Reactive Intermediates

:

Model Substrate Studies

A thesis

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by

Stephen J van Eyk

University of Canterbury

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Contents

Abstract

The reactions of cinnamyl chloride and crotyl chloride with various aldehydes, RCHO; R=Me, Et, iPr, $CH_3(CH_2)_5$, $PhCH_2$, Ph, p-MeOPh, p-NCPh, to form homoallylic alcohols under the control of Sn-Al, Cr(II), Zn and Mg were examined and the stereochemistry of the products determined. Stereoselectivity and regioselectivity of these reactions are compared and explained with reference to cyclic and linear mechanisms and the metal involved, frontier molecular orbital energies and molecular modelling experiments.

An attempt was made to extend control of the relative stereochemistry of the Sn-Al reaction to systems with more than two contiguous carbon centers. The aldehydes, $RCH(CH_3)CHO$; R=Me, Ph, tBu, reacting with cinnamyl chloride under control of Sn-Al resulted in moderate Cram selectivity, this diastereofacial selectivity increasing with the bulk of the aldehydes' R group. Glyceraldehyde gave very poor diastereofacial selectivity.

Dialdehydes terephthaldecarboxaldehyde and glyoxal were reacted with cinnamyl chloride mediated by Sn-Al and the relative stereochemistries of the major products deduced. Competition experiments of crotyl bromide and cinnamyl chloride with aryl aldehydes, p-R-C_6H_4CHO; R=H, Me, MeO, NC, O_2N, under the control of tin mediated conditions (Sn-Al) and of crotyl organotin and cinnamyl organotin (allylic-SnL_3; L=Ph, nBu) catalysed by either $BF_3.OEt_2$ or heat were carried out and the results of these experiments discussed in the light of frontier molecular orbital theory.

Molecular mechanics calculations were performed to evaluate the steric stability of rotamers of *threo* and *erythro* homoallylic alcohols and these used in association with electronic effects to explain the diastereoselectivity

of the linear mechanism. Conformational analysis using MM calculations were undertaken in an attempt to rationalize the stereoselectivity at the cyclic transition state.

Synthetic pathways to β,γ-epoxy ketones were explored and the synthesis of 38, 44, and 50 effected by a number of different paths to maximize yields; the diastereoselectivities of the epoxidations of intermediate hydroxy and acetoxy alkenes was investigated.

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Abstract
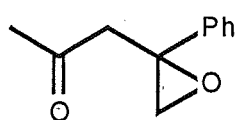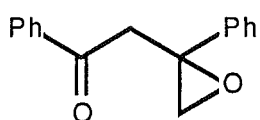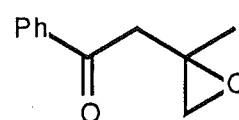
Introduction

In the synthesis of organic molecules at least three problems must be dealt with: the carbon skeleton must be built; the appropriate functionalities must be introduced and the correct stereochemistry induced. In modern chemistry it is no longer sufficient to deal with only the first two of these objectives. Highly developed techniques are now readily available for certain organic systems (notably rigid cyclic or conformationally non-dynamic systems) to produce pure racemates and less often pure enantiomers.

The control of stereochemistry in conformationally non-rigid open chain compounds is more difficult. The size of the synthetic problem can become enormous when the elaboration of complex molecules such as polyether, ansamycin, and macrolide antibiotics is attempted. They and their synthons often have functional groups of similar reactivity hence selective methods and reagents need to be available to the synthetic organic chemist. Recently the biological activities and commercial importance of molecules such as monensin, α-multistriatin and nonactin have stimulated efforts to design methodological tools which provide products with relative and absolute asymmetric induction in high yields[1] . These methods include crossed aldol reactions, reaction of organometallic compounds with carbonyl compounds, ring opening reactions of cyclic compounds, [75TL2643] epoxidation of allylic alcohols,[81TL2017, 83PA1823] hydroboration of olefinic compounds,[78JA2933, 80JA7385] reduction of carbonyl derivatives, [80TL1641, 80TL2467] sigmatropic rearrangements[79AC0563, 80JA1155] and selected reactions of carbohydrates[79AR0159, 80JA1439].

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[1]   For reviews see 80TD0003, 82AC0555, 82HC0357

Introduction

β-Methyl alkanol units in both the *erythro* and *threo* configurations are characteristic structural elements of a number of macrolide and polyether antibiotics and the diastereoselective synthesis of β-hydroxycarbonyl and of homoallylic alcohols is applicable to the synthesis of these materials. The stereoselective formation of C-C bonds between prochiral centres is most generally accomplished by the addition reaction of metal enolates[2] or 2-alkenylmetal derivatives[3] to aldehydes.

