)
C16—C11—C9	123.8 (2)	C7—S1—C1	89.27 (12)
C12—C11—C9	118.2 (2)		
N1—C2—C3—C4	−177.9 (2)	C16—C11—C12—C13	−1.9 (4)
C7—C2—C3—C4	−0.5 (4)	C9—C11—C12—C13	179.3 (2)
C2—C3—C4—C5	−0.3 (4)	C11—C12—C13—C14	1.1 (4)
C3—C4—C5—C6	0.5 (4)	C12—C13—C14—C15	0.1 (4)
C4—C5—C6—C7	0.1 (4)	C13—C14—C15—C16	−0.5 (4)
C5—C6—C7—C2	−1.0 (4)	C14—C15—C16—C11	−0.3 (4)

C5—C6—C7—S1	177.4 (2)	C12—C11—C16—C15	1.4 (4)
C3—C2—C7—C6	1.2 (4)	C9—C11—C16—C15	−179.9 (2)
N1—C2—C7—C6	178.9 (2)	C1—C8—C17—C18	68.7 (3)
C3—C2—C7—S1	−177.43 (19)	C10—C8—C17—C18	−78.1 (3)
N1—C2—C7—S1	0.2 (3)	C9—C8—C17—C18	−146.4 (2)
N1—C1—C8—C17	−159.5 (2)	C8—C17—C18—C23	3.6 (3)
S1—C1—C8—C17	24.2 (3)	C8—C17—C18—C19	−176.9 (2)
N1—C1—C8—C10	−11.8 (3)	C23—C18—C19—C20	2.9 (3)
S1—C1—C8—C10	171.81 (16)	C17—C18—C19—C20	−176.7 (2)
N1—C1—C8—C9	53.2 (3)	C18—C19—C20—C21	−1.5 (4)
S1—C1—C8—C9	−123.15 (19)	C19—C20—C21—C22	−0.3 (4)
C1—C8—C9—C11	139.2 (2)	C20—C21—C22—C23	0.7 (4)
C17—C8—C9—C11	−6.7 (3)	C21—C22—C23—C18	0.8 (3)
C10—C8—C9—C11	−113.7 (3)	C19—C18—C23—C22	−2.5 (3)
C1—C8—C9—C10	−107.2 (2)	C17—C18—C23—C22	177.0 (2)
C17—C8—C9—C10	106.9 (2)	C8—C1—N1—C2	−176.3 (2)
C11—C9—C10—C8	110.2 (3)	S1—C1—N1—C2	0.2 (3)
C1—C8—C10—C9	102.9 (2)	C3—C2—N1—C1	177.3 (2)
C17—C8—C10—C9	−110.3 (2)	C7—C2—N1—C1	−0.3 (3)
C10—C9—C11—C16	2.8 (4)	C6—C7—S1—C1	−178.6 (2)
C8—C9—C11—C16	75.3 (3)	C2—C7—S1—C1	−0.08 (18)
C10—C9—C11—C12	−178.5 (2)	N1—C1—S1—C7	−0.07 (19)
C8—C9—C11—C12	−106.0 (3)	C8—C1—S1—C7	176.54 (19)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell

e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

2-((1*S*,2*S*)-2-(But-3-en-1-yl)cyclopropyl)-4,5-diphenyloxazole 76d

Crystal data

$C_{22}H_{21}NO$	$F(000) = 336$
$M_r = 315.40$	
Triclinic, $P\bar{1}$	$D_x = 1.206$ Mg m^{-3}
Hall symbol:	Melting point: 35-38 °C
$a = 8.3248$ (11) Å	radiation, $\lambda = 1.54178$ Å
$b = 9.9043$ (12) Å	Cell parameters from 4244 reflections
$c = 11.0379$ (14) Å	$\theta = 4.2$–$63.5°$
$\alpha = 79.536$ (7)°	$\mu = 0.57$ mm^{-1}
$\beta = 77.832$ (8)°	$T = 100$ K
$\gamma = 81.303$ (7)°	Block, translucent colourless
$V = 868.79$ (19) Å^3	0.40 × 0.35 × 0.08 mm
$Z = 2$	

Data collection

? diffractometer	2686 independent reflections
Radiation source: ?	1223 reflections with $I > 2\sigma(I)$
?	$R_{int} = 0.091$
Detector resolution: 8.3333 pixels mm^{-1}	$\theta_{max} = 65.3°$, $\theta_{min} = 4.2°$
?	$h = -5 \rightarrow 9$
Absorption correction: multi-scan SADABS V2008/1 (Bruker AXS)	$k = -11 \rightarrow 11$
$T_{min} = 0.81$, $T_{max} = 0.96$	$l = -12 \rightarrow 11$
4779 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map

Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.052$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.252$	$w = 1/[\sigma^2(F_o^2) + (0.1522P)^2 + 0.035P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.06$	$(\Delta/\sigma)_{max} = 0.001$
2686 reflections	$\Delta\rho_{max} = 0.37$ e Å^{-3}
217 parameters	$\Delta\rho_{min} = -0.52$ e Å^{-3}
0 restraints	Extinction correction: none
constraints	Extinction coefficient: ?
Primary atom site location: structure-invariant direct methods	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2874 (4)	0.8624 (4)	0.4910 (3)	0.0375 (9)
C2	0.0913 (3)	0.8542 (3)	0.3914 (2)	0.0287 (7)
C3	0.1564 (3)	0.9754 (3)	0.3487 (3)	0.0312 (8)
C4	0.4005 (3)	0.8243 (3)	0.5784 (3)	0.0360 (9)
H4	0.4785	0.8933	0.5744	0.043*
C5	0.4658 (3)	0.6769 (3)	0.6162 (2)	0.0390 (9)
H5A	0.5808	0.6574	0.6311	0.047*
H5B	0.4301	0.6056	0.5786	0.047*

C6	0.3388 (3)	0.7488 (3)	0.7092 (2)	0.0360 (8)
H6	0.2247	0.7214	0.7241	0.043*
C7	0.3890 (3)	0.7877 (3)	0.8215 (2)	0.0376 (9)
H7A	0.4991	0.8212	0.7946	0.045*
H7B	0.309	0.8646	0.8515	0.045*
C8	0.3963 (3)	0.6694 (3)	0.9288 (2)	0.0398 (8)
H8A	0.2883	0.6321	0.9522	0.048*
H8B	0.4813	0.5947	0.9002	0.048*
C9	0.4353 (3)	0.7093 (3)	1.0402 (2)	0.0403 (9)
H9	0.5397	0.7409	1.0327	0.048*
C10	0.3343 (3)	0.7041 (3)	1.1496 (3)	0.0466 (9)
H10A	0.2291	0.673	1.1599	0.056*
H10B	0.3667	0.7314	1.2182	0.056*
C11	−0.0397 (3)	0.7913 (3)	0.3610 (2)	0.0287 (7)
C12	−0.0354 (3)	0.6485 (3)	0.3778 (2)	0.0332 (8)
H12	0.0539	0.5921	0.4098	0.04*
C13	−0.1561 (3)	0.5868 (3)	0.3495 (2)	0.0377 (8)
H13	−0.1499	0.4888	0.3622	0.045*
C14	−0.2864 (3)	0.6658 (3)	0.3027 (2)	0.0354 (8)
H14	−0.3698	0.6231	0.2821	0.043*
C15	−0.2946 (3)	0.8086 (3)	0.2861 (2)	0.0325 (8)
H15	−0.3846	0.8643	0.2545	0.039*
C16	−0.1732 (3)	0.8697 (3)	0.3151 (2)	0.0298 (7)
H16	−0.1806	0.9677	0.3036	0.036*
C17	0.1300 (3)	1.0928 (3)	0.2490 (2)	0.0291 (8)
C18	0.1036 (3)	1.0712 (3)	0.1346 (2)	0.0360 (9)
H18	0.097	0.9801	0.1216	0.043*
C19	0.0869 (3)	1.1811 (3)	0.0388 (3)	0.0399 (9)

H19	0.0665	1.1655	−0.0387	0.048*
C20	0.0999 (3)	1.3129 (3)	0.0560 (3)	0.0426 (10)
H20	0.0902	1.3878	−0.0104	0.051*
C21	0.1268 (3)	1.3369 (3)	0.1682 (3)	0.0395 (9)
H21	0.135	1.4282	0.1796	0.047*
C22	0.1420 (3)	1.2270 (3)	0.2655 (3)	0.0356 (9)
H22	0.1607	1.2437	0.3432	0.043*
O1	0.1782 (2)	0.7798 (2)	0.48239 (18)	0.0439 (7)
N1	0.2790 (2)	0.9798 (2)	0.41511 (18)	0.0253 (6)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0261 (19)	0.054 (2)	0.0391 (17)	−0.0146 (17)	−0.0045 (11)	−0.0181 (16)
C2	0.0267 (16)	0.0317 (17)	0.0239 (13)	0.0053 (13)	−0.0052 (9)	−0.0008 (12)
C3	0.0243 (16)	0.0355 (19)	0.0340 (16)	0.0040 (15)	−0.0058 (11)	−0.0120 (14)
C4	0.0347 (18)	0.0336 (19)	0.0372 (18)	−0.0050 (15)	−0.0061 (12)	0.0006 (15)
C5	0.0336 (16)	0.038 (2)	0.0421 (17)	0.0021 (15)	−0.0045 (11)	−0.0063 (15)
C6	0.0392 (18)	0.0264 (17)	0.0387 (17)	−0.0048 (14)	−0.0024 (11)	−0.0006 (14)
C7	0.0317 (18)	0.0369 (19)	0.0384 (16)	0.0067 (14)	−0.0056 (11)	−0.0010 (14)
C8	0.0378 (17)	0.0375 (18)	0.0381 (16)	0.0038 (14)	−0.0030 (11)	−0.0020 (14)
C9	0.0360 (18)	0.043 (2)	0.0343 (16)	0.0060 (14)	−0.0068 (11)	0.0046 (14)
C10	0.0436 (18)	0.048 (2)	0.0417 (17)	0.0063 (15)	−0.0019 (11)	−0.0073 (16)
C11	0.0278 (18)	0.0236 (17)	0.0308 (15)	−0.0035 (14)	0.0017 (10)	−0.0022 (12)
C12	0.0287 (16)	0.0289 (18)	0.0382 (15)	−0.0042 (15)	−0.0023 (10)	0.0006 (13)
C13	0.0335 (18)	0.0288 (17)	0.0467 (17)	−0.0068 (15)	−0.0014 (11)	0.0001 (14)
C14	0.0311 (17)	0.0358 (19)	0.0399 (16)	−0.0143 (16)	−0.0039 (10)	−0.0016 (14)
C15	0.0284 (16)	0.036 (2)	0.0328 (14)	−0.0079 (15)	−0.0069 (9)	−0.0007 (14)
C16	0.0306 (17)	0.0281 (16)	0.0282 (15)	−0.0038 (14)	−0.0022 (9)	−0.0017 (12)

C17	0.0220 (15)	0.0282 (19)	0.0348 (15)	−0.0007 (13)	0.0005 (11)	−0.0077 (14)
C18	0.0330 (16)	0.0349 (19)	0.0408 (17)	−0.0085 (14)	0.0000 (12)	−0.0124 (14)
C19	0.0383 (17)	0.041 (2)	0.0358 (16)	−0.0080 (16)	−0.0019 (11)	0.0016 (15)
C20	0.0355 (18)	0.038 (2)	0.0459 (18)	−0.0047 (15)	0.0033 (12)	0.0013 (16)
C21	0.0298 (17)	0.0290 (18)	0.0511 (19)	−0.0024 (13)	0.0049 (12)	0.0004 (15)
C22	0.0238 (17)	0.034 (2)	0.0499 (17)	−0.0036 (15)	0.0027 (11)	−0.0215 (16)
O1	0.0450 (14)	0.0466 (15)	0.0355 (12)	0.0029 (12)	−0.0064 (9)	−0.0024 (10)
N1	0.0243 (13)	0.0247 (13)	0.0295 (12)	0.0012 (11)	−0.0098 (8)	−0.0086 (10)

Geometric parameters (Å, °)

C1—N1	1.305 (4)	C10—H10A	0.95
C1—O1	1.340 (3)	C10—H10B	0.95
C1—C4	1.450 (4)	C11—C16	1.388 (4)
C2—C3	1.357 (4)	C11—C12	1.389 (3)
C2—O1	1.397 (3)	C12—C13	1.367 (4)
C2—C11	1.458 (4)	C12—H12	0.95
C3—N1	1.386 (3)	C13—C14	1.374 (4)
C3—C17	1.473 (4)	C13—H13	0.95
C4—C5	1.496 (4)	C14—C15	1.386 (3)
C4—C6	1.523 (3)	C14—H14	0.95
C4—H4	1.0	C15—C16	1.372 (4)
C5—C6	1.503 (3)	C15—H15	0.95
C5—H5A	0.99	C16—H16	0.95
C5—H5B	0.99	C17—C18	1.385 (4)
C6—C7	1.516 (4)	C17—C22	1.396 (3)
C6—H6	1.0	C18—C19	1.386 (4)
C7—C8	1.511 (4)	C18—H18	0.95
C7—H7A	0.99	C19—C20	1.375 (4)
C7—H7B	0.99	C19—H19	0.95

C8—C9	1.469 (4)	C20—C21	1.371 (4)
C8—H8A	0.99	C20—H20	0.95
C8—H8B	0.99	C21—C22	1.394 (4)
C9—C10	1.315 (3)	C21—H21	0.95
C9—H9	0.95	C22—H22	0.95
N1—C1—O1	113.3 (3)	C9—C10—H10A	120.0
N1—C1—C4	124.2 (3)	C9—C10—H10B	120.0
O1—C1—C4	122.5 (3)	H10A—C10—H10B	120.0
C3—C2—O1	107.5 (3)	C16—C11—C12	117.2 (3)
C3—C2—C11	134.2 (3)	C16—C11—C2	122.3 (3)
O1—C2—C11	118.3 (3)	C12—C11—C2	120.5 (3)
C2—C3—N1	108.2 (3)	C13—C12—C11	121.8 (3)
C2—C3—C17	134.8 (3)	C13—C12—H12	119.1
N1—C3—C17	117.0 (3)	C11—C12—H12	119.1
C1—C4—C5	121.6 (3)	C12—C13—C14	120.3 (3)
C1—C4—C6	118.9 (2)	C12—C13—H13	119.8
C5—C4—C6	59.74 (16)	C14—C13—H13	119.8
C1—C4—H4	115.1	C13—C14—C15	119.1 (3)
C5—C4—H4	115.1	C13—C14—H14	120.4
C6—C4—H4	115.1	C15—C14—H14	120.4
C4—C5—C6	61.04 (17)	C16—C15—C14	120.2 (3)
C4—C5—H5A	117.7	C16—C15—H15	119.9
C6—C5—H5A	117.7	C14—C15—H15	119.9
C4—C5—H5B	117.7	C15—C16—C11	121.4 (3)
C6—C5—H5B	117.7	C15—C16—H16	119.3
H5A—C5—H5B	114.8	C11—C16—H16	119.3
C5—C6—C7	119.9 (2)	C18—C17—C22	118.8 (3)
C5—C6—C4	59.23 (16)	C18—C17—C3	120.7 (3)

