

**THE STUDY OF NITRILE YLIDES WITH CONJUGATION
IN HETEROCYCLIC SYNTHESIS**

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A thesis presented for the degree of Doctor of Philosophy

University of Edinburgh

1996



Dedication

This thesis is dedicated to

Mum, Dad and Morna

Declaration

I declare that this thesis is my own composition and that the work of which it is a record was carried out by myself unless otherwise acknowledged. No part of this thesis has been submitted in any other application for a higher degree.

Jon-Paul Strachan 1996.

Courses Attended

The following is a statement of the courses attended during the period of research:-

1. Merck, Sharp and Dohme, Medicinal Chemistry Lectures, Prof. R. Baker and Dr. P. Leeson, Department of Chemistry, University of Edinburgh, 1994, 1995 and 1996.
2. NMR of Biological Molecules, Dr. P. Barlow and Dr. I. Sadler, Department of Chemistry, University of Edinburgh, 1995.
3. Chemical Development in the Pharmaceutical Industry, Smith-Kline Beecham, various speakers, Department of Chemistry, University of Edinburgh, 1994.

4. Industrial Fine Organic Chemistry, Prof. A. McKillop (University of East Anglia), Department of Chemistry, University of Edinburgh, 1996.
5. Hydrogen Peroxide and its Derivatives in Industry, Solvay Interox, various speakers, Department of Chemistry, University of Edinburgh, 1994.
6. Industrial Biocatalysts, Smith-Kline Beecham, various speakers, Department of Chemistry, University of Edinburgh, 1994.
7. Industrial Chemistry, Zeneca Grangemouth, various speakers, Department of Chemistry, University of Edinburgh, 1995.
8. Organic Research Seminars, various speakers, Department of Chemistry, University of Edinburgh, 3 years attendance.
9. Current Topics in Organic Chemistry, various speakers, Department of Chemistry, University of Edinburgh, 3 years attendance.
10. Royal Society of Chemistry, Perkin Division (Scottish Section), annual meetings, various speakers, 3 years attendance.

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Abstract

This research was concerned with the generation and reaction of diene- and triene-conjugated nitrile ylides. The amide precursors were synthesised from readily available reactants *via* Pd(0) catalysed cross coupling reactions and the nitrile ylides were generated by the 1,3-dehydrochlorination of imidoyl chlorides.

Two series of triene-conjugated nitrile ylides were studied; firstly, those in which the $\alpha,\beta;\gamma,\delta$ bonds were aromatic and then those with an aromatic ring only in the α,β position. The first series reacted *via* a [3+2] cycloaddition across the olefinic double bond, when this was activated towards cycloaddition, to give a dibenz[e,g]indole. The presence of a methyl group at the 2 or 2'-position of the biaryl unit prevented cyclisation and dimeric products were then observed. When no methyl group was present reaction occurred *via* 1,7-electrocyclisation at the free ortho position of the γ,δ aromatic ring to give dibenz[c,e]azepines.

The second series of nitrile ylides in which the $\gamma,\delta;\epsilon,\zeta$ double bonds are olefinic cyclised at 0 °C to give cyclopropa[c]isoquinolines as primary products. In cases where the terminal double bond was *cis* these products reacted further by a Cope rearrangement to give 1,4-bridged isoquinolines. In cases where the terminal double bond was *trans* the primary product rearranged on heating *via* a [1,5] carbon shift accompanied by a complex skeletal rearrangement to give an azatetracyclotridecatetraene and to a lesser extent *via* an equilibration

between *exo* and *endo* isomers accompanied by a Cope rearrangement to give 1,4-bridged isoquinolines.

The diene-conjugated nitrile ylides cyclised at room temperature to give cyclopropa[c]isoquinolines in a stereospecific reaction. Thermal decomposition of these products involved an equilibration between *exo* and *endo* isomers accompanied by ring expansion to give 1*H*-2-benzazepines or a [1,5]-sigmatropic hydrogen shift to give 1*H*-isoquinolines or followed another reaction path to give 5*H*-2-benzazepines.

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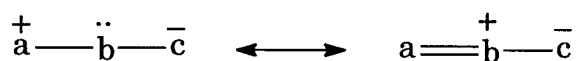
Introduction

1. 1,3-Dipoles

1.1 Structure

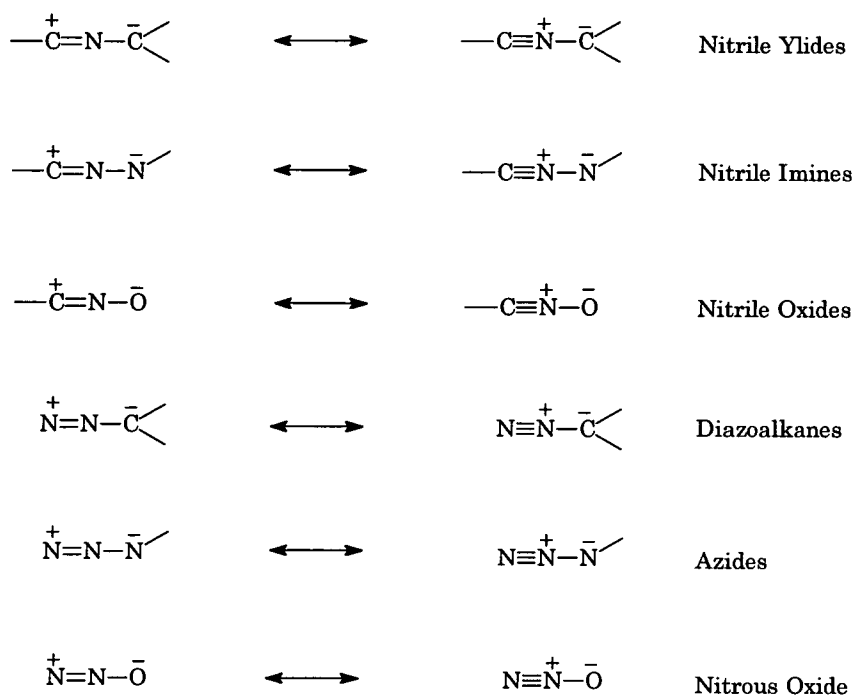
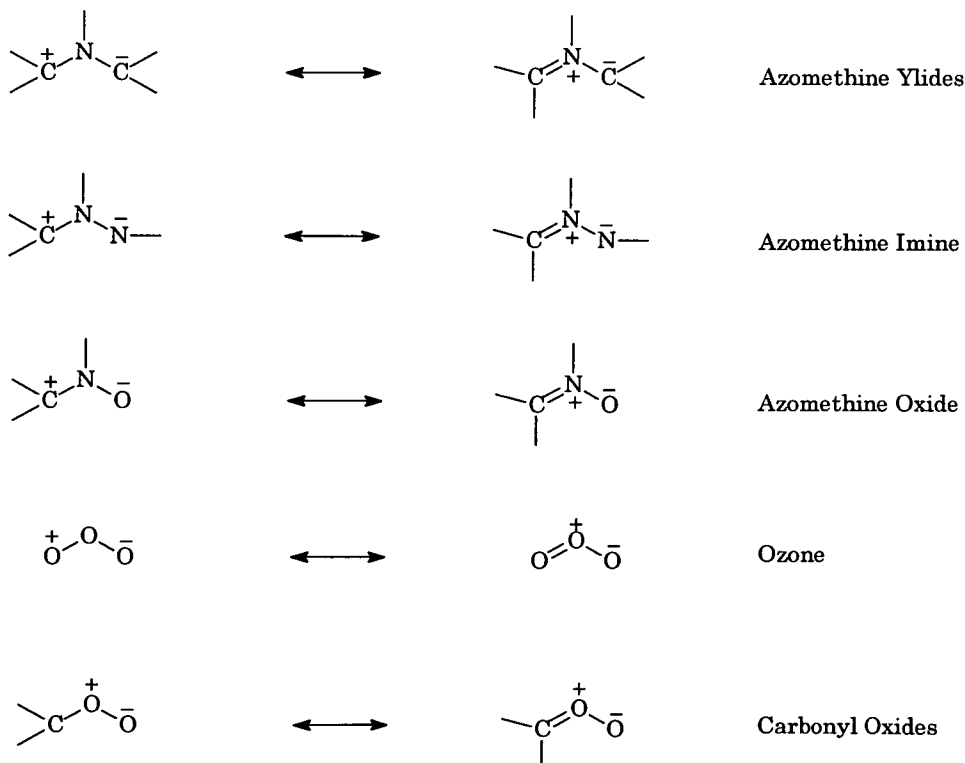
The term 1,3-dipole applies to a class of reactive intermediates which may be defined¹ as systems **a-b-c** in which **a** has an electron sextet and **c** has an unshared electron pair, *i.e.* **a** has a formal positive charge and **c** has a formal negative charge.

1,3-Dipoles are isoelectronic with both the allyl and propargyl anion, possessing four π -electrons spread over the **a-b-c** system. Dipoles in which the positive centre **a** is an electron deficient carbon, nitrogen or oxygen atom are, in general, too unstable for long lived existence. The system may, however, be stabilised if atom **b** is capable of donating an electron pair as shown below.



This donation of the electron pair leads to the formation of a more stable “all octet” configuration in which the site of the formal positive charge is shifted to atom **b**.

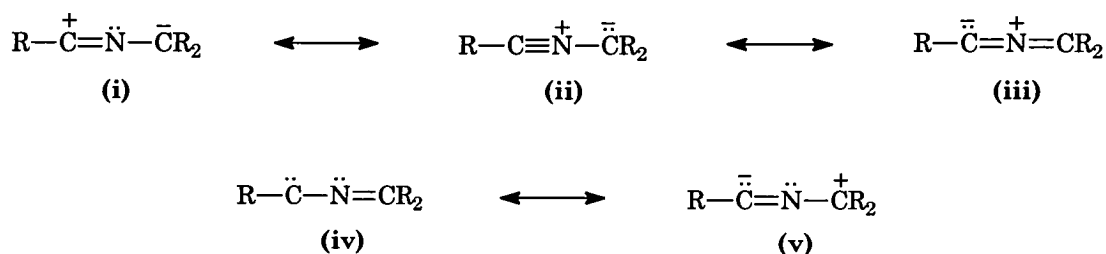
Octet stabilised 1,3-dipoles may be divided into two classes, those with an orthogonal double bond, *i.e.* the allenyl-propargyl type, and those without an orthogonal double bond, *i.e.* the allyl type, as shown in Table 1.

Table 1. 1,3-Dipoles with octet stabilisation**(a) 1,3-Dipoles of the allenyl-propargyl type****(b) 1,3-Dipoles of the allyl type**

Allenyl-propargyl type 1,3-dipoles have nitrogen as the central atom **b** since it is the only element capable of donating an electron pair whilst in the neutral trivalent state. Allyl type 1,3-dipoles can have nitrogen or oxygen as the central atom.

The geometry of the two types of dipoles are different. Allenyl-propargyl dipoles tend to be linear due to the presence of an extra orthogonal double bond, whereas allyl type dipoles are bent.

The structure of 1,3-dipoles is best represented through a series of resonance structures, *e.g.* the canonical forms (i)-(v) for a nitrile ylide shown in Scheme 1.



Scheme 1

The all octet structures (ii) and (iii) are the most stable representations of the nitrile ylide although the term 1,3-dipole applies strictly to structures (i) and (v), and structure (iv) represents the carbene form. It is, however, accepted that the term 1,3-dipole is applicable to the molecule as a whole as it best describes the observed reactivity.

1.2 Reactions

1,3-Dipoles react readily with most multiple bond systems^{1,2} (d=e); (the dipolarophile) *via* a [3+2] cycloaddition reaction to give a five membered cyclic product. The reaction leads to the formation of two new σ -bonds at the **a** and **c** termini, to give a product with no net charge. 1,3-Dipolar cycloadditions can occur as both inter- and intramolecular

reactions. If the 1,3-dipole is attached to a system through which its conjugation can be extended then there is also the possibility of an electrocyclic reaction.

1.2.1 Intermolecular 1,3-Dipolar Cycloadditions

The general features of mechanism and patterns of reactivities and selectivities in 1,3-dipolar cycloaddition reactions were established by Huisgen *et al*^{1,3} in the sixties.

These reactions are thermally allowed $4\pi + 2\pi$ processes which possess certain characteristic features. (i) Neither rate nor stereochemistry of the reaction is markedly affected by solvent polarity. (ii) The products are 5-membered rings with the stereochemistry of the dipolarophile retained. (iii) The reactions exhibit low enthalpies of and large negative entropies of activation. (iv) The reaction rates are increased by conjugation in the dipolarophile, but reduced by steric effects in dipole and dipolarophile.

There has been much debate over the mechanism of 1,3-dipolar cycloadditions, primarily between Huisgen^{3,4} and Firestone.^{5,6,7}

Huisgen¹ originally proposed a concerted [3+2] mechanism involving a cyclic transition state with no discrete intermediate. This was reinforced by the Woodward and Hoffmann rules,⁸ which showed that this mechanism is allowed on the basis of conservation of orbital symmetry. A later proposal by Firestone^{5,6,7} involves a two step mechanism in which the formation of a discrete spin-paired diradical is the rate determining step. In this case the stereochemistry of the reaction was explained in terms of ring-closure being energetically more favourable than bond rotation in the diradical. Firestone also suggested that the effects of conjugation and solvent effects could be better explained by the diradical mechanism.

Fukui⁹ had earlier postulated that reactions take place in the direction of maximum frontier molecular orbital overlap. This results

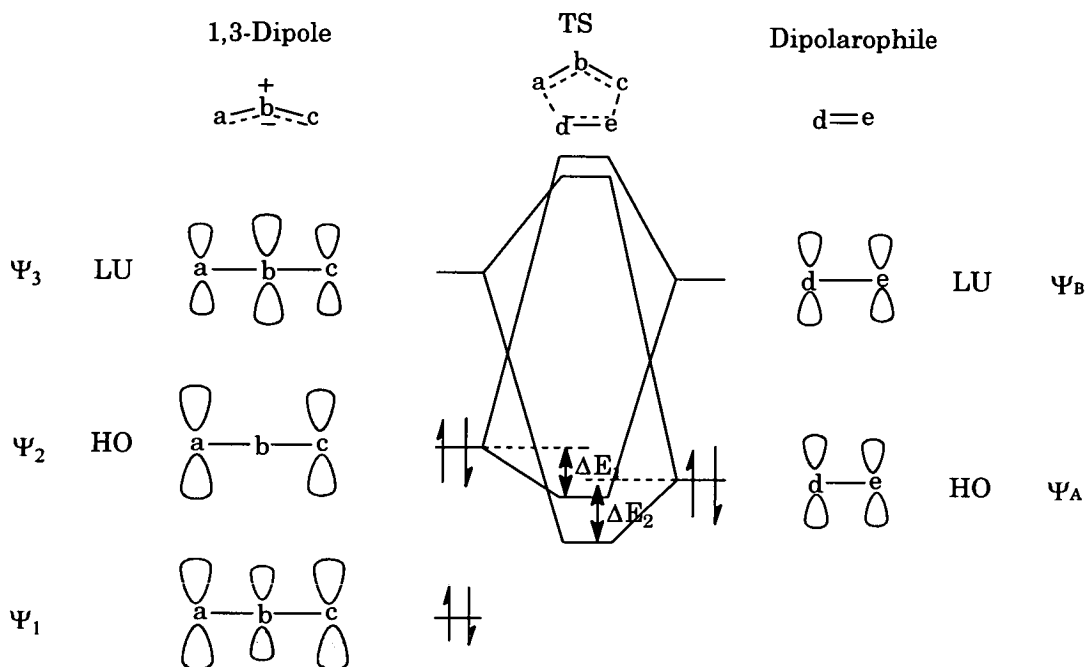
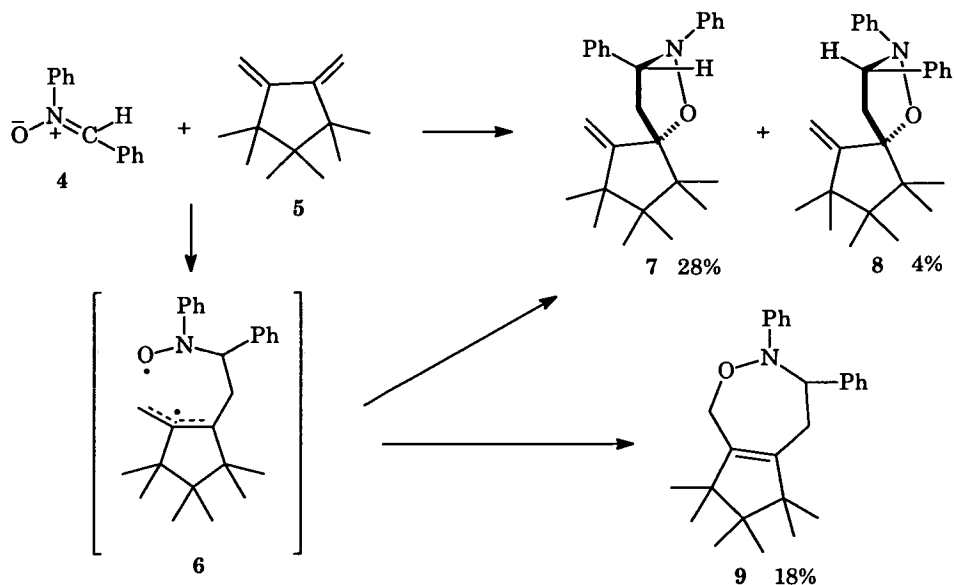


Figure 1

Sustmann's PMO model of concerted cycloadditions^{13,14} envisages two cases in which the stepwise mechanism might compete with the concerted one. Firstly, if the energy differences between the two interacting HO-LU pairs are large and of the same magnitude then the sum of the two energy gains $\Delta E_1 + \Delta E_2$ is small. This corresponds to a minimum of rate and a diradical mechanism may be expected to compete if radical stabilising substituents are present.

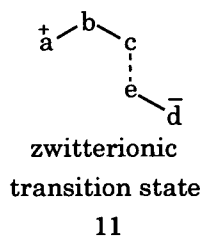
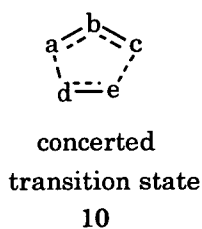
The first example of this pathway was reported by Baran and Mayr.¹⁵ The sterically hindered 1,3-diene **5** combined with diphenyl nitrene **4** to give 32% of the diastereomeric [3+2] adducts and 18% of a [3+4] adduct **9**. Orbital symmetry forbids the formation of **9** by a concerted $[4\pi + 4\pi]$ process, therefore the diradical **6** must be formed. This intermediate, stabilised as a nitroxyl radical and an allyl radical, looks attractive and would give the observed products *via* 1.5- and 1.7-recombination, Scheme 2.

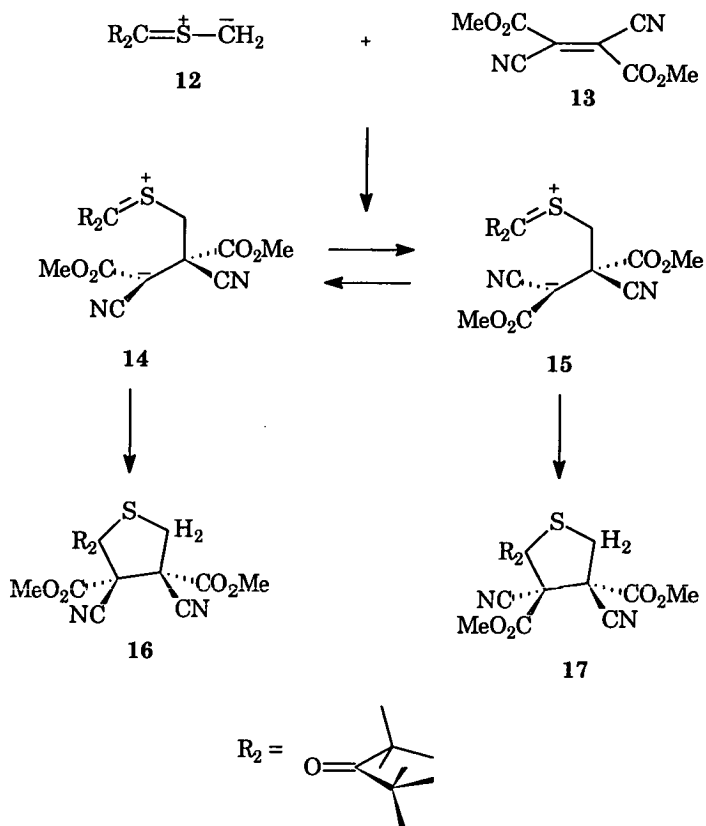


Scheme 2

A second limiting case for the two-step reaction might be expected when the interaction HO (1,3-dipole)-LU (dipolarophile) is strongly dominant in the transition state. This situation would arise when the π -molecular orbital energies of HO (1,3-dipole) and LU (dipolarophile) are similar and those of HO (dipolarophile) and LU (1,3-dipole) are widely different, Figure 2.

Further lifting of the π -molecular orbitals of the 1,3-dipole and/or lowering of those of the dipolarophile will, *in extremis*, lead to the second interaction energy gain (ΔE_2) being negligibly small. ΔE_2 will no longer be able to pay the entropy price required for the highly ordered transition state for the concerted reaction and a unidirectional electron flow will occur leading to a zwitterionic intermediate.





Scheme 3

Houk has carried out extensive molecular orbital calculations which give theoretical values to the orbital coefficients for a series of dipoles and dipolarophiles. This data, therefore, allows the prediction of the product(s) for any given experiment using various dipoles and dipolarophiles, provided that the dominant f.m.o interaction can be identified. The major difficulty was that the f.m.o.'s of both the dipoles and the dipolarophiles vary over a wide energy range. The identification of the dominant f.m.o. interaction was simplified by the classification of the dipoles into three groups, depending on the energy of their f.m.o.'s by Sustmann.¹⁷ The three types of interaction are shown in Figure 3: In each case the major interaction(s) are shown by an arrow.

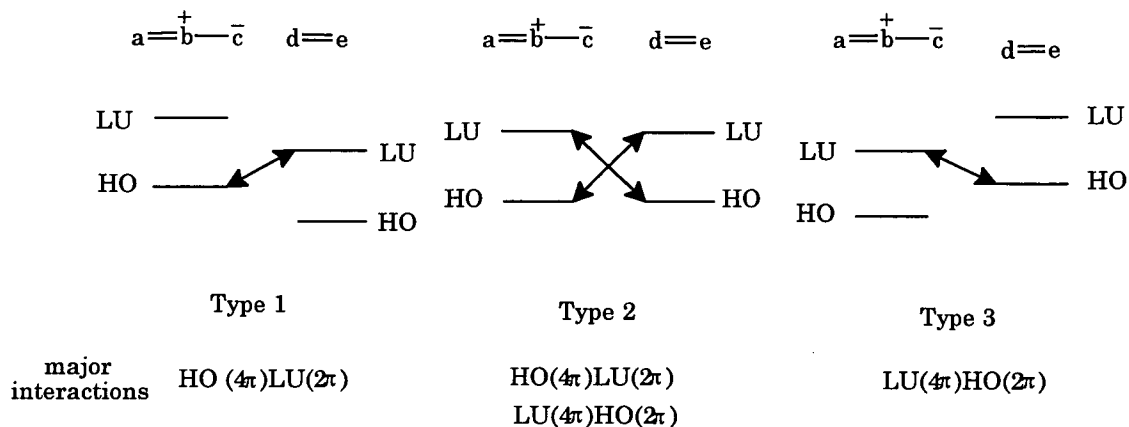


Figure 3

The main 1,3-dipoles in Type 1 are nitrile ylides and diazoalkanes, in Type 2 are nitrile imines, nitrile oxides and azides, and in Type 3 are nitrous oxide and ozone.

Type 1. This is a system where the energy of the f.m.o.'s of the dipoles are high. The major stabilising effect in the transition state is between HO (dipole)-LU (dipolarophile). The introduction of substituents onto either the dipole or the dipolarophile will have an effect on the energy of the f.m.o.'s and hence the transition state of the reaction. An electron donating substituent attached to the dipole raises the energies of both the HOMO and LUMO. Thus the major interaction becomes more stabilising to the transition state. Therefore, electron donating substituents attached to the dipole accelerate the reaction. Electron withdrawing substituents attached to the dipole have the opposite effect and lower both the HOMO and the LUMO of the dipole, and this leads to a reduction in the major stabilising interaction and therefore, the reaction is retarded.

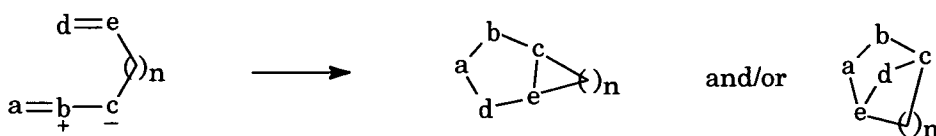
Conjugated substituents raise the HOMO and lower the LUMO and this leads to an increase in the dominant f.m.o. interaction and an increased reaction rate.

The effect of substituents on the dipolarophile parallels the effect on the dipole. For example the effect of an electron withdrawing group on the f.m.o. of the dipolarophile leads to an increase in the reaction rate. Although the minor f.m.o. stabilising interaction HOMO (dipolarophile)-LUMO (dipole) has not been discussed, the same treatment can be applied to the relationship of this effect on the transition state. However, the minor stabilising interaction influences the transition state to a much lesser extent and is, therefore, commonly ignored.

The reactivity of Type 2, 1,3-dipoles is different from that of Type 1, 1,3-dipoles. The addition of either electron donating, electron withdrawing or conjugating groups to the dipole increases the reaction rate. This is due to the formation of a major f.m.o. stabilising interaction previously missing from the unsubstituted dipole. The reactivity of Type 3, 1,3-dipoles is opposite to Type 1, 1,3-dipoles.

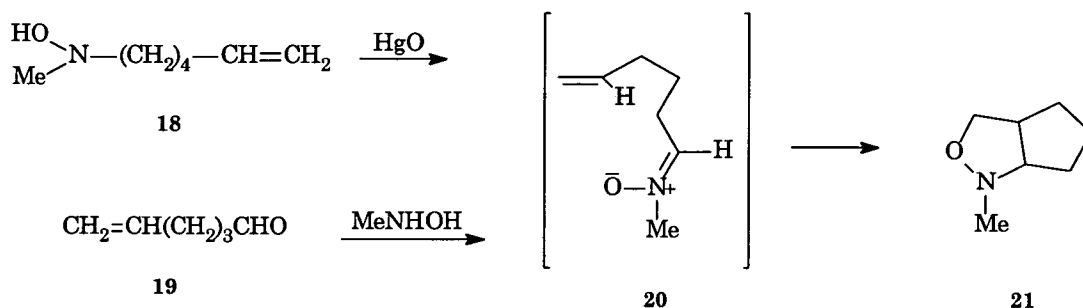
1.2.2 Intramolecular 1,3-Dipolar Cycloadditions

Intramolecular 1,3-dipolar cycloadditions require a molecule which contains both the 1,3-dipole and a dipolarophilic group. The cyclisation occurs *via* a [3+2] mechanism, as described for the intermolecular case, to form a fused five-membered heterocycle.



Lebel and Whang¹⁸ reported the first example of an intramolecular 1,3-dipolar cycloaddition in 1959. The nitrene **20**, prepared either by

oxidation of an *N*-alkenylhydroxylamine **18** by mercuric oxide or by condensation of an unsaturated aldehyde **19** with *N*-methylhydroxylamine, gave a fused bicyclic isoxazolidine **21**, Scheme 4.



Scheme 4

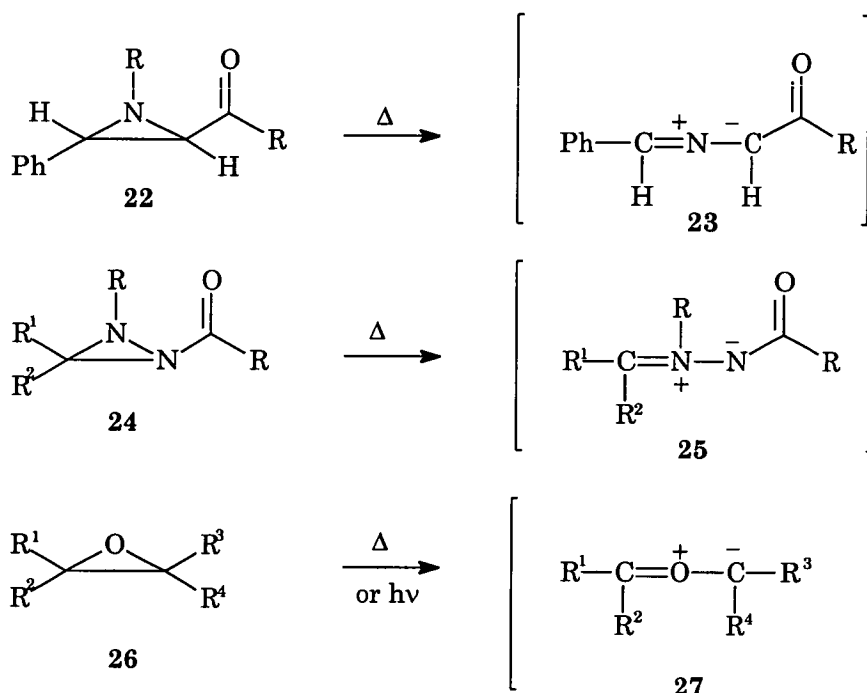
Several reviews^{19,20,21} of intramolecular cycloadditions have been published and numerous papers have reported the use of this reaction in the synthesis of natural products.^{22,23} Nitrile ylides, nitrile imines, azomethine imines, azides, diazoalkanes, nitrones, nitrile oxides and carbonyl oxides have all been shown to undergo intramolecular cycloaddition.²⁰

1.2.3 Electrocyclic Reactions

In cases where the 1,3-dipole is in direct conjugation with the dipolarophile there is the possibility of an electrocyclic reaction.²⁴ An electrocyclic reaction is defined²⁵ as one in which an unsaturated system undergoes a ring closure in a process that can be regarded as a cyclic electron shift, the net result being the conversion of a π -bond into a σ -bond. Electrocyclic processes belong to the class of one-step pericyclic reactions which conform to the principle of conservation of orbital symmetry. The stereochemical course of these reactions may be predicted by inspection of the symmetry of the highest occupied molecular orbital.

1,3-Dipolar electrocyclic reactions fall into three main classes; (i) 4π -1,3-retroelectrocyclisation, (ii) 6π -1,5-electrocyclisation and (iii) 8π -1,7-electrocyclisation.

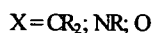
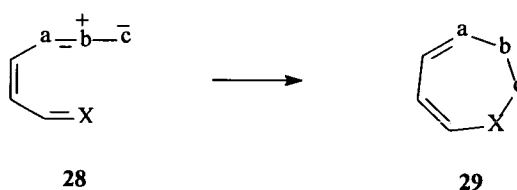
1,3-Retroelectrocyclisations have been widely used for the generation of 1,3-dipoles, especially nitrile ylides, azomethine ylides **23**, *via* the thermolysis of aziridines **22**,²⁶ azomethine imines **25**, *via* the thermolysis of diaziridines **24**²⁷ and carbonyl ylides **27**, *via* the thermolysis or photolysis of oxiranes **26**, Scheme 5.^{28,29}



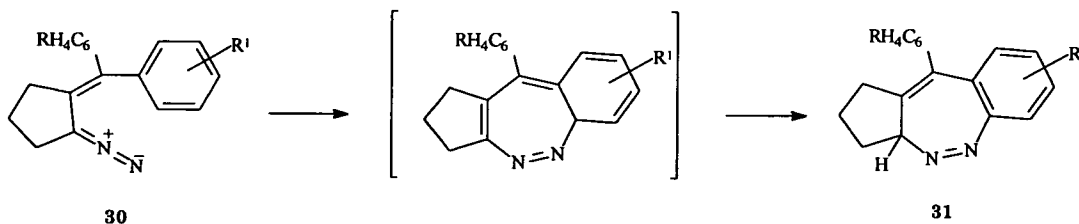
Scheme 5

1,3-Dipoles of both the allenyl-propargyl and the allyl type are capable of 6π -1,5-electrocyclisation when conjugated with a double bond, to form charge free five-membered rings. 1,5-Electrocyclisations of 1,3-dipoles has been used in the synthesis of many monocyclic and fused unsaturated, aromatic and heteroaromatic systems and has been the subject of major reviews.^{30,31}

1,7-Electrocyclisation may compete with 1,5-electrocyclisation when the 1,3-dipole is in conjugation with an $\alpha,\beta,\gamma,\delta$ -unsaturated system. These electrocyclisations involve an 8π -electron system and are isoelectronic with the ring closure of the heptatrienyl anion. On the basis of conservation of orbital symmetry these reactions are predicted to proceed, thermally, *via* a conrotatory ring closure to form seven membered heterocycles, *e.g.* **28** to **29**.



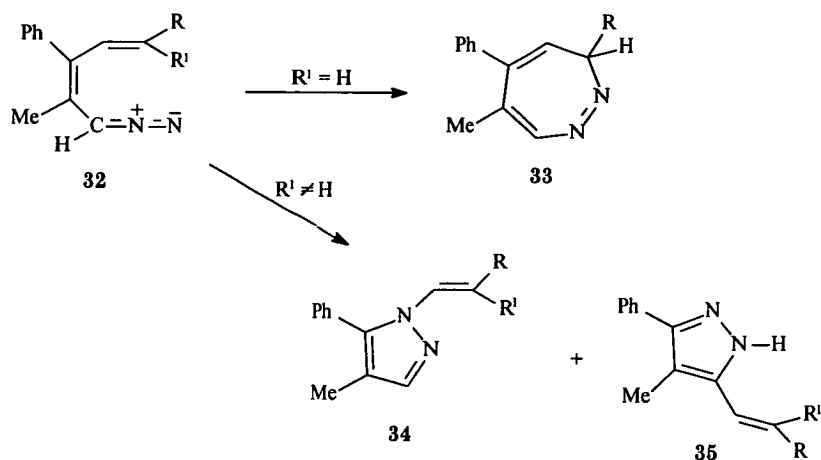
A variety of $\alpha,\beta,\gamma,\delta$ -unsaturated 1,3-dipoles have been shown to undergo reactions of this type.³¹ The most thoroughly studied 1,3-dipolar systems found to undergo 1,7-electrocyclisations were diazocompounds. Diazoalkanes of the type **30** undergo 1,7-electrocyclisation to give the benzodiazepines **31**.³² The initially formed diazepine undergoes a 1,5-hydrogen migration to give the isolated product, Scheme 6.



Scheme 6

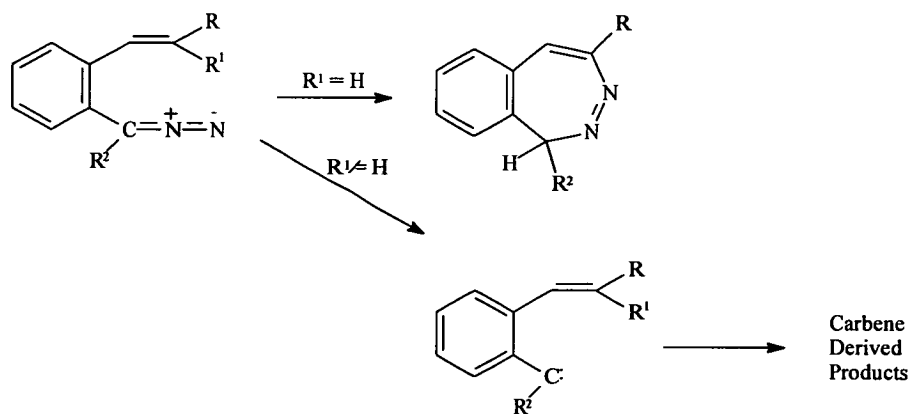
Systems of these types have been shown to be sensitive to steric effects in the conjugated system³³ and also to substituents on the

terminus of the double bond. The diazocompound **32** with $\alpha,\beta,\gamma,\delta$ -olefinic unsaturation, undergoes 1,7-electrocyclisation followed by a [1,5]-sigmatropic hydrogen shift when $R^1 = H$. When $R^1 \neq H$, the reaction proceeds *via* 1,5-electrocyclisation followed by successive [1,5]-vinyl and hydrogen migrations to give the pyrazoles **34** and **35**, Scheme 7.



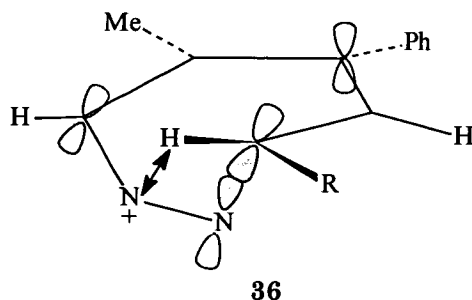
Scheme 7

When the α,β -unsaturation is aromatic in character, 1,7-electrocyclisation followed by a [1,5]-hydrogen shift occurs when a *cis*-hydrogen is present on the terminal double bond. When no *cis*-hydrogen is present the diazocompound loses nitrogen and reacts to give carbene derived compounds, Scheme 8.



Scheme 8

The mechanism of these 1,7-electrocyclisation reactions was postulated by Robertson and Sharp³⁴ to proceed *via* a helical transition state **36**. This transition state leads to the minimum distortion of the diazo group from its preferred linear geometry. Recent *ab-initio* calculations by Houk³⁵ have supported this hypothesis.



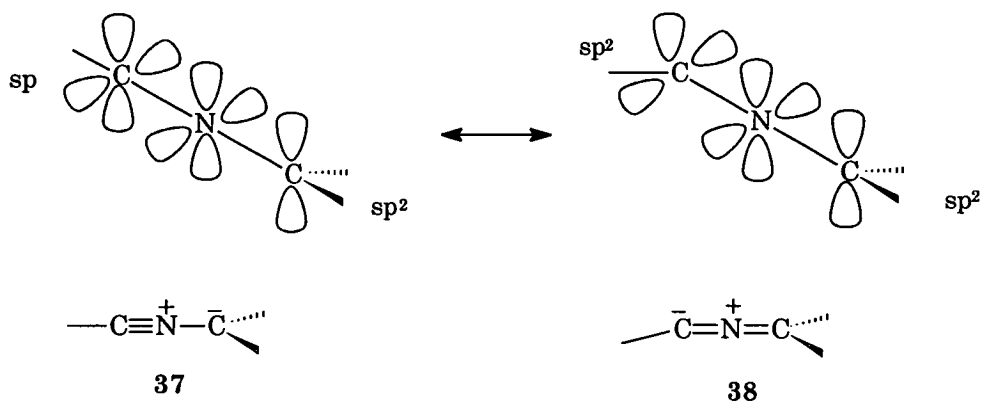
2. Nitrile Ylides

2.1 Structure Of Nitrile Ylides

Nitrile ylides belong to the class of 1,3-dipoles generally called nitrilium betaines; they are based upon a C-N-C system and have an orthogonal double bond.

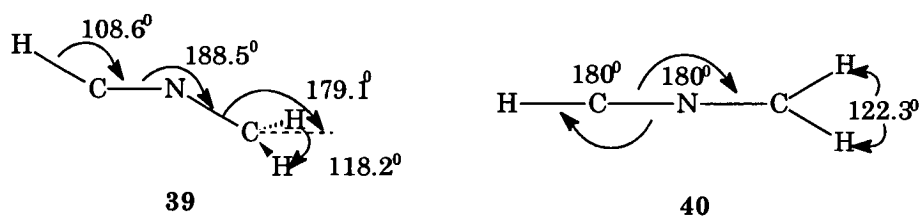
Nitrile ylides are the least stable of the nitrilium betaines and are only isolable in a matrix at very low temperature.³⁶

As mentioned previously the existence of a π -bond in the plane perpendicular to the allyl system generally leads to the allenyl-propargyl 1,3-dipoles adopting a linear conformation. In 1963 Huisgen¹ suggested that, in order to maximise allyl resonance and give maximum overlap for the orthogonal double bond, nitrile ylides would have a preferred linear and planar conformation **37**, the bent form **38** being less important.



Molecular orbital calculations^{10, 11} were made on the assumption that the nitrile ylide had a linear geometry. These calculations gave the coefficients for the frontier molecular orbitals. However predictions based upon this model always led to the opposite regioisomer to that obtained experimentally.

Houk concluded that these calculations must, therefore, be wrong and carried out further MO calculations with geometry optimisation.³⁷ These *ab initio* calculations indicated that the geometry of the nitrile ylide is appreciably different from the linear-planar conformation suggested by Huisgen. He concluded that the bent nitrile ylide **39** is more stable than the linear structure **40** by 11.1 kcalmol⁻¹ and thus resembles a bent allenyl anion rather than a planar propargyl anion.



Houk's calculations show that the bent nitrile ylide HOMO is heavily localised at the nitrile terminus (C-1), but still resembles the normal three-orbital, 4 π -electron system of other 1,3-dipoles, so that concerted cycloadditions can still occur.

The preference for H-C-N bending has been attributed to the mixing of the very high lying HOMO in nitrile ylides with the vacant orbital which is mainly σ_{CH^*} in character.

Figure 4 shows the f.m.o.'s and gross heavy atomic charges for the optimised geometry of formonitrile methylyde.

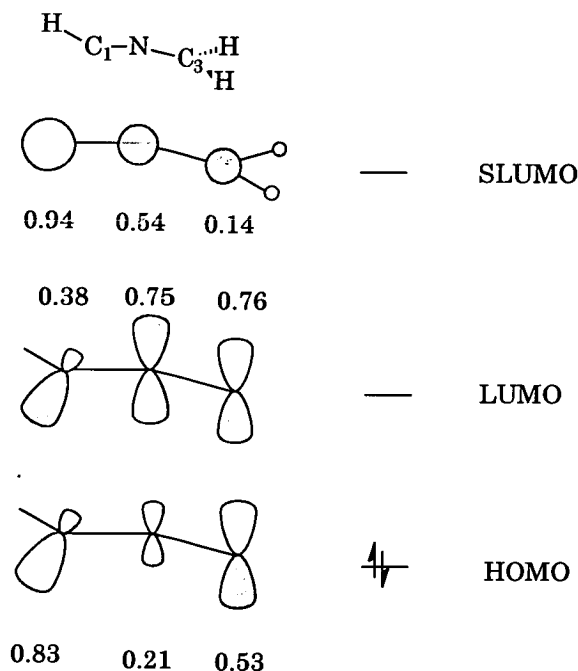


Figure 4

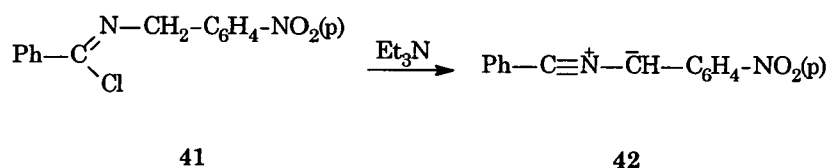
The large HOMO coefficient at C-1 makes this the more nucleophilic terminus. Thus regioselectivity of the cycloadditions to electron deficient alkenes where C-1 adds to the more electrophilic terminus can be accounted for.

The destabilisation of the linear relative to the bent conformation can be compensated for by placing electron withdrawing groups on the methylene (C-3) terminus. This results in the HOMO decreasing in energy and becoming more localised at the C-3 terminus. Thus bending results in less mixing of the HOMO with the σ_{CH^*} orbital. This loss of

stabilisation is compensated for by the increase in allyl resonance in the planar form. For example bis(trifluoromethyl)benzotrile ylide adds to electron deficient alkenes to give the opposite regioisomers to those of simple nitrile ylides.³⁸ Thus electron acceptors at C-3 stabilise the linear relative to the bent species and electron donors at C-3 favour the bent form.

2.2 Generation

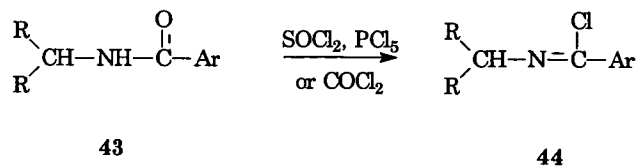
The first reported nitrile ylide³⁹ was generated by Huisgen as part of a programme of research into nitrilium betaines. By analogy to the generation of nitrile oxides by treatment of hydroxamic acid chlorides with bases, the corresponding imidoyl chlorides were expected to form nitrile ylides under similar conditions. Thus *N*-(*p*-nitrobenzyl)benzimidoyl chloride **41** was treated with triethylamine in benzene at 0-20 °C to give benzonitrile-*p*-nitrophenylmethanide **42**, Scheme 9.



Scheme 9

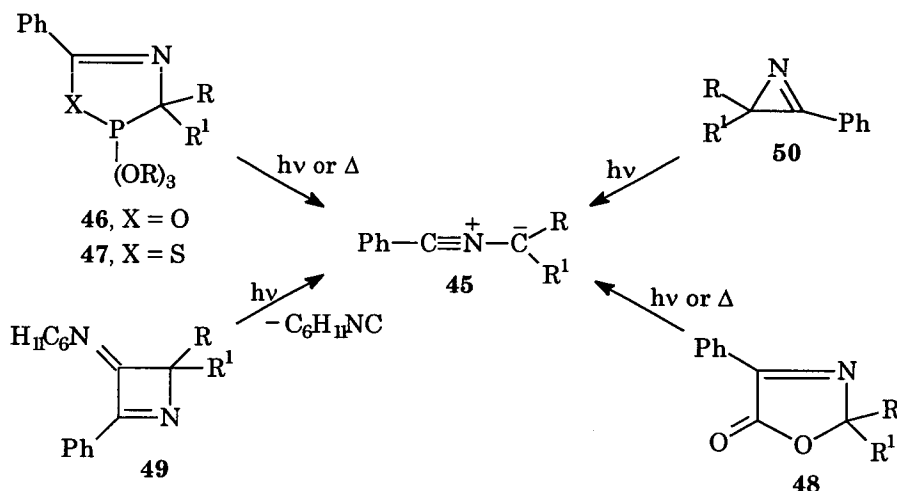
The 1,3-dipolar nature of the intermediate was demonstrated by the formation of cycloadducts when the reaction was carried out in the presence of trapping agents.

The base catalysed dehydrohalogenation of imidoyl chlorides represents a general route to nitrile ylides as the synthesis of the starting materials **44** involves a straightforward chlorination of the readily made amides **43**, Scheme 10.



Scheme 10

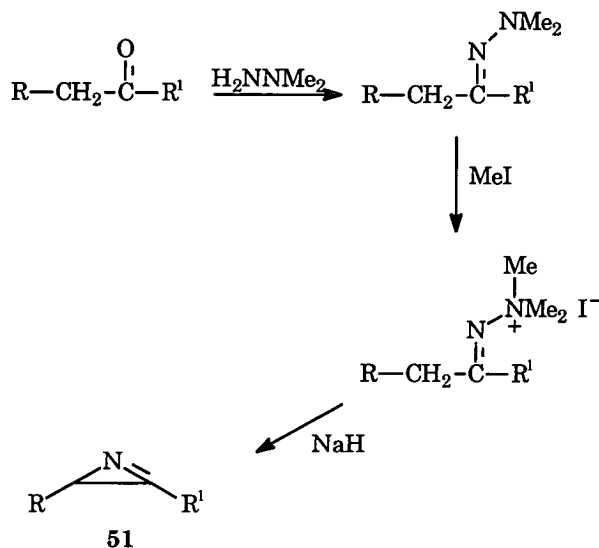
The chlorination of the amide may generally be achieved by treatment with thionyl chloride, phosphorus pentachloride or phosgene.⁴⁰



Other thermal routes to nitrile ylides **45** include (i) the elimination of a phosphoric acid ester from 2,3-dihydro-1,4,2λ⁵-oxazaphospholes **46**,^{41,42} (ii) elimination of alkyl thiophosphates from 2,3-dihydro-1,4,2λ⁵-thiazaphospholes **47**,^{43,44} and (iii) thermal extrusion of carbon dioxide from 3-oxazolin-5-ones **48**,⁴⁵ Scheme 11.

Nitrile ylides may also be generated by photochemical means. Two of the thermolytic precursors to nitrile ylides, *i.e.* 2,3-dihydro-1,4,2λ⁵-oxazaphospholes **46** and 3-oxazolin-5-ones **48** also give the nitrile ylide on photolysis. 3-Imino-1-azetidines **49** lose isocyanides to give nitrile ylides photochemically.³⁸ The most thoroughly studied method of nitrile ylide generation is the photolytic ring-opening of 2*H*-azirines **50**,⁴⁶ Scheme 11.

The usefulness of this approach stems from the fact that a wide range of substituted 2*H*-azirines **51** are available by photolysis of vinyl azides⁴⁷ or by the modified Neber reaction,⁴⁸ Scheme 12.



Scheme 12

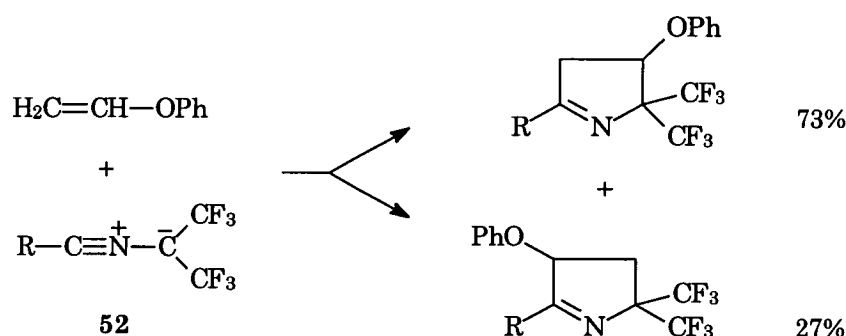
2.3 Reactions of Nitrile Ylides

2.3.1 Intermolecular Reactions of Nitrile Ylides

Nitrile ylides undergo typical 1,3-dipolar reactions such as dimerisation³⁶ and [3+2] cycloadditions to multiple bonds to form five-membered heterocycles.⁴⁸

The 1,3-dipolar cycloaddition reactions of nitrile ylides with all dipolarophiles, except the very electron rich, are HOMO controlled according to Sustmann's classification.¹³ That is, the dominant frontier orbital interaction is that between the 1,3-dipole HOMO and the dipolarophile LUMO. This explains the reactivity of nitrile ylides towards electron-deficient multiple bonds. Dipolarophiles of this type have LUMO's which are lower in energy and which can, therefore, mix better with the nitrile ylide HOMO.

Substituents on the nitrile (C-1) terminus have been shown to have little effect on the HO-LU separation of nitrile ylides⁴⁹ and therefore have no substantial reactivity or regioselectivity effect on the reaction with electron deficient double bonds. Substitution at the methylene (C-3) terminus, however, does affect both regioselectivity and reaction rate. Electron-withdrawing or conjugating groups, lead to slower reaction of the nitrile ylide. Electron-withdrawing groups at the C-3 terminus affect the regioselectivity of the nitrile ylide cycloaddition by making the energy difference between the bent and linear conformations much smaller, as explained earlier. For example, Burger⁵⁰ found that two trifluoromethyl groups on the methylene carbon of the nitrile ylide **52** gave a mixture of regioisomers in the reaction with phenyl vinyl ether, Scheme 13.

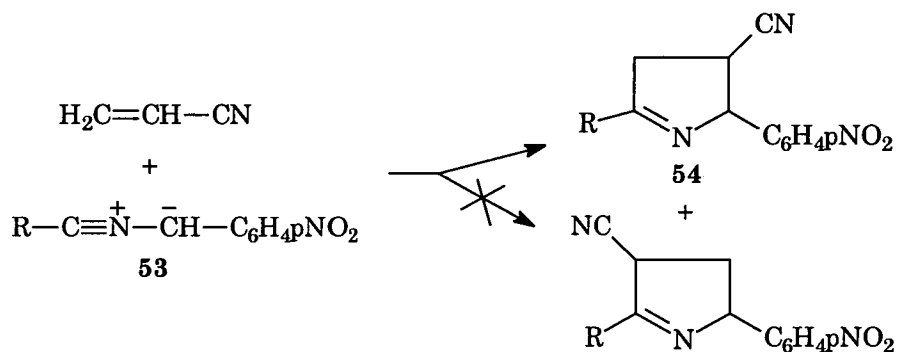


Scheme 13

Increasing the LU energy of the dipolarophile through electron donating substituents suppresses the rate of 1,3-dipolar cycloaddition whereas electron-withdrawing or conjugating groups on the dipolarophile lower the LU energy and accelerate cycloaddition.^{51,52}

In unsymmetrically substituted dipolarophiles with electron-withdrawing or conjugated substituents at only one end, the larger coefficient in the LUMO is at the dipolarophile terminus remote from the substituents. As described earlier, the preferred mode of reaction involves attachment of the dipole and dipolarophile termini with the

larger coefficients. Thus, in the reaction of the nitrile ylide **53** with acrylonitrile the C-1 terminus of the 1,3-dipole becomes attached to the unsubstituted end of the dipolarophile, Scheme 14.



Scheme 14

Nitrile ylides have also been shown to undergo 1,3-dipolar cycloaddition with C=S, C=N, C=O and cumulated double bonds⁵³ as well as with carbon-carbon triple bonds to give pyrroles.

Reactions of nitrile ylides with *E* and *Z* alkenes have shown that the reaction is stereospecific, with the stereochemistry of the alkene being retained in the product. This provides strong evidence for the proposed concerted mechanism.⁵⁴

The mechanism of the 1,3-dipolar cycloaddition of nitrile ylides has been proposed to proceed *via* a "parallel-planes" transition state. That is, the 1,3-dipole and dipolarophile approach each other to form a two-plane orientation complex,¹ Figure 5.

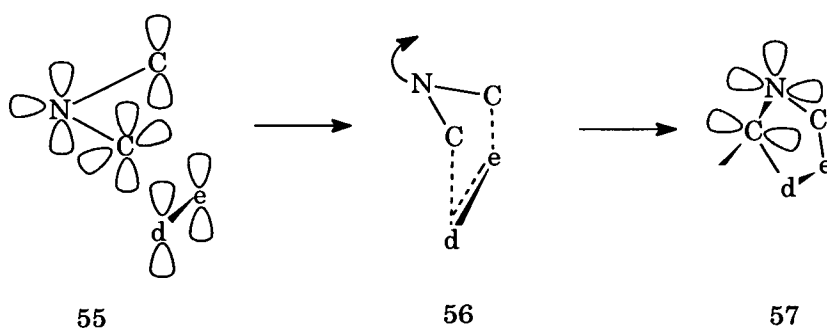
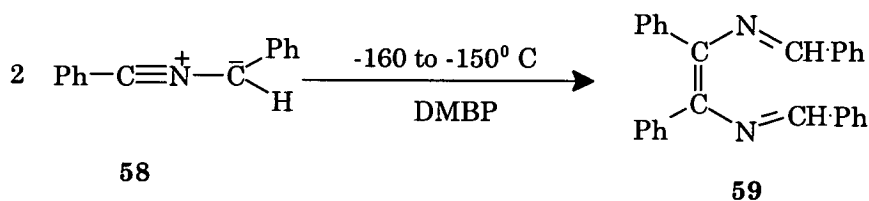


Figure 5

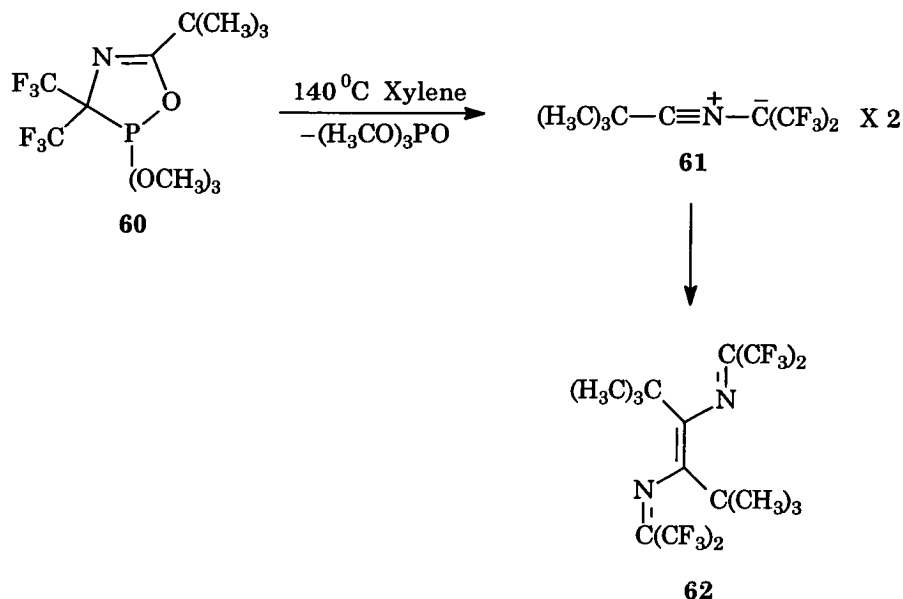
During the activation process the "linear" bond system of the nitrile ylide must bend in order to place the termini in contact with the termini of the π -bond system in the dipolarophile. This involves disruption of the orthogonal double bond, but leaves the allylic π -system intact. The nitrogen is moved upwards (the path is indicated by an arrow) until it reaches the plane of the remaining four centres in **57**.

Nitrile ylides produced photochemically from *2H*-azirines are stable in glassy matrices at -196 °C. When the DMBP matrix for benzonitrilio phenylmethanide **58** is warmed to -150 °C, a new compound 2,5-diaza-1,3,5-hexatriene **59** is rapidly formed. Nitrile ylide **58** reacts at -150 °C by a direct head-to-head coupling reaction, a type of [1+1] "cycloaddition"; that is **58** reacts with itself as though it corresponds to a resonance-stabilised carbene,⁵⁵ Scheme 15.



Scheme 15

Burger and co-workers⁵⁶ observed that heating 5-*tert*-butyl-3,3-bis(trifluoromethyl)-2,2,2-trimethoxy-2,3-dihydro-1,4,2 λ^5 -oxazaphosphole **60** in xylene at 140 °C results in a 70% yield of *E*-2,5-diazahexa-1,3,5-triene **62** and trimethyl phosphate. The intermediate involved in this reaction is most likely the nitrile ylide **61** which furnishes **62**, by a head-to-head combination, Scheme 16.



Scheme 16

2.3.2 Intramolecular Reactions of Nitrile Ylides

As discussed previously 1,3-dipolar cycloadditions proceed *via* a “parallel-planes” transition state. In molecules which contain both a nitrile ylide and a dipolarophilic moiety, normal 1,3-dipolar cycloaddition may take place if the two groups can attain this geometry. If this geometry cannot be attained then a different mode of reaction becomes dominant.

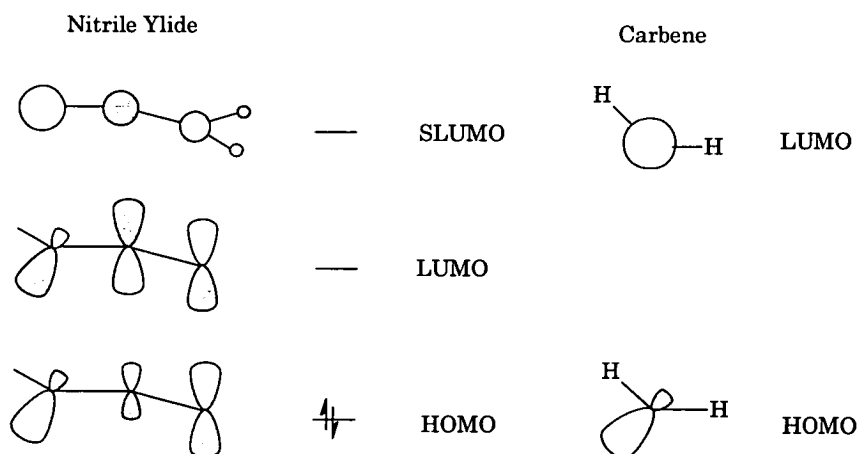
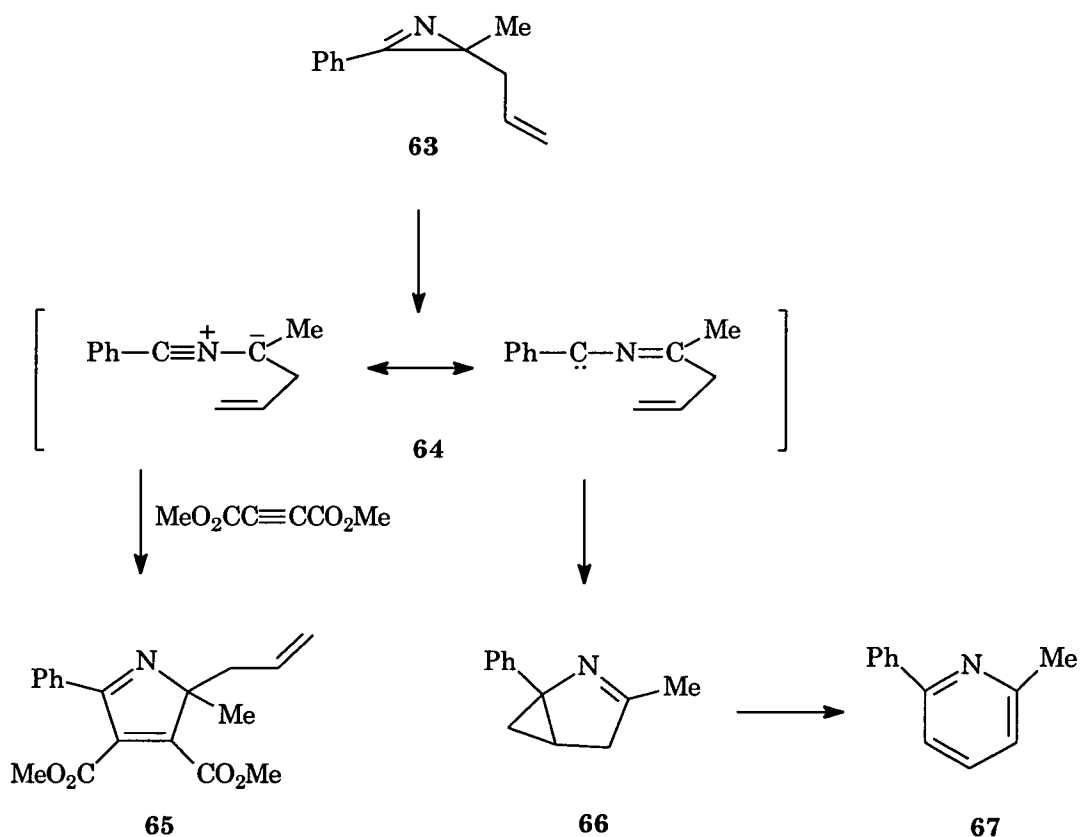


Figure 6

Houk's calculations³⁷ have shown that for the bent nitrile ylide geometry, the HOMO and LUMO bear a strong resemblance to the HOMO and LUMO of a singlet carbene, Figure 6.

Since singlet carbenes readily react with double bonds then an analogous 1,1-cycloaddition of nitrile ylides with double bonds might be expected. This type of reaction was first observed by Padwa and Carlsen in 1975.⁵⁷ When a deaerated solution of 2-allyl-2-methyl-3-phenyl-2*H*-azirine **63** was irradiated in cyclohexane, an extremely rapid and clean conversion to 3-methyl-1-phenyl-2-azabicyclo[3.1.0]hex-2-ene **66** was observed, Scheme 17.

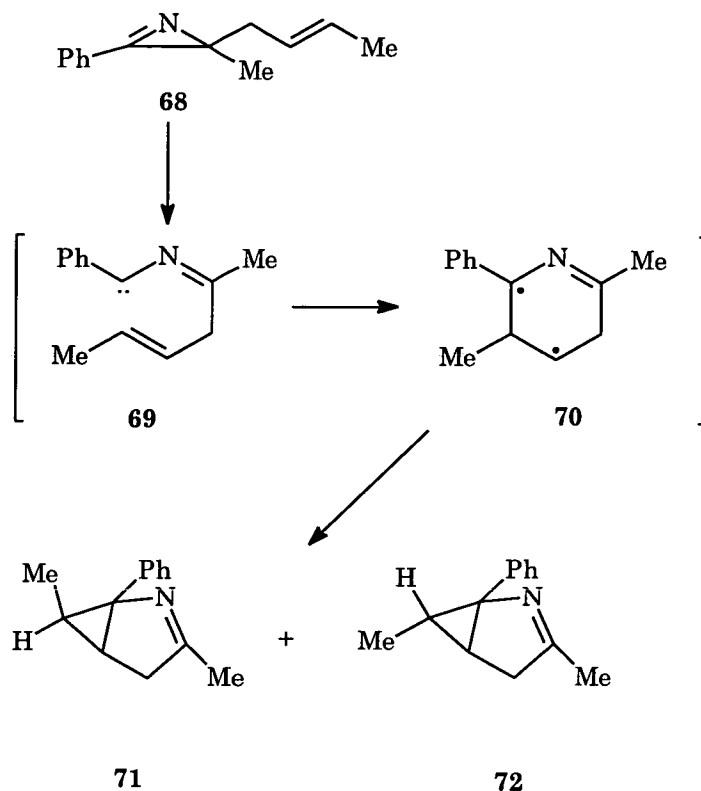


Scheme 17

The intermediacy of the nitrile ylide **64** in this process was demonstrated by trapping with a reactive dipolarophile. When carried out in the presence of dimethyl acetylenedicarboxylate the 1,1-cycloaddition was entirely suppressed and only the cycloadduct **65** derived from 1,3-dipolar cycloaddition was isolated.

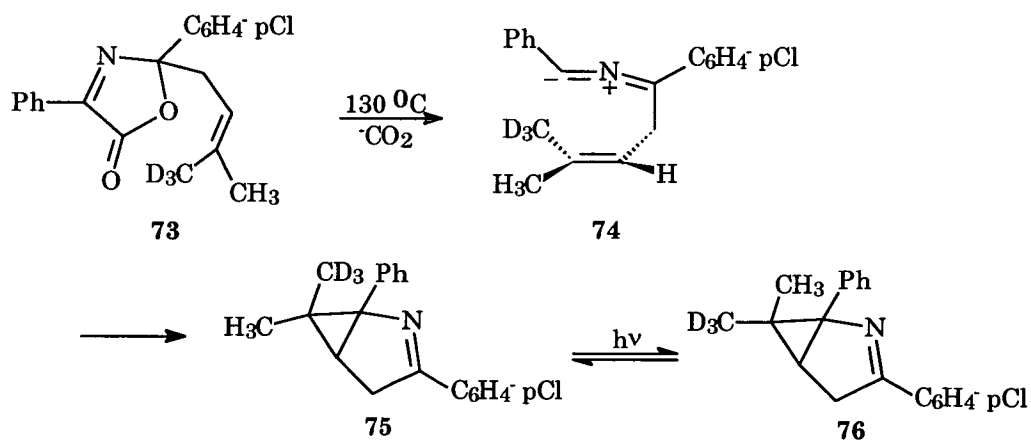
The carbene like reactivity of nitrile ylides arises when the parallel-planes complex required for 1,3-dipolar cycloaddition cannot be attained. The two-plane transition state requires a high degree of order, and geometric constraints may prevent the four centres required for reaction from coming together with the required geometry. The transition state for 1,1-cycloaddition has lower geometric requirements as only three centres are involved.

In 1977 Padwa and Carlsen⁵⁸ proposed a stepwise carbenic reaction of allyl-substituted nitrile ylides to explain the fact that the reaction gave a mixture of products, Scheme 18. It was suggested that photolysis of the azirine **68** led to formation of the nitrile ylide **69**. Padwa proposed that attack of the carbene carbon of the dipole at the terminal position of the allyl double bond generated a six membered intermediate **70**. Subsequent collapse of this intermediate was proposed to give the mixture of 2-azabicyclohexene products **71** and **72**.



Scheme 18

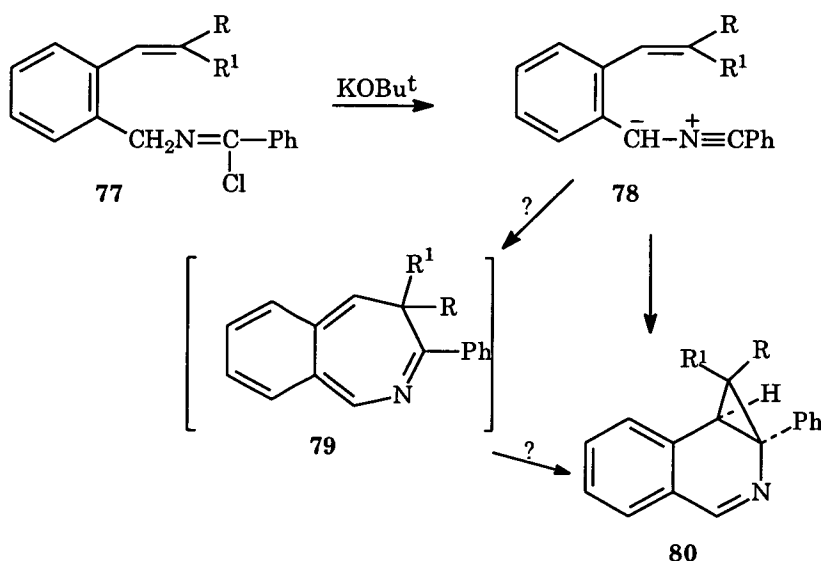
The “non-concertedness” of this reaction was surprising given that singlet carbenes undergo concerted cycloaddition with olefins.⁵⁹ Fischer and Steglich,⁶⁰ who generated analogous nitrile ylides by thermal methods demonstrated that the reaction was in fact concerted.