Monensin
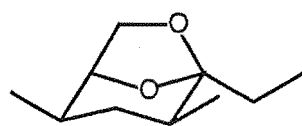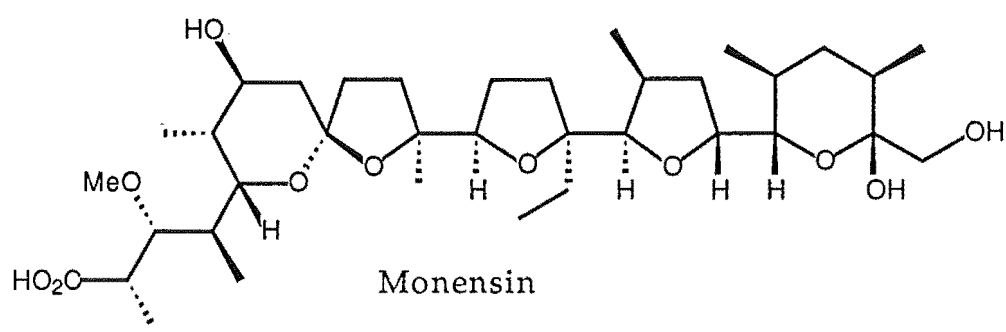
α-Multistriatin
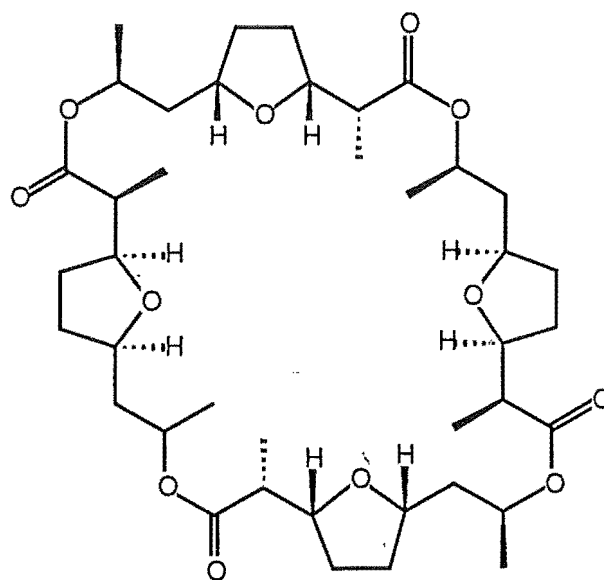
Nonactin

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2   77JA0247, 77JA8109, 79JA2501, 75TL1225, 77TL4651, 80JO1066, 73JA3310, 75JL2201, 79TL1665, 79TL2225, 79TL2229, 79TL3937, 79JA6120, 74JM0373, 77JA7705, 74JA7503, 79TL4029.

3   80TL0303, 79TL4653, 79AC0306, 80JA2118, 72JM0020, 80JA4548, 77JA3179, 82CL1299, 83OM0191, 85JO5396, 82BJ0561, 87JM0177, 85TL4211, 87AR0243.

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The aldol condensation is fundamental to biosynthesis, however the same products can be produced by the synthetically analogous allylation of carbonyl compounds to produce homoallylic alcohols and subsequent oxidative cleavage of the double bond. Homoallylic alcohols have become one of the most useful intermediates in acyclic synthesis because of the facility the hydroxyl group and the C=C double bond offer for chemical modification. This dual functionality allows easy entry to a variety of bifunctionalized molecules and furthermore can undergo a facile one-carbon homologation to δ-lactones via hydroformylation[84TL4051] or can be epoxidised thereby introducing a third chiral centre.[81JA3229]

Allylations of aldehydes or ketones to give homoallylic alcohols can be achieved using conventional organometallic reactions (eg Grignard or Barbier reactions) or in the presence of catalysts.[85JO0045] Mild conditions have recently been developed which allow or even require aqueous conditions or the presence of metallic salts in a lower valence state. Electro-chemical recycling of the organometallic has been developed and is likely to become important in large scale manufacture of organic chemicals. The allylation reaction can be highly stereospecific and with careful selection of the organometallic reagent and reaction conditions both *threo* and *erythro* homoallylic alcohols can be produced from the same aldehyde and allylic moiety. The formation of C-C bonds using organotin compounds has received occasional attention and it is the intent of this thesis to expand on the use of tin for allylation of carbonyl compounds.