C7—C6—C4	119.4 (2)	C22—C17—C3	120.3 (3)
C5—C6—H6	115.6	C17—C18—C19	120.6 (3)
C7—C6—H6	115.6	C17—C18—H18	119.7
C4—C6—H6	115.6	C19—C18—H18	119.7
C8—C7—C6	113.4 (2)	C20—C19—C18	120.0 (3)
C8—C7—H7A	108.9	C20—C19—H19	120.0
C6—C7—H7A	108.9	C18—C19—H19	120.0
C8—C7—H7B	108.9	C21—C20—C19	120.4 (3)
C6—C7—H7B	108.9	C21—C20—H20	119.8
H7A—C7—H7B	107.7	C19—C20—H20	119.8
C9—C8—C7	113.3 (3)	C20—C21—C22	119.9 (3)
C9—C8—H8A	108.9	C20—C21—H21	120.0
C7—C8—H8A	108.9	C22—C21—H21	120.0
C9—C8—H8B	108.9	C21—C22—C17	120.2 (3)
C7—C8—H8B	108.9	C21—C22—H22	119.9
H8A—C8—H8B	107.7	C17—C22—H22	119.9
C10—C9—C8	124.0 (3)	C1—O1—C2	104.9 (3)
C10—C9—H9	118.0	C1—N1—C3	106.0 (3)
C8—C9—H9	118.0		
O1—C2—C3—N1	−2.1 (2)	C13—C14—C15—C16	0.5 (3)
C11—C2—C3—N1	179.1 (2)	C14—C15—C16—C11	0.2 (3)
O1—C2—C3—C17	174.9 (2)	C12—C11—C16—C15	−0.8 (3)
C11—C2—C3—C17	−3.9 (4)	C2—C11—C16—C15	179.50 (18)
N1—C1—C4—C5	−150.0 (2)	C2—C3—C17—C18	−38.8 (3)
O1—C1—C4—C5	31.2 (3)	N1—C3—C17—C18	138.0 (2)
N1—C1—C4—C6	139.7 (3)	C2—C3—C17—C22	145.4 (3)
O1—C1—C4—C6	−39.1 (4)	N1—C3—C17—C22	−37.8 (3)
C1—C4—C5—C6	−107.3 (3)	C22—C17—C18—C19	−1.0 (3)

C4—C5—C6—C7	−108.5 (3)	C3—C17—C18—C19	−176.80 (19)
C1—C4—C6—C5	111.7 (3)	C17—C18—C19—C20	1.4 (3)
C1—C4—C6—C7	−139.1 (3)	C18—C19—C20—C21	−1.0 (3)
C5—C4—C6—C7	109.2 (3)	C19—C20—C21—C22	0.4 (3)
C5—C6—C7—C8	−81.9 (3)	C20—C21—C22—C17	0.0 (3)
C4—C6—C7—C8	−151.2 (2)	C18—C17—C22—C21	0.4 (3)
C6—C7—C8—C9	−176.55 (18)	C3—C17—C22—C21	176.16 (18)
C7—C8—C9—C10	117.0 (3)	N1—C1—O1—C2	−0.3 (2)
C3—C2—C11—C16	−28.2 (3)	C4—C1—O1—C2	178.5 (2)
O1—C2—C11—C16	153.1 (2)	C3—C2—O1—C1	1.5 (2)
C3—C2—C11—C12	152.1 (3)	C11—C2—O1—C1	−179.46 (17)
O1—C2—C11—C12	−26.6 (3)	O1—C1—N1—C3	−1.0 (2)
C16—C11—C12—C13	0.6 (3)	C4—C1—N1—C3	−179.8 (2)
C2—C11—C12—C13	−179.70 (19)	C2—C3—N1—C1	1.9 (2)
C11—C12—C13—C14	0.2 (3)	C17—C3—N1—C1	−175.71 (19)
C12—C13—C14—C15	−0.8 (3)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2011.6.0.0; cell refinement: *SAINT* V7.68A (Bruker AXS, 2009); data reduction: *SAINT* V7.68A (Bruker AXS, 2009); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)-4,5-diphenyloxazole 77a

Crystal data

$C_{31}H_{25}NO$	
M_r = 427.52	D_x = 1.265 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Melting point: 140-146 °C
Hall symbol: ?	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 5.9692 (6) Å	Cell parameters from 1843 reflections
b = 16.5956 (16) Å	θ = 3.5–23.4°
c = 22.656 (2) Å	μ = 0.08 mm^{-1}
V = 2244.4 (4) Å^3	T = 100 K
Z = 4	Needle, colourless
F(000) = 904	0.48 × 0.05 × 0.05 mm

Data collection

Bruker APEX-II CCD diffractometer	3785 independent reflections
Radiation source: sealed tube	2989 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.068
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 24.7°, θ_{min} = 1.5°
φ and ω scans	h = −6→7
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	k = −19→19
T_{min} = 0.96, T_{max} = 1.00	l = −26→26
15263 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.041$	$w = 1/[\sigma^2(F_o^2) + (0.0382P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.084$	$(\Delta/\sigma)_{max} < 0.001$
$S = 1.01$	$\Delta\rho_{max} = 0.17$ e Å^{-3}
3785 reflections	$\Delta\rho_{min} = -0.22$ e Å^{-3}
298 parameters	Extinction correction: none
0 restraints	Extinction coefficient: ?
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 1 (2)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.4730 (4)	0.67683 (15)	0.17918 (9)	0.0239 (6)
C2	0.4376 (4)	0.57282 (14)	0.12330 (9)	0.0217 (6)
C3	0.2792 (4)	0.62656 (13)	0.10641 (9)	0.0203 (5)
C4	0.5459 (4)	0.73956 (13)	0.22028 (9)	0.0199 (5)
C5	0.5321 (4)	0.82660 (14)	0.19500 (9)	0.0227 (5)
H5	0.4635	0.8295	0.1548	0.027*

C6	0.3732 (4)	0.79991 (14)	0.24172 (10)	0.0241 (6)
H6A	0.2153	0.7909	0.2301	0.029*
H6B	0.3932	0.8226	0.2818	0.029*
C7	0.7129 (4)	0.88662 (13)	0.20480 (9)	0.0201 (5)
C8	0.8814 (4)	0.89489 (14)	0.16267 (10)	0.0238 (6)
H8	0.877	0.8629	0.1279	0.029*
C9	1.0539 (4)	0.94872 (14)	0.17067 (11)	0.0284 (6)
H9	1.1669	0.9537	0.1414	0.034*
C10	1.0643 (4)	0.99563 (14)	0.22104 (10)	0.0265 (6)
H10	1.186	1.0315	0.2273	0.032*
C11	0.8950 (4)	0.98935 (16)	0.26190 (11)	0.0312 (6)
H11	0.8985	1.0223	0.2962	0.037*
C12	0.7199 (4)	0.93598 (15)	0.25395 (11)	0.0292 (6)
H12	0.6035	0.9332	0.2825	0.035*
C13	0.7387 (4)	0.71807 (14)	0.26061 (9)	0.0238 (6)
H13A	0.8228	0.768	0.2697	0.029*
H13B	0.8412	0.6817	0.2389	0.029*
C14	0.6757 (4)	0.67775 (13)	0.31860 (9)	0.0204 (5)
C15	0.8295 (4)	0.67909 (14)	0.36461 (9)	0.0260 (6)
H15	0.9693	0.7054	0.3592	0.031*
C16	0.7830 (5)	0.64296 (14)	0.41807 (10)	0.0320 (6)
H16	0.8903	0.6446	0.449	0.038*
C17	0.5808 (5)	0.60443 (14)	0.42665 (10)	0.0337 (7)
H17	0.5479	0.5798	0.4635	0.04*
C18	0.4265 (5)	0.60195 (14)	0.38115 (10)	0.0310 (6)
H18	0.2875	0.5751	0.3866	0.037*
C19	0.4739 (4)	0.63845 (13)	0.32763 (10)	0.0249 (6)
H19	0.3665	0.6365	0.2967	0.03*

C20	0.4908 (4)	0.49026 (14)	0.10488 (10)	0.0207 (5)
C21	0.7010 (4)	0.45833 (14)	0.11557 (10)	0.0266 (6)
H21	0.8143	0.4914	0.1323	0.032*
C22	0.7485 (4)	0.37847 (14)	0.10219 (11)	0.0323 (6)
H22	0.8935	0.3573	0.1099	0.039*
C23	0.5862 (5)	0.32982 (15)	0.07780 (10)	0.0302 (6)
H23	0.6187	0.2751	0.0688	0.036*
C24	0.3764 (4)	0.36081 (15)	0.06655 (10)	0.0280 (6)
H24	0.2644	0.3274	0.0495	0.034*
C25	0.3280 (4)	0.44034 (14)	0.07988 (9)	0.0238 (6)
H25	0.1828	0.4611	0.072	0.029*
C26	0.1100 (4)	0.63246 (13)	0.06011 (9)	0.0190 (5)
C27	0.1392 (4)	0.59556 (13)	0.00521 (9)	0.0219 (6)
H26	0.2708	0.5651	−0.0023	0.026*
C28	−0.0216 (4)	0.60313 (13)	−0.03807 (10)	0.0248 (6)
H27	−0.0023	0.5767	−0.0749	0.03*
C29	−0.2103 (4)	0.64884 (13)	−0.02809 (10)	0.0267 (6)
H28	−0.3201	0.6542	−0.0582	0.032*
C30	−0.2408 (4)	0.68704 (13)	0.02554 (10)	0.0247 (6)
H29	−0.3707	0.7188	0.0322	0.03*
C31	−0.0813 (4)	0.67875 (14)	0.06942 (10)	0.0227 (5)
H30	−0.1026	0.7049	0.1063	0.027*
N1	0.5617 (3)	0.60656 (11)	0.17005 (7)	0.0184 (4)
O1	0.2994 (3)	0.69326 (9)	0.14300 (6)	0.0263 (4)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0202 (13)	0.0365 (15)	0.0151 (11)	−0.0102 (12)	−0.0007 (10)	0.0047 (12)

C2	0.0219 (14)	0.0240 (13)	0.0191 (12)	−0.0076 (12)	0.0044 (11)	0.0028 (11)
C3	0.0263 (14)	0.0181 (12)	0.0165 (11)	−0.0046 (11)	0.0011 (10)	−0.0041 (10)
C4	0.0191 (13)	0.0203 (13)	0.0203 (12)	−0.0035 (11)	−0.0005 (10)	0.0016 (10)
C5	0.0227 (13)	0.0237 (13)	0.0218 (12)	0.0016 (11)	−0.0025 (10)	0.0013 (11)
C6	0.0199 (13)	0.0283 (14)	0.0241 (12)	−0.0038 (11)	0.0003 (11)	0.0013 (11)
C7	0.0204 (14)	0.0190 (13)	0.0209 (11)	0.0018 (11)	−0.0042 (10)	0.0039 (10)
C8	0.0264 (14)	0.0215 (13)	0.0236 (12)	0.0000 (12)	0.0030 (11)	−0.0065 (11)
C9	0.0290 (15)	0.0255 (14)	0.0307 (14)	0.0015 (13)	0.0076 (12)	0.0025 (12)
C10	0.0274 (14)	0.0158 (13)	0.0363 (15)	0.0003 (12)	−0.0044 (12)	0.0024 (11)
C11	0.0339 (16)	0.0342 (16)	0.0256 (13)	−0.0025 (13)	−0.0005 (12)	−0.0070 (12)
C12	0.0261 (15)	0.0371 (15)	0.0246 (13)	−0.0040 (13)	0.0037 (12)	−0.0035 (12)
C13	0.0200 (14)	0.0263 (14)	0.0251 (12)	−0.0030 (12)	−0.0036 (11)	−0.0004 (11)
C14	0.0261 (14)	0.0149 (12)	0.0203 (12)	0.0050 (11)	−0.0015 (10)	−0.0023 (11)
C15	0.0293 (15)	0.0216 (13)	0.0271 (13)	0.0038 (12)	−0.0066 (11)	−0.0037 (11)
C16	0.0439 (18)	0.0283 (14)	0.0239 (13)	0.0091 (14)	−0.0098 (13)	0.0009 (12)
C17	0.0539 (19)	0.0226 (14)	0.0247 (13)	0.0062 (15)	0.0024 (14)	0.0076 (12)
C18	0.0384 (16)	0.0214 (13)	0.0331 (14)	−0.0010 (13)	0.0049 (13)	0.0025 (12)
C19	0.0295 (15)	0.0211 (13)	0.0243 (12)	−0.0004 (12)	−0.0018 (11)	0.0008 (12)
C20	0.0219 (14)	0.0221 (13)	0.0180 (11)	−0.0033 (11)	0.0022 (10)	0.0042 (11)
C21	0.0231 (15)	0.0271 (14)	0.0298 (14)	−0.0039 (12)	0.0008 (11)	0.0036 (12)
C22	0.0255 (15)	0.0314 (15)	0.0399 (14)	0.0059 (14)	0.0040 (12)	0.0092 (13)
C23	0.0403 (16)	0.0196 (13)	0.0306 (14)	0.0047 (13)	0.0099 (13)	0.0055 (12)
C24	0.0334 (16)	0.0234 (14)	0.0272 (13)	−0.0032 (12)	0.0001 (11)	0.0036 (12)
C25	0.0276 (15)	0.0216 (13)	0.0222 (12)	0.0021 (12)	0.0015 (11)	0.0054 (11)
C26	0.0207 (13)	0.0156 (12)	0.0208 (12)	−0.0048 (11)	−0.0009 (10)	0.0048 (10)
C27	0.0251 (14)	0.0174 (13)	0.0233 (13)	0.0004 (11)	−0.0005 (11)	0.0032 (11)
C28	0.0359 (16)	0.0183 (13)	0.0202 (11)	−0.0012 (13)	−0.0038 (11)	−0.0001 (11)
C29	0.0297 (16)	0.0224 (13)	0.0281 (13)	−0.0056 (12)	−0.0105 (12)	0.0035 (11)