Scheme 19

Thermolysis of the 3-oxazolin-5-one **73** gave the nitrile ylide **74** which reacted *via* 1,1-cycloaddition to give the 2-azabicyclo[3.1.0]hexene **75** with total retention of stereochemistry. Subsequent irradiation of the product caused an equilibrium of the *endo*- and *exo*-isomers to be set-up, thus accounting for the product mixture observed by Padwa, Scheme 19.

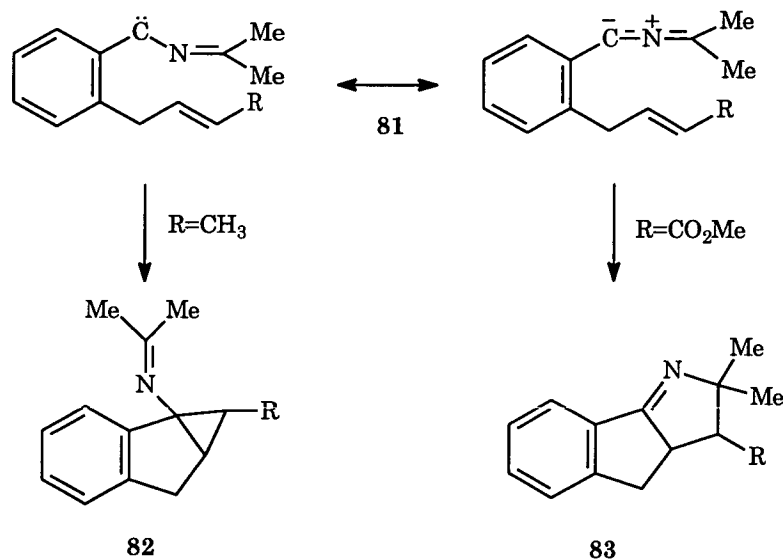
Sharp⁶¹ also found that the nitrile ylides **78** generated by dehydrochlorination of the imidoyl chloride **77** underwent reaction which gave the products expected from a concerted 1,1-cycloaddition. In all cases there was a complete retention of stereochemistry, consistent with a concerted reaction. The nitrile ylide **78** possesses an $\alpha,\beta,\gamma,\delta$ -conjugated system and it is possible that the reaction proceeds *via* 1,7-electrocyclisation to give the benzazepine **79**, which rapidly ring-collapses to the cyclopropa[*c*]isoquinoline **80**, Scheme 20.



Scheme 20

The mode of intramolecular cycloaddition also depends on substituents.^{46, 62} For example nitrile ylide **81**, $\text{R}=\text{Me}$, reacts cleanly *via* 1,1-cycloaddition to give **82**, but the presence of electron withdrawing

groups on the double bond **81**, $R=CO_2Me$, leads to a switch in mechanism with **83** being the only isolated product,⁴⁶ Scheme 21.



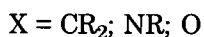
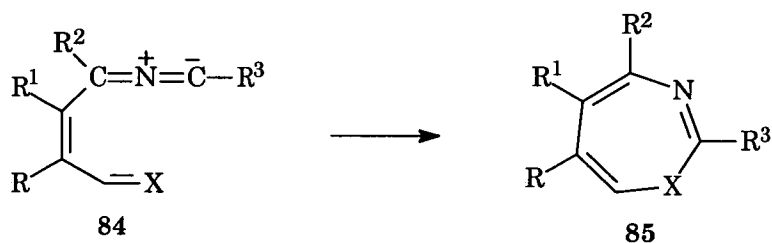
Scheme 21

The dual reactivity of nitrile ylides in intramolecular cycloadditions, as demonstrated by the above reactions, can be explained by the flexibility of the 1,3-dipole. The linear form is understood to be the species which reacts in 1,3-dipolar cycloadditions *via* a transition state which involves bending of the 1,3-dipole, whereas the bent form is responsible for the carbene-like 1,1-cycloadditions. The ability to bend and rehybridise with only a small energy demand is crucial for the attainment of the transition-state geometries required for both 1,1- and 1,3-cycloaddition.

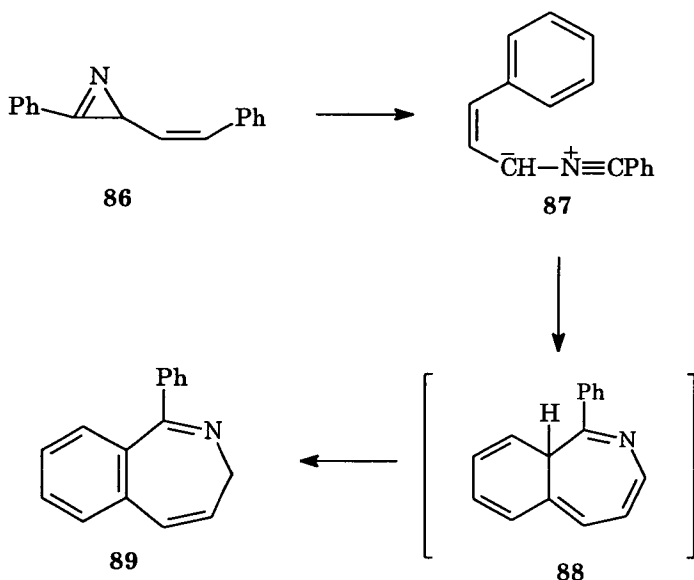
2.3.3 1,7-Electrocyclisation Reactions of Nitrile Ylides

Nitrile ylides of the type **84** which possess $\alpha,\beta,\gamma,\delta$ -conjugation are isoelectronic with the heptatrienyl anion. This system is known to undergo thermal conrotatory electrocycloisatation to the cycloheptadienyl

anion, therefore the analogous reaction of the nitrile ylide would be expected to give products of the type **85**.

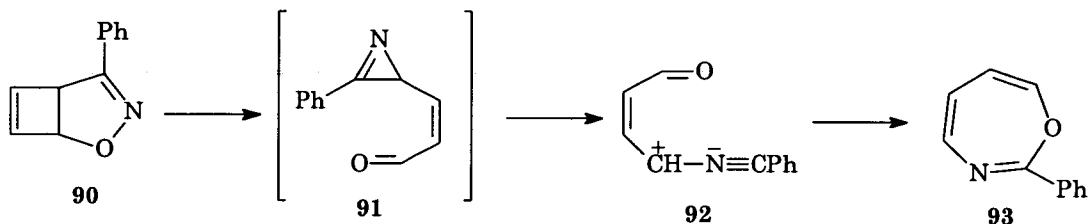


Padwa and co-workers⁶³ found that irradiation of *Z*-3-phenyl-2-styryl-2*H*-azirine **86** in benzene gave 1-phenyl-3*H*-2-benzazepine **89** as the one major product. The formation of this product was explained in terms of a 1,7-electrocyclisation of the nitrile ylide **87** followed by a [1,5] sigmatropic hydrogen shift, Scheme 22.



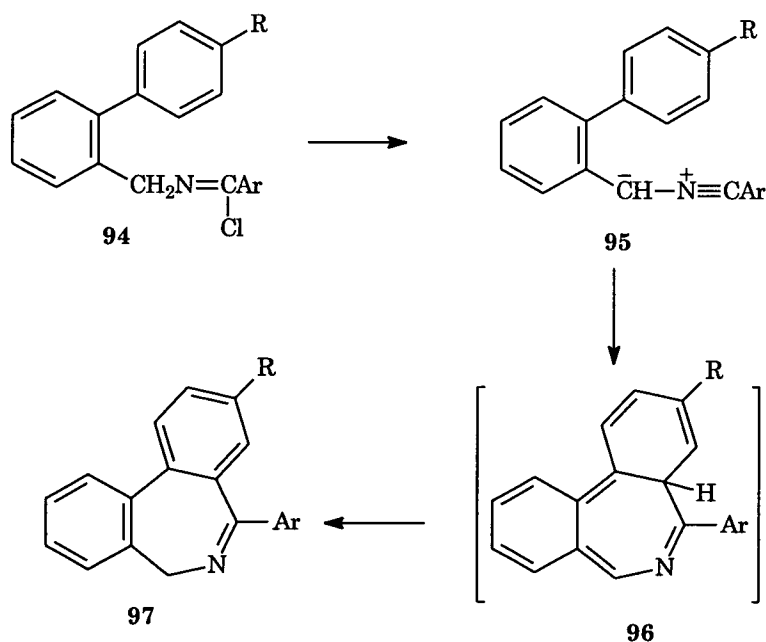
Scheme 22

Photolysis of the bicyclic isoxazoline **90** is believed to involve the intermediacy of the *Z*-azirine **91**. This species could not be isolated but ring-opens to the nitrile ylide **92**. The 1,7-electrocyclisation of the nitrile ylide gives 2-phenyl-1,3-oxazepine **93**,⁶⁴ Scheme 23.



Scheme 23

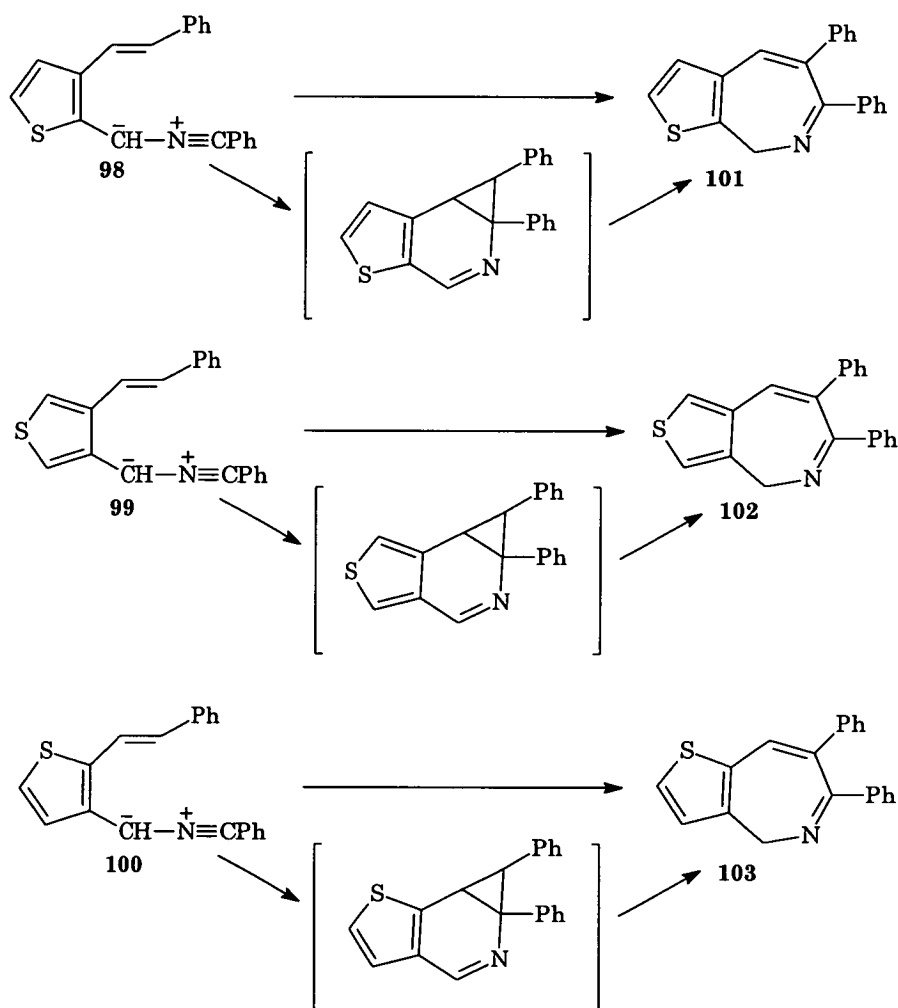
The scope of 1,7-electrocyclisations of nitrile ylides has been broadened by the work of Sharp and co-workers. Nitrile ylides of the type **95**, thermally generated *via* the 1,3-dehydrochlorination of imidoyl chlorides **94** were shown to undergo 1,7-electrocyclisation to give dibenz[*c,e*]azepines **97**,⁶⁵ Scheme 24.



Scheme 24

The versatility of 1,7-electrocyclisation reactions of nitrile ylides of this type was extended by incorporation of a heterocyclic moiety into the $\alpha,\beta,\gamma,\delta$ -unsaturated system. Nitrile ylides of the types **98**, **99** and **100** were all shown to give the products expected from 1,7-electrocyclisation **101**, **102** and **103** respectively,⁶⁶ Scheme 25.

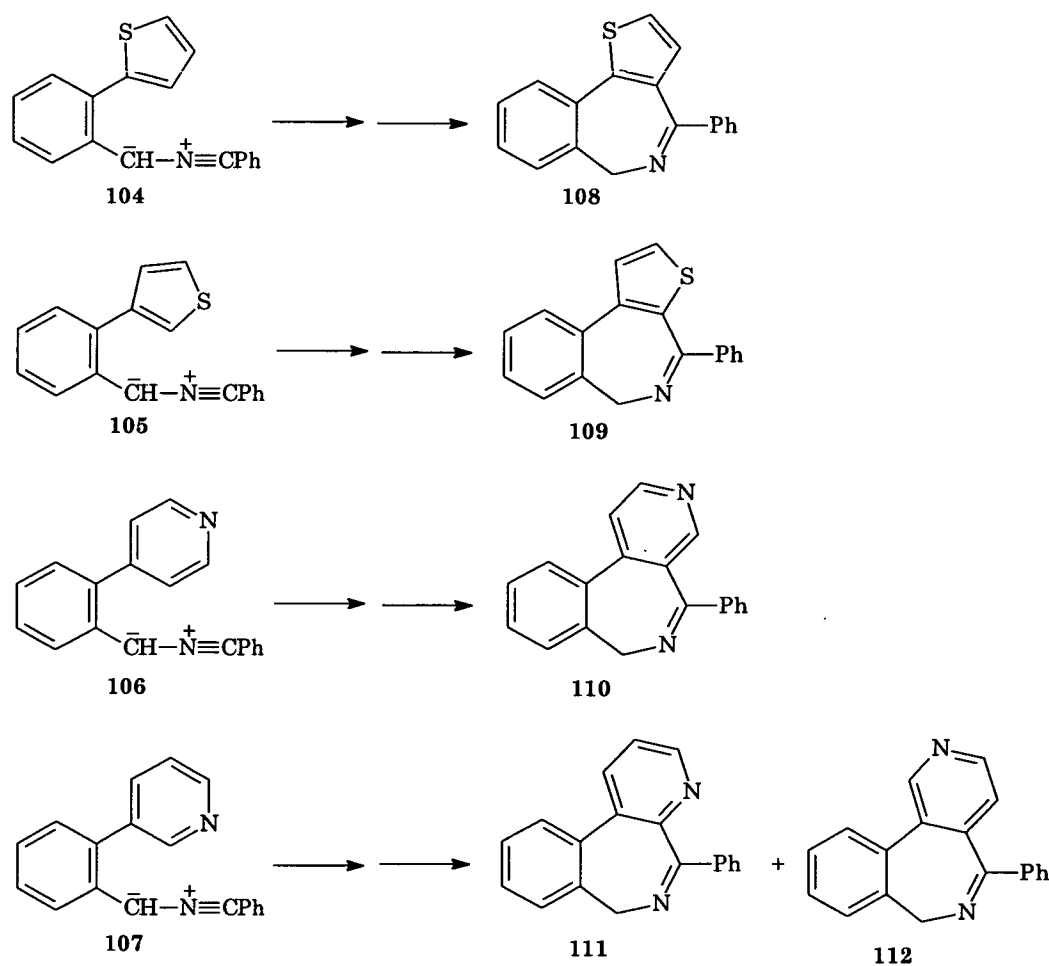
It is not absolutely clear whether these products derive directly from the 1,7-electrocyclisation reaction followed by 1,5-hydrogen migration or from the 1,1-cycloaddition of the nitrile ylide across the olefinic γ,δ -double bond followed by ring expansion.



Scheme 25

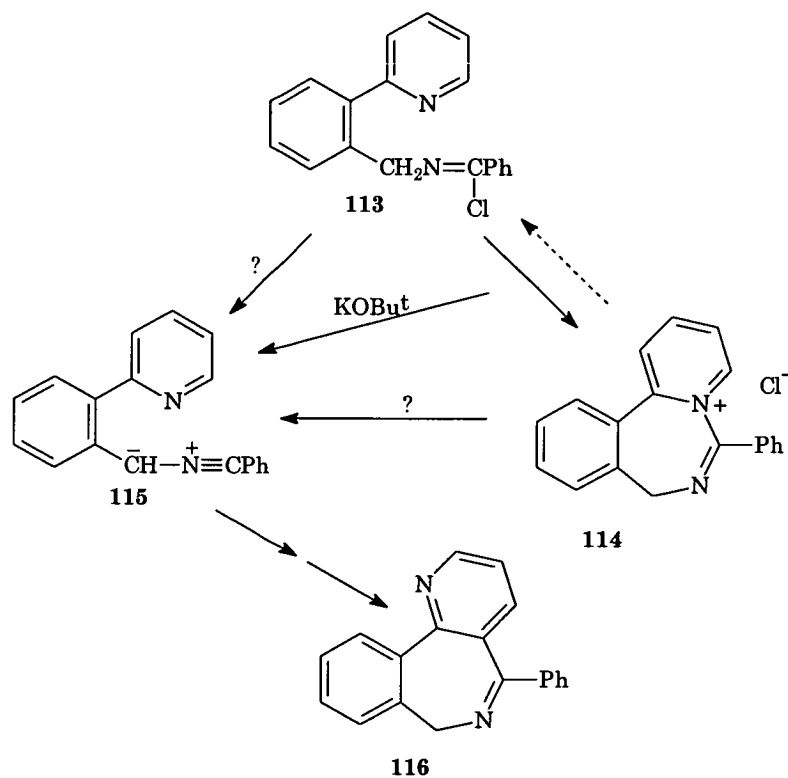
Sharp and Reece⁶⁷ have generated the nitrile ylides **104**, **105**, **106**, **107**, which have been observed to undergo 1,7-electrocyclisation to give the products **108**, **109**, **110**, **111**, **112**, Scheme 26. This represented the first electrocyclisations of a nitrile ylide onto a heterocyclic moiety.

Both of the thiophene nitrile ylides **104** and **105** cyclised as expected to give the azepines **108** and **109**, respectively. As expected from earlier work on diazo cyclisations,⁶⁸ **105** cyclised only at the 2-position of the thiophene ring rather than the 4-position.



Three isomeric pyridine-containing systems **106**, **107** and **115** have also been studied. These contrast with the thiophene analogues in that

azepine formation now requires the electrocyclic substitution of electron-deficient heterocyclic rings. The 4-substituted derivative **106** cyclised to give 5-phenyl-7*H*-pyrido[3,4-*d*][2]benzazepine **110** in good yield. The 3-substituted analogue **107** cyclised at both of the *ortho* positions to give a mixture of the two isomers 5-phenyl-7*H*-pyrido[2,3-*d*][2]benzazepine **111** and 5-phenyl-7*H*-pyrido[4,3-*d*][2]benzazepine **112**. On the basis of other work⁶⁹ which has shown that the reaction rate is increased by the proximity of electron-withdrawing groups to the cyclisation site it seems likely that the major product is compound **111**.



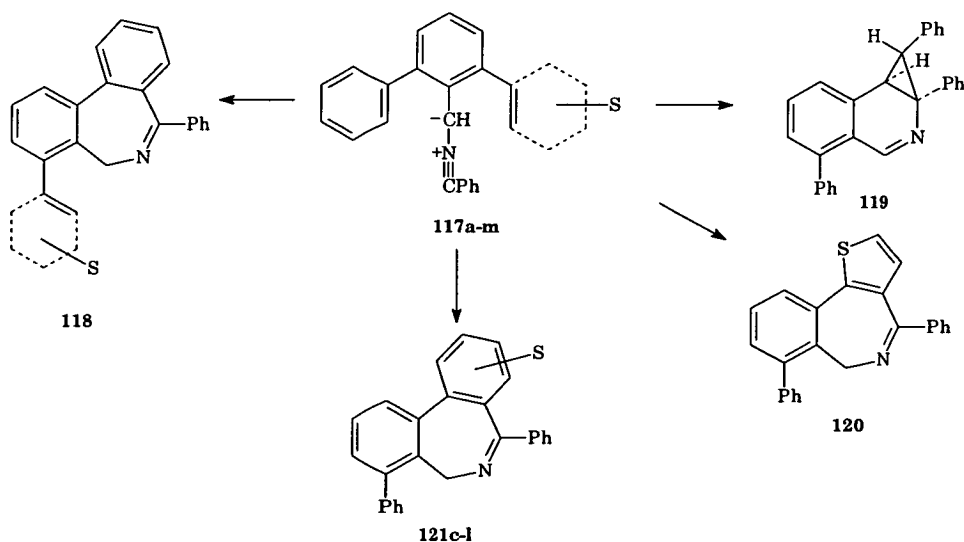
Scheme 27

The 2-pyridyl compound **115** which has one of the two potential cyclisation sites occupied by the pyridine nitrogen atom cyclised at the free *ortho* position. It seems likely that 5-phenyl-7*H*-pyrido[3,2-*d*][2]benzazepine **116** is formed in the usual way *via* the nitrile ylide **115**

which itself may be formed either directly from the imidoyl chloride **113** or *via* the deprotonation and ring opening of compound **114**, Scheme 27.

Although the basic reaction mechanism is known there are still major gaps in the understanding of the factors controlling these electrocycisation reactions. Cullen and Sharp⁷⁰ reported the first attempt to obtain data for the cyclisation of nitrile ylides. The objective was to study the effects of substituents of various types close to the cyclisation site.

The cyclisations involving the olefinic double bond **117a** and the thiophene ring **117b**, confirm the reactivity order expected on the basis of the electrocycisation mechanism, *i.e.* that the activation energy increases with the aromatic character of the γ,δ -double bond. The results concerning the effects of substituents in the aromatic ring, show a distinct pattern of reactivity but one which cannot be explained with any degree of certainty. With the exception of the *ortho* substituted case **117m**, where the effect is steric in origin, the overall pattern observed is that the reactivity of the ring is at a minimum when it is unsubstituted and is increased by both electron-donating and -withdrawing substituents, Scheme 28 and Table 2.



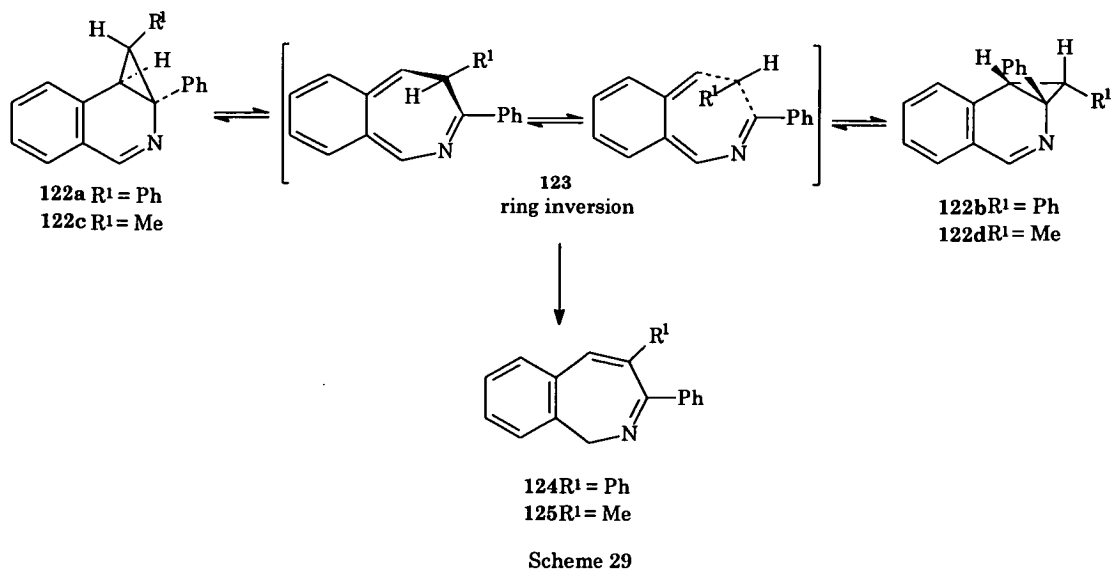
Scheme 28

Table 2.

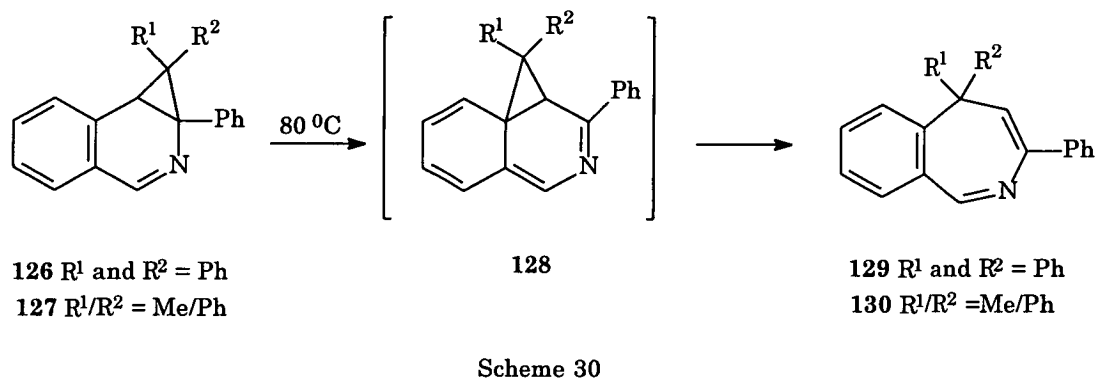
Reactant	Substituent	Products	Ratios
117a	<i>E</i> -2-phenylethenyl	119/118	>100
117b	2-Thienyl	120/118	>100
117c	3,5-Dimethylphenyl	121c/118	8.3
117d	3,5-Bis(trifluoromethyl)phenyl	121d/118	32
117e	3-Nitrophenyl	121e/118	>100
117f	3-Methoxyphenyl	121f/118	5.6 : 0.8
117g	4-Methylphenyl	121g/118	1.5
117h	4-Trifluoromethylphenyl	121h/118	12.8
117i	4-Dimethylaminophenyl	121i/118	1.3
117j	4-Methoxyphenyl	121j/118	1.6
117k	4-Chlorophenyl	121k/118	2.2
117l	4-Fluorophenyl	121l/118	1.2
117m	2-Methylphenyl	118	>100

3. Thermal Rearrangement of Cyclopropa[c]isoquinolines

The reactions of cyclopropa[c]isoquinolines fall into two distinct categories depending on the nature of the substituents at C-1 of the reactant. In cases where one of the substituents was hydrogen, **122a-d**, then the reaction gave the *1H*-2-benzazepines **124** and **125**, apparently *via* the path shown in Scheme 29.⁶⁶



The thermolysis of the cyclopropa[*c*]isoquinolines **126** and **127a/b** which have no hydrogen at C-1 follows a different path, Scheme 30.

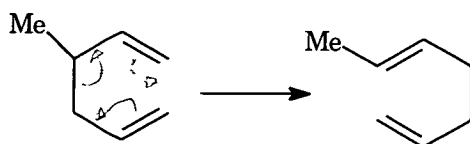


The reactions were slower than those of **122a-d** and gave the 5*H*-2-benzazepines **129** and **130**.

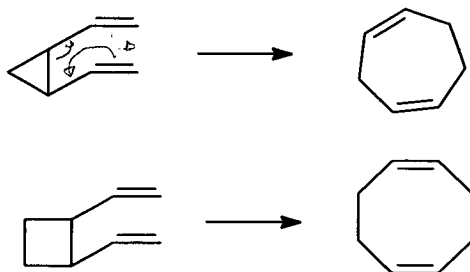
4. Cope and Hetero-Cope Rearrangement

When 1,5-dienes are heated, they isomerise, in a [3,3]-sigmatropic rearrangement known as the Cope rearrangement.⁷¹ A Cope rearrangement can only be detected when the diene is not symmetrical about the 3,4-bond. Any 1,5-diene gives this rearrangement; for example,

3-methyl-1,5-hexadiene heated to 300 °C gives 1,5-heptadiene.⁷² The reaction is obviously reversible and produces an equilibrium mixture of the two 1,5-dienes, which is richer in the thermodynamically more stable isomer.

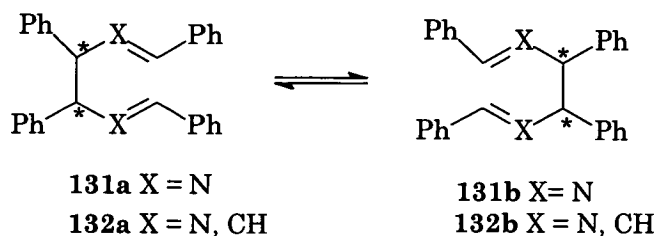


The 1,5-diene system may be inside a ring or part of an allenic system⁷³ but the reaction does not take place when one of the double bonds is part of an aromatic system. When the two double bonds are in vinylic groups attached to adjacent ring positions, the product is a ring four carbons larger. This has been applied to divinylcyclopropanes and cyclobutanes.



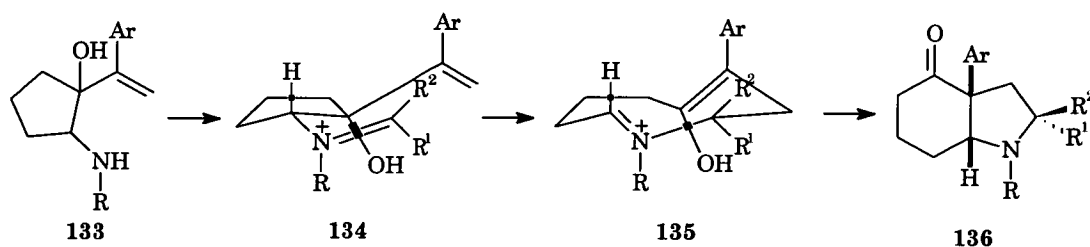
Cis-1,2-divinylcyclopropanes give this rearrangement so rapidly that they generally cannot be isolated at room temperature,⁷⁴ though exceptions are known.⁷⁵

Chiral 1,2-diaminoethanes have been synthesised *via* the diaza-Cope rearrangement **131a** to **131b**.⁷⁶ The tetraarylmonoaza Cope system **132a** has also been found to undergo stereospecific valence isomerisation to form novel chiral 3-alkenylamines and their derivatives, Scheme 31.⁷⁷



Scheme 31

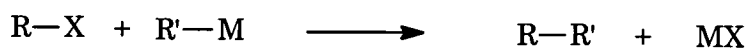
The aza-Cope rearrangement has been used for alkaloid synthesis.⁷⁸ The cationic aza-Cope rearrangement of iminium ions derived from *cis*-2-amino-1-(1-arylethenyl)cyclopentanols **133** selectively yield *cis*-octahydroindole products **136**, Scheme 32.



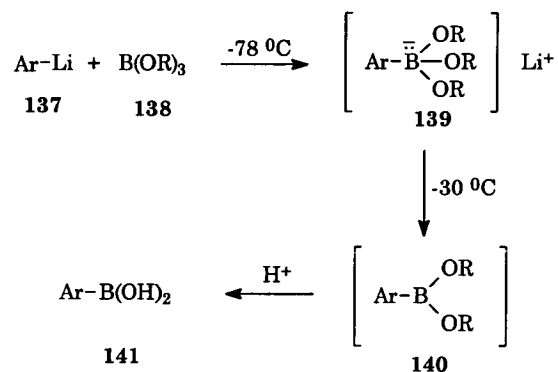
Scheme 32

5. Palladium Mediated Coupling Reactions

Until recently, there were few organic reactions which could generate carbon-carbon bonds between unsaturated systems. However, this area of synthesis was revolutionised by the discovery that transition metals such as palladium and nickel are very effective in catalysing cross-coupling reactions of unsaturated organic halides (R-X) and a range of unsaturated organometallic derivatives (R'-M).

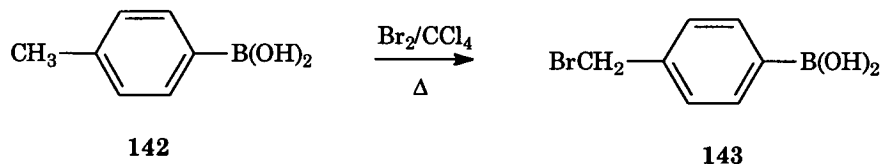


A range of organometallic reagents, boronic acids, boranes and organotin reagents have been used in this area. Boronic acids are readily prepared from organolithium or Grignard compounds with the appropriate alkyl borate,^{79, 80} Scheme 33. The most commonly used alkyl borates are trimethyl and triisopropyl borate.



Scheme 33

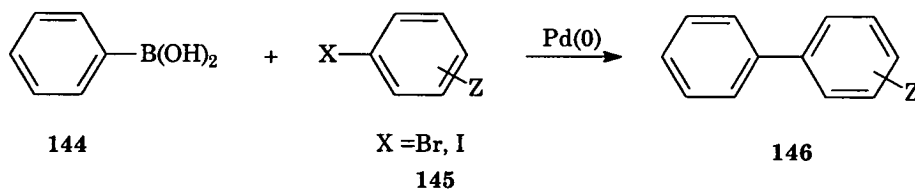
The boronic acids, dependant on the ease of preparation of the organolithium or Grignard compounds, are normally formed in high yields from their halides. This functional group is stable enough to allow several reactions,⁸¹ for example bromination of the methyl group in 4-methylphenylboronic acid **142**, Scheme 34.



Scheme 34

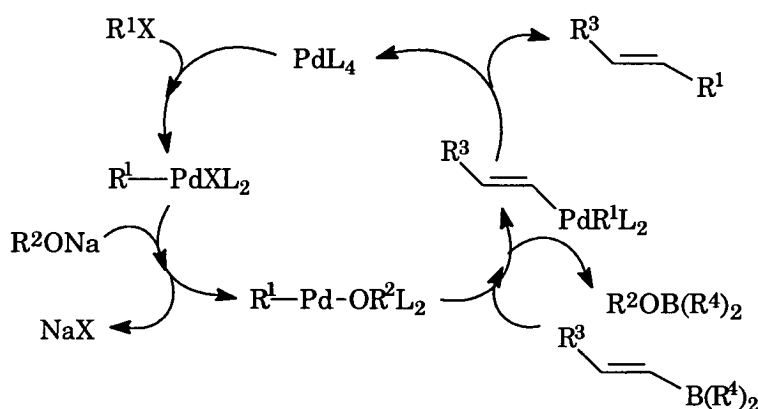
The most important reaction is palladium cross coupling reactions with unsaturated organic halides. The original research into the cross-coupling reaction of boronic acids was carried out by Suzuki,⁸² who

optimised the conditions required for the coupling of phenylboronic acid 144 to various substituted aryl halides, Scheme 35.



Scheme 35

The maximum yields were obtained using a 10% excess of the boronic acid, equimolar amount of sodium carbonate solution and 3 mol% of the tetrakis(triphenylphosphine)palladium (0) over the bromo compound. Gronowitz⁸³ refined the method by introducing DME as the solvent in preference to Suzuki's benzene. A mechanism for the cross-coupling reaction of boron containing compounds was suggested by Suzuki,⁸⁴ as the catalytic cycle shown in Figure 7.



Catalytic cycle for tetrakis(triphenylphosphine) palladium (0)

Figure 7

Discussion

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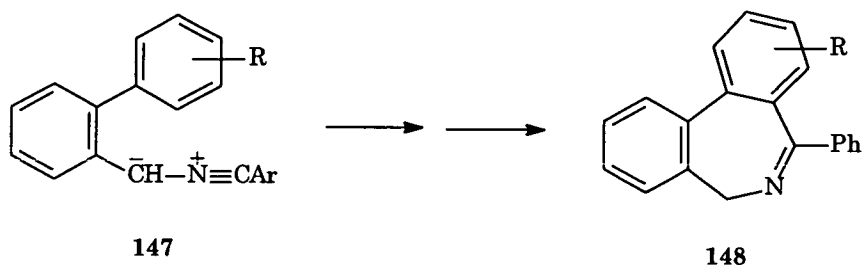
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Discussion

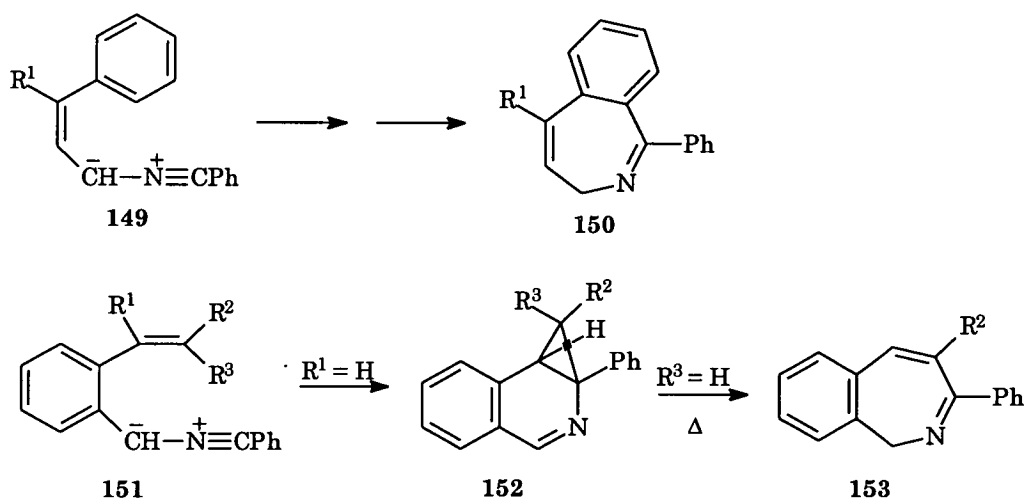
1. Program of Research

This thesis is concerned with the reactions of diene- and triene-conjugated nitrile ylides. Previous work⁸⁵ had shown that intermediates of the type **147** cyclise to give dibenzazepines **148**, Scheme 36.



Scheme 36

The cyclisation also occurs readily in systems of the type **149** where the α,β -unsaturation is olefinic and the γ,δ -unsaturation forms part of an aromatic ring,⁸⁶ Scheme 37.

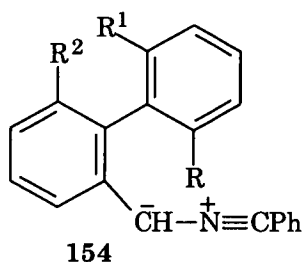


Scheme 37

When the γ,δ -unsaturation is olefinic *e.g.* **151** the nitrile ylides cyclise to give cyclopropa[c]isoquinolines **152** as the primary isolated products. These are formally derived *via* 1,1-cycloaddition of the nitrile ylide to the olefinic double bond.⁶⁶ These cyclopropa[c]isoquinolines are isomerised to benzazepines **153** upon heating, when R^2 or $R^3 = H$, Scheme 37.

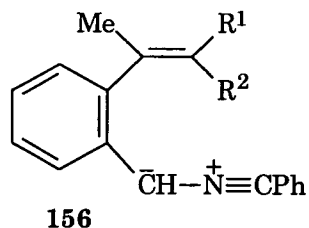
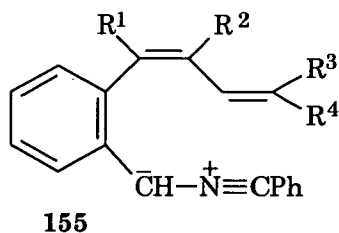
The overall objective of this research was to undertake an exploratory study of systems analogous to the above but having the conjugation extended by one more double bond.

The first objective was to generate nitrile ylides of the type **154** and find out how they would react when subjected to the conditions which were required for cyclisation in the previous $\alpha,\beta:\gamma,\delta$ -systems. The extent of the research into these nitrile ylides was to be determined by the nature of the results.



$R = H, CH=CHPh, CH=CH_2, CH=CHCO_2Me$
 $R^1 = H, Me$
 $R^2 = H, Me$

The second objective was to generate and study the nitrile ylides **155** where α,β -unsaturation forms part of a phenyl ring and the $\gamma,\delta:\epsilon,\zeta$ -unsaturation is olefinic. As a consequence of this work a number of diene-conjugated nitrile ylides of the type **156** were also studied.



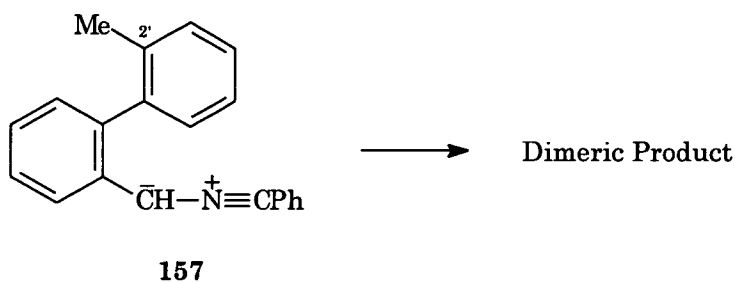
Section One

1.1 Synthetic Studies on the Reactions of Benzonitrile-2-(2-alkenylaryl)benzyl Ylides

Preamble

The system chosen for the first part of the project was the triene-conjugated nitrile ylide of the type 154. Previous work with diene-conjugated nitrile ylides of the type 147 in which both the α,β - and the γ,δ -double bonds are aromatic had shown that they react *via* a 1,7-electrocyclisation on to the aryl ring followed by a [1,5]-sigmatropic hydrogen shift to give the benzazepines 148, Scheme 36.

Subsequent work showed that when a methyl group is located at the 2' position, 157, 1,7-electrocyclisation on to the phenyl ring becomes uncompetitive and dimerisation⁸⁵ takes place, Scheme 38.



Scheme 38

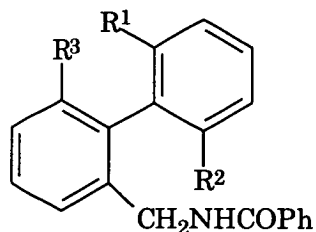
The failure of **157** to cyclise must be due to the steric interaction of the 2'-methyl group with the *ortho*-hydrogen atom in the adjacent ring which restricts rotation about the bond joining the two benzene rings. It is thought that 1,7-electrocyclisation normally takes place *via* a helical transition state^{34,66} which involves some degree of twist in the conjugated system, but in this case it appears that the steric effect of the methyl group so much inhibits conjugation between the two benzene rings that an electrocyclisation reaction is not possible.

It was decided to investigate whether replacement of the methyl group by an olefinic moiety would lead to new reactivity at the ϵ,ζ -double bond. There are many possible reaction paths available to **154**, when $R^1, R^2 = H$, *e.g.* [3+2] cycloaddition, 1,1-cycloaddition across the olefinic double bond, 1,7-electrocyclisation on to the free position of the appropriate phenyl ring, 1,9-electrocyclisation and dimerisation. These will be discussed in more detail later.

1.2 Synthesis of *N*-[2-(2-Alkenylaryl)benzyl]benzamides

In recent years, several routes to biaryls have been developed with various organometallic derivatives. The route developed by Suzuki⁸⁵ using arylboronic acids was the one which had previously been utilised in the group and shown to be very useful. In all cases the synthesis of the title compounds was achieved *via* the palladium(0) catalysed cross-coupling of aryl halides with 2-*N*-benzoylaminomethylphenylboronic acid **165**, Scheme 41, or *via* the coupling of *N*-benzoyl-2-bromobenzylamine **159** with arylboronic acids. The range of amides synthesised as precursors to the nitrile ylides of the type **154** are summarised below.

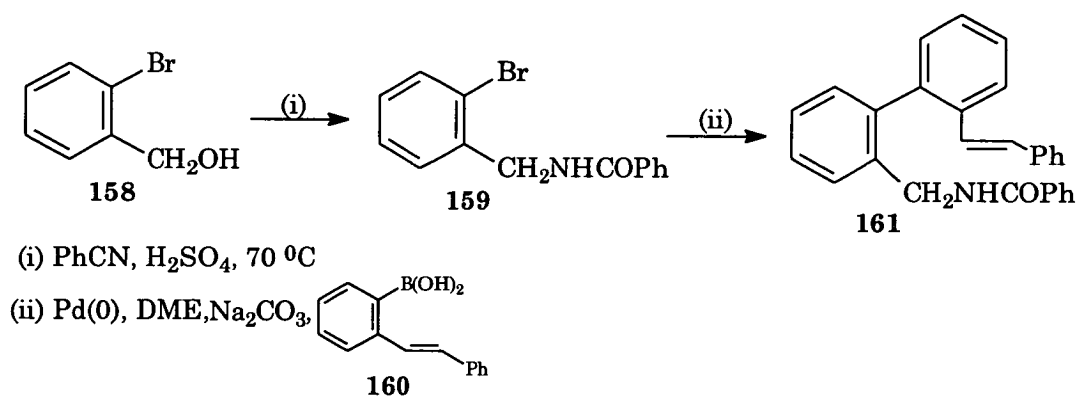




Compound	R ¹	R ²	R ³
161	H	CH=CHPh	H
166	H	CH=CHCO ₂ Me	H
169	H	CH=CH ₂	H
174	CH ₃	CH=CH ₂	H
178	H	H	CH ₃
179	H	CH=CH ₂	CH ₃

(a) *N*-[2-(2-(*E*-2-Phenylethenyl)phenyl)benzyl]benzamide **161**

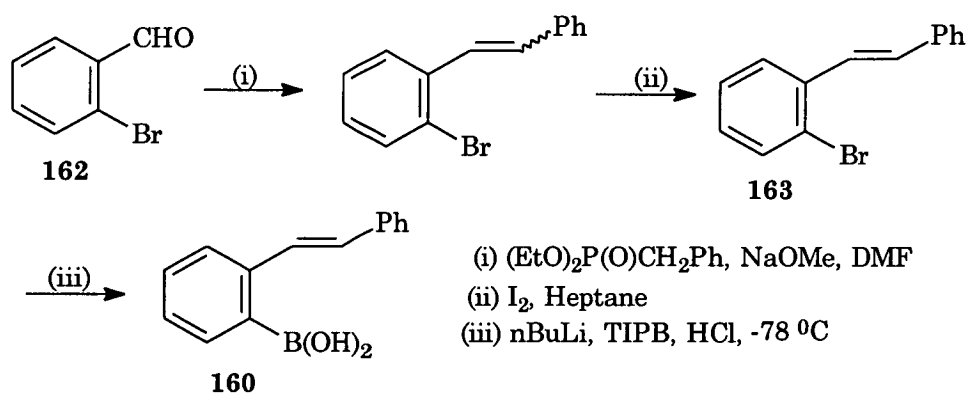
The synthesis of the amide **161** is shown in Scheme 39. The key step is the coupling of *N*-benzoyl-2-bromobenzylamine **159** with 2-(*E*-2-phenylethenyl)phenylboronic acid **160**.



Scheme 39

The first reaction undertaken in this multi-step synthesis was the Ritter reaction,⁸⁷ which was achieved in a 70% yield by the slow addition of concentrated sulfuric acid to a mixture of benzonitrile, which also acts as solvent, and 2-bromobenzyl alcohol **158** at 70 °C.

The boronic acid **160**, required in step (ii), was synthesised in two steps, Scheme 40. The first step was to prepare the *E*-alkene **163**, from **162** *via* the Wadsworth Emmons⁸⁸ olefination reaction or *via* the Wittig reaction. The former proved to be the more successful and simpler method resulting in a 95% yield. Both reactions gave mixtures of *E* and *Z*-isomers which required isomerisation. Heating the isomeric mixture at reflux in heptane with iodine, converted the *Z*-isomer into the required *E*-isomer.

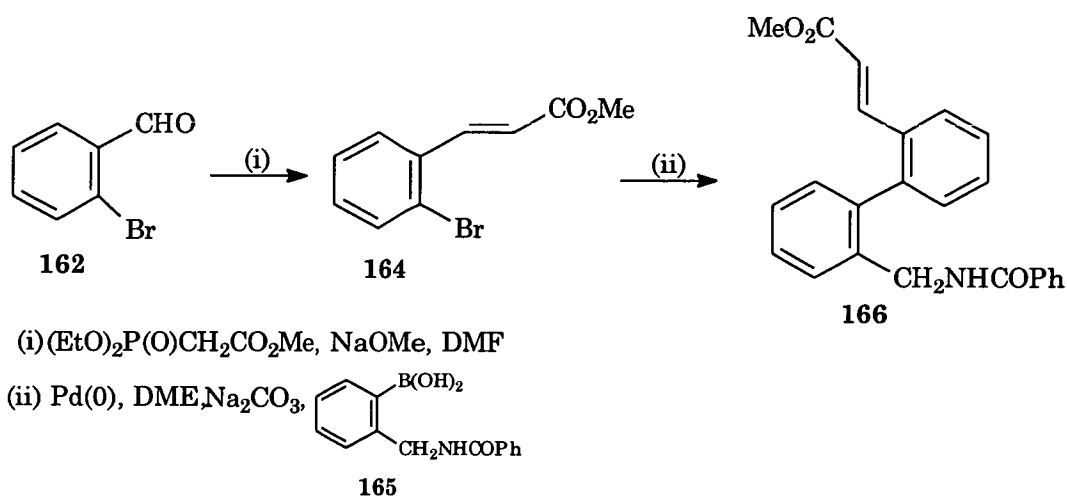


Scheme 40

Triisopropylborate was added dropwise to the lithiated derivative of **163** in THF at -78 °C, to convert the bromo group into its boronic acid derivative in a 70% yield. 2-(*E*-2-Phenylethenyl)phenylboronic acid **160** and compound **159** were then coupled using a Pd(0) catalysed cross coupling reaction producing **161** in a 70% yield after dry-flash chromatography and recrystallisation.

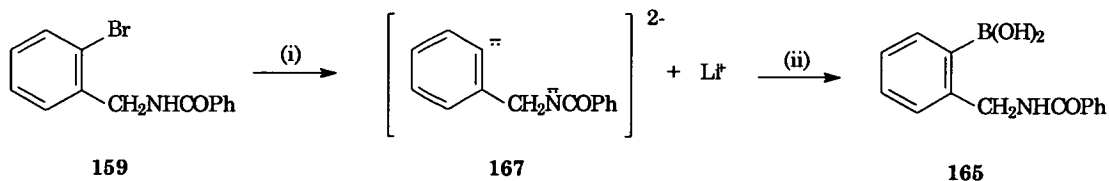
(b) *N*-[2-(2-(2-Carbomethoxyethenyl)phenyl)benzyl]benzamide **166**

The amide **166** was synthesised as shown in Scheme 41. Methyl-3-(2-bromophenyl)prop-2-enoate **164** was synthesised in a 95% yield using methyldiethylphosphonoacetate and 2-bromobenzaldehyde in the Wadsworth Emmons reaction. The product **164** was found to be the *E*-isomer in >95% by ¹H nmr spectroscopy which gave the coupling constant between the olefinic protons as 16 Hz.



Scheme 41

The preparation of the boronic acid **165**, Scheme 42, involved the formation of the dilithiated derivative of **159** and its reaction with a borate ester. The dianion **167** was generated by sequential treatment of **159** with methyllithium to deprotonate selectively the amide and then with *tert*-butyllithium to effect metal-halogen exchange.⁸⁹ Reaction with triisopropylborate gave **165** in a 90% yield.



(i) MeLi, ^tBuLi, -78°C

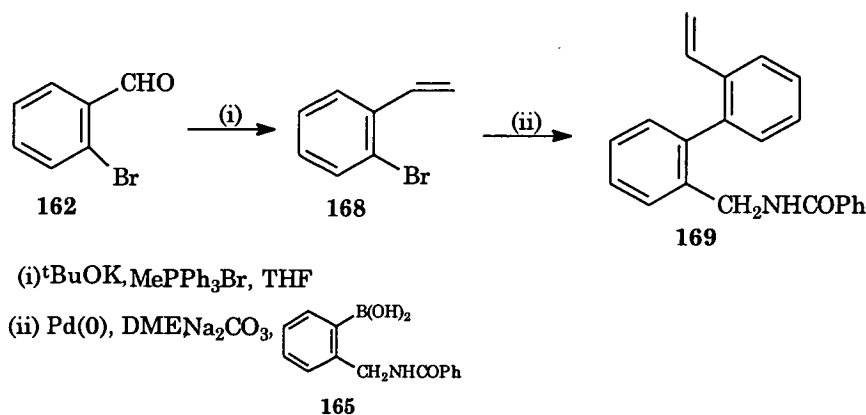
(ii) TIPB, HCl

Scheme 42

The Pd(0) catalysed cross-coupling reaction between **164** and **165**, Scheme 41, gave the desired amide **166** in a 70% yield. The olefinic protons in the amide **166** are seen as doublets in the ¹H nmr spectrum at δ 6.5 and δ 7.5 with coupling constants J 16.0 Hz. Therefore, reactions involving the ε,ζ-double bond should be easily detected by ¹H nmr spectroscopy.

(c) N-[2-(2-Ethenylphenyl)benzyl]benzamide 169

The amide **169** was synthesised as shown in Scheme 43.



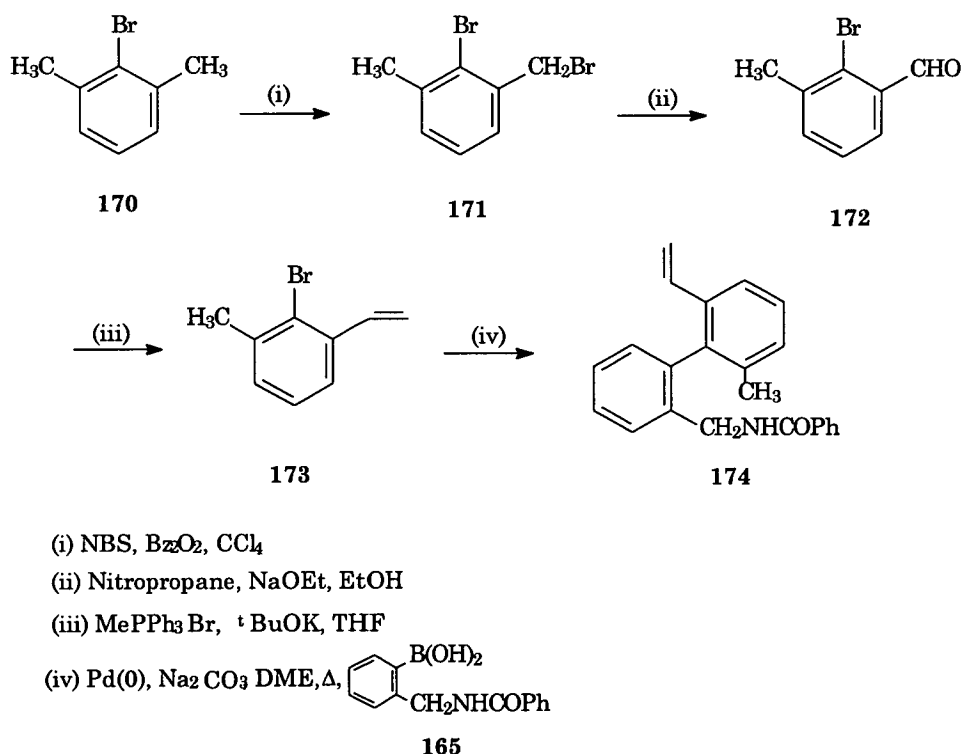
Scheme 43

2-Bromostyrene **168** was synthesised *via* the Wittig reaction in a 75% yield, but, was found to polymerise readily at room temperature, therefore, care was taken in the storage of this compound. The key step

was the Pd(0) catalysed cross coupling reaction which had gone to completion after 20 hours. The product **169** was isolated in a 78% yield after dry-flash chromatography and crystallisation. The olefinic protons are easily seen at δ 5.11, δ 5.63 and δ 6.38, in the ^1H nmr spectrum. Therefore, any reaction involving the ϵ,ζ -double bond will be easily detected unlike the amide **161** where the olefinic protons are amongst the aromatic multiplet.

(d) *N*-[2-(2-Ethenyl-6-methylphenyl)benzyl]benzamide **174**

The amide **174** was synthesised *via* the coupling of **165** and **173**, as shown in Scheme 44.



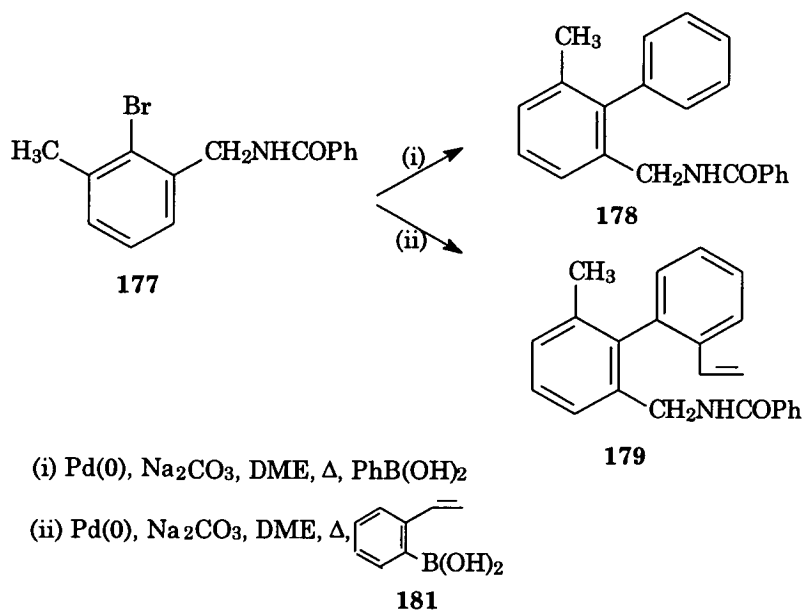
Scheme 44

Bromination of **170** with *N*-bromosuccinimide in carbon tetrachloride gave 2-bromo-3-methylbenzyl bromide **171** (53%), separated

from the dibrominated compound and unreacted starting material by distillation under vacuum. Using the methodology of Hass and Bender⁹⁰ the benzyl bromide **171** was converted to the aldehyde **172** in a 70% yield. 2-Ethenyl-6-methylbromobenzene **173** was then synthesised in 76% yield, *via* the Wittig reaction.

(e) *N*-[3-Methyl-2-phenylbenzyl]benzamide **178** and *N*-[3-Methyl-2-(2-ethenylphenyl)benzyl]benzamide **179**

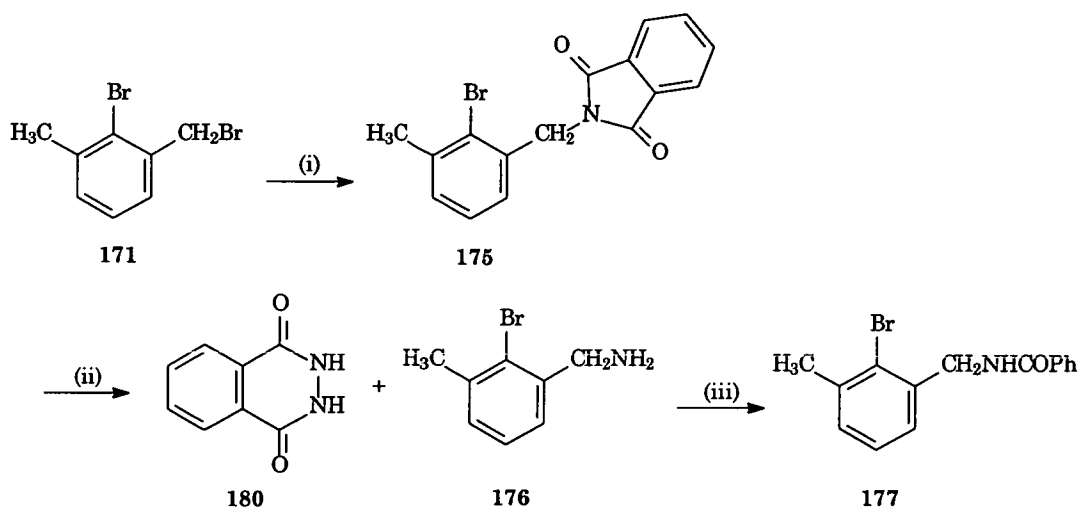
The next objective was to synthesise the amides **178** and **179** *via* the coupling of compound **177** with phenylboronic acid and 2-ethenylphenylboronic acid **181**, respectively; Scheme 45.



Scheme 45

Bromination of one of the methyl groups in **170** using NBS gave compound **171**. Reaction of this with potassium phthalimide in DMF⁹¹ gave **175** in the first stage of the Gabriel reaction,⁹² Scheme 46. This phthalimido derivative **175** was then cleaved with hydrazine hydrate⁹³ to

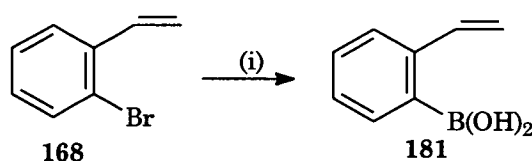
give the amine **176** and phthaloyl hydrazide **180**. The amine was converted to *N*-benzoyl-2-bromo-3-methylbenzylamine **177** with benzoyl chloride in a 78% yield.



- (i) K.Pthal., DMF
(ii) Hydrazine Hydrate, MeOH
(iii) Benzoyl Chloride, Na_2CO_3 , DCM

Scheme 46

2-Ethenylphenylboronic acid **181** was synthesised from 2-bromostyrene with *n*-butyllithium and TIPB in a 52% yield, Scheme 47.



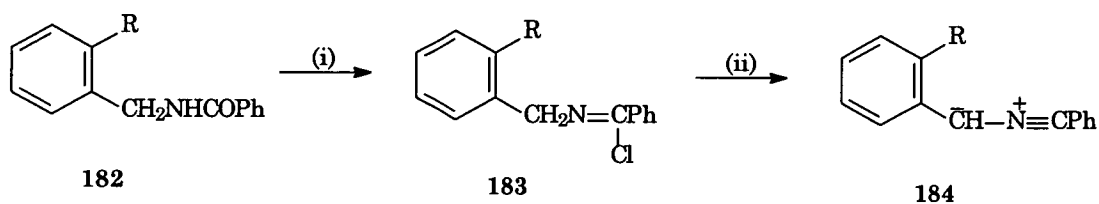
- (i) *n*BuLi, TIPB, HCL, $-78\text{ }^\circ\text{C}$

Scheme 47

1.3 Generation and Reaction of the Nitrile Ylides Derived From Substituted *N*-[2-(2-Alkenylaryl)benzyl]benzimidoyl Chlorides

In this research the nitrile ylides were generated by the 1,3-dehydrochlorination of imidoyl chlorides. The preparation of imidoyl chlorides from amides was carried out using either thionyl chloride, phosphorus pentachloride or chloromethylenedimethylammonium chloride. The method of choice involved the use of thionyl chloride as both by-products, being gaseous, could be readily removed. Amides of the type **182** were chlorinated using a large excess of thionyl chloride in ether at reflux overnight. Any remaining by-products, HCl and SO₂, were removed under high vacuum at room temperature.

Nitrile ylides of the type **184** were generated at 0 °C by dissolving the imidoyl chloride **183** in dry THF and adding two equivalents of solid potassium *tert*-butoxide, Scheme 49.



(i) SOCl₂, Ether, Δ

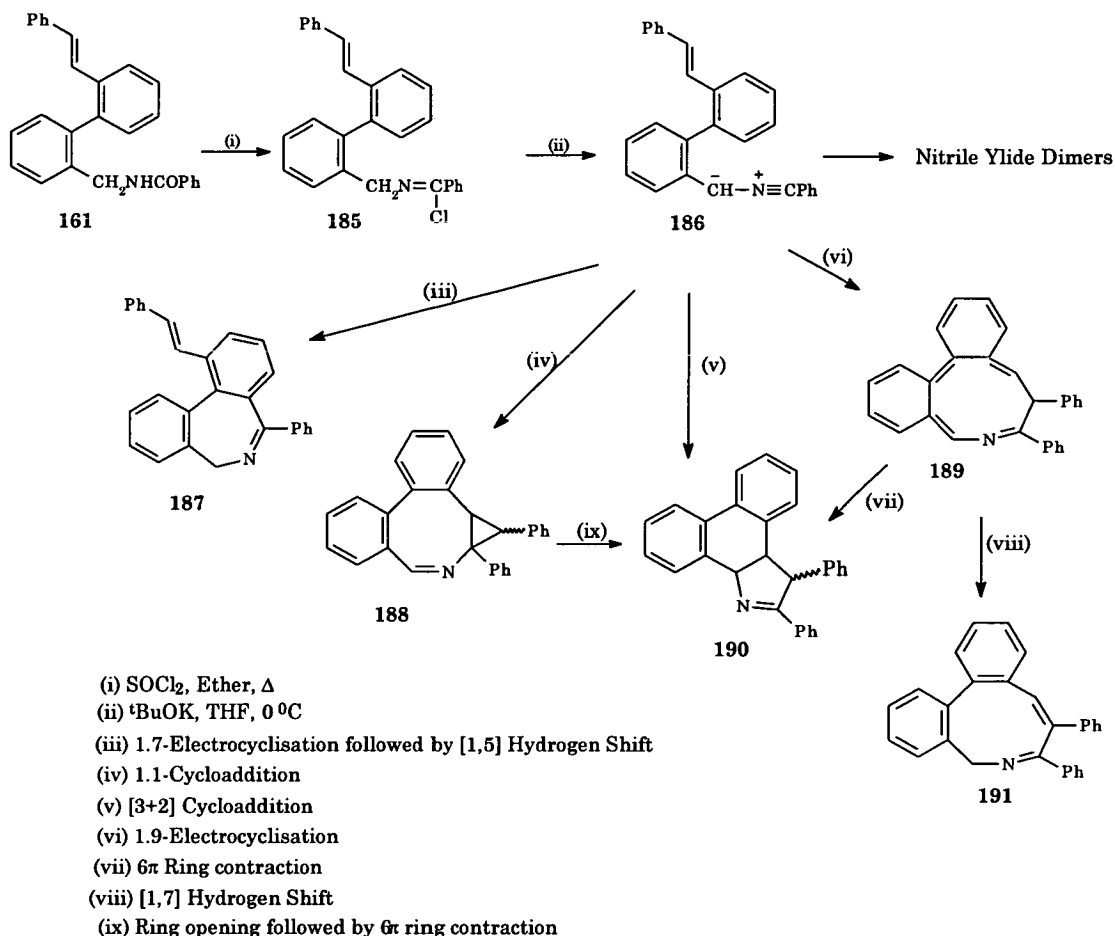
(ii) ^tBuOK, THF, 0° C

Scheme 49

The excess of potassium *tert*-butoxide was added to ensure that sufficient base was present to dehydrochlorinate the imidoyl chloride as well as react with any residual by-products from the chlorination and any adventitious moisture.

(a) Benzonitrile-2-(2-(*E*-2-phenylethenyl)phenyl)benzyl Ylide 186

The first reactions to be investigated in this study were those of the nitrile ylide 186, Scheme 50.



Scheme 50

N-[2-(2-(*E*-2-Phenylethenyl)phenyl)benzyl]benzamide 161 was converted to the imidoyl chloride 185, as described above. The product was then examined by ^1H nmr spectroscopy and the conversion into 185 was checked by the change in chemical shift and the coupling of the methylene protons. Compound 161 has a pair of doublet of doublets (each methylene proton is coupled to the other, which in turn are coupled to the NH proton), and 185 has a singlet which, as usual for imidoyl chlorides,

occurs slightly downfield of the amide CH_2 absorptions. This method of confirmation of the identity of the imidoyl chloride was used with all such conversions in this research. The imidoyl chloride **185** was then dissolved in dry THF at 0 °C, and a two-fold excess of solid potassium *tert*-butoxide was added. Analysis of the product mixture showed two well defined spots which had different R_f values from the amide **161**. These compounds were separated by dry-flash chromatography and analysed by nmr and mass spectroscopy. The faster running "yellow" spot was thought to be a nitrile ylide dimer from its ^1H nmr spectrum which had a singlet at δ 9.79, assigned as the signal from the $\text{HC}=\text{N}$ proton and from its mass spectrum, $(\text{M}+1)^+$, 743.3426. The structure of the nitrile ylide dimer is thought to be similar to the dimeric product **200**, page 67.

The material corresponding to the second tlc spot was thought to be the 1.7-electrocyclisation product, *i.e.*, a dibenzazepine. The ^1H nmr spectrum showed the methylene protons as the expected pair of doublets at δ 3.99 and δ 4.89 (J 10 Hz). However on examination of the ^1H nmr spectrum the integrals did not have the ratios expected for the pure dibenzazepine **187**. The sample was analysed by HPLC which showed it to be a mixture of two products which were inseparable by chromatography. This result indicated the presence of one monomeric cyclised product and several other products thought to be nitrile ylide dimers, the structures of which are not known.