The Use of Tin in Diastereoselective Carbon-Carbon Bond-forming Reactions
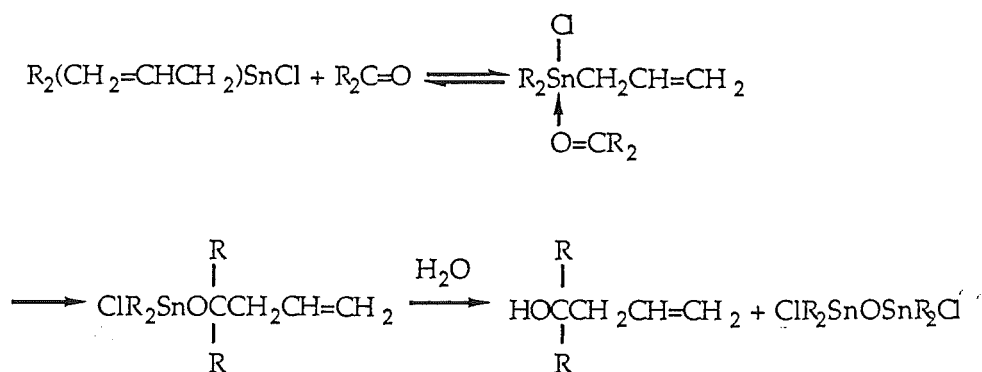
Allylic-organotins: Thermal reaction

It has been known for some time that allylic organotins and allylic organotin halides can be used as reagents for the formation of homoallylic alcohols.
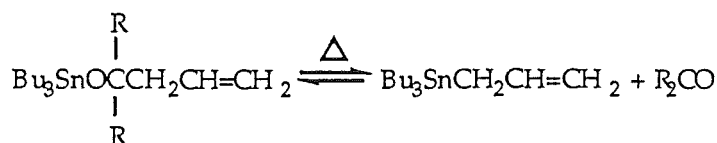
Introduction

Tagliavini et. al.[77IC0047] suggested that after the formation of the allylic dialkyltin halide[4] a coordination step (where the carbonyl coordinates to the tin atom) may facilitate the overall reaction (Scheme 1.1). At that time no mention is made of a cyclic transition state and there was no relative stereo-chemistry to be considered. In later papers[78IC0041, 78JM0037, 79IC0263] they suggested that this reaction may be reversible (Scheme 1.2) since allyl dialkyl carbinols on reaction with (Bu$_3$Sn)$_2$O and (Bu$_2$SnCl)$_2$O produced water, the corresponding ketones and the mixed allyltins: Bu$_3$Sn(CH$_2$CH=CH$_2$) and Bu$_2$Sn(CH$_2$CH=CH$_2$)Cl respectively. The elimination reaction (and presumably the addition reaction) was explained in terms of a pericyclic transition state[5] (Scheme 1.3) in which nucleophilic attack of the terminal olefinic carbon to the tin atom takes place together with the breaking of the Sn-O and the C-C bonds.

Scheme 1.1

$$R_2(CH_2=CHCH_2)SnCl + R_2C=O \rightleftharpoons R_2\overset{\overset{Cl}{|}}{Sn}CH_2CH=CH_2$$
$$\underset{\uparrow}{O=CR_2}$$

$$\longrightarrow ClR_2Sn\overset{\overset{R}{|}}{O}\underset{\underset{R}{|}}{C}CH_2CH=CH_2 \overset{H_2O}{\longrightarrow} HO\overset{\overset{R}{|}}{\underset{\underset{R}{|}}{C}}CH_2CH=CH_2 + ClR_2SnOSnR_2Cl$$

Scheme 1.2

$$Bu_3SnO\overset{\overset{R}{|}}{\underset{\underset{R}{|}}{C}}CH_2CH=CH_2 \overset{\Delta}{\rightleftharpoons} Bu_3SnCH_2CH=CH_2 + R_2CO$$
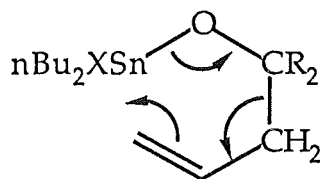
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[4]   These and other allylic alkyltin halides are easily formed from the corresponding alkyltin halides and an allylic Grignard reagent and other methods as described in the referenced articles.