C30	0.0219 (14)	0.0205 (13)	0.0317 (13)	0.0005 (12)	0.0010 (11)	0.0058 (12)
C31	0.0276 (14)	0.0210 (13)	0.0194 (12)	−0.0060 (12)	0.0037 (11)	−0.0007 (11)
N1	0.0203 (10)	0.0189 (10)	0.0161 (9)	−0.0028 (9)	0.0012 (8)	0.0010 (9)
O1	0.0309 (10)	0.0247 (9)	0.0233 (8)	−0.0030 (8)	−0.0018 (8)	−0.0009 (8)

Geometric parameters (Å, °)

C1—N1	1.297 (3)	C15—C16	1.380 (3)
C1—O1	1.349 (3)	C15—H15	0.95
C1—C4	1.463 (3)	C16—C17	1.379 (4)
C2—C3	1.355 (3)	C16—H16	0.95
C2—N1	1.409 (3)	C17—C18	1.383 (4)
C2—C20	1.467 (3)	C17—H17	0.95
C3—O1	1.388 (2)	C18—C19	1.385 (3)
C3—C26	1.459 (3)	C18—H18	0.95
C4—C13	1.512 (3)	C19—H19	0.95
C4—C6	1.517 (3)	C20—C21	1.384 (3)
C4—C5	1.556 (3)	C20—C25	1.397 (3)
C5—C7	1.486 (3)	C21—C22	1.389 (3)
C5—C6	1.489 (3)	C21—H21	0.95
C5—H5	1.0	C22—C23	1.377 (4)
C6—H6A	0.99	C22—H22	0.95
C6—H6B	0.99	C23—C24	1.377 (4)
C7—C12	1.383 (3)	C23—H23	0.95
C7—C8	1.393 (3)	C24—C25	1.384 (3)
C8—C9	1.375 (3)	C24—H24	0.95
C8—H8	0.95	C25—H25	0.95
C9—C10	1.383 (3)	C26—C31	1.392 (3)
C9—H9	0.95	C26—C27	1.397 (3)
C10—C11	1.374 (3)	C27—C28	1.378 (3)

C10—H10	0.95	C27—H26	0.95
C11—C12	1.382 (3)	C28—C29	1.376 (3)
C11—H11	0.95	C28—H27	0.95
C12—H12	0.95	C29—C30	1.383 (3)
C13—C14	1.522 (3)	C29—H28	0.95
C13—H13A	0.99	C30—C31	1.383 (3)
C13—H13B	0.99	C30—H29	0.95
C14—C19	1.385 (3)	C31—H30	0.95
C14—C15	1.389 (3)		
N1—C1—O1	113.5 (2)	C16—C15—C14	121.3 (2)
N1—C1—C4	128.3 (2)	C16—C15—H15	119.4
O1—C1—C4	118.1 (2)	C14—C15—H15	119.4
C3—C2—N1	108.53 (19)	C17—C16—C15	120.1 (2)
C3—C2—C20	133.3 (2)	C17—C16—H16	120.0
N1—C2—C20	118.1 (2)	C15—C16—H16	120.0
C2—C3—O1	107.18 (19)	C16—C17—C18	119.4 (2)
C2—C3—C26	136.9 (2)	C16—C17—H17	120.3
O1—C3—C26	115.8 (2)	C18—C17—H17	120.3
C1—C4—C13	116.3 (2)	C17—C18—C19	120.2 (2)
C1—C4—C6	118.1 (2)	C17—C18—H18	119.9
C13—C4—C6	118.64 (19)	C19—C18—H18	119.9
C1—C4—C5	114.24 (18)	C18—C19—C14	120.9 (2)
C13—C4—C5	118.80 (19)	C18—C19—H19	119.6
C6—C4—C5	57.93 (14)	C14—C19—H19	119.6
C7—C5—C6	123.8 (2)	C21—C20—C25	118.3 (2)
C7—C5—C4	121.93 (19)	C21—C20—C2	120.3 (2)
C6—C5—C4	59.73 (14)	C25—C20—C2	121.2 (2)
C7—C5—H5	113.7	C20—C21—C22	120.8 (2)

C6—C5—H5	113.7	C20—C21—H21	119.6
C4—C5—H5	113.7	C22—C21—H21	119.6
C5—C6—C4	62.34 (15)	C23—C22—C21	120.2 (2)
C5—C6—H6A	117.5	C23—C22—H22	119.9
C4—C6—H6A	117.5	C21—C22—H22	119.9
C5—C6—H6B	117.5	C22—C23—C24	119.7 (2)
C4—C6—H6B	117.5	C22—C23—H23	120.2
H6A—C6—H6B	114.6	C24—C23—H23	120.2
C12—C7—C8	118.1 (2)	C23—C24—C25	120.4 (2)
C12—C7—C5	122.6 (2)	C23—C24—H24	119.8
C8—C7—C5	119.2 (2)	C25—C24—H24	119.8
C9—C8—C7	121.0 (2)	C24—C25—C20	120.6 (2)
C9—C8—H8	119.5	C24—C25—H25	119.7
C7—C8—H8	119.5	C20—C25—H25	119.7
C8—C9—C10	120.5 (2)	C31—C26—C27	118.6 (2)
C8—C9—H9	119.7	C31—C26—C3	119.7 (2)
C10—C9—H9	119.7	C27—C26—C3	121.6 (2)
C11—C10—C9	118.7 (2)	C28—C27—C26	120.4 (2)
C11—C10—H10	120.6	C28—C27—H26	119.8
C9—C10—H10	120.6	C26—C27—H26	119.8
C10—C11—C12	121.1 (2)	C29—C28—C27	120.2 (2)
C10—C11—H11	119.4	C29—C28—H27	119.9
C12—C11—H11	119.4	C27—C28—H27	119.9
C11—C12—C7	120.5 (2)	C28—C29—C30	120.3 (2)
C11—C12—H12	119.8	C28—C29—H28	119.8
C7—C12—H12	119.8	C30—C29—H28	119.8
C4—C13—C14	115.94 (19)	C29—C30—C31	119.7 (2)
C4—C13—H13A	108.3	C29—C30—H29	120.2

C14—C13—H13A	108.3	C31—C30—H29	120.2
C4—C13—H13B	108.3	C30—C31—C26	120.7 (2)
C14—C13—H13B	108.3	C30—C31—H30	119.7
H13A—C13—H13B	107.4	C26—C31—H30	119.7
C19—C14—C15	118.1 (2)	C1—N1—C2	105.22 (19)
C19—C14—C13	123.3 (2)	C1—O1—C3	105.58 (18)
C15—C14—C13	118.5 (2)		
N1—C2—C3—O1	−1.2 (2)	C15—C16—C17—C18	0.4 (4)
C20—C2—C3—O1	175.2 (2)	C16—C17—C18—C19	−0.6 (4)
N1—C2—C3—C26	175.3 (2)	C17—C18—C19—C14	0.2 (4)
C20—C2—C3—C26	−8.3 (5)	C15—C14—C19—C18	0.3 (3)
N1—C1—C4—C13	−4.9 (3)	C13—C14—C19—C18	179.2 (2)
O1—C1—C4—C13	179.11 (19)	C3—C2—C20—C21	159.5 (2)
N1—C1—C4—C6	−155.5 (2)	N1—C2—C20—C21	−24.3 (3)
O1—C1—C4—C6	28.6 (3)	C3—C2—C20—C25	−24.8 (4)
N1—C1—C4—C5	139.4 (2)	N1—C2—C20—C25	151.4 (2)
O1—C1—C4—C5	−36.6 (3)	C25—C20—C21—C22	−0.5 (3)
C1—C4—C5—C7	−137.6 (2)	C2—C20—C21—C22	175.4 (2)
C13—C4—C5—C7	5.8 (3)	C20—C21—C22—C23	0.2 (4)
C6—C4—C5—C7	113.3 (2)	C21—C22—C23—C24	0.2 (4)
C1—C4—C5—C6	109.2 (2)	C22—C23—C24—C25	−0.3 (3)
C13—C4—C5—C6	−107.5 (2)	C23—C24—C25—C20	0.0 (3)
C7—C5—C6—C4	−110.3 (2)	C21—C20—C25—C24	0.4 (3)
C1—C4—C6—C5	−102.4 (2)	C2—C20—C25—C24	−175.4 (2)
C13—C4—C6—C5	107.8 (2)	C2—C3—C26—C31	153.4 (3)
C6—C5—C7—C12	−14.6 (3)	O1—C3—C26—C31	−30.3 (3)
C4—C5—C7—C12	−87.3 (3)	C2—C3—C26—C27	−29.5 (4)
C6—C5—C7—C8	166.3 (2)	O1—C3—C26—C27	146.8 (2)

C4—C5—C7—C8	93.6 (3)	C31—C26—C27—C28	−1.8 (3)
C12—C7—C8—C9	2.1 (3)	C3—C26—C27—C28	−179.0 (2)
C5—C7—C8—C9	−178.8 (2)	C26—C27—C28—C29	1.6 (3)
C7—C8—C9—C10	0.3 (4)	C27—C28—C29—C30	−0.5 (3)
C8—C9—C10—C11	−2.2 (4)	C28—C29—C30—C31	−0.4 (3)
C9—C10—C11—C12	1.6 (4)	C29—C30—C31—C26	0.1 (3)
C10—C11—C12—C7	0.9 (4)	C27—C26—C31—C30	1.0 (3)
C8—C7—C12—C11	−2.7 (4)	C3—C26—C31—C30	178.2 (2)
C5—C7—C12—C11	178.2 (2)	O1—C1—N1—C2	0.4 (2)
C1—C4—C13—C14	−87.8 (2)	C4—C1—N1—C2	−175.8 (2)
C6—C4—C13—C14	62.6 (3)	C3—C2—N1—C1	0.6 (2)
C5—C4—C13—C14	129.6 (2)	C20—C2—N1—C1	−176.5 (2)
C4—C13—C14—C19	20.9 (3)	N1—C1—O1—C3	−1.1 (2)
C4—C13—C14—C15	−160.3 (2)	C4—C1—O1—C3	175.43 (19)
C19—C14—C15—C16	−0.5 (3)	C2—C3—O1—C1	1.4 (2)
C13—C14—C15—C16	−179.4 (2)	C26—C3—O1—C1	−175.95 (18)
C14—C15—C16—C17	0.1 (4)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker *APEX2*; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

2-((1*R*,2*R*)-2-Phenylcyclopropyl)benzo[*d*]oxazole 79a

Crystal data

$C_{32}H_{26}N_2O_2$	
M_r = 470.55	D_x = 1.300 Mg m^{-3}
Monoclinic, $P2_1/n$	Melting point: 37-43 °C
Hall symbol:	radiation, λ = 0.71073 Å
a = 17.900 (3) Å	Cell parameters from 1987 reflections
b = 5.6246 (7) Å	θ = 2.7–23.3°
c = 24.101 (4) Å	μ = 0.08 mm^{-1}
β = 97.843 (4)°	T = 100 K
V = 2403.8 (6) Å^3	Needle, translucent colourless
Z = 4	0.40 × 0.05 × 0.04 mm
F(000) = 992	

Data collection

diffractometer	5947 independent reflections
Radiation source:	3344 reflections with $I > 2\sigma(I)$
?	R_{int} = 0.085
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.3°, θ_{min} = 1.5°
?	h = −23→23
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	k = −7→7
T_{min} = 0.86, T_{max} = 1.00	l = −32→32
22658 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.057$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.140$	$w = 1/[\sigma^2(F_o^2) + (0.0592P)^2 + 0.3835P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.98$	$(\Delta/\sigma)_{max} < 0.001$
5947 reflections	$\Delta\rho_{max} = 0.31$ e Å^{-3}
325 parameters	$\Delta\rho_{min} = -0.28$ e Å^{-3}
0 restraints	Extinction correction: none
constraints	Extinction coefficient:
Primary atom site location: structure-invariant direct methods	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1A	0.59458 (8)	0.7243 (3)	0.03458 (6)	0.0281 (4)
O1B	0.06714 (8)	0.2848 (3)	0.06116 (6)	0.0273 (4)
N1A	0.66557 (9)	1.0535 (3)	0.03302 (7)	0.0219 (4)
N1B	0.08850 (10)	−0.0526 (3)	0.11106 (7)	0.0191 (4)
C3A	0.55584 (13)	1.1211 (4)	−0.10803 (9)	0.0269 (5)
H3A	0.5486	1.2184	−0.1405	0.032*