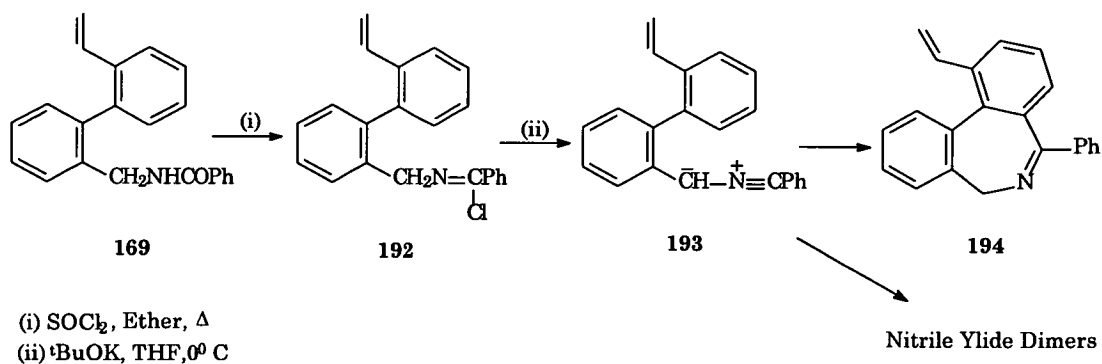
Attempts were made to see whether or not the yield of the monomeric product could be improved and the amount of dimerisation minimised. Formation of dimers is obviously favoured at high nitrile ylide concentrations therefore a series of dilution experiments was carried out in order to keep the concentration of the nitrile ylide low throughout the reaction. These involved doubling the amount of solvent and adding a solution of the imidoyl chloride *via* a syringe over periods of two, six and fifteen hours to a solution of the base potassium *tert*-butoxide in THF.

These experiments had some success and resulted in improving the yield of the monomeric product from 11% to a best yield of 32%. There was also a reduction in the formation of nitrile ylide dimers, but, 12% of the amide was recovered from the fifteen hour dilution experiment.

The olefinic protons in the cyclised product could not be distinguished from the aromatic multiplet in the ^1H nmr spectrum and therefore, it was not possible to say definitely whether or not the olefinic group had been involved in the reaction. The appearance of doublets at δ 3.99 and δ 4.89 in the ^1H nmr spectrum of the monomeric product are indicative of the dibenzazepine structure. This leads us to believe that the main reaction product is 11-(*E*-2-phenylethenyl)-7-phenyl-5*H*-dibenz[*c,e*]azepine **187** resulting from a 1,7-electrocyclisation on to the phenyl ring at the 2' position even though this is a difficult reaction due to steric effects. At first sight the styryl group would appear to be bulkier than the methyl group (Scheme 38). However, a 1,7-electrocyclisation occurred when the styryl group and not the methyl group was located at the 2' position. Therefore, it can be seen from this that the styryl group has less of an inhibitive effect than the methyl group.

(b) Benzonitrile-2-(2-ethenylphenyl)benzyl Ylide **193**

Due to the difficulty in determining whether or not the ϵ,ζ -double bond in nitrile ylide **186** was involved in any reaction, it was decided to study the nitrile ylide **193**. *N*-[2-(2-Ethenylphenyl)benzyl]benzamide **169** was converted to the imidoyl chloride **192** as described earlier and the product was checked by ^1H nmr spectroscopy to confirm complete conversion, Scheme 51.



Scheme 51

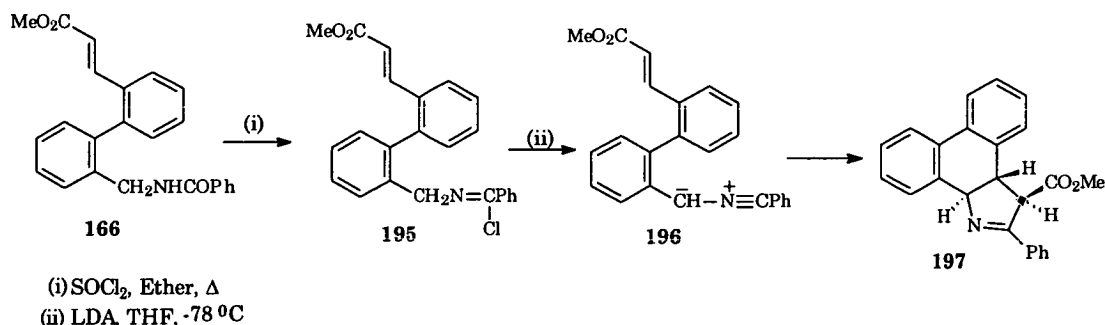
The imidoyl chloride **192** was dissolved in dry THF at 0°C , and reacted with a two-fold excess of solid potassium *tert*-butoxide as usual. Analysis of the product mixture showed four well defined spots, three of which had different R_f values from the starting material **169**. These compounds were separated by dry-flash chromatography and examined by nmr and mass spectroscopy.

The ^1H nmr spectrum showed that the material corresponding to the second tlc spot consisted of the dibenzazepine **194** and another product. The presence of the dibenzazepine was shown by the pair of doublets at δ 3.93 and δ 4.84 (J 10 Hz), which correspond to the methylene protons. Examination of the ^1H nmr spectrum integrals showed that they did not have the ratios expected for the pure dibenzazepine. The product **194** resisted all attempts at recrystallisation and therefore the unidentified impurity could not be removed. The two other products to be isolated after dry-flash chromatography are thought to be nitrile ylide dimers from their ^1H nmr and mass spectra. These structures will be discussed later, pages 68 and 69.

(c) Benzonitrile-2-(2-(2-carbomethoxyphenyl)phenyl)benzyl Ylide 196

Since, surprisingly, there had been no apparent reaction of the ϵ,ζ -double bond in either nitrile ylide **186** or **193**, it was decided to try and

induce a reaction by activating it. The first attempt at activating the olefinic bond was to change its phenyl substituent for a methyl ester, *i.e.* nitrile ylide **196**, Scheme 52. By increasing the major stabilising energy E_1 as in Sustmann Type 1 cycloaddition, it was expected to activate the double bond to cycloaddition.



Scheme 52

The imidoyl chloride **195**, synthesised as described earlier was then treated with LDA to generate the nitrile ylide **196**. Potassium *tert*-butoxide was not used as in the earlier cases in order to avoid possible ester exchange. Initially the LDA was added in quickly at 0°C and then in a subsequent reaction at -78°C over a period of two hours. The latter procedure produced the cleaner reaction resulting in one major separable product which, after dry-flash chromatography and crystallisation gave a crystalline solid in a 50% yield. The ^1H nmr spectrum showed three methine signals, δ 3.72 (1 H, m, CH), 4.41 (1 H, dd, J 3 Hz, 12 Hz, CH), δ 4.80 (1 H, dd, J 3 Hz, 13 Hz, CH), and no longer showed the doublets at δ 6.5 and δ 7.5 which corresponded to the olefinic protons of the starting material. This indicated that a reaction had taken place across the ϵ,ζ -double bond. The mass spectrum confirmed that this product was monomeric, $(M+1)^+$, 353.1411, HPLC analysis showed the presence of only one compound and X-ray crystallography confirmed the structure, Figure 8.

3-Methoxycarbonyl-2-phenyl-3a,11b-dihydro-3H-dibenzo[e,g]indole

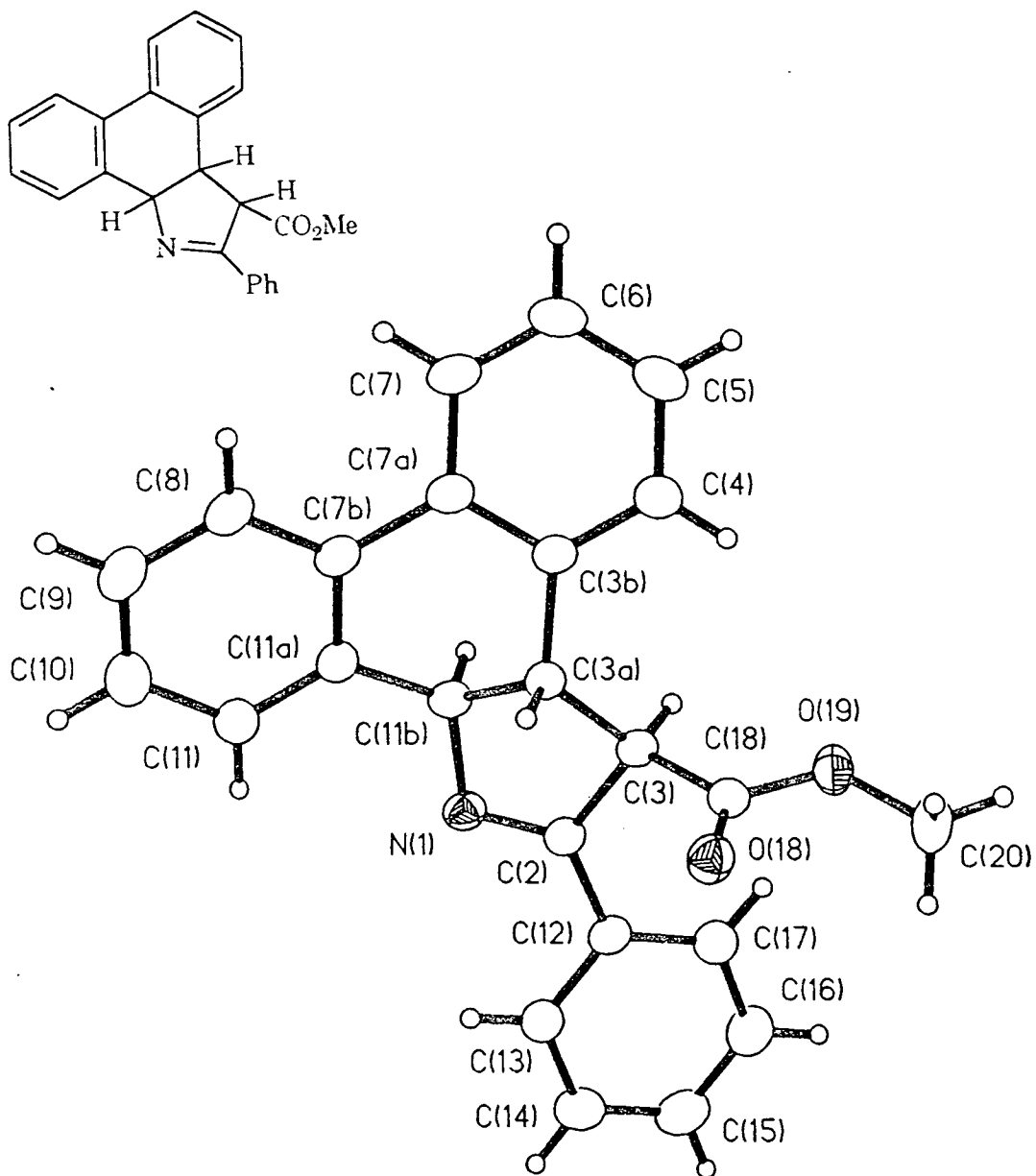


Figure 8

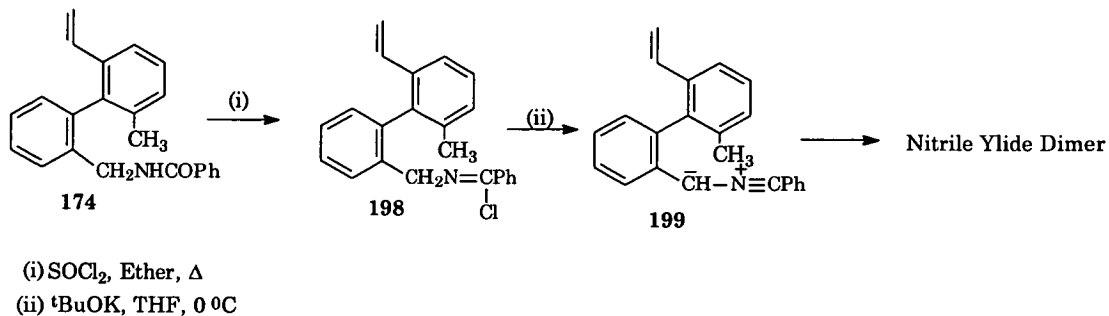
The hydrogens on C₃-C_{3a} and C_{3a}-C_{11b} in the pyrrole ring were found by X-ray crystallography to have an anti relationship with respect to each other. Therefore, the nitrile ylide **196** reacted *via* [3+2] cycloaddition across the ϵ,ζ -double bond. There are several other possible reaction pathways available for the nitrile ylide **196**, as illustrated for nitrile ylide **186** in Scheme 50. If compound **197** had been derived from either a 1,9-electrocyclisation followed by a 6π thermal disrotatory ring contraction or *via* a 1,1-cycloaddition, followed by ring opening and a 6π thermal disrotatory ring contraction, then a mixture of isomers would be expected in which the methine protons in the pyrrole ring would have had a different relationship with respect to each other.

(d) Benzonitrile-2-(2-ethenyl-6-methylphenyl)benzyl Ylide **199**

The first nitrile ylides to be studied in this series were **186** and **193**, Schemes 50 and 51. No reaction was observed with the ϵ,ζ -double bond but a 1,7-electrocyclisation at the 2' position did occur although sterically hindered, along with some dimerisation.

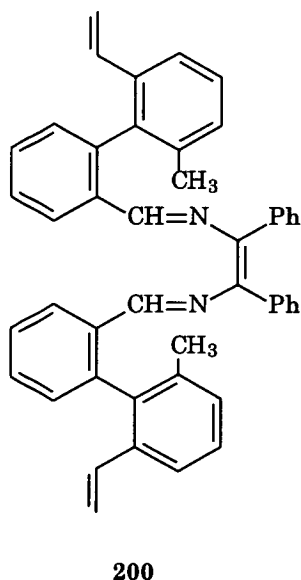
In an attempt to block this reaction path and thus promote reaction at the ϵ,ζ -double bond without directly activating it, a methyl group was placed at the 2' position of the biaryl unit.

N-[2-(2-Ethenyl-6-methylphenyl)benzyl]benzamide **174** was converted into its imidoyl chloride **198** as described earlier and dissolved in dry THF at 0 °C, and reacted with a two-fold excess of solid potassium *tert*-butoxide, Scheme 53.

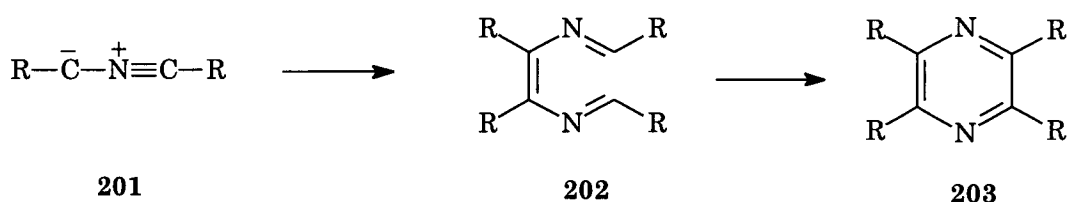


Scheme 53

Analysis of the product mixture showed two well defined spots, both of which had different R_f values from the amide 174. These compounds were separated by dry-flash chromatography and mass spectroscopy showed these compounds to be dimeric, $(M+1)^+$, 619.3108. The ^1H nmr spectrum of the faster running compound showed two singlets at δ 9.61 and δ 9.62, which correspond to the $\text{HC}=\text{N}$ protons. Attempts to crystallise a sample for X-ray analysis were unsuccessful. However the product has been tentatively assigned the structure **200**. Nitrile ylides **186** (^1H nmr spectrum showed a singlet at δ 9.79), and **193** (^1H nmr spectrum showed a singlet at δ 9.75), are also thought to give dimers of this structure.



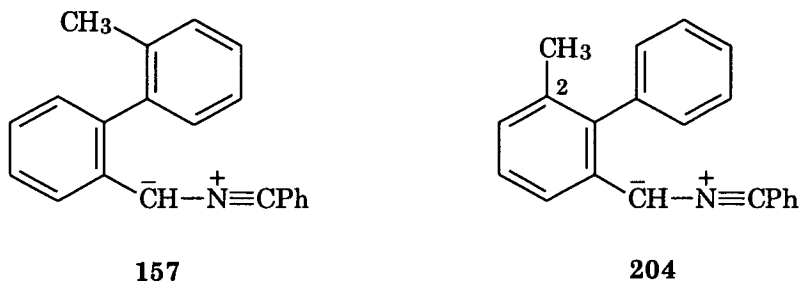
This assignment was based on both the spectroscopic data obtained and the known behaviour of nitrile ylides. It is known that nitrile ylides undergo dimerisation in a 'head-to-head' manner,⁵⁵ which is generally followed by electrocycloisatation and oxidation to pyrazines **203**, Scheme 54. Examination of the ¹H nmr spectrum showed that the material corresponding to the faster running tlc spot consisted of the dimer **200** and another product. The integrals for the HC=N protons and the aromatic multiplet did not have the expected ratio, but it was not possible to say from the nmr data whether the other product was the result of an electrocycloisatation to the pyrazines.



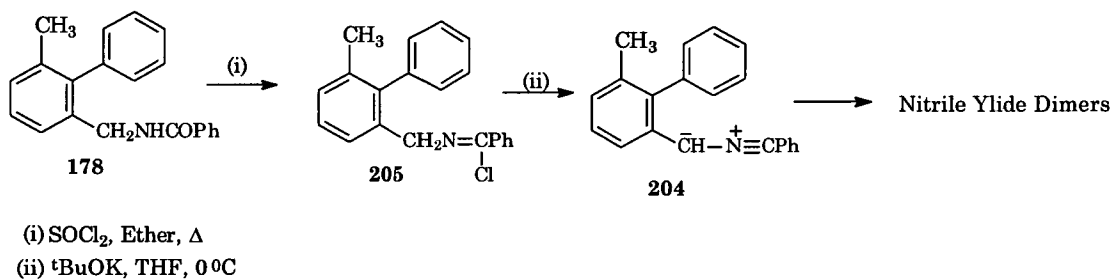
Scheme 54

(e) Benzonitrile-3-methyl-2-phenylbenzyl Ylide **204**

A methyl group located at the 2'-position of the biaryl unit blocks any reaction with the ϵ,ζ -double bond in nitrile ylide **199** and only dimeric products were observed. It was hoped that a methyl group at the 2-position in the nitrile ylide **212**, Scheme 57, would block the 1,7-electrocycloisatation pathway and allow a reaction at the ϵ,ζ -double bond. However, it had not been established previously whether a methyl group located at the 2-position of the biaryl unit in nitrile ylide **204** would hinder electrocycloisatation in the same manner as in nitrile ylide **157**.

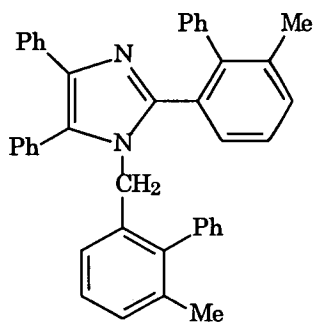


N-[3-Methyl-2-phenylbenzyl]benzamide **178** was converted to the imidoyl chloride **205** as described earlier, then dissolved in dry THF at 0 °C, and reacted with a two-fold excess of solid potassium *tert*-butoxide, Scheme 55.

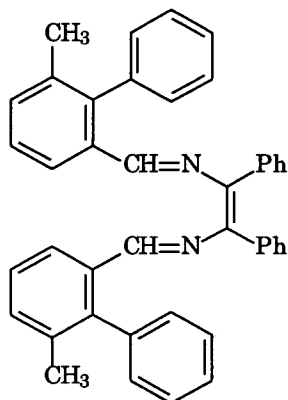


Scheme 55

Analysis of the product mixture showed three well defined spots, of which two had different R_f values from the amide **178**. These compounds were separated by dry-flash chromatography and mass spectroscopy showed these compounds to be dimeric, $(M+1)^+$, 567.2799. The minor reaction product is thought to have a similar structure to **200**, *i.e.* a 2,5-diaza-1,3,5-hexatriene **207**.

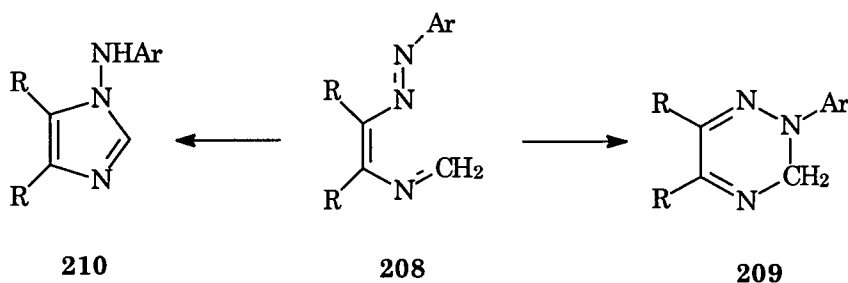


206



207

The main product's ^1H nmr spectrum showed two methyl signals, δ 1.84 (s, CH_3), δ 2.21 (s, CH_3), a methylene signal δ 3.96 (br, CH_2) and a large aromatic multiplet δ 6.39-7.54 (m, Ar-H). This spectrum is not consistent with an electrocyclication of **207** to the pyrazines, but, work by Butler *et al*⁹⁴ has shown that 1,2,5-triaza-1,3,5-hexatriazenes **208** can undergo a 6π electrocyclication to give **209** or they can rearrange to give 1-anilinoimidazoles **210** in low yield, Scheme 56. It is thought that **207**, which is similar to **208**, may undergo a similar rearrangement to give compound **206**. The minor product derived from nitrile ylide **193** (^1H nmr spectrum showed a methylene signal at δ 4.05), is also thought to have a structure similar to **206**.

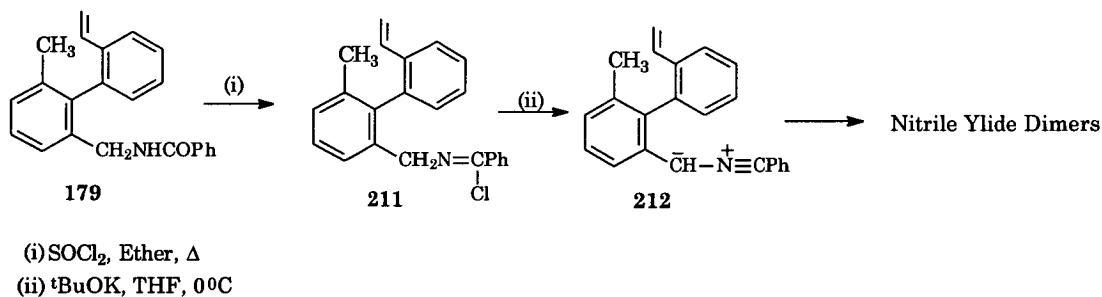


Scheme 56

It has now been established that the methyl group located at the 2-position of the biaryl unit in nitrile ylide **204** blocked the 1,7-electrocyclisation pathway as expected, but, surprisingly the main dimeric product was thought to be **206**, formed from a rearrangement of **207**.

(f) Benzonitrile-3-methyl-2-(2-ethenylphenyl)benzyl Ylide **212**

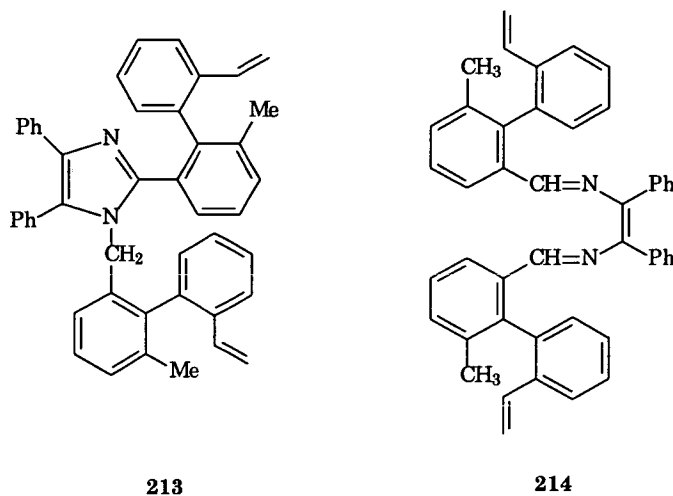
N-[3-Methyl-2-(2-ethenylphenyl)benzyl]benzamide **179** was converted to the imidoyl chloride **211** by heating at reflux with a large excess of thionyl chloride in ether for 48 hours. The solvent and excess thionyl chloride were removed under high vacuum. The imidoyl chloride was then dissolved in dry THF at 0 °C and reacted with a two-fold excess of solid potassium *tert*-butoxide, Scheme 57.



Scheme 57

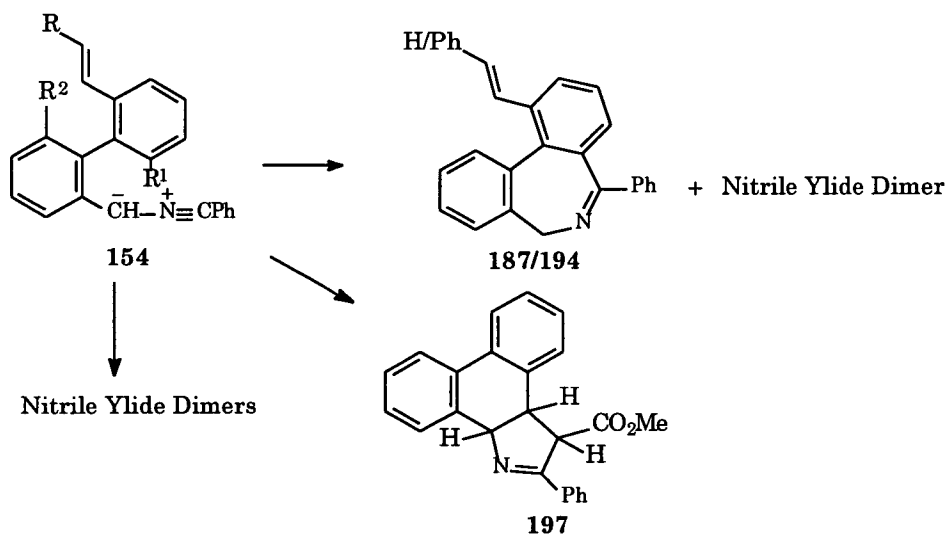
Analysis of the product mixture showed three well defined spots, of which two had different R_f values from the amide **179**. These compounds were separated by dry-flash chromatography and mass spectroscopy showed these compounds to be dimeric, $(M+1)^+$, 619.3150. The main reaction product has been tentatively assigned the structure **213** from its ^1H nmr spectrum which showed two methyl signals δ 1.79 (s, CH_3), δ 2.03 (s, CH_3) and a methylene signal δ 4.08 (d, J 5.9 Hz, CH_2). The minor reaction product is thought to be **214**, *i.e.* a 2,5-diaza-1,3,5-hexatriene from

its ^1H nmr spectrum which showed two singlets at δ 9.59 and δ 9.60 which correspond to the $\text{HC}=\text{N}$ protons.



Summary

(i) Nitrile ylides of the type **154**, showed that when $\text{R} = \text{H}$ or Ph and $\text{R}^{1/2} = \text{H}$, reaction occurred *via* a 1,7-electrocyclisation followed by a [1,5]-sigmatropic hydrogen shift to give the dibenz[*c,e*]azepines **187** and **194** along with substantial dimerisation, Scheme 58.



Scheme 58

(ii) A [3+2] cycloaddition across the ϵ,ζ -double bond was observed when $R = \text{CO}_2\text{Me}$ and $R^{1/2} = \text{H}$, to give a dibenz[e,g]indole **197**.

(iii) Cyclisation was prevented when R^1 or $R^2 = \text{Me}$, *via* its steric limitation in the transition state and only dimeric products were observed.

Conclusions

The first objective of the project, as described in Section 1.1, was to gain an insight into how triene-conjugated nitrile ylides in which both the α,β - and the γ,δ -double bonds are aromatic reacted. It was found that 1,7-electrocyclisation onto the γ,δ -aromatic ring was severely inhibited by styryl and ethenyl groups although this reaction became more competitive when the nitrile ylide concentration was minimised. This implies that the steric bulk of the two olefinic groups is less than that of a methyl group located at the 2- or 2'-position, which completely inhibits electrocyclisation. The steric interaction of the 2- or 2'-methyl group with the *ortho*-hydrogen in the adjacent ring must restrict rotation about the bond joining the two aromatic rings to a greater extent than either of the olefinic groups. Therefore, the helical transition state for 1,7-electrocyclisation, which requires some degree of twist in the conjugation can be attained with the 'smaller' olefinic groups.

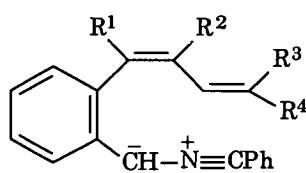
Blocking the 2'-position of the biaryl unit failed to promote any reaction of the nitrile ylide with the ϵ,ζ -double bond and only by activating it towards cycloaddition with an electron withdrawing group was a reaction observed.

Section Two

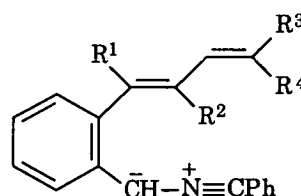
2.1 Synthetic Studies on the Reactions of Benzonitrile-2-alkadienylbenzyl Ylides

Preamble

The system chosen for the second part of the project was the triene-conjugated nitrile ylide of the type **155a,b**.



155a

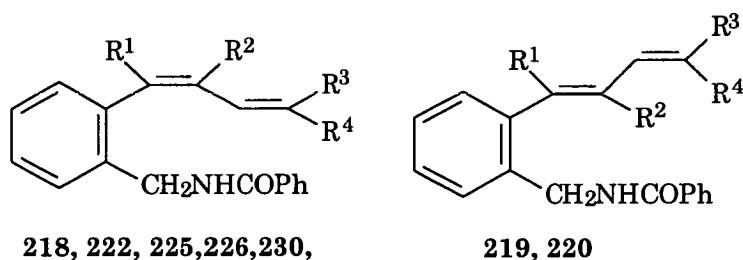


155b

Results obtained in the previous section showed that the presence of an *ortho*-substituted aromatic ring in the γ,δ -position had severely inhibited 1,7-electrocyclisation reactions at the δ carbon of the triene system because of steric effects. It was decided to investigate whether replacement of the γ,δ -phenyl substituent by an olefinic moiety would lead to new reactivity at either the γ,δ - or the ϵ,ζ -double bond. There are many reaction paths available to **155a,b**, for example, [3+2] or 1,1-cycloaddition, 1,7- or 1,9-electrocyclisation and dimerisation reactions, these will be discussed later in this section.

2.2 Synthesis of the *N*-[2-Alkadienylbenzyl]benzamides

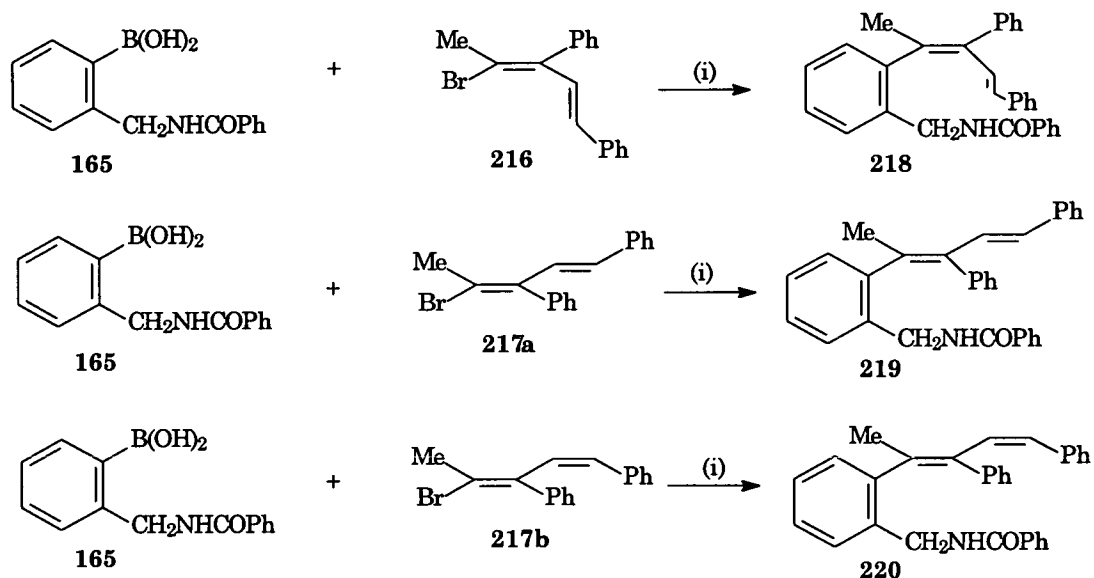
The most obvious route to the title compounds would involve the Pd(0) catalysed cross coupling of 2-*N*-benzoylaminomethylphenylboronic acid **165** and a series of bromodienes. The range of amides synthesised as precursors to the nitrile ylides of the type **155a,b** are summarised below.



Compound	R ¹	R ²	R ³	R ⁴
218	Me	Ph	H	Ph
219	Me	Ph	Ph	H
220	Me	Ph	H	Ph
222	Me	Ph	H	CO ₂ Me
225	Me	Ph	Me	Me
226	Me	Ph	H	Me
230	R ¹ , R ² = (CH ₂) ₃		H	Ph
231	R ¹ , R ² = (CH ₂) ₃		H	CO ₂ Me

(a) *N*-[2-*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl]benzyl]benzamide **218**, *N*-[2-*E,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl]benzyl]benzamide **219** and *N*-[2-*Z,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl]benzyl]benzamide **220**

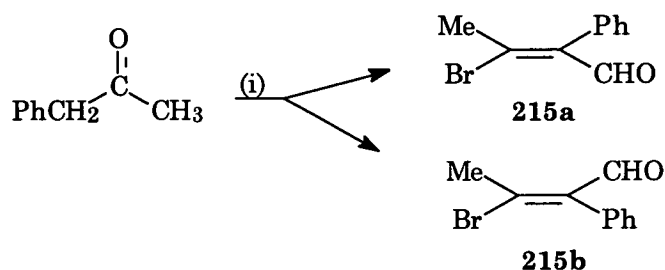
The amides **218**, **219** and **220** were synthesised as shown in Scheme 59.



(i) Pd(0), Na₂CO₃, DME, Δ

Scheme 59

The first reaction undertaken in these synthesis was Arnold's⁹⁶ bromoformylation reaction, Scheme 60. This was carried out in a 36% yield by the slow addition of the phenylacetone in chloroform to a mixture of phosphorus tribromide, DMF and chloroform at 0 °C, Scheme 60. The reaction was quenched by the slow addition of ice and solid sodium bicarbonate.



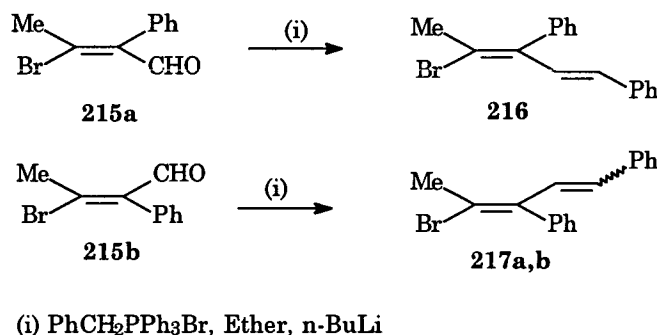
(i) PBr₃, DMF, CHCl₃, 0 °C

Scheme 60

Attempted separation of the isomers by dry-flash, wet-flash and gravity column chromatography failed, therefore, medium pressure liquid

chromatography was used. The *Z*-3-bromo-2-phenyl-2-butenal **215a** and *E*-isomer **215b** were separated in 25% and 10% respectively. Heating the *E*-isomer at reflux for 2 h in heptane with iodine gave a 2:1 isomeric mixture of the *Z* and *E*-isomers.

The bromodienes **216** and **217a,b** were synthesised by the Wittig reaction, Scheme 61. Several attempts were made using the Wadsworth Emmons olefination reaction but the bromodienes were only ever isolated in very low yields.



Scheme 61

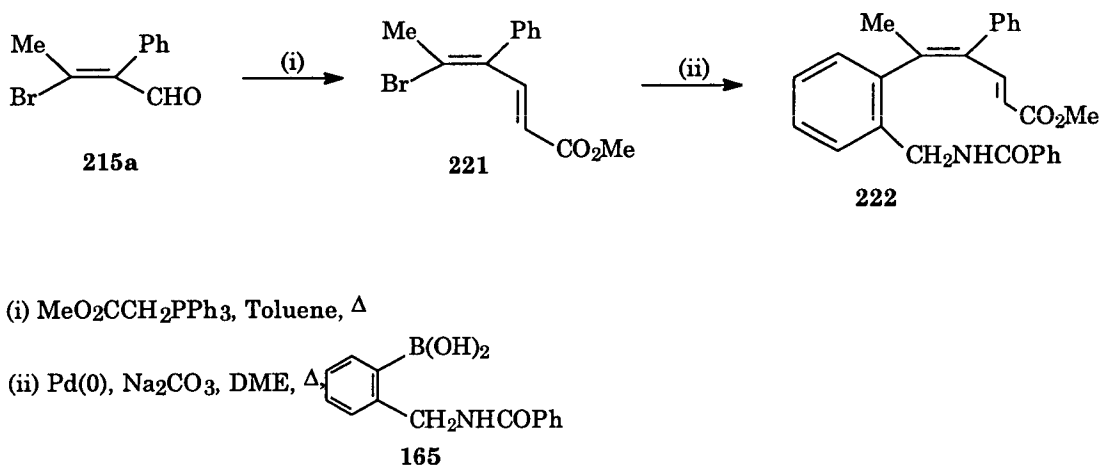
^1H Nmr spectroscopy showed that *E,E*-4-bromo-1,3-diphenylpenta-1,3-diene **216** was the exclusive product isolated in a 85% yield from **215a**. However, in the reaction of **215b** a 2:1 isomeric ratio of *Z,Z* and *E,Z*-4-bromo-1,3-diphenylpenta-1,3-dienes **217a,b** was synthesised in a combined yield of 66%. The isomers were separated by MPLC.

The boronic acid **165**, synthesised as described earlier, Scheme 42, was coupled with the bromodienes **216** and **217a,b** to give the amides **218**, **219** and **220** in 77%, 77% and 48% yields respectively.

(b) *N*-[2-(Methyl-*E,E*'-phenylhexa-2',4'-dienoat-5'-yl)benzyl]benzamide **222**

The amide **222** was synthesised as shown in Scheme 62. Step (i) in this synthesis was the Wittig reaction. The aldehyde **215a** and

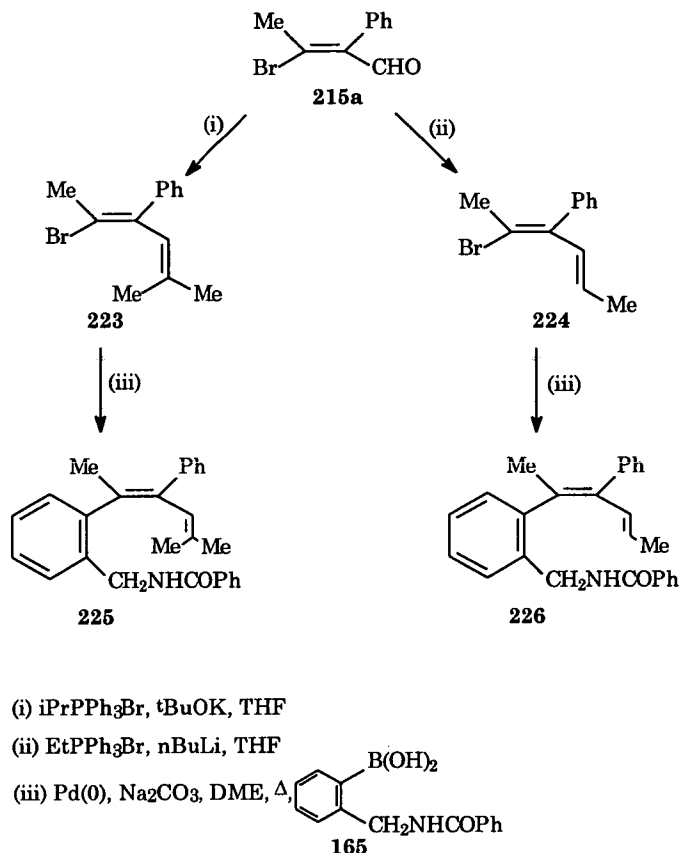
methyl(triphenylphosphoranoylidene)acetate were heated at reflux in toluene for 3 hours to give methyl-*E,E*-5-bromo-4-phenylhexa-2,4-dienoate **221** in a 92% yield. The Pd(0) catalysed cross coupling reaction of the boronic acid **165** and the bromodiene **221** gave the amide **222** in a 88% yield after dry-flash chromatography and recrystallisation.



Scheme 62

(c) *N*-[2-(*E*-5'-Methyl-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide **225** and *N*-[2-(*E,E*-3'-Phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide **226**

The amides **225** and **226** were synthesised as shown in Scheme 63. *E*-2-Bromo-5-methyl-3-phenylhexa-2,4-diene **223** and *E,E*-2-bromo-3-phenylhexa-2,4-diene **224** were synthesised by the Wittig reaction in 54% and 52%. Different bases (*n*-BuLi or *t*BuOK) and solvents (THF or ether), were used in an attempt to improve the yields, but this proved unsuccessful. The bromodiene **223** was relatively stable at room temperature, however, **224** was less stable with decomposition evident after only a few hours at room temperature. The bromodienes were used immediately to ensure the best possible yields from the Pd(0) catalysed cross coupling reactions.

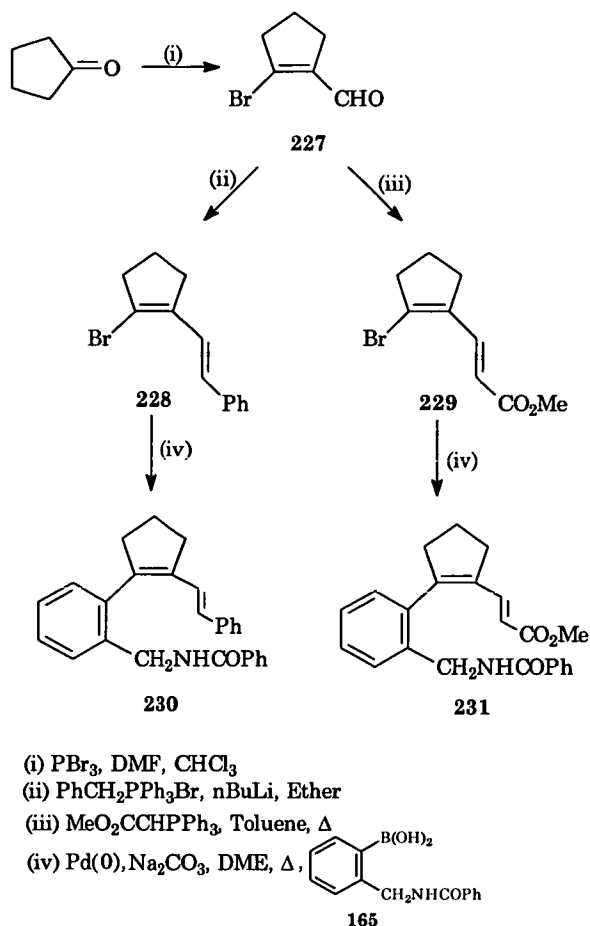


Scheme 63

The $Pd(0)$ catalysed cross coupling reaction of the boronic acid **165** and the bromodiene **223** gave the amide **225** in a 41% yield after dry-flash chromatography and recrystallisation. The coupling reaction of the boronic acid **165** with the bromodiene **224** gave a product mixture which showed several spots by tlc. The amide **226** was isolated from the impurities by dry-flash chromatography and MPLC in a 35% yield.

(d) *N*-[2-(2'-(*E*-2-Phenylethenyl)cyclopent-1'-enyl)benzyl]benzamide **230** and *N*-[2-(2'-(2-Carbomethoxyethenyl)cyclopent-1'-enyl)benzyl]benzamide **231**

The amides **230** and **231** were synthesised as shown in Scheme 64. The first reaction in this synthesis, the conversion of cyclopentanone to 1-bromo-2-formylcyclopentene **227** was achieved in a 66% yield.



Scheme 64

The bromodienes **228a,b** were synthesised *via* the Wittig reaction as a mixture of isomers in a 1:1 ratio. 1-Bromo-2-(*E*-2-phenylethenyl)cyclopentene **228** was separated as a brown oil from the *Z*-isomer using MPLC in a 42% yield. Two attempts were made to increase the *E/Z* ratio in the product mixture. The first was the Wadsworth Emmons reaction, but no product was obtained. The second involved heating the isomers at reflux in heptane with iodine for two hours, but, decomposition occurred readily and no starting material was recovered after dry-flash chromatography. The bromodiene **229** was synthesised as a yellow crystalline solid *via* both the Wittig and the Wadsworth Emmons reactions in yields of between 60-70%. ^1H Nmr spectroscopy showed that the *E*-isomer was the only product obtained from either reaction. The

Pd(0) catalysed cross coupling reactions of **228** and **229**, Scheme 64, gave the amides **230** and **231** in 93% and 86% yields after dry-flash chromatography and recrystallisation.

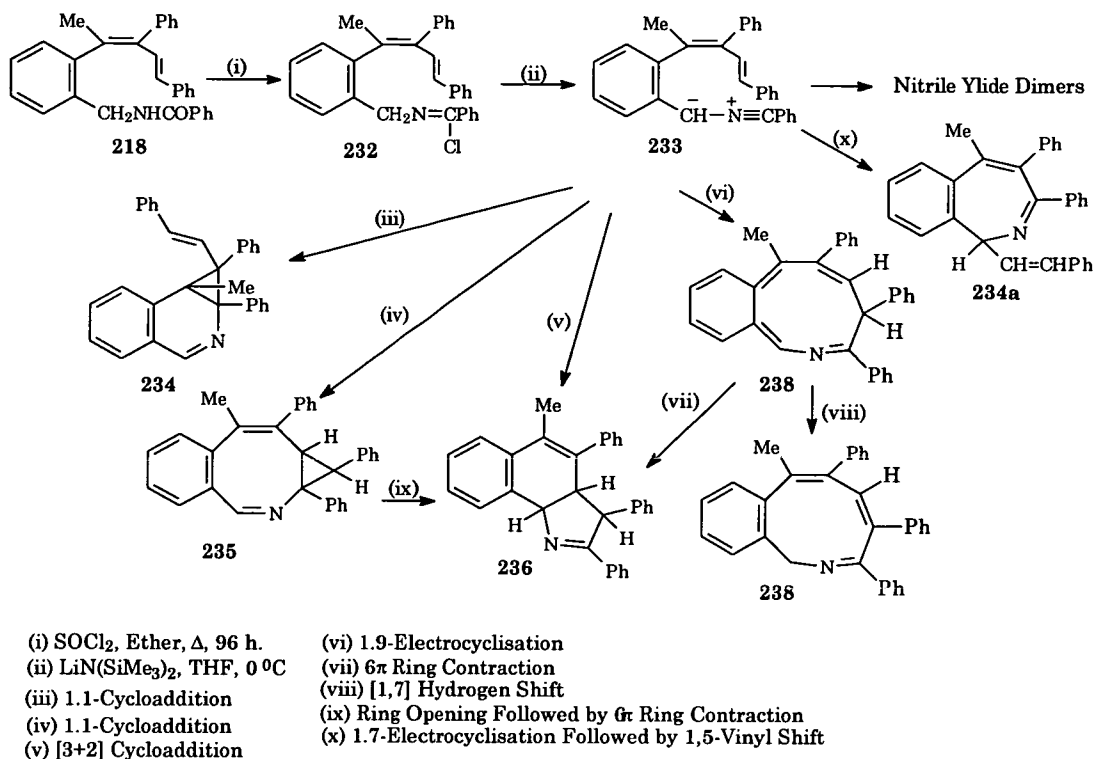
2.3 Generation and Reaction of the Nitrile Ylides Derived From Substituted *N*-[2-Alkadienylbenzyl]benzimidoyl Chlorides

In this research the nitrile ylides were generated by the 1,3-dehydrochlorination of imidoyl chlorides. The latter were prepared from their respective amides using thionyl chloride or chloromethylenedimethylammonium chloride. The method of choice involved the use of thionyl chloride as both by-products, being gaseous, could be readily removed. However, it is not as powerful as some of the other chlorinating reagents and usually requires heating to bring about the reaction. Chloromethylenedimethylammonium chloride,⁹⁶ is generally generated *in situ* by the reaction of thionyl chloride with DMF. This is a highly reactive reagent and earlier work in the group has shown that it can bring about conversions to the imidoyl chloride at room temperature or below in cases where the previous reagents have been ineffective at elevated temperatures.

(a) Benzonitrile-2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl Ylide 233

The first reactions to be investigated in this study were of the nitrile ylide **233**, Scheme 65.

N-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide **218** was converted to the imidoyl chloride **232** using a large excess of thionyl chloride in ether at reflux for 96 h. However initial attempts at generating **232** proved to be surprisingly difficult.



Scheme 65

The standard method for generating imidoyl chlorides, thionyl chloride in ether at reflux for 20-24 h, resulted in only a 15% conversion to the imidoyl chloride. It was thought that prolonged heating would result in polymerisation or decomposition of the amide, therefore, different methods were tried to generate the imidoyl chloride.

Previous work on nitrile ylides of the type 151 in which the γ,δ -double bond was olefinic had shown that the method of choice for the formation of the imidoyl chlorides was phosphorus pentachloride in ether at reflux for 24 h. However no imidoyl chloride formation was observed by ^1H nmr spectroscopy using this technique.

Before attempting further preparative work a small scale experiment was carried out with monitoring by ^1H nmr spectroscopy using chloromethylenedimethylammonium chloride produced from perdeuteriated DMF. The amide 218 was dissolved in DMF-d_7 then transferred to a nmr tube fitted with a septum cap under nitrogen.

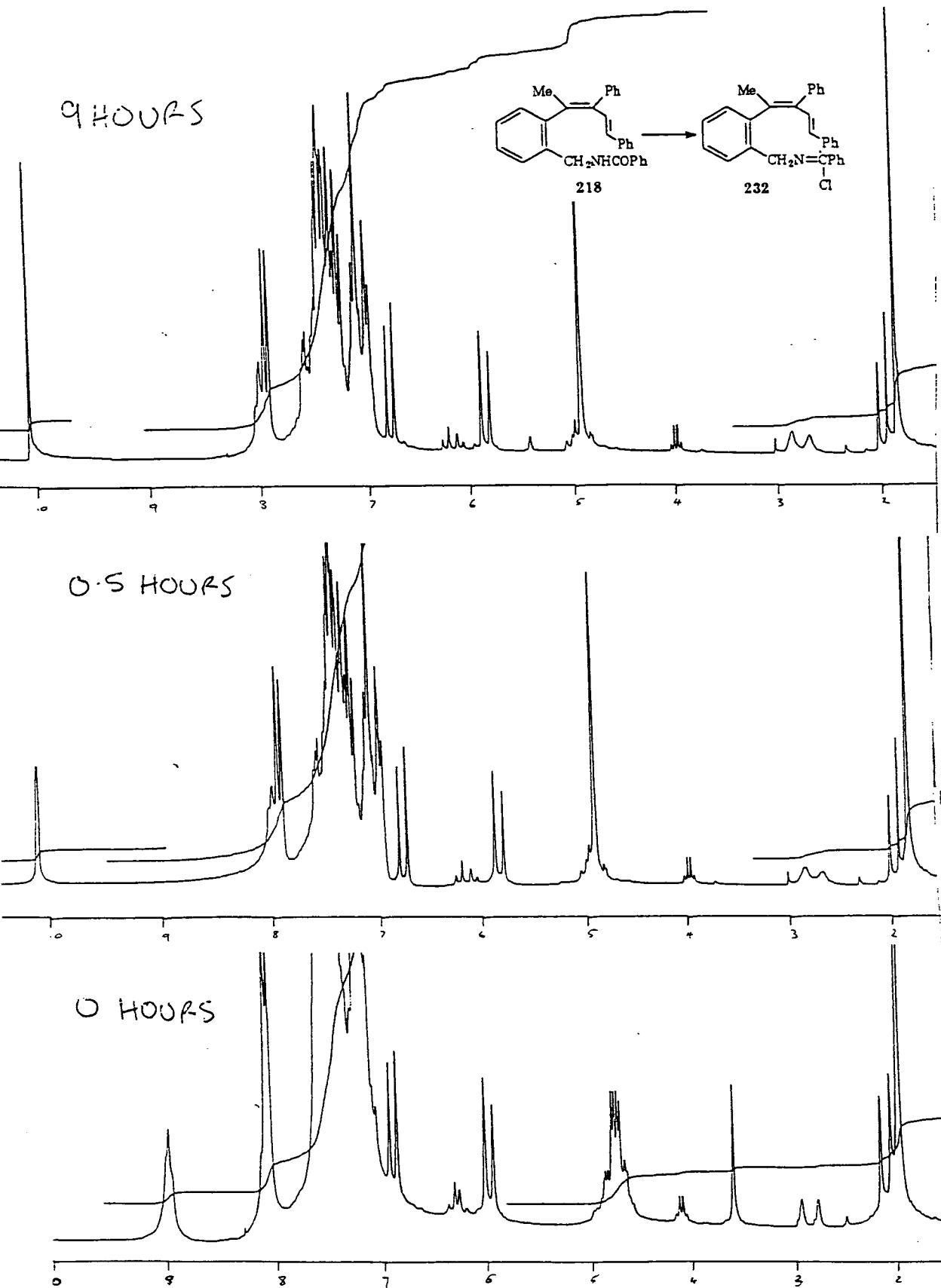


Figure 9

The reagent was then prepared by adding thionyl chloride by syringe to a 5 cm³ round bottom flask, fitted with a Suba-seal, which contained DMF-d₇. After 5 minutes this solution was added to the nmr tube containing the amide solution. The combined solution was examined by ¹H nmr spectroscopy after 0.5, 2, 4 and 9 h, Figure 9.

It can be seen from Figure 9 that *N*-[2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride **232** was obtained within 30 minutes as shown by the strong singlet peak at δ 4.90 (s, CH₂), which occurs slightly downfield from the amides CH₂ adsorption δ 4.74 (pair of dd, CH₂), and the disappearance of the NH peak at δ 8.96 (1 H, br). It is thought the singlet at δ 10.07 results from the formation of DMF-d₆.

Although the formation of the imidoyl chloride **232** was confirmed by ¹H nmr spectroscopy, generation and reaction of the nitrile ylide **233** proved to be rather more difficult, and several of the following attempts were unsuccessful. In all but one case the imidoyl chloride was kept under high vacuum at 30-40 °C for 2-3 h to remove the excess DMF and thionyl chloride. The product was dissolved in dry THF at 0 °C, and a two-fold excess of solid potassium *tert*-butoxide was added. Analysis of the product mixture showed one well-defined spot by tlc that had the same R_f value as the amide **218**. ¹H nmr spectroscopy confirmed the reaction had failed and only starting material was recovered after dry-flash chromatography.

For the second attempt at generating **233**, the amount of THF in which the imidoyl chloride was dissolved was doubled, and for the third attempt LDA was used as the base, but, again, in both cases only starting material was recovered.

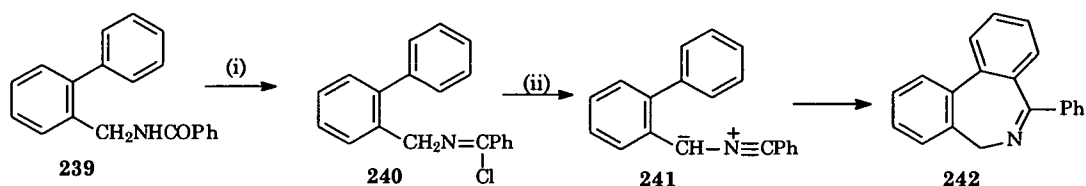
Previous work in the group had shown that a nitrile ylide could be generated without the removal of excess DMF and thionyl chloride. Therefore, the imidoyl chloride **232** in DMF was diluted in THF and a

two-fold excess of solid potassium *tert*-butoxide was added. Analysis of the reaction mixture again showed only the presence of starting material.

Since these reactions were being carried out under conditions known to generate the imidoyl chloride it was concluded that the problem must lie in the 1,3-dehydrochlorination step. To try and understand why the generation and reaction of the nitrile ylide **233** from the imidoyl chloride **232** was proving to be so difficult benzonitrile-2-phenylbenzyl ylide **241** was generated and reacted under different conditions, Scheme 66.

N-2-Phenylbenzylbenzamide **239** was synthesised by a Pd(0) catalysed cross coupling reaction between *N*-benzoyl-2-bromobenzylamine **159** and phenylboronic acid. The amide **239** was chlorinated using a large excess of thionyl chloride in ether at reflux overnight and the by-products and excess solvent were removed under vacuum at room temperature.

It had been shown previously that 1,3-dehydrochlorination of the imidoyl chloride **240** with a two-fold excess of solid potassium *tert*-butoxide generated benzonitrile-2-phenylbenzyl ylide **241** that cyclised to give 7-phenyl-5*H*-dibenz[*c,e*]azepine **242** in a 76% yield. Therefore, a series of non nucleophilic bases under various conditions were studied. The results were then compared to the standard cyclisation conditions with potassium *tert*-butoxide.



(i) SOCl_2 , Ether, Δ
(ii) $t\text{BuOK}$, LDA, $\text{LiN}(\text{SiMe}_3)_2$, or LiTMP

Scheme 66

The three bases studied were lithium diisopropylamide, lithium bis(trimethylsilyl)amide and lithium tetramethylpiperidide. The results and conditions are summarised in Table 3.

Base	moleq	Temp °C	% Yield
^t BuOK	2.0	0	76
LDA	1.1	-78	50
LiTMP	1.1	-78	66
LiN(SiMe ₃) ₂	1.1	-78	64
LiN(SiMe ₃) ₂	1.1	0	75
LiN(SiMe ₃) ₂	1.0	0	75
LiN(SiMe ₃) ₂	2.0	0	75

At -78 °C lithium tetramethylpiperidide gave the dibenzazepine **242** in a 66% yield and lithium bis(trimethylsilyl)amide gave **242** in a 64% yield. Lithium bis(trimethylsilyl)amide is readily available from Aldrich as a 1.0 M solution in THF, and therefore, it was decided to study this base further. At 0 °C the dibenzazepine was obtained in a 75% yield when 1.0, 1.1 and 2.0 molar equivalents of lithium bis(trimethylsilyl)amide were used. This work therefore showed that this convenient base could be used effectively for the generation of nitrile ylides *via* the 1,3-dehydrochlorination of imidoyl chlorides.

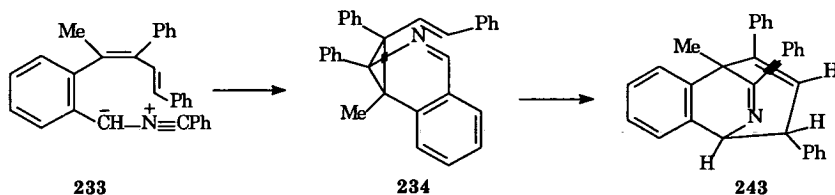
It was known that the imidoyl chloride **232** could be generated from the amide **218** with the chlorinating agent chloromethylenedimethylammonium chloride after 0.5 h but no success had been obtained in generating the nitrile ylide by the subsequent addition of either KOBu^t or LDA. It was decided to look further at the alternative route to the imidoyl chloride *via* reaction of the amide with thionyl chloride in ether. Some early work had shown that the conversion was *ca* 15% after 20 h. Further experiments with nmr

monitoring showed that the conversion was complete after 96 h and that no significant decomposition had occurred. Using the imidoyl chloride **232** prepared by this route the nitrile ylide **233** was generated at 0 °C by dissolving it in dry THF and adding 1.5 equivalents of lithium bis(trimethylsilyl)amide by syringe. The excess of base was added to ensure that sufficient base was present to dehydrochlorinate the imidoyl chloride as well as react with any residual by-products from the chlorination.

This procedure produced a clean reaction giving one primary product which after dry-flash chromatography and recrystallisation from ethyl acetate and hexane gave a crystalline solid in a 65% yield. The ^1H nmr spectrum no longer showed the doublets at δ 5.90 and δ 6.73 which corresponded to the olefinic protons of the amide **218**. This indicated that the reaction that had taken place involved the ϵ,ζ -double bond, but it was not known how the nitrile ylide **233** had cyclised. Mass spectroscopy confirmed that the product was monomeric, $(\text{M}+1)^+$, 412.2044. The ^1H nmr spectrum was similar to the spectrum obtained for 3-methoxycarbonyl-2-phenyl-3a,11b-dihydro-3*H*-dibenz[e,g]indole **197**, in that it showed three methine adsorptions at δ 3.90 (m, CH), δ 5.26 (m, CH), and δ 5.51 (m, CH). One of these has a very similar chemical shift to that in compound **197** but the other two are more deshielded.

X-ray crystallography showed that the product was 8-methyl-9,11,13-triphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene **243**, Figure 10. There are several reaction pathways open to nitrile ylide **233**, as shown in Scheme 65. However the structure obtained from X-ray crystallography, Figure 10, showed that the product could not have been obtained from a [3+2] cycloaddition as was the case for nitrile ylide **196**, Scheme 52. Work by Sharp and co-workers on nitrile ylides of the type **151** in which the γ,δ -double bond is olefinic has shown that they cyclise to give cyclopropa[c]isoquinolines **152**, Scheme 37. Therefore the reaction

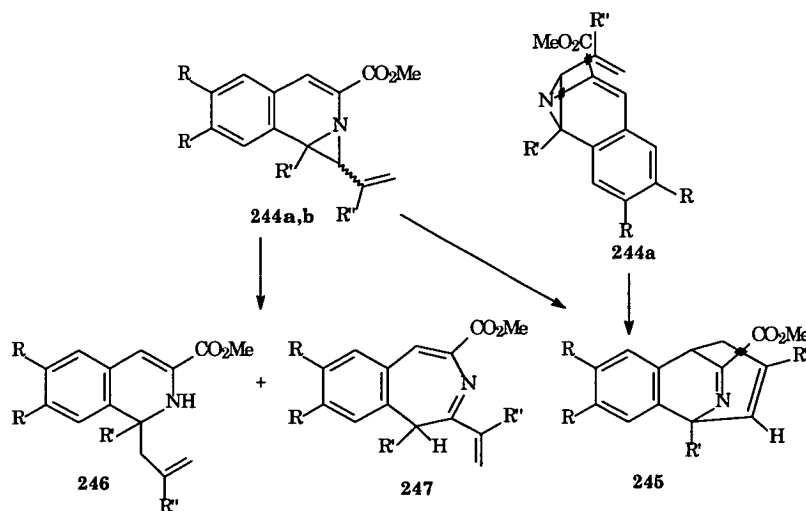
pathway was most likely *via* a 1,1-cycloaddition to give **234** as a non isolable intermediate which immediately underwent an aza-Cope rearrangement, Scheme 67.



Scheme 67

This conversion is somewhat similar to recent work done by Claus Vogel *et al*⁹⁷, who reported that intramolecular reactions of vinyl azides with 1,3-dienes, formed 6-aza-bicyclo[3.2.2]nonatrienes **245** and are most likely formed by a 3-aza-Cope rearrangement of the *cis*-1,2-divinylaziridines **244a**, Scheme 68. 1,2-Divinylaziridines are known to undergo a rapid aza-Cope rearrangement even at temperatures as low as $-20\text{ }^{\circ}\text{C}$.⁹⁸

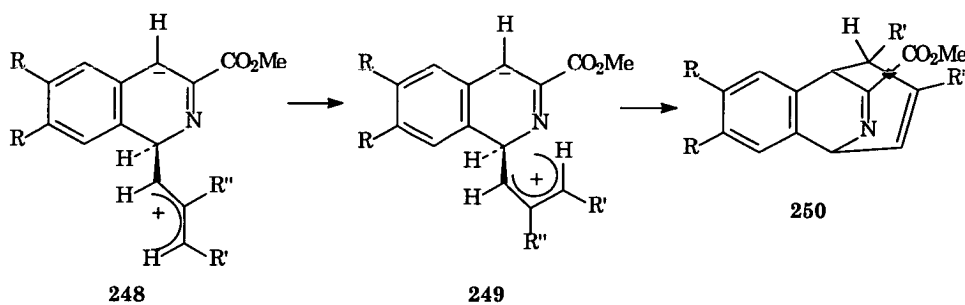
The formation of the other two products can be rationalised by assuming the *cis*- and *trans*-1,2-divinylaziridines **244a,b** are intermediates.



Scheme 68

1,2-H-shifts taking place at the aziridine result in a mixture of the isoquinoline **246** and the 3*H*-benzazepine **247**, analogous to cases that did not have the additional vinyl group.⁹⁹

Vogel¹⁰⁰ later suggested that the *cis*-divinylaziridine is not the intermediate but rather that the vinylnitrene, formed from the vinylazide by thermolytic loss of N₂, adds to the *ortho* double bond through one of its dipolar resonance structures, to give the dipolar intermediates **248** and **249**, Scheme 69.

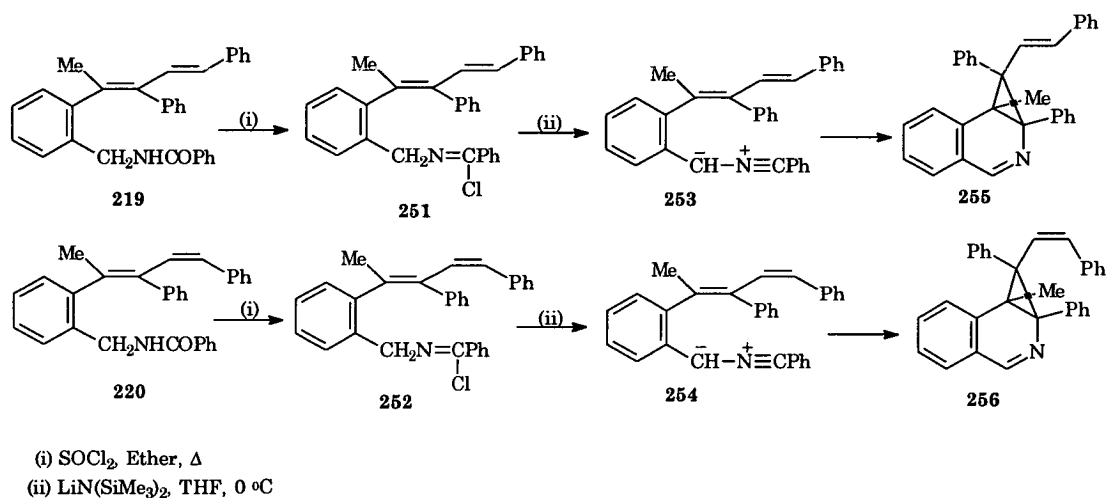


Scheme 69

(b) Benzonitrile-2-(*E,Z*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl Ylide **253** and Benzonitrile-2-(*Z,Z*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl Ylide **254**

To gain further evidence for the proposed reaction mechanism the nitrile ylides **253** and **254** were studied. Sharp and co-workers have shown that nitrile ylides of the type **151** cyclise to give the cyclopropa[*c*]isoquinolines **152**, Scheme 37. It has been shown that the reaction is wholly stereospecific in that the *trans* substituent at the terminal position in **151** goes into the *exo* position of the product **152**. The primary products obtained from the cyclisation of **253** and **254** would be the *exo*-phenylethenylcyclopropa[*c*]isoquinolines **255** and **256**. These products do not have the required geometry for an aza-Cope rearrangement, Scheme 70, but Sharp showed that on heating, the

cyclopropa[*c*]isoquinolines undergo an equilibration of the *exo/endo* isomers *via* electrocyclic ring opening followed by ring inversion and reclosure. In cases where $R^2 = H$ and $R^3 \neq H$ this equilibration is accompanied by a slower [1,5] hydrogen shift to give the 1*H*-2-benzazepine, Scheme 37. Therefore it was expected that the thermolysis of the *exo*-phenylethenyl isomers **255** and **256** would result in an equilibrium of *exo* and *endo* isomers being established. The *endo* isomer would then undergo an aza-Cope rearrangement to give compound **243**.



Scheme 70

The amides **219** and **220** were again converted into the imidoyl chlorides **251** and **252** using a large excess of thionyl chloride in ether at reflux for 96 h, and the nitrile ylides **253** and **254** were generated at $0\text{ }^\circ\text{C}$ by using 1.5 equivalents of lithium bis(trimethylsilyl)amide as in the previous case.

This procedure gave after dry-flash chromatography and crystallisation, compounds **255** and **256**, Scheme 70, as colourless crystalline solids in 65% and 82% yields respectively. The ^1H nmr spectra with singlets at δ 7.78 and δ 7.77 are indicative of cyclopropa[*c*]isoquinolines and X-ray crystallography confirmed the structure of compound **255**, Figure 11.