[5]   This transition state has been previously suggested for reversible Grignard reactions.[69JA5162, 70CF1077]

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Scheme 1.3

$$nBu_2XSn \diagdown \overset{O}{\diagup} CR_2$$
$$CH_2$$

The reaction of 2-butenyl di-n-butyltin chloride with aldehydes, RCHO; R=CH$_3$, C$_2$H$_5$, C$_2$H$_5$(CH$_3$)CH, (CH$_3$)$_2$CH, C$_6$H$_5$, gives *threo* and *erythro* homoallylic alcohols in high yields[82JM0149] and the ratio of products is independent of the *trans:cis* ratio of 2-butenyl di-n-butyltin chloride; e.g. *i*-PrCHO reacts with 66.6:33.3 *trans* and *cis* Bu$_2$ClSnCrot to give 66.6:33.3 *threo* and *erythro* homoallylic alcohols and with 50:50 *trans* and *cis* Bu$_2$ClSnCrotyl to give the same (66.6:33.3) ratio of *threo* and *erythro* homoallylic alcohols.

The *threo:erythro* ratio of 2:1 obtained, which is independent of the *trans:cis* crotyltin ratio, shows that formation of the *threo* isomer is twice that of the *erythro* isomer. Either *cis trans* interconversion of the reactant occurs under the reaction conditions and the addition is stereospecific or the product ratio is thermodynamically determined.

These results should be compared with those of Yamamoto et. al.[80JA4548] who realized total (100%) *erythro* selective coupling via the thermal[72JM0020] reaction of *cis*-crotyl tri-n-butyltin (and also via the Lewis acid mediated reaction).

Allylic-organotins: Lewis acid mediated reaction
It has been stated that in general, the *trans*-crotyl metal compound, such as M = Li,[80TL0303] B,[80CL0993] Al,[80JA2118] Zn,[87JM0177] Ti,[81TL0243] Zr[81TL2895] or Cr[81TL1037]..., reacts with aldehydes to produce the corresponding *threo*-homoallylic alcohols predominantly if the geometry of the double bond is

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retained during the reaction, while the *cis* derivative gives the *erythro* isomer preferentially.[84TD2239]

The *erythro* selective synthesis is of special value for the synthesis of bio-organic molecules (e.g. macrolide antibiotics). Few easy synthetic pathways are available to form the *cis*-allylic metal derivative,[80JA4548] therefore if an *erythro* selective reaction process could be found for *trans*-allylic metal derivatives a number of synthetic problems could be solved.

Yamamoto et. al.[80JA7107] used the Lewis acid mediated addition[79CL0919] of crotyl tri-n-butyltins to aldehydes (R = C_6H_5, $(CH_3)_2CH$, $(C_2H_5)_2CH$, $(CH_3)_2CHCH_2$, CH_3CH_2, CH_3) and found that *erythro*-homoallylic alcohol products were produced preferentially (90-98%) in good (82-90%) yield independent of the *trans* to *cis* ratio of the crotyl metal derivatives. Thus *trans*-crotyl tri-n-butyltin reacted with benzaldehyde in the presence of $BF_3.OEt_2$ to give 98% of the *erythro*-homoallylic alcohol in a 90% yield and *cis*-crotyl tri-n-butyltin under the same conditions gave 99% of the *erythro*-homoallylic alcohol in similar yield. Further, mixtures of *trans*- and *cis*-crotyl tri-n-butyltin under similar conditions gave comparable results.

Yamamoto suggests the reaction goes through a linear mechanism[6] (similar consideration is made for aldol addition[79JA7723]). If the *trans*-crotyltin undergoes a facile isomerization to the *cis* isomer via 1,3-tin migration (Scheme 1.4), the *erythro* selectivity of this reaction can be understood by the reaction occuring via a cyclic transition state. However this is excluded by the following two experiments:

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[6] See Schemes 2.2 and 2.3. The linear and cyclic mechanisms are more fully presented in the discussion section of this document.

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- the reaction of *trans*-crotyl tributyltin with benzaldehyde in the

presence of $BF_3.OEt_2$ was quenched immediately at -78°C with MeOH-

H_2O. No isomerization of the recovered crotyltin could be detected

- the reaction of the isomeric 1-methylallyltin,[76JM0155] with

benzaldehyde under the same conditions produced 1-phenyl-

3-penten-1-ol in high yield.