C2A	0.61024 (12)	1.1833 (4)	−0.06433 (9)	0.0261 (5)
H2A	0.6407	1.3207	−0.066	0.031*
C1A	0.61831 (11)	1.0356 (4)	−0.01791 (9)	0.0207 (5)
C7A	0.64861 (12)	0.8704 (4)	0.06148 (9)	0.0265 (5)
C8A	0.68200 (13)	0.8128 (4)	0.11834 (9)	0.0261 (5)
H8A	0.7131	0.9421	0.1385	0.031*
C10A	0.70955 (12)	0.5600 (4)	0.13277 (9)	0.0250 (5)
H10A	0.699	0.4417	0.1017	0.03*
C11A	0.78289 (12)	0.5284 (4)	0.16944 (8)	0.0222 (5)
C12A	0.80870 (14)	0.6836 (4)	0.21289 (9)	0.0296 (5)
H12A	0.778	0.8131	0.2211	0.036*
C13A	0.87846 (14)	0.6509 (4)	0.24410 (9)	0.0324 (6)
H13A	0.8956	0.7594	0.2733	0.039*
C14A	0.92395 (13)	0.4613 (4)	0.23327 (9)	0.0273 (5)
H14A	0.9721	0.4398	0.2546	0.033*
C4A	0.51106 (13)	0.9193 (4)	−0.10588 (9)	0.0272 (5)
H4A	0.4738	0.8839	−0.1367	0.033*
C6A	0.57427 (11)	0.8336 (4)	−0.01688 (9)	0.0205 (5)
C5A	0.51959 (12)	0.7695 (4)	−0.05988 (9)	0.0245 (5)
H5A	0.4895	0.6311	−0.0582	0.029*
C9A	0.64146 (13)	0.6555 (4)	0.15493 (10)	0.0301 (5)
H9A	0.6463	0.6939	0.1953	0.036*
H9B	0.5916	0.5917	0.1388	0.036*
C16A	0.82876 (12)	0.3392 (4)	0.15935 (9)	0.0237 (5)
H16A	0.8121	0.2309	0.13	0.028*
C15A	0.89811 (13)	0.3049 (4)	0.19104 (9)	0.0248 (5)
H15A	0.9282	0.1726	0.1837	0.03*
C14B	0.39894 (13)	0.5900 (4)	0.25120 (9)	0.0306 (6)

H14B	0.4386	0.6173	0.281	0.037*
C13B	0.40291 (13)	0.4009 (4)	0.21488 (10)	0.0321 (6)
H13B	0.4455	0.2984	0.2198	0.038*
C12B	0.34571 (12)	0.3609 (4)	0.17189 (10)	0.0284 (5)
H12B	0.3495	0.2318	0.147	0.034*
C11B	0.28201 (12)	0.5068 (4)	0.16408 (9)	0.0211 (5)
C10B	0.21870 (12)	0.4635 (4)	0.11874 (9)	0.0227 (5)
H10B	0.1758	0.5783	0.1173	0.027*
C8B	0.19610 (12)	0.2063 (4)	0.10337 (9)	0.0247 (5)
H8B	0.2301	0.0818	0.1227	0.03*
C7B	0.11650 (12)	0.1411 (4)	0.09252 (9)	0.0262 (5)
C6B	0.01184 (12)	−0.0410 (4)	0.09017 (8)	0.0209 (5)
C5B	−0.04668 (13)	−0.1968 (4)	0.09561 (9)	0.0259 (5)
H5B	−0.0388	−0.3386	0.117	0.031*
C4B	−0.11692 (13)	−0.1363 (4)	0.06849 (9)	0.0280 (5)
H4B	−0.1584	−0.2383	0.0716	0.034*
C3B	−0.12875 (13)	0.0718 (4)	0.03640 (9)	0.0261 (5)
H3B	−0.1778	0.106	0.0178	0.031*
C1B	−0.00101 (12)	0.1667 (4)	0.05933 (8)	0.0196 (4)
C2B	−0.07044 (12)	0.2284 (4)	0.03127 (9)	0.0233 (5)
H2B	−0.0779	0.3699	0.0097	0.028*
C15B	0.33685 (13)	0.7387 (4)	0.24382 (9)	0.0285 (5)
H15B	0.3342	0.8703	0.2682	0.034*
C16B	0.27858 (12)	0.6960 (4)	0.20096 (9)	0.0236 (5)
H16B	0.2357	0.7971	0.1967	0.028*
C9B	0.23113 (13)	0.3605 (4)	0.06321 (9)	0.0275 (5)
H9D	0.1983	0.4175	0.0295	0.033*
H9C	0.2837	0.3249	0.0574	0.033*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1A	0.0258 (9)	0.0286 (8)	0.0307 (9)	−0.0018 (7)	0.0068 (7)	0.0044 (7)
O1B	0.0239 (8)	0.0275 (8)	0.0326 (9)	−0.0030 (7)	0.0110 (7)	0.0004 (7)
N1A	0.0150 (9)	0.0269 (10)	0.0241 (9)	−0.0024 (8)	0.0041 (7)	0.0029 (8)
N1B	0.0211 (9)	0.0181 (9)	0.0189 (9)	−0.0018 (8)	0.0049 (7)	−0.0021 (7)
C3A	0.0274 (12)	0.0286 (12)	0.0263 (12)	0.0091 (11)	0.0091 (10)	0.0068 (10)
C2A	0.0237 (12)	0.0231 (11)	0.0332 (13)	−0.0002 (10)	0.0100 (10)	0.0045 (10)
C1A	0.0140 (10)	0.0236 (11)	0.0257 (11)	0.0013 (9)	0.0073 (9)	−0.0007 (9)
C7A	0.0189 (11)	0.0313 (12)	0.0299 (12)	0.0043 (10)	0.0061 (10)	−0.0017 (10)
C8A	0.0257 (12)	0.0258 (12)	0.0277 (12)	−0.0007 (10)	0.0068 (10)	−0.0001 (10)
C10A	0.0276 (12)	0.0225 (11)	0.0263 (12)	−0.0008 (10)	0.0086 (10)	−0.0006 (9)
C11A	0.0274 (12)	0.0226 (11)	0.0184 (10)	−0.0023 (10)	0.0091 (9)	0.0026 (9)
C12A	0.0408 (14)	0.0230 (11)	0.0250 (12)	0.0102 (11)	0.0046 (11)	−0.0011 (10)
C13A	0.0454 (15)	0.0264 (12)	0.0231 (12)	0.0050 (12)	−0.0035 (11)	−0.0022 (10)
C14A	0.0283 (12)	0.0260 (12)	0.0270 (12)	0.0018 (10)	0.0017 (10)	0.0032 (10)
C4A	0.0206 (11)	0.0336 (13)	0.0272 (12)	0.0036 (10)	0.0025 (10)	−0.0037 (10)
C6A	0.0168 (10)	0.0218 (11)	0.0242 (11)	0.0037 (9)	0.0075 (9)	0.0019 (9)
C5A	0.0191 (11)	0.0221 (11)	0.0340 (13)	−0.0013 (9)	0.0093 (10)	−0.0049 (10)
C9A	0.0264 (12)	0.0386 (14)	0.0269 (12)	−0.0022 (11)	0.0098 (10)	0.0020 (11)
C16A	0.0262 (12)	0.0239 (11)	0.0231 (11)	−0.0029 (10)	0.0110 (9)	−0.0015 (9)
C15A	0.0259 (12)	0.0218 (11)	0.0287 (12)	0.0004 (10)	0.0107 (10)	0.0006 (9)
C14B	0.0214 (12)	0.0458 (15)	0.0245 (12)	−0.0080 (11)	0.0026 (10)	0.0085 (11)
C13B	0.0227 (12)	0.0330 (13)	0.0409 (14)	0.0056 (11)	0.0056 (11)	0.0086 (11)
C12B	0.0224 (11)	0.0250 (11)	0.0391 (13)	0.0020 (10)	0.0083 (10)	0.0009 (10)
C11B	0.0185 (10)	0.0221 (11)	0.0244 (11)	−0.0007 (9)	0.0084 (9)	0.0033 (9)
C10B	0.0193 (10)	0.0209 (10)	0.0291 (11)	0.0028 (9)	0.0071 (9)	0.0008 (9)
C8B	0.0200 (11)	0.0228 (11)	0.0319 (12)	0.0025 (9)	0.0060 (10)	−0.0001 (10)
C7B	0.0231 (11)	0.0338 (13)	0.0228 (11)	0.0025 (11)	0.0070 (9)	−0.0052 (10)

C6B	0.0262 (11)	0.0187 (10)	0.0195 (10)	−0.0012 (9)	0.0092 (9)	−0.0038 (9)
C5B	0.0390 (14)	0.0187 (11)	0.0226 (11)	−0.0061 (10)	0.0138 (10)	−0.0031 (9)
C4B	0.0283 (12)	0.0302 (12)	0.0280 (12)	−0.0108 (11)	0.0130 (10)	−0.0089 (10)
C3B	0.0220 (11)	0.0309 (12)	0.0269 (12)	−0.0004 (10)	0.0086 (10)	−0.0084 (10)
C1B	0.0202 (11)	0.0191 (10)	0.0216 (10)	−0.0036 (9)	0.0106 (9)	−0.0049 (9)
C2B	0.0250 (12)	0.0203 (11)	0.0261 (11)	0.0005 (9)	0.0094 (10)	−0.0028 (9)
C15B	0.0275 (13)	0.0317 (13)	0.0279 (12)	−0.0030 (11)	0.0093 (10)	−0.0013 (10)
C16B	0.0211 (11)	0.0237 (11)	0.0280 (11)	0.0023 (10)	0.0106 (9)	0.0018 (9)
C9B	0.0211 (11)	0.0316 (12)	0.0314 (12)	−0.0013 (10)	0.0093 (10)	−0.0012 (10)

Geometric parameters (Å, °)

O1A—C7A	1.363 (3)	C9A—H9B	0.99
O1A—C6A	1.387 (2)	C16A—C15A	1.379 (3)
O1B—C7B	1.350 (3)	C16A—H16A	0.95
O1B—C1B	1.384 (2)	C15A—H15A	0.95
N1A—C7A	1.296 (3)	C14B—C15B	1.383 (3)
N1A—C1A	1.396 (3)	C14B—C13B	1.385 (3)
N1B—C7B	1.303 (3)	C14B—H14B	0.95
N1B—C6B	1.397 (3)	C13B—C12B	1.372 (3)
C3A—C2A	1.378 (3)	C13B—H13B	0.95
C3A—C4A	1.394 (3)	C12B—C11B	1.397 (3)
C3A—H3A	0.95	C12B—H12B	0.95
C2A—C1A	1.385 (3)	C11B—C16B	1.393 (3)
C2A—H2A	0.95	C11B—C10B	1.483 (3)
C1A—C6A	1.385 (3)	C10B—C9B	1.502 (3)
C7A—C8A	1.455 (3)	C10B—C8B	1.534 (3)
C8A—C9A	1.504 (3)	C10B—H10B	1.0
C8A—C10A	1.530 (3)	C8B—C7B	1.460 (3)
C8A—H8A	1.0	C8B—C9B	1.499 (3)

C10A—C11A	1.490 (3)	C8B—H8B	1.0
C10A—C9A	1.496 (3)	C6B—C5B	1.386 (3)
C10A—H10A	1.0	C6B—C1B	1.387 (3)
C11A—C16A	1.386 (3)	C5B—C4B	1.378 (3)
C11A—C12A	1.393 (3)	C5B—H5B	0.95
C12A—C13A	1.379 (3)	C4B—C3B	1.403 (3)
C12A—H12A	0.95	C4B—H4B	0.95
C13A—C14A	1.388 (3)	C3B—C2B	1.384 (3)
C13A—H13A	0.95	C3B—H3B	0.95
C14A—C15A	1.376 (3)	C1B—C2B	1.376 (3)
C14A—H14A	0.95	C2B—H2B	0.95
C4A—C5A	1.385 (3)	C15B—C16B	1.385 (3)
C4A—H4A	0.95	C15B—H15B	0.95
C6A—C5A	1.373 (3)	C16B—H16B	0.95
C5A—H5A	0.95	C9B—H9D	0.99
C9A—H9A	0.99	C9B—H9C	0.99
C7A—O1A—C6A	103.93 (16)	C14A—C15A—H15A	119.8
C7B—O1B—C1B	103.69 (16)	C16A—C15A—H15A	119.8
C7A—N1A—C1A	104.50 (17)	C15B—C14B—C13B	119.5 (2)
C7B—N1B—C6B	104.00 (17)	C15B—C14B—H14B	120.2
C2A—C3A—C4A	121.9 (2)	C13B—C14B—H14B	120.2
C2A—C3A—H3A	119.1	C12B—C13B—C14B	120.4 (2)
C4A—C3A—H3A	119.1	C12B—C13B—H13B	119.8
C3A—C2A—C1A	116.7 (2)	C14B—C13B—H13B	119.8
C3A—C2A—H2A	121.6	C13B—C12B—C11B	121.1 (2)
C1A—C2A—H2A	121.6	C13B—C12B—H12B	119.4
C6A—C1A—C2A	120.6 (2)	C11B—C12B—H12B	119.4
C6A—C1A—N1A	108.75 (18)	C16B—C11B—C12B	118.0 (2)

C2A—C1A—N1A	130.60 (19)	C16B—C11B—C10B	119.98 (19)
N1A—C7A—O1A	115.42 (19)	C12B—C11B—C10B	122.05 (19)
N1A—C7A—C8A	125.4 (2)	C11B—C10B—C9B	121.90 (19)
O1A—C7A—C8A	119.2 (2)	C11B—C10B—C8B	118.85 (18)
C7A—C8A—C9A	120.9 (2)	C9B—C10B—C8B	59.17 (14)
C7A—C8A—C10A	119.95 (19)	C11B—C10B—H10B	115.1
C9A—C8A—C10A	59.07 (14)	C9B—C10B—H10B	115.1
C7A—C8A—H8A	115.1	C8B—C10B—H10B	115.1
C9A—C8A—H8A	115.1	C7B—C8B—C9B	120.9 (2)
C10A—C8A—H8A	115.1	C7B—C8B—C10B	119.94 (19)
C11A—C10A—C9A	121.73 (19)	C9B—C8B—C10B	59.36 (14)
C11A—C10A—C8A	118.45 (19)	C7B—C8B—H8B	115.1
C9A—C10A—C8A	59.61 (14)	C9B—C8B—H8B	115.1
C11A—C10A—H10A	115.2	C10B—C8B—H8B	115.1
C9A—C10A—H10A	115.2	N1B—C7B—O1B	116.07 (19)
C8A—C10A—H10A	115.2	N1B—C7B—C8B	124.1 (2)
C16A—C11A—C12A	118.0 (2)	O1B—C7B—C8B	119.9 (2)
C16A—C11A—C10A	118.86 (19)	C5B—C6B—C1B	120.8 (2)
C12A—C11A—C10A	123.1 (2)	C5B—C6B—N1B	130.8 (2)
C13A—C12A—C11A	120.6 (2)	C1B—C6B—N1B	108.40 (18)
C13A—C12A—H12A	119.7	C4B—C5B—C6B	116.8 (2)
C11A—C12A—H12A	119.7	C4B—C5B—H5B	121.6
C12A—C13A—C14A	120.7 (2)	C6B—C5B—H5B	121.6
C12A—C13A—H13A	119.7	C5B—C4B—C3B	121.8 (2)
C14A—C13A—H13A	119.7	C5B—C4B—H4B	119.1
C15A—C14A—C13A	118.9 (2)	C3B—C4B—H4B	119.1
C15A—C14A—H14A	120.5	C2B—C3B—C4B	121.4 (2)
C13A—C14A—H14A	120.5	C2B—C3B—H3B	119.3