7b-1-*endo*-Phenyl-1a-phenyl-1-(*E*-2-phenylethenyl)cyclopropa[*c*]isoquinoline

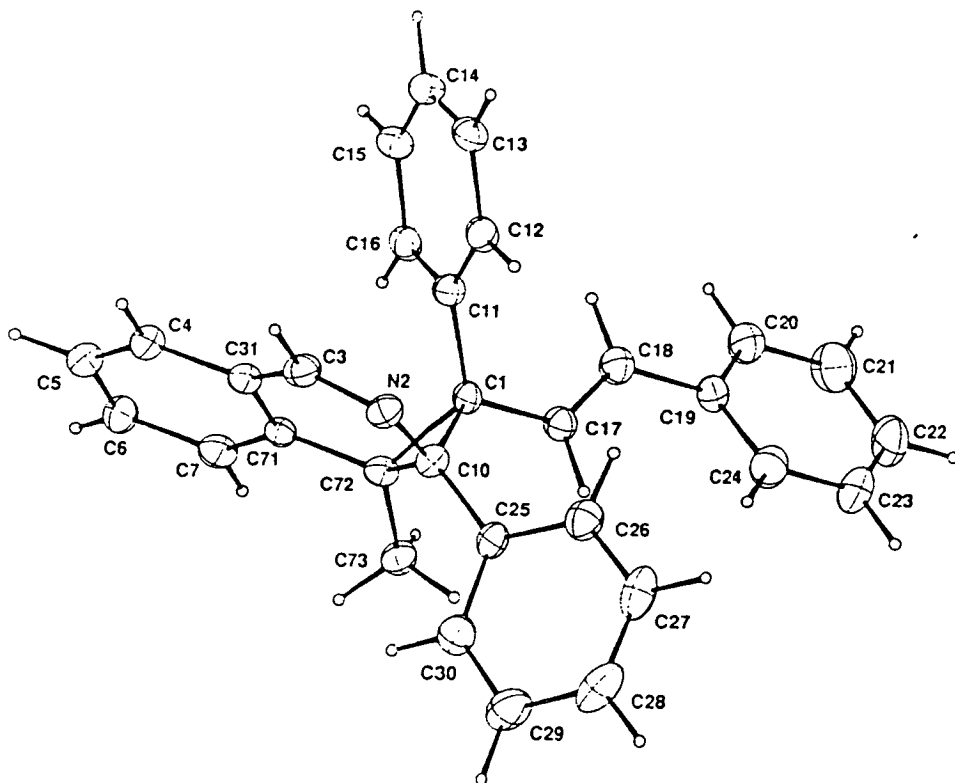
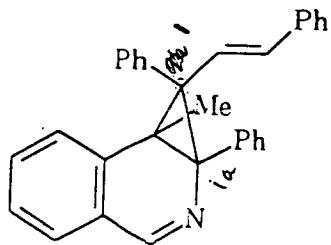


Figure 11

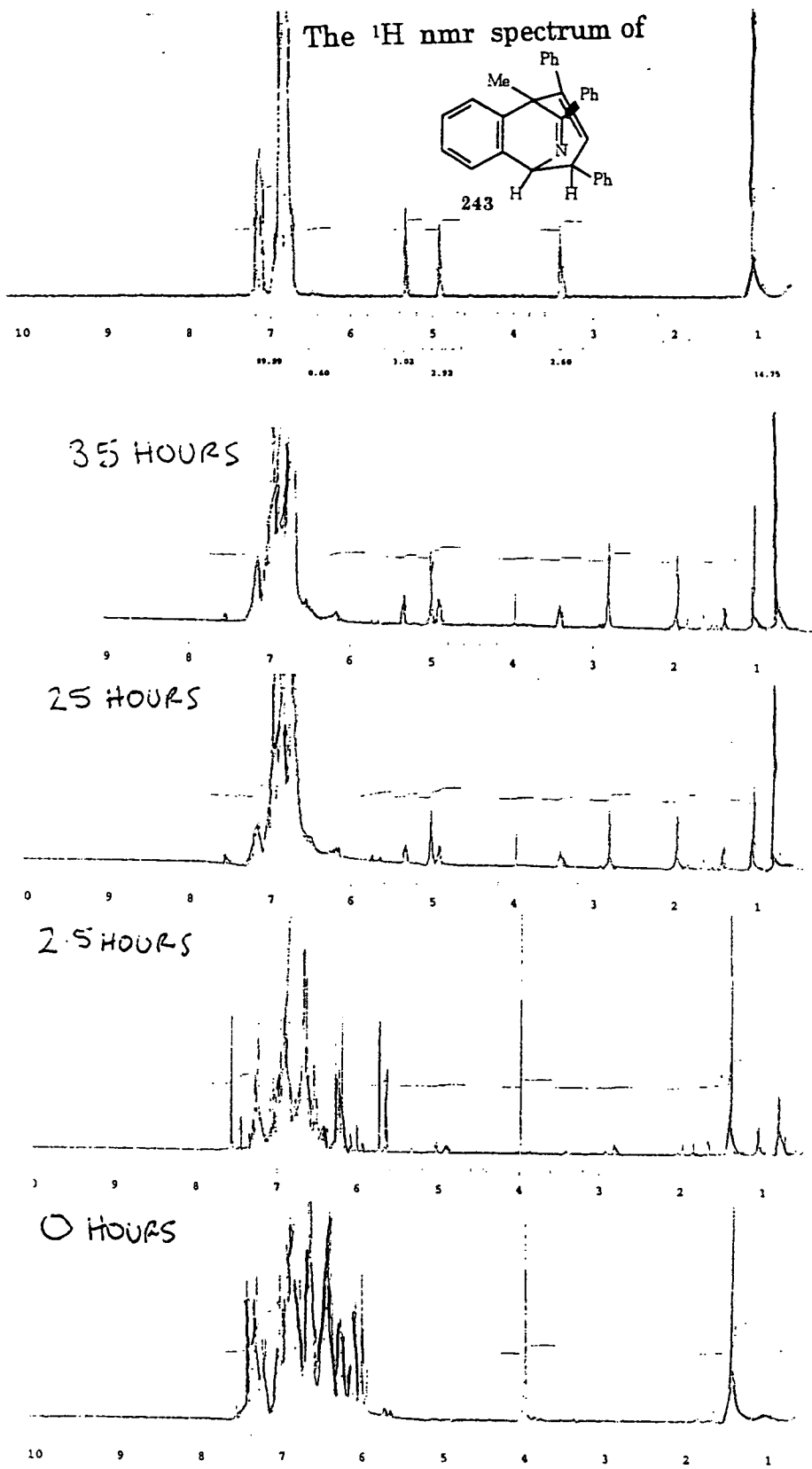
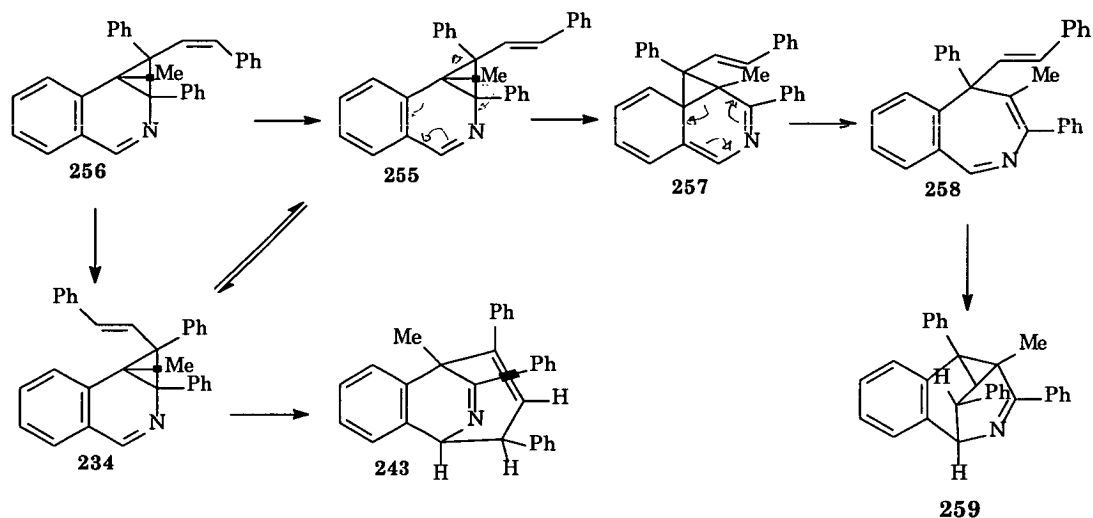


Figure 12

The products, as solutions in perdeuteriobenzene, were heated under reflux for 35 h with nmr monitoring, Figure 12. Compound **255** gave two products **243** and **259** in 35% and 65% respectively, isolated by MPLC and crystallisation. The minor product **243** had identical nmr spectra and mp to the product obtained in the previous case from the nitrile ylide **233**. The structure of the major product **259** was determined by X-ray crystallography, Figure 13.



Scheme 71

Surprisingly the expected product **243** was the minor component. The relatively low yield of **243** in this reaction must be due to the high steric strain in its precursor **234** which results in it being present in only very low concentration in the equilibrium with compound **255**.

The thermal isomerisation of compound **256** gave the same products and interestingly, nmr monitoring showed that the first step in this process was the isomerisation of the *Z*-phenylethenyl group, *i.e.* **256** → **255**.

Of the several possible mechanisms for the formation of compound **259**, the most likely is *via* the path shown in Scheme 71; this involves three steps, a [1,5] walk to give the intermediate **257** which then

10-Methyl-8,11,13-triphenyl-12-azatetracyclo[7.3.1.0.2.70.8.10]
trideca-2(7),3,5,11-tetraene

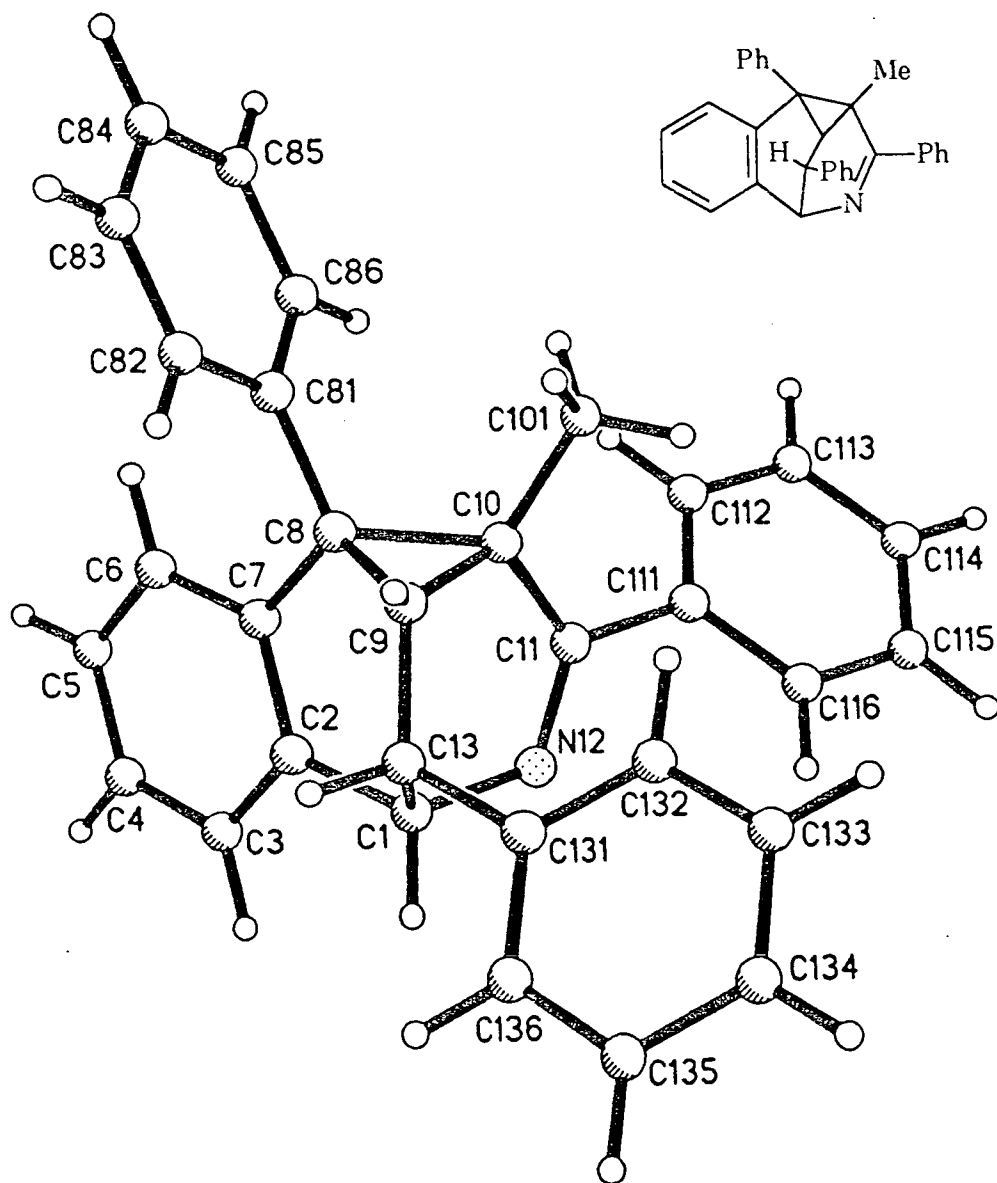
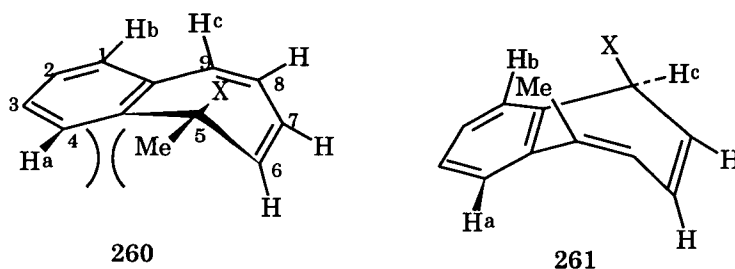


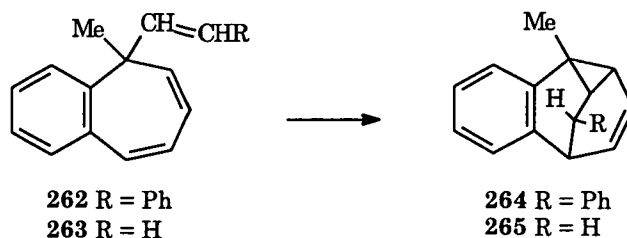
Figure 13

undergoes an electrocyclic ring expansion to give the benzazepine **258** followed by an internal Diels-Alder reaction to give the product 3,4-benzo-6-azatricyclo[3.3.1.0^{2,8}]nona-3,6-diene **259**, in yields of 65% and 68%.

Evidence which supports the internal Diels-Alder reaction comes from work carried out by Battye and Jones¹⁰¹ on the relative migratory aptitudes of doubly and triply bonded groups in a cycloheptatriene system. As shown in structure **260** a 5,5-disubstituted benzocycloheptene is destabilised by the *peri* interaction of a C-5 substituent with an *ortho*-proton, H_a, of the benzene group. A 1,5-shift of X in structure **260** would relieve this interaction replacing it with the interaction of H_b with H_c.



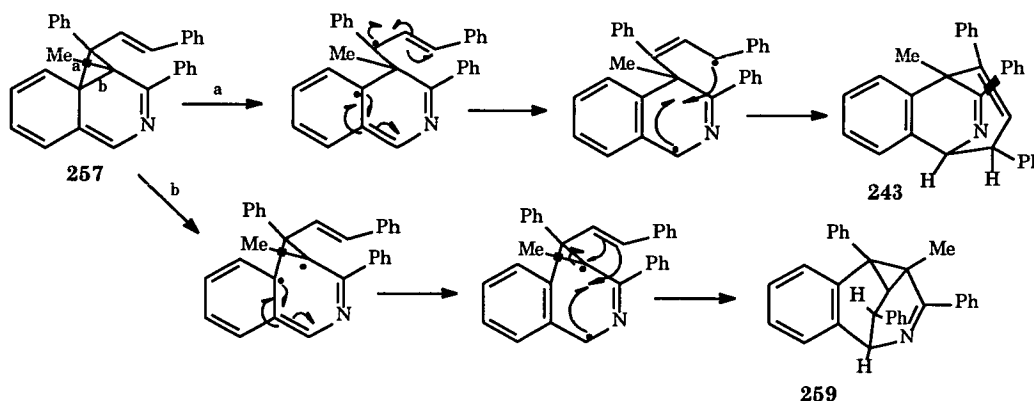
This rearrangement is seen when X = CHO, CN and C≡CPh, but when X = CH=CH₂ or *E*-CH=CHPh, internal Diels-Alder reactions are observed. The products **264** and **265** were obtained after heating the olefins **262** (100 °C, 7 h) and **263** (90 °C, 4.5 h), as shown in Scheme 72.



Scheme 72

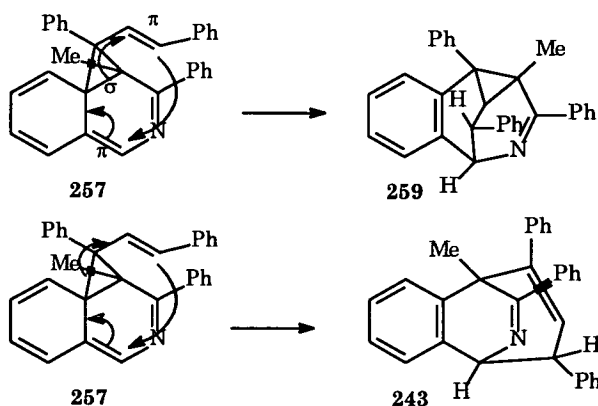
There are other possible reaction routes that could account for the formation of the observed products from the intermediate **257**. The first

would require homolytic cleavage of the **a** or **b** bond in the cyclopropane ring, as shown in Scheme 73, which would give either **243** or **259**, respectively. Cleavage of the **a** bond would be favoured due to the stability of the allyl radical. Therefore, the major product expected from the diradical mechanism would be **243** and not **259** as was found experimentally.



Scheme 73

The second possibility would involve a concerted ($\pi 2s + \pi 2s + \sigma 2s$) rearrangement of **257** to give **259** directly, or, a Cope rearrangement to give **243**, Scheme 74.



Scheme 74

7,15-diphenyl-16-azatetracyclo[6.6.2.0^{1.5}.0^{9.14}]
hexadeca-5,9(14),10,12,15-pentaene

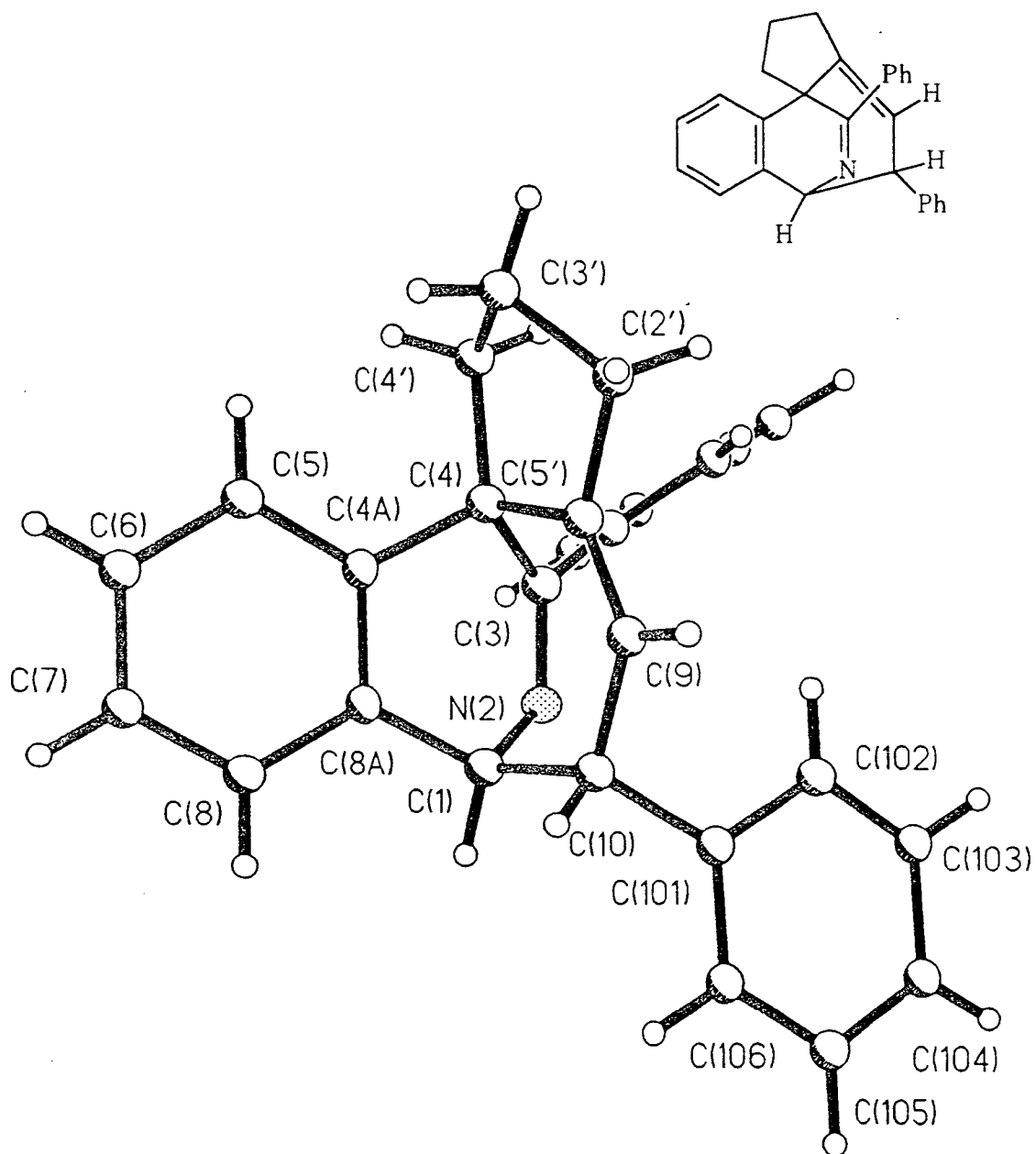
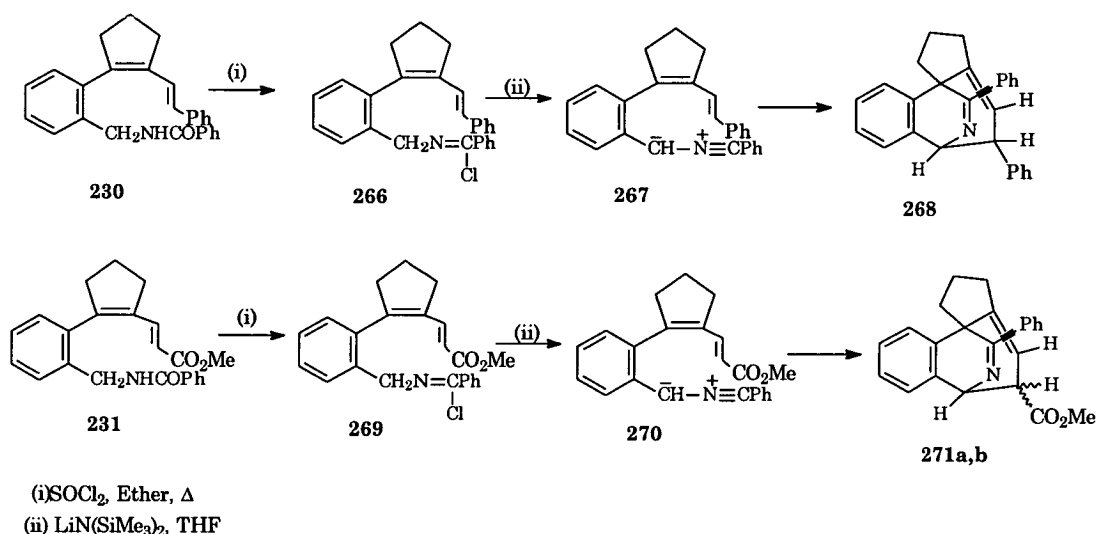


Figure 14

(c) Benzonitrile-2-(2'-(*E*-2-phenylethenyl)cyclopent-1'-enyl)benzyl Ylide 267 and Benzonitrile-2-(2'-(methyl-*E*-propenoate)cyclopent-1'-enyl)benzyl Ylide 270

The amide **230** was heated at reflux for 20 h in an excess of thionyl chloride and ether, and the amide **231** was heated at reflux for 96 h, to give the imidoyl chlorides **266** and **269** respectively. The nitrile ylides **267** and **270** were generated *via* the 1,3-dehydrochlorination of the imidoyl chlorides **266** and **269** with a 1.5 molar equivalent of lithium bis(trimethylsilyl)amide in THF at 0 °C, Scheme 75.



Scheme 75

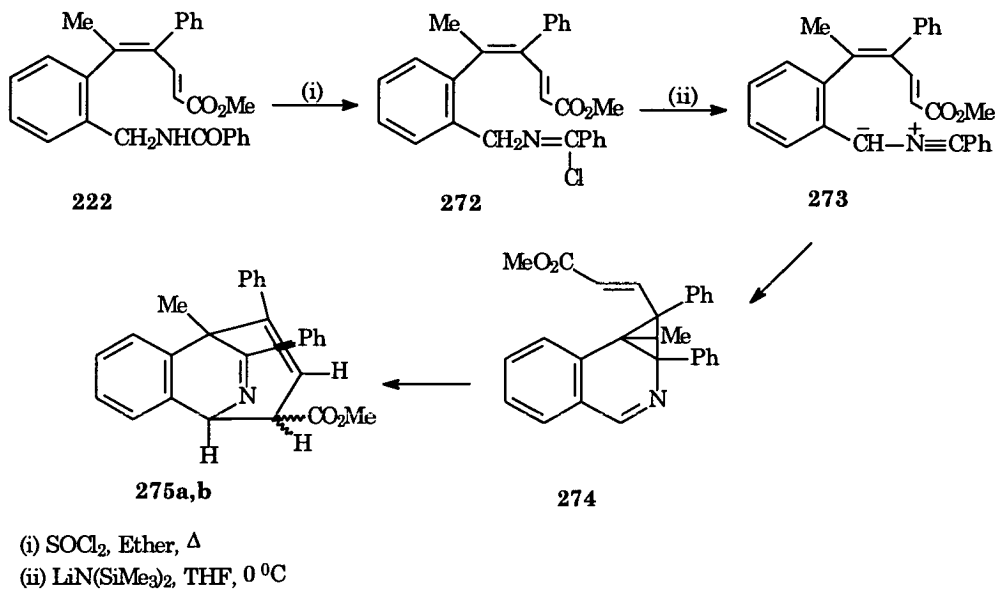
This procedure produced a clean reaction for nitrile ylide **267** resulting in one primary product which was isolated after dry-flash chromatography. This proved to be compound **268** isolated as a brown crystalline solid in a 63% yield. The structure of **268** was determined by comparison of the ¹H nmr spectrum (three methine protons at δ 3.76, δ 5.20 and δ 5.49) with the spectrum for compound **243** and by X-ray crystallography, Figure 14. Analysis of the product mixture from nitrile ylide **270** showed several spots by tlc with different R_f values from the amide. The minor products from this reaction could not be identified, but

are thought to be due to thermal fragmentation of the imidoyl chloride. The nitrile ylide **270** cyclised to give 7-methoxycarbonyl-15-phenyl-16-azatetracyclo[6.6.0.^{1,5}0.^{9,14}]hexa-5,9(14),10,12,15-pentaene **271a,b**, as a mixture of epimers, isolated in a 42% yield. The structures were deduced from comparison of the ¹H nmr spectra (δ 3.57 (m, CH), δ 5.22 (d, CH), δ 5.62 (m, CH), and δ 3.33 (br, CH), δ 5.11 (br, CH), δ 5.72 (br, CH)). The initial isomeric ratio was found to be 5:1; however, isomerisation was found to have occurred even at low temperatures and was later found to be 2:1. The epimers **271a,b** could not be separated by any of the chromatography techniques available.

(d) Benzonitrile-2-(methyl-*E,E*-4'-phenylhexa-2',4'-dienoat-5'-yl)benzyl Ylide **273**

The amide **222** was chlorinated using thionyl chloride in ether at reflux for 144 h. The imidoyl chloride **272** was dissolved in dry THF and a 1.5 molar equivalent of lithium bis(trimethylsilyl)amide was added to generate the nitrile ylide **273**, Scheme 76. Analysis of the product mixture showed several spots with different R_f values from the amide **222** that could not be identified after chromatography; however it is thought that they are due to thermal fragmentation of the imidoyl chloride. The nitrile ylide **273** cyclised *via* a 1,1-cycloaddition to the non isolable intermediate **274** which underwent an aza-Cope rearrangement to give 11-methoxycarbonyl-8-methyl-9,11-diphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene **275a,b** as a mixture of epimers. The epimers **275a,b**, identified by comparison with the ¹H nmr spectrum of product **243**, (δ 3.75 (m, CH), δ 5.32 (d, CH), and δ 5.63 (t, CH)) and (δ 3.77 (m, CH), δ 5.21 (m, CH), and δ 5.73 (m, CH)), were isolated in a disappointingly low yield of 20%. The initial isomeric ratio was found to be 2:1, but isomerisation was found to have occurred even at

low temperatures. Partial separation of the epimers **275a,b** was achieved using MPLC but all attempts at crystallisation failed.



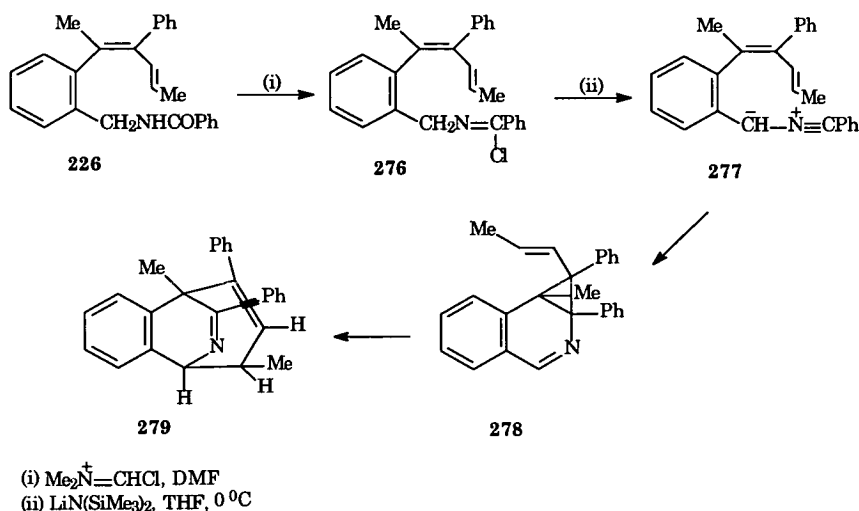
Scheme 76

The nitrile ylides **270** and **273** had several reaction pathways open to them including 1,1- and [3+2] cycloaddition, as shown for nitrile ylide **233**, Scheme 65. The methyl ester attached to the ϵ,ζ -double bond was expected to increase the major stabilising energy E_1 , as in Sustmann Type 1 cycloaddition, thus activating them towards [3+2] cycloaddition. However, no product was obtained from any of the reaction pathways open to the nitrile ylides **270** and **273** other than *via* 1,1-cycloaddition followed by an aza-Cope rearrangement.

(e) Benzonitrile-2-(*E,E*-3'-phenylhexa-2',4'-dien-2'-yl)benzyl Ylide **277**

The amide **226** was chlorinated with chloromethylenedimethylammonium chloride. Generation of the imidoyl chloride **276** was found to be complete after 30 minutes by ^1H nmr spectroscopy. Earlier attempts at chlorinating the amide with thionyl chloride and ether at reflux for 12 h resulted in major decomposition. The

of lithium bis(trimethylsilyl)amide was added to generate the nitrile ylide **277**, Scheme 77.



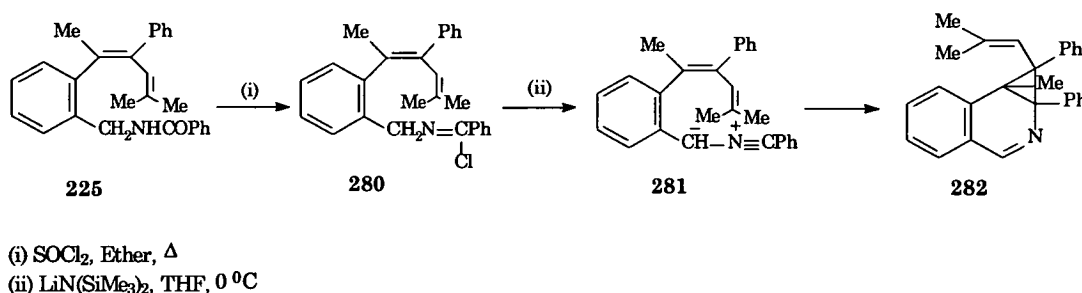
Scheme 77

The nitrile ylide **277** cyclised to give 8,11-dimethyl-9,13-diphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene **279**, identified by comparison with the other ¹H nmr spectra, as colourless crystals in a 46% yield after chromatography and crystallisation.

(f) Benzonitrile-2-(*E*-5'-methyl-3'-phenylhexa-2',4'-dien-2'-yl)benzyl Ylide **281**

The amide **225** was chlorinated with chloromethylenedimethylammonium chloride and generation of the imidoyl chloride **280** was found to be complete after 30 minutes. ¹H Nmr spectroscopy showed that a 30% conversion of the amide **225** to the imidoyl chloride **280** had occurred with substantial decomposition, when heated at reflux for 24 h with thionyl chloride and ether. The imidoyl chloride **280** was dissolved in dry THF and a 5.0 molar equivalent of lithium bis(trimethylsilyl)amide was added to generate the nitrile ylide **281**, Scheme 78.

lithium bis(trimethylsilyl)amide was added to generate the nitrile ylide **281**, Scheme 78.

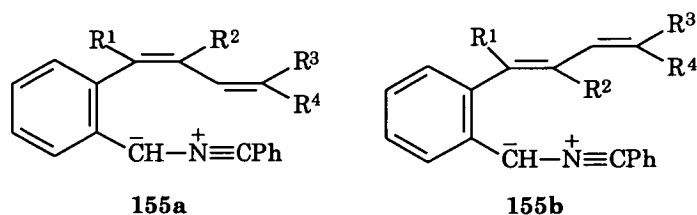


Scheme 78

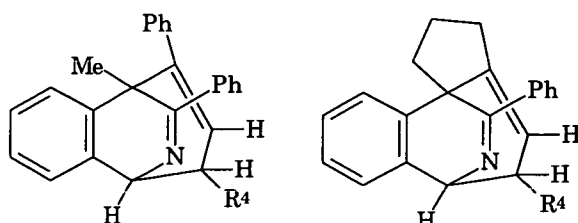
One successful generation and reaction of the nitrile ylide **281** gave a 1:1 mixture of the amide **225** and the cyclopropa[*c*]isoquinoline **282**. This result is surprising in that **282** should have the required *cis* geometry for the aza-Cope rearrangement. However it is thought that the *cis*-methyl prevents the compound from aligning properly in the transition state and thus preventing the rearrangement.

The product **282** is not very stable and a substantial loss of material was observed with chromatography reducing the yield from 50% to approximately 20% (^1H nmr spectra of the crude reaction showed a 1:1 ratio of product to amide). It was intended to monitor the aza-Cope rearrangement by ^1H nmr spectroscopy but decomposition of the product **282** had occurred at room temperature before this could be attempted.

Summary



(i) When $R^1 = \text{Me}$, $R^2 = \text{Ph}$ and $R^3 = \text{H}$, nitrile ylides of the type **155a**, cyclised *via* 1.1-cycloaddition to a non isolable cyclopropa[c]isoquinoline which undergoes a fast aza-Cope rearrangement to give 12-azatricyclotridecapentaenes **243**, **275a,b**, **279**, and when $R^{1/2} = (\text{CH}_2)_3$, cyclised to give 16-azatetracyclohexadecapentaenes **268** and **271a,b**.



$R^3 = \text{H}$, $R^4 = \text{Ph}$ **243**

$R^3 = \text{H}$, $R^4 = \text{CO}_2\text{Me}$ **275a,b**

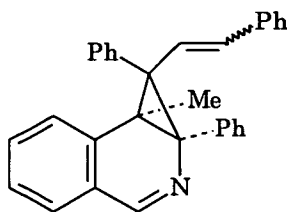
$R^3 = \text{H}$, $R^4 = \text{Me}$ **279**

$R^4 = \text{Ph}$ **268**

$R^4 = \text{CO}_2\text{Me}$ **271a,b**

(ii) When $R^4 = \text{Me}$, the nitrile ylide **155a** cyclised *via* 1.1-cycloaddition to give a cyclopropa[c]isoquinoline as the primary product, which did not undergo an aza-Cope rearrangement.

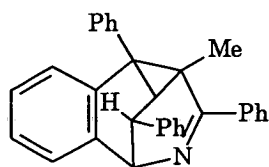
(iii) The nitrile ylide of the type **155b** cyclised *via* 1.1-cycloaddition in a wholly stereospecific manner to give the cyclopropa[c]isoquinolines **255** and **256** as the primary products isolated.



255 or 256

(iv) Thermal isomerisation of **255** and **256** gave the 12-azatricyclotridecapentaene **243** as the minor product *via* an aza-Cope

rearrangement and the bridged benzazepine **259** as the major product in three steps, *via* a 1,5-walk, an electrocyclic ring opening and an internal Diels-Alder reaction.

**259**

Conclusions

The second objective of this project, as described in Section 2.1, was to study the reactions of triene-conjugated nitrile ylides in which the γ,δ - and the ϵ,ζ -double bonds are olefinic. In view of the known chemistry of the analogous diene system, it seems likely the primary products derived from these triene-conjugated nitrile ylides are cyclopropa[c]isoquinolines which then undergo a fast aza-Cope rearrangement. The products isolated from these reactions, the bridged isoquinolines, have their structure closely related to that of the isopavine alkaloids. Only when the ζ carbon was disubstituted did the reactant fail to follow the same reaction path as the other nitrile ylides and a cyclopropa[c]isoquinoline was isolated. This observation is consistent with the suggested aza-Cope mechanism since the presence of a *cis* group larger than a hydrogen atom would be expected to hinder the transition state required for a concerted reaction.

Predictably, the cyclopropa[c]isoquinoline with its 1-alkenyl group in the *exo* position (1-phenyl group in the *endo* position), proved to be kinetically stable at the reaction temperature and was isolated. Heating the compound at reflux in perdeuteriobenzene surprisingly gave the bridged isoquinoline as the minor product. This must be due to the high steric strain in the rearranged cyclopropa[c]isoquinoline with its 1-phenyl

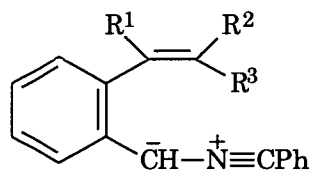
group in the *exo* position (1-alkenyl group in the *endo* position), which results in it being present in only very low concentration in the equilibrium mixture. The first two steps in the formation of the major product from the thermolysis parallel those observed in related reactions, and the final step is closely similar to known chemistry in an all-carbon analogue.

Section Three

3.1 Synthetic Studies on the Reactions of Benzonitrile-2-alkenylbenzyl Ylides

Preamble

The third area of research concerned diene-conjugated nitrile ylides of the type **156**.



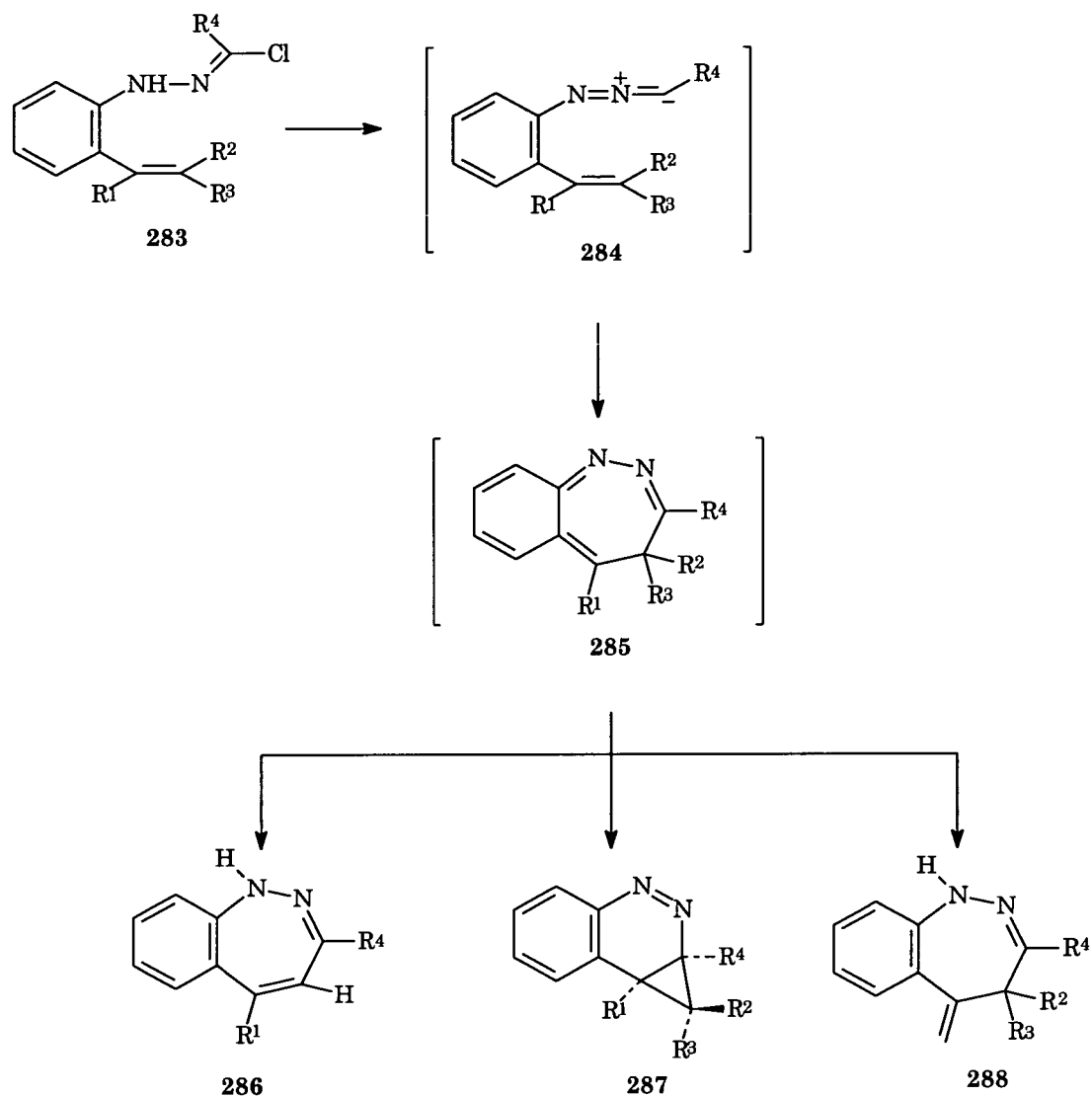
156

There are several reaction paths available to nitrile ylides of this type depending on the nature of the substituents R^1 , R^2 , and R^3 . Previous work on diene-conjugated nitrile ylides **151**, showed that they react *via* a 1,1-cycloaddition to give cyclopropa[*c*]isoquinolines **152**, Scheme 37. Depending on the substituents R^2 and R^3 , thermolysis of the cyclopropa[*c*]isoquinolines **152** can give 1*H*-2-benzazepines or 5*H*-2-benzazepines.

Work by Zecchi¹⁰² on the nitrile imines **284**, Scheme 79, analogous to the nitrile ylide **156** showed that in general these systems had a similar pattern of reactivity to the nitrile ylides, *i.e.* giving compounds of the type **286** and **287** depending on the nature of the substituents. However it was also found that an additional product, the 5-methylene-1*H*-1,2-benzodiazepine **288** was also obtained in the two cases where R^1 was a methyl group.

Although many examples of nitrile ylides of the type **156** had previously been studied in the group no work had been done on

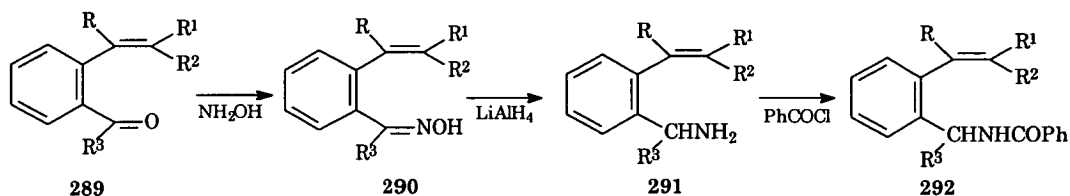
compounds where $R^1 = \text{Me}$. It was therefore thought to be of interest to find out if they would follow a similar path to the nitrile imines and lead to 5-methylene-1*H*-2-benzazepines.



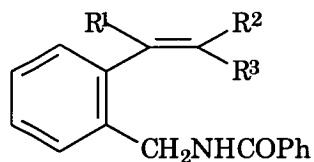
Scheme 79

3.2 Synthesis of *N*-[2-Alkenylbenzyl]benzamides

Previously the benzamides **292** used as precursors to the nitrile ylides of the type **151**, were prepared from unsaturated aldehydes and ketones, *e.g.* **289**, by the general method shown in Scheme 80.



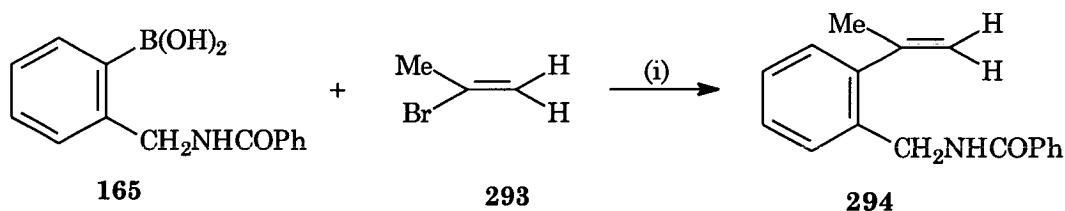
Work carried out by a fourth year undergraduate student had shown that this was not a satisfactory route to the amides **292** when $R \neq H$. Therefore the route chosen was *via* Suzuki's Pd(0) catalysed cross coupling reaction with 2-*N*-benzoylaminomethylphenylboronic acid **165** and a series of alkenyl bromides as developed earlier in this work. The range of amides synthesised as precursors to the nitrile ylides of the type **156** are summarised below.



Compound	R ¹	R ²	R ³
294	Me	H	H
298a	Me	Ph	H
304	Me	Me	Me
308a	Me	Ph	Me
308b	Me	Me	Ph
302	Me	Ph	Ph
312	Et	Me	Me

(a) *N*-[2-(Propen-2'-yl)benzyl]benzamide **294**

The route to the amide **294** was as shown in Scheme 81. 2-Bromopropene, commercially available from Avocado, was coupled with the boronic acid **165** to give the amide **294** as a white solid in a 65% yield.



(i) Pd(0), Na₂CO₃, DME, Δ

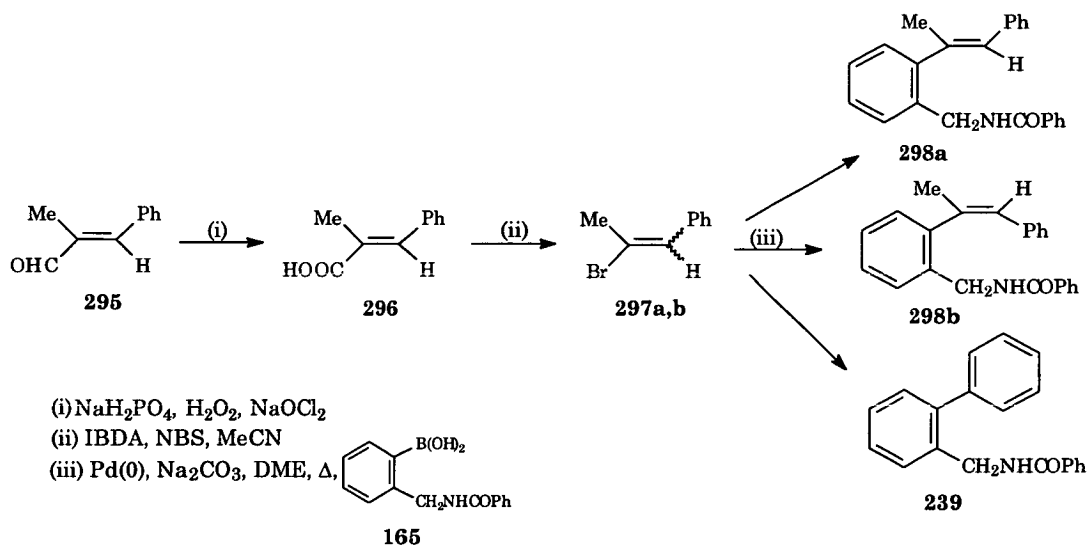
Scheme 81

The amide **294** synthesised from this coupling reaction was separated from the starting materials readily by dry-flash chromatography. One of the main failings of the previous method, outlined in Scheme 79, was that the amide required dry-flash chromatography and MPLC to remove all the impurities.

(b) *N*-[2-(*E*-1'-Phenylpropen-2'-yl)benzyl]benzamide **298a**

The amides **298a,b** were synthesised as shown in Scheme 82. 2-Bromo-1-phenylpropene **297a,b** was synthesised as a mixture of isomers *via* an oxidative bromo-decarboxylation of α -methyl-*trans*-cinnamic acid using the methodology of Dahl *et al.*¹⁰³ It was not clear from the paper whether this particular reaction was stereospecific. This was because α -methylcinnamic acid is only available from Aldrich as a mixture of isomers. In this work the pure *trans* isomer **296** was obtained by a mild oxidation¹⁰⁴ of α -methyl-*trans*-cinnamaldehyde. Bromodecarboxylation gave a 2:1 mixture of the *E* and *Z* isomers **297a** and **297b** which could not

be separated by dry- or wet-flash chromatography. Therefore, it can be seen that this particular reaction is non stereospecific.

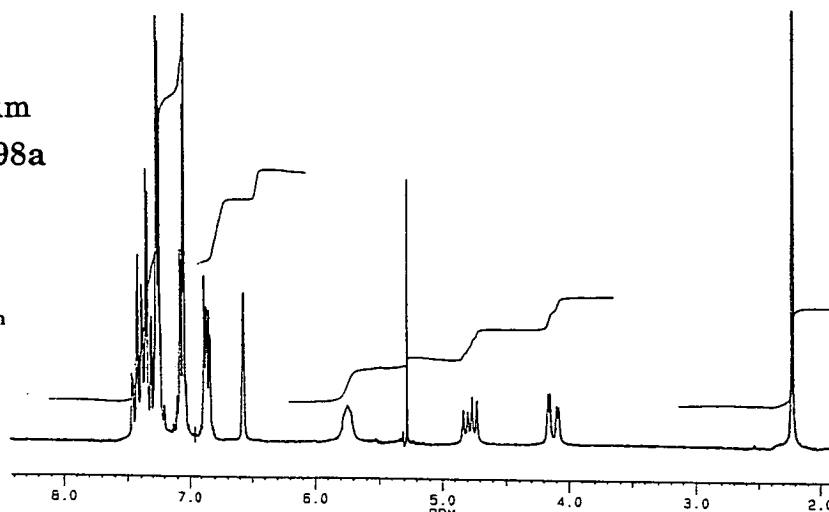
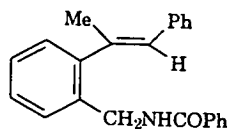


Scheme 82

The alkenyl bromides **297a,b** were coupled as a mixture with **165**, as shown in Scheme 82, to give three products, **298a**, **298b** and **239** as the major product. The three products were separated by MPLC. This was the first and only occasion that one of the phenyl ligands from the catalyst was incorporated in the coupling reaction. However, this phenomenon has been observed by other groups.¹⁰⁵

The amides **298a** and **298b** were identified from their ^1H nmr spectra. The amide **298a** gave a ^1H nmr spectrum which showed that the methylene protons were non-equivalent, δ 4.09 (1 H, dd, J 3.4 Hz, 14.1 Hz, CH_2) and δ 4.73 (1 H, dd, J 7.5 Hz, 14.1 Hz, CH_2), whereas the amide **298b** gave a ^1H nmr spectrum which showed that the methylene protons were equivalent, δ 4.72 (2 H, d, J 5.5 Hz, CH_2), Figure 15.

^1H nmr spectrum
of the amide **298a**



^1H nmr spectrum
of the amide **298b**

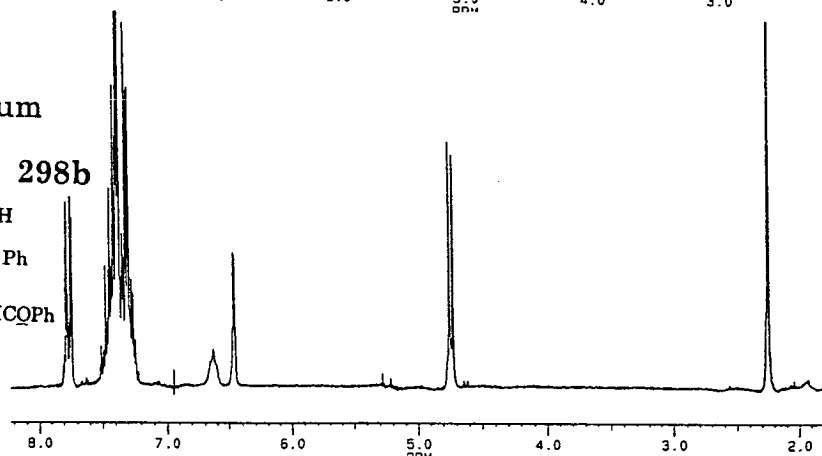
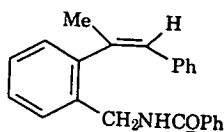
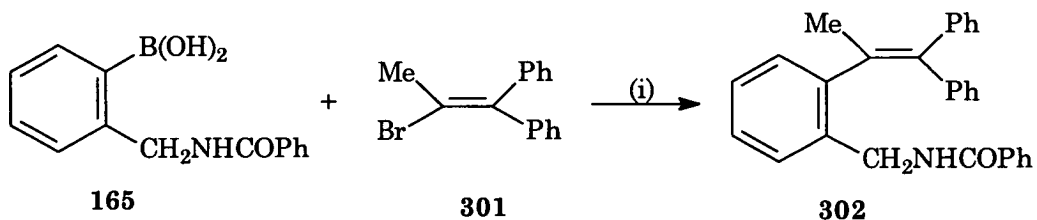


Figure 15

It appears that the methyl group in the amide **298a** restricts rotation of the olefinic moiety to which it is attached, due to a steric interaction with the *ortho*-hydrogen in the adjacent phenyl ring. This restrictive effect of the methyl group results in the appearance of the methylene protons as diastereotopic. However, this effect is not seen in the amide **298b** and the methylene protons are seen in the ^1H nmr spectrum as a doublet.

(c) *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzamide **302**

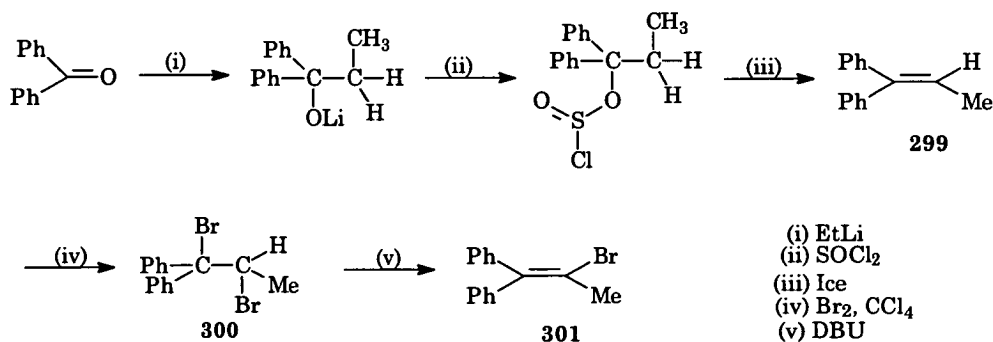
The amide **302** was synthesised as shown in Scheme 83. The Pd(0) catalysed cross coupling reaction of the boronic acid **165** and 2-bromo-1,1-diphenylpropene **301** gave the amide **302** as a white solid in a 54% yield.



(i) Pd(0), Na_2CO_3 , DME, Δ

Scheme 83

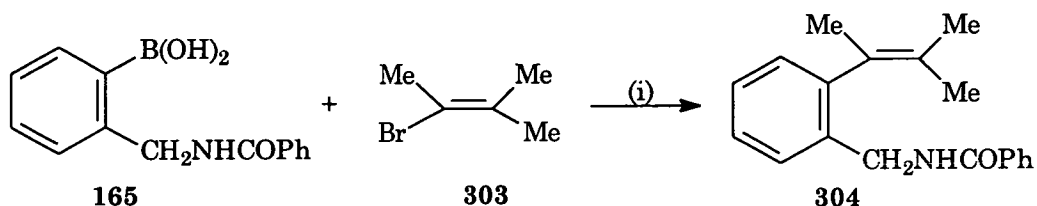
The bromoalkene **301** was prepared as shown in Scheme 84. The first attempted synthesis of 1,1-diphenylpropene **299** was *via* the Grignard reaction, which was to be followed by a dehydration of the tertiary alcohol. However, the Grignard reaction gave benzhydrol in 70% as the only product and not the expected 1,1-diphenylpropanol. Therefore, the methodology developed by Olah¹⁰⁶ for the synthesis of hindered olefins was employed. Thionyl chloride was added with vigorous stirring to the reaction product of ethyllithium and benzophenone in ether at -78°C . This reaction gave 1,1-diphenylpropene **299** as a white solid in a 24% yield, Scheme 84. Bromination of the alkene **299** gave the dibromo compound **300**, which subsequently underwent spontaneous dehydrobromination in deuteriochloroform over a seven day period. The base DBU effected the dehydrobromination more readily and gave 2-bromo-1,1-diphenylpropene **293** in a 65% yield.



Scheme 84

(d) *N*-[2-(3'-Methylbut-2'-enyl)benzyl]benzamide 304

The Pd(0) catalysed cross coupling reaction of the boronic acid **165** and 2-bromo-3-methylprop-2-ene **303**, commercially available from Avocado, gave the amide **304** as a white solid in a 70% yield, Scheme 85.

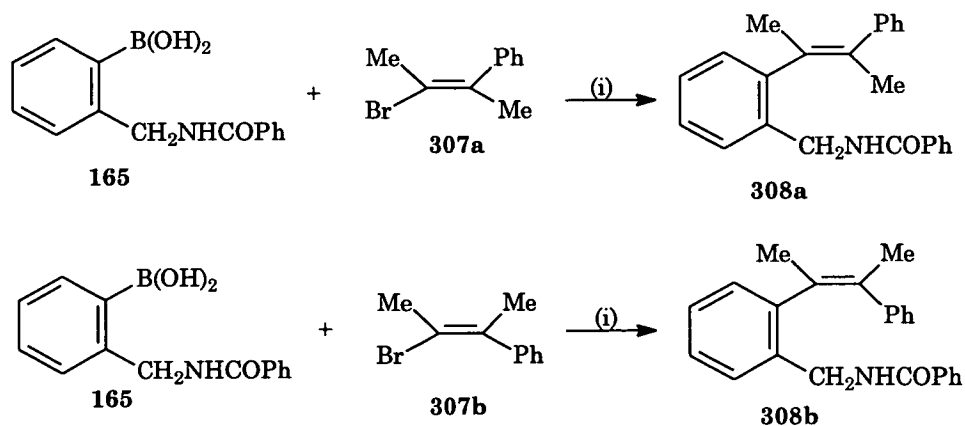


(i) Pd(0), Na₂CO₃, DME, Δ

Scheme 85

(e) *N*-[2-(*E*-3'-Phenylbut-2'-enyl)benzyl]benzamide 308a and *N*-[2-(*Z*-3'-Phenylbut-2'-enyl)benzyl]benzamide 308b

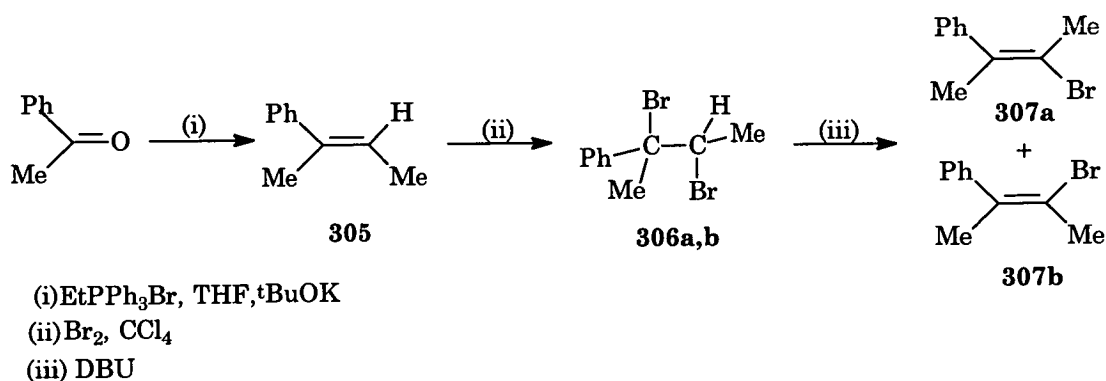
The Pd(0) catalysed cross coupling reaction of the boronic acid **165** and *E*-2-bromo-3-phenylbut-2-ene **307a** gave the amide **308a** as a white solid in a 63% yield. The coupling reaction of **165** and *Z*-2-bromo-3-phenylbut-2-ene **307b** gave the amide **308b** as a white solid in a 78% yield, Scheme 86.



(i) Pd(0), Na₂CO₃, DME, Δ

Scheme 86

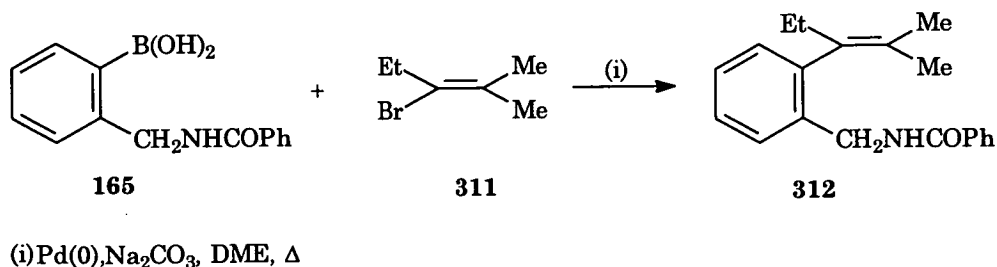
E-2-Phenylbut-2-ene **305** was synthesised *via* a Wittig reaction from acetophenone in 65% yield. Bromination of **305** gave 2,3-dibromo-3-phenylbutane **306a,b** as a mixture of diastereomers that were used without purification, because, decomposition was found to have occurred during chromatography on silica. Dehydrobromination of **306a,b** with DBU, Scheme 87, gave *E*-2-bromo-3-phenylbut-2-ene **307a** as the minor product and *Z*-2-bromo-3-phenylbut-2-ene **307b** as the major product in a ratio of 3:1. The isomers were separated in 10% and 28% respectively by dry-flash chromatography.



Scheme 87

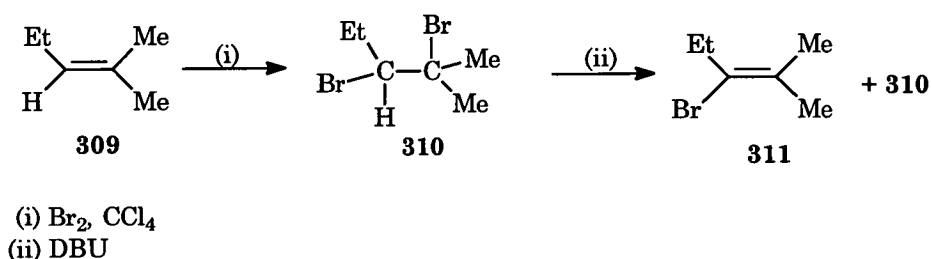
(f) *N*-[2-(2'-Methylpent-2'-en-3'-yl)benzyl]benzamide **312**

The amide **312** was synthesised as shown in Scheme 88. The Pd(0) catalysed cross coupling reaction of the boronic acid **165** and 3-bromo-2-methylpent-2-ene **311** gave the amide **312** as a white solid in 45% yield.



Scheme 88

Bromination of 2-methylpent-2-ene **309**, commercially available from Aldrich, gave 2,3-dibromo-2-methylpentane **310** as an orange oil that was purified by distillation under vacuum. Dehydrobromination of **310** with DBU gave a mixture of the product **311** and starting material in a ratio of 2:1. The mixture was distilled under vacuum at room temperature, and then a further 1.5 molar equivalents of DBU was added, Scheme 89. The product **311** was again distilled under vacuum, but the ^1H nmr spectrum showed that there was still approximately 10% of the unreacted dibromo compound **310** present. It was decided to use the mixture without further purification because it is known that saturated bromo compounds cannot be coupled with boronic acids using the Suzuki reaction.



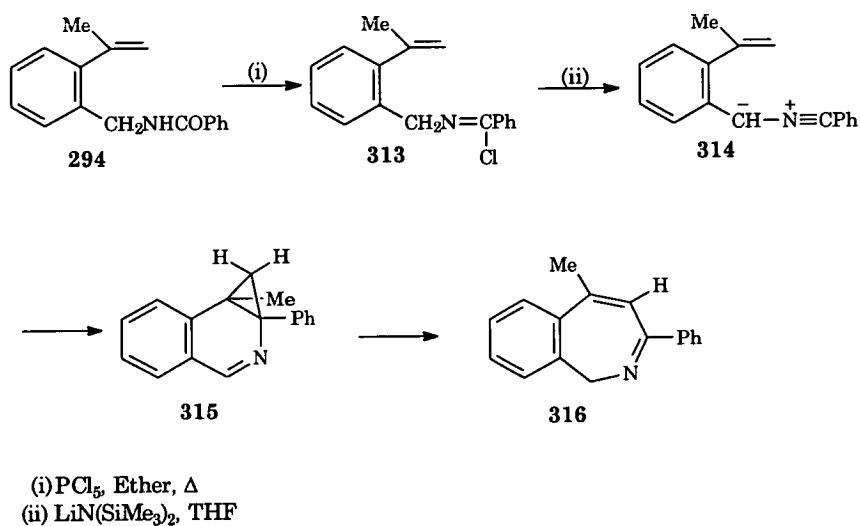
Scheme 89

3.3 Generation and Reaction of the Nitrile Ylides Derived from Substituted *N*-[2-Alkenylbenzyl]benzimidoyl Chlorides

In this research the nitrile ylides were generated by the 1,3-dehydrochlorination of imidoyl chlorides. The latter were prepared from their respective amides using phosphorus pentachloride or chloromethylenedimethylammonium chloride and were used without purification.

(a) Benzonitrile-2-(propen-2'-yl)benzyl Ylide 314

The amide **294** was converted to the imidoyl chloride **313**, by heating at reflux with phosphorus pentachloride in dry ether for 24 h. Evaporation of the ether left an oil that was kept at 30-40 °C on a high vacuum rotary evaporator for *ca.* 3 h to remove the phosphorus oxychloride. The crude benzimidoyl chloride **313** was dissolved in dry THF and the solution was kept at 0 °C under nitrogen. The nitrile ylide **314** was generated at 0 °C by the addition of 1.5 molar equivalents of lithium bis(trimethylsilyl)amide, as shown in Scheme 90.