Scheme **1.4**
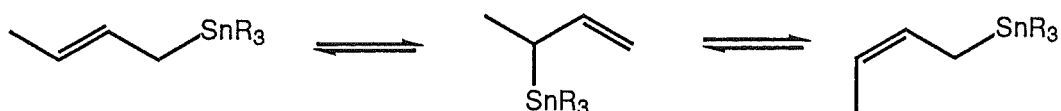
In a later paper[84TD2239] Yamamoto suggests that the Lewis acid changes the

transition state structure by coordinating to the aldehyde oxygen and

preventing coordination of the aldehyde to the tin atom thereby excluding

the possibility of forming a cyclic transition state. The Lewis acid activates

the carbonyl group and also acts as a stereosteering group. The effects of

other Lewis acids ($TiCl_4$, $SnCl_4$, BCl_3, cyclopentyldichloroborane) are also

reported; $BF_3.OEt_2$ gave the best results in both diastereoselectivity and yield.

Recently an X-ray crystal structure of a boron triflouride adduct of

benzaldehyde and heteronuclear Overhauser experiments shows that the

Lewis acid is indeed complexed *anti* to the phenyl group of benzaldehyde

both in the solid phase and in solution.[86JA2405]

Koreeda and Tanaka[82CL1299] using the same Lewis acid conditions as

Yamamoto found that *trans*-crotyl triphenyltin reacted with benzaldehyde to

give 5:1 *erythro-* and *threo*-homoallylic alcohols but *trans*-cinnamyl

triphenyltin reacted with benzaldehyde to give 1:99 *erythro-* and *threo*-

homoallylic alcohols. Keck et. al.[84TL3927] further investigated this reaction

and substituted other Lewis acids ($MgBr_2$, ZnI_2, $SnCl_4$, $TiCl_4$). The reaction

mediated by $TiCl_4$ is of special note. Here the order of reagent addition

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determines the *threo erythro* diastereoselectivity. Thus addition of crotyl tri-n-butyltin to a solution containing the Lewis acid and cyclohexane-carboxaldehyde produces 90:7 *erythro-* to *threo-* homoallylic alcohols (and 3% of the α-adduct) whereas addition of the aldehyde to a solution prepared from Lewis acid and crotyl tri-n-butyltin results in 4:91 *erythro-* to *threo-* homoallylic alcohols (and 5% of the α-adduct). In contrast the $BF_3.OEt_2$ mediated reactions are unaffected by the order of addition of reagents.

In addition Yamamoto[84TD2239] discovered the Lewis acid $AlCl_3.iPrOH$ mediated reaction of crotyl tri-alkyltin with certain aldehydes gave the α-adduct. Thus reaction with RCHO (R = Ph, Et, nPr, nBu) gave 83 - 95% of the (linear) α-adduct, 17 - 5% of the (branched) γ-adduct; (R = n-C_9H_{19}, Me_2CHCH_2) gave 60:40 α- and γ-adducts; (R = iPr, MeCH=CH, PhC=O) gave the γ-adduct only. Where the linear adduct was formed the ratio *trans:cis* was around 90:10 in all cases. A number of other factors (order of reagent addition, replacing iPrOH with other alcohols) were examined and found to be important in determining the regioselectivity of the reaction.

Yamamoto writes (Scheme 1.5) "the regioreversed addition can be understood by the following routes. Transmetallation from (i) with the aid of $AlCl_3.iPrOH$, presumably $AlCl_2(O\text{-}iPr)$, would proceed through S_E2' process to produce the α-methylallyl aluminium derivative (ii), which reacts with aldehydes to give (v). At higher temperature and/or over a prolonged period of time, (ii) undergoes rearrangement to the more stable isomer (iii), which reacts with aldehydes to give (iv). $AlCl_3$ and other strong Lewis acids produce (iv) via path A. The combination of the soft Lewis acid ($AlCl_3.iPrOH$) and the reactive aldehydes gives (v) via path B. Unreactive aldehydes and ketones permit further rearrangement to (iii), resulting in (iv) via path C. Presumably, the addition of aldehydes prior to the addition of (i) makes path A favourable."