C5A—C4A—C3A	121.6 (2)	C4B—C3B—H3B	119.3
C5A—C4A—H4A	119.2	C2B—C1B—O1B	128.85 (19)
C3A—C4A—H4A	119.2	C2B—C1B—C6B	123.28 (19)
C5A—C6A—C1A	123.4 (2)	O1B—C1B—C6B	107.84 (18)
C5A—C6A—O1A	129.15 (19)	C1B—C2B—C3B	115.9 (2)
C1A—C6A—O1A	107.39 (18)	C1B—C2B—H2B	122.0
C6A—C5A—C4A	115.7 (2)	C3B—C2B—H2B	122.0
C6A—C5A—H5A	122.1	C14B—C15B—C16B	120.1 (2)
C4A—C5A—H5A	122.1	C14B—C15B—H15B	120.0
C10A—C9A—C8A	61.31 (14)	C16B—C15B—H15B	120.0
C10A—C9A—H9A	117.6	C15B—C16B—C11B	120.9 (2)
C8A—C9A—H9A	117.6	C15B—C16B—H16B	119.5
C10A—C9A—H9B	117.6	C11B—C16B—H16B	119.5
C8A—C9A—H9B	117.6	C8B—C9B—C10B	61.47 (14)
H9A—C9A—H9B	114.7	C8B—C9B—H9D	117.6
C15A—C16A—C11A	121.3 (2)	C10B—C9B—H9D	117.6
C15A—C16A—H16A	119.3	C8B—C9B—H9C	117.6
C11A—C16A—H16A	119.3	C10B—C9B—H9C	117.6
C14A—C15A—C16A	120.4 (2)	H9D—C9B—H9C	114.7
C4A—C3A—C2A—C1A	−0.1 (3)	C15B—C14B—C13B—C12B	−0.1 (3)
C3A—C2A—C1A—C6A	1.3 (3)	C14B—C13B—C12B—C11B	−0.8 (3)
C3A—C2A—C1A—N1A	−177.5 (2)	C13B—C12B—C11B—C16B	0.6 (3)
C7A—N1A—C1A—C6A	−0.3 (2)	C13B—C12B—C11B—C10B	−178.5 (2)
C7A—N1A—C1A—C2A	178.6 (2)	C16B—C11B—C10B—C9B	148.0 (2)
C1A—N1A—C7A—O1A	1.0 (2)	C12B—C11B—C10B—C9B	−32.9 (3)
C1A—N1A—C7A—C8A	−178.7 (2)	C16B—C11B—C10B—C8B	−142.3 (2)
C6A—O1A—C7A—N1A	−1.3 (2)	C12B—C11B—C10B—C8B	36.9 (3)
C6A—O1A—C7A—C8A	178.43 (18)	C11B—C10B—C8B—C7B	137.7 (2)

N1A—C7A—C8A—C9A	157.6 (2)	C9B—C10B—C8B—C7B	−110.4 (2)
O1A—C7A—C8A—C9A	−22.1 (3)	C11B—C10B—C8B—C9B	−111.9 (2)
N1A—C7A—C8A—C10A	−132.6 (2)	C6B—N1B—C7B—O1B	0.1 (2)
O1A—C7A—C8A—C10A	47.7 (3)	C6B—N1B—C7B—C8B	−179.40 (19)
C7A—C8A—C10A—C11A	137.7 (2)	C1B—O1B—C7B—N1B	−0.3 (2)
C9A—C8A—C10A—C11A	−112.1 (2)	C1B—O1B—C7B—C8B	179.24 (18)
C7A—C8A—C10A—C9A	−110.3 (2)	C9B—C8B—C7B—N1B	152.7 (2)
C9A—C10A—C11A—C16A	145.8 (2)	C10B—C8B—C7B—N1B	−137.2 (2)
C8A—C10A—C11A—C16A	−144.2 (2)	C9B—C8B—C7B—O1B	−26.8 (3)
C9A—C10A—C11A—C12A	−35.8 (3)	C10B—C8B—C7B—O1B	43.3 (3)
C8A—C10A—C11A—C12A	34.3 (3)	C7B—N1B—C6B—C5B	179.6 (2)
C16A—C11A—C12A—C13A	1.1 (3)	C7B—N1B—C6B—C1B	0.1 (2)
C10A—C11A—C12A—C13A	−177.4 (2)	C1B—C6B—C5B—C4B	0.8 (3)
C11A—C12A—C13A—C14A	−0.8 (4)	N1B—C6B—C5B—C4B	−178.5 (2)
C12A—C13A—C14A—C15A	−0.4 (3)	C6B—C5B—C4B—C3B	0.6 (3)
C2A—C3A—C4A—C5A	−0.7 (3)	C5B—C4B—C3B—C2B	−1.1 (3)
C2A—C1A—C6A—C5A	−1.7 (3)	C7B—O1B—C1B—C2B	−177.4 (2)
N1A—C1A—C6A—C5A	177.38 (19)	C7B—O1B—C1B—C6B	0.3 (2)
C2A—C1A—C6A—O1A	−179.55 (18)	C5B—C6B—C1B—C2B	−1.9 (3)
N1A—C1A—C6A—O1A	−0.5 (2)	N1B—C6B—C1B—C2B	177.59 (18)
C7A—O1A—C6A—C5A	−176.7 (2)	C5B—C6B—C1B—O1B	−179.80 (17)
C7A—O1A—C6A—C1A	1.0 (2)	N1B—C6B—C1B—O1B	−0.3 (2)
C1A—C6A—C5A—C4A	0.8 (3)	O1B—C1B—C2B—C3B	178.81 (19)
O1A—C6A—C5A—C4A	178.17 (19)	C6B—C1B—C2B—C3B	1.4 (3)
C3A—C4A—C5A—C6A	0.4 (3)	C4B—C3B—C2B—C1B	0.1 (3)
C11A—C10A—C9A—C8A	106.7 (2)	C13B—C14B—C15B—C16B	1.1 (3)
C7A—C8A—C9A—C10A	108.6 (2)	C14B—C15B—C16B—C11B	−1.3 (3)
C12A—C11A—C16A—C15A	−0.3 (3)	C12B—C11B—C16B—C15B	0.4 (3)

C10A—C11A—C16A—C15A	178.29 (19)	C10B—C11B—C16B—C15B	179.58 (19)
C13A—C14A—C15A—C16A	1.3 (3)	C7B—C8B—C9B—C10B	108.8 (2)
C11A—C16A—C15A—C14A	−0.9 (3)	C11B—C10B—C9B—C8B	106.9 (2)

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2012.6.0.0; cell refinement: *SAINT* V8.18C (Bruker AXS Inc., 2011); data reduction: *SAINT* V8.18C (Bruker AXS Inc., 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

2-((1*R*,2*S*)-1-Methyl-2-phenylcyclopropyl)benzo[*d*]oxazole 80a

Crystal data

$C_{17}H_{15}NO$	$F(000) = 264$
$M_r = 249.30$	
Triclinic, $P\bar{1}$	$D_x = 1.284$ Mg m^{-3}
Hall symbol: ?	Melting point: 35-41 °C
$a = 5.9023$ (3) Å	radiation, $\lambda = 1.54178$ Å
$b = 8.7324$ (4) Å	Cell parameters from 5747 reflections
$c = 13.3472$ (7) Å	$\theta = 5.4–63.7°$
$\alpha = 92.843$ (3)°	$\mu = 0.63$ mm^{-1}
$\beta = 95.426$ (3)°	$T = 100$ K
$\gamma = 109.067$ (2)°	Plate, translucent colourless
$V = 644.90$ (6) Å^3	0.40 × 0.20 × 0.04 mm
$Z = 2$	

Data collection

diffractometer	2038 independent reflections
Radiation source: ?	1971 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.022$
Detector resolution: 8.3333 pixels mm^{-1}	$\theta_{max} = 63.7°$, $\theta_{min} = 5.4°$
	$h = -6 \rightarrow 5$
Absorption correction: multi-scan *SADABS* V2012/1 (Bruker AXS Inc.)	$k = -8 \rightarrow 10$
$T_{min} = 0.84$, $T_{max} = 0.98$	$l = -13 \rightarrow 15$
7037 measured reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map

Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.044$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.122$	$w = 1/[\sigma^2(F_o^2) + (0.0713P)^2 + 0.366P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} < 0.001$
2038 reflections	$\Delta\rho_{max} = 0.33$ e Å^{-3}
173 parameters	$\Delta\rho_{min} = -0.24$ e Å^{-3}
0 restraints	Extinction correction: none
? constraints	Extinction coefficient: ?
Primary atom site location: structure-invariant direct methods	

Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.24984 (18)	0.29782 (12)	0.05979 (8)	0.0208 (3)
N1	−0.1280 (2)	0.12883 (14)	0.06764 (9)	0.0173 (3)
C1	−0.0185 (3)	0.42337 (19)	−0.16767 (12)	0.0253 (4)
H1	0.0146	0.4936	−0.2205	0.03*
C2	0.1689 (3)	0.42546 (18)	−0.09593 (11)	0.0218 (4)
H3	0.33	0.4952	−0.0976	0.026*
C3	0.1059 (3)	0.31975 (17)	−0.02221 (11)	0.0173 (3)
C4	0.0945 (3)	0.18310 (18)	0.10965 (11)	0.0196 (4)

C5	0.1869 (3)	0.13656 (18)	0.20451 (11)	0.0187 (4)
C6	0.3618 (3)	0.27570 (19)	0.27761 (12)	0.0225 (4)
H8	0.4032	0.3856	0.2513	0.027*
C7	0.3385 (3)	0.27488 (18)	0.38807 (12)	0.0221 (4)
C8	0.1721 (4)	0.3330 (3)	0.42691 (14)	0.0479 (6)
H7	0.0701	0.3707	0.3825	0.057*
C9	0.1493 (4)	0.3379 (3)	0.52907 (14)	0.0488 (6)
H6	0.0343	0.3803	0.5538	0.059*
C10	0.2894 (3)	0.2828 (2)	0.59441 (12)	0.0269 (4)
H2	0.2736	0.2862	0.6646	0.032*
C11	−0.2552 (3)	0.3202 (2)	−0.16398 (12)	0.0257 (4)
H15	−0.3785	0.323	−0.2143	0.031*
C12	−0.3151 (3)	0.21445 (19)	−0.08939 (12)	0.0234 (4)
H14	−0.4759	0.1446	−0.0873	0.028*
C13	−0.1278 (3)	0.21581 (18)	−0.01774 (11)	0.0182 (3)
C14	0.4537 (4)	0.2224 (3)	0.55714 (15)	0.0520 (6)
H4	0.5511	0.1816	0.6018	0.062*
C15	0.4803 (4)	0.2197 (3)	0.45466 (15)	0.0467 (6)
H5	0.5979	0.1791	0.4304	0.056*
C16	0.4523 (3)	0.1595 (2)	0.22259 (12)	0.0255 (4)
H10	0.5006	0.0799	0.2621	0.031*
H9	0.5515	0.1999	0.1675	0.031*
C17	0.0090 (3)	−0.00362 (19)	0.24778 (12)	0.0233 (4)
H11	−0.13	0.0269	0.2638	0.035*
H12	0.0871	−0.0302	0.3094	0.035*
H13	−0.0455	−0.0986	0.1982	0.035*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0187 (6)	0.0227 (6)	0.0195 (6)	0.0052 (4)	0.0027 (4)	0.0007 (4)
N1	0.0163 (6)	0.0196 (6)	0.0163 (6)	0.0060 (5)	0.0055 (5)	−0.0013 (5)
C1	0.0364 (9)	0.0235 (8)	0.0186 (8)	0.0137 (7)	0.0025 (7)	−0.0003 (6)
C2	0.0235 (8)	0.0200 (8)	0.0207 (8)	0.0054 (6)	0.0047 (6)	−0.0018 (6)
C3	0.0185 (8)	0.0184 (7)	0.0150 (7)	0.0071 (6)	0.0011 (6)	−0.0037 (6)
C4	0.0239 (8)	0.0193 (8)	0.0185 (8)	0.0099 (6)	0.0081 (6)	−0.0015 (6)
C5	0.0187 (8)	0.0191 (8)	0.0196 (8)	0.0073 (6)	0.0057 (6)	−0.0008 (6)
C6	0.0207 (8)	0.0217 (8)	0.0229 (8)	0.0038 (6)	0.0038 (6)	0.0012 (6)
C7	0.0215 (8)	0.0190 (7)	0.0225 (8)	0.0028 (6)	0.0019 (6)	0.0001 (6)
C8	0.0641 (14)	0.0806 (16)	0.0230 (10)	0.0565 (13)	0.0040 (9)	0.0075 (10)
C9	0.0539 (13)	0.0897 (17)	0.0238 (10)	0.0511 (13)	0.0090 (9)	0.0047 (10)
C10	0.0292 (9)	0.0272 (9)	0.0183 (8)	0.0013 (7)	0.0024 (7)	0.0007 (6)
C11	0.0283 (9)	0.0288 (9)	0.0215 (8)	0.0151 (7)	−0.0052 (7)	−0.0068 (7)
C12	0.0183 (8)	0.0258 (8)	0.0251 (8)	0.0081 (6)	0.0005 (6)	−0.0086 (6)
C13	0.0182 (7)	0.0193 (7)	0.0179 (8)	0.0075 (6)	0.0045 (6)	−0.0040 (6)
C14	0.0686 (15)	0.0816 (16)	0.0236 (10)	0.0516 (14)	−0.0033 (10)	0.0038 (10)
C15	0.0477 (12)	0.0796 (16)	0.0272 (10)	0.0424 (12)	0.0007 (9)	−0.0003 (10)
C16	0.0201 (8)	0.0343 (9)	0.0240 (8)	0.0107 (7)	0.0059 (6)	0.0028 (7)
C17	0.0252 (8)	0.0211 (8)	0.0228 (8)	0.0060 (7)	0.0048 (6)	0.0011 (6)