Scheme 90

The reaction gave one product which was identified as 7b-methyl-1a-phenyl-1H-cyclopropa[c]isoquinoline **315** from its ^1H nmr spectrum. The singlet at δ 8.29, assigned as the $\text{HC}=\text{N}$ proton is characteristic of the cyclopropa[c]isoquinolines **152**, Scheme 37. The product was isolated as a yellow oil by dry-flash chromatography, but, partial isomerisation was found to have occurred at room temperature over a period of 24 h to give 5-methyl-3-phenyl-1H-2-benzazepine **316**. Thermal isomerisation of the cyclopropa[c]isoquinoline **315** in benzene for 12 h gave a quantitative conversion to the benzazepine **316**, which was identified from its ^1H nmr

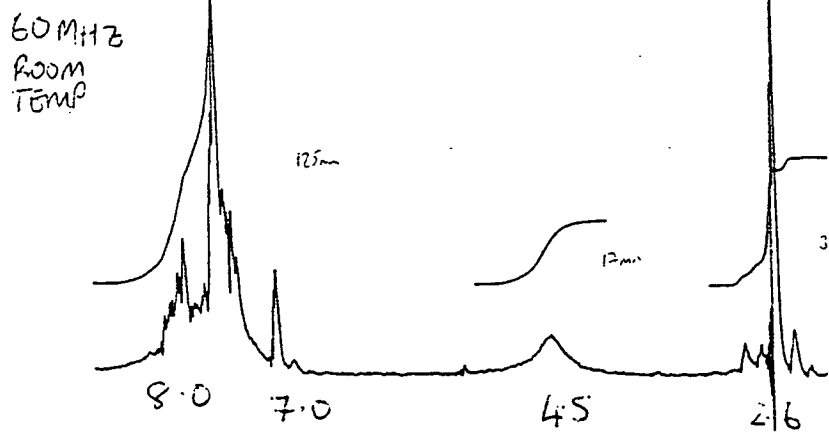
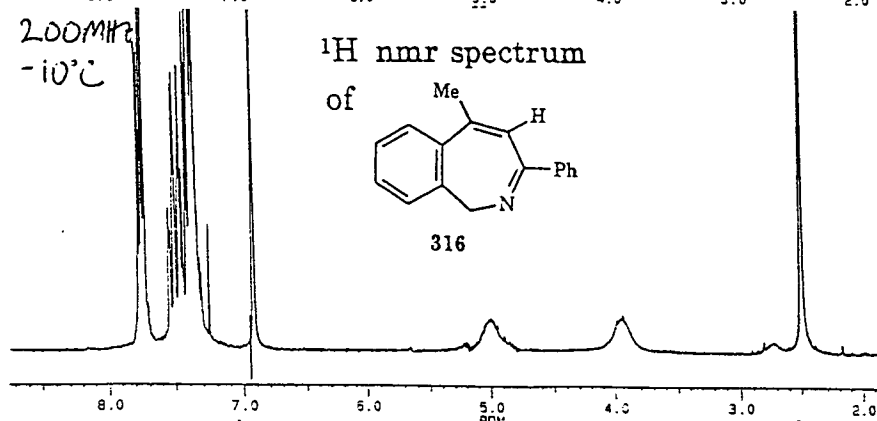
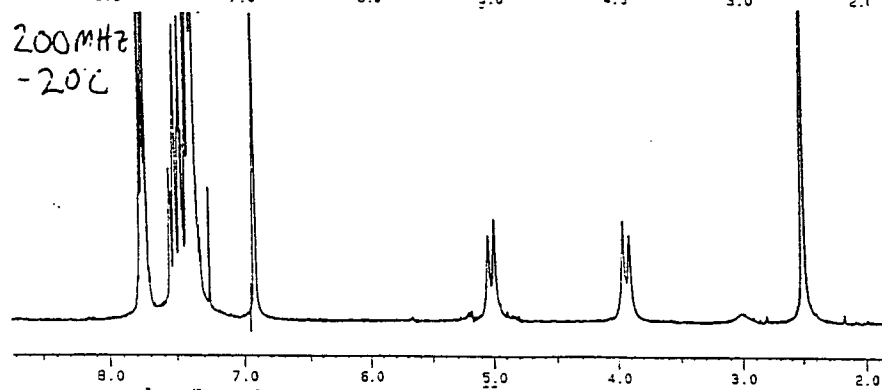
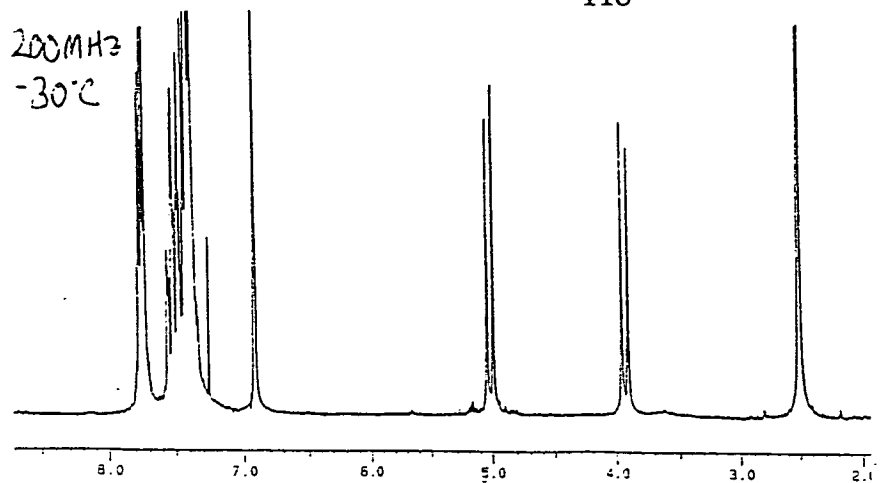


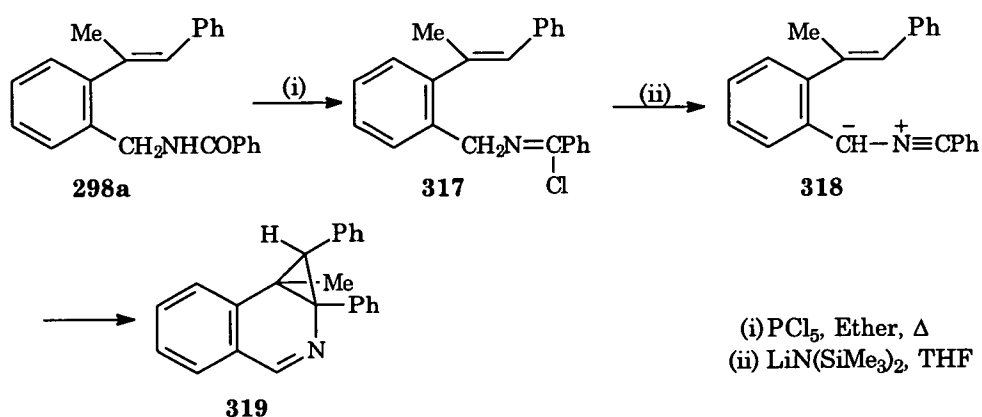
Figure 16

spectrum. Examination of the ^1H nmr spectrum of the benzazepine **316** at 25 °C showed a broad peak at δ 4.5 (this was observed on the 60 MHz nmr machine), which on cooling resolved to give two doublets (J 10 Hz), at δ 3.90 (axial) and δ 4.98 (equatorial) due to the absorption of the methylene protons, Figure 16. The coalescence of the doublets at room temperature is due to the ring inversion of the seven membered ring. At the lower temperature the ring inversion is slow on the nmr time scale and the methylene protons absorb at different chemical shifts and couple to each other. As the temperature is raised the rate of ring inversion increases and the peaks broaden, coalesce and eventually give a singlet at the midpoint of the original pair of doublets.

The molecular formula was confirmed by an accurate mass measurement, $(M+1)^+$, 234.1283, and elemental analysis.

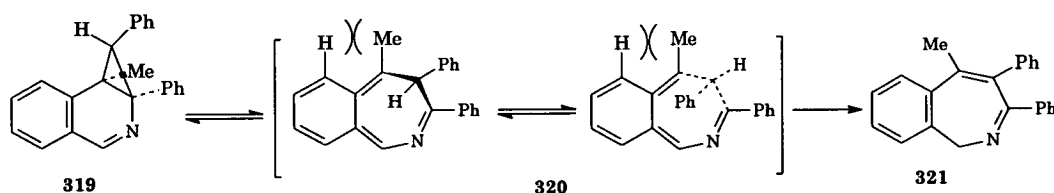
(b) Benzonitrile-2-(*E*-1'-phenylpropen-2'-yl)benzyl Ylide **318**

The imidoyl chloride **317** was prepared from the amide **298a** by heating at reflux with phosphorus pentachloride in ether for 24 h. The cyclopropa[*c*]isoquinoline **319** was then obtained in a 66% yield by the reaction of **317**, with lithium bis(trimethylsilyl)amide in the usual manner, Scheme 91.



Scheme 91

Sharp and co-workers showed that when $R^1, R^3 = H$, the cyclopropa[c]isoquinolines **152**, Scheme 37, ring open to form a new seven membered ring which is followed by a [1,5] hydrogen migration to give the 1*H*-2-benzazepine **153**. Thermal isomerisation of the cyclopropa[c]isoquinoline **319** in toluene for 24 h gave the 1*H*-2-benzazepine **321**, *via* the path shown in Scheme 92. The [1,5]-hydrogen shift giving **321** is probably a sigmatropic shift. The temperature and time required for the isomerisation was quite surprising considering that a similar cyclopropa[c]isoquinoline **152**, which did not have a methyl group at the C-7b carbon only required to be heated at reflux for 12 h in benzene. However, it seems likely that the intermediates **320** are destabilised by a *peri* interaction between the hydrogen and the methyl group as shown in Scheme 92.

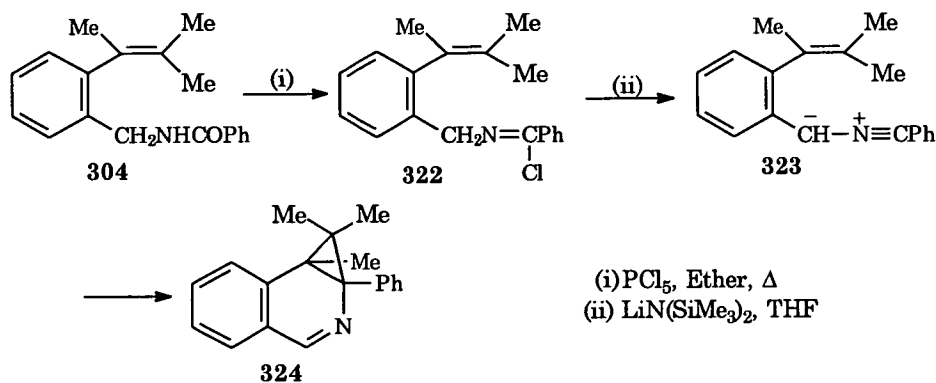


The ^1H nmr spectrum of the 1*H*-2-benzazepine **321** obtained at 25 $^{\circ}\text{C}$ was similar to the spectrum of the benzazepine **316** at -30 $^{\circ}\text{C}$. The methylene protons gave two doublets (J 10 Hz), at δ 4.14 and δ 4.96. The molecular formula was confirmed by an accurate mass measurement, $(M+1)^+$, 310.1596.

(c) Benzonitrile-2-(3'-methylbut-2'-enyl)benzyl Ylide **323**

Zecchi isolated the 5-methylene-4,4-dimethyl-1*H*-1,2-benzodiazepine **288** and the cyclopropacinnoline **287** from the nitrile imine **284** when $R^{1,2,3} = \text{Me}$. The product **288** was as a result of a [1,5]

hydrogen migration from the methyl group at the C-5 position in the intermediate **285**. Therefore, it was decided to investigate the reactions of the nitrile ylide **323** which is analogous to the nitrile imine **284**, Scheme 79. The imidoyl chloride **322** was prepared from the amide **304** by heating at reflux with phosphorus pentachloride in ether for 60 h. The cyclopropa[*c*]isoquinoline **324** was then obtained in a 75% yield by the reaction of **322**, with lithium bis(trimethylsilyl)amide in the usual manner, Scheme 93. The product was identified by comparisons with the other ^1H nmr spectra. The singlet at δ 8.30 assigned as the HC=N proton is indicative of a cyclopropa[*c*]isoquinoline.



Scheme 93

Thermal isomerisation of the cyclopropa[*c*]isoquinoline **324** was found not to have gone to completion after heating at reflux in toluene for over a week. Therefore, *p*-xylene, a higher boiling solvent was used. It was found that the cyclopropa[*c*]isoquinoline **324** isomerised to give 4-methyl-3-phenyl-4-propen-2'-yl-1*H*-isoquinoline **325** at reflux in *p*-xylene for 24 h, Scheme 94.

4-Methyl-3-phenyl-4-propen-2'-ylisoquinoline

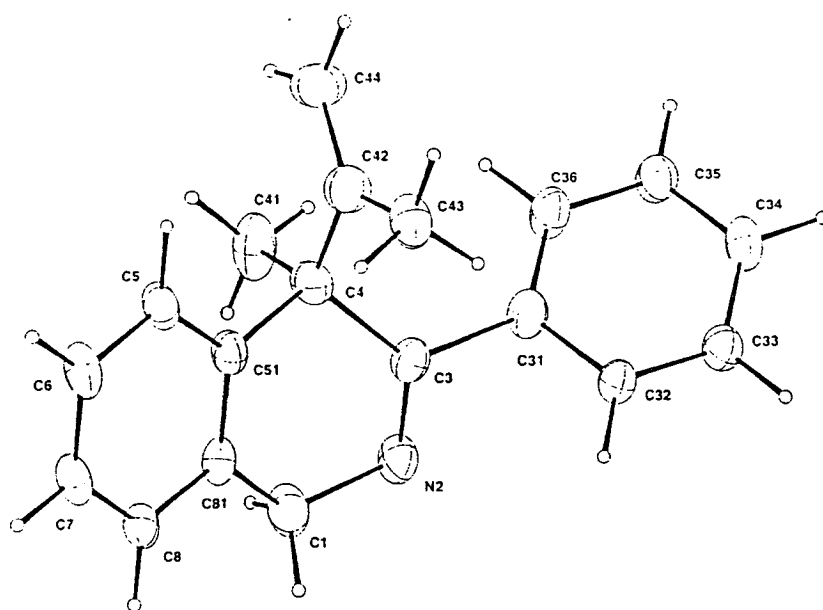
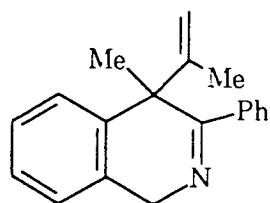
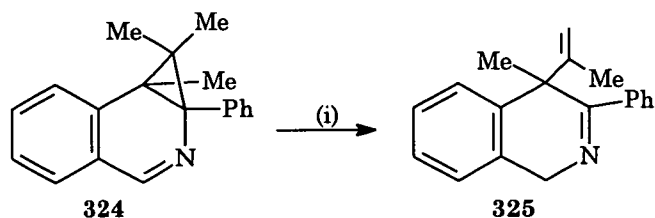


Figure 17



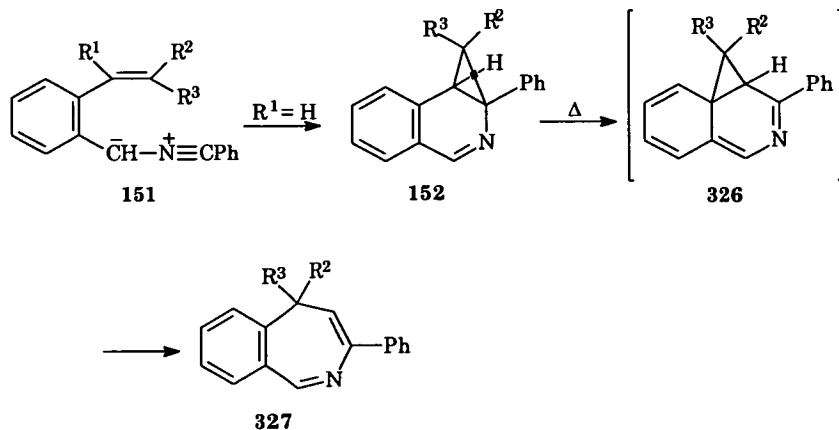
(i) *p*-Xylene, Δ , 24 h

Scheme 94

The structure of the product **325** was established by X-ray crystallography, Figure 17. It appears that the reaction proceeds *via* a homo [1,5]-sigmatropic hydrogen shift,¹⁰⁷ which is well known and is similar to the one shown below.



When R^1 , R^2 and $R^3 = \text{Me}$, the nitrile ylide **323** cyclised as expected to give the cyclopropa[*c*]isoquinoline **324**. The surprising feature was that thermolysis of the product **324** gave the isoquinoline **325** apparently *via* a [1,5] sigmatropic hydrogen shift (this reaction was not base catalysed, because heating **324** with base in toluene for 48 h gave only starting material). Previous work on diene-conjugated nitrile ylides of the type **151** showed that when the δ carbon was disubstituted a [1,5] carbon walk was followed by an electrocyclic ring opening to give the 5*H*-2-benzazepines.

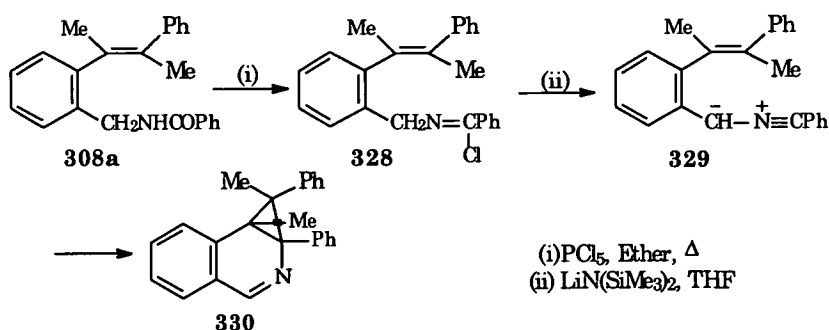


Scheme 95

(d) Benzonitrile-2-(*E*-3'-phenylbut-2'-enyl)benzyl Ylide 329

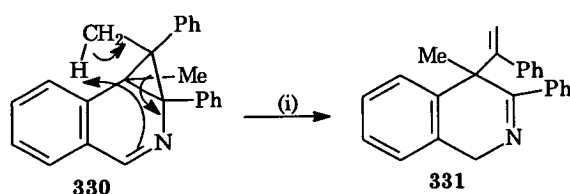
In view of the complete difference in reaction path for the thermolysis of **324** it was of interest to explore further the influence of the substituents on these reactions. Therefore, the R^2 methyl group in **323** (nitrile ylide **329**) and subsequently the R^3 methyl group (nitrile ylide **333**) were to be replaced by phenyl substituents to see if the two mechanisms became competitive and if a 5*H*-2-benzazepine could be isolated.

The imidoyl chloride **328** was prepared from the amide **308a** by heating with phosphorus pentachloride in ether at reflux for 60 h. The cyclopropa[*c*]isoquinoline **330** was obtained in a 70% yield from the reaction of **328**, with lithium bis(trimethylsilyl)amide in the usual manner, Scheme 96.



Scheme 96

The cyclopropa[*c*]isoquinoline **330**, was heated at reflux in *p*-xylene for 48 h and gave only 4-methyl-3-phenyl-4-(1'-phenylethenyl)-1*H*-isoquinoline **331**, *via* a homo [1,5]-sigmatropic hydrogen shift, as shown in Scheme 97. The structure of the product **331** was determined by comparison with the ^1H nmr spectrum for the isoquinoline **325**. The ^1H nmr spectrum of the product **330** showed a singlet at δ 1.71 (CH_3), a doublet at δ 4.59 (1 H, ring CH_2), a doublet at δ 5.41 (1 H, olefinic CH_2), a doublet at δ 5.54 (1 H, olefinic CH_2), and a doublet at δ 6.69 (1 H, ring CH_2). There was no evidence to suggest that the 5*H*-2-benzazepine was formed from this isomerisation reaction. Therefore, the homo [1,5] hydrogen shift remains the energetically favoured reaction even though it becomes slower with a phenyl substituent at C-1 position of the cyclopropa[*c*]isoquinoline ring.

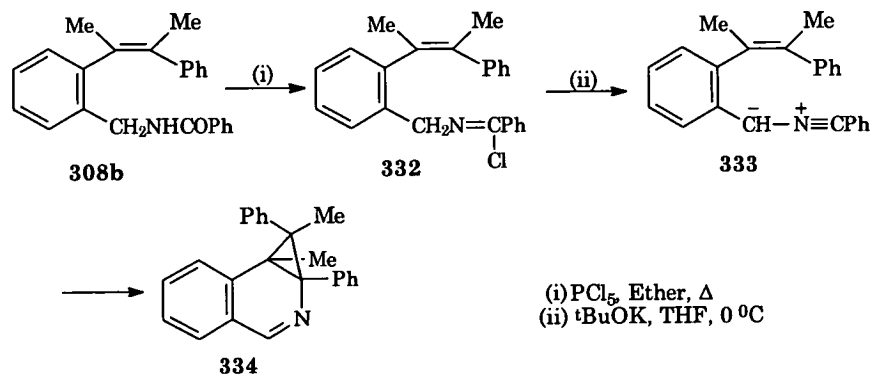


(i) *p*-Xylene, Δ , 48 h

Scheme 97

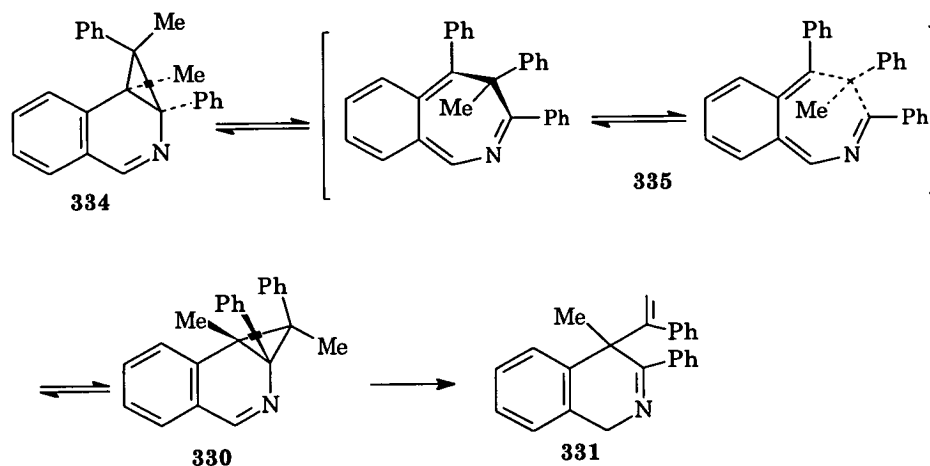
(e) Benzonitrile-2-(*Z*-3'-phenylbut-2'-enyl)benzyl Ylide **333**

The imidoyl chloride **332** was prepared from the amide **308b** by heating at reflux with phosphorus pentachloride in ether for 60 h. The nitrile ylide **333** was generated at 0 $^{\circ}\text{C}$ by dissolving the imidoyl chloride **332** in dry THF and adding two equivalents of potassium *tert*-butoxide, Scheme 98. This procedure gave the cyclopropa[*c*]isoquinoline **334** as an oil in 72% yield.



Scheme 98

It was expected that the thermal isomerisation of **334** would be slower than for cyclopropa[*c*]isoquinoline **330**, because the methyl group is in the *exo* position and not the required *endo* position. Therefore, an equilibrium, Scheme 99, has to be established between **334** and **330** before the hydrogen shift can occur.



Scheme 99

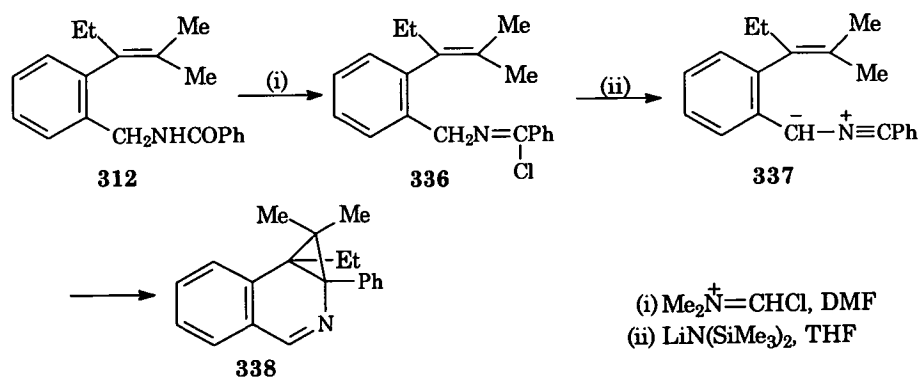
After heating **334** at reflux for 48 h in *p*-xylene a mixture of **330** and **331** was obtained. This showed that an equilibration between *exo* and *endo* isomers had been established and was apparently the slow step in the isomerisation to give compound **331**. This was a surprising result since

previous work⁶⁶ showed that an equilibration between *exo* and *endo* isomers of cyclopropa[c]isoquinolines is established fairly rapidly and that they are then slowly converted into benzazepines. The course of these thermal rearrangements was monitored by ¹H nmr spectroscopy. However, the reactions of **330** and **334** could not be monitored by ¹H nmr spectroscopy due to the nature of the solvents required for isomerisation

(f) Benzonitrile-2-(2'-methylpent-2'-en-3'-yl)benzyl Ylide **337**

The cyclopropa[c]isoquinolines **324**, **330** and **334** isomerised *via* a homo [1,5] hydrogen shift to give the isoquinolines **325** and **331** respectively. One feature all three had in common was the methyl group at the C-7b position, therefore, it was decided to replace it with an ethyl group to see if this affected the hydrogen migration.

The standard method of generating imidoyl chlorides, phosphorus pentachloride and ether at reflux, was not satisfactory for the amide **312**. The imidoyl chloride **336** was prepared from the amide **312** by reaction with chloromethylenedimethylammonium chloride.

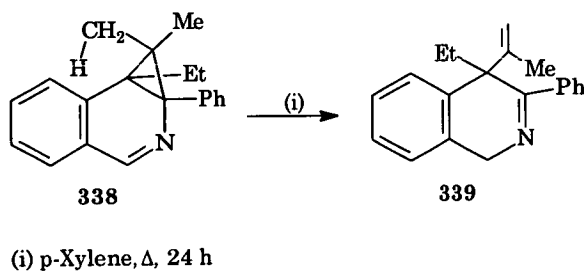


Scheme 100

The nitrile ylide **337** was generated at 0 °C by dissolving the imidoyl chloride **336** in dry THF and adding four equivalents of lithium bis(trimethylsilyl)amide, Scheme 100. This procedure gave the cyclopropa[c]isoquinoline **338** as an oil in 80%. The structure was

established by comparison with the ^1H nmr spectrum for the cyclopropa[c]isoquinoline **324**. The singlet at δ 8.21 assigned as the $\text{HC}=\text{N}$ proton is characteristic of the cyclopropa[c]isoquinoline structure.

By heating at reflux in *p*-xylene for 24 h the cyclopropa[c]isoquinoline **338**, was isomerised to 4-ethyl-3-phenyl-4-propen-2'-yl-1*H*-isoquinoline **339**, *via* a homo [1,5]-sigmatropic hydrogen shift, as shown in Scheme 101. It is therefore apparent that the effect of the ethyl group is no different to that of a methyl at the same position.



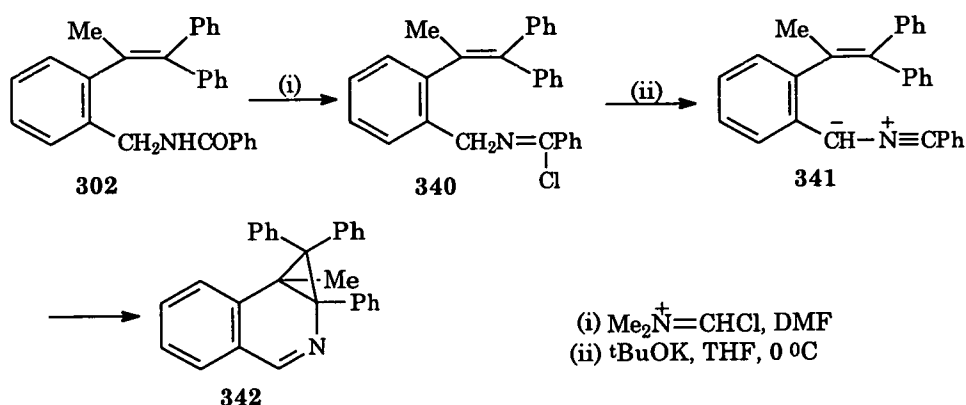
Scheme 101

(g) Benzonitrile-2-(1',1'-diphenylpropen-2'-yl)benzyl Ylide **341**

Previous work on diene-conjugated nitrile ylides of the type **151** in which the δ carbon was disubstituted gave the cyclopropa[c]isoquinolines **152**. Isomerisation of **152** ($\text{R}^{2/3} = \text{Ph}$) in toluene resulted in an equilibrium between the reactant and the 5*H*-2-benzazepine in the ratio *ca.* 2:1 being established after 24 h. The cyclopropa[c]isoquinoline **342** therefore has this pathway open to it and also a possible pathway *via* a [1,5] hydrogen shift from the methyl group which would give the 5-methylene-1*H*-2-benzazepine, *i.e.* a parallel to the formation of compound **288**, Scheme 79.

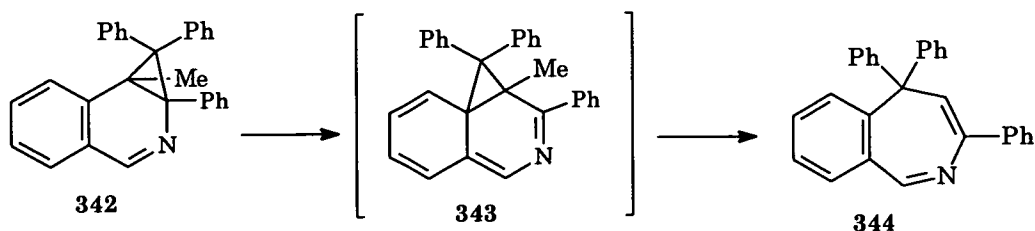
Numerous attempts were made to convert the amide **302** into the imidoyl chloride **340**. The one method that proved successful was to generate the chlorinating agent chloromethylenedimethylammonium chloride *in situ*. Some of the failures included thionyl chloride in ether, phosphorus pentachloride in ether and even adding preformed

chloromethylenedimethylammonium chloride to the amide in DMF. The nitrile ylide **341** was generated at 0 °C by dissolving the imidoyl chloride **340** in dry THF and adding six equivalents of potassium *tert*-butoxide, Scheme 102. This procedure gave the cyclopropa[*c*]isoquinoline **342** as a yellow solid in 67%. The product was identified by comparison with the other ¹H nmr spectra.



Scheme 102

Thermal isomerisation of **342** on a small scale gave **344** in a 40% yield after heating at reflux in *p*-xylene for six days, apparently *via* the path shown in Scheme 103. The product was separated from the cyclopropa[*c*]isoquinoline **342** by dry-flash chromatography. It is thought the product **344** is a 5*H*-2-benzazepine from the data collected, however, a full analysis was not possible as the product decomposed before this was completed.



Scheme 103

Summary and Conclusions

The third objective of the project, as described in Section 3.1, was to study the reactions of diene-conjugated nitrile ylides with a methyl group in the γ -position.

(i) All of the diene-conjugated nitrile ylides of the type **156** cyclised to give the cyclopropa[c]isoquinolines.

(ii) Thermolysis of cyclopropa[c]isoquinolines with a hydrogen at the C-1 position resulted in an electrocyclic ring opening followed by a [1,5] hydrogen shift to give the *1H*-2-benzazepines **316** and **321**. This route is clearly the preferred reaction path when a C-1 hydrogen atom is present.

(iii) Thermolysis of the cyclopropa[c]isoquinolines with a methyl group at C-1 position and no hydrogen at this site gave the isoquinolines *via* a homo [1,5] hydrogen shift. This appears to be the preferred path for cyclopropa[c]isoquinolines with a 1^y or 2^y alkyl group at C-1 and in all the cases studied is favoured over the alternative [1,5] carbon walk leading to the *5H*-2-benzazepine.

(iv) Thermolysis of a cyclopropa[c]isoquinoline with two phenyl groups at the C-1 position gave the *5H*-2-benzazepine.

(v) In no case was there a reaction which paralleled the formation of **288**, Scheme 79, observed in the analogous nitrile imines. Such a reaction could in principle take place *via* a [1,5] hydrogen shift from the alkyl group at the C-7b position but such a transition state would require much distortion of the molecule. In the nitrile imine reaction the mechanism of the formation of compound **288** is not discussed in the original paper but it seems possible that it is a base-catalysed process. In the light of this an attempt was made to effect a similar reaction by treating **324** with strong base, but, no reaction occurred.

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A. SYMBOLS AND ABBREVIATIONS

NMR	nuclear magnetic resonance
Hz	hertz
MHz	megahertz
δ	chemical shift
p.p.m.	parts per million
<i>J</i>	coupling constant
br	broad
s	singlet
d	doublet
dd	doublet of doublets
t	triplet
q	quartet
quat.	quaternary
m	multiplet
IR	infra-red
ν	wave numbers
EI	electron ionisation mass spectrometry
FAB	fast atom bombardment mass spectrometry
<i>m/z</i>	mass to charge ratio
M^+	mass of molecular ion
$(M+1)^+$	mass of molecular ion
tlc	thin layer chromatography
MPLC	medium pressure liquid chromatography
HPLC	high pressure liquid chromatography
DME	ethylene glycol dimethyl ether

DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulphoxide
DCM	dichloromethane
THF	tetrahydrofuran
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
mol	moles
mmol	millimoles
w/v	weight/volume
mp	melting point
bp	boiling point
h	hours
min	minutes
p.s.i.	pounds per square inch

B. INSTRUMENTATION AND GENERAL TECHNIQUES

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

^1H NMR spectra were recorded either at 250.133 MHz on a Bruker AC250 (250 MHz), at 200.13 MHz on a Bruker WP200 (200 MHz) or at 199.975 MHz on a Gemini Varian (200 MHz) spectrometer. Routine continuous wave spectra were obtained on a Joel PMX 60SI (60 MHz) instrument. ^{13}C NMR spectra were recorded at 62.900 MHz on the Bruker AC250 (63 MHz) or at 50.320 MHz on the Bruker WP200 (50 MHz) instruments.

Carbon multiplicity was established by distortionless enhancement by polarisation transfer (DEPT). Spectra were recorded in deuteriochloroform, unless otherwise stated; chemical shifts (δ_{H} , δ_{C}) are quoted in parts per million, relative to tetramethylsilane, and coupling constants (J) are quoted in Hz. Standard 200 and 250 MHz ^1H spectra have an accuracy of 0.3 Hz per point and are quoted as recorded. Standard 50 and 63 MHz ^{13}C spectra have an accuracy of 0.5 Hz per point and are quoted as recorded. The AC250 was operated by Mr. J. R. A. Millar, the WP200 by Mr. J. R. A. Millar, Mr. W. Kerr.

MASS SPECTROSCOPY

Low resolution electron impact mass spectra were recorded at 70 eV by Miss E. Stevenson on an A.E.I. MS902 instrument. High resolution and FAB mass spectra were recorded by Mr. A. Taylor on a Kratos MS50TC instrument.

ELEMENTAL ANALYSIS

Microanalyses were obtained by Mrs. L. Eades on a Perkin Elmer 240 CHN Elemental Analyser.

X-RAY CRYSTALLOGRAPHY

X-ray crystallographic data were obtained and refined by Dr. S. Parsons on a Stoë STADI-4 four circle diffractometer with graphite monochromator.

INFRA-RED SPECTROSCOPY

Liquid samples were examined as thin films and solid samples as nujol mulls on sodium chloride plates using a Bio-Rad FTS-7 spectrometer.

CHROMATOGRAPHY

Thin-layer chromatography was carried out on pre-coated aluminium sheets (0.2 mm silica gel, Merck, grade 60) impregnated with a UV fluorescent indicator, or on pre-coated aluminium sheets (0.2 mm aluminium oxide, neutral (Type E), Merck, grade 60) impregnated with a UV fluorescent indicator. Components in the developed chromatograms were detected by their quenching of fluorescence under ultra-violet light. Dry-flash chromatography was carried out on silica gel (Fluka, Kieselgel GF₂₅₄; for thin layer chromatography) using the method of Harwood.¹⁰⁸ Wet-flash column chromatography was carried out on either silica gel (Merck, grade 60, 230-400 mesh, 60 Å) or alumina (Aldrich, activated, neutral, Brockmann grade 1) using the method of Still.¹⁰⁹

SOLVENTS

Tetrahydrofuran was distilled from sodium benzophenone ketal as required. HPLC grade hexane and ethyl acetate were used without further purification. Ether was generally dried by storage over sodium wire; when necessary it was dried further by distillation from sodium benzophenone ketal. Cyclohexane, ethylene glycol dimethyl ether, dichloromethane and *N,N*-dimethylformamide were distilled from calcium hydride as required. 'Super-dry' ethanol was prepared as described in Vogel¹¹⁰ and was stored over molecular sieve (4 Å). All other dry solvents were obtained by storing over molecular sieve (4 Å).

MELTING POINTS

Melting points were determined using a Gallenkamp melting-point apparatus and are uncorrected.

HIGH-PRESSURE LIQUID CHROMATOGRAPHY

Analytical chromatograms were obtained using a solvent metering pump (model 110A) and sample injection valve (model 210) supplied by Altex Scientific Inc. A variable wavelength ultraviolet monitor (CE212) supplied by Cecil Instruments was used as the peak detector at a wavelength of 254 nm. The peaks were measured with a Pye Unicam CDP integrator.

Pre-packed HPLC columns supplied by "HPLC technology" were used throughout. Alphasil5SILICA packed in a 250 x 4.6 mm column was used for normal phase with Alphasil5ODS packed in a 250 x 4.6 mm column for reverse phase. Reverse phase was used unless otherwise stated. Standard HPLC grade solvents were used throughout.

MEDIUM PRESSURE LIQUID CHROMATOGRAPHY

Glass columns (100 x 2.5 cm) packed with silica gel (Merck Kieselgel, grade 60, 230-240 mesh) were used and were cleaned between separations by back flushing with dry ethyl acetate. Samples were pre-absorbed onto a small scrubber column (25 x 1.5 cm), packed as above, which protected the main column from contamination. The diaphragm-type pump (100 p.s.i. maximum) was supplied by Metering Pumps Ltd.

DRYING AGENTS

Magnesium sulphate was used unless otherwise stated.

I. Preparation of starting materials

(i) N-Benzoyl-2-bromobenzylamine 159

To benzonitrile (10 cm³) was added concentrated sulfuric acid (6.24 g, 42.4 mmol) under nitrogen. The solution was heated to 70 °C and 2-bromobenzylalcohol (7.92 g, 42.4 mmol) in benzonitrile (20 cm³) was added dropwise and stirred for 6 h. The reaction mixture was allowed to cool to room temperature and was left stirring overnight. Sodium carbonate (50% w/v, 100 cm³) was added slowly to neutralise the reaction. Ethyl acetate (2 x 100 cm³) was added, the organic layer separated and washed with a saturated sodium chloride solution (50 cm³). The organic layer was dried and the solvent removed *in vacuo*. Wet-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded *N*-benzoyl-2-bromobenzylamine as a white crystalline solid (8.70 g, 70%), mp 134 °C, from ethanol, lit.⁶⁷, 133-134 °C, (Found: 290.0165. C₁₄H₁₃⁷⁹BrNO requires (M+1)⁺, 290.0181); δ_H(200 MHz, CDCl₃) 4.77 (2 H, d, J 6.0 Hz, CH₂), 6.33 (1 H, br, NH), 7.33-8.07 (9 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 44.1 (CH₂), 123.5 (quat.), 126.8 (CH), 127.2 (CH), 128.4 (2 x CH), 129.1 (CH), 130.2 (CH), 131.5 (CH), 131.8 (CH), 132.6 (CH), 134.0 (quat.), 137.0 (quat.), 167.3 (quat.); *m/z* (FAB) 292 (M+1, 40%), 291 (75), 290 (100), 289 (70), 288 (60), 210 (100), 105 (75), 77 (55); ν_{max}(Nujol)/cm⁻¹ 1629 (C=O), 3289 (NH).

(ii) 2-Bromo-3-methylbenzyl bromide 171

A mixture of bromo-*meta*-xylene (29.6 g, 0.16 mol), *N*-bromosuccinimide (28.0 g, 0.16 mol) and dry benzoyl peroxide (1.94 g, 5% initiator) in carbon tetrachloride (200 cm³) was heated at reflux overnight under nitrogen. The reaction was allowed to cool to room temperature and the succinimide formed was filtered off. The solvent was removed *in vacuo* and dichloromethane (100 cm³) was added. The organic solution

was then washed with sodium carbonate solution (5% w/v, 2 x 50 cm³) and then water (2 x 50 cm³). The organic layer was dried, filtered and the solvent removed *in vacuo* to give a brown oil. Distillation of the product gave 2-bromo-3-methylbenzyl bromide as a clear oil (22.38 g, 53%), bp 50 °C/0.05 mmHg, lit.¹¹¹, 67-68 °C/1 x 10⁻¹ Torr, (Found: 261.8994. C₈H₈⁷⁹Br₂ requires M⁺, 261.8993); δ_H(200 MHz, CDCl₃) 2.44 (3 H, s, CH₃), 4.65 (2 H, s, CH₂), 7.17-7.31 (3 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 23.7 (CH₃), 34.5 (CH₂), 126.9 (quat.), 127.1 (CH), 128.5 (CH), 130.8 (CH), 137.1 (quat.), 139.2 (quat.); *m/z* (EI) 264 (M⁺, 11%), 264 (22), 262 (11), 185 (100), 183 (100), 104 (25), 103 (20).

(iii) 6-Methyl-2-(phthalimidomethyl)bromobenzene 175

This was made by the Gabriel synthesis⁹¹ using the method of Sheehan and Bolhofer.⁹² A mixture of 2-bromo-3-methylbenzyl bromide (9.9 g, 37.5 mmol), and dry potassium phthalimide (7.65 g, 41.3 mmol), in *N,N*-dimethylformamide (60 cm³) was stirred at room temperature under nitrogen overnight. The solvent was removed *in vacuo* and DCM (30 cm³) was added. The organic solution was washed with aqueous sodium hydroxide solution (2M, 30 cm³) and then water (2 x 30 cm³). The organic layer was then dried, filtered and the solvent removed *in vacuo* to give a white solid (9.41 g, 76%), mp 159 °C from toluene-ethanol (Found: 330.0133. C₁₆H₁₃N⁷⁹Br requires (M+1)⁺, 330.0133); δ_H(200 MHz, CDCl₃) 2.41 (3 H, s, CH₃), 4.97 (2 H, s, CH₂), 6.88-7.25 (3 H, m, Ar-H), 7.68-7.91 (4 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 23.4 (CH₃), 42.3 (CH₂), 123.3 (2 x CH), 124.9 (CH), 126.8 (CH), 129.7 (CH), 131.8 (quat.), 134.0 (2 x CH), 134.9 (quat.), 138.7 (quat.), 167.8 (quat.); *m/z* (FAB) 332 (M+1, 2.4%), 330 (2.1%), 325 (16), 217 (100), 215 (18); ν_{max}(Nujol)/cm⁻¹ 1710 (C=O).

(iv) 2-Bromo-3-methylbenzylamine 176

This was made using the Ing-Manske⁹³ procedure. A mixture of 6-methyl-2-(phthalimidomethyl)bromobenzene (9.37 g, 28.4 mmol), and

hydrazine hydrate (1.64 g, 51.6 mmol), in methanol (120 cm³) was heated at reflux for 1 h. The solvent was removed *in vacuo* and ether (100 cm³) was added. The organic layer was washed with aqueous sodium hydroxide solution (2M, 50 cm³) and then water (2 x 50 cm³). The organic layer was dried, filtered and the solvent removed *in vacuo* to give a yellow oil. This product was used without further purification (5.0 g, 88%), (Found: 198.999. C₈H₁₀N⁷⁹Br requires M⁺, 198.9997); δ_{H} (250 MHz, CDCl₃) 1.78 (2 H, s, NH₂), 2.38 (3 H, s, CH₃), 3.87 (2 H, s, CH₂), 7.08-7.25 (3 H, m, Ar-H); δ_{C} (63 MHz, CDCl₃) 23.7 (CH₃), 47.3 (CH₂), 125.9 (quat.), 126.2 (CH), 127.6 (CH), 129.2 (CH), 138.4 (quat.), 142.2 (quat.); *m/z* (EI) 200 (M⁺, 19%), 198 (16), 184 (10), 169 (15), 131 (22), 120 (100), 91 (36), 69 (12), 30 (15); ν_{max} (Film)/cm⁻¹ 3370 (NH).

(v) N-Benzoyl-2-bromo-3-methylbenzylamine 177

2-Bromo-3-methylbenzylamine (5.0 g, 25.0 mmol) was dissolved in DCM (100 cm³). Sodium carbonate (10.84 g, 37.9 mmol) was added and the mixture stirred for 10 minutes. Benzoyl chloride (7.0 g, 50 mmol) was added and the mixture stirred at room temperature under dry nitrogen overnight. Water (100 cm³) was added and the mixture was stirred for a further 1 h. The organic layer was separated, washed with water (2 x 50 cm³), dried and the solvent removed *in vacuo* to give a white solid (5.93 g, 78%), mp 137-138 °C from ethanol (Found: C, 59.0; H, 4.6; N, 4.5%; (M+1)⁺, 304.0338. C₁₅H₁₄BrN requires C, 59.2; H, 4.6; N, 4.6%; (M+1)⁺, 304.0337); δ_{H} (200 MHz, CDCl₃) 2.41 (3 H, s, CH₃), 4.68 (2 H, d, J 6.0 Hz, CH₂), 6.90 (1 H, br, NH), 7.14-7.80 (8 H, m, Ar-H); δ_{C} (50 MHz, CDCl₃) 23.5 (CH₃), 44.8 (CH₂), 126.2 (quat.), 126.8 (2 x CH), 127.0 (CH), 127.6 (CH), 128.4 (2 x CH), 130.0 (CH), 131.4 (CH), 134.1 (quat.), 137.3 (quat.), 138.6 (quat.), 167.1 (quat.); *m/z* (FAB) 306 (M+1, 97%), 305 (22), 304 (100), 226 (19), 183 (27); ν_{max} (Nujol)/cm⁻¹ 1705 (C=O), 3288 (NH).

(vi) 2-Formyl-6-methylbromobenzene 172

This reaction was carried out using the methodology of Hass and Bender.⁹⁰ Sodium metal (1.30 g) was dissolved in 'super dry' ethanol (50 cm³) under nitrogen and the sodium ethoxide thus prepared was then added to a solution of 2-nitropropane (5.02 g, 56.5 mmol) in 'super dry' ethanol (50 cm³). After stirring under nitrogen for 1 h it was added, using a double tipped needle to a solution of 2-bromo-3-methylbenzyl bromide (8.54 g, 35.3 mmol) in 'super dry' ethanol (50 cm³). The reaction was stirred at room temperature under nitrogen for 48 h. The ethanol was removed *in vacuo* and then ether (100 cm³) was added to dissolve the organic material present. The organic layer was washed with aqueous sodium hydroxide solution (10% w/v, 100 cm³) and then water (2 x 100 cm³). The organic layer was dried, filtered and the solvent removed *in vacuo* to give a white solid (4.92 g, 70%), mp 51-53 °C from hexane, lit.¹¹², 53-54 °C, (Found: 197.9667. C₈H₇⁷⁹BrO requires M⁺, 197.9680); δ_{H} (200 MHz, CDCl₃) 2.46 (3 H, s, CH₃), 7.00-7.74 (3 H, m, Ar-H), 10.43 (1 H, s, CHO); δ_{C} (50 MHz, CDCl₃) 22.7 (CH₃), 127.2 (CH), 127.3 (CH), 129.4 (quat.), 133.9 (quat.), 136.1 (CH), 139.5 (quat.), 192.6 (quat.); *m/z* (EI) 200 (M⁺, 66%), 199 (100), 198 (67), 169 (26), 131 (12), 119 (18), 90 (27), 89 (23), 69 (48); ν_{max} (Nujol)/cm⁻¹ 1700 (C=O).

(vii) Benzyltriphenylphosphonium bromide

A mixture of benzyl bromide (42.76 g, 0.25 mol) and triphenylphosphine (72.13 g, 0.275 mol) in dry cyclohexane (250 cm³) was heated at reflux for 2 h under nitrogen. The reaction was allowed to cool to room temperature and the white precipitate formed was filtered off and washed with ether (3 x 50 cm³). The product benzyltriphenylphosphonium bromide was used without further purification (86.67 g, 80%), mp 289-291 °C, lit.¹¹³, 295-296 °C from ether.

(viii) Methyltriphenylphosphonium bromide

Available commercially from Aldrich.

(ix) Ethyltriphenylphosphonium bromide

Available commercially from Aldrich.

(x) Isopropyltriphenylphosphonium iodide

Available commercially from Avocado.

(xi) Methyl(triphenylphosphoranylidene)acetate

Available commercially from Aldrich.

(xii) 2-Bromostyrene 168

Potassium *tert*-butoxide (5.20 g, 45.8 mmol) in THF (50 cm³) was added dropwise to a solution of methyltriphenylphosphonium bromide (16.44 g, 45.8 mmol) in THF (150 cm³). The reaction was stirred at room temperature for 1.5 h under nitrogen. A solution of 2-bromobenzaldehyde (8.39 g, 45.8 mmol) in THF (10 cm³) was added dropwise and stirred for 1 h. Aqueous ammonium chloride (25% w/v, 100 cm³) was added and the mixture stirred for 5 minutes. DCM (100 cm³) was added, the organic layer was separated and the aqueous layer extracted with DCM (2 x 50 cm³). The combined organic layers were dried, filtered and the solvent removed *in vacuo*. The product was passed through a small pad of alumina (hexane) to yield 2-bromostyrene as a clear oil (6.29 g, 75%), bp 40 °C/0.1 mmHg, lit.¹¹⁴, 60-61 °C/3.0 Torr, (Found: 181.9744. C₈H₇⁷⁹Br requires M⁺, 181.9731); δ_H(200 MHz, CDCl₃) 5.35 (1 H, dd, J 1.0 Hz, J 11.0 Hz, CH₂), 5.67 (1 H, dd, J 1.0 Hz, J 17.5 Hz, CH₂), 7.02-7.33 (3 H, m, CH), 7.54-7.60 (2 H, m, CH); δ_C(50 MHz, CDCl₃) 116.6 (CH₂), 123.5 (quat.), 126.6 (CH), 127.3 (CH), 128.9 (CH), 132.7 (CH), 135.6 (CH), 137.3 (quat.); *m/z* (EI) 184 (M⁺, 56%), 182 (60), 103 (68), 102 (13), 77 (34), 69 (100); ν_{max}(Film)/cm⁻¹ 1636 (C=C).

(xiii) 2-Bromostilbene 163

Sodium metal (1.91 g) was dissolved in 'super dry' ethanol (100 cm³) under nitrogen and the sodium ethoxide thus prepared was then added over a period of 1 h to a mixture of benzyltriphenylphosphonium bromide (34.96 g, 80.7 mmol) and 2-bromobenzaldehyde (14.93 g, 80.7 mmol) in 'super dry' ethanol (150 cm³). The reaction was left stirring under nitrogen overnight. Aqueous ammonium chloride (25% w/v, 100 cm³) was added and the mixture was stirred for 5 minutes. DCM (100 cm³) was added, the organic layer was separated and the aqueous layer was extracted with DCM (2 x 50 cm³). The combined organic layers were dried, filtered and the solvent removed *in vacuo*. The product was passed through a small pad of alumina (hexane) to give a mixture of the *Z* and *E* isomers. A mixture of the isomers and iodine (0.15 g) in heptane (100 cm³) were heated at reflux overnight. The reaction was cooled to room temperature and washed with sodium thiosulphate solution (10% w/v, 50 cm³). DCM (100 cm³) was added and the organic layer was extracted, dried, filtered and the solvent removed *in vacuo*. Distillation of the product gave 2-bromostilbene as a clear oil (12.79 g, 61%), bp 115 °C/0.15 mmHg, lit.¹¹⁵, 115 °C/0.15 mmHg (Found: 258.0047. C₁₄H₁₁⁷⁹Br requires M⁺, 258.005); δ_H(200 MHz, CDCl₃) 7.00-8.00 (11 H, m, CH); δ_C(50 MHz, CDCl₃) 124.0 (quat.), 126.6 (CH), 126.7 (2 x CH), 127.3 (CH), 127.4 (CH), 127.9 (CH), 128.6 (2 x CH), 128.7 (CH), 131.3 (CH), 132.9 (CH), 136.9 (quat.), 137.0 (quat.); *m/z* (EI) 260 (M⁺, 68%), 259 (10), 179 (100), 178 (83); ν_{max}(Film)/cm⁻¹ 2900 (CH).

(xiv) Methyl-3-(2-bromophenyl)prop-2-enoate 164

Methyl diethylphosphonoacetate (12.02 g, 57.7 mmol) and 2-bromobenzaldehyde (10.59 g, 57.2 mmol) were dissolved in DMF (100 cm³). Sodium methoxide (3.40 g, 62.9 mmol) was added and the mixture stirred for 1.5 h. Water (100 cm³) was added and the mixture was extracted with DCM (2 x 100 cm³). The organic layer was dried, filtered

and the solvent removed *in vacuo*. The product was passed through a small pad of alumina (hexane) to give a yellow oil. Distillation of the product gave methyl-3-(2-bromophenyl)prop-2-enoate as a colourless oil (13.11 g, 95%), bp 120 °C/0.05 mmHg, lit.¹¹⁶, 170-171 °C/1.6 x 10¹ Torr, (Found: 239.9777. C₁₀H₉⁷⁹BrO requires M⁺, 239.978); δ_H(200 MHz, CDCl₃) 3.77 (3 H, s, CH₃), 6.31 (1 H, d, J 15.9 Hz, CH), 7.13-7.56 (4 H, m, Ar-H), 7.97 (1 H, d, J 15.9 Hz, CH); δ_C(50 MHz, CDCl₃) 51.7 (CH₃), 120.4 (CH), 125.1 (quat.), 127.5 (2 x CH), 131.1 (CH), 134.2 (CH), 134.3 (quat.), 143.0 (CH), 166.6 (quat.); *m/z* (EI) 242 (M⁺, 5%), 240 (5), 211 (8), 161 (100), 102 (34), 75 (14); ν_{max}(Film)/cm⁻¹ 1634 (C=C), 1720 (C=O).

(xv) 2-Ethenyl-6-methylbromobenzene 173

Potassium *tert*-butoxide (1.63 g, 14.3 mmol) in THF (50 cm³) was added dropwise to a solution of methyltriphenylphosphonium bromide (5.12 g, 14.3 mmol) in THF (100 cm³). The reaction was stirred at room temperature for 1 h under dry nitrogen. A solution of 2-formyl-6-methylbromobenzene (2.86 g, 14.3 mmol) in THF (10 cm³) was added dropwise and stirred for 1 h. Aqueous ammonium chloride (25% w/v, 50 cm³) was added and the mixture stirred for 5 minutes. DCM (100 cm³) was added, the organic layer separated and the aqueous layer extracted with DCM (2 x 25 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography of the product eluting with hexane afforded 2-ethenyl-6-methylbromobenzene as a clear oil (2.14 g, 76%), bp 100 °C/2.0 mmHg, (Found: 195.9893. C₉H₉⁷⁹Br requires M⁺, 195.9888); δ_H(200 MHz, CDCl₃) 2.43 (3 H, s, CH₃), 5.31 (1 H, dd, J 1.0 Hz, J 11.0 Hz, CH), 5.60 (1 H, dd, J 1.0 Hz, J 17.0 Hz, CH), 7.06-7.39 (4 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 23.8 (CH₃), 116.4 (CH₂), 124.3 (CH), 126.1 (quat.), 126.7 (CH), 129.8 (CH), 136.7 (CH), 138.1 (quat.), 138.5 (quat.); *m/z* (EI) 198 (M⁺, 77%), 196 (76), 117 (82), 115 (78), 40 (100); ν_{max}(Film)/cm⁻¹ 3035 (CH), 1624 (C=C).

II. Preparation of Bromoacraldehydes

(i) Z-3-Bromo-2-phenyl-2-butenal 215a and E-3-Bromo-2-phenyl-2-butenal 215b

These two isomers were prepared by a modification of the method of Arnold *et al.*⁹⁵ Phosphorus tribromide (50.7 g, 0.186 mol) was added over 30 min with stirring and ice cooling to a solution of DMF (16.4 g, 0.22 mol) in dry chloroform (50 cm³). After 30 min a white precipitate formed and phenylacetone (10.0 g, 75 mmol) in dry chloroform (30 cm³) was added dropwise and stirred for 24 h at room temperature. The solvent was removed *in vacuo*, cooled in ice and ice (1500 g) added. To the mixture was added, with cooling, solid sodium bicarbonate solution until neutral. The mixture was extracted with ether (3 x 500 cm³), washed with saturated sodium bicarbonate solution (2 x 200 cm³), water (200 cm³) and dried. The solvent was then removed *in vacuo* to give a yellow oil. Medium pressure liquid chromatography on silica, eluting with hexane-ether, (4:1) gave a) *Z*-3-bromo-2-phenyl-2-butenal as a yellow oil (4.29 g, 25%), bp 80 °C/0.4 mmHg, lit⁹⁵, 83 °C/0.4 mmHg, (Found: 224.9931. C₁₀H₁₀⁷⁹BrO requires (M+1)⁺, 224.9915); δ_H(200 MHz, CDCl₃) 2.49 (3 H, s, CH₃), 7.04-7.45 (5 H, m, Ar-H), 10.26 (1 H, s, CHO); δ_C(50 MHz, CDCl₃) 29.0 (CH₃), 128.1 (CH), 128.3 (2 x CH), 129.2 (2 x CH), 133.5 (quat.), 139.4 (quat.), 143.8 (quat.), 192.9 (CHO); *m/z* (FAB) 227 (M+1, 37%), 225 (M+1, 39%), 209 (10), 193 (12), 175 (12), 161 (52), 147 (22), 129 (100), 115 (77), 103 (17), 91 (46), 77 (32); ν_{max}(Film)/cm⁻¹ 1603 (C=C), 1682 (C=O).

b) *E*-3-bromo-2-phenyl-2-butenal as a yellow oil (1.71 g, 10%), (Found 224.9931. C₁₀H₁₀⁷⁹BrO requires (M+1)⁺, 224.9915); δ_H(200 MHz, CDCl₃) 2.98 (3 H, s, CH₃), 7.12-7.46 (5 H, m, Ar-H), 10.09 (1 H, s, CHO); δ_C(50 MHz, CDCl₃) 25.7 (CH₃), 128.1 (CH), 128.6 (2 x CH), 129.2 (2 x CH), 136.5 (quat.), 142.2 (quat.), 147.3 (quat.), 186.3 (CHO); *m/z* (FAB) 227

(M+1, 50%), 225 (M+1, 15), 207 (16), 193 (17), 175 (16), 161 (59), 149 (19), 135 (22), 128 (75), 115 (78), 91 (68), 73 (100); $\nu_{\max}(\text{Film})/\text{cm}^{-1}$ 1616 (C=C), 1676 (C=O).

(ii) 1-Bromo-2-formylcyclopentene 227

Phosphorus tribromide (70.0 g, 0.228 mol) was added over 30 min with stirring and ice cooling to a solution of DMF (20.14 g, 0.276 mol) in dry chloroform (80 cm³). After 30 min a white precipitate formed and cyclopentanone (7.75 g, 92.1 mmol) in dry chloroform (50 cm³) was added dropwise and stirred for 24 h at room temperature. The solvent was removed *in vacuo*, cooled in ice and ice (2000 g) added. Solid sodium bicarbonate was added to the mixture until neutral. The mixture was extracted with ether (3 x 500 cm³), washed with saturated sodium bicarbonate solution (2 x 200 cm³), water (200 cm³) and dried. The solvent was removed *in vacuo* to give a yellow liquid. Dry-flash column chromatography on silica, eluting with hexane-ether (2:1) gave 1-bromo-2-formylcyclopentene as an oil (10.64 g, 66%), bp 55 °C/2.0 mmHg, lit.⁹⁵, 45-47 °C/1.5 mmHg, (Found: 174.9752. C₆H₈⁷⁹BrO requires (M+1)⁺, 174.9759); δ_{H} (200 MHz, CDCl₃) 1.94 (2 H, m, CH₂), 2.44 (2 H, m, CH₂), 2.82 (2 H, m, CH₂), 9.86 (1 H, s, CHO); δ_{C} (50 MHz, CDCl₃) 21.2 (CH₂), 29.1 (CH₂), 42.4 (CH₂), 139.8 (quat.), 141.3 (quat.), 189.0 (quat.); *m/z* (FAB) 177 (M+1, 42%), 175 (58), 173 (21), 159 (33), 143 (15), 125 (16), 111 (41), 91 (39), 79 (95), 73 (100); $\nu_{\max}(\text{Film})/\text{cm}^{-1}$ 1674 (C=O).

III. Preparation of Boronic acids

(i) 2-(*E*-2-Phenylethenyl)phenylboronic acid 160

n-Butyllithium (7.69 cm³ of a 2.21 M solution in hexanes) was added dropwise with stirring to a solution of 2-bromostilbene (3.99 g, 15.4 mmol) in THF (50 cm³) at -78 °C under dry nitrogen. The mixture was stirred at -78 °C for 1 h then triisopropylborate (3.76 g, 20 mmol) was

added dropwise. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 10 minutes then allowed to warm to room temperature. The mixture was neutralised with 2 M hydrochloric acid and extracted with ether (50 cm^3). The ether layer was washed with water (25 cm^3), dried, filtered and the solvent removed *in vacuo*. The product was crystallised from chloroform to give 2-(*E*-2-phenylethenyl)phenylboronic acid as a white solid (2.11 g, 61%), mp $208\text{--}210\text{ }^{\circ}\text{C}$; δ_{H} (200 MHz, d_6 DMSO) 7.10 (1 H, d, J 16.4 Hz, CH), 7.61 (1 H, d, J 16.4 Hz, CH), 7.21-7.77 (9 H, m, Ar-H), 8.00 (2 H, br, OH); δ_{C} (50 MHz, d_6 DMSO) 124.5 (CH), 126.4 (2 x CH), 126.7 (CH), 127.6 (CH), 128.4 (CH), 128.9 (2 x CH), 129.1 (CH), 130.1 (CH), 133.7 (CH), 137.6 (2 x quat.), 140.3 (quat.); ν_{max} (Nujol)/ cm^{-1} 3398 (OH), 1343 (BO).

(ii) 2-Ethenylphenylboronic acid 181

n-Butyllithium (14.5 cm^3 , of a 2.15 M solution in hexanes) was added dropwise with stirring to a solution of 2-bromostyrene (5.2 g, 28.4 mmol) in THF (150 cm^3) at $-78\text{ }^{\circ}\text{C}$ under dry nitrogen. The mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 h then triisopropylborate (8.53 cm^3 , 36.9 mmol) was added dropwise. The mixture was stirred for 10 minutes then allowed to warm to room temperature. The mixture was neutralised with 2 M hydrochloric acid and extracted with ether (50 cm^3). The ether layer was washed with water (25 cm^3), dried, filtered and the solvent removed *in vacuo*. The product was crystallised from water to give 2-ethenylphenylboronic acid as a white solid (2.19 g, 52%), mp $102\text{--}104\text{ }^{\circ}\text{C}$ from water, lit.¹¹⁷, $108\text{--}109\text{ }^{\circ}\text{C}$; δ_{H} (200 MHz, d_6 DMSO) 5.18 (1 H, dd, J 11.0 Hz, CH_2), 5.64 (1 H, dd, J 10.6 Hz, CH_2), 6.74-8.03 (7 H, m, CH, OH); δ_{C} (50 MHz, d_6 DMSO) 114.2 (CH_2), 124.2-132.2 (CH), 140.5 (quat.); ν_{max} (Nujol)/ cm^{-1} 3367 (OH), 1346 (BO).

(iii) Phenylboronic acid

Available commercially from Aldrich.

(iv) 2-*N*-Benzoylaminomethylphenylboronic acid 165

This was made using the methodology developed by Reece.⁸⁹ Methyllithium (38.4 cm³ of a 1.5 M solution in ether) was added dropwise with stirring to a solution of *N*-benzoyl-2-bromobenzylamine (9.57 g, 32.6 mmol) in THF (30 cm³) at -78 °C under dry nitrogen. The mixture was stirred at -78 °C for 1 h then *tert*-butyllithium (71.1 cm³ of a 1.49 M solution in pentane) was added dropwise. The mixture was stirred at -78 °C for 1 h then triisopropylborate (36.1 g, 44.3 cm³, 0.192 mol) was added dropwise. After 10 minutes the reaction was allowed to warm to room temperature. The mixture was neutralised with 2 M hydrochloric acid and extracted with ether (50 cm³). The ether layer was washed with water (25 cm³), dried, filtered and the solvent removed *in vacuo*. The product was crystallised from DMSO/water to give 2-*N*-benzoylaminomethylphenylboronic acid as a pale green crystalline solid (7.90 g, 95%), mp 166-168 °C, lit.,⁸⁹ 166-168 °C; δ_{H} (200 MHz, d₆DMSO) 4.59 (2 H, d, J 5.9 Hz, CH₂), 7.19-7.92 (9 H, m, Ar-H), 8.52 (2 H, br, OH), 9.19 (1 H, d, J 5.8 Hz, NH); δ_{C} (50 MHz, d₆DMSO) 43.2 (CH₂), 126.0 (CH), 127.4 (2 x CH), 128.5 (2 x CH), 129.3 (CH), 131.6 (CH), 133.7 (CH), 134.2 (quat.), 143.1 (quat.), 166.9 (quat.); ν_{max} (Nujol)/cm⁻¹ 3375 (OH), 3266 (NH), 1602 (C=O).

IV. Preparation of substituted Bromoalkadienes**(i) *E,E*-4-Bromo-1,3-diphenylpenta-1,3-diene 216**

n-Butyllithium (1.07 cm³, 2.5 M solution in hexanes) was added dropwise to a stirred solution of benzyltriphenylphosphonium bromide (1.15 g, 2.68 mmol) in dry ether (30 cm³) at 0 °C and then stirred for 1 h at room temperature to generate the ylid. *Z*-3-bromo-2-phenylbut-2-enal (0.6 g, 2.68 mmol) in dry ether (10 cm³) was added dropwise and stirred

for 1 h. The reaction was hydrolysed by the addition of ammonium chloride solution (10% w/v, 20 cm³). The aqueous layer was separated, extracted with ether (2 x 50 cm³) and the combined organic phase washed with water (50 cm³) and dried. The solvent was removed *in vacuo* to give a yellow oil. Dry-flash column chromatography on silica, eluting with hexane gave *E,E*-4-bromo-1,3-diphenylpenta-1,3-diene as a clear oil which solidified on standing (0.68 g, 85%), mp 53-55 °C from pentane, lit.³⁴ 51-54 °C, (Found: 298.0382. C₁₇H₁₅⁷⁹Br requires (M+1)⁺, 298.0357); δ_{H} (200 MHz, CDCl₃) 2.27 (3 H, s, CH₃), 5.99 (1 H, d, J 15.9 Hz, CH), 7.06-7.50 (10 H, m, Ar-H), 7.58 (1 H, d, J 16.0 Hz, CH); δ_{C} (50 MHz, CDCl₃) 27.2 (CH₃), 123.3 (quat.), 126.6 (2 x CH), 127.4 (CH), 127.5 (CH), 127.6 (CH), 128.4 (3 x CH), 129.4 (2 x CH), 130.5 (CH), 134.2 (CH), 137.1 (quat.), 138.0 (quat.), 138.8 (quat.); *m/z* (FAB) 301 (M+1, 25%), 300 (M+1, 49), 299 (19), 298 (46), 279 (84), 251 (47), 234 (34), 227 (24), 219 (100), 215 (68), 204 (88), 191 (45), 165 (55), 141 (71), 131 (19); ν_{max} (Nujol)/cm⁻¹ 1573 (diene).

(ii) *E,Z*-4-Bromo-1,3-diphenylpenta-1,3-diene 217a and *Z,Z*-4-Bromo-1,3-diphenylpenta-1,3-diene 217b

n-Butyllithium (4.52 cm³, 2.5 M solution in hexanes) was added dropwise to a stirred solution of benzyltriphenylphosphonium bromide (5.66 g, 11.3 mmol) in THF (100 cm³) at 0 °C and stirred for 1 h at room temperature to generate the ylid. *E*-3-bromo-2-phenylbut-2-enal (2.54 g, 11.3 mmol) in THF (10 cm³) was added dropwise and stirred at room temperature for 1 h. The reaction was hydrolysed by the addition of ammonium chloride solution (10% w/v, 50 cm³). The aqueous layer was separated, extracted with ether (2 x 50 cm³) and the combined organic phase washed with water (50 cm³) and dried. The solvent was removed *in vacuo* to give a yellow oil. Dry-flash column chromatography followed by MPLC on silica, eluting with hexane gave a) *E,Z*-4-bromo-1,3-diphenylpenta-1,3-diene as a clear oil (0.75 g, 22%), (Found: 298.0364.