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Scheme 1.5
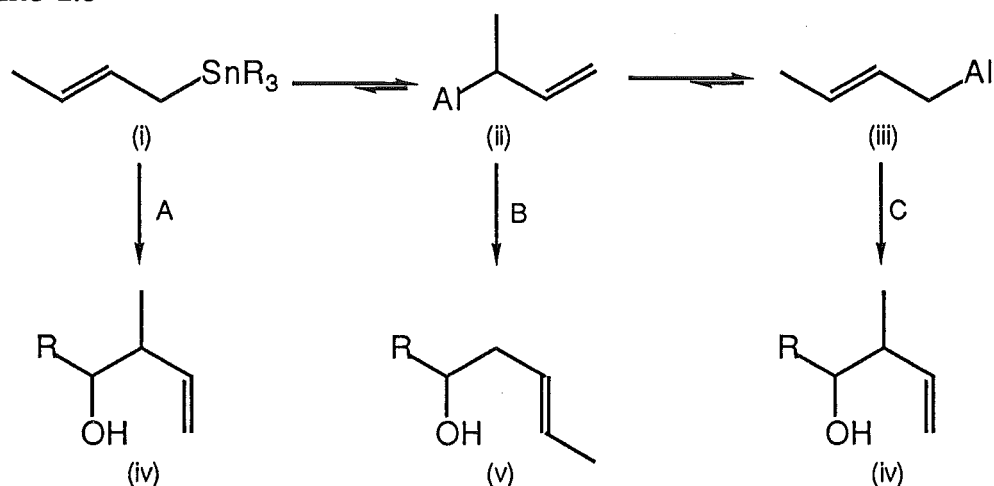
This plethora of results led Denmark and Weber[84JA7970] to design a system to evaluate the relative importance of synclinal[7] versus antiperiplanar reactive geometries (Scheme 1.6) and so help to explain a little more of the role of the metal centre, the Lewis acid and the allylic function. Reaction of the model aldehyde (Scheme 1.6, i) in the presence of various Lewis acids (TiCl$_4$, BF$_3$.OEt$_2$, AlCl$_3$, Et$_2$AlCl, ZrCl$_4$, SnCl$_4$, FeCl$_3$, CF$_3$COOH) and also the thermal reaction of the model aldehyde produces the cyclization products (Scheme 1.6, *syn*-ii, *anti*-iii) in *syn:anti* ratios greater than 80:20. This *syn* selectivity implies the preferred transition state of the *erythro* (*syn*) selective Lewis acid catalyzed allylic alkyltin - aldehyde reaction has synclinal geometry rather than the previously supposed antiperiplanar (linear) transition state geometry. However it would seem that intramolecular steric interactions might force this reaction to take on a synclinal geometry and the antiperiplanar versus synclinal transition state question should be further investigated. A second point of issue is the disposition of the tributyltin group. Denmark suggests, on the basis of recent studies, that the tin group is

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7   Note that while the cyclic chair transition state has the double bonds arranged in synclinal orientation, a synclinal geometry does not necessarily imply a cyclic transition state. That is, the observation of a synclinal orientation of double bonds does not necessarily imply an interaction between the metal atom and the carbonyl oxygen in the transition state.

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orientated *anti* to the approaching aldehyde giving the synclinal transition
state shown in Scheme **1.6**.

Scheme **1.6**

synclinal   syn (ii)

(i)