Geometric parameters (Å, °)

O1—C4	1.3669 (18)	C8—C9	1.383 (3)
O1—C3	1.3813 (18)	C8—H7	0.95
N1—C4	1.300 (2)	C9—C10	1.357 (3)
N1—C13	1.400 (2)	C9—H6	0.95
C1—C2	1.387 (2)	C10—C14	1.366 (3)
C1—C11	1.400 (2)	C10—H2	0.95
C1—H1	0.95	C11—C12	1.383 (2)

C2—C3	1.376 (2)	C11—H15	0.95
C2—H3	0.95	C12—C13	1.388 (2)
C3—C13	1.390 (2)	C12—H14	0.95
C4—C5	1.460 (2)	C14—C15	1.391 (3)
C5—C16	1.507 (2)	C14—H4	0.95
C5—C17	1.510 (2)	C15—H5	0.95
C5—C6	1.538 (2)	C16—H10	0.99
C6—C16	1.486 (2)	C16—H9	0.99
C6—C7	1.494 (2)	C17—H11	0.98
C6—H8	1.0	C17—H12	0.98
C7—C8	1.374 (3)	C17—H13	0.98
C7—C15	1.374 (3)		
C4—O1—C3	104.22 (11)	C10—C9—H6	119.6
C4—N1—C13	104.51 (12)	C8—C9—H6	119.6
C2—C1—C11	121.54 (15)	C9—C10—C14	118.57 (16)
C2—C1—H1	119.2	C9—C10—H2	120.7
C11—C1—H1	119.2	C14—C10—H2	120.7
C3—C2—C1	115.54 (15)	C12—C11—C1	122.10 (15)
C3—C2—H3	122.2	C12—C11—H15	119.0
C1—C2—H3	122.2	C1—C11—H15	119.0
C2—C3—O1	128.73 (14)	C11—C12—C13	116.48 (15)
C2—C3—C13	123.69 (14)	C11—C12—H14	121.8
O1—C3—C13	107.56 (13)	C13—C12—H14	121.8
N1—C4—O1	115.16 (13)	C12—C13—C3	120.64 (15)
N1—C4—C5	126.11 (14)	C12—C13—N1	130.79 (14)
O1—C4—C5	118.70 (13)	C3—C13—N1	108.54 (13)
C4—C5—C16	118.31 (13)	C10—C14—C15	120.91 (18)
C4—C5—C17	114.65 (13)	C10—C14—H4	119.5

C16—C5—C17	119.14 (13)	C15—C14—H4	119.5
C4—C5—C6	116.29 (13)	C7—C15—C14	120.77 (19)
C16—C5—C6	58.42 (10)	C7—C15—H5	119.6
C17—C5—C6	118.64 (13)	C14—C15—H5	119.6
C16—C6—C7	122.81 (14)	C6—C16—C5	61.85 (10)
C16—C6—C5	59.73 (10)	C6—C16—H10	117.6
C7—C6—C5	119.32 (13)	C5—C16—H10	117.6
C16—C6—H8	114.7	C6—C16—H9	117.6
C7—C6—H8	114.7	C5—C16—H9	117.6
C5—C6—H8	114.7	H10—C16—H9	114.7
C8—C7—C15	117.37 (16)	C5—C17—H11	109.5
C8—C7—C6	119.89 (15)	C5—C17—H12	109.5
C15—C7—C6	122.73 (16)	H11—C17—H12	109.5
C7—C8—C9	121.56 (17)	C5—C17—H13	109.5
C7—C8—H7	119.2	H11—C17—H13	109.5
C9—C8—H7	119.2	H12—C17—H13	109.5
C10—C9—C8	120.80 (18)		
C11—C1—C2—C3	0.2 (2)	C5—C6—C7—C15	98.2 (2)
C1—C2—C3—O1	−178.07 (14)	C15—C7—C8—C9	0.8 (3)
C1—C2—C3—C13	0.2 (2)	C6—C7—C8—C9	−178.4 (2)
C4—O1—C3—C2	177.89 (15)	C7—C8—C9—C10	−1.0 (4)
C4—O1—C3—C13	−0.59 (15)	C8—C9—C10—C14	0.0 (3)
C13—N1—C4—O1	−1.21 (17)	C2—C1—C11—C12	−0.4 (3)
C13—N1—C4—C5	176.72 (14)	C1—C11—C12—C13	0.1 (2)
C3—O1—C4—N1	1.17 (16)	C11—C12—C13—C3	0.3 (2)
C3—O1—C4—C5	−176.93 (13)	C11—C12—C13—N1	178.02 (15)
N1—C4—C5—C16	157.40 (15)	C2—C3—C13—C12	−0.5 (2)
O1—C4—C5—C16	−24.7 (2)	O1—C3—C13—C12	178.11 (13)

N1—C4—C5—C17	8.6 (2)	C2—C3—C13—N1	−178.65 (14)
O1—C4—C5—C17	−173.58 (12)	O1—C3—C13—N1	−0.08 (16)
N1—C4—C5—C6	−136.01 (15)	C4—N1—C13—C12	−177.20 (16)
O1—C4—C5—C6	41.86 (19)	C4—N1—C13—C3	0.75 (16)
C4—C5—C6—C16	−108.50 (15)	C9—C10—C14—C15	1.1 (4)
C17—C5—C6—C16	108.40 (15)	C8—C7—C15—C14	0.3 (3)
C4—C5—C6—C7	138.44 (15)	C6—C7—C15—C14	179.5 (2)
C16—C5—C6—C7	−113.06 (16)	C10—C14—C15—C7	−1.3 (4)
C17—C5—C6—C7	−4.7 (2)	C7—C6—C16—C5	107.36 (16)
C16—C6—C7—C8	−153.63 (18)	C4—C5—C16—C6	105.03 (15)
C5—C6—C7—C8	−82.6 (2)	C17—C5—C16—C6	−107.54 (15)
C16—C6—C7—C15	27.2 (2)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes. Data collection: Bruker Instrument Service v2012.12.0.3; cell refinement: *SAINT* V8.27B (Bruker AXS Inc., 2012); data reduction: *SAINT* V8.27B (Bruker AXS Inc., 2012); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

2-((1*S*,2*S*)-1-Benzyl-2-phenylcyclopropyl)benzo[*d*]oxazole 80b

Crystal data

$C_{23}H_{19}NO$	
M_r = 325.39	D_x = 1.252 Mg m^{-3}
Monoclinic, $P2_1$	Melting point: 96-106 °C
Hall symbol:	radiation, λ = 0.71073 Å
a = 5.976 (3) Å	Cell parameters from 5268 reflections
b = 16.911 (7) Å	θ = 2.4–28.1°
c = 8.636 (4) Å	μ = 0.08 mm^{-1}
β = 98.563 (9)°	T = 100 K
V = 863.0 (6) Å^3	Block, lustrous colourless
Z = 2	0.38 × 0.26 × 0.06 mm
F(000) = 344	

Data collection

diffractometer	4309 independent reflections
Radiation source:	3666 reflections with $I > 2\sigma(I)$
	R_{int} = 0.079
Detector resolution: 8.3333 pixels mm^{-1}	θ_{max} = 28.7°, θ_{min} = 2.4°
	h = −7→8
Absorption correction: multi-scan *SADABS* V2008/1 (Bruker AXS Inc.)	k = −22→22
T_{min} = 0.77, T_{max} = 1.00	l = −11→11
14327 measured reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.066$	$w = 1/[\sigma^2(F_o^2) + (0.0672P)^2 + 0.7691P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.161$	$(\Delta/\sigma)_{max} = 0.001$
$S = 1.01$	$\Delta\rho_{max} = 0.49$ e Å^{-3}
4309 reflections	$\Delta\rho_{min} = -0.29$ e Å^{-3}
226 parameters	Extinction correction: none
1 restraint	Extinction coefficient:
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0 (2)
Secondary atom site location: difference Fourier map	

Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.9248 (5)	0.50962 (16)	0.6307 (3)	0.0189 (5)
C2	1.0615 (5)	0.40346 (17)	0.7385 (3)	0.0205 (5)
C3	0.8403 (5)	0.38752 (15)	0.6690 (3)	0.0196 (6)
C4	0.7388 (6)	0.31498 (18)	0.6773 (4)	0.0288 (7)
H4	0.5883	0.305	0.6284	0.035*
C5	0.8697 (7)	0.25724 (18)	0.7614 (4)	0.0365 (8)

H5	0.8066	0.2062	0.7711	0.044*
C6	1.0916 (7)	0.27187 (19)	0.8323 (4)	0.0368 (8)
H6	1.1761	0.2305	0.8877	0.044*
C7	1.1904 (6)	0.34487 (18)	0.8236 (4)	0.0292 (7)
H7	1.3403	0.355	0.8735	0.035*
C8	0.8886 (4)	0.59226 (15)	0.5803 (3)	0.0151 (5)
C9	0.9374 (4)	0.65345 (15)	0.7142 (3)	0.0154 (5)
H9	0.9915	0.6299	0.8193	0.018*
C10	1.0972 (4)	0.64363 (16)	0.5983 (3)	0.0196 (5)
H10A	1.2445	0.618	0.6349	0.023*
H10B	1.1029	0.6864	0.5208	0.023*
C11	0.7884 (4)	0.72442 (15)	0.7181 (3)	0.0163 (5)
C12	0.8267 (5)	0.79580 (15)	0.6450 (4)	0.0215 (6)
H12	0.9533	0.8011	0.591	0.026*
C13	0.6801 (6)	0.85894 (16)	0.6509 (4)	0.0265 (6)
H13	0.7067	0.907	0.5998	0.032*
C14	0.4958 (5)	0.85303 (16)	0.7301 (4)	0.0235 (6)
H14	0.3969	0.8968	0.734	0.028*
C15	0.4571 (5)	0.78282 (17)	0.8036 (4)	0.0231 (6)
H15	0.3306	0.7781	0.8578	0.028*
C16	0.6025 (5)	0.71914 (16)	0.7985 (3)	0.0188 (5)
H16	0.5752	0.6713	0.8503	0.023*
C17	0.6951 (4)	0.60778 (14)	0.4503 (3)	0.0165 (5)
H17A	0.683	0.6656	0.4332	0.02*
H17B	0.5532	0.59	0.4858	0.02*
C18	0.7115 (4)	0.56863 (14)	0.2951 (3)	0.0142 (5)
C19	0.9101 (5)	0.53472 (17)	0.2587 (3)	0.0200 (6)
H19	1.0437	0.536	0.3336	0.024*

C20	0.9147 (5)	0.49894 (18)	0.1137 (4)	0.0243 (6)
H20	1.0505	0.4753	0.0913	0.029*
C21	0.7223 (5)	0.49762 (17)	0.0022 (3)	0.0233 (6)
H21	0.7264	0.4736	−0.0968	0.028*
C22	0.5234 (5)	0.53159 (17)	0.0359 (3)	0.0212 (6)
H22	0.3905	0.5308	−0.0398	0.025*
C23	0.5202 (5)	0.56663 (15)	0.1810 (3)	0.0171 (5)
H23	0.3837	0.5899	0.2032	0.021*
N1	1.1092 (4)	0.48150 (13)	0.7124 (3)	0.0176 (5)
O1	0.7528 (3)	0.45683 (11)	0.5981 (2)	0.0198 (4)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0245 (14)	0.0182 (12)	0.0150 (12)	0.0018 (10)	0.0059 (10)	−0.0046 (9)
C2	0.0223 (13)	0.0221 (13)	0.0163 (12)	0.0040 (10)	0.0003 (10)	−0.0045 (10)
C3	0.0269 (14)	0.0165 (13)	0.0152 (12)	0.0036 (10)	0.0029 (11)	−0.0025 (9)
C4	0.0406 (19)	0.0237 (15)	0.0219 (15)	−0.0073 (13)	0.0035 (14)	−0.0032 (11)
C5	0.070 (3)	0.0153 (14)	0.0241 (16)	−0.0066 (14)	0.0051 (16)	0.0006 (11)
C6	0.060 (2)	0.0251 (16)	0.0225 (16)	0.0141 (15)	−0.0037 (15)	0.0016 (12)
C7	0.0345 (17)	0.0278 (15)	0.0229 (15)	0.0110 (13)	−0.0033 (13)	0.0002 (11)
C8	0.0153 (11)	0.0143 (11)	0.0157 (12)	−0.0003 (9)	0.0027 (9)	−0.0036 (9)
C9	0.0149 (12)	0.0170 (12)	0.0136 (12)	−0.0013 (9)	−0.0002 (10)	−0.0043 (9)
C10	0.0151 (12)	0.0212 (13)	0.0232 (13)	−0.0024 (10)	0.0054 (10)	−0.0034 (10)
C11	0.0170 (12)	0.0163 (12)	0.0140 (12)	−0.0013 (9)	−0.0029 (10)	−0.0057 (9)
C12	0.0241 (15)	0.0161 (13)	0.0244 (14)	−0.0030 (10)	0.0034 (11)	−0.0010 (10)
C13	0.0349 (17)	0.0136 (13)	0.0296 (16)	−0.0019 (11)	0.0006 (13)	0.0003 (10)
C14	0.0235 (14)	0.0166 (13)	0.0283 (15)	0.0049 (10)	−0.0034 (12)	−0.0090 (11)
C15	0.0207 (14)	0.0240 (14)	0.0240 (15)	0.0019 (11)	0.0011 (11)	−0.0071 (11)

C16	0.0213 (13)	0.0163 (12)	0.0185 (12)	−0.0016 (10)	0.0017 (10)	−0.0033 (10)
C17	0.0169 (12)	0.0149 (12)	0.0174 (12)	0.0033 (9)	0.0013 (10)	−0.0046 (9)
C18	0.0146 (12)	0.0109 (11)	0.0171 (12)	−0.0018 (8)	0.0022 (10)	0.0005 (9)
C19	0.0145 (12)	0.0259 (14)	0.0196 (13)	−0.0003 (10)	0.0019 (10)	−0.0045 (10)
C20	0.0183 (14)	0.0342 (16)	0.0222 (14)	−0.0017 (11)	0.0089 (11)	−0.0070 (11)
C21	0.0299 (15)	0.0280 (15)	0.0128 (13)	−0.0059 (12)	0.0059 (11)	−0.0030 (10)
C22	0.0229 (14)	0.0238 (13)	0.0153 (13)	−0.0045 (10)	−0.0022 (11)	−0.0012 (10)
C23	0.0170 (12)	0.0162 (12)	0.0178 (13)	0.0019 (9)	0.0010 (10)	−0.0011 (9)
N1	0.0149 (11)	0.0192 (11)	0.0170 (11)	0.0034 (8)	−0.0035 (8)	−0.0014 (8)
O1	0.0193 (10)	0.0180 (9)	0.0222 (10)	−0.0011 (7)	0.0029 (8)	−0.0020 (7)