$C_{17}H_{15}^{79}Br$ requires $(M+1)^+$, 298.0357); δ_H (200 MHz, $CDCl_3$) 2.72 (3 H, s, CH_3), 5.98 (1 H, d, J 15.7 Hz, CH), 7.14-7.49 (11 H, m, CH); δ_C (50 MHz, $CDCl_3$) 25.2 (CH_3), 123.9 (quat.), 125.6 (CH), 126.4 (2 x CH), 127.2 (CH), 127.6 (CH), 128.1 (2 x CH), 128.5 (2 x CH), 129.4 (2 x CH), 133.1 (CH), 137.1 (quat.), 140.1 (quat.), 140.8 (quat.); m/z (FAB) 300 ($M+1$, 15%), 298 (18), 204 (53), 202 (69), 176 (14), 115 (100); ν_{max} (Film)/ cm^{-1} 1598 (diene).

b) *Z,Z*-4-bromo-1,3-diphenylpenta-1,3-diene as a clear oil (1.50 g, 44%) (Found: 300.0334. $C_{17}H_{15}^{81}Br$ requires $(M+1)^+$, 300.0338); δ_H (200 MHz, $CDCl_3$) 2.24 (3 H, s, CH_3), 6.09 (1 H, d, J 12.0 Hz, CH), 6.60 (1 H, d, J 12.0 Hz, CH), 7.20-7.50 (10 H, m, CH); δ_C (50 MHz, $CDCl_3$) 27.0 (CH_3), 121.1 (quat.), 127.4 (CH), 127.5 (CH), 127.9 (2 x CH), 128.0 (2 x CH), 128.3 (CH), 128.4 (2 x CH), 128.9 (2 x CH), 131.3 (CH), 136.6 (quat.), 136.7 (quat.), 140.6 (quat.); m/z (FAB) 300 ($M+1$, 14%), 298 (16), 239 (11), 205 (28), 189 (22), 178 (21), 152 (23), 141 (57), 128 (25), 102 (16); ν_{max} (Film)/ cm^{-1} 1598 (diene).

(iii) Methyl *E,E*-5-bromo-4-phenylhexa-2,4-dienoate 221

Methyl(triphenylphosphoranoylidene)acetate (3.72 g, 11.1 mmol) and *Z*-3-bromo-2-phenylbut-2-enal (2.5 g, 11.1 mmol) in dry toluene (100 cm^3) were heated at reflux for 3 h under nitrogen. The reaction was cooled to room temperature and the solvent removed *in vacuo*. Wet-flash column chromatography on silica, eluting with hexane gave methyl *E,E*-5-bromo-4-phenylhexa-2,4-dienoate as a yellow solid (2.87 g, 92%), mp 56-57 °C from hexane (Found: C, 55.8; H, 5.0%; $(M+1)^+$, 281.0186. $C_{13}H_{13}BrO_2$ requires C, 55.5; H, 4.7%; $(M+1)^+$, 281.0177); δ_H (250 MHz, $CDCl_3$) 2.25 (3 H, s, CH_3), 3.70 (3 H, s, CH_3), 5.31 (1 H, d, J 15.6 Hz, CH), 7.04-7.41 (5 H, m, Ar-H), 8.02 (1 H, d, J 15.6 Hz, CH); δ_C (63 MHz, $CDCl_3$) 27.8 (CH_3), 51.5 (CH_3), 123.0 (CH, olefinic), 127.8 (CH), 128.7 (2 x CH), 129.0 (2 x CH), 130.9 (quat.), 136.6 (quat.), 137.6 (quat.), 145.2 (CH, olefinic), 167.2 (quat.); m/z (FAB) 283 ($M+1$, 99%), 282 (38), 281 (100),

249 (42), 221 (19), 201 (61), 169 (35), 149 (29), 128 (48), 115 (75); $\nu_{\max}(\text{Nujol})/\text{cm}^{-1}$ 1724 (C=O).

(iv) *E*-2-Bromo-5-methyl-3-phenylhexa-2,4-diene 223

Potassium *tert*-butoxide (1.25 g, 11.1 mmol) in THF (10 cm³) was added dropwise to a stirred solution of isopropyltriphenylphosphonium bromide (4.80 g, 11.1 mmol) in THF (100 cm³) at 0 °C and stirred for 1 h at room temperature to generate the ylid. *Z*-3-bromo-2-phenylbut-2-enal (2.50 g, 11.1 mmol) in THF (10 cm³) was added dropwise and stirred at room temperature for 1 h. The reaction was hydrolysed by the addition of ammonium chloride solution (10% w/v, 50 cm³). The aqueous layer was separated, extracted with ether (2 x 50 cm³) and the combined organic phase washed with water (50 cm³) and dried. The solvent was removed *in vacuo* to give a green oil. Wet-flash column chromatography on silica, eluting with hexane gave *E*-2-bromo-5-methyl-3-phenylhexa-2,4-diene as an oil, which was used without further purification (1.51 g, 54%), (Found: 251.0433. C₁₃H₁₅⁷⁹Br requires (M+1)⁺, 251.0435); δ_{H} (200 MHz, CDCl₃) 1.27 (3 H, s, CH₃), 1.78 (3 H, s, CH₃), 2.30 (3 H, s, CH₃), 6.07 (1 H, br, CH), 7.13-7.35 (5 H, m, Ar-H); δ_{C} (50 MHz, CDCl₃) 19.6 (CH₃), 26.4 (CH₃), 26.5 (CH₃), 121.7 (CH), 126.8 (CH), 128.1 (2 x CH), 129.0 (2 x CH), 137.2 (quat.), 138.1 (quat.), 140.2 (quat.), 145.8 (quat.); *m/z* (FAB) 252 (M+1, 12%), 251 (23), 227 (10), 203 (30), 195 (72), 187 (100), 170 (61), 155 (28), 141 (45), 128 (51), 115 (92), 77 (23); $\nu_{\max}(\text{Film})/\text{cm}^{-1}$ 1625, 1683 (diene).

(v) *E,E*-2-Bromo-3-phenylhexa-2,4-diene 224

n-Butyllithium (4.44 cm³, 2.5 M solution in hexanes) was added dropwise to a stirred solution of ethyltriphenylphosphonium bromide (4.12 g, 11.1 mmol) in THF (100 cm³) at 0 °C and stirred for 1 h at room temperature to generate the ylid. *Z*-3-bromo-2-phenylbut-2-enal (2.50 g, 11.1 mmol) in THF (10 cm³) was added dropwise and stirred at room temperature for 1 h. The reaction was hydrolysed by the addition of

ammonium chloride solution (10% w/v, 50 cm³). The aqueous layer was separated, extracted with ether (2 x 50 cm³) and the combined organic phase washed with water (50 cm³) and dried. The solvent was removed *in vacuo* to give a pale green oil. Wet-flash column chromatography on silica, eluting with hexane gave *E,E* and *E,Z*-2-bromo-3-phenylhexa-2,4-diene in a ratio (4:1) and was used without further purification (1.37 g, 52%), (Found: 237.0297. C₁₂H₁₃⁷⁹Br requires (M+1)⁺, 237.0279); δ_{H} (200 MHz, CDCl₃) 1.29 (3 H, m, CH₃)*, 1.73 (3 H, d, J 6.0 Hz, CH₃), 2.12 (3 H, s, CH₃)*, 2.27 (3 H, s, CH₃), 5.16 (1 H, q, J 7.0 Hz, 16.0 Hz, CH)*, 5.58 (1 H, q, J 6.0 Hz, 11.0 Hz, CH), 6.74 (1 H, d, J 16.0 Hz, CH)*, 6.83 (1 H, d, J 11.0 Hz, CH), 6.88-7.98 (10 H, m, Ar-H); δ_{C} (50 MHz, CDCl₃) 17.0 (CH₃), 18.4 (CH₃)*, 25.6 (CH₃)*, 27.6 (CH₃), 127.1 (CH), 127.5 (CH), 128.0 (CH), 128.1 (CH), 128.2 (2 x CH), 128.5 (CH), 128.8 (CH), 129.3 (CH), 131.0 (quat.), 138.6 (quat.), 141.6 (quat.); *m/z* (FAB) 237 (M+1, 24%), 235 (20), 205 (12), 189 (59), 173 (90), 155 (55), 141 (47), 128 (54), 115 (100), 77 (52); ν_{max} (Film)/cm⁻¹ 1597, 1625, 1682 (diene).

* major isomer absorptions.

(vi) 1-Bromo-2-(*E*-2-phenylethenyl)cyclopentene 228

n-Butyllithium (2.15 M, 11.2 cm³ solution in hexanes) was added dropwise to a stirred suspension of benzyltriphenylphosphonium bromide (12.0 g, 24.0 mmol) in dry ether (150 cm³) and stirred at room temperature for 1 h to generate the ylid. 1-Bromo-2-formylcyclopentene (4.2 g, 24.0 mmol) in dry ether (50 cm³) was added dropwise and stirred at room temperature for 1 h. The reaction was hydrolysed by the addition of ammonium chloride (10% w/v, 100 cm³). The aqueous layer was separated, extracted with ether (2 x 100 cm³) and the combined organic phase washed with water (100 cm³) and dried. The solvent was removed *in vacuo* to give a brown oil which was subject to wet-flash column chromatography on silica, eluting with hexane. The isomers were separated by MPLC on silica, eluting with hexane to give 1-bromo-2-(*E*-2-

phenylethenyl)cyclopentene as a brown oil⁹⁵ (2.5 g, 42%), (Found: 248.0192. $C_{13}H_{13}^{79}Br$ requires $(M+1)^+$, 248.0201); δ_H (250 MHz, $CDCl_3$) 1.96-2.11 (2 H, m, CH_2), 2.24-2.40 (2 H, m, CH_2), 2.56-2.84 (2 H, m, CH_2), 6.50 (1 H, d, J 16.1 Hz, CH), 7.06 (1 H, d, J 16.0 Hz, CH), 7.21-7.89 (5 H, m, Ar-H); δ_C (63 MHz, $CDCl_3$) 21.4 (CH_2), 31.1 (CH_2), 40.7 (CH_2), 121.5 (quat.), 122.9 (olefinic CH), 126.5 (2 x CH), 127.6 (2 x CH), 128.5 (CH), 131.4 (olefinic CH), 137.1 (quat.), 137.8 (quat.); m/z (FAB) 250 ($M+1$, 10%), 249 (5), 248 (9), 201 (18), 169 (19), 141 (21), 128 (15), 91 (49); ν_{max} (Nujol)/ cm^{-1} 1570 (diene).

(vii) Methyl 3-(2-bromocyclopent-1-enyl)propenoate 229

Methyl(triphenylphosphoranoylidene)acetate (7.68 g, 22.9 mmol) and 1-bromo-2-formylcyclopentene (4.0 g, 22.9 mmol) in dry toluene (100 cm^3) were heated at reflux for 3 h under nitrogen. The reaction was cooled to room temperature and the solvent removed *in vacuo*. Wet-flash column chromatography on silica, eluting with hexane-ether (4:1) gave methyl 3-(2-bromocyclopent-1-enyl)propenoate as a yellow crystalline solid (3.49 g, 66%), mp 63-64 °C from ethanol (Found: C, 47.1; H, 5.0%; $(M+1)^+$, 231.0008. $C_9H_{11}BrO_2$ requires C, 46.8; H, 4.8%; $(M+1)^+$, 231.0021); δ_H (250 MHz, $CDCl_3$) 2.01-2.07 (2 H, m, CH_2), 2.41-2.50 (2 H, m, CH_2), 2.75-2.82 (2 H, m, CH_2), 3.75 (3 H, s, CH_3), 5.78 (1 H, d, J 15.8 Hz, CH), 7.51 (1 H, d, J 15.8 Hz, CH); δ_C (50 MHz, $CDCl_3$) 21.3 (CH_2), 30.8 (CH_2), 41.3 (CH_2), 51.5 (CH_3), 120.2 (CH), 130.1 (quat.), 136.7 (quat.), 137.8 (CH), 167.2 (quat.); m/z (FAB) 233 ($M+1$, 44%), 232 (15), 231 (45), 217 (17), 183 (12), 151 (41), 119 (51), 109 (49), 69 (54), 57 (86), 43 (91), 29 (100); ν_{max} (Nujol)/ cm^{-1} 1627 (C=C), 1725 (C=O).

V. Preparation of substituted Alkenyl bromides

(i) 2-Bromopropene 293

Commercially available from Avocado.

(ii) α -Methyl-*trans*-cinnamic acid 296

This was made using Dalcanale and Montanari's method.¹⁰⁴ Sodium chlorite (4.54 g, 50.25 mmol) in water (40 cm³) was added dropwise over a period of 1 h to a stirred mixture of α -methyl-*trans*-cinnamaldehyde (3.00 g, 20.1 mmol), acetonitrile (30 cm³), NaH₂PO₄ (0.66 g) in water (25 cm³) with hydrogen peroxide (27.5%, 2.64 cm³, 21.36 mmol) at 10 °C. The reaction was allowed to warm to room temperature and stirred overnight. Sodium thiosulphate (0.2 g) was added to destroy any unreacted HOCl and H₂O₂. The reaction mixture was acidified with aqueous hydrochloric acid (10% w/v, 100 cm³) and the precipitate was washed with water (2 x 50 cm³) to give α -methyl-*trans*-cinnamic acid as a white solid (2.35 g, 80%), mp 78-80 °C, lit.,¹⁰⁴ 79-81 °C, (Found: 162.0681. C₁₀H₁₀O₂ requires M⁺, 162.0681); δ_{H} (250 MHz, CDCl₃) 2.17 (3 H, d, J 1.5 Hz, CH₃), 7.25-7.48 (5 H, m, Ar-H), 7.86 (1 H, d, J 1.5 Hz, CH), 11.53 (1 H, br, OH); δ_{C} (63 MHz, CDCl₃) 13.6 (CH₃), 127.5 (quat.), 128.3 (2 x CH), 128.6 (2 x CH), 129.7 (CH), 135.5 (quat.), 141.0 (CH), 174.4 (quat.); *m/z* (EI) 162 (M⁺, 23), 161 (M⁺, 48), 115 (100); ν_{max} (Nujol)/cm⁻¹ 1680 (C=O).

(iii) 2-Bromo-1-phenylpropene 297a,b

This was made using the oxidative bromo decarboxylation methodology as described by Dahl *et al.*¹⁰³ α -Methyl-*trans*-cinnamic acid (6.53 g, 40.3 mmol) and iodobenzene diacetate (6.60 g, 20.15 mmol) in acetonitrile (160 cm³) and water (80 cm³) were stirred at 60 °C for 1 h. *N*-bromosuccinimide (7.13 g, 40.3 mmol) was added and the reaction mixture was stirred for a further 1 h at 60 °C. The reaction was allowed to cool to room temperature and the solvent removed *in vacuo*. The aqueous layer was washed with ether (3 x 50 cm³). The organic layer was dried and the solvent was removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane gave 2-bromo-1-phenylpropene as a mixture of *E* and *Z* isomers (2:1) (1.67 g, 21%),

(Found: 195.9884. $C_9H_9^{79}Br$ requires M^+ , 195.9888); δ_H (250 MHz, $CDCl_3$) 2.47 (3 H, d, J 1.4 Hz, CH_3)*, 2.50 (3 H, d, J 1.3 Hz, CH_3), 6.73 (1 H, br s, CH), 6.99 (1 H, br, CH)*, 7.20-7.59 (m, Ar-H), lit.¹¹⁸ for *E* isomer, $\delta_H(CDCl_3)$ 2.48 (3 H, d, J 1.3 Hz, CH_3), 6.99 (1 H, br, CH), 7.37-7.50 (5 H, m, Ar-H); δ_C (50 MHz, $CDCl_3$) 24.8 (CH_3), 30.5 (CH_3), 123.5 (quat.), 127.1 (2 x CH), 127.4 (CH), 127.9 (CH), 128.2 (3 x CH), 128.3 (3 x CH), 128.6 (CH), 136.4 (quat.); m/z (EI) 198 (M^+ , 73%), 196 (M^+ , 74), 117 (100), 115 (93), 91 (41); $\nu_{max}(\text{Film})/cm^{-1}$ 2909 (CH). * major isomer absorptions.

(iv) 1,1-Diphenylpropene 299

This reaction was carried out using the methodology of Olah.¹⁰⁶ Lithium metal was added to *n*-pentane (50 cm³) in a three necked flask flushed with nitrogen. A solution of ethyl bromide (10.9 g, 0.10 mol) in *n*-pentane (12 cm³) was added dropwise at 30 °C. After stirring under nitrogen for 1 h the ethyllithium was added, using a double tipped needle, to a solution of benzophenone (6.37 g, 35.0 mmol) in dry ether (100 cm³) at -78 °C. The reaction was stirred for 30 min at -78 °C then thionyl chloride (8.33 g, 70.0 mmol) was added dropwise with good stirring. The reaction mixture was allowed to warm to room temperature and poured into a separating funnel with ice (200 g). The organic layer was separated and the aqueous layer was extracted with ether (3 x 50 cm³). The combined fractions were dried, filtered and the solvent removed *in vacuo* to give a white solid. Dry-flash column chromatography on silica, eluting with hexane gave 1,1-diphenylpropene (1.63 g, 24%), mp 49-51 °C from hexane, lit.¹¹⁹ mp 51-52 °C, (Found: 194.1093. $C_{15}H_{14}$ requires M^+ , 194.1096); δ_H (250 MHz, $CDCl_3$) 1.82 (3 H, d, J 7.1 Hz, CH_3), 6.20-6.29 (1 H, q, J 7.0 Hz, CH), 7.23-7.47 (10 H, m, Ar-H); δ_C (63 MHz, $CDCl_3$) 15.6 (CH_3), 124.0 (CH), 126.6 (CH), 126.7 (CH), 127.1 (2 x CH), 127.9 (2 x CH), 128.0 (2 x CH), 129.9 (2 x CH), 139.9 (quat.), 142.3 (quat.), 142.8 (quat.);

m/z (EI) 194 (M^+ , 40%), 193 (28), 178 (18), 165 (15), 115 (30), 40 (100); ν_{\max} (Nujol)/ cm^{-1} 2933 (CH).

(v) 1,2-Dibromo-1,1-diphenylpropane 300

Bromine (0.86 g, 5.32 mmol) was added dropwise to a solution of 1,1-diphenylpropene (1.0 g, 5.14 mmol) in carbon tetrachloride (30 cm^3) and stirred for 30 min at room temperature. The solvent and excess bromine were removed *in vacuo* to give 1,2-dibromo-1,1-diphenylpropane as an orange oil which was not purified further. δ_{H} (60 MHz, CDCl_3) 2.95 (3 H, d, J 14.4 Hz, CH_3), 5.40 (1 H, q, J 14.4 Hz, CH), 7.20-7.95 (10 H, m, Ar-H), lit.¹²¹ δ_{H} (CCl_4) 2.82 (CH_3), 5.26 (CH), 7.03-7.86 (Ar-H).

(vi) 2-Bromo-1,1-diphenylpropene 301

Dehydrobromination of the dibromo compound occurred over a period of seven days in a nmr tube.

DBU (1.56 g, 10.28 mmol) was added dropwise to a solution of 1,2-dibromo-1,1-diphenylpropane (1.82 g, 5.14 mmol) in DMSO (20 cm^3) and stirred at room temperature for 30 min. Water (10 cm^3) was added and the reaction mixture was extracted with DCM (2 x 20 cm^3). The organic layer was dried, filtered and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane gave 2-bromo-1,1-diphenylpropene as a brown oil (0.91 g, 65%), (Found: 272.0198. $\text{C}_{15}\text{H}_{13}^{79}\text{Br}$ requires M^+ , 272.0201); δ_{H} (250 MHz, CDCl_3) 2.46 (3 H, s, CH_3), 7.18-7.38 (10 H, m, Ar-H), lit.¹²⁰ δ_{H} (CCl_4) 2.43 (3 H, s, CH_3), 7.21 (10 H, Ar-H); δ_{C} (63 MHz, CDCl_3) 27.3 (CH_3), 121.0 (quat.), 127.0 (CH), 127.1 (CH), 127.9 (2 x CH), 128.2 (2 x CH), 129.0 (2 x CH), 129.1 (2 x CH), 140.6 (quat.), 141.6 (quat.), 143.1 (quat.); m/z (EI) 274 (M^+ , 8%), 272 (8), 194 (30), 178 (12), 115 (20); ν_{\max} (Nujol)/ cm^{-1} 1687 (C=C), 2917 (CH).

(vii) 2-Bromo-3-methylbut-2-ene 303

Commercially available from Avocado.

(viii) E-2-Phenylbut-2-ene 305

Potassium *tert*-butoxide (3.03 g, 26.9 mmol) in THF (10 cm³) was added dropwise to a stirred suspension of ethyltriphenylphosphonium bromide (10.0 g, 26.9 mmol) in THF (100 cm³) and stirred at room temperature for 1 h to generate the ylid. Acetophenone (3.24 g, 26.9 mmol) in THF (25 cm³) was added dropwise and stirred at room temperature for 1 h. The reaction was hydrolysed by the addition of ammonium chloride (10% w/v, 100 cm³). The aqueous layer was separated, extracted with ether (2 x 100 cm³) and the combined organic phase washed with water (100 cm³) and dried. The solvent was removed *in vacuo* to give a yellow oil. Wet-flash column chromatography on silica, eluting with hexane gave *E*-2-phenylbut-2-ene as a clear oil (2.30 g, 65%), bp 175-180 °C, lit.¹²¹ bp for *Z* isomer 194 °C, bp for *E* isomer 174 °C, (Found: 133.1019. C₁₀H₁₂ requires (M+1)⁺, 133.1017); δ_H(200 MHz, CDCl₃) 1.81 (3 H, m, CH₃), 2.03 (3 H, t, CH₃), 5.80-5.91 (1 H, m, CH), 7.16-7.39 (5 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 14.2 (CH₃), 15.3 (CH₃), 122.3 (CH), 125.4 (2 x CH), 126.3 (CH), 128.0 (2 x CH), 135.4 (quat.), 143.9 (quat.); *m/z* (FAB) 135 (M+1, 19%), 134 (22), 133 (100), 132 (27), 117 (31), 115 (20), 105 (49), 91 (23), 78 (14); ν_{max}(Film)/cm⁻¹ 1646 (C=C).

(ix) 2,3-Dibromo-3-phenylbutane 306a,b

Bromine (2.91 g, 18.0 mmol) was added dropwise to a solution of *E*-2-phenylbut-2-ene (2.30 g, 17.4 mmol) in carbon tetrachloride (50 cm³) and stirred for 30 min at room temperature. The solvent and excess bromine were removed *in vacuo* to give 2,3-dibromo-3-phenylbutane as a mixture of diastereomers and as an orange oil which was not purified further (5.04 g, 100%), (Found: 290.9225. C₁₀H₁₂Br₂ requires (M+1)⁺, 290.9208); δ_H(200 MHz, CDCl₃) 1.61 (3 H, d, J 6.6 Hz, CH₃), 2.06 (3 H, d, J 7.0 Hz, CH₃)*, 2.28 (3 H, s, CH₃)*, 2.38 (3 H, s, CH₃), 4.81 (2 H, pair of q, J 7.0 Hz, CH), 7.26-7.66 (m, CH); δ_C(63 MHz, CDCl₃) 22.6 (CH₃), 23.2

(CH₃), 25.0 (CH₃), 29.9 (CH₃), 58.2 (CH), 60.3 (CH), 70.3 (quat.), 71.5 (quat.), 126.4 (2 x CH), 127.9 (2 x CH), 128.0 (2 x CH), 128.1 (2 x CH), 128.2 (CH), 128.6 (CH), 140.4 (quat.), 144.4 (quat.); *m/z* (FAB) 291 (M+1, 10%), 289 (6), 213 (79), 211 (63), 171 (12), 131 (100), 117 (40), 115 (56), 103 (18), 77 (28); ν_{\max} (Film)/cm⁻¹ 2986 (CH). * major isomer absorptions.

(x) E-2-Bromo-3-phenylbut-2-ene 307a and Z-2-Bromo-3-phenylbut-2-ene 307b

DBU (2.58 g, 17.0 mmol) was added dropwise to a solution of 2,3-dibromo-3-phenylbutane (4.96 g, 17.0 mmol) in DMSO (10 cm³) and stirred at room temperature for 30 min. Water (30 cm³) was added and the reaction mixture was extracted with DCM (2 x 40 cm³). The organic layer was dried, filtered and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane gave a) *E*-2-bromo-3-phenylbut-2-ene as a clear oil (0.36 g, 10%), (Found: 210.0048. C₁₀H₁₁⁷⁹Br requires M⁺, 210.0044); δ_{H} (250 MHz, CDCl₃) 2.06 (3 H, q, J 2.1 Hz, CH₃), 2.46 (3 H, q, J 2.2 Hz, CH₃), 7.18-7.47 (5 H, m, Ar-H), lit.¹²² δ_{H} (CDCl₃) 1.95 (3 H, q, J 1.5 Hz, CH₃), 2.85 (3 H, q, J 1.5 Hz, CH₃), 7.2 (5 H, Ar-H); δ_{C} (63 MHz, CDCl₃) 21.5 (CH₃), 25.5 (CH₃), 116.7 (quat.), 126.7 (CH), 127.7 (2 x CH), 128.0 (2 x CH), 135.4 (quat.), 144.6 (quat.); *m/z* (EI) 212 (M⁺, 29%), 210 (30), 131 (76), 115 (57), 91 (100), 77 (22); ν_{\max} (Nujol)/cm⁻¹ 1650 (C=C). b) *Z*-2-bromo-3-phenylbut-2-ene as a clear oil (1.02 g, 28%), (Found: 210.0048. C₁₀H₁₂⁷⁹Br requires M⁺, 210.0044); δ_{H} (250 MHz, CDCl₃) 2.20 (3 H, t, J 1.4 Hz, CH₃), 2.21 (3 H, t, J 1.2 Hz, CH₃), 7.14-7.40 (5 H, m, Ar-H) lit.¹²³ δ_{H} (CDCl₃) 2.14 (6 H, s, CH₃), 7.45-7.9 (5 H, m, Ar-H); δ_{C} (63 MHz, CDCl₃) 25.8 (CH₃), 26.4 (CH₃), 119.7 (quat.), 136.8 (CH), 127.7 (2 x CH), 128.2 (2 x CH), 135.9 (quat.), 141.6 (quat.); *m/z* (EI) 212 (M⁺, 29%), 210 (M⁺, 30), 131 (76), 129 (29), 116 (36), 115 (57), 103 (11), 91 (100), 77 (22); ν_{\max} (Film)/cm⁻¹ 1650 (C=C).

(xi) 2,3-Dibromo-2-methylpentane 310

Bromine (7.55 g, 46.70 mmol) was added dropwise to a solution of 2-methylpent-2-ene (3.80 g, 45.15 mmol) in carbon tetrachloride (100 cm³) and stirred for 30 min at room temperature. The solvent and excess bromine were removed *in vacuo* to give 2,3-dibromo-2-methylpentane as an orange oil. Dry-flash column chromatography on silica, eluting with hexane gave 2,3-dibromo-2-methylpentane (5.51 g, 50%), (Found: 242.9203. C₆H₁₂Br₂ requires 242.9208); δ_{H} (200 MHz, CDCl₃) 1.13 (3 H, t, J 7.0 Hz, CH₃), 1.80 (3 H, s, CH₃), 1.98 (3 H, s, CH₃), 2.45 (2 H, m, CH₂), 4.10 (1 H, dd, J 2.0 Hz, 11.0 Hz, CHBr), lit.¹²³ δ_{H} (300 MHz, CDCl₃) 1.14 (3 H, t, J 7.3 Hz, CH₃), 1.80 (1 H, ddq, J 7.3, 11.0, 14.5 Hz, CH₂), 1.81 (3 H, s, CH₃), 1.99 (3 H, s, CH₃), 2.48 (1 H, ddq, J 1.7, 7.3, 14.5 Hz CH₂), 4.13 (1 H, dd, J 1.7, 11.0 Hz, CHBr); δ_{C} (63 MHz, CDCl₃) 13.1 (CH₃), 28.0 (CH₃), 29.1 (CH₂), 35.3 (CH₃), 68.8 (quat.), 69.2 (CH); *m/z* (EI) 243 (M⁺, 11%), 163 (24), 121 (23), 119 (21), 84 (100), 67 (12), 55 (34).

(xii) 3-Bromo-2-methylpent-2-ene 311

DBU (1.64 g, 10.80 mmol) was added dropwise to 2,3-dibromo-2-methylpentane (1.75 g, 7.17 mmol) and stirred at room temperature for 30 min. Distillation at 25 °C/0.05 mmHg gave a mixture of starting material and product (1:2). DBU (0.54 g, 3.60 mmol) was added dropwise to the mixture and stirred at room temperature for 30 min. Distillation of the reaction mixture gave 3-bromo-2-methylpent-2-ene as a clear oil with 12% starting material which was not purified further (1.02 g, 88%), bp 25 °C/0.05 mmHg, lit.¹²⁴ bp 136-140 °C, (Found: 162.0047. C₆H₁₁⁷⁹Br requires 162.0044); δ_{H} (200 MHz, CDCl₃) 1.08 (3 H, t, CH₃), 1.75 (3 H, s, CH₃), 1.85 (3 H, s, CH₃), 2.48 (2 H, q, CH₂); δ_{C} (63 MHz, CDCl₃) 13.0 (CH₃), 19.9 (CH₃), 25.1 (CH₃), 31.0 (CH₂), 123.4 (quat.), 129.0 (quat.); *m/z* (EI) 165 (M⁺, 26%), 164 (54), 163 (30), 162 (59), 149 (16), 121 (14), 83 (100), 67 (64).

VI. Preparation of N-[2-Arylbenzyl]benzamides

(i) N-2-Phenylbenzylbenzamide 239

This was made *via* Suzuki's⁸² palladium catalysed cross-coupling reaction using the Gronowitz⁸³ modifications. *N*-Benzoyl-2-bromobenzylamine (3.0 g, 10.34 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.54 g, 0.46 mmol, 4.4% mol catalyst) were stirred in 1,2-dimethoxyethane (40 cm³) under dry nitrogen for 20 minutes. Phenylboronic acid (1.39 g, 11.37 mmol) and sodium carbonate (2.96 g, 10.34 mmol) in water (14.3 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and dichloromethane (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-2-phenylbenzylbenzamide as a white solid (2.05 g, 69%), mp 95-97 °C, lit.⁶⁷ mp 95-96 °C from ethanol (Found: 288.1377. C₂₀H₁₇NO requires (M+1)⁺, 288.1388); δ_H(200 MHz, CDCl₃) 4.62 (2 H, d, J 5.6 Hz, CH₂), 6.23 (1 H, br, NH), 7.25-7.50 (14 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 41.9 (CH₂), 126.7 (2 x CH), 127.2 (CH), 127.4 (CH), 127.7 (CH), 128.3 (4 x CH), 128.6 (CH), 128.8 (2 x CH), 130.1 (CH), 131.2 (CH), 134.2 (quat.), 135.3 (quat.), 140.6 (quat.), 141.5 (quat.), 166.9 (quat.); *m/z* (FAB) 289 (M+1, 53%), 288 (M+1, 73), 239 (10), 202 (14), 179 (84), 166 (90), 152 (45), 134 (35), 122 (62), 115 (48), 91 (30), 77 (100); ν_{max}(Nujol)/cm⁻¹ 1625 (C=O), 3320 (NH).

(ii) N-[2-(2-(*E*-2-Phenylethenyl)phenyl)benzyl]benzamide 161

N-Benzoyl-2-bromobenzylamine (3.58 g, 12.2 mmol) and Pd(0) (0.63 g, 0.56 mmol, 4.6% mol catalyst) were stirred in DME (45 cm³) under dry nitrogen for 20 minutes. *E*-2-(2-Phenylethenyl)phenylboronic

acid (3.00 g, 13.4 mmol) and sodium carbonate (3.52 g, 12.2 mmol) in water (20.0 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(2-(*E*-2-phenylethenyl)phenyl)benzyl]benzamide as a brown solid (2.99 g, 63%), mp 139-141 °C from ethanol (Found: C, 86.1; H, 5.6; N, 3.5%; M⁺, 389.1756. C₂₈H₂₃NO requires C, 86.3; H, 5.9; N, 3.6%; M⁺, 389.1778); δ_H(200 MHz, CDCl₃) 4.11-4.35 (1 H, dd, J 5.2 Hz, 19.7 Hz, CH₂), 4.46-4.73 (1 H, dd, J 6.4 Hz, 14.6 Hz, CH₂), 6.13 (1 H, br, NH), 6.95-7.84 (20 H, m, CH); δ_C(50 MHz, CDCl₃) 41.8 (CH₂), 125.1 (CH), 126.2 (CH), 126.4 (2 x CH), 126.6 (2 x CH), 127.4 (CH), 127.5 (CH), 127.7 (CH), 128.0 (CH), 128.2 (3 x CH), 128.6 (2 x CH), 129.1 (CH), 130.0 (2 x CH), 130.1 (CH), 131.1 (CH), 133.0 (quat.), 135.4 (quat.), 136.5 (quat.), 136.7 (quat.), 139.6 (quat.), 140.1 (quat.), 166.7 (quat.); *m/z* (EI) 389 (M⁺, 5%), 268 (20), 105 (58), 77 (28); ν_{max}(Nujol)/cm⁻¹ 1636 (C=O), 3404 (NH).

(iii) *N*-[2-(2-Ethenylphenyl)benzyl]benzamide 169

2-Bromostyrene (2.64 g, 14.4 mmol) and Pd(0) (0.75 g, 0.65 mmol, 4.5% mol catalyst) were stirred in DME (50 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (4.05 g, 15.84 mmol) and sodium carbonate (4.14 g, 14.4 mmol) in water (35 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(2-ethenylphenyl)benzyl]benzamide as a brown solid (3.51 g, 78%), mp 109-

111 °C from ethanol (Found: (M+1)⁺, 314.1545. C₂₂H₁₉NO requires (M+1)⁺, 314.1545); δ_H(250 MHz, CDCl₃) 4.30-4.48 (2 H, pair of dd, J 5.7 Hz, 14.8 Hz, CH₂), 5.11 (1 H, dd, J 1.1 Hz, 11.0 Hz, CH₂), 5.63 (1 H, dd, J 1.1 Hz, 17.6 Hz, CH₂), 6.21 (1 H, br, NH), 6.38 (1 H, dd, J 11.0 Hz, 17.6 Hz, CH), 7.17-7.73 (13 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 41.9 (CH₂), 115.3 (CH₂), 125.0 (CH), 126.7 (2 x CH), 127.3 (CH), 127.6 (CH), 127.9 (CH), 128.3 (2 x CH), 128.8 (CH), 130.0 (CH), 131.2 (CH), 134.7 (CH), 135.0 (quat.), 135.7 (quat.), 136.2 (quat.), 139.2 (quat.), 140.1 (quat.), 166.8 (quat.); *m/z* (FAB) 315 (M+1, 23%), 314 (45), 303 (15), 290 (21), 193 (100), 178 (69), 165 (55), 152 (13), 134 (18); ν_{max}(Nujol)/cm⁻¹ 1638 (C=O), 3299 (NH).

(iv) N-[2-(2-(2-Carbomethoxyethenyl)phenyl)benzyl]

benzamide 166

Methyl 3-(2-bromophenyl)prop-2-enoate (2.49 g, 10.3 mmol) and Pd(0) (0.54 g, 0.46 mmol, 4.4% mol catalyst) were stirred in DME (40 cm³) under dry nitrogen for 20 minutes. Sodium carbonate (2.96 g, 10.33 mmol) in water (14.3 cm³) and 2-*N*-benzoylaminomethylphenylboronic acid (2.90 g, 11.37 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Distillation of the product gave *N*-[2-(2-(2-carbomethoxyethenyl)phenyl)benzyl]benzamide as an orange glass (3.03 g, 79%), bp 210-220 °C/0.1 mmHg (Found: C, 76.9; H, 5.9; N, 3.9%; (M+1)⁺, 372.15996. C₂₃H₂₁NO₃ requires C, 76.7; H, 6.2; N, 3.7%; (M+1)⁺, 372.15998); δ_H(250 MHz, CDCl₃) 3.63 (3 H, s, CH₃), 4.19-4.27 (1 H, dd, J 5.1 Hz, 14.8 Hz, CH₂), 4.45-4.53 (1 H, dd, J 6.1 Hz, 14.8 Hz, CH₂), 6.27 (1 H, d, J 16.1 Hz, CH), 6.32 (1 H, br, NH), 7.14-8.09 (14 H, m, CH); δ_C(63 MHz, CDCl₃) 41.6 (CH₂), 51.4 (CH₃), 118.7 (CH), 126.1 (CH), 126.7 (2 x CH), 127.4 (CH), 127.9 (CH), 128.2 (2 x CH), 128.3 (CH),

128.7 (CH), 129.9 (CH), 130.1 (CH), 130.4 (CH), 131.2 (CH), 133.9 (quat.), 136.1 (quat.), 138.9 (quat.), 141.2 (quat.), 142.4 (CH), 166.8 (quat.), 167.0 (quat.); m/z (FAB) 372 (M+1, 50%), 279 (100), 191 (52), 179 (35), 165 (25).

(v) N-[2-(2-Ethenyl-6-methylphenyl)benzyl]benzamide 174

2-Bromo-3-methylstyrene (0.95 g, 4.82 mmol) and Pd(0) (0.25 g, 0.22 mmol, 4.5% mol catalyst) were stirred in DME (20 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (1.35 g, 5.30 mmol) and sodium carbonate (1.38 g, 4.82 mmol) in water (10 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(2-ethenyl-6-methylphenyl)benzyl]benzamide as a brown solid (1.23 g, 78%), mp 111-113 °C from ethanol-cyclohexane (Found: C, 84.6; H, 6.9; N, 4.5%; (M+1)⁺, 328.1703. C₂₃H₂₁NO requires C, 84.4; H, 6.5; N, 4.3%; (M+1)⁺, 328.1701); δ_{H} (250 MHz, CDCl₃) 1.97 (3 H, s, CH₃), 4.04-4.12 (1 H, dd, J 5.1 Hz, 14.7 Hz, CH₂), 4.41-4.49 (1 H, dd, J 6.7 Hz, 14.7 Hz, CH₂), 5.03 (1 H, dd, J 1.3 Hz, 11.0 Hz, CH), 5.56 (1 H, dd, J 1.3 Hz, 17.5 Hz, CH), 6.15 (1 H, br, NH), 6.27 (1 H, dd, J 11.0 Hz, 17.6 Hz, CH), 7.08-7.81 (12 H, m, Ar-H); δ_{C} (63 MHz, CDCl₃) 20.4 (CH₃), 42.0 (CH₂), 115.0 (CH₂), 122.5 (CH), 126.7 (2 x CH), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.3 (2 x CH), 129.2 (CH), 129.5 (CH), 129.6 (CH), 131.2 (CH), 135.3 (CH), 135.8 (quat.), 136.0 (quat.), 136.3 (quat.), 138.7 (quat.), 139.0 (quat.), 166.8 (quat.); m/z (FAB) 329 (M+1, 7%), 328 (22), 302 (39), 279 (38), 207 (39), 193 (18), 181 (40), 165 (29), 134 (14), 105 (100); ν_{max} (Nujol)/cm⁻¹ 1638 (C=O), 3320 (NH).

(vi) N-[3-Methyl-2-phenylbenzyl]benzamide 178

N-Benzoyl-2-bromo-3-methylbenzylamine (1.22 g, 4.01 mmol) and Pd(0) (0.21 g, 0.18 mmol, 4.5% mol catalyst) were stirred in DME (15 cm³) under dry nitrogen for 20 minutes. Phenylboronic acid (0.54 g, 4.41 mmol) and sodium carbonate (1.15 g, 4.01 mmol) in water (4.0 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[3-methyl-2-phenylbenzyl]benzamide as a white solid (0.75 g, 62%), mp 124-126 °C from ethanol (Found: C, 83.7; H, 6.6; N, 4.7%; (M+1)⁺, 302.1549. C₂₁H₁₉NO requires C, 83.7; H, 6.4; N, 4.7%; (M+1)⁺, 302.1545); δ_H(250 MHz, CDCl₃) 2.05 (3 H, s, CH₃), 4.34 (2 H, d, J 5.8 Hz, CH₂), 6.23 (1 H, br, NH), 7.16-7.67 (13 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 20.5 (CH₃), 42.3 (CH₂), 126.0 (CH), 126.7 (2 x CH), 127.2 (CH), 127.5 (CH), 128.3 (2 x CH), 128.6 (2 x CH), 128.8 (2 x CH), 129.0 (CH), 131.2 (CH), 134.2 (quat.), 135.8 (quat.), 136.5 (quat.), 139.5 (quat.), 141.2 (quat.), 166.7 (quat.); *m/z* (FAB) 303 (M+1, 26%), 302 (77), 181 (100), 166 (33), 165 (43), 152 (12), 122 (15), 105 (72), 77 (48); ν_{max}(Nujol)/cm⁻¹ 1639 (C=O), 3299 (NH).

(vii) N-[3-Methyl-2-(2-ethenylphenyl)benzyl]benzamide 179

N-Benzoyl-2-bromo-3-methylbenzylamine (1.0 g, 3.4 mmol) and Pd(0) (0.18 g, 0.15 mmol, 4.5% mol catalyst) were stirred in DME (15 cm³) under dry nitrogen for 20 minutes. 2-Ethenylphenylboronic acid (0.55 g, 3.74 mmol) and sodium carbonate (0.98 g, 3.4 mmol) in water (3.5 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was

added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[3-methyl-2-(2-ethenylphenyl)benzyl]benzamide as a white solid (0.73 g, 65%), mp 131-132 °C from ethanol (Found: 328.1694. C₂₃H₂₁NO requires (M+1)⁺, 328.1701); δ_H(200 MHz, CDCl₃) 1.97 (3 H, s, CH₃), 4.13-4.40 (2 H, pair of dd, J 6.0 Hz, 14.7 Hz, CH₂), 5.06-5.12 (1 H, dd, J 1.1 Hz, 11.0 Hz, CH₂), 5.59-5.68 (1 H, dd, J 1.0 Hz, 17.6 Hz, CH₂), 6.20 (1 H, br, NH), 6.25-6.39 (1 H, dd, J 11.0 Hz, 17.6 Hz, CH), 7.09-7.48 (9 H, m, Ar-H), 7.61-7.82 (3 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 20.2 (CH₃), 42.2 (CH₂), 115.3 (CH₂), 125.1 (CH), 126.4 (CH), 126.7 (2 x CH), 127.8 (CH), 128.1 (CH), 128.2 (2 x CH), 129.0 (CH), 129.3 (CH), 131.1 (CH), 134.2 (CH), 135.4 (quat.), 136.0 (quat.), 136.6 (quat.), 138.1 (quat.), 139.5 (quat.), 166.6 (quat.); *m/z* (FAB) 330 (M+1, 12%), 329 (15), 328 (37), 306 (38), 279 (12), 217 (38), 207 (36), 192 (18), 183 (21), 165 (19), 122 (14), 109 (42), 91 (67), 46 (100); ν_{max}(Nujol)/cm⁻¹ 1635 (C=O), 3288 (NH).

VII. Preparation of *N*-[2-Alkadienylbenzyl]benzamides

(i) *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]

benzamide 218

E,E-2-Bromo-3,5-diphenylpenta-2,4-diene (1.0 g, 3.36 mmol) and Pd(0) (0.19 g, 0.22 mmol, 5.6% mol catalyst) were stirred in DME (20 cm³) under dry nitrogen for 20 minutes. Sodium carbonate (0.97 g, 3.36 mmol) in water (5.5 cm³) and 2-*N*-benzoylaminomethylphenylboronic acid (0.95 g, 3.70 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(*E,E*-1',3'-

diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide as a yellow solid (1.11 g, 77%), mp 81-83 °C from ethanol (Found: C, 86.7; H, 6.5; N, 3.3%; (M+1)⁺, 430.2174. C₃₁H₂₇NO requires C, 86.7; H, 6.3; N, 3.3%; (M+1)⁺, 430.2171); δ_H(200 MHz, CDCl₃) 1.92 (3 H, s, CH₃), 4.39-4.49 (1 H, dd, J 4.2 Hz, 14.2 Hz, CH₂), 4.85-4.96 (1 H, dd, 6.9 Hz, 14.3 Hz, CH₂), 5.90-5.98 (1 H, d, J 16.1 Hz, CH), 6.42 (1 H, br, NH), 6.73-6.81 (1 H, d, J 16.0 Hz, CH), 6.93-7.68 (19 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 23.4 (CH₃), 41.9 (CH₂), 126.2 (CH), 126.7 (CH), 126.9 (CH), 127.3 (CH), 127.7 (CH), 128.0 (CH), 128.2 (2 x CH), 128.4 (4 x CH), 128.8 (CH), 129.6 (CH), 129.7 (2 x CH), 131.1 (CH), 131.6 (CH), 133.8 (quat.), 135.4 (quat.), 137.0 (quat.), 137.4 (quat.), 138.7 (quat.), 138.9 (quat.), 142.5 (quat.), 166.8 (quat.); *m/z* (FAB) 431 (M+1, 16%), 430 (32), 429 (17), 338 (18), 315 (19), 308 (49), 291 (40), 279 (60), 265 (39), 239 (45), 229 (56), 215 (100), 202 (90), 178 (52), 171 (31), 152 (42), 134 (26); ν_{max}(Nujol)/cm⁻¹ 1635 (C=O), 3336 (NH).

(ii) *N*-[2-(*E,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]

benzamide 219

E,Z-4-Bromo-1,3-diphenylpenta-1,3-diene (0.65 g, 2.17 mmol) and Pd(0) (0.12 g, 0.11 mmol, 4.8% mol catalyst) were stirred in DME (10 cm³) under dry nitrogen for 20 minutes. Sodium carbonate (0.62 g, 2.17 mmol) in water (3.0 cm³) and 2-*N*-benzoylaminomethylphenylboronic acid (0.64 g, 2.39 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a yellow solid. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(*E,Z*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide as a white solid (0.72 g, 77%), mp 116-118 °C from hexane-ethyl acetate (Found: C, 86.6; H, 6.5; N, 3.0%; (M+1)⁺, 428.2001. C₃₁H₂₇NO requires C, 86.7; H, 6.3; N, 3.3%; (M+1)⁺, 428.2014); δ_H(200 MHz, CDCl₃) 2.36 (3 H, s, CH₃),

4.18 (1 H, dd, J 4.4 Hz, 14.9 Hz, CH₂), 4.68 (1 H, dd, J 6.8 Hz, 14.3 Hz, CH₂), 5.84 (1 H, br, NH), 6.14 (1 H, d, J 16.0 Hz, CH), 6.99-7.82 (20 H, m, CH); δ_c (63 MHz, CDCl₃) 21.7 (CH₃), 41.1 (CH₃), 126.3 (2 x CH), 126.9 (CH), 127.4 (CH), 127.5 (CH), 128.2 (CH), 128.4 (2 x CH), 128.5 (2 x CH), 129.6 (CH), 130.6 (2 x CH), 131.3 (CH), 132.6 (CH), 134.1 (quat.), 134.3 (quat.), 135.7 (quat.), 137.6 (quat.), 139.4 (quat.), 143.4 (quat.), 167.1 (quat.); *m/z* (FAB) 431 (M+1, 38%), 430 (100), 428 (14), 339 (14), 322 (14), 309 (70), 291 (52), 279 (45), 265 (45), 252 (40), 239 (41), 216 (75), 202 (78), 189 (39), 179 (52), 166 (29), 152 (32), 131 (17); ν_{\max} (Nujol)/cm⁻¹ 1635 (C=O), 3345 (NH).

(iii) N-[2-(Z,Z-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide 220

Z,Z-4-Bromo-1,3-diphenylpenta-1,3-diene (1.20 g, 4.01 mmol) and Pd(0) (0.22 g, 0.19 mmol, 4.8% mol catalyst) were stirred in DME (10 cm³) under dry nitrogen for 20 minutes. Sodium carbonate (1.14 g, 4.01 mmol) in water (5.6 cm³) and 2-*N*-benzoylaminomethylphenylboronic acid (1.18 g, 4.61 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(*Z,Z*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide as a white solid (0.83 g, 48%), mp 135.5-137.5 °C from hexane-ethyl acetate (Found: C, 86.6; H, 6.5; N, 3.0%; (M+1)⁺, 428.2007. C₃₁H₂₇NO requires C, 86.7; H, 6.3; N, 3.3%; (M+1)⁺, 428.2014); δ_H (200 MHz, CDCl₃) 2.00 (3 H, d, J 1.1 Hz, CH₃), 4.04 (1 H, dd, J 3.7 Hz, 14.5 Hz, CH₂), 4.64 (1 H, dd, J 7.5 Hz, 14.5 Hz, CH₂), 5.43 (1 H, br, NH), 6.48 (1 H, dd, J 1.1 Hz, 12.1 Hz, CH), 6.65 (1 H, d, J 12.1 Hz, CH), 6.94-7.82 (19 H, m, Ar-H); δ_c (63 MHz, CDCl₃) 24.0 (CH₃), 41.0 (CH₂), 126.3 (CH), 126.9 (2 x CH), 127.1 (CH), 127.2 (CH),

127.3 (CH), 127.5 (2 x CH), 128.0 (2 x CH), 128.1 (2 x CH), 128.2 (2 x CH), 129.2 (CH), 129.2 (CH), 129.5 (2 x CH), 130.3 (CH), 131.1 (CH), 134.2 (quat.), 134.3 (quat.), 134.5 (quat.), 134.6 (quat.), 137.3 (quat.), 139.7 (quat.), 142.8 (quat.), 167.1 (quat.); m/z (FAB) 431 (M+1, 34%), 430 (100), 429 (28), 339 (10), 309 (70), 291 (51), 279 (38), 265 (44), 252 (39), 239 (39), 229 (52), 218 (40), 215 (42), 205 (55), 193 (41), 178 (41), 166 (25), 151 (18), 131 (19); ν_{\max} (Nujol)/ cm^{-1} 1634 (C=O), 3340 (NH).

(iv) *N*-[2-(Methyl-*E,E*-4'-phenylhexa-2',4'-dienoat-5'-yl)benzyl]

benzamide 222

Methyl *E,E*-5-bromo-4-phenylhexa-2,4-dienoate (1.8 g, 6.4 mmol) and Pd(0) (0.32 g, 0.28 mmol, 4.4% mol catalyst) were stirred in DME (30 cm^3) under dry nitrogen for 20 minutes. Sodium carbonate (1.83 g, 6.4 mmol) in water (10 cm^3) and 2-*N*-benzoylaminomethylphenylboronic acid (1.80 g, 7.04 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm^3) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown solid. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(methyl *E,E*-4'-phenylhexa-2',4'-dienoat-5'-yl)benzyl]benzamide as a yellow solid (2.32 g, 88%), mp 140-142 °C from pentane-DCM* (Found: C, 78.9; H, 6.4; N, 3.0%; (M+1)⁺, 412.1920. $\text{C}_{27}\text{H}_{25}\text{NO}_3$ requires C, 78.9; H, 6.1; N, 3.4%; (M+1)⁺, 412.1913); δ_{H} (250 MHz, CDCl_3) 1.93 (3 H, s, CH_3), 3.49 (3 H, s, CH_3), 4.45-4.53 (1 H, dd, J 5.0 Hz, 14.4 Hz, CH_2), 4.68-4.76 (1 H, dd, J 5.8 Hz, 14.4 Hz, CH_2), 5.19 (1 H, d, J 16.0 Hz, CH), 6.52 (1 H, br, NH), 7.71-7.48 (13 H, m, CH), 7.71-7.76 (2 H, m, Ar-H); δ_{C} (63 MHz, CDCl_3) 24.0 (CH_3), 41.6 (CH_2), 51.1 (CH_3), 119.9 (CH), 126.8 (2 x CH), 127.3 (CH), 128.0 (CH), 128.1 (CH), 128.2 (2 x CH), 128.4 (CH), 128.5 (2 x CH), 129.3 (CH), 131.2 (CH), 133.9 (quat.), 134.7 (quat.), 137.4 (quat.), 137.5 (quat.), 141.3 (quat.), 144.2 (CH), 145.4 (quat.), 166.9 (quat.), 167.5

(quat.); m/z (FAB) 412 (M+1, 38%), 380 (50), 259 (67), 230 (16), 215 (40), 189 (10), 165 (19), 105 (100), 91 (25), 77 (27); ν_{\max} (Nujol)/ cm^{-1} 1545 (amide), 1721 (ester), 3312 (amide).

* isothermal distillation.

(v) *N*-[2-(*E*-5'-Methyl-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]

benzamide 225

E-5-Bromo-2-methyl-5-phenylhexa-2,4-diene (0.65 g, 2.6 mmol) and Pd(0) (0.14 g, 0.12 mmol, 4.8% mol catalyst) were stirred in DME (10 cm^3) under dry nitrogen for 20 minutes. Sodium carbonate (0.74 g, 2.58 mmol) in water (3.5 cm^3) and 2-*N*-benzoylaminomethylphenylboronic acid (0.76 g, 2.84 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm^3) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a yellow solid. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(*E*-5'-methyl-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide as a white solid (0.40 g, 41%), mp 131-132 °C from ethyl acetate (Found: C, 85.2; H, 7.4; N, 3.6%; (M+1)⁺, 382.2179. $\text{C}_{27}\text{H}_{27}\text{NO}$ requires C, 85.0; H, 7.1; N, 3.7%; (M+1)⁺, 382.2171); δ_{H} (200 MHz, CDCl_3) 0.90 (3 H, s, CH_3), 1.42 (3 H, s, CH_3), 1.85 (3 H, s, CH_3), 4.33 (1 H, dd, J 4.1 Hz, 14.0 Hz, CH_2), 4.71 (1 H, dd, J 6.5 Hz, 14.0 Hz, CH_2), 5.59 (1 H, s, CH), 6.33 (1 H, br, NH), 6.91-7.67 (14 H, m, CH); δ_{C} (63 MHz, CDCl_3) 19.5 (CH_3), 22.9 (CH_3), 27.4 (CH_3), 42.0 (CH_2), 125.2 (CH), 126.4 (CH), 126.8 (2 x CH), 127.2 (CH), 127.9 (CH), 128.1 (2 x CH), 128.4 (2 x CH), 129.4 (CH), 129.5 (2 x CH), 131.2 (CH), 134.5 (quat.), 134.7 (quat.), 135.1 (quat.), 135.6 (quat.), 137.4 (quat.), 141.6 (quat.), 143.8 (quat.), 167.1 (quat.); m/z (FAB) 383 (M+1, 36%), 382 (100), 381 (44), 366 (12), 338 (11), 276 (24), 261 (63), 245 (62), 243 (45), 231 (69), 220 (63), 216 (85), 202 (90), 190 (49), 178 (16), 166 (46), 155 (67), 141 (80), 131 (40); ν_{\max} (Nujol)/ cm^{-1} 1635 (C=O), 3316 (NH).

(vi) N-[2-(*E,E*-3'-Phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide 226

2-Bromo-3-phenylhexa-2,4-diene (0.80 g, 3.37 mmol) and Pd(0) (0.19 g, 0.17 mmol, 5.0% mol catalyst) were stirred in DME (15 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminoethylphenylboronic acid (1.00 g, 3.71 mmol) and sodium carbonate (0.96 g, 3.37 mmol) in water (4.5 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(*E,E*-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide as a white solid (0.42 g, 35%), mp 138-140 °C from hexane-ethyl acetate (Found: C, 84.9; H, 6.9; N, 3.4%; (M+1)⁺, 368.2026. C₂₆H₂₅NO requires C, 85.0; H, 6.9; N, 3.8%; (M+1)⁺, 268.2014); δ_H(200 MHz, CDCl₃) 1.47 (3 H, d, J 6.8 Hz, CH₃), 1.81 (3 H, s, CH₃), 4.41 (1 H, dd, J 4.4 Hz, 14.4 Hz, CH₂), 4.78 (1 H, dd, J 6.8 Hz, 14.4 Hz, CH₂), 5.05 (1 H, q, CH), 5.93 (1 H, d, J 15.7 Hz, CH), 6.42 (1 H, br, NH), 7.10-7.75 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 18.2 (CH₃), 23.0 (CH₃), 42.1 (CH₂), 126.6 (CH), 126.8 (2 x CH), 127.4 (CH), 128.0 (CH), 128.2 (2 x CH), 128.3 (2 x CH), 128.9 (CH), 129.4 (2 x CH), 129.6 (2 x CH), 131.1 (CH), 131.4 (CH), 133.5 (quat.), 134.3 (quat.), 135.2 (quat.), 138.6 (quat.), 139.6 (quat.), 143.0 (quat.), 166.9 (quat.); *m/z* (FAB) 369 (M+1, 67%), 368 (80), 367 (22), 366 (38), 247 (87), 231 (76), 216 (54), 205 (79), 191 (28), 178 (26), 165 (24), 155 (43), 141 (53), 134 (100); ν_{max}(Nujol)/cm⁻¹ 1633 (C=O), 3365 (NH).

(vii) N-[2-(2'-(*E*-2-Phenylethenyl)cyclopent-1'-enyl)benzyl]**benzamide 230**

1-Bromo-2-(*E*-2-phenylethenyl)cyclopentene (1.40 g, 5.64 mmol) and Pd(0) (0.28 g, 0.25 mmol, 4.4% mol catalyst) were stirred in DME (30

cm³) under dry nitrogen for 20 minutes. Sodium carbonate (1.61 g, 5.64 mmol) in water (9.0 cm³) and 2-*N*-benzoylaminomethylphenylboronic acid (1.54 g, 6.20 mmol) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(2'-(*E*-2-phenylethenyl)cyclopent-1'-enyl)benzyl]benzamide as a brown solid (1.65 g, 93%), mp 132-134 °C from pentane-DCM* (Found: C, 84.2; H, 6.7; N, 3.6%; (M+1)⁺, 380.2020. C₂₇H₂₅NO requires C, 84.5; H, 7.1; N, 3.6%; (M+1)⁺, 380.2014); δ_H(250 MHz, CDCl₃) 2.01-2.13 (2 H, m, CH₂), 2.75-2.82 (4 H, m, CH₂), 4.61 (2 H, br, CH₂), 6.44 (1 H, br, NH), 6.49 (1 H, d, J 16.1 Hz, CH), 6.66 (1 H, d, J 16.1 Hz, CH), 7.11-7.68 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 22.3 (CH₂), 32.7 (CH₂), 39.7 (CH₂), 42.1 (CH₂), 123.1 (CH), 126.2 (2 x CH), 126.6 (2 x CH), 127.2 (CH), 127.5 (CH), 127.6 (CH), 128.2 (2 x CH), 128.4 (2 x CH), 129.2 (CH), 129.3 (CH), 130.3 (CH), 131.1 (CH), 133.9 (quat.), 136.0 (quat.), 137.1 (quat.), 137.8 (quat.), 138.2 (quat.), 142.0 (quat.), 166.8 (quat.); *m/z* (FAB) 381 (M+1, 14%), 380 (58), 379 (21), 378 (12), 288 (13), 279 (100), 274 (14), 258 (61), 229 (45), 203 (30), 181 (28), 165 (83), 154 (34), 141 (43); ν_{max}(Nujol)/cm⁻¹ 1634 (C=O), 3337 (NH).

* isothermal distillation.

(viii) *N*-[2-(2'-(2-Carbomethoxyethenyl)cyclopent-1'-enyl)benzyl]benzamide 231

Methyl 3-(2-bromocyclopent-1-enyl)propenoate (2.42 g, 10.47 mmol) and Pd(0) (0.48 g, 0.42 mmol, 4.0% mol catalyst) were stirred in DME (50 cm³) under dry nitrogen for 20 minutes. Sodium carbonate (3.00 g, 10.47 mmol) in water (15 cm³) and 2-*N*-benzoylaminomethylphenylboronic acid (2.93 g, 11.52 mmol) were added and the mixture heated at reflux for 20

h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (100 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave *N*-[2-(2'-(2-carbomethoxyethenyl)cyclopent-1'-enyl)benzyl]benzamide as a yellow solid (3.25 g, 86%), mp 117-118 °C from ethanol (Found: C, 76.1; H, 6.2; N, 3.6%; (M+1)⁺, 362.1754. C₂₃H₂₃NO₃ requires C, 76.4; H, 6.4; N, 3.9%; (M+1)⁺, 362.1756); δ_H(250 MHz, CDCl₃) 1.97-2.09 (2 H, m, CH₂), 2.59-2.65 (2 H, m, CH₂), 2.79 (2 H, br, CH₂), 3.60 (3 H, s, CH₃), 4.46 (2 H, br, CH₂), 5.71 (1 H, d, J 15.7 Hz, CH), 6.49 (1 H, br, NH), 7.13 (1 H, d, J 15.7 Hz, CH), 7.04-7.73 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 22.1 (CH₂), 32.2 (CH₂), 40.2 (CH₂), 41.8 (CH₂), 51.3 (CH₃), 118.6 (CH), 126.8 (2 x CH), 127.6 (CH), 128.1 (CH), 128.2 (2 x CH), 128.9 (CH), 129.0 (CH), 131.2 (CH), 133.9 (quat.), 135.5 (quat.), 136.5 (quat.), 136.7 (quat.), 138.6 (quat.), 150.7 (quat.), 166.9 (quat.), 167.5 (quat.); *m/z* (FAB) 363 (M+1, 9%), 362 (11), 302 (17), 279 (50), 181 (27), 153 (13), 129 (11), 105 (86), 91 (23), 77 (46), 60 (38), 46 (98), 30 (100); ν_{max}(Nujol)/cm⁻¹ 1641 (C=C), 1700 (C=O), 3342 (NH).

VIII. Preparation of *N*-[2-Alkenylbenzyl]benzamides

(i) *N*-[2-(Propen-2'-yl)benzyl]benzamide 294

2-Bromopropene (1.52 g, 12.0 mmol) and Pd(0) (0.66 g, 0.58 mmol, 4.8% mol catalyst) were stirred in DME (50 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (3.38 g, 13.2 mmol) and sodium carbonate (3.42 g, 12.0 mmol) in water (16.5 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (100 cm³) was added. The organic layer was separated, dried and the solvent removed

in vacuo to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(propen-2'-yl)benzyl]benzamide as a white solid (1.96 g, 65%), mp 92-93 °C from ethanol (Found: C, 81.1; N, 6.8; H, 5.5%; (M+1)⁺, 252.1391. C₁₇H₁₇NO requires C, 81.2; H, 6.8; N, 5.6%; (M+1)⁺, 252.1388); δ_H(200 MHz, CDCl₃) 2.07 (3 H, dd, J 1.0 Hz, CH₃), 4.64 (2 H, d, J 5.5 Hz, CH₂), 4.90 (1 H, m, CH), 5.24 (1 H, m, CH), 6.57 (1 H, br, NH), 7.14-7.51 (7 H, m, Ar-H), 7.72-7.79 (2 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 24.8 (CH₃), 41.8 (CH₂), 115.5 (CH₂), 126.7 (CH), 127.2 (CH), 127.3 (CH), 128.2 (CH), 128.4 (CH), 128.7 (CH), 131.2 (CH), 134.3 (quat.), 143.5 (quat.), 144.8 (quat.), 167.0 (quat.); *m/z* (FAB) 254 (M+1, 51%), 253 (36), 252 (100), 251 (20), 250 (35), 239 (46), 207 (17), 202 (14), 179 (17), 165 (23), 163 (40), 146 (72), 141 (20), 131 (65); ν_{max}(Nujol)/cm⁻¹ 1636 (C=O), 3331 (NH).

(ii) *N*-[2-(*E*-1'-Phenylpropen-2'-yl)benzyl]benzamide 298a

2-Bromo-1-phenylpropene (1.70 g, 8.63 mmol) and Pd(0) (0.45 g, 0.40 mmol, 4.6% mol catalyst) were stirred in DME (35 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminoethylphenylboronic acid (2.42 g, 9.49 mmol) and sodium carbonate (2.47 g, 8.63 mmol) in water (11.9 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (100 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica followed by MPLC, eluting with hexane-ethyl acetate (9:1) gave a) *N*-[2-(*E*-1'-phenylpropen-2'-yl)benzyl]benzamide as a white solid (0.59 g, 21%), mp 147-148 °C from hexane-ethanol (Found: C, 84.4; H, 6.5; N, 4.3%; (M+1)⁺, 328.1701. C₂₃H₂₁NO requires C, 84.4; H, 6.5; N, 4.3%; (M+1)⁺, 328.1701); δ_H(250 MHz, CDCl₃) 2.22 (3 H, d, J 1.4 Hz, CH₃), 4.09 (1 H, dd, J 3.4 Hz, 14.1 Hz, CH₂), 4.73 (1 H, dd, J 7.5 Hz, 14.1 Hz, CH₂), 5.74 (1 H, br, NH), 6.57 (1 H, d, J 1.3 Hz, CH), 6.83-7.46

(14 H, m, Ar-H); δ_{C} (63 MHz, CDCl_3) 28.1 (CH_3), 41.5 (CH_2), 126.6 (CH), 126.7 (CH), 127.6 (CH), 127.7 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 130.3 (CH), 131.0 (CH), 133.9 (quat.), 134.0 (quat.), 136.9 (quat.), 137.7 (quat.), 141.8 (quat.), 166.6 (quat.); m/z (FAB) 331 (M+1, 7%), 330 (64), 329 (47), 328 (70), 327 (51), 239 (22), 222 (36), 205 (100), 179 (69), 165 (32), 134 (18), 129 (55), 115 (43); ν_{max} (Nujol)/ cm^{-1} 1632 (C=O), 3317 (NH).

b) *N*-[2-(*Z*-1'-Phenylpropen-2'-yl)benzyl]benzamide as a white solid (0.28 g, 10%), mp 112-113 °C from hexane-ethanol (Found: C, 84.4; H, 6.5; N, 4.3%; (M+1)⁺, 328.1701. $\text{C}_{23}\text{H}_{21}\text{NO}$ requires C, 84.4; H, 6.5; N, 4.3%; (M+1)⁺, 328.1701); δ_{H} (250 MHz, CDCl_3) 2.24 (3 H, d, J 1.5 Hz, CH_3), 4.72 (2 H, d, J 5.5 Hz, CH_2), 6.45 (1 H, d, J 1.4 Hz, CH), 6.57 (1 H, br, NH), 7.24-7.77 (14 H, m, Ar-H); δ_{C} (63 MHz, CDCl_3) 20.2 (CH_3), 41.9 (CH_2), 126.6 (CH), 126.7 (CH), 127.3 (CH), 127.5 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 129.9 (CH), 134.2 (quat.), 134.5 (quat.), 137.2 (quat.), 137.8 (quat.), 145.3 (quat.), 167.1 (quat.); m/z (FAB) 330 (M+1, 33%), 329 (38), 328 (67), 327 (26), 288 (16), 239 (17), 222 (26), 205 (100), 191 (42), 179 (50), 165 (26), 152 (20), 141 (16), 131 (28), 115 (35), 91 (52), 77 (43); ν_{max} (Nujol)/ cm^{-1} 1632 (C=O), 3317 (NH).

c) *N*-[2-Phenylbenzyl]benzamide as a white solid (1.12 g, 40%), mp 95-96 °C from hexane-ethanol (Found: 288.1377. $\text{C}_{20}\text{H}_{17}\text{NO}$ requires (M+1)⁺, 288.1388); δ_{H} (200 MHz, CDCl_3) 4.62 (2 H, d, J 5.6 Hz, CH_2), 6.23 (1 H, br, NH), 7.25-7.50 (12 H, m, Ar-H); δ_{C} (50 MHz, CDCl_3) 41.9 (CH_2), 126.7 (CH), 127.2 (CH), 127.4 (CH), 127.7 (CH), 128.3 (CH), 128.6 (CH), 128.8 (CH), 130.1 (CH), 131.2 (CH), 134.2 (quat.), 135.3 (quat.), 140.6 (quat.), 141.5 (quat.), 166.9 (quat.); m/z (FAB) 289 (M+1, 53%), 288 (M+1, 73), 239 (10), 202 (14), 184 (26), 179 (84), 166 (90), 152 (45), 134 (35), 122 (62), 115 (48), 91 (30), 77 (100); ν_{max} (Nujol)/ cm^{-1} 1625 (C=O), 3320 (NH).

(iii) N-[2-(3'-Methylbut-2'-enyl)benzyl]benzamide 304

2-Bromo-3-methylbut-2-ene (1.59 g, 10.66 mmol) and Pd(0) (0.56 g, 0.49 mmol, 4.6% mol catalyst) were stirred in DME (40 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (3.00 g, 11.73 mmol) and sodium carbonate (3.06 g, 10.66 mmol) in water (15 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (100 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown solid. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(3'-methylbut-2'-enyl)benzyl]benzamide as a white solid (2.10 g, 70%), mp 105 °C from hexane-ethanol (Found: C, 81.4; H, 8.0; N, 4.7%; (M+1)⁺, 280.16998. C₁₉H₂₁NO requires C, 81.7; H, 7.6; N, 5.0%; (M+1)⁺, 280.17014); δ_H(250 MHz, CDCl₃) 1.42 (3 H, d, J 1.4 Hz, CH₃), 1.80 (3 H, d, J 0.4 Hz, CH₃), 1.90 (3 H, d, J 0.9 Hz, CH₃), 4.51 (2 H, m, CH₂), 6.45 (1 H, br, NH), 7.01-7.77 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 19.7 (CH₃), 20.6 (CH₃), 21.8 (CH₃), 41.6 (CH₂), 126.5 (CH), 126.7 (2 x CH), 127.5 (CH), 128.2 (CH), 128.4 (2 x CH), 128.9 (CH), 131.2 (CH), 134.3 (quat.), 134.7 (2 x quat.), 144.5 (quat.), 167.0 (quat.); *m/z* (FAB) 281 (M+1, 45%), 280 (77), 279 (11), 278 (20), 174 (21), 160 (37), 159 (81), 143 (59), 128 (50), 117 (53), 115 (33), 105 (100), 91 (60), 77 (52); ν_{max}(Nujol)/cm⁻¹ 1637 (C=O), 3327 (NH). One quat. carbon obscured by aromatic carbons.