antiperiplanar   anti (iii)
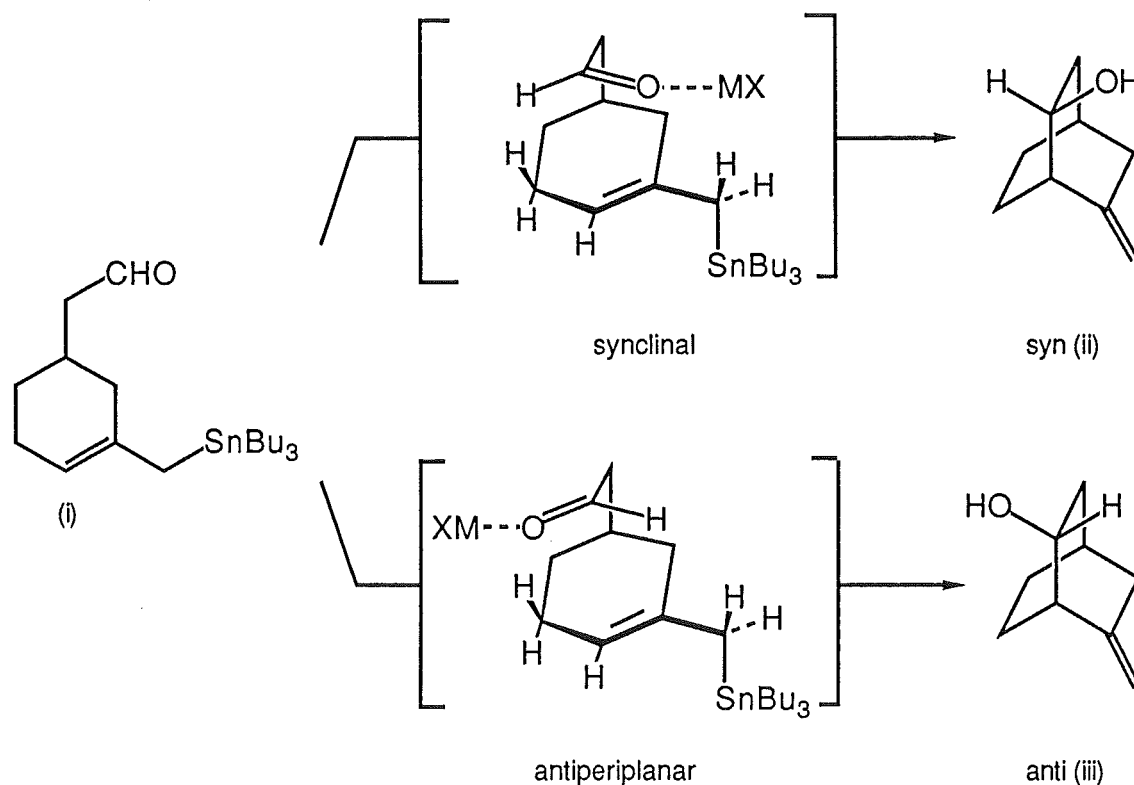
Metallic tin: Grignard or Barbier-like reactions

Mukaiyama et. al. had formed[80CL1507] allyltin dihaloiodide through
oxidative addition of allyl iodide to stannous halide, and reacted this with
carbonyl compounds to give homoallylic alcohols. Unfortunately this
reaction was limited to allyl iodides. In a later paper[81CL1527] they employed
metallic tin (rather than stannous halide) and found that not only allyl
iodide but also allyl bromide reacts under these mild conditions to give the
homoallyl alcohols. The following experiment typifies the reaction and is
used to demonstrate the mildness of the conditions. A suspension of
metallic tin (1.1 mmol), allyl iodide (1.0 mmol) and benzaldehyde (0.8
mmol) in 3 ml of THF was stirred for 0.5 hours before working up. Yields
obtained ranged from 76% to 88% for various aldehydes and 50% for

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4-phenyl-2-butanone. When crotyl bromide was reacted with benzaldehyde under these conditions a 59:41 *threo* to *erythro* diastereoselectivity was observed.[8] Mukaiyama realized the reaction mechanism was not clear but assumed initial formation of diallyltin dihalide which was suggested to react with aldehyde with concomitant rearrangement of the allylic fragment and after hydrolysis to form the homoallyl alcohols.

Two years later Nokami et. al.[83OM0191] added water to accelerate the reaction and aluminium (powder or foil) to improve the product yield. This new system was used to allylate aldehydes and ketones with allyl bromide or crotyl chloride (the latter reaction capable of producing two diastereo-isomers). For example, the heterogeneous mixture of acetaldehyde (20 mmol), crotyl bromide (19.4 mmol), was dissolved in ether (5 ml) and water (3 ml), tin powder (8.4 mmol), aluminium powder (18.5 mmol) and a catalytic quantity of hydrobromic acid were added and the mixture stirred vigorously before workup. Allyl bromide reacting under these conditions generally gave better yields with aldehydes (around 70%) than with ketones (around 50%). Reaction of crotyl bromide with various aldehydes gave yields ranging from 76% to 96% (64% with crotyl aldehyde) and diastereo-selectivities favouring the *erythro*-homoallylic alcohol ranging 53:47 to 73:27. Different solvent systems gave different results. Thus $THF-H_2O$ gave better yields and diastereoselectivities than Et_2O-H_2O.