Geometric parameters (Å, °)

C1—N1	1.306 (4)	C11—C16	1.397 (4)
C1—O1	1.359 (3)	C12—C13	1.387 (4)
C1—C8	1.470 (4)	C12—H12	0.95
C2—N1	1.376 (4)	C13—C14	1.384 (5)
C2—C3	1.394 (4)	C13—H13	0.95
C2—C7	1.395 (4)	C14—C15	1.381 (4)
C3—C4	1.375 (4)	C14—H14	0.95
C3—O1	1.388 (3)	C15—C16	1.388 (4)
C4—C5	1.387 (5)	C15—H15	0.95
C4—H4	0.95	C16—H16	0.95
C5—C6	1.397 (6)	C17—C18	1.511 (4)
C5—H5	0.95	C17—H17A	0.99
C6—C7	1.375 (5)	C17—H17B	0.99
C6—H6	0.95	C18—C23	1.394 (4)
C7—H7	0.95	C18—C19	1.395 (4)
C8—C10	1.508 (4)	C19—C20	1.395 (4)
C8—C17	1.510 (4)	C19—H19	0.95

C8—C9	1.547 (3)	C20—C21	1.386 (4)
C9—C10	1.491 (4)	C20—H20	0.95
C9—C11	1.498 (4)	C21—C22	1.390 (4)
C9—H9	1.0	C21—H21	0.95
C10—H10A	0.99	C22—C23	1.389 (4)
C10—H10B	0.99	C22—H22	0.95
C11—C12	1.397 (4)	C23—H23	0.95
N1—C1—O1	115.1 (2)	C13—C12—C11	120.1 (3)
N1—C1—C8	125.5 (2)	C13—C12—H12	119.9
O1—C1—C8	119.3 (2)	C11—C12—H12	119.9
N1—C2—C3	108.7 (2)	C14—C13—C12	121.1 (3)
N1—C2—C7	131.0 (3)	C14—C13—H13	119.5
C3—C2—C7	120.2 (3)	C12—C13—H13	119.5
C4—C3—O1	129.5 (3)	C15—C14—C13	119.3 (3)
C4—C3—C2	123.2 (3)	C15—C14—H14	120.4
O1—C3—C2	107.3 (2)	C13—C14—H14	120.4
C3—C4—C5	115.9 (3)	C14—C15—C16	120.3 (3)
C3—C4—H4	122.0	C14—C15—H15	119.9
C5—C4—H4	122.0	C16—C15—H15	119.9
C4—C5—C6	121.9 (3)	C15—C16—C11	120.9 (3)
C4—C5—H5	119.0	C15—C16—H16	119.6
C6—C5—H5	119.0	C11—C16—H16	119.6
C7—C6—C5	121.5 (3)	C8—C17—C18	116.1 (2)
C7—C6—H6	119.3	C8—C17—H17A	108.3
C5—C6—H6	119.3	C18—C17—H17A	108.3
C6—C7—C2	117.3 (3)	C8—C17—H17B	108.3
C6—C7—H7	121.4	C18—C17—H17B	108.3
C2—C7—H7	121.4	H17A—C17—H17B	107.4

C1—C8—C10	115.7 (2)	C23—C18—C19	117.8 (2)
C1—C8—C17	116.6 (2)	C23—C18—C17	118.9 (2)
C10—C8—C17	120.4 (2)	C19—C18—C17	123.3 (2)
C1—C8—C9	114.3 (2)	C20—C19—C18	120.8 (3)
C10—C8—C9	58.43 (17)	C20—C19—H19	119.6
C17—C8—C9	118.5 (2)	C18—C19—H19	119.6
C10—C9—C11	123.1 (2)	C21—C20—C19	120.4 (3)
C10—C9—C8	59.49 (17)	C21—C20—H20	119.8
C11—C9—C8	120.4 (2)	C19—C20—H20	119.8
C10—C9—H9	114.3	C20—C21—C22	119.7 (3)
C11—C9—H9	114.3	C20—C21—H21	120.2
C8—C9—H9	114.3	C22—C21—H21	120.2
C9—C10—C8	62.07 (17)	C23—C22—C21	119.5 (3)
C9—C10—H10A	117.6	C23—C22—H22	120.2
C8—C10—H10A	117.6	C21—C22—H22	120.2
C9—C10—H10B	117.6	C22—C23—C18	121.9 (3)
C8—C10—H10B	117.6	C22—C23—H23	119.1
H10A—C10—H10B	114.6	C18—C23—H23	119.1
C12—C11—C16	118.4 (2)	C1—N1—C2	105.0 (2)
C12—C11—C9	123.0 (2)	C1—O1—C3	103.9 (2)
C16—C11—C9	118.6 (2)		
N1—C2—C3—C4	−178.3 (3)	C16—C11—C12—C13	−1.0 (4)
C7—C2—C3—C4	−1.0 (4)	C9—C11—C12—C13	179.0 (3)
N1—C2—C3—O1	0.6 (3)	C11—C12—C13—C14	0.7 (4)
C7—C2—C3—O1	177.9 (3)	C12—C13—C14—C15	−0.4 (4)
O1—C3—C4—C5	−178.1 (3)	C13—C14—C15—C16	0.3 (4)
C2—C3—C4—C5	0.6 (4)	C14—C15—C16—C11	−0.7 (4)
C3—C4—C5—C6	−0.4 (5)	C12—C11—C16—C15	1.0 (4)

C4—C5—C6—C7	0.8 (6)	C9—C11—C16—C15	−179.0 (2)
C5—C6—C7—C2	−1.2 (5)	C1—C8—C17—C18	−62.0 (3)
N1—C2—C7—C6	177.9 (3)	C10—C8—C17—C18	87.0 (3)
C3—C2—C7—C6	1.3 (4)	C9—C8—C17—C18	155.2 (2)
N1—C1—C8—C10	12.5 (4)	C8—C17—C18—C23	166.8 (2)
O1—C1—C8—C10	−170.8 (2)	C8—C17—C18—C19	−13.9 (4)
N1—C1—C8—C17	162.9 (3)	C23—C18—C19—C20	−1.0 (4)
O1—C1—C8—C17	−20.3 (3)	C17—C18—C19—C20	179.6 (3)
N1—C1—C8—C9	−52.7 (4)	C18—C19—C20—C21	1.0 (4)
O1—C1—C8—C9	124.1 (2)	C19—C20—C21—C22	−0.6 (4)
C1—C8—C9—C10	106.3 (3)	C20—C21—C22—C23	0.2 (4)
C17—C8—C9—C10	−110.0 (3)	C21—C22—C23—C18	−0.2 (4)
C1—C8—C9—C11	−140.7 (2)	C19—C18—C23—C22	0.6 (4)
C10—C8—C9—C11	112.9 (3)	C17—C18—C23—C22	−180.0 (2)
C17—C8—C9—C11	2.9 (4)	O1—C1—N1—C2	0.0 (3)
C11—C9—C10—C8	−108.5 (3)	C8—C1—N1—C2	176.9 (3)
C1—C8—C10—C9	−103.9 (2)	C3—C2—N1—C1	−0.4 (3)
C17—C8—C10—C9	106.8 (3)	C7—C2—N1—C1	−177.3 (3)
C10—C9—C11—C12	−17.8 (4)	N1—C1—O1—C3	0.4 (3)
C8—C9—C11—C12	−89.2 (3)	C8—C1—O1—C3	−176.7 (2)
C10—C9—C11—C16	162.1 (2)	C4—C3—O1—C1	178.3 (3)
C8—C9—C11—C16	90.8 (3)	C2—C3—O1—C1	−0.6 (3)

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes. Data collection: Bruker Instrument Service

v2012.6.0.0; cell refinement: *SAINT* V8.18C (Bruker AXS Inc., 2011); data reduction: *SAINT* V8.18C (Bruker AXS Inc., 2011); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008).

5 REFERENCES

1 Smith, M. B.; March, J. *March's 'Advanced organic chemistry reactions, mechanisms, and structure*,' 6th Ed.; Wiley-Interscience. p. 218-219.

2 (*a*) Wilberg, F. J. *Acc. Chem. Res.* **1996**, *29*, 229; (*b*) Coulson, C. A.; Goodwin, T. H. *J. Chem. Soc*. **1962**, 2851-2854; (*c*) Peters, D. *Tetrahedron* **1963**, *19*, 1539-1546; (*d*) Hoffman, R.; Davidson, R. B. *J. Am. Chem. Soc.* **1971**, *93*, 5699-5705.

3 Graham, J. D.; Rogers, M. T. *J. Am. Chem. Soc.* **1962**, 84, 2249-2252.

4 Wiberg, K. B.; Rablen, P. R. *J. Am. Chem. Soc.* **1987**, *109*, 1001-1012.

5 Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Guy Orpen, A.; Taylor, R. *J. Chem. Soc. Perkin Trans. 2* **1987**, *12*, S1-S19.

6 Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117-3179.

7 Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051-3060.

8 (*a*) Brackmann, F.; De Meijere, A. *Chem. Rev.* **2007**, *107*, 4493. (*b*) Wessjohann, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev.* **2003**, *103*, 1625. (*c*) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589.

9 (*a*) Pellissier, H. *Tetrahedron* **2008**, *64*, 7041-7095. (*b*) Ojima, I. *Comprehensive Asymmetric Synthesis*, 2nd Ed.; Wiley-VCH Inc.: New York, **2000**; p 864.

10 Charette, A. B.; Juteau, H.; Lebel, H.; Molinaro, C. *J. Am. Chem. Soc.* **1998**, *120,* 11943-11952.

11 Dargel, T. K.; Koch, W. *J. Chem. Soc. Perkin Trans. 2* **1996**, 877-881.

12 Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651-2652.

13 (*a*) Liu, P.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 10772-10773; (*b*) Ghosh, A. K.; Liu, C. *Org. Lett.* **2001**, *3*, 635-638; (*c*) Charette, A. B.; Lebel, H. *J. Am. Chem. Soc.* **1996**, *118*, 10327-10328.

14 (*a*) Motherwell, W. B.; Bégis, G.; Cladingboel, D. E.; Jerome, L.; Sheppard, T. D. *Tetrahedron* **2007**, *63*, 6462-6476; (*b*) Ishikawa, S.; Sheppard, T. D.; D'Oyley, J. M.; Kamimura, A; Motherwell, W. B. *Angew. Chem. Int. Ed.* **2013**, *52*, 10060 –10063; (*c*) Bégis, G.; Cladingboel, D. E.; Jerome, L.; Motherwell, W. B.; Sheppard, T. D. *Eur. J. Org. Chem.* **2009**, 1532-1548.

15 Aggarwal ,V. K.; Fulton, J. R.; Sheldon C. G.; De Vicente, J. *J. Am. Chem Soc.* **2003**, 125, 6034-6035.

16 Deng, X.-M.; Cai, P.; Ye, S.; Sun, X.-L.; Liao, W.-W.; Li, K.; Tang, Y.; Wu, Y.-D.; Dai, L.-X. *J. Am. Chem. Soc.* **2006**, *128*, 9730–9740.

17 Kunz, R. K., Macmillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 3240-3241.

18 Beaulieu, P. L.; Gillard, J.; Bailey, M. D.; Boucher, C.; Duceppe, J.-S.; Simoneau, B. *J. Org. Chem.* **2005**, *15*, 5869-5879.

19 Wadsworth W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733.

20 (*a*) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1954**, *87*, 1318; (*b*) Wittig, G.; Haag, W. *Chem. Ber.* **1955**, *88*, 1654.

21 (*a*) Denney, D. B.; Boskin, M. J. *J. Am. Chem. Soc.* **1959**, *81*, 6330; (*b*) Denney, D. B.; Vill, J. J.; Boskin, M. J. *J. Am. Chem. Soc.* **1962**, *84*, 3944-3946.

22 Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41.

23 (*a*) Vilkas, M.; Abraham, N. A. *Compt. Rend.* **1958**, *246*, 1434. (*b*) Bohlmann, F.; Inhoffen, E. *Chem. Ber.* **1956**, *89*, 1276.

24 Horner, L.; Hoffman, H.; Wippel, H. G.; Klahre, G. *Chem. Ber.* **1959**, *92*, 2499.

25 Arbuzov, A. E.; F.Razumov, A. F. *J. Russ. Phys. Chem. Soc.* **1929**, *61*, 623.

26 Tömösközi, I. *Tetrahedron* **1963**, *19*, 1969-1979.

27 Eliel, E. L.; Delmonte, D. W. *J. Org. Chem.* **1956**, *21*, 596.

28 (*a*) Cram, D. J.; Elhafez, F. A. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828; (*b*) Prelog, V. *Helv. Chim. Acta* **1953**, *36*, 308; (*c*) Doering, W. E.; Levy, L. K. *J. Am. Chem. Soc.* **1955**, *77*, 509; (*d*) Cram, D. J.; Nielsen, W. D.; Rickborn, B. *J. Am. Chem. Soc.* **1960**, *82*, 6415.

29 (*a*) Inouye, Y.; Inamasu, S.; Ohno, M.; Sugita, T.; Walborsky, H. M. *J. Am. Chem. Soc.* **1961**, *83*, 2962; (*b*) Walborsky, H. M.; Sugita, T.; Ohno, M.; Inouye, Y. *J. Am. Chem. Soc.* **1960**, *82*, 5255; (*c*) Prelog, V.; Scherrer, H. *Helv. Chim. Acta* **1959**, *42*, 2227; (*d*) Berson, J. A.; Greenbaum, M. A. *J. Am. Chem. Soc.* **1959**, *81*, 6456; (*e*) Van Auken, T. V.; Rinehart, K. L. *J. Am. Chem. Soc.* **1962**, *84*, 3736; (*f*) Mills, J. A.; Klyne, W. *Progress in stereochemistry, Ed. Klyne* **1954**, *1*, 189-195.