(iv) N-[2-(*E*-3'-Phenylbut-2'-enyl)benzyl]benzamide 308a

E-2-Bromo-3-phenylbut-2-ene (0.28 g, 1.33 mmol) and Pd(0) (0.074 g, 0.065 mmol, 4.9% mol catalyst) were stirred in DME (6.0 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (0.39 g, 1.46 mmol) and sodium carbonate (0.38 g, 1.33 mmol) in water (1.9 cm³) were added and the mixture heated at reflux for 20 h. The

reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(*E*-3'-phenylbut-2'-enyl)benzyl]benzamide as a white solid (0.45 g, 63%), mp 141-143 °C from hexane-ethyl acetate (Found: C, 84.8; H, 7.1; N, 4.0%; (M+1)⁺, 342.1844. C₂₄H₂₃NO requires C, 84.4; H, 6.8; N, 4.1%; (M+1)⁺, 342.1858); δ_H(200 MHz, CDCl₃) 2.06 (3 H, s, CH₃), 2.13 (3 H, s, CH₃), 3.93 (1 H, dd, J 4.0 Hz, 14.6 Hz, CH₂), 4.56 (1 H, dd, J 7.3 Hz, 14.3 Hz, CH₂), 5.36 (1 H, br, NH), 7.06-7.54 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 20.5 (CH₃), 22.5 (CH₃), 41.1 (CH₂), 125.9 (CH), 126.8 (CH), 126.9 (2 x CH), 127.1 (CH), 127.5 (2 x CH), 128.2 (2 x CH), 128.6 (2 x CH), 128.7 (CH), 129.8 (CH), 131.2 (CH), 131.4 (quat.), 133.0 (quat.), 134.3 (quat.), 134.4 (quat.), 143.6 (quat.), 143.8 (quat.), 167.1 (quat.); *m/z* (FAB) 343 (M+1, 31%), 342 (100), 341 (12), 236 (23), 220 (64), 216 (18), 202 (60), 189 (29), 178 (41), 165 (30), 152 (27), 141 (58); ν_{max}(Nujol)/cm⁻¹ 1635 (C=O), 3301 (NH).

(v) *N*-[2-(*Z*-3'-Phenylbut-2'-enyl)benzyl]benzamide 308b

Z-2-Bromo-3-phenylbut-2-ene (1.02 g, 4.83 mmol) and Pd(0) (0.27 g, 0.24 mmol, 4.9% mol catalyst) were stirred in DME (20 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (1.43 g, 5.31 mmol) and sodium carbonate (1.38 g, 4.83 mmol) in water (6.5 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(*Z*-3'-phenylbut-2'-enyl)benzyl]benzamide as a white solid (1.24 g, 78%), mp

125-127 °C from hexane-ethyl acetate (Found: C, 84.6; H, 7.0; N, 4.1%; (M+1)⁺, 342.1855. C₂₄H₂₃NO requires C, 84.4; H, 6.8; N, 4.1%; (M+1)⁺, 342.1858); δ_H(200 MHz, CDCl₃) 1.67 (3 H, s, CH₃), 1.78 (3 H, s, CH₃), 4.59 (2 H, dd, J 3.4 Hz, 5.5 Hz, CH₂), 6.32 (1 H, br, NH), 6.91-7.72 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 22.2 (CH₃), 22.4 (CH₃), 41.6 (CH₂), 126.3 (CH), 126.7 (2 x CH), 127.0 (CH), 127.8 (CH), 128.0 (2 x CH), 128.1 (2 x CH), 128.4 (CH), 128.5 (2 x CH), 128.7 (CH), 131.3 (CH), 134.3 (quat.), 134.4 (quat.), 134.6 (quat.), 143.2 (quat.), 143.6 (quat.), 167.1 (quat.); *m/z* (FAB) 343 (M+1, 36%), 342 (100), 341 (29), 265 (12), 252 (12), 236 (29), 216 (26), 205 (70), 192 (45), 179 (66), 165 (33), 152 (31), 143 (60), 131 (22); ν_{max}(Nujol)/cm⁻¹ 1636 (C=O), 3344 (NH).

(vi) N-[2-(2'-Methylpent-2'-en-3'-yl)benzyl]benzamide 312

3-Bromo-2-methylpent-2-ene (0.50 g, 3.07 mmol) and Pd(0) (0.17 g, 0.15 mmol, 4.9% mol catalyst) were stirred in DME (15 cm³) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (0.91 g, 3.38 mmol) and sodium carbonate (0.88 g, 3.07 mmol) in water (4.2 cm³) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm³) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a red solid. Dry-flash column chromatography followed by MPLC on silica, eluting with hexane-ethyl acetate (9:1) gave *N*-[2-(2'-methylpent-2'-en-3'-yl)benzyl]benzamide as a white solid (0.37 g, 41%), mp 105 °C from hexane-ethyl acetate (Found: C, 81.8; H, 5.2; N, 4.5%; (M+1)⁺, 280.16998. C₂₀H₂₃NO requires C, 81.9; H, 7.9; N, 4.8%; (M+1)⁺, 280.17014); δ_H(200 MHz, CDCl₃) 0.88 (3 H, t, CH₃), 1.42 (3 H, s, CH₃), 1.82 (3 H, s, CH₃), 2.10 (1 H, q, CH₂), 2.46 (1 H, q, CH₂), 4.52 (2 H, dd, J 2.9 Hz, 5.5 Hz, CH₂), 6.25 (1 H, br, NH), 7.00-7.78 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 12.6 (CH₃), 19.3 (CH₃), 22.1 (CH₃), 27.1 (CH₂), 41.7 (CH₂), 126.7 (2 x CH), 127.2 (CH), 128.1 (CH), 128.5 (2 x CH), 129.8 (CH),

131.3 (CH), 134.4 (quat.), 134.6 (quat.), 135.2 (quat.), 143.0 (quat.), 167.0 (quat.); m/z (FAB) 281 (M+1, 45%), 280 (77), 279 (11), 278 (20), 174 (21), 159 (81), 143 (59), 129 (46), 117 (53), 115 (33), 105 (100), 91 (60), 77 (52); ν_{\max} (Nujol)/ cm^{-1} 1636 (C=O), 3340 (NH).

(vii) *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzamide 302

2-Bromo-1,1-diphenylpropene (0.70 g, 2.56 mmol) and Pd(0) (0.14 g, 0.12 mmol, 4.7% mol catalyst) were stirred in DME (15 cm^3) under dry nitrogen for 20 minutes. 2-*N*-Benzoylaminomethylphenylboronic acid (0.72 g, 2.81 mmol) and sodium carbonate (0.73 g, 2.56 mmol) in water (3.5 cm^3) were added and the mixture heated at reflux for 20 h. The reaction mixture was allowed to cool to room temperature and passed through a pad of alumina. The DME was removed *in vacuo* and DCM (50 cm^3) was added. The organic layer was separated, dried and the solvent removed *in vacuo* to give a brown solid. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) to give *N*-[2-(1',1'-diphenylpropen-2'-yl)benzyl]benzamide as a white solid (0.56 g, 54%), mp 144-146 °C from hexane-ethanol (Found: C, 86.4; H, 6.4; N, 3.3%; (M+1)⁺, 404.2001. C₂₉H₂₅NO requires C, 86.3; H, 6.3; N, 3.5%; (M+1)⁺, 404.2014); δ_{H} (250 MHz, CDCl₃) 2.11 (3 H, s, CH₃), 4.15 (1 H, dd, J 3.6 Hz, 14.4 Hz, CH₂), 4.83 (1 H, dd, J 7.6 Hz, 14.4 Hz, CH₂), 5.54 (1 H, br, NH), 6.89-7.59 (19 H, m, Ar-H); δ_{C} (63 MHz, CDCl₃) 24.6 (CH₃), 40.8 (CH₂), 126.1 (CH), 126.7 (CH), 126.9 (2 x CH), 127.2 (CH), 127.3 (CH), 127.4 (2 x CH), 128.1 (2 x CH), 128.2 (2 x CH), 129.1 (CH), 129.7 (CH), 129.8 (2 x CH), 130.2 (2 x CH), 131.2 (CH), 133.9 (quat.), 134.2 (quat.), 134.5 (quat.), 139.6 (quat.), 141.9 (quat.), 142.4 (quat.), 142.9 (quat.), 167.1 (quat.); m/z (FAB) 405 (M+1, 72%), 404 (48), 403 (20), 339 (10), 296 (24), 284 (45), 267 (58), 254 (41), 239 (41), 229 (23), 216 (31), 205 (76), 192 (48), 178 (42), 167 (54), 152 (22), 141 (15), 122 (73), 103 (29); ν_{\max} (Nujol)/ cm^{-1} 1640 (C=O), 3291 (NH).

IX. Generation and Reaction of Substituted Nitrile Ylides derived from N-[2-Arylbenzyl]benzimidoyl chlorides

(i) Generation and Reaction of the Nitrile Ylide derived from N-[2-Phenylbenzyl]benzimidoyl chloride 240

N-[2-Phenylbenzyl]benzamide (0.30 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³) were heated at reflux under dry nitrogen overnight. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (20 cm³) was added and the solution cooled to 0 °C. Solid potassium *tert*-butoxide (0.80 g, 2.08 mmol) was added in one portion with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 2 h, allowed to warm to room temperature and stirred for 1 h. Ammonium chloride (25% w/v, 20 cm³) was added and the mixture stirred for 10 minutes. The mixture was extracted with DCM (2 x 20 cm³), the combined organic fractions were dried and the solvent removed *in vacuo* to give a yellow foam. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5*H*-dibenz[*c,e*]azepine as a white crystalline solid (0.22 g, 80%), mp 95-96 °C from cyclohexane (Found: 270.1285. C₂₀H₁₅N requires (M+1)⁺, 270.1283); δ_H(250 MHz, CDCl₃) 3.94 (1 H, d, J 10.4 Hz, CH₂), 4.89 (1 H, d, J 10.5 Hz, CH₂), 7.25-7.77 (13 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 55.2 (CH₂), 126.2 (CH), 127.5 (CH), 127.6 (CH), 127.8 (2 x CH), 127.9 (CH), 128.0 (CH), 128.7 (CH), 129.3 (2 x CH), 129.4 (CH), 129.5 (CH), 130.3 (CH), 133.9 (quat.), 138.0 (quat.), 140.5 (quat.), 140.7 (quat.), 140.8 (quat.), 168.3 (quat.); *m/z* (FAB) 271 (M+1, 46%), 270 (100), 268 (43), 165 (50), 104 (25), 91 (22); ν_{max}(Nujol)/cm⁻¹ 1610 (C=N).

(ii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-Phenylbenzyl]benzimidoyl chloride 240 using alternative bases

Preparation of Lithium Diisopropylamide

n-Butyllithium (0.46 cm³, 2.5 M solution in hexanes) was added dropwise at 0 °C to a solution of diisopropylamide (0.15 g, 1.44 mmol) in freshly distilled THF (5 cm³), under nitrogen. The solution was left to stir at room temperature for a further 30 mins.

(1) Using Lithium Diisopropylamide as Base

The imidoyl chloride was prepared as in (i) using *N*-[2-phenylbenzyl]benzamide (0.3 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to -78 °C. Lithium diisopropylamide (1.15 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at -78 °C for 2 h, allowed to warm to room temperature and stirred for a 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5*H*-dibenz[*c,e*]azepine as a white crystalline solid (0.14 g, 50%).

(2) Using Lithium Bis(trimethylsilyl)amide as Base

The imidoyl chloride was prepared as in (i) using *N*-[2-phenylbenzyl]benzamide (0.3 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to -78 °C. Lithium bis(trimethylsilyl)amide (1.15 cm³, 1.15 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at -78 °C for 2 h, allowed to warm to room temperature and stirred for a 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on

silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5*H*-dibenz[*c,e*]azepine as a white crystalline solid (0.18 g, 64%).

(2b)

The imidoyl chloride was prepared as in (i) using *N*-[2-phenylbenzyl]benzamide (0.3 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.15 cm³, 1.15 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 2 h, allowed to warm to room temperature and stirred for a 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5*H*-dibenz[*c,e*]azepine as a white crystalline solid (0.21 g, 75%).

(2c)

The imidoyl chloride was prepared as in (i) using *N*-[2-phenylbenzyl]benzamide (0.3 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.04 cm³, 1.04 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5*H*-dibenz[*c,e*]azepine as a white crystalline solid (0.21 g, 75%).

(2d)

The imidoyl chloride was prepared as in (i) using *N*-[2-phenylbenzyl]benzamide (0.3 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³). After drying the imidoyl chloride was

dissolved in THF (20 cm³) and cooled to 0 °C. Lithium bis(trimethylsilyl)amide (2.08 cm³, 2.08 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5H-dibenz[c,e]azepine as a white crystalline solid (0.21 g, 75%).

Preparation of Lithium Tetramethylpiperidide

n-Butyllithium (0.46 cm³, 2.5 M solution in hexanes) was added dropwise at 0 °C to a solution of tetramethylpiperidide (0.20 g, 1.44 mmol) in freshly distilled THF (5 cm³), under nitrogen. The solution was left to stir at room temperature for a further 30 mins.

(3) Using Lithium Tetramethylpiperidide as Base

The imidoyl chloride was prepared as in (i) using *N*-[2-phenylbenzyl]benzamide (0.3 g, 1.04 mmol), dry ether (20 cm³) and thionyl chloride (5.46 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to -78 °C. Lithium tetramethylpiperidide (1.15 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at -78 °C for 2 h, allowed to warm to room temperature and stirred for a further 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 7-phenyl-5*H*-dibenz[c,e]azepine as a white crystalline solid (0.18 g, 66%).

(iii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(2-(*E*-2-Phenylethenyl)phenyl)benzyl]benzimidoyl chloride 185

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-(*E*-2-phenylethenyl)phenyl)benzyl]benzamide (0.75 g, 1.93 mmol), dry ether (35 cm³) and thionyl chloride (11.2 cm³). After drying the imidoyl chloride

was dissolved in THF (35 cm³) and cooled to 0 °C. Solid potassium *tert*-butoxide (0.43 g, 3.86 mmol) was added in one portion with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 30 min, allowed to warm to room temperature and stirred for a further 30 min. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded three products.

(a) 11-(*E*-2-Phenylethenyl)-7-phenyl-5*H*-dibenz[*c,e*]azepine and a nitrile ylide dimer which were inseparable as a yellow glassy foam (0.24 g)*, (Found: 372.1762. C₂₈H₂₁N requires (M+1)⁺, 372.1752); δ_H(200 MHz, CDCl₃) 3.99 (1 H, d, J 10.2 Hz, CH₂), 4.89 (1 H, d, J 10.2 Hz, CH₂), 7.10-7.90 (19 H, m, Ar-H, olefinic CH); δ_C(50 MHz, CDCl₃) 55.0 (CH₂), 126.1 (CH), 126.4 (CH), 126.5 (2 x CH), 127.3 (CH), 127.6 (CH), 127.8 (2 x CH), 127.9 (CH), 128.1 (CH), 128.6 (2 x CH), 128.8 (CH), 129.3 (2 x CH), 129.4 (CH), 129.9 (CH), 131.9 (CH), 134.7 (quat.), 136.1 (quat.), 137.3 (quat.), 139.1 (quat.), 140.6 (quat.), 142.1 (quat.), 168.2 (C=N); *m/z* (FAB) 373 (M+1, 82%), 372 (100), 265 (55), 217 (50), 179 (45), 106 (70); ν_{max}(Nujol)/cm⁻¹ 1711 (C=N).

*HPLC analysis showed the cyclised product to be 50% of this mixture.

(b) A nitrile ylide dimer (0.12 g) which resisted recrystallisation from any solvent system (Found: 743.3477. C₅₆H₄₃N₂ requires 743.3426); δ_H(200 MHz, CDCl₃) 6.74-8.10 (m, Ar-H, olefinic CH), 9.79 (s, HC=N); δ_C(50 MHz, CDCl₃) 122.6-144.4 (quat., CH), 191.9 (HC=N); *m/z* (FAB) 744 (M+1, 20%), 743 (30), 475 (16), 473 (11), 373 (55), 372 (100), 294 (12), 280 (18), 265 (34), 252 (33), 226 (24), 204 (20), 194 (17), 178 (78), 115 (40), 104 (24).

(1) Addition over 2 hours

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-(*E*-2-phenylethenyl)phenyl)benzyl]benzamide (0.75 g, 1.93 mmol), dry ether (35 cm³) and thionyl chloride (11.2 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and added slowly over a period of two

hours to a solution of potassium *tert*-butoxide (0.43 g, 3.86 mmol) in THF (20 cm³) at 0 °C, allowed to warm to room temperature and stirred for a further 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded three products.

(a) 11-(*E*-2-Phenylethenyl)-7-phenyl-5*H*-dibenz[*c,e*]azepine and a nitrile ylide dimer which were inseparable as a yellow glassy foam (0.13 g). HPLC analysis showed the mixture to be 62% cyclised product and 38% dimeric product.

(b) A nitrile ylide dimer (0.09 g) which resisted recrystallisation from any solvent system.

(2) Addition over 6 hours

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-(*E*-2-phenylethenyl)phenyl)benzyl]benzamide (0.75 g, 1.93 mmol), dry ether (35 cm³) and thionyl chloride (11.2 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and added slowly over a period of 6 hours to a solution of potassium *tert*-butoxide (0.43 g, 3.86 mmol) in THF (20 cm³) at 0 °C, allowed to warm to room temperature and stirred for a further 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded three products.

(a) 11-(*E*-2-Phenylethenyl)-7-phenyl-5*H*-dibenz[*c,e*]azepine and a nitrile ylide dimer which were inseparable as a yellow glassy foam (0.23g). HPLC analysis showed the mixture to be 80% cyclised product and 20% dimeric product.

(b) A nitrile ylide dimer (0.03 g) which resisted recrystallisation from any solvent system.

(3) Addition over 15 hours

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-(*E*-2-phenylethenyl)phenyl)benzyl]benzamide (0.75 g, 1.93 mmol), dry ether (35 cm³) and thionyl chloride (11.2 cm³). After drying the imidoyl chloride was dissolved in THF (40 cm³) and added slowly over a period of 15 hours to a solution of potassium *tert*-butoxide (0.43 g, 3.86 mmol) in THF (40 cm³) at 0 °C, allowed to warm to room temperature and stirred for a further 10 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded four products.

(a) 11-(*E*-2-Phenylethenyl)-7-phenyl-5*H*-dibenz[*c,e*]azepine and a nitrile ylide dimer which were inseparable as a yellow glassy foam (0.26 g). HPLC analysis showed the mixture to be 89% cyclised product and 11% dimeric product.

(b) A nitrile ylide dimer (0.01 g) which resisted recrystallisation from any solvent system.

(c) *N*-[2-(2-(*E*-2-phenylethenyl)phenyl)benzyl]benzamide (0.09 g, 12%).

(iv) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(2-Ethenylphenyl)benzyl]benzimidoyl chloride 192

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-ethenylphenyl)benzyl]benzamide (0.5 g, 1.59 mmol), dry ether (30 cm³) and thionyl chloride (9.19 cm³). After drying the imidoyl chloride was dissolved in THF (25 cm³) and cooled to 0 °C. Solid potassium *tert*-butoxide (0.36 g, 3.20 mmol) was added in one portion with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a further hour. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded four products.

(a) 11-Ethenyl-7-phenyl-5*H*-dibenz[*c,e*]azepine as an impure yellow solid which resisted recrystallisation from any solvent system (0.12 g, 25%), (Found: 296.1421. $C_{22}H_{17}N$ requires $(M+1)^+$, 296.1439); δ_H (250 MHz, $CDCl_3$) 3.93 (1 H, d, J 10.2 Hz, CH_2), 4.84 (1 H, d, J 10.2 Hz, CH_2), 5.30 (1 H, dd, J 1.3 Hz, 11.0 Hz, CH_2), 5.78 (1 H, dd, J 1.3 Hz, 17.0 Hz, CH_2), 6.80 (1 H, dd, J 11.0 Hz, 17.4 Hz, CH), 7.24-7.78 (12 H, m, Ar-H); δ_C (63 MHz, $CDCl_3$) 54.9 (CH_2), 115.3 (CH_2), 126.0 (CH), 126.3 (CH), 127.1 (CH), 127.8 (2 x CH), 128.2 (CH), 129.3 (2 x CH), 129.4 (CH), 130.8 (CH), 132.0 (CH), 134.5 (quat.), 136.5 (quat.), 137.0 (CH), 138.8 (quat.), 140.5 (quat.), 141.9 (quat.), 168.3 (quat.); m/z (FAB) 296 ($M+1$, 83%), 280 (12), 269 (19), 253 (31), 217 (20), 193 (76), 178 (57), 165 (55), 135 (43), 105 (44).

(b) A nitrile ylide dimer which resisted recrystallisation from any solvent system (0.17 g), (Found: 591.2796. $C_{44}H_{34}N_2$ requires $(M+1)^+$, 591.2800); δ_H (200 MHz, $CDCl_3$) 5.14 (dd, J 1.0 Hz, 11.0 Hz, CH_2), 5.63 (dd, J 1.0 Hz, 17.5 Hz, CH_2), 6.34 (dd, J 11.0 Hz, 17.5 Hz, CH), 6.50-8.07 (m, Ar-H), 9.75 (s, HC=N); m/z (FAB) 591 ($M+1$, 32%), 431 (38), 411 (17), 371 (37), 294 (34), 280 (27), 217 (45), 178 (78), 165 (73), 152 (32).

(c) A nitrile ylide dimer which resisted recrystallisation from any solvent system (0.09 g), (Found: 591.2799. $C_{44}H_{34}N_2$ requires $(M+1)^+$, 591.2800); δ_H (250 MHz, $CDCl_3$) 4.05 (s, CH_2), 4.82-4.98 (m, olefinic CH_2), 5.38-5.47 (m, olefinic CH_2), 6.40 (br, olefinic CH), 6.83-7.61 (m, Ar-H); δ_C (50 MHz, $CDCl_3$) 46.1 (CH_2), 114.3 (CH_2), 114.6 (CH_2), 124.8-134.2 (CH, quat.), 134.9 (quat.), 135.6 (quat.), 135.7 (quat.), 138.0 (quat.), 138.5 (quat.), 147.2 (quat.); m/z (FAB) 591 ($M+1$, 77%), 507 (11), 431 (18), 411 (17), 399 (41), 371 (32), 294 (14), 280 (17), 217 (56), 193 (70), 178 (78), 165 (73), 152 (32), 105 (31).

(d) *N*-[2-(2-ethenylphenyl)benzyl]benzamide (0.04 g, 8%).

(v) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(2-(2-Carbomethoxyethenyl)phenyl)benzyl]benzimidoyl chloride 195

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-(2-carbomethoxyethenyl)phenyl)benzyl]benzamide (0.79 g, 2.13 mmol), dry ether (35 cm³) and thionyl chloride (11.18 cm³). After drying the imidoyl chloride was dissolved in THF (40 cm³) and cooled to -78 °C. Lithium diisopropylamide (5.5 mmol), prepared as shown on page 188, was added in over a two hour period with rapid stirring under dry nitrogen. The mixture was stirred at -78 °C for a further 1 h, then warmed to room temperature. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) gave 3-methoxycarbonyl-2-phenyl-3a,11b-dihydro-3*H*-dibenzo[e,g]indole as a crystalline solid (0.38 g, 50%), mp 199 °C from hexane-ethyl acetate (Found: C, 81.7; H, 5.5; N, 3.9%; (M+1)⁺, 353.1411. C₂₄H₁₉NO₂ requires C, 81.6; H, 5.4; N, 4.0%; (M+1)⁺, 353.1416); δ_H(200 MHz, CDCl₃) 3.67 (3 H, s, CH₃), 3.72 (1 H, m, CH), 4.41 (1 H, dd, J 3.0 Hz, 12.0 Hz, CH), 4.80 (1 H, dd, J 3.0 Hz, 12.0 Hz, CH), 7.25-7.48 (8 H, m, Ar-H), 7.76-8.02 (5 H, m, Ar-H); δ_C(50 MHz, CDCl₃) 52.4 (CH), 52.5 (CH), 55.8 (CH₃), 74.4 (CH), 123.3 (CH), 123.9 (CH), 124.7 (2 x CH), 127.0 (2 x CH), 127.3 (CH), 127.5 (CH), 127.9 (2 x CH), 128.5 (2 x CH), 130.7 (2 x CH), 133.4 (quat.), 134.1 (quat.), 134.8 (quat.), 135.4 (quat.), 138.3 (quat.), 172.0 (quat.), 172.5 (quat.); *m/z* (FAB) 354 (M+1, 75%), 351 (100), 320 (75), 293 (70), 103 (65), 72 (100); ν_{max}(Nujol)/cm⁻¹ 1728 (C=O).

¹H nmr decoupling experiments; irradiation at δ 4.80 collapsed the dd at δ 4.41 to a d (J 13.0 Hz). Irradiation at δ 4.41 collapsed the dd at δ 4.80 to a d (J 13.0 Hz) and the signal at δ 3.67 became more complex. Irradiation at δ 3.72 resulted in the signals at δ 4.41 and δ 4.80 becoming very complex.

(vi) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(2-Ethenyl-6-methylphenyl)benzyl]benzimidoyl chloride 198

The imidoyl chloride was prepared as in (i) using *N*-[2-(2-ethenyl-6-methylphenyl)benzyl]benzamide (0.30 g, 0.87 mmol), dry ether (25 cm³) and thionyl chloride (4.55 cm³). After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to 0 °C. Solid potassium *tert*-butoxide (0.18 g, 1.73 mmol) was added in one portion with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a further 30 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded two products.

(a) A nitrile ylide dimer which resisted recrystallisation from any solvent system (0.2 g), (Found: 619.3108. C₄₆H₃₈N₂ requires 619.3113); δ_H(200 MHz, CDCl₃) 1.77 (s, CH₃), 1.99 (s, CH₃), 4.94 (pair dd, CH olefinic), 5.43 (pair dd, CH olefinic), 6.05 (pair dd, CH olefinic), 6.98-8.08 (m, Ar-H), 9.61 (s, CH), 9.62 (s, CH); δ_C(50 MHz, CDCl₃) 20.6 (CH₃), 20.7 (CH₃), 114.4 (CH₂), 115.5 (CH₂), 122.0 (CH), 122.5 (CH), 126.3-137.1 (CH and quat.), 141.4 (quat.), 144.0 (quat.), 158.4 (CH), 192.0 (CH); *m/z* (FAB) 619 (M+1, 35%), 521 (57), 461 (14), 413 (64), 391 (42), 327 (27), 308 (19), 294 (22), 279 (56), 205 (71), 193 (100), 133 (85).

(b) Unidentifiable product (0.05 g).

(vii) Generation and Reaction of the Nitrile Ylide derived from *N*-[3-Methyl-2-phenylbenzyl]benzimidoyl chloride 205

The imidoyl chloride was prepared as in (i) using *N*-[3-methyl-2-phenylbenzyl]benzamide (0.255 g, 0.80 mmol), dry ether (25 cm³) and thionyl chloride (4.60 cm³). After drying the imidoyl chloride was dissolved in THF (15 cm³) and cooled to 0 °C. Solid potassium *tert*-butoxide (0.17 g, 1.60 mmol) was added in one portion with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a further 30 minutes. The

usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded two dimeric products.

(a) A nitrile ylide dimer which resisted recrystallisation from any solvent system (0.12 g), (Found: 567.2799. $C_{42}H_{34}N_2$ requires 567.2800); δ_H (250 MHz, $CDCl_3$) 1.84 (s, CH_3), 2.21 (s, CH_3), 3.96 (br, CH_2), 6.39-7.54 (m, Ar-H); δ_C (63 MHz, $CDCl_3$) 20.2 (CH_3), 20.8 (CH_3), 45.8 (CH_2), 122.7 (CH), 125.9 (CH), 126.3 (CH), 126.4 (CH), 126.8 (CH), 127.2 (CH), 127.3 (CH), 127.8 (CH), 128.1 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.5 (CH), 130.7 (CH), 131.2 (CH), 134.6 (quat.), 135.5 (quat.), 135.6 (quat.), 135.8 (quat.), 136.8 (quat.), 138.7 (quat.), 138.8 (quat.), 139.1 (quat.), 141.5 (quat.), 147.4 (quat.); m/z (FAB) 567 (M+1, 100%), 566 (75), 399 (41), 387 (75), 265 (16), 204 (19), 192 (24), 178 (73), 165 (16), 115 (37).

(b) A nitrile ylide dimer which resisted recrystallisation from any solvent system (0.05 g), (Found: 567.2797. $C_{42}H_{34}N_2$ requires 567.2800); δ_H (250 MHz, $CDCl_3$) 2.02 (s, CH_3), 6.38-7.80 (m, CH), 9.70 (s, HC=N); m/z (FAB) 567 (M+1, 100%), 566 (60), 397 (25), 385 (20), 265 (36), 205 (15), 191 (12), 178 (35), 165 (46), 115 (20).

(viii) Generation and Reaction of the Nitrile Ylide derived from *N*-[3-Methyl-2-(2-ethenylphenyl)benzyl]benzimidoyl chloride 211

The imidoyl chloride was prepared by heating *N*-[3-methyl-2-(2-ethenylphenyl)benzyl]benzamide (0.3 g, 0.92 mmol), dry ether (30 cm³) and thionyl chloride (5.28 cm³) at reflux under dry nitrogen for 48 h. After drying the imidoyl chloride was dissolved in THF (20 cm³) and cooled to 0 °C. Solid potassium *tert*-butoxide (0.21 g, 1.87 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, allowed to warm to room temperature and stirred for a further 30 minutes. The usual work-up as in (i) and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded two dimeric products.

(a) A nitrile dimer which resisted recrystallisation from any solvent system (0.1 g), (Found: 619.3150. $C_{46}H_{38}N_2$ requires 619.3113); δ_H (250 MHz, $CDCl_3$) 1.92 (s, CH_3), 2.04 (s, CH_3), 4.98 (dd, J 1.0, 11.0 Hz, CH olefinic), 5.09 (dd, J 1.0, 11.0 Hz, CH olefinic), 5.48 (dd, J 0.8, 16.0 Hz, CH, olefinic), 5.61 (dd, J 1.1, 16.7 Hz, CH olefinic), 6.07 (m, CH olefinic), 6.80-7.89 (m, Ar-H), 9.59 (s, HC=N), 9.60 (s, HC=N); δ_C (63 MHz, $CDCl_3$) 19.6 (CH_3), 19.9 (CH_3), 114.7 (CH_2), 115.8 (CH_2), 123.9-135.3 (CH and quat.), 135.9-144.3 (quat.), 159.0 (CH); m/z (FAB) 619 (M+1, 17%), 521 (55), 413 (100), 385 (23), 311 (21), 279 (17), 239 (22), 221 (54).

(b) A nitrile ylide dimer which resisted recrystallisation from any solvent system (0.06 g), (Found: 619.3093. $C_{46}H_{38}N_2$ requires 619.3113); δ_H (250 MHz, $CDCl_3$) 1.79 (s, CH_3), 2.03 (s, CH_3), 4.08 (d, J 5.9 Hz, CH_2), 4.77 (m, CH, olefinic), 5.41 (m, CH, olefinic), 6.40-6.49 (m, CH olefinic), 6.82-7.60 (m, Ar-H); δ_C (63 MHz, $CDCl_3$) 19.8 (CH_3), 20.5 (CH_3), 46.8 (CH_2), 114.1 (CH_2), 114.8 (CH_2), 122.6-135.5 (CH), 135.6-146.8 (quat.); m/z (FAB) 620 (M+2, 70%), 619 (100), 425 (24), 414 (48), 397 (21), 385 (22), 335 (16), 207 (49), 192 (77), 179 (78), 165 (62), 105 (23).

X. Generation and Reaction of Substituted Nitrile Ylides derived from *N*-[2-Alkadienylbenzyl]benzimidoyl chlorides

(i) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

N-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.5 g, 1.17 mmol), thionyl chloride (5.90 cm³) and dry ether (40 cm³) were heated at reflux under dry nitrogen for 96 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Lithium

bis(trimethylsilyl)amide (1.75 cm³, 1.75 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 20 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 8-methyl-9,11,13-triphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene as a yellow crystalline solid (0.31 g, 65%), mp 181-182 °C from hexane-ethyl acetate (Found: C, 90.6; H, 6.4; N, 3.1%; (M+1)⁺, 412.2044. C₃₁H₂₅N requires C, 90.5; H, 6.1; N, 3.4%; (M+1)⁺, 412.2065); δ_H(250 MHz, CDCl₃) 1.33 (3 H, s, CH₃), 3.90 (1 H, m, CH), 5.26 (1 H, m, CH), 5.51 (1 H, m, CH), 7.15-7.61 (19 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 21.6 (CH₃), 45.6 (quat.), 48.0 (CH), 67.2 (CH), 120.8 (CH), 125.3 (CH), 126.3 (CH), 126.8 (CH), 127.0 (CH), 127.1 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 129.3 (CH), 138.9 (quat.), 139.7 (quat.), 140.6 (quat.), 141.9 (quat.), 144.1 (quat.), 144.3 (quat.), 181.1 (quat.); *m/z* (FAB) 414 (M+1, 67%), 413 (75), 412 (100), 362 (18), 334 (16), 320 (18), 307 (34), 293 (31), 278 (28), 253 (19), 239 (20), 215 (73), 191 (57), 165 (26), 128 (23), 91 (92); ν_{max}(Nujol)/cm⁻¹ 1600 (C=N).

(ii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 251

N-[2-(*E,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.5 g, 1.17 mmol), dry ether (40 cm³) and thionyl chloride (5.80 cm³) were heated at reflux under dry nitrogen for 96 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.75 cm³, 1.75 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1

h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 20 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 7b-methyl-1-*endo*-phenyl-1a-phenyl-1-(*E*-2-phenylethenyl)cyclopropa[*c*]isoquinoline as a yellow crystalline solid (0.32 g, 65%), mp 167-169 °C from pentane-DCM* (Found: C, 90.9; H, 6.5; N, 3.2%; (M+1)⁺, 412.2050. C₃₁H₂₅N requires C, 90.5; H, 6.1; N, 3.4%; (M+1)⁺, 412.2065); δ_{H} (200 MHz, CDCl₃) 1.80 (3 H, s, CH₃), 5.59 (1 H, d, J 15.7 Hz, CH), 6.16 (1 H, d, J 15.7 Hz, CH), 6.76-7.62 (19 H, m, Ar-H), 7.78 (1 H, s, HC=N); δ_{C} (63 MHz, CDCl₃) 19.8 (CH₃), 37.7 (quat.), 39.9 (quat.), 65.0 (quat.), 125.6 (CH), 125.7 (CH), 125.8 (2 x CH), 126.0 (CH), 126.1 (CH), 126.8 (CH), 127.2 (CH), 127.3 (CH), 127.6 (CH), 128.3 (3 x CH), 128.6 (2 x CH), 131.3 (2 x CH), 131.9 (CH), 132.5 (2 x CH), 134.3 (quat.), 134.7 (CH), 137.6 (quat.), 139.2 (quat.), 139.4 (quat.), 155.7 (HC=N); *m/z* (FAB) 413 (M+1, 85%), 412 (89), 307 (41), 292 (11), 220 (62), 215 (13), 191 (13), 165 (26), 153 (28), 138 (100), 124 (16), 105 (63), 90 (81); ν_{max} (Nujol)/cm⁻¹ 1624 (C=N).

* isothermal distillation.

(iii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*Z,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 252

N-[2-(*Z,Z*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.5 g, 1.17 mmol), dry ether (40 cm³) and thionyl chloride (5.80 cm³) were heated at reflux under dry nitrogen for 96 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.75 cm³, 1.75 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1

h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 20 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 7b-methyl-1-endo-phenyl-1a-phenyl-1-(*Z*-2-phenylethenyl)cyclopropa[*c*]isoquinoline as a colourless crystalline solid (0.34 g, 70%), mp 134-136 °C from pentane-DCM* (Found: C, 90.2; H, 6.3; N, 3.3%; (M+1)⁺, 412.2085. C₃₁H₂₅N requires C, 90.5; H, 6.1; N, 3.4%; (M+1)⁺, 412.2065); δ_H(250 MHz, CDCl₃) 1.80 (3 H, s, CH₃), 6.15 (1 H, d, J 12.1 Hz, CH), 6.53-7.81 (20 H, m, Ar-H, olefinic CH), 7.77 (1 H, s, HC=N); δ_C(63 MHz, CDCl₃) 21.1 (CH₃), 35.3 (quat.), 36.0 (quat.), 63.6 (quat.), 125.2 (CH), 125.7 (CH), 126.1 (CH), 126.2 (CH), 126.3 (CH), 126.4 (CH), 126.9 (CH), 127.3 (2 x CH), 127.4 (CH), 128.2 (2 x CH), 128.4 (CH), 128.7 (2 x CH), 130.7 (CH), 131.3 (2 x CH), 131.9 (CH), 132.8 (CH), 133.4 (CH), 135.2 (quat.), 137.2 (quat.), 138.7 (quat.), 155.0 (HC=N); *m/z* (FAB) 414 (M+1, 17%), 413 (100), 412 (78), 396 (22), 334 (23), 320 (13), 308 (33), 292 (11), 220 (82), 215 (34), 206 (10), 191 (35), 165 (26), 138 (54), 115 (26), 105 (69), 91 (43); ν_{max}(Nujol)/cm⁻¹ 1624 (C=N). * isothermal distillation.

(iv) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E*-5'-methyl-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]benzimidoyl chloride 280

Thionyl chloride (0.048 cm³, 0.65 mmol) was added to *N*-[2-(*E*-5'-methyl-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide (0.2 g, 0.52 mmol) in dry DMF (0.6 g, 7.7 mmol) and stirred under a nitrogen atmosphere for 30 minutes. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (10 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (2.08 cm³, 2.08 mmol) was added dropwise with rapid stirring under dry

nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 15 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 10 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave (a) 7b-Methyl-1-*exo*-phenyl-1a-phenyl-1-(2'-methylprop-1'-enyl)cyclopropa[c]isoquinoline as a yellow solid (0.05 g, 20%), which decomposes at room temperature, (Found: (M+1)⁺, 364.2059. C₂₇H₂₅N requires (M+1)⁺, 364.2065); δ_H(250 MHz, CDCl₃) 1.25 (3 H, s, CH₃), 1.34 (3 H, s, CH₃), 1.57 (3 H, s, CH₃), 4.64 (1 H, s, CH), 7.06-7.67 (14 H, m, Ar-H), 8.25 (1 H, s, HC=N); δ_C(63 MHz, CDCl₃) 19.0 (CH₃), 21.2 (CH₃), 25.0 (CH₃), 35.5 (quat.), 36.4 (quat.), 62.5 (quat.), 122.7 (CH), 125.6 (CH), 126.2 (CH), 126.8 (CH), 127.6 (2 x CH), 127.8 (2 x CH), 128.4 (CH), 130.5 (2 x CH), 131.0 (2 x CH), 131.7 (quat.), 137.5 (quat.), 137.8 (quat.), 139.7 (quat.), 155.3 (HC=N); *m/z* (FAB) 362 (M+1, 100%), 348 (15), 289 (12), 260 (32), 245 (17), 215 (21), 178 (22), 143 (65), 117 (29); ν_{max}(Nujol)/cm⁻¹ 1624 (C=N). (b) Starting material (0.05 g, 20%).

(v) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E,E*-3'-Phenylhexa-2',4'-dien-2'-yl)benzyl]benzimidoyl chloride 276

Thionyl chloride (0.053 cm³, 0.72 mmol) was added to *N*-[2-(*E,E*-3'-phenylhexa-2',4'-dien-2'-yl)benzyl]benzamide (0.2 g, 0.6 mmol) in dry DMF (0.72 g, 9.2 mmol) and stirred under a nitrogen atmosphere for 30 minutes. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (10 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (3.52 cm³, 3.52 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 10 cm³) was added and the

mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 10 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 8,11-dimethyl-9,13-diphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene as a clear crystalline solid (0.11 g, 46%), mp 149-150 °C from pentane-DCM* (Found: C, 89.0; H, 6.9; N, 3.9%; (M+1)⁺, 350.1909. C₂₆H₂₃N requires C, 89.3; H, 6.6; N, 4.0%; (M+1)⁺, 350.1909); δ_H(250 MHz, CDCl₃) 1.16 (3 H, s, CH₃), 1.34 (3 H, t, CH₃), 2.57 (1 H, m, CH), 4.91 (1 H, t, CH), 5.16 (1 H, d, J 1.6 Hz, CH), 6.93-7.39 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 17.9 (CH₃), 21.5 (CH₃), 37.0 (CH), 45.1 (quat.), 66.2 (CH), 120.5 (CH), 125.3 (CH), 126.1 (CH), 126.6 (CH), 126.7 (CH), 127.3 (2 x CH), 127.6 (2 x CH), 127.9 (2 x CH), 128.0 (CH), 128.5 (2 x CH), 132.0 (CH), 139.1 (quat.), 139.6 (quat.), 141.9 (quat.), 142.3 (quat.), 144.0 (quat.), 181.3 (quat.); *m/z* (FAB) 350 (M+1, 100%), 246 (77), 231 (19), 215 (24);; ν_{max}(Nujol)/cm⁻¹ 1624 (C=N). * isothermal distillation.

(vi) Generation and Reaction of the Nitrile Ylide derived from N-[2-(Methyl *E,E*-4'-phenylhexa-2',4'-dienoat-5'-yl)benzyl] benzimidoyl chloride 272

N-[2-(Methyl-*E,E*-4'-phenylhexa-2',4'-dienoate-5'-yl)benzyl] benzamide (0.5 g, 1.22 mmol), dry ether (6.20 cm³) and thionyl chloride (50 cm³) were heated at reflux under dry nitrogen for 144 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.83 cm³, 1.83 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer separated and the aqueous layer extracted with DCM (2 x 20 cm³). The combined organic layers were dried and the solvent

removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded 11-methoxycarbonyl-8-methyl-9,13-diphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene as a mixture of diastereoisomers which resisted crystallisation from all solvent systems (96 mg, 20%); (Found: (M+1)⁺, 394.1816. C₂₇H₂₃NO₂ requires (M+1)⁺, 394.1810); δ_{H} (250 MHz, CDCl₃) 1.18 (s, CH₃), 1.21 (s, CH₃)^{*}, 3.61 (s, ester CH₃), 3.75 (m, CH)^{*}, 3.77 (m, CH), 5.21 (m, CH), 5.32 (1 H, d, J 1.8 Hz, CH)^{*}, 5.63 (1 H, t, 1.8 Hz, CH)^{*}, 5.73 (m, CH), 6.99-7.68 (m, Ar-H); δ_{C} (63 MHz, CDCl₃) 21.4 (CH₃), 24.0 (CH₃), 44.0 (CH), 45.7 (CH), 46.0 (quat.), 46.1 (quat.), 52.1 (CH₃), 52.4 (CH₃), 61.2 (CH), 62.5 (CH), 120.7 (CH), 120.9 (CH), 123.6-145.4 (CH and quat.), 170.5 (quat.), 171.1 (quat.); *m/z* (FAB) 395 (M+1, 100%), 394 (65), 289 (25), 231 (12), 226 (11), 220 (34), 215 (27), 176 (21), 165 (25); ν_{max} (Nujol)/cm⁻¹ 1644 (C=N), 1735 (C=O). * major isomer absorptions.

(vii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(2'-(*E*-2-Phenylethenyl)cyclopent-1'-enyl)benzyl]benzimidoyl chloride 266

N-[2-(2'-(*E*-2-Phenylethenyl)cyclopent-1'-enyl)benzyl]benzamide (0.5 g, 1.32 mmol), dry ether (50 cm³) and thionyl chloride (6.60 cm³) were heated at reflux under dry nitrogen for 24 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.98 cm³, 1.98 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 20 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 7,15-diphenyl-16-

azatetracyclo[6.6.2.0^{1,5}.0^{9,14}]hexadeca-5,9(14),10,12,15-pentaene as a brown crystalline solid (0.3 g, 63%), mp 144-146 °C from hexane-ethyl acetate (Found: C, 89.7; H, 6.8; N, 3.7%; (M+1)⁺, 362.1908. C₂₇H₂₃N requires C, 89.7; H, 6.4; N, 3.9%; (M+1)⁺, 362.1909); δ_H(250 MHz, CDCl₃) 1.81-2.62 (6 H, m, CH₂), 3.76 (1 H, t, J 2.6 Hz, CH), 5.20 (1 H, t, J 1.6 Hz, CH), 5.49 (1 H, dd, J 2.0 Hz, 2.7 Hz, CH), 7.18-7.55 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 24.8 (CH₂), 33.6 (CH₂), 34.5 (CH₂), 45.0 (CH), 53.5 (quat.), 68.6 (CH), 119.3 (CH), 120.2 (CH), 125.5 (CH), 126.0 (CH), 126.5 (CH), 126.7 (CH), 127.4 (CH), 127.8 (CH), 128.2 (CH), 128.3 (CH), 139.1 (quat.), 139.4 (quat.), 141.2 (quat.), 142.5 (quat.), 146.8 (quat.), 181.4 (quat.); *m/z* (FAB) 364 (M+1, 17%), 363 (38), 362 (100), 258 (24), 229 (12), 215 (17), 203 (11), 167 (17), 152 (12), 128 (12), 104 (11), 91 (36); ν_{max}(Nujol)/cm⁻¹ 1621 (C=N).

(viii) Generation and Reaction of the Nitrile Ylide derived from N-[2-(2'-(2-Carbomethoxyethenyl)cyclopent-1'-enyl)benzyl]benzimidoyl chloride 269

N-[2-(2'-(2-Carbomethoxyethenyl)cyclopent-1'-enyl)benzyl]benzamide (0.5 g, 1.38 mmol), dry ether (50 cm³) and thionyl chloride (7.0 cm³) were heated at reflux under dry nitrogen for 96 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (2.08 cm³, 2.08 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 20 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (4:1) afforded 7-methoxycarbonyl-15-phenyl-16-azatetracyclo[6.6.2.0^{1,5}.0^{9,14}]hexadeca-5,9(14),10,12,15-pentaene as a

mixture of diastereoisomers which were partially separated by MPLC eluting with hexane-ethyl acetate (6:1), (0.2 g, 42%). (a) (Found: (M+1)⁺, 344.1648. C₂₃H₂₁NO₂ requires (M+1)⁺, 344.16501); δ_H(200 MHz, CDCl₃) 1.73-2.75 (6 H, m, CH₂), 3.57 (1 H, m, CH), 3.64 (3 H, s, CH₃), 5.22 (1 H, d, J 2.7 Hz, CH), 5.62 (1 H, m, CH), 7.01-7.73 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 24.8 (CH₂), 33.3 (CH₂), 34.4 (CH₂), 42.9 (CH), 52.3 (CH₃), 53.8 (quat.), 63.7 (CH), 114.2 (CH), 120.4 (CH), 126.0 (CH), 126.2 (CH), 127.0 (CH), 127.6 (2 x CH), 127.9 (2 x CH), 128.6 (CH), 137.1 (quat.), 142.3 (quat.), 147.3 (quat.), 171.8 (quat.); *m/z* (FAB) 344 (M+1, 76%), 255 (13), 240 (46), 223 (16), 181 (53), 165 (23), 105 (100); ν_{max}(Nujol)/cm⁻¹ 1625 (C=N), 1734 (C=O). (b) (Found: (M+1)⁺, 344.1647. C₂₃H₂₁NO₂ requires (M+1)⁺, 344.1651); δ_H(200 MHz, CDCl₃) 1.71-2.57 (6 H, m, CH₂), 3.33 (1 H, br, CH), 3.78 (3 H, s, CH₃), 5.11 (1 H, br, CH), 5.72 (1 H, br, CH), 7.15-7.43 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 24.9 (CH₂), 33.4 (CH₂), 34.5 (CH₂), 41.3 (CH), 52.0 (CH₃), 54.2 (quat.), 62.8 (CH), 114.0 (CH), 120.2 (CH), 126.0 (CH), 126.8 (CH), 126.9 (CH), 127.3 (2 x CH), 128.0 (2 x CH), 128.2 (CH), 128.4 (CH), 137.1 (quat.), 143.6 (quat.), 146.7 (quat.), 171.4 (quat.); *m/z* (FAB) 344 (M+1, 82%), 343 (38), 255 (13), 240 (67), 223 (15), 181 (73), 165 (30), 105 (100); ν_{max}(Nujol)/cm⁻¹ 1625 (C=N), 1731 (C=O).

(ix) Attempted Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

(1) Attempted Generation of *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

N-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.05 g, 0.116 mmol), dry ether (5.0 cm³) and thionyl chloride (0.67 cm³) were heated at reflux under dry nitrogen for 24 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h.

(2) Attempted Generation of *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

N-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.05 g, 0.116 mmol), dry ether (5.0 cm³) and thionyl chloride (28 mg, 0.13 mmol) were heated at reflux under dry nitrogen for 24 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h.

(3) Attempted Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

Thionyl chloride (0.013 cm³, 0.174 mmol) was added to *N*-[2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.05 g, 0.116 mmol) in dry d₇DMF (0.5 cm³) under a nitrogen atmosphere. The reaction was monitored by ¹H nmr spectroscopy and formation of the imidoyl chloride was found to be complete after 30 minutes. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (5 cm³) was added and the solution cooled to 0 °C. Solid potassium *tert*-butoxide (0.04 g, 0.348 mmol) was added with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 5 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 5 cm³). The combined organic layers were dried and the solvent removed *in vacuo* to yield only starting material.

(4) Attempted Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E,E*-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

Thionyl chloride (0.013 cm³, 0.174 mmol) was added to *N*-[2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.05 g, 0.116 mmol) in dry d₇DMF (0.5 cm³) under a nitrogen atmosphere. The reaction was

monitored by ^1H nmr spectroscopy and formation of the imidoyl chloride was found to be complete after 30 minutes. Dry THF (10 cm³) was added and the solution cooled to 0 °C. Solid potassium *tert*-butoxide (0.50 g, 0.464 mmol) was added with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 5 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 5 cm³). The combined organic layers were dried and the solvent removed *in vacuo* to yield only starting material.

(5) Attempted Generation and Reaction of the Nitrile Ylide derived from N-[2-(E,E-1',3'-Diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride 232

Thionyl chloride (0.013 cm³, 0.174 mmol) was added to *N*-[2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide (0.05 g, 0.116 mmol) in dry d₇DMF (0.5 cm³) under a nitrogen atmosphere. Formation of the imidoyl chloride was complete after 30 minutes. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (10 cm³) was added and the solution cooled to 0 °C. Lithium diisopropylamide (0.348 mmol), prepared as shown on page 188, was added with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 5 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 5 cm³). The combined organic layers were dried and the solvent removed *in vacuo* to yield only starting material.

^1H Nmr spectrum of *N*-[2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzimidoyl chloride; δ_{H} (200 MHz, d₇DMF) 1.82 (3 H, s, CH₃), 4.90 (2 H, s, CH₂), 5.78 (1 H, d, J 16.1 Hz, CH), 6.70 (1 H, d, J 16.1 Hz, CH), 6.94-8.01 (19 H, m, Ar-H).

^1H Nmr spectrum of *N*-[2-(*E,E*-1',3'-diphenylpenta-1',3'-dien-4'-yl)benzyl]benzamide; δ_{H} (200 MHz, $d_7\text{DMF}$) 1.95 (3 H, s, CH_3), 4.71 (2 H, m, CH_2), 5.91 (1 H, d, J 16.0 Hz, CH), 6.70 (1 H, d, J 16.1 Hz, CH), 6.94-8.01 (19 H, m, Ar-H), 8.96 (1 H, br, NH).

XI. Generation and Reaction of Substituted Nitrile Ylides derived from *N*-[2-Alkenylbenzyl]benzimidoyl chlorides

(i) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(Propen-2'-yl)benzyl]benzimidoyl chloride 313

N-[2-(Propen-2'-yl)benzyl]benzamide (0.5 g, 1.99 mmol), dry ether (40 cm^3) and phosphorus pentachloride (0.54 g, 2.2 mmol) were heated at reflux under dry nitrogen for 24 h. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 $^{\circ}\text{C}$ for 2-3 h. Dry THF (30 cm^3) was added and the solution cooled to 0 $^{\circ}\text{C}$. Lithium bis(trimethylsilyl)amide (2.99 cm^3 , 2.99 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 $^{\circ}\text{C}$ for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 30 cm^3) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 30 cm^3). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 7b-methyl-1a-phenyl-1*H*-cyclopropa[*c*]isoquinoline as a yellow oil (0.35 g, 75%), (Found: $(\text{M}+1)^+$, 234.1279. $\text{C}_{17}\text{H}_{15}\text{N}$ requires $(\text{M}+1)^+$, 234.1283); δ_{H} (250 MHz, CDCl_3) 0.18 (1 H, d, J 5.1 Hz, CH_2), 1.29 (3 H, s, CH_3), 2.51 (1 H, d, J 5.1 Hz, CH_2), 7.25-7.63 (9 H, m, Ar-H), 8.29 (1 H, s, $\text{HC}=\text{N}$); δ_{C} (63 MHz, CDCl_3) 19.0 (CH_3), 24.6 (CH_2), 31.0 (quat.), 57.4 (quat.), 123.5 (quat.), 124.7 (CH), 125.5 (CH), 127.0 (CH), 128.1 (2 x CH), 129.1 (2 x CH), 129.5 (CH), 131.2

(CH), 140.2 (quat.), 140.6 (quat.), 153.8 (CH); m/z (FAB) 235 (M+1, 73%), 234 (84), 233 (75), 219 (70), 205 (37), 180 (22), 167 (22), 156 (33), 141 (23), 128 (92), 116 (35), 105 (49), 91 (100); ν_{\max} (Nujol)/ cm^{-1} 1615 (C=N).

(ii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E*-1'-Phenylpropen-2'-yl)benzyl]benzimidoyl chloride 317

N-[2-(*E*-1'-Phenylpropen-2'-yl)benzyl]benzamide (0.24 g, 0.31 mmol), dry ether (12 cm^3) and phosphorus pentachloride (0.20 g, 0.34 mmol) were heated at reflux under dry nitrogen for 24 h. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (12 cm^3) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (1.10 cm^3 , 1.10 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 15 cm^3) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 15 cm^3). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 7b-methyl-1-*exo*-phenyl-1a-phenyl-1*H*-cyclopropa[*c*]isoquinoline as a white crystalline solid (0.15 g, 66%), mp 156-158 °C from pentane-DCM* (Found: C, 89.4; H, 6.2; N, 4.2%; (M+1)⁺, 310.1591. C₂₃H₁₉N requires C, 89.3; H, 6.2; N, 4.5%; (M+1)⁺, 310.1596); δ_{H} (250 MHz, CDCl₃) 1.54 (3 H, s, CH₃), 3.30 (1 H, s, CH), 6.76-7.76 (14 H, m, Ar-H), 8.07 (1 H, d, J 0.7 Hz, HC=N); δ_{C} (63 MHz, CDCl₃) 21.1 (CH₃), 30.3 (CH, C-1), 34.6 (quat., C-7b), 61.2 (quat., C-1a), 125.6 (CH), 125.7 (CH), 125.9 (CH), 127.2 (CH), 128.2 (CH), 129.2 (CH), 131.2 (CH), 132.0 (CH), 132.8 (quat.), 136.9 (quat.), 141.8 (quat.), 155.2 (HC=N); m/z (FAB) 310 (M+1, 67%), 309 (100), 308 (68), 304 (17), 296 (60), 279 (24), 265 (28), 252 (36), 230 (39), 220 (76), 216 (62), 205 (51), 193 (21), 178 (61), 165 (45), 152 (28), 139 (24); ν_{\max} (Nujol)/ cm^{-1} 1600 (C=N).

* isothermal distillation.

(iii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(3'-Methylbut-2'-enyl)benzyl]benzimidoyl chloride 322

N-[2-(3'-Methylbut-2'-enyl)benzyl]benzamide (0.75 g, 2.68 mmol), dry ether (75 cm³) and phosphorus pentachloride (0.75 g, 3.59 mmol) were heated at reflux under dry nitrogen for 60 h. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (40 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (4.04 cm³, 4.04 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 40 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 25 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 1,1a,7b-trimethyl-1a-phenylcyclopropa[*c*]isoquinoline as a white crystalline solid (0.53 g, 75%), mp 143-144 °C from hexane-ethanol (Found: C, 87.5; H, 7.5; N, 5.1%; (M+1)⁺, 261.1515. C₁₉H₁₉N requires C, 87.3; H, 7.3; N, 5.4%; (M+1)⁺, 261.1518); δ_H(250 MHz, CDCl₃) 0.69 (3 H, s, CH₃), 1.35 (3 H, s, CH₃), 1.49 (3 H, s, CH₃), 7.25-7.55 (9 H, m, Ar-H), 8.30 (1 H, s, HC=N); δ_C(63 MHz, CDCl₃) 15.7 (CH₃), 18.8 (CH₃), 18.9 (quat.), 20.1 (CH₃), 31.9 (quat.), 62.4 (quat.), 125.5 (CH), 125.6 (CH), 126.1 (CH), 126.8 (CH), 128.1 (CH), 128.3 (2 x CH), 130.8 (2 x CH), 131.2 (CH), 139.1 (quat.), 140.6 (quat.), 154.5 (quat.); *m/z* (EI) 261 (M⁺, 27%), 260 (100), 158 (33), 143 (80), 141 (12), 128 (34), 115 (20), 103 (11); ν_{max}(Nujol)/cm⁻¹ 1618 (C=N).

(iv) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*Z*-3'-Phenylbut-2'-enyl)benzyl]benzimidoyl chloride 332

N-[2-(*Z*-3'-Phenylbut-2'-enyl)benzyl]benzamide (0.5 g, 1.50 mmol), dry ether (25 cm³) and phosphorus pentachloride (0.43 g, 2.0 mmol) were heated at reflux under dry nitrogen for 60 h. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (25 cm³) was added and the solution cooled to 0 °C. Solid potassium *tert*-butoxide (0.34 g, 3.0 mmol) was added with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 25 cm³) was added and the mixture stirred for 10 minutes. The organic layer separated and the aqueous layer extracted with DCM (2 x 25 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 1,7b-dimethyl-1-*endo*-phenyl-1a-phenylcyclopropa[*c*]isoquinoline as a white oil (0.35 g, 72%), (Found: (M+1)⁺, 324.1763. C₂₄H₂₁N requires (M+1)⁺, 324.1752); δ_H(200 MHz, CDCl₃) 1.01 (3 H, s, CH₃), 1.58 (3 H, s, CH₃), 7.13-7.75 (14 H, m, Ar-H), 8.47 (1 H, s, HC=N); δ_C(63 MHz, CDCl₃) 20.8 (CH₃), 22.6 (CH₃), 28.8 (quat.), 32.8 (quat.), 61.9 (quat.), 125.9 (CH), 126.3 (CH), 126.4 (CH), 126.5 (CH), 127.3 (quat.), 127.6 (2 x CH), 127.9 (2 x CH), 128.6 (CH), 130.5 (2 x CH), 131.0 (2 x CH), 132.0 (CH), 138.3 (quat.), 140.7 (quat.), 141.4 (quat.), 156.0 (HC=N); *m/z* (FAB) 324 (M+1, 100%), 323 (36), 220 (39), 205 (10), 153 (21); ν_{max}(Nujol)/cm⁻¹ 1625 (C=N).

(v) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(*E*-3'-Phenylbut-2'-enyl)benzyl]benzimidoyl chloride 328

N-[2-(*E*-3'-Phenylbut-2'-enyl)benzyl]benzamide (0.20 g, 0.59 mmol), dry ether (10 cm³) and phosphorus pentachloride (0.17 g, 1.37 mmol) were heated at reflux under dry nitrogen for 60 h. The solvent was removed *in*

vacuo and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (10 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (2.36 cm³, 2.36 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 10 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 10 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 1,7b-dimethyl-1-*exo*-phenyl-1a-phenylcyclopropa[c]isoquinoline as a white solid (0.13 g, 70%), mp 179-181 °C from pentane-DCM* (Found: C, 88.9; H, 6.4; N, 4.0%; (M+1)⁺, 324.1752. C₂₄H₂₁N requires C, 89.1; H, 6.5; N, 4.3%; (M+1)⁺, 324.1752); δ_H(200 MHz, CDCl₃) 1.49 (3 H, s, CH₃), 1.68 (3 H, s, CH₃), 7.03-7.64 (14 H, m, Ar-H), 7.75 (1 H, s, HC=N); δ_C(63 MHz, CDCl₃) 18.9 (CH₃), 23.4 (CH₃), 33.5 (quat.), 34.3 (quat.), 62.7 (quat.), 125.2 (CH), 125.4 (2 x CH), 127.0 (CH), 127.1 (2 x CH), 128.0 (CH), 128.4 (2 x CH), 131.0 (2 x CH), 131.2 (CH), 131.5 (quat.), 139.3 (quat.), 139.9 (quat.), 140.6 (quat.), 154.6 (HC=N); *m/z* (FAB) 324 (M+1, 100%), 323 (52), 220 (54), 205 (15); ν_{max}(Nujol)/cm⁻¹ 1623 (C=N). * isothermal distillation.

(vi) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(2'-Methylpent-2'-en-3'-yl)benzyl]benzimidoyl chloride 336

Thionyl chloride (0.06 cm³, 0.81 mmol) was added to *N*-[2-(2'-methylpent-2'-en-3'-yl)benzyl]benzamide (0.2 g, 0.68 mmol) in dry DMF (0.8 g, 10.2 mmol) and stirred under a nitrogen atmosphere for 30 minutes. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (15 cm³) was added and the solution cooled to 0 °C. Lithium bis(trimethylsilyl)amide (2.72 cm³, 2.72 mmol) was added dropwise with rapid stirring under dry nitrogen. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room

temperature. Ammonium chloride (25% w/v, 15 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 15 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) afforded 7b-ethyl-1,1-dimethyl-1a-phenylcyclopropa[c]isoquinoline as a yellow oil (0.15 g, 80%), (Found: (M+1)⁺, 276.1761. C₂₀H₂₁N requires (M+1)⁺, 276.1752); δ_{H} (200 MHz, CDCl₃) 0.59 (3 H, s, CH₃), 1.00 (3 H, t, CH₃), 1.34 (3 H, s, CH₃), 1.44 (1 H, q, CH₂), 2.09 (1 H, q, CH₂), 7.18-7.41 (9 H, m, Ar-H), 8.21 (1 H, s, HC=N); δ_{C} (63 MHz, CDCl₃) 12.4 (CH₃), 16.5 (CH₃), 19.1 (quat.), 20.3 (CH), 23.1 (CH₂), 37.1 (quat.), 62.6 (quat.), 125.6 (CH), 126.5 (quat.), 127.0 (CH), 127.4 (CH), 128.3 (2 x CH), 128.6 (CH), 130.7 (2 x CH), 130.9 (CH), 137.2 (quat.), 140.8 (quat.), 154.8 (HC=N); *m/z* (FAB) 277 (M+1, 73%), 276 (62), 275 (100), 260 (21), 246 (86), 234 (87), 218 (27), 204 (20), 172 (82), 157 (61), 143 (72), 105 (35); ν_{max} (Nujol)/cm⁻¹ 1626 (C=N).

(vii) Generation and Reaction of the Nitrile Ylide derived from *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzimidoyl chloride 340

Thionyl chloride (0.034 cm³, 0.46 mmol) was added to *N*-[2-(1',1'-diphenylpropen-2'-yl)benzyl]benzamide (0.15 g, 0.39 mmol) in dry DMF (0.46 g, 5.89 mmol) and stirred under a nitrogen atmosphere for 30 minutes. The solvent was removed *in vacuo* and the residue dried under high vacuum at 30-40 °C for 2-3 h. Dry THF (15 cm³) was added and the solution cooled to 0 °C. Potassium *tert*-butoxide (0.26 g, 2.34 mmol) was added in one portion. The mixture was stirred at 0 °C for 1 h, then allowed to warm to room temperature. Ammonium chloride (25% w/v, 15 cm³) was added and the mixture stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with DCM (2 x 15 cm³). The combined organic layers were dried and the solvent removed *in vacuo*. Dry-flash column chromatography on silica, eluting with hexane-

ethyl acetate (9:1) afforded 7b-methyl-1,1,1a-triphenylcyclopropa[c]isoquinoline as a yellow solid (0.10 g, 67%), mp 178-180 °C from pentane-DCM* (Found: C, 90.2; H, 6.2; N, 3.3%; (M+1)⁺, 386.1935. C₂₉H₂₃N requires C, 90.4; H, 6.0; N, 3.6%; (M+1)⁺, 386.1909); δ_H(200 MHz, CDCl₃) 1.76 (3 H, s, CH₃), 6.77-7.80 (19 H, m, Ar-H), 7.83 (1 H, s, HC=N); δ_C(63 MHz, CDCl₃) 22.3 (CH₃), 35.4 (quat.), 42.9 (quat.), 62.6 (quat.), 125.1 (CH), 125.8 (CH), 125.9 (CH), 126.1 (CH), 126.6 (CH), 127.7 (2 x CH), 127.9 (2 x CH), 128.3 (CH), 130.8 (2 x CH), 131.1 (2 x CH), 131.7 (CH), 138.4 (quat.), 140.0 (quat.), 140.1 (quat.), 140.4 (quat.), 155.8 (HC=N); *m/z* (FAB) 386 (M+1, 99%), 385 (M+1, 100), 369 (20), 282 (44), 268 (20), 239 (15), 220 (36), 205 (20), 178 (32), 165 (82), 115 (10), 93 (16); ν_{max}(Film)/cm⁻¹ 1625 (C=N). * isothermal distillation.

(1) Attempted Generation of *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzimidoyl chloride 340

N-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzamide (0.1 g, 0.25 mmol), dry ether (10 cm³) and phosphorus pentachloride (68 mg, 0.32 mmol) were heated at reflux under dry nitrogen for 48 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. The ¹H nmr spectrum showed the presence of starting material and no imidoyl chloride.

(2) Attempted Generation of *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzimidoyl chloride 340

N-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzamide (0.1 g, 0.25 mmol), dry ether (10 cm³) and phosphorus pentachloride (68 mg, 0.32 mmol) were heated at reflux under dry nitrogen for 168 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. The ¹H nmr spectrum showed the presence of starting material and no imidoyl chloride.

(3) Attempted Generation of *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzimidoyl chloride 340

N-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzamide (0.05 g, 0.116 mmol), dry ether (5 cm³), dry THF (5 cm³) and phosphorus pentachloride (28 mg, 0.13 mmol) were heated at reflux under dry nitrogen for 48 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. The ¹H nmr spectrum showed the presence of starting material and no imidoyl chloride.

(4) Attempted Generation of *N*-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzimidoyl chloride 340

N-[2-(1',1'-Diphenylpropen-2'-yl)benzyl]benzamide (0.1 g, 0.25 mmol), dry ether (10 cm³) and thionyl chloride (1.26 cm³) were heated at reflux under dry nitrogen for 48 h. The solvent was removed *in vacuo* and the residue dried under high vacuum for 2-3 h. The ¹H nmr spectrum showed the presence of starting material and no imidoyl chloride.

XII. Thermal Isomerisation of Cyclopropa[c]isoquinolines

(i) Thermal Isomerisation of 7b-Methyl-1-endo-phenyl-1a-phenyl-1-(*E*-2-phenylethenyl)cyclopropa[c]isoquinoline 255

7b-Methyl-1-endo-phenyl-1a-phenyl-1-(*E*-2-phenylethenyl)cyclopropa[c]isoquinoline (0.05 g, 0.133 mmol) in dry C₆D₆ (0.7 cm³) was heated under reflux for 35 h. The reaction was monitored by ¹H nmr spectroscopy and was found to be complete after 35 h. Evaporation of the solvent gave a brown oil. Dry-flash column chromatography and MPLC on silica, eluting with hexane-ethyl acetate (9:1) gave 8-methyl-9,11,13-triphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene as a crystalline solid (0.17 g, 35%), and 10-methyl-8,11,13-triphenyl-12-azatetracyclo[7.3.1.0.2,7.0.8,10]trideca-2(7),3,5,11-tetraene as a clear

crystalline solid (0.33 g, 65%), mp 116-118 °C from pentane-DCM* (Found: (M+1)⁺, 412.2057. C₃₁H₂₅N requires (M+1)⁺, 412.2065); δ_H(200 MHz, CDCl₃) 1.14 (3 H, s, CH₃), 2.53 (1 H, t, J 2.2 Hz, CH), 3.30 (1 H, s, CH), 5.10 (1 H, t, J 1.8 Hz, CH), 6.89-7.51 (19 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 23.5 (CH₃), 31.7 (quat.), 34.2 (CH), 37.0 (CH), 45.0 (quat.), 64.0 (CH), 125.9 (CH), 126.2 (CH), 126.6 (CH), 127.3 (2 x CH), 127.8 (3 x CH), 127.9 (2 x CH), 128.1 (CH), 128.3 (CH), 128.4 (2 x CH), 129.5 (CH), 130.1 (CH), 132.6 (CH), 135.5 (quat.), 137.0 (quat.), 138.1 (quat.), 141.2 (quat.), 170.1 (quat.); *m/z* (FAB) 413 (M+1, 45%), 412 (44), 411 (100), 396 (11), 321 (12), 309 (19), 276 (14), 246 (12), 228 (14), 215 (18), 192 (10), 165 (24), 115 (16), 93 (13); ν_{max}(Nujol)/cm⁻¹ 1620 (C=N). * isothermal distillation.