30 (*a*) Tömösközi, I. *Tetrahedron* **1966**, *22*, 179-182. (*b*) Inouye, Y.; Inamasu, S.; Ohno, M.; Sugita, T.; Walborski, H. M. *Tetrahedron* **1964**, *20*, 1695-1699. (*c*) Doering, W., von E.; Kirmse, W. *Tetrahedron* **1960**, *11*, 272.

31 Izydore, R. A.; Ghirardelli, R. G. *J. Org. Chem.* **1973**, *38*, 1790-1793.

32 Fitzsimmons, B. J.; Fraser-Reid, B. *Tetrahedron,* **1984**, *40*, 1279-1287.

33 Petter, R. C. *Tetrahedron Lett.* **1989**, *30*, 399-402.

34 Abbot, M. T.; Udenfriend, S. *In Molecular Mechanisms of Oxygen Activation*; O. Hayaishi, Ed. Academic Press: New York **1974**, 168-214.

35 (*a*) Rich, A.; Crick, F. H. C. *J. Mol. Biol.* **1961**, *3*, 483. (*b*) Berg, R. A.; Prockop, D. J. *Biochem. Biophys. Res. Comm.* **1973**, *52*, 115.

36 (*a*) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. (*b*) Suckling, C. K. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 537.

37 (*a*) Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185-4190; (b) Gloer, K. B.; Calogeropoulou, T.; Jackson, J. A.; Wiemer, D. F. *J. Org. Chem.* **1990**, *55*, 2842-2846; (*c*) An, Y. Z.; Wiemer, D. F. *J. Org. Chem.* **1992**, *57*, 317-321; (*d*) Lee, K.; Wiemer, D. F. *J. Org. Chem.* **1991**, *56*, 5556-5560.

38 Jacks, T. E.; Nibbe, H.; Wiemer, D. F. *J. Org. Chem.* **1993**, *58*, 4584-4588.

39 Sparatore, F.; La Rotonda, M. I.; Paglietti, G.; Ramundo, E.; Silipo, C.; Vittoria, A. *Farmaco Ed Sci.* **1978**, *33*, 901.

40 (*a*) Wender, P. A.; Cooper, C. A. *Tetrahedron* **1986**, *42*, 2985; (*b*) Hubert, A. J. *J. Chem. Soc. C.* **1969**, 1334; (*c*) Katritzky, A. R.; Rachwal, S.; Hitchings, G. J. *Tetrahedron* **1991**, *47*, 2683; (*d*) Katritzky, A. R.; Yang, Z.; Cundy, D. J. *Aldrichimica Acta* **1994**, *27*, 31; (*e*) Katritzky, A. R.; Lan, X. *Chem. Soc. Rev.* **1994**, *23*, 363; (*f*) Katritzky, A. R.; Lan, X.; Fan, W.-Q. *Synthesis* **1994**, 445.

41 Katritzky, A. R.; Wu, H.; Xie, L.; Jiang, J. *J. Heterocycl. Chem.* **1995**, *32*, 595.

42 Zhu, J.; Price, B. A.; Zhao, S. X.; Skonezny, P. M. *Tetrahedron Lett.* **2000**, *41*, 4011.

43 Singh, A. K.; Rao, M. N.; Simpson, J. H.; Li, W.; Thronton, J. E.; Kuehner, D.E.; Kacsur, D. J. *Org. Process Res. Dev.* **2002**, *6*, 618-620.

44 (*a*) Armstrong, A.; Scutt, J. N. *Org Lett* **2003**, *5*, 2331-2334. (*b*) Armstrong, A.; Scutt, J. N. *Chem. Comm.* **2004**, *46*, 510-511.

45 Asai, A.; Hasegawa, A.; Ochiai, K.; Yamashita, Y.; Mizukami, T. *J. Antibiot.* **2000**, *53*, 81-83.

46 (*a*) O'Donnell, M. J.; Bennett, W. D.; Wu, S. *J. Am. Chem. Soc.* **1989**, *111*, 2353-2355. (*b*) O'Donnell, M. J.; Wu, S.; Huffman, J. C. *Tetrahedron* **1994**, *50*, 4507-4518; (*c*) Corey, E., J.; Xu, F.; Noe, M. C. *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415. (*d*) Lygo, B.; Wainwright, P. G. *Tetrahedron Lett.* **1997**, *38*, 8595-8598.

47 Delhaye, L.; Merschaert, A.; Delbeke, P.; Briône, W. *Organic Process Research and development* **2007**, *11*, 689-692.

48 Bray, C. D.; De Faveri, G. *J. Org. Chem.* **2010**, *75*, 4652-4655.

49 (*a*) Chang, Y. H.; Pinnick, H. W. *J. Org. Chem.* **1978**, *43*, 373. (*b*) Corey, E. J.;Weatherhead-Kloster, R. A. *Org. Lett.* **2006**, *8*, 171. (*c*) Tanikaga, R.; Yamada, S.; Nishikawa, T.; Matsui, A. *Tetrahedron* **1998**, *31*, 8933. (*d*) Tanaka, K.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2071.

50 (*a*) Baldwin, J. E.; Adlington, R. M.; Bebbington, D. *Tetrahedron* **1994**, *50*, 12015. (*b*) Lai, M. T.; Oh, E.; Shih, Y.; Liu, H. W. *J. Org. Chem.* **1992**, *57*, 2471.

51 Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 2871.

52 Kazuta, Y.; Matsuda, A.; Shuto, S. *J. Org. Chem.* **2002**, *67*, 1669.

53 Trost, B. M.; Cossy, J.; Burkes, J. *J. Am. Chem. Soc.* **1983**, *105*, 1052.

54 (*a*) Bernard, A. M.; Frongia, A.; Piras, P. P.; Secci, F. *Synlett* **2004**, 1064. (*b*) Aïssa, C. *J. Org. Chem.* **2006**, *71*, 360.

55 Hayashi, N.; Hirokawa, Y.; Shibata, I.; Yasuda, M.; Baba, A. *J. Am. Chem. Soc.* **2008**, *130*, 2912.

56 Aïssa, C. *J. Org. Chem.* **2006**, *71*, 360-363.

57 (*a*) Krawczyk, H.; Wąsek, K; Kędzia, J. *Synlett* **2005**, *17*, 2648-2652. (*b*) Krawczyk, H.; Wąsek, K; Kędzia, J.; Wojciechowski, J.; Wolf, W. M. *Org Biomol. Chem.* **2008**, *6*, 308-318.

58 Krawczyk, H.; Wąsek, K; Kędzia, J. *Synthesis* **2009**, 1473-1476.

59 Clarke, C.; Fox, D. J.; Pedersen, D. S.; Warren, S. *Org. Biomol. Chem.* **2009**, *7*, 1323-1328.

60 (*a*) Janecki, T.; Blaszczyk, E. *Tetrahedron Lett*. **2001**, *42*, 2919-2922. (*b*) ; Stritzke, K.; Schulz, S.; Nishida, R. *Eur. J. Org. Chem.* **2002**, *22*, 3884-3892. (*c*) Ersoy, O.; Fleck, R.; Blanco, M.-J.; Masamune, S. *Bioorg. Med. Chem.* **1999**, *7*, 279-286.

61 (*a*) Patai, S.; Schwartz, A. *J. Org. Chem.* **1960**, *25*, 1232-1233. (*b*) Lehnert, W. *Tetrahedron* **1974**, *30*, 301-305.

62 Ianni, A.; Waldvogel, S. R. *Synthesis* **2006**, 2103-2112.

63 Jackson, J. A.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1989**, *54*, 4750-4754.

64 Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456-463.

65 Panne, P.; DeAngelis, A.; Fox, J. M. *Org. Lett.* **2008**, *10*, 2987-2989.

66 Muray, E.; Rifè, J.; Branchadell, V.; Ortuño, R. M. *J. Org. Chem.* **2002**, *67*, 4520-4525

67 Kennewell, P. D.; Matharu, S. S.; Taylor, J. B.; Westwood, R.; Sammes, P. G. *J. Chem. Soc.*, *Perkin Trans. 1* **1982**, 2563.

68 Bray, C. D.; Minicone, F. *Chem. Commun.* **2010**, *46*, 5867-5869.

69 Kumar, P.; Dubey, A.; Harbindu, A. *Org. Biomol. Chem.* **2010**, *10*, 6987-6994.

70 Sokolsky, A.; Smith, A. B. *Org. Lett.* **2012**, *14*, 4470-4473.

71 Wang, M.-X; Feng, G.-Q *New J. Chem.* **2002**, *26*, 1575-1583.

72 Zhang, X. M.; Bordwell, F. G.; Van Der Puy, M.; Fried, H. E. *J. Org. Chem.* **1993**, *58*, 3060-3066.

73 Bordwell, F. G.; Algrim, D.; Vanier, N. R. *J. Org. Chem.* **1977**, *42*, 1817-1819.

74 Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Conforth, F. J.; Drucker, G. E., Margolin, Z., McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006-7014.

75 Sanz, L. M.; Jimenez-Diaz, M.B.; Crespo, B.; De-Cozar, C.; Almela, M. J.; Angulo-Barturen, I.; Castaneda, P.; Ibanez, J.; Fernandez, E. P.; Ferrer, S.; Herreros, E.; Lozano, S.; Martinez, M. S.; Rueda, L.; Burrows, J. N.; Garcia-Bustos, J. F.; Gamo, F. J.; *Antimicrob. Chemother.* **2011**, *55*, 5740-5745.

76 Haly, B.; Bharadwaj, R.; Sanghvi, Y. S. *Synlett* **1996**, *7*, 687.

77 Ando, K.; Tsuji, E.; Ando, Y.; Kunitomo, J.-I.; Kobayashi, R.; Yokomizo, T.; Shimizu, T.; Yamashita, M.; Otha, S.; Nabe, T.; Kohno, S.; Onishi, Y. *Org. Biomol. Chem.* **2005**, *3*, 2129-2139.

78 Concellon, J. M.; Rodriguez-Solla, H.; Gomez, C. *Angew. Chem. Int. Ed.* **2002**, *41*, 1917-1919.

79 Netz, D. F.; Seidel, J. L. *Tetrahedron Lett.* **1992**, *33*, 1957-1958.

80 Bordwell, F. G.; Van der Puy, M.; Vanier, N. R. *J. Org. Chem.* **1976**, *41*, 1885-1886

81 Jang, W. B.; Jeon, H. J.; Oh, D. Y. *Synth. Commun.* **1998**, *28*, 1253-1256.

82 Carran, J.; Waschbuesch, R.; Savignac, P. *Phosphorus, Sulfur Silicon Relat. Elem.* **1997**, *123*, 209-218.

83 Okazaki, H.; Onishi, K.; Soeda, M.; Ikefuji, Y.; Tamura, R; Mochida, I. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3167-3174.

84 Anthony, N. G.; Breen, D.; Clarke, J.; Donoghue, G.; Drummond, A. J.; Ellis, E. M.; Gemmell, C. G.; Helesbeux, J.-J.; Hunter, I. S.; Khalaf, A. I.; Mackay, S. P.; *et al. J. Med. Chem.* **2007**, *50*, 6116-6125.

85 Yao, M.-L.; Deng, M.-Z. *New J. Chem.* **2000**, *24*, 425-428.

86 Fraser, R. R.; Mansour, T. S.; Savard, S. *J. Org. Chem.* **1985**, *50*, 3232-3234.

87 Riccardi, R.; Bresesti, M. *Ann. Chim.* **1959**, *49*, 1891-1895.

88 Lartia, R.; Allain, C.; Bordeau, G.; Schmidt, F.; Fiorini-Debuisschert, C.; Charra, F.; Teulade-Fichou, M.-P. *J. Org. Chem.* **2008**, *73*, 1732-1744.

89 Minami, T.; Isonaka, T.; Okada, Y.; Ichikawa, J. *J. Org. Chem.* **1993**, *58*, 7009-7015.

90 Liu, X.; Liu, H.; Zhou, W.; Zheng, H.; Yin, X.; Li, Y.; Guo, Y.; Zhu, M.; Ouyang, C.; Zhu, D.; Xia, A. *Langmuir* **2010**, *26*, 3179-3185.

91 Hulvat, J. F.; Sofos, M.; Tajima, K.; Stupp, S. I. *J. Am. Chem. Soc.* **2005**, *127*, 366-372.

92 Detert, H.; Schollmeyer, D.; Sugiono, E. *Eur. J. Org. Chem.* **2001**, *15*, 2927-2938.

93 McElhanon, J. R.; Wu, M.-J.; Escobar, M.; Chaudhry, U.; Hu, C.-L.; McGrath, D. V. *J. Org. Chem.* **1997**, *62*, 908-915.

94 Bordwell, F. G.; Cheng, J.-P.; Ji, G.-Z.; Satish, A. V.; Zhang, X. *J. Am. Chem. Soc.* **1991**, *113*, 9790-9795.

95 Sun, L.; Goerner, H. *J. Phys. Chem.* **1993**, *97*, 11186-11193.

96 McCauley, J. A.; Theberge, C. R.; Romano, J. J.; Billings, S. B.; Anderson, K. D.; Claremon, D. A.; Freidinger, R. M.; Bednar, R. A.; Mosser, S. D.; Gaul, S. L.; Connolly, T. M.; *et al. J. Med. Chem.* **2004**, *47*, 2089-2096.

97 Lion, C. J.; Matthews, C. S.; Stevens, M. F. G.; Westwell, A. D. *J. Med. Chem.* **2005**, *48*, 1292-1295.

98 Fields E. K. *J. Am. Chem. Soc.* **1952**, *74*, 1528-1530.

99 (*a*) Csuk, R.; Schabel, M. J.; Scholz, Y. Von *Tetrahedron: Asymmetry* **1996**, *7*, 3505-3512; (*b*) Aggarwal, V. K.; Vicente, J. de; Bonnert, R. V. *Org. Lett.* **2001**, *3*, 2785-2788.

100 Krawczyk, H.; Wasek, K.; Kedzia, J. *Synlett* **2005**, *17*, 2648-2652.

101 Jackson, J. A.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1989**, *54*, 4750-4754.

102 Lehnert,W. *Tetrahedron* **1974**, *30*, 301-305.