(ii) Thermal Isomerisation of 7b-Methyl-1-endo-phenyl-1a-phenyl-1-(Z-2-phenylethenyl)cyclopropa[c]isoquinoline 256

7b-Methyl-1-endo-phenyl-1a-phenyl-1-(Z-2-phenylethenyl)cyclopropa[c]isoquinoline (0.06 g, 0.146 mmol) in dry C₆D₆ (0.7 cm³) was heated under reflux for 35 h. The reaction was monitored by ¹H nmr spectroscopy and was found to be complete after 35 h. Evaporation of the solvent gave a brown oil. Dry-flash column chromatography and MPLC on silica, eluting with hexane-ethyl acetate gave 8-methyl-9,11,13-triphenyl-12-azatricyclo[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene as a crystalline solid (18 mg, 32%), and 10-methyl-8,11,13-triphenyl-12-azatetracyclo[7.3.1.0.2,7^{0,8,10}]trideca-2(7),3,5,11-tetraene as a clear crystalline solid (32 mg, 68%).

(iii) Thermal Isomerisation of 7b-methyl-1a-phenyl-1H-cyclopropa[c]isoquinoline 315

7b-Methyl-1a-phenyl-1H-cyclopropa[c]isoquinoline (0.1 g, 0.43 mmol) in dry benzene (2 cm³) was heated under reflux for 12 h. Evaporation of the solvent gave a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 5-

methyl-3-phenyl-1*H*-2-benzazepine as a brown crystalline solid (0.1 g, 100%), mp 111-112 °C from pentane-DCM* (Found: C, 87.4; H, 6.8; N, 5.9%; (M+1)⁺, 234.1264. C₁₇H₁₅N requires C, 87.5; H, 6.5; N, 6.0%; (M+1)⁺, 234.1283); δ_H(200 MHz, CDCl₃, 245 K) 2.49 (3 H, d, J 1.2 Hz, CH₃), 3.90 (1 H, d, J 10.5 Hz, CH₂), 4.98 (1 H, d, J 10.5 Hz, CH₂), 6.90 (1 H, J 1.3 Hz, CH), 7.25-7.78 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 23.8 (CH₃), 56.3 (CH₂), 107.5 (CH), 124.2 (CH), 125.5 (CH), 126.0 (CH), 127.6 (2 x CH), 127.9 (CH), 128.0 (2 x CH), 129.3 (CH), 129.9 (CH), 137.6 (quat.), 137.8 (quat.), 138.7 (quat.), 147.4 (quat.), 165.1 (quat.); *m/z* (FAB) 236 (M+1, 43%), 235 (90), 234 (91), 222 (53), 218 (71), 207 (70), 203 (28), 193 (36), 181 (21), 165 (28), 147 (65), 135 (27); ν_{max}(Nujol)/cm⁻¹ 1618 (C=N). * isothermal distillation.

(iv) Thermal Isomerisation of 7b-Methyl-1-*exo*-phenyl-1a-phenyl-1*H*-cyclopropa[c]isoquinoline 319

7b-Methyl-1-*exo*-phenyl-1a-phenyl-1*H*-cyclopropa[c]isoquinoline (0.1 g, 0.32 mmol) in dry toluene (5 cm³) was heated under reflux for 24 h. Evaporation of the solvent gave a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 5-methyl-3,4-diphenyl-1*H*-2-benzazepine as a yellow glassy foam (0.07 g, 75%), (Found: (M+1)⁺, 310.1606. C₂₃H₁₉N requires (M+1)⁺, 310.1596); δ_H(200 MHz, CDCl₃) 2.43 (3 H, s, CH₃), 4.14 (1 H, d, J 9.9 Hz, CH₂), 4.96 (1 H, d, J 9.9 Hz, CH₂), 7.05-7.63 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 21.6 (CH₃), 55.8 (CH₂), 126.8 (CH), 126.9 (CH), 127.0 (CH), 127.1 (CH), 127.4 (2 x CH), 127.7 (2 x CH), 128.3 (CH), 128.4 (CH), 128.6 (2 x CH), 130.6 (2 x CH), 136.6 (quat.), 138.8 (quat.), 139.4 (quat.), 139.6 (quat.), 139.7 (quat.), 143.0 (quat.), 167.3 (C=N); *m/z* (FAB) 311 (M+1, 33%), 310 (100), 308 (12), 215 (62), 178 (75); ν_{max}(Nujol)/cm⁻¹ 1606 (C=N).

(v) Thermal Isomerisation of 1,1,7b-Trimethyl-1a-phenylcyclopropa[c]isoquinoline 324

1,1,7b-Trimethyl-1a-phenylcyclopropa[c]isoquinoline (0.1 g, 0.38 mmol) in dry *p*-xylene (5 cm³) was heated under reflux for 24 h. Evaporation of the solvent gave a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 4-methyl-3-phenyl-4-propen-2'-ylisoquinoline as a white solid (0.1 g, 100 %), mp 68-69 °C from pentane (Found: C, 87.6; H, 7.6; N, 5.0%; (M+1)⁺, 262.1601. C₁₉H₁₉N requires C, 87.4; H, 7.3; N, 5.3%; (M+1)⁺, 262.1596); δ_H(200 MHz, CDCl₃) 1.49 (3 H, d, J 0.8 Hz, CH₃), 1.61 (3 H, s, CH₃), 5.06 (2 H, d, J 2.3 Hz, CH₂), 5.11 (1 H, t, J 1.2 Hz, CH₂), 5.26 (1 H, s, CH₂), 7.17-7.88 (9 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 20.9 (CH₃), 25.1 (CH₃), 48.5 (quat.), 56.0 (CH₂), 112.8 (CH₂), 123.8 (CH), 124.8 (CH), 125.4 (CH), 126.4 (CH), 127.1 (CH), 127.5 (CH), 127.6 (CH), 128.4 (CH), 132.6 (quat.), 134.3 (quat.), 138.3 (quat.), 140.7 (quat.), 147.5 (quat.), 171.4 (quat.); *m/z* (EI) 262 (M+1, 27%), 261 (100), 159 (33), 144 (80), 141 (12), 128 (34), 115 (20), 103 (11); ν_{max}(Nujol)/cm⁻¹ 1628 (C=N).

(vi) Thermal Isomerisation of 1,7b-Dimethyl-1-exo-phenyl-1a-phenylcyclopropa[c]isoquinoline 330

1,7b-Dimethyl-1-exo-phenyl-1a-phenylcyclopropa[c]isoquinoline (0.06 g, 0.18 mmol) in dry *p*-xylene (2 cm³) was heated under reflux for 48 h. Evaporation of the solvent gave a brown oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 4-methyl-3-phenyl-4-(1'-phenylethenyl)isoquinoline as a colourless oil (0.05 g, 83%), (Found: (M+1)⁺, 324.1743. C₂₄H₂₁N requires (M+1)⁺, 324.1752); δ_H(200 MHz, CDCl₃) 1.71 (3 H, s, CH₃), 4.59 (1 H, d, J 20.9 Hz, CH₂), 4.69 (1 H, d, J 20.5 Hz, CH₂), 5.41 (1 H, d, J 0.7 Hz, CH₂), 5.54 (1 H, d, J 0.7 Hz, CH₂), 6.55-7.45 (14 H, m, Ar-H); δ_C(63 MHz, CDCl₃) 26.1 (CH₃), 48.6 (quat.), 52.9 (CH₂), 115.3 (CH₂), 125.0 (CH), 125.5 (CH), 126.5 (CH), 126.6

(CH), 127.2 (CH), 127.4 (2 x CH), 127.5 (2 x CH), 127.8 (2 x CH), 127.9 (2 x CH), 128.2 (CH), 131.7 (quat.), 138.7 (quat.), 141.0 (quat.), 141.1 (quat.), 151.5 (quat.), 171.7 (quat.); m/z (FAB) 276 (M+1, 20%), 262 (15), 250 (19), 234 (11), 128 (15), 115 (16), 105 (100); ν_{\max} (Nujol)/ cm^{-1} 1638 (C=N).

(vii) Thermal Isomerisation of 1,7b-Dimethyl-1-endo-phenyl-1a-phenylcyclopropa[c]isoquinoline 334

1,7b-Dimethyl-1-endo-phenyl-1a-phenylcyclopropa[c]isoquinoline (0.15 g, 0.46 mmol) in dry *para*-xylene (5 cm^3) was heated under reflux for 48 h. Evaporation of the solvent gave a yellow oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 4-methyl-3-phenyl-4-(1'-phenylethenyl)isoquinoline as a colourless oil (0.1 g, 66%) and 1,7b-dimethyl-1-exo-phenyl-1a-phenylcyclopropa[c]isoquinoline (0.03 g, 20%).

(viii) Thermal Isomerisation of 7b-Ethyl-1,1-dimethyl-1a-phenylcyclopropa[c]isoquinoline 338

7b-Ethyl-1,1-dimethyl-1a-phenylcyclopropa[c]isoquinoline (0.05 g, 0.18 mmol) in dry *p*-xylene (3 cm^3) was heated under reflux for 24 h. Evaporation of the solvent and dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 4-ethyl-3-phenyl-4-propen-2'-ylisoquinoline as a yellow oil (45 mg, 90 %), (Found: (M+1)⁺, 274.1685. $\text{C}_{20}\text{H}_{21}\text{N}$ requires (M+1)⁺, 274.1752); δ_{H} (200 MHz, CDCl_3) 0.46 (3 H, t, J 7.3 Hz, CH_3), 1.52 (3 H, d, 0.7 Hz, CH_3), 2.01 (2 H, q, CH_2), 5.01 (1 H, t, 1.1 Hz, CH_2), 5.05 (2 H, s, CH_2), 5.19 (1 H, s, CH_2), 7.03-7.65 (9 H, m, Ar-H); δ_{C} (63 MHz, CDCl_3) 9.0 (CH_3), 21.5 (CH_3), 30.2 (CH_2), 52.2 (quat.), 53.1 (CH_2), 111.8 (CH_2), 124.3 (CH), 125.5 (CH), 126.4 (CH), 127.1 (CH), 127.6 (2 x CH), 127.8 (2 x CH), 128.5 (CH), 132.0 (quat.), 135.6 (quat.), 140.7 (quat.), 148.9 (quat.), 169.0 (quat.); m/z (FAB) 276 (M+1, 20%), 262 (15), 250 (19), 234 (11), 128 (15), 115 (16), 105 (100); ν_{\max} (Nujol)/ cm^{-1} 1628 (C=N).

(ix) Thermal Isomerisation of 7b-Methyl-1,1,1a-triphenylcyclopropa[c]isoquinoline 342

7b-Methyl-1,1,1a-triphenylcyclopropa[c]isoquinoline (0.05 g, 0.13 mmol) in dry *p*-xylene (3 cm³) was heated under reflux for 168 h. Evaporation of the solvent gave a yellow oil. Dry-flash column chromatography on silica, eluting with hexane-ethyl acetate (9:1) gave 3,5,5-triphenyl-2-benzazepine as a yellow oil (0.02 g, 40 %), (Found: (M+1)⁺, 386.1939. C₂₉H₂₃N requires (M+1)⁺, 386.1909); δ_H(200 MHz, CDCl₃) 1.74 (3 H, s, CH₃), 6.78-7.55 (19 H, m, Ar-H), 8.39 (1 H, br, HC=N); *m/z* (FAB) 387 (M+1, 37%), 386 (100), 323 (14), 307 (14), 282 (15), 270 (15), 254 (15), 220 (28), 215 (23), 199 (24), 181 (30), 165 (49), 149 (27), 131 (39), 105 (100); and starting material (0.01 g).

(x) Attempted Base Catalysed Isomerisation of 1,1,7b-Trimethyl-1a-phenylcyclopropa[c]isoquinoline 324

(a) 1,1,7b-Trimethyl-1a-phenylcyclopropa[c]isoquinoline (0.05 g, 0.19 mmol) and lithium bis(trimethylsilylamide) (0.19 cm³, 0.19 mmol) were stirred in THF (5 cm³) at room temperature for 168 h under dry nitrogen. No 4-methyl-3-phenyl-4-propen-2'-ylisoquinoline was obtained from this reaction.

(b) 1,1,7b-Trimethyl-1a-phenylcyclopropa[c]isoquinoline (0.05 g, 0.19 mmol) and lithium bis(trimethylsilylamide) (0.19 cm³, 0.19 mmol) were heated in toluene (5 cm³) at reflux for 48 h. No 4-methyl-3-phenyl-4-propen-2'-ylisoquinoline was obtained from this reaction.

Appendix 1

3-Methoxycarbonyl-2-phenyl-3a,11b-dihydro-3H-dibenzo[e,g]indole

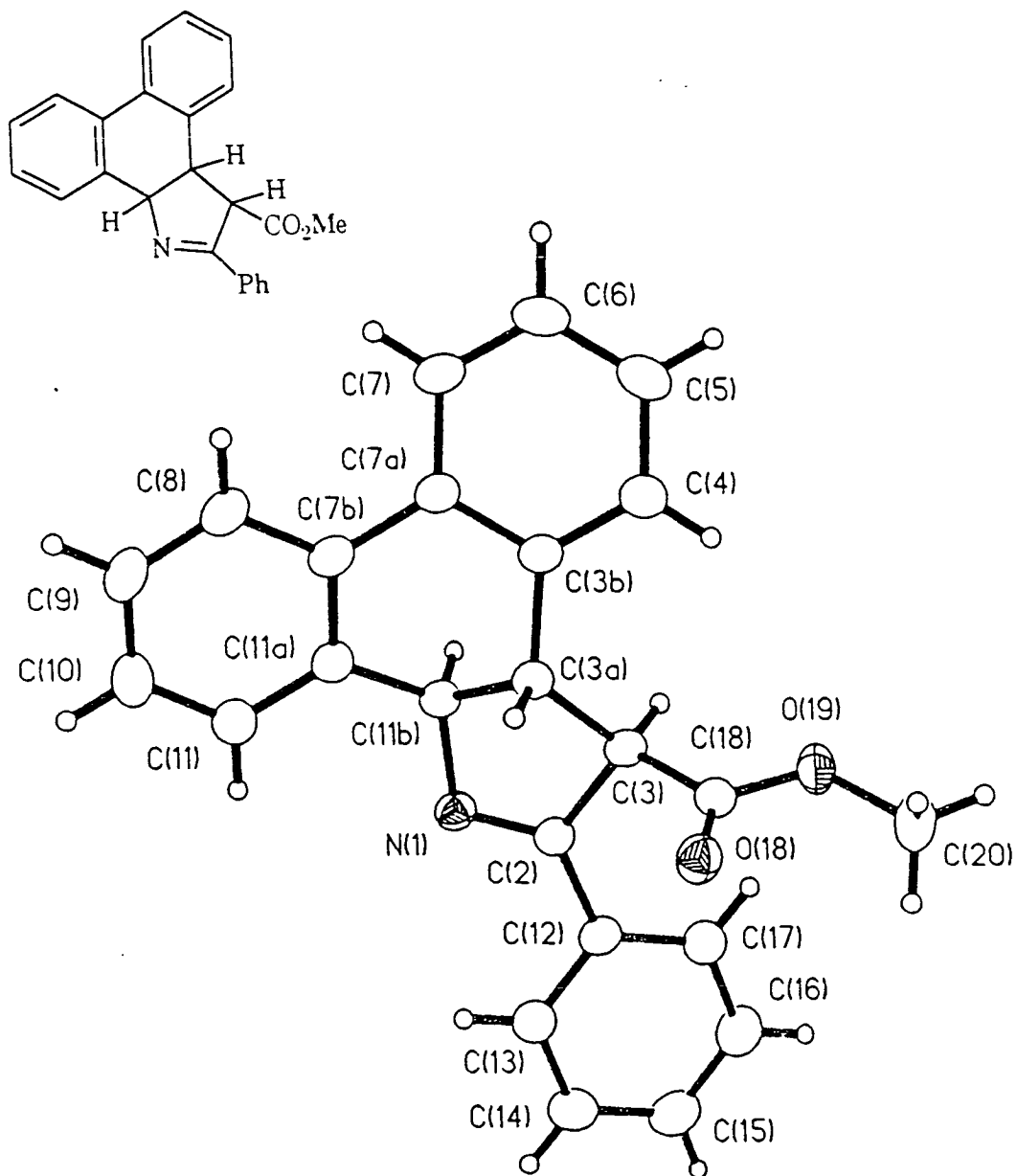


Figure 8

Table 1. Crystal data and structure refinement for INDCOM.

Identification code	INDCOM
Empirical formula	C ₂₄ H ₁₉ N O ₂
Formula weight	353.40
Temperature	295(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/a
Unit cell dimensions	a = 8.369(4) Å alpha = 90 deg. b = 20.174(5) Å beta = 106.70(4) deg. c = 11.159(5) Å gamma = 90 deg.
Volume	1804.6(13) Å ³
Z	4
Density (calculated)	1.301 Mg/m ³
Absorption coefficient	0.083 mm ⁻¹
F(000)	744
Crystal size	0.8 x 0.5 x 0.2 mm
Theta range for data collection	2.73 to 24.97 deg.
Index ranges	-9 ≤ h ≤ 9, 0 ≤ k ≤ 23, 0 ≤ l ≤ 13
Reflections collected	3314
Independent reflections	3148 [R(int) = 0.0294]
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3134 / 0 / 245
Goodness-of-fit on F ²	1.013
Final R indices [I > 2σ(I)]	R1 = 0.0469, wR2 = 0.1032
R indices (all data)	R1 = 0.0831, wR2 = 0.1254
Extinction coefficient	0.0081(13)
Largest diff. peak and hole	0.175 and -0.160 e.Å ⁻³

Table 3. Selected bond lengths [Å] and angles [deg] for 1.

N(1)-C(2)	1.274(3)
N(1)-C(11B)	1.466(3)
C(2)-C(12)	1.478(3)
C(2)-C(3)	1.546(3)
C(3)-C(18)	1.506(3)
C(3)-C(3A)	1.528(3)
C(3A)-C(3B)	1.510(3)
C(3A)-C(11B)	1.520(3)
C(3B)-C(4)	1.383(3)
C(3B)-C(7A)	1.406(3)
C(4)-C(5)	1.389(3)
C(5)-C(6)	1.371(4)
C(6)-C(7)	1.374(3)
C(7)-C(7A)	1.396(3)
C(7A)-C(7B)	1.485(3)
C(7B)-C(8)	1.390(3)
C(7B)-C(11A)	1.408(3)
C(8)-C(9)	1.380(3)
C(9)-C(10)	1.381(4)
C(10)-C(11)	1.383(3)
C(11)-C(11A)	1.381(3)
C(11A)-C(11B)	1.490(3)
C(18)-O(18)	1.201(3)
C(18)-O(19)	1.333(3)
O(19)-C(20)	1.444(3)
C(2)-N(1)-C(11B)	107.1(2)
N(1)-C(2)-C(12)	122.2(2)
N(1)-C(2)-C(3)	114.4(2)
C(12)-C(2)-C(3)	123.2(2)
C(18)-C(3)-C(3A)	114.0(2)
C(18)-C(3)-C(2)	113.0(2)
C(3A)-C(3)-C(2)	99.0(2)
C(3B)-C(3A)-C(11B)	108.1(2)
C(3B)-C(3A)-C(3)	122.7(2)
C(11B)-C(3A)-C(3)	100.6(2)
C(4)-C(3B)-C(7A)	120.0(2)
C(4)-C(3B)-C(3A)	123.8(2)
C(7A)-C(3B)-C(3A)	116.2(2)
C(3B)-C(4)-C(5)	120.7(2)
C(6)-C(5)-C(4)	119.4(2)
C(5)-C(6)-C(7)	120.6(2)

C(6)-C(7)-C(7A)	121.2(2)
C(7)-C(7A)-C(3B)	118.0(2)
C(7)-C(7A)-C(7B)	122.1(2)
C(3B)-C(7A)-C(7B)	119.9(2)
C(8)-C(7B)-C(11A)	118.2(2)
C(8)-C(7B)-C(7A)	122.5(2)
C(11A)-C(7B)-C(7A)	119.3(2)
C(9)-C(8)-C(7B)	121.0(2)
C(8)-C(9)-C(10)	120.3(2)
C(9)-C(10)-C(11)	119.8(2)
C(11A)-C(11)-C(10)	120.3(2)
C(11)-C(11A)-C(7B)	120.5(2)
C(11)-C(11A)-C(11B)	124.7(2)
C(7B)-C(11A)-C(11B)	114.9(2)
N(1)-C(11B)-C(11A)	120.3(2)
N(1)-C(11B)-C(3A)	105.8(2)
C(11A)-C(11B)-C(3A)	110.6(2)
C(17)-C(12)-C(13)	118.8(2)
C(17)-C(12)-C(2)	121.7(2)
C(13)-C(12)-C(2)	119.4(2)
C(14)-C(13)-C(12)	120.3(2)
C(15)-C(14)-C(13)	120.3(3)
C(16)-C(15)-C(14)	120.0(2)
C(15)-C(16)-C(17)	120.4(3)
C(12)-C(17)-C(16)	120.2(2)
O(18)-C(18)-O(19)	123.6(2)
O(18)-C(18)-C(3)	124.1(2)
O(19)-C(18)-C(3)	112.4(2)
C(18)-O(19)-C(20)	116.2(2)

Symmetry transformations used to generate equivalent atoms:

Appendix 2

8-Methyl-9,11,13-triphenyl-12-azatricyclo
[6.3.2.0^{2,7}]trideca-2(7),3,5,9,12-pentaene

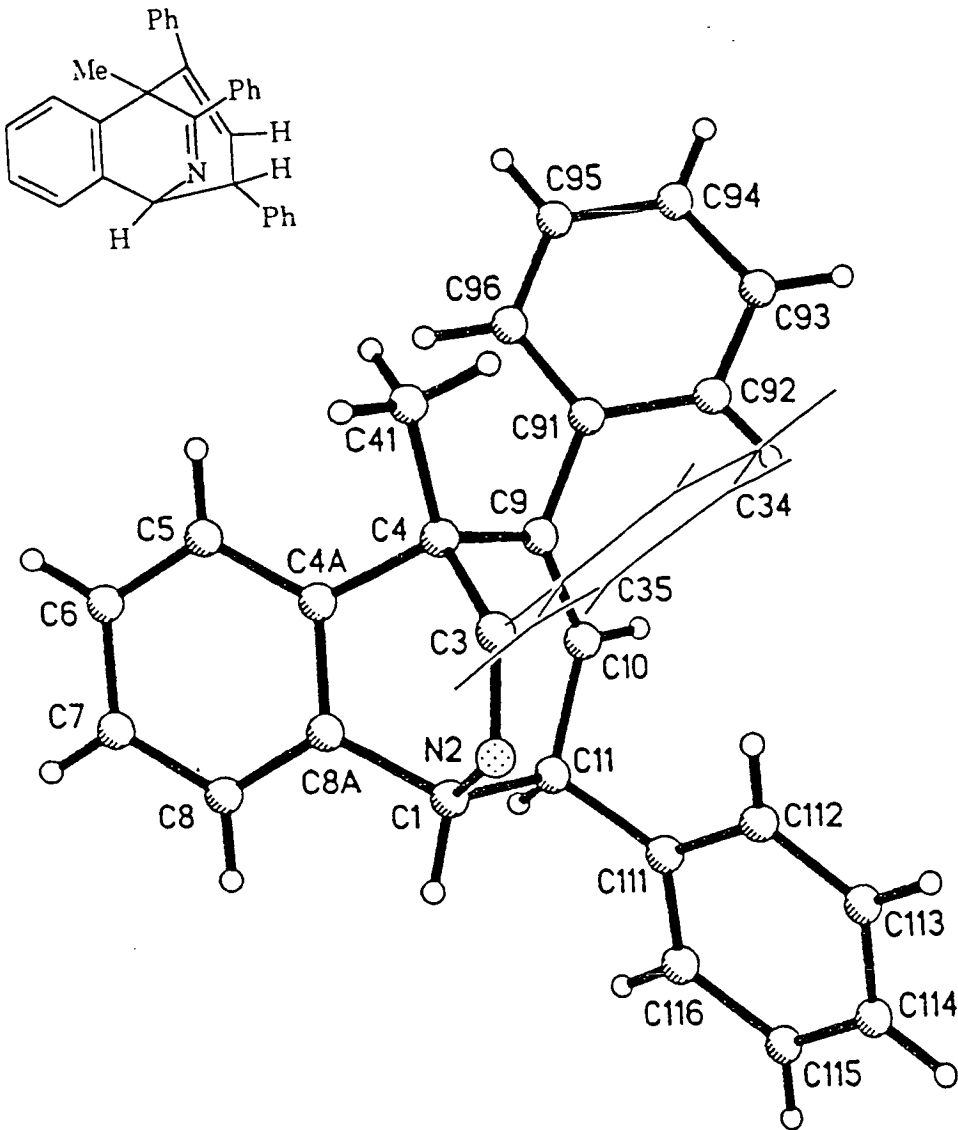


Figure 10

Table 1. Crystal data and structure refinement for jps280 at 150(2) K.

Empirical formula	C31 H25 N
Formula weight	411.52
Wavelength	1.54184 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 10.3624(7) Å alpha = 90 deg. b = 19.1821(13) Å beta = 94.549(4) deg. c = 11.1715(5) Å gamma = 90 deg.
Volume	2213.6(2) Å ³
Z	4
Density (calculated)	1.235 Mg/m ³
Absorption coefficient	0.538 mm ⁻¹
F(000)	872
Crystal description	Colourless lump
Crystal size	0.35 x 0.31 x 0.06 mm
Theta range for data collection	4.59 to 60.07 deg.
Index ranges	-11 ≤ h ≤ 11, -20 ≤ k ≤ 21, -6 ≤ l ≤ 12
Reflections collected	3928
Independent reflections	3223 [R(int) = 0.0232]
Scan type	omega-theta
Data / restraints / parameters	3219/0/290 (Full-matrix least-squares on F ²)
Goodness-of-fit on F ²	1.024
Conventional R [F > 4sigma(F)]	R1 = 0.0438 [2464 data]
R indices (all data)	R1 = 0.0634, wR2 = 0.1193
Extinction coefficient	0.0029(3)
Final maximum delta/sigma	0.000
Weighting scheme	calc w = 1 / [s ² (Fo ²) + (0.0672P) ² + 0.4838P] where P = (Fo ² + 2Fc ²) / 3
Largest diff. peak and hole	0.205 and -0.206 e.Å ⁻³

Table 3. Bond lengths [Å], angles and torsions [deg] for 1.

C(1)-N(2)	1.465(3)
C(1)-C(8A)	1.506(3)
C(1)-C(11)	1.551(3)
N(2)-C(3)	1.276(3)
C(3)-C(31)	1.493(3)
C(3)-C(4)	1.550(3)
C(31)-C(32)	1.388(3)
C(31)-C(36)	1.394(3)
C(32)-C(33)	1.384(3)
C(33)-C(34)	1.373(4)
C(34)-C(35)	1.385(4)
C(35)-C(36)	1.388(3)
C(4)-C(41)	1.533(3)
C(4)-C(4A)	1.536(3)
C(4)-C(9)	1.555(3)
C(4A)-C(8A)	1.393(3)
C(4A)-C(5)	1.397(3)
C(5)-C(6)	1.389(3)
C(6)-C(7)	1.378(3)
C(7)-C(8)	1.390(3)
C(8)-C(8A)	1.385(3)
C(9)-C(10)	1.334(3)
C(9)-C(91)	1.491(3)
C(91)-C(92)	1.391(3)
C(91)-C(96)	1.400(3)
C(92)-C(93)	1.386(3)
C(93)-C(94)	1.383(3)
C(94)-C(95)	1.376(3)
C(95)-C(96)	1.386(3)
C(10)-C(11)	1.507(3)
C(11)-C(111)	1.522(3)
C(111)-C(112)	1.385(3)
C(111)-C(116)	1.385(3)
C(112)-C(113)	1.395(3)
C(113)-C(114)	1.381(4)
C(114)-C(115)	1.366(4)
C(115)-C(116)	1.387(3)
N(2)-C(1)-C(8A)	111.5(2)
N(2)-C(1)-C(11)	108.8(2)
C(8A)-C(1)-C(11)	111.7(2)
C(3)-N(2)-C(1)	115.4(2)
N(2)-C(3)-C(31)	116.3(2)
N(2)-C(3)-C(4)	122.8(2)
C(31)-C(3)-C(4)	120.7(2)
C(32)-C(31)-C(36)	118.8(2)
C(32)-C(31)-C(3)	120.5(2)
C(36)-C(31)-C(3)	120.5(2)
C(33)-C(32)-C(31)	120.8(2)
C(34)-C(33)-C(32)	120.3(2)
C(33)-C(34)-C(35)	119.6(2)
C(34)-C(35)-C(36)	120.5(2)
C(35)-C(36)-C(31)	120.0(2)
C(41)-C(4)-C(4A)	111.7(2)
C(41)-C(4)-C(9)	109.8(2)
C(4A)-C(4)-C(9)	106.8(2)
C(41)-C(4)-C(3)	114.8(2)
C(4A)-C(4)-C(3)	108.4(2)
C(3)-C(4)-C(9)	104.8(2)

C(8A)-C(4A)-C(5)	118.6(2)
C(8A)-C(4A)-C(4)	116.3(2)
C(5)-C(4A)-C(4)	125.1(2)
C(6)-C(5)-C(4A)	120.2(2)
C(7)-C(6)-C(5)	120.6(2)
C(6)-C(7)-C(8)	119.9(2)
C(8A)-C(8)-C(7)	119.7(2)
C(8)-C(8A)-C(4A)	121.0(2)
C(8)-C(8A)-C(1)	122.4(2)
C(4A)-C(8A)-C(1)	116.6(2)
C(10)-C(9)-C(91)	118.5(2)
C(10)-C(9)-C(4)	122.0(2)
C(91)-C(9)-C(4)	119.5(2)
C(92)-C(91)-C(96)	117.8(2)
C(92)-C(91)-C(9)	120.2(2)
C(96)-C(91)-C(9)	122.0(2)
C(93)-C(92)-C(91)	121.4(2)
C(94)-C(93)-C(92)	119.7(2)
C(95)-C(94)-C(93)	120.1(2)
C(94)-C(95)-C(96)	120.2(2)
C(95)-C(96)-C(91)	120.8(2)
C(9)-C(10)-C(11)	129.9(2)
C(10)-C(11)-C(111)	112.0(2)
C(10)-C(11)-C(1)	114.4(2)
C(111)-C(11)-C(1)	110.9(2)
C(112)-C(111)-C(116)	118.2(2)
C(112)-C(111)-C(11)	121.7(2)
C(116)-C(111)-C(11)	120.0(2)
C(111)-C(112)-C(113)	120.5(2)
C(114)-C(113)-C(112)	120.1(3)
C(115)-C(114)-C(113)	119.8(2)
C(114)-C(115)-C(116)	120.1(3)
C(111)-C(116)-C(115)	121.2(3)
C(8A)-C(1)-N(2)-C(3)	47.2(2)
C(11)-C(1)-N(2)-C(3)	-76.4(2)
C(1)-N(2)-C(3)-C(31)	170.4(2)
C(1)-N(2)-C(3)-C(4)	-5.2(3)
N(2)-C(3)-C(31)-C(32)	-119.5(2)
C(4)-C(3)-C(31)-C(32)	56.2(3)
N(2)-C(3)-C(31)-C(36)	54.7(3)
C(4)-C(3)-C(31)-C(36)	-129.6(2)
C(36)-C(31)-C(32)-C(33)	-0.8(3)
C(3)-C(31)-C(32)-C(33)	173.4(2)
C(31)-C(32)-C(33)-C(34)	1.0(4)
C(32)-C(33)-C(34)-C(35)	0.1(4)
C(33)-C(34)-C(35)-C(36)	-1.4(3)
C(34)-C(35)-C(36)-C(31)	1.5(3)
C(32)-C(31)-C(36)-C(35)	-0.4(3)
C(3)-C(31)-C(36)-C(35)	-174.7(2)
N(2)-C(3)-C(4)-C(41)	-159.5(2)
C(31)-C(3)-C(4)-C(41)	25.0(3)
N(2)-C(3)-C(4)-C(4A)	-38.2(2)
C(31)-C(3)-C(4)-C(4A)	146.3(2)
N(2)-C(3)-C(4)-C(9)	76.6(2)
C(31)-C(3)-C(4)-C(9)	-98.8(2)
C(41)-C(4)-C(4A)-C(8A)	159.8(2)
C(3)-C(4)-C(4A)-C(8A)	39.8(2)
C(9)-C(4)-C(4A)-C(8A)	-72.7(2)
C(41)-C(4)-C(4A)-C(5)	-20.7(3)
C(3)-C(4)-C(4A)-C(5)	-140.8(2)
C(9)-C(4)-C(4A)-C(5)	106.8(2)
C(8A)-C(4A)-C(5)-C(6)	-0.6(3)
C(4)-C(4A)-C(5)-C(6)	180.0(2)

C(4A)-C(5)-C(6)-C(7)	0.8(3)
C(5)-C(6)-C(7)-C(8)	-0.1(3)
C(6)-C(7)-C(8)-C(8A)	-0.8(3)
C(7)-C(8)-C(8A)-C(4A)	1.0(3)
C(7)-C(8)-C(8A)-C(1)	-177.6(2)
C(5)-C(4A)-C(8A)-C(8)	-0.3(3)
C(4)-C(4A)-C(8A)-C(8)	179.2(2)
C(5)-C(4A)-C(8A)-C(1)	178.4(2)
C(4)-C(4A)-C(8A)-C(1)	-2.1(3)
N(2)-C(1)-C(8A)-C(8)	135.4(2)
C(11)-C(1)-C(8A)-C(8)	-102.7(2)
N(2)-C(1)-C(8A)-C(4A)	-43.3(2)
C(11)-C(1)-C(8A)-C(4A)	78.7(2)
C(41)-C(4)-C(9)-C(10)	-173.0(2)
C(4A)-C(4)-C(9)-C(10)	61.3(2)
C(3)-C(4)-C(9)-C(10)	-52.4(2)
C(41)-C(4)-C(9)-C(91)	6.3(2)
C(4A)-C(4)-C(9)-C(91)	-119.4(2)
C(3)-C(4)-C(9)-C(91)	126.9(2)
C(10)-C(9)-C(91)-C(92)	52.3(3)
C(4)-C(9)-C(91)-C(92)	-127.1(2)
C(10)-C(9)-C(91)-C(96)	-124.4(2)
C(4)-C(9)-C(91)-C(96)	56.3(3)
C(96)-C(91)-C(92)-C(93)	-0.6(3)
C(9)-C(91)-C(92)-C(93)	-177.4(2)
C(91)-C(92)-C(93)-C(94)	0.0(3)
C(92)-C(93)-C(94)-C(95)	0.4(3)
C(93)-C(94)-C(95)-C(96)	-0.1(3)
C(94)-C(95)-C(96)-C(91)	-0.5(3)
C(92)-C(91)-C(96)-C(95)	0.9(3)
C(9)-C(91)-C(96)-C(95)	177.6(2)
C(91)-C(9)-C(10)-C(11)	179.3(2)
C(4)-C(9)-C(10)-C(11)	-1.4(3)
C(9)-C(10)-C(11)-C(111)	126.0(2)
C(9)-C(10)-C(11)-C(1)	-1.3(3)
N(2)-C(1)-C(11)-C(10)	63.9(2)
C(8A)-C(1)-C(11)-C(10)	-59.6(2)
N(2)-C(1)-C(11)-C(111)	-64.0(2)
C(8A)-C(1)-C(11)-C(111)	172.6(2)
C(10)-C(11)-C(111)-C(112)	-49.7(3)
C(1)-C(11)-C(111)-C(112)	79.5(2)
C(10)-C(11)-C(111)-C(116)	133.1(2)
C(1)-C(11)-C(111)-C(116)	-97.7(2)
C(116)-C(111)-C(112)-C(113)	1.1(3)
C(11)-C(111)-C(112)-C(113)	-176.1(2)
C(111)-C(112)-C(113)-C(114)	-1.6(4)
C(112)-C(113)-C(114)-C(115)	0.6(4)
C(113)-C(114)-C(115)-C(116)	1.0(4)
C(112)-C(111)-C(116)-C(115)	0.5(4)
C(11)-C(111)-C(116)-C(115)	177.7(2)
C(114)-C(115)-C(116)-C(111)	-1.5(4)

Symmetry transformations used to generate equivalent atoms:

Appendix 3

7b-1-*endo*-Phenyl-1a-phenyl-1-(*E*-2-phenylethenyl)cyclopropa[*c*]isoquinoline

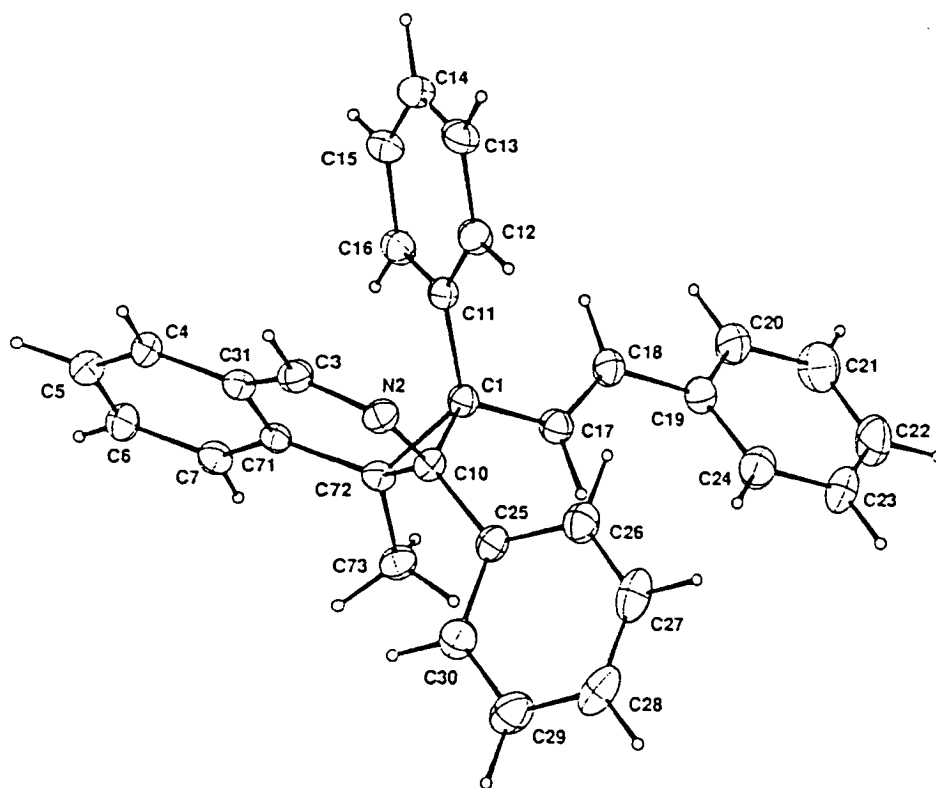
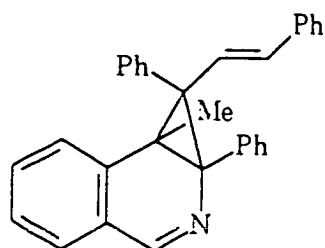


Figure 11

Table 1. Crystal data and structure refinement for xjpsc3 at 220 K.

Empirical formula	C31 H25 N1
Formula weight	411.55
Wavelength	1.54180 A
Crystal system	Monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 21.503(8) A alpha = 90 deg. b = 6.613(4) A beta = 94.38(3) deg. c = 16.214(5) A gamma = 90 deg.
Volume	2298.89 A ³
Z	4.00
Number of reflections for cell	46
Theta range for cell	20 to 22 deg.
Density (calculated)	1.19 Mg/m ³
Absorption coefficient	0.49 mm ⁻¹
F(000)	874.10
Crystal description	colourless plate
Crystal size	0.62 x 0.31 x 0.04 mm
Theta range for data collection	2.50 to 60.00 deg.
Index ranges	-24<=h<=24, 0<=k<=7, 0<=l<=18
Reflections collected	3953
Independent reflections	2951 [R(int) = 0.06]
Scan type	2\q/\w
Data / parameters	2127/290
Goodness-of-fit	1.1401
R	0.0575
Rw	0.0584
Number of reflections used	2127
Observed criterion	>2.00\s(I)
Refinement type	Full-matrix least-squares on F -CRYSTALS
Extinction coefficient	101(23)
Final maximum delta/sigma	0.018580
Weighting scheme	Chebychev 3-term polynomial

Table 5: Bond lengths and angles for xjpsc3 at 220K.

C(1) - C(10)	1.542(4)
C(1) - C(72)	1.558(3)
C(1) - C(11)	1.499(4)
C(1) - C(17)	1.493(4)
C(10) - N(2)	1.446(3)
C(10) - C(72)	1.553(4)
C(10) - C(25)	1.502(4)
N(2) - C(3)	1.287(3)
C(3) - C(31)	1.449(4)
C(31) - C(4)	1.402(4)
C(31) - C(71)	1.399(4)
C(4) - C(5)	1.390(4)
C(5) - C(6)	1.377(4)
C(6) - C(7)	1.397(4)
C(7) - C(71)	1.402(4)
C(71) - C(72)	1.488(4)
C(72) - C(73)	1.513(4)
C(11) - C(12)	1.398(4)
C(11) - C(16)	1.387(4)
C(12) - C(13)	1.387(4)
C(13) - C(14)	1.388(5)
C(14) - C(15)	1.372(5)
C(15) - C(16)	1.383(4)
C(17) - C(18)	1.320(4)
C(18) - C(19)	1.483(4)
C(19) - C(20)	1.377(4)
C(19) - C(24)	1.387(4)
C(20) - C(21)	1.391(4)
C(21) - C(22)	1.376(5)
C(22) - C(23)	1.361(5)
C(23) - C(24)	1.383(5)
C(25) - C(26)	1.391(4)
C(25) - C(30)	1.381(4)
C(26) - C(27)	1.379(5)
C(27) - C(28)	1.372(5)
C(28) - C(29)	1.370(5)
C(29) - C(30)	1.387(4)

C(10) - C(1) - C(72)	60.1(2)
C(10) - C(1) - C(11)	118.6(2)
C(72) - C(1) - C(11)	120.3(2)
C(10) - C(1) - C(17)	117.7(2)
C(72) - C(1) - C(17)	116.3(2)
C(11) - C(1) - C(17)	113.8(2)
C(1) - C(10) - N(2)	117.5(2)
C(1) - C(10) - C(72)	60.5(2)
N(2) - C(10) - C(72)	120.5(2)
C(1) - C(10) - C(25)	121.6(2)
N(2) - C(10) - C(25)	108.7(2)
C(72) - C(10) - C(25)	121.3(2)
C(10) - N(2) - C(3)	118.7(2)
N(2) - C(3) - C(31)	126.1(3)
C(3) - C(31) - C(4)	119.6(3)
C(3) - C(31) - C(71)	119.6(2)
C(4) - C(31) - C(71)	120.4(3)
C(31) - C(4) - C(5)	120.3(3)
C(4) - C(5) - C(6)	119.4(3)
C(5) - C(6) - C(7)	121.2(3)
C(6) - C(7) - C(71)	120.0(3)
C(31) - C(71) - C(7)	118.7(2)
C(31) - C(71) - C(72)	119.9(2)
C(7) - C(71) - C(72)	121.4(2)
C(1) - C(72) - C(10)	59.4(2)
C(1) - C(72) - C(71)	118.0(2)
C(10) - C(72) - C(71)	114.4(2)
C(1) - C(72) - C(73)	117.2(2)
C(10) - C(72) - C(73)	121.4(2)
C(71) - C(72) - C(73)	115.2(2)
C(1) - C(11) - C(12)	119.9(2)
C(1) - C(11) - C(16)	121.0(2)
C(12) - C(11) - C(16)	118.9(2)
C(11) - C(12) - C(13)	120.1(3)
C(12) - C(13) - C(14)	120.0(3)
C(13) - C(14) - C(15)	120.0(2)
C(14) - C(15) - C(16)	120.3(3)
C(11) - C(16) - C(15)	120.7(3)
C(1) - C(17) - C(18)	126.2(2)
C(17) - C(18) - C(19)	125.3(3)
C(18) - C(19) - C(20)	120.0(3)
C(18) - C(19) - C(24)	121.5(3)
C(20) - C(19) - C(24)	118.4(3)
C(19) - C(20) - C(21)	121.3(3)
C(20) - C(21) - C(22)	119.6(3)
C(21) - C(22) - C(23)	119.1(3)
C(22) - C(23) - C(24)	121.9(3)
C(19) - C(24) - C(23)	119.5(3)
C(10) - C(25) - C(26)	120.7(2)
C(10) - C(25) - C(30)	120.4(2)
C(26) - C(25) - C(30)	118.6(3)
C(25) - C(26) - C(27)	120.1(3)
C(26) - C(27) - C(28)	120.4(3)
C(27) - C(28) - C(29)	120.4(3)
C(28) - C(29) - C(30)	119.3(3)
C(25) - C(30) - C(29)	121.1(3)

Appendix 4

10-Methyl-8,11,13-triphenyl-12-azatetracyclo[7.3.1.0.2.70.8.10]
trideca-2(7),3,5,11-tetraene

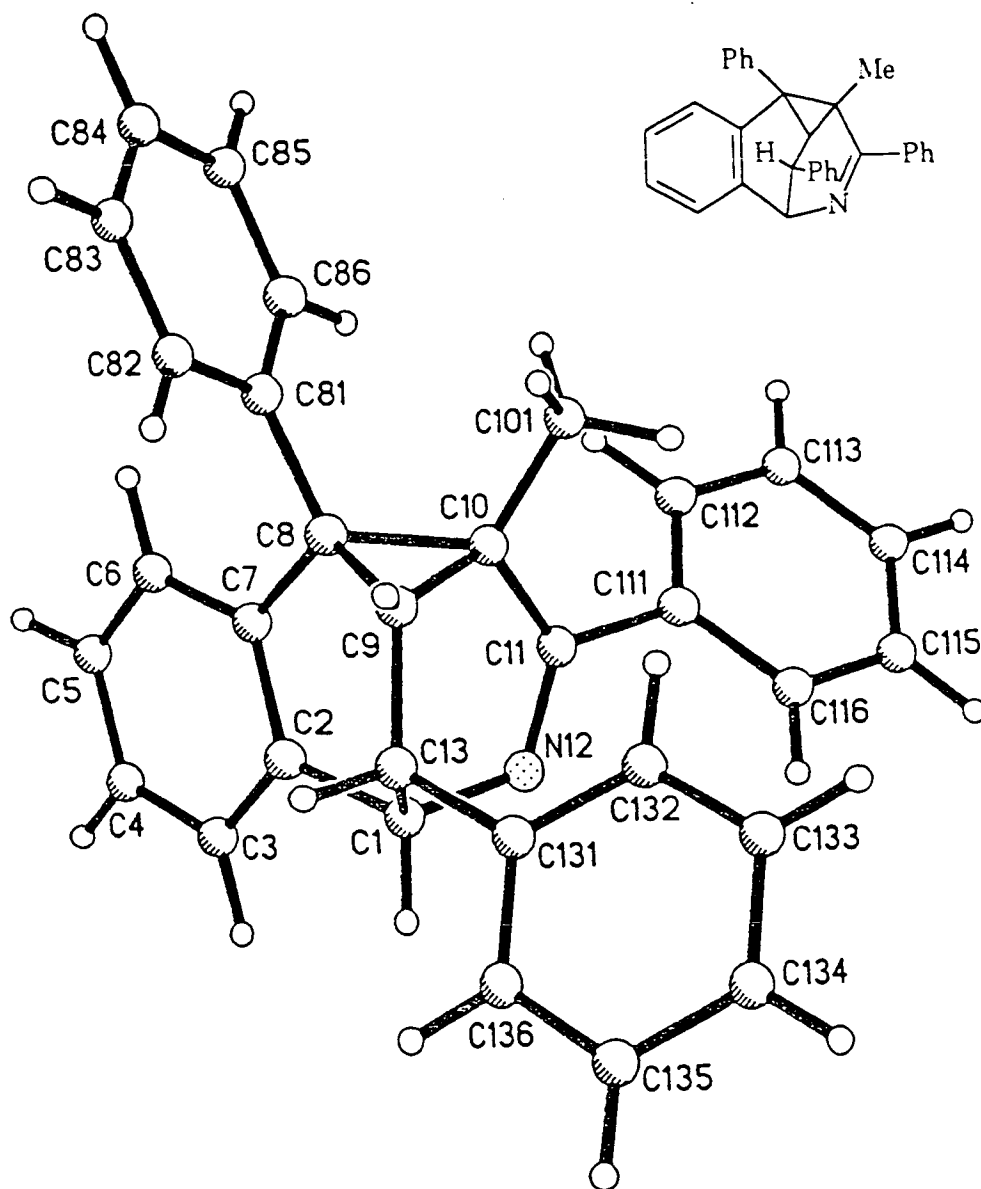


Figure 13

Table 1. Crystal data and structure refinement for xjpsc4 at 220 K.

Empirical formula	C32 H27 N1 Cl2
Formula weight	496.48
Wavelength	1.54180 Å
Crystal system	Monoclinic
Space group	C 1 2/c 1
Unit cell dimensions	a = 26.662 Å alpha = 90 deg. b = 9.496 Å beta = 108.080 deg. c = 21.929 Å gamma = 90 deg.
Volume	5277.90 Å ³
Z	8.00
Number of reflections for cell	31
Theta range for cell	10 to 22 deg.
Density (calculated)	1.25 Mg/m ³
Absorption coefficient	2.38 mm ⁻¹
F(000)	2089.90
Crystal description	colourless lump
Crystal size	0.45 x 0.27 x 0.16 mm
Theta range for data collection	2.50 to 60.00 deg.
Index ranges	-29<=h<=28, 0<=k<=10, 0<=l<=24
Reflections collected	4229
Independent reflections	3276 [R(int) = 0.02]
Scan type	omega-theta
Data / parameters	2103/329
Goodness-of-fit	1.1068
R	0.0774
Rw	0.0855
Observed criterion	>2.00\ s(I)
Refinement type	Full-matrix least-squares on F ² -CRYSTALS
Final maximum delta/sigma	0.040169
Weighting scheme	Chebychev 5-term polynomial
Largest diff. peak and hole	0.68 and -0.40 e.Å ⁻³

Table 5: Bond lengths and angles for xjpsc4 at 220 K.

C(1) - N(2)	1.477(6)
C(1) - C(90)	1.497(8)
C(1) - C(11)	1.550(7)
N(2) - C(3)	1.286(6)
C(3) - C(31)	1.504(7)
C(3) - C(4)	1.484(7)
C(31) - C(32)	1.384(7)
C(31) - C(36)	1.397(7)
C(32) - C(33)	1.389(8)
C(33) - C(34)	1.381(9)
C(34) - C(35)	1.363(9)
C(35) - C(36)	1.389(8)
C(4) - C(41)	1.517(7)
C(4) - C(5)	1.583(7)
C(4) - C(10)	1.536(7)
C(5) - C(50)	1.506(7)
C(5) - C(51)	1.500(7)
C(5) - C(10)	1.504(7)
C(50) - C(6)	1.401(8)
C(50) - C(90)	1.399(7)
C(51) - C(52)	1.397(7)
C(51) - C(56)	1.402(7)
C(52) - C(53)	1.370(8)
C(53) - C(54)	1.388(9)
C(54) - C(55)	1.389(9)
C(55) - C(56)	1.385(8)
C(6) - C(7)	1.377(8)
C(7) - C(8)	1.359(9)
C(8) - C(9)	1.375(8)
C(9) - C(90)	1.391(7)
C(10) - C(11)	1.509(7)
C(11) - C(111)	1.511(7)
C(111) - C(112)	1.392(7)
C(111) - C(116)	1.388(8)
C(112) - C(113)	1.374(8)
C(113) - C(114)	1.374(8)
C(114) - C(115)	1.375(9)
C(115) - C(116)	1.395(8)
C(100) - CL(100)	1.751(9)
C(100) - CL(101)	1.716(9)
C(100) - CL(102)	1.722(9)

N(2) - C(1) - C(90)	106.6(4)
N(2) - C(1) - C(11)	112.0(4)
C(90) - C(1) - C(11)	110.7(4)
C(1) - N(2) - C(3)	116.8(4)
N(2) - C(3) - C(31)	115.4(4)
N(2) - C(3) - C(4)	124.8(4)
C(31) - C(3) - C(4)	119.7(4)
C(3) - C(31) - C(32)	122.1(4)
C(3) - C(31) - C(36)	119.5(4)
C(32) - C(31) - C(36)	118.4(5)
C(31) - C(32) - C(33)	121.1(5)
C(32) - C(33) - C(34)	119.0(5)
C(33) - C(34) - C(35)	121.2(5)
C(34) - C(35) - C(36)	119.7(5)
C(31) - C(36) - C(35)	120.6(5)
C(3) - C(4) - C(41)	118.0(4)
C(3) - C(4) - C(5)	119.5(4)
C(41) - C(4) - C(5)	117.1(4)
C(3) - C(4) - C(10)	115.3(4)
C(41) - C(4) - C(10)	114.9(4)
C(5) - C(4) - C(10)	57.7(3)
C(4) - C(5) - C(50)	119.1(4)
C(4) - C(5) - C(51)	116.0(4)
C(50) - C(5) - C(51)	115.3(4)
C(4) - C(5) - C(10)	59.6(3)
C(50) - C(5) - C(10)	116.6(4)
C(51) - C(5) - C(10)	119.1(4)
C(5) - C(50) - C(6)	121.9(5)
C(5) - C(50) - C(90)	118.7(4)
C(6) - C(50) - C(90)	119.2(5)
C(5) - C(51) - C(52)	121.6(5)
C(5) - C(51) - C(56)	120.1(4)
C(52) - C(51) - C(56)	118.3(5)
C(51) - C(52) - C(53)	121.8(5)
C(52) - C(53) - C(54)	119.6(5)
C(53) - C(54) - C(55)	119.9(5)
C(54) - C(55) - C(56)	120.4(5)
C(51) - C(56) - C(55)	120.1(5)
C(50) - C(6) - C(7)	119.8(5)
C(6) - C(7) - C(8)	120.6(5)
C(7) - C(8) - C(9)	121.0(5)
C(8) - C(9) - C(90)	119.9(5)
C(1) - C(90) - C(50)	118.9(4)
C(1) - C(90) - C(9)	121.6(5)
C(50) - C(90) - C(9)	119.5(5)
C(4) - C(10) - C(5)	62.7(3)
C(4) - C(10) - C(11)	115.7(4)
C(5) - C(10) - C(11)	119.7(4)
C(1) - C(11) - C(10)	107.6(4)
C(1) - C(11) - C(111)	111.1(4)
C(10) - C(11) - C(111)	113.8(4)
C(11) - C(111) - C(112)	122.9(5)
C(11) - C(111) - C(116)	119.7(5)
C(112) - C(111) - C(116)	117.4(5)
C(111) - C(112) - C(113)	120.9(5)
C(112) - C(113) - C(114)	121.3(6)
C(113) - C(114) - C(115)	119.1(5)
C(114) - C(115) - C(116)	119.8(5)
C(111) - C(116) - C(115)	121.4(5)
CL(100) - C(100) - CL(101)	107.7(5)

Appendix 5

7,15-diphenyl-16-azatetracyclo[6.6.2.0^{1,5}.0^{9,14}]
hexadeca-5,9(14),10,12,15-pentaene

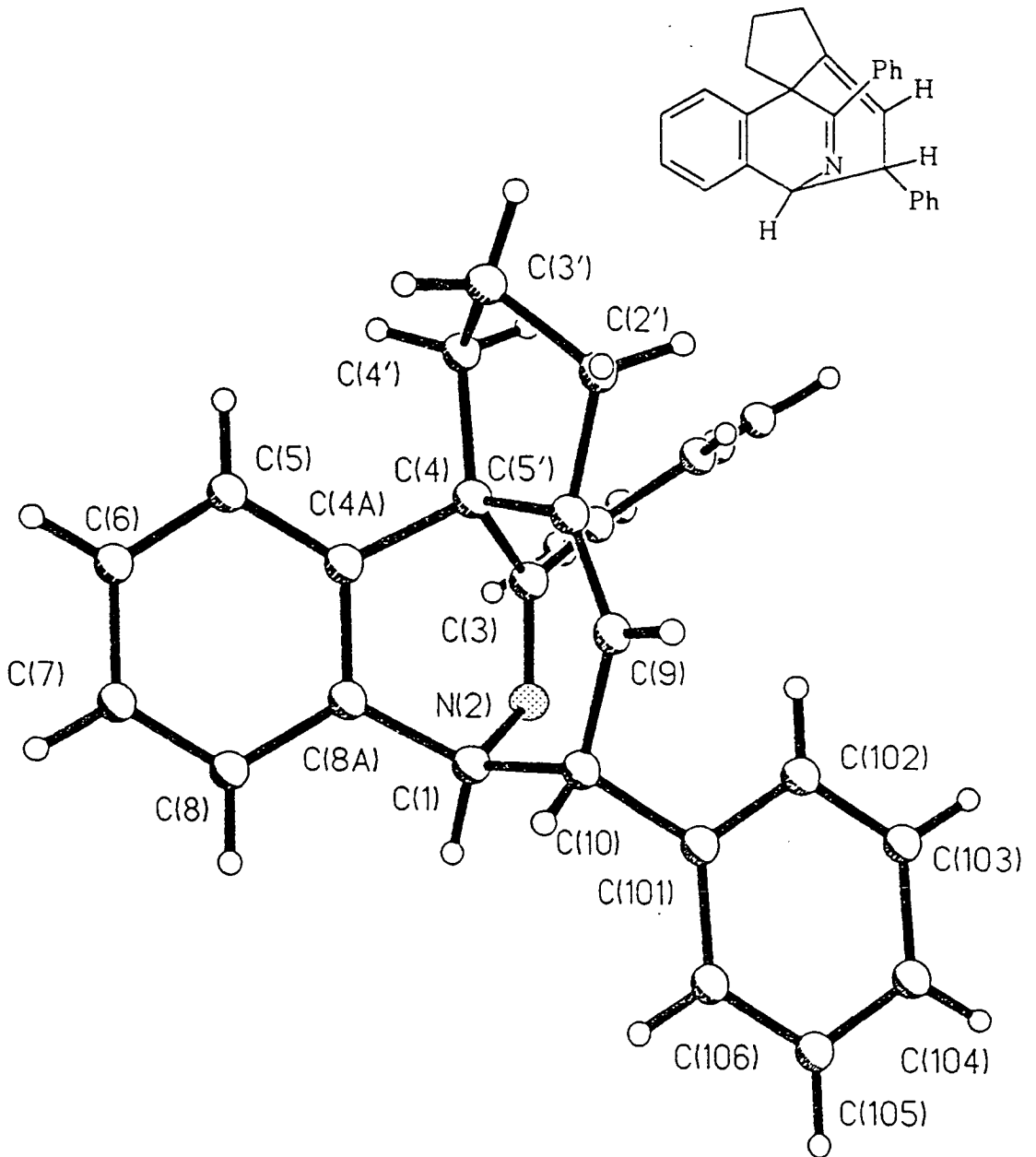


Figure 14

Table 1. Crystal data and structure refinement for 1.

Identification code	jps260
Empirical formula	$C_{27}H_{23}N$
Formula weight	361.46
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions	$a = 8.304(3) \text{ Å}$ $\alpha = 90^\circ$ $b = 11.722(5) \text{ Å}$ $\beta = 91.57(4)^\circ$ $c = 19.804(8) \text{ Å}$ $\gamma = 90^\circ$
Volume, Z	$1927.0(13) \text{ Å}^3$, 4
Density (calculated)	1.246 Mg/m^3
Absorption coefficient	0.072 mm^{-1}
F(000)	768
Crystal size	0.50 x 0.27 x 0.20 mm
θ range for data collection	2.63 to 20.07°
Limiting indices	$-8 \leq h \leq 8$, $0 \leq k \leq 11$, $0 \leq l \leq 19$
Reflections collected	2580
Independent reflections	1804 ($R_{\text{int}} = 0.0708$)
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1802 / 0 / 254
Goodness-of-fit on F^2	1.005
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.1132$, $wR2 = 0.2605$
R indices (all data)	$R1 = 0.2096$, $wR2 = 0.3487$
Extinction coefficient	0.011(5)
Largest diff. peak and hole	0.370 and -0.516 eÅ^{-3}

Table 3. Bond lengths [Å] and angles [°] for 1.

C(1)-N(2)	1.487(13)	C(1)-C(8A)	1.49(2)
C(1)-C(10)	1.55(2)	N(2)-C(3)	1.284(13)
C(3)-C(31)	1.502(14)	C(3)-C(4)	1.54(2)
C(4)-C(4')	1.53(2)	C(4)-C(4A)	1.54(2)
C(4)-C(5')	1.55(2)	C(4A)-C(8A)	1.38(2)
C(4A)-C(5)	1.39(2)	C(5)-C(6)	1.40(2)
C(6)-C(7)	1.38(2)	C(7)-C(8)	1.35(2)
C(8)-C(8A)	1.43(2)	C(9)-C(5')	1.32(2)
C(9)-C(10)	1.51(2)	C(10)-C(101)	1.51(2)
C(2')-C(3')	1.49(2)	C(2')-C(5')	1.50(2)
C(3')-C(4')	1.55(2)	C(31)-C(36)	1.38(2)
C(31)-C(32)	1.40(2)	C(32)-C(33)	1.41(2)
C(33)-C(34)	1.37(2)	C(34)-C(35)	1.35(2)
C(35)-C(36)	1.40(2)	C(101)-C(106)	1.38(2)
C(101)-C(102)	1.42(2)	C(102)-C(103)	1.36(2)
C(103)-C(104)	1.39(2)	C(104)-C(105)	1.39(2)
C(105)-C(106)	1.37(2)		
N(2)-C(1)-C(8A)	111.4(9)	N(2)-C(1)-C(10)	107.5(8)
C(8A)-C(1)-C(10)	113.4(9)	C(3)-N(2)-C(1)	114.2(9)
N(2)-C(3)-C(31)	114.5(10)	N(2)-C(3)-C(4)	123.3(9)
C(31)-C(3)-C(4)	121.7(11)	C(4')-C(4)-C(3)	118.3(9)
C(4')-C(4)-C(4A)	114.2(9)	C(3)-C(4)-C(4A)	105.7(8)
C(4')-C(4)-C(5')	104.1(9)	C(3)-C(4)-C(5')	107.8(8)
C(4A)-C(4)-C(5')	106.0(8)	C(8A)-C(4A)-C(5)	121.1(10)
C(8A)-C(4A)-C(4)	115.5(10)	C(5)-C(4A)-C(4)	123.4(11)
C(4A)-C(5)-C(6)	118.4(11)	C(7)-C(6)-C(5)	120.6(12)
C(8)-C(7)-C(6)	121.4(12)	C(7)-C(8)-C(8A)	119.1(12)
C(4A)-C(8A)-C(8)	119.3(11)	C(4A)-C(8A)-C(1)	117.7(10)
C(8)-C(8A)-C(1)	122.9(11)	C(5')-C(9)-C(10)	128.0(11)
C(9)-C(10)-C(101)	113.0(10)	C(9)-C(10)-C(1)	114.2(9)
C(101)-C(10)-C(1)	112.4(9)	C(3')-C(2')-C(5')	106.2(10)
C(2')-C(3')-C(4')	102.6(10)	C(4)-C(4')-C(3')	104.3(9)
C(9)-C(5')-C(2')	128.1(11)	C(9)-C(5')-C(4)	124.7(10)
C(2')-C(5')-C(4)	107.2(10)	C(36)-C(31)-C(32)	118.8(10)
C(36)-C(31)-C(3)	121.7(10)	C(32)-C(31)-C(3)	119.4(10)
C(31)-C(32)-C(33)	119.7(11)	C(34)-C(33)-C(32)	120.4(11)
C(35)-C(34)-C(33)	119.7(11)	C(34)-C(35)-C(36)	121.2(13)
C(31)-C(36)-C(35)	120.1(11)	C(106)-C(101)-C(102)	117.4(11)
C(106)-C(101)-C(10)	122.9(12)	C(102)-C(101)-C(10)	119.4(12)
C(103)-C(102)-C(101)	118.6(12)	C(102)-C(103)-C(104)	123.1(12)
C(105)-C(104)-C(103)	118.7(13)	C(106)-C(105)-C(104)	118.3(13)
C(105)-C(106)-C(101)	123.7(12)		

Symmetry transformations used to generate equivalent atoms:

Table 1. Crystal data and structure refinement for labour(1974) at 150 K.

Empirical formula	C19 H19 N1
Formula weight	261.37
Wavelength	1.54180 A
Crystal system	Monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 8.657(6) A alpha = 90 deg. b = 24.09(2) A beta = 94.95(8) deg. c = 7.071(8) A gamma = 90 deg.
Volume	1469.14 A ³
Z	4.00
Number of reflections for cell	15
Theta range for cell	20 to 22 deg.
Density (calculated)	1.18 Mg/m ³
Absorption coefficient	0.48 mm ⁻¹
F(000)	561.32
Crystal description	colourless block
Crystal size	0.47 x 0.35 x 0.19 mm
Theta range for data collection	2.5 to 60.00 deg.
Index ranges	-9<=h<=9, -26<=k<=19, 0<=l<=7
Reflections collected	0
Independent reflections	1670 [R(int) = 0.06]
Scan type	2\q/\w
Data / parameters	1159/182
Goodness-of-fit	1.0066
R	0.0973
Rw	0.1073
Number of reflections used	1159
Observed criterion	>3.00\s(I)
Refinement type	Full-matrix least-squares on F -CRYSTALS
Extinction coefficient	69(28)
Final maximum delta/sigma	0.028989

Table 5: Bond lengths and angles.

C(1) - N(2)	1.467(7)
C(1) - C(81)	1.512(7)
N(2) - C(3)	1.252(7)
C(3) - C(31)	1.516(7)
C(3) - C(4)	1.559(7)
C(31) - C(32)	1.400(7)
C(31) - C(36)	1.380(7)
C(32) - C(33)	1.366(7)
C(33) - C(34)	1.397(8)
C(34) - C(35)	1.368(8)
C(35) - C(36)	1.398(7)
C(4) - C(41)	1.584(7)
C(4) - C(42)	1.457(9)
C(4) - C(51)	1.556(6)
C(42) - C(43)	1.51(1)
C(42) - C(44)	1.353(9)
C(51) - C(5)	1.393(7)
C(51) - C(81)	1.367(7)
C(5) - C(6)	1.393(7)
C(6) - C(7)	1.364(8)
C(7) - C(8)	1.392(7)
C(8) - C(81)	1.395(7)
N(2) - C(1) - C(81)	113.3(5)
C(1) - N(2) - C(3)	120.1(4)
N(2) - C(3) - C(31)	115.9(4)
N(2) - C(3) - C(4)	123.4(4)
C(31) - C(3) - C(4)	120.5(4)
C(3) - C(31) - C(32)	118.6(4)
C(3) - C(31) - C(36)	123.2(4)
C(32) - C(31) - C(36)	117.9(4)
C(31) - C(32) - C(33)	122.0(5)
C(32) - C(33) - C(34)	119.4(5)
C(33) - C(34) - C(35)	119.5(4)
C(34) - C(35) - C(36)	120.8(5)
C(31) - C(36) - C(35)	120.3(4)
C(3) - C(4) - C(41)	107.3(5)
C(3) - C(4) - C(42)	112.6(4)
C(41) - C(4) - C(42)	111.5(6)
C(3) - C(4) - C(51)	107.3(4)
C(41) - C(4) - C(51)	108.2(4)
C(42) - C(4) - C(51)	109.8(5)
C(4) - C(42) - C(43)	112.2(6)
C(4) - C(42) - C(44)	122.6(8)
C(43) - C(42) - C(44)	125.0(7)
C(4) - C(51) - C(5)	122.6(5)
C(4) - C(51) - C(81)	118.6(4)
C(5) - C(51) - C(81)	118.7(4)
C(51) - C(5) - C(6)	120.5(5)
C(5) - C(6) - C(7)	120.1(5)
C(6) - C(7) - C(8)	120.2(4)
C(7) - C(8) - C(81)	119.1(5)
C(1) - C(81) - C(51)	119.1(4)
C(1) - C(81) - C(8)	119.4(5)
C(51) - C(81) - C(8)	121.4(5)

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