Luche et. al.[85TL1449] has found that homoallylic alcohols can be formed from allylic halides and aldehydes or ketones by using metallic tin under sonication in a water - tetrahydrofuran solvent mixture. It would appear

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8   Note this diastereoselectivity does not make sense in the light of later experiments by Nokami[83OM0191] et. al. where *erythro* selectivity would have been expected. However, this ratio had been determined from n.m.r. spectra and different and disagreeing spectra have been assigned to the *threo* and *erythro* product homoallylic alcohols at different times.[70JL0106] cf [74CA0496] A definitive assignment of these spectra has been provided by Coxon and Hii.[77AJ0835]

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that the function of the sonication (or in Nokami's system, the function of the aluminium) is to activate the metallic tin and to thus allow the formation of the allylic organotin. Luche has also investigated the kinetic selectivity of the reaction. This allows discrimination between aldehydes and ketones and he finds that for an equimolar mixture of benzaldehyde and acetophenone sonicated in the presence of 1.2 equivalents each of allyl bromide and tin that 90% of the aldehyde had undergone reaction whereas no trace of reaction with ketone was apparent. In a later paper[87JM0177] Luche writes about this reaction "...several mechanisms, involving 6-membered cyclic or acyclic processes according to the organometallic used, have been proposed to account of the stereoselectivity. In our systems, the presence of water probably precludes the presence of organometallic species, and so the transition state must be different. Although no direct evidence has yet been obtained for a free radical intermediate in solution or absorbed on the metal surface,[9] it can be regarded as highly probable."[10]

Torii et. al.[84TL6017, 85JO5396, 86TL2395] uses this type of reaction but electrochemically recycles the allylic tin reagent. In doing so he has carried out three different reactions *in situ*; generation of the organometallic reagent, allylation of the carbonyl compound and regeneration of the metal. Typical of Torii's procedure is the following experiment: a mixture of benzaldehyde (7.5 mmol), allyl bromide (15 mmol), tin powder (0.75 mmol) and cyclohexene[11] (30 mmol) was dissolved in methanol (3 ml) and acetic acid (0.75 ml) and stirred at room temperature for 2 h and then electrolysed in an undivided beaker type cell at 50 - 55°C using platinum foil electrodes

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[9]   The formation of organolithium and organomagnesium compounds is thought to involve a single electron transfer from the metal to the carbon-halogen bond. This first step necessarily occurs on the solid surface. It is reasonable to assume that this initial process applies also to other metals.

[10] In fact organotin compounds are known to be relatively stable to aqueous conditions but see ref 82JA3481.

[11] Cyclohexene was employed for trapping bromine formed at the anode.

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$(2 * 1.5 \text{ cm}^2)$ under a constant current (50 mA for 16 h, 3.9 F/mol). This gives a 91% yield of the homoallyl alcohol; only 11% of the homoallyl alcohol was obtained when no current was passed.

This system has clarified certain mechanistic details. If the tin reagent is to be recycled then the tetravalent tin remaining after the allylation reaction has to be reduced to the active divalent or zero valent tin. This is then able to react with allyl bromide and regenerate the allyltin reagent. The reaction process is illustrated in Scheme 1.7. Diallyltin dibromide (iii) is produced from a metallic tin (or divalent tin) and allyl bromide in methanol and reacts with benzaldehyde to give allyl dibromotin monoalkoxide. This undergoes alkoxy exchange with methanol to produce the homoallyl alcohol (i) and allyl dibromotin methoxide (iv). In contrast to the reaction in tetrahydrofuran, the reaction rate of diallyltin dibromide with benzaldehyde in methanol is so fast as to avoid loss of the diallyltin dibromide reagent by electroreduction.[12] Allyl dibromotin methoxide (iv) is electroreduced to di and/or zero valent tin,[13] which completes the cycle by reacting with allyl bromide thus regenerating diallyltin dibromide.

Supporting evidence of this cycle is found in the cyclic voltammogram of (iii) in methanol. A reduction peak (circa -1.0 V vs. Ag/AgNO$_3$) is clearly seen, which upon adding benzaldehyde, disappears and shifts to a new peak (circa -0.8 V) corresponding to (iv) or its related alkoxide. This is less negative than the original, suggesting allyl dibromotin methoxide (iv) is more easily reduced than diallyltin dibromide (iii).

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[12]   On electrolysing diallyltin dibromide in methanol and then adding benzaldehyde, a trace of (i) was obtained and benzaldehyde was recovered, suggesting (iii) is also electroreducible.

[13]   Although the structure of the Sn(II) compound in this electrolysis is not clear at this moment, it is known the allylic reagent produced from stannous halides and allyl bromide reacts with carbonyl compounds, providing the corresponding homoallyl alcohols.

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Scheme **1.7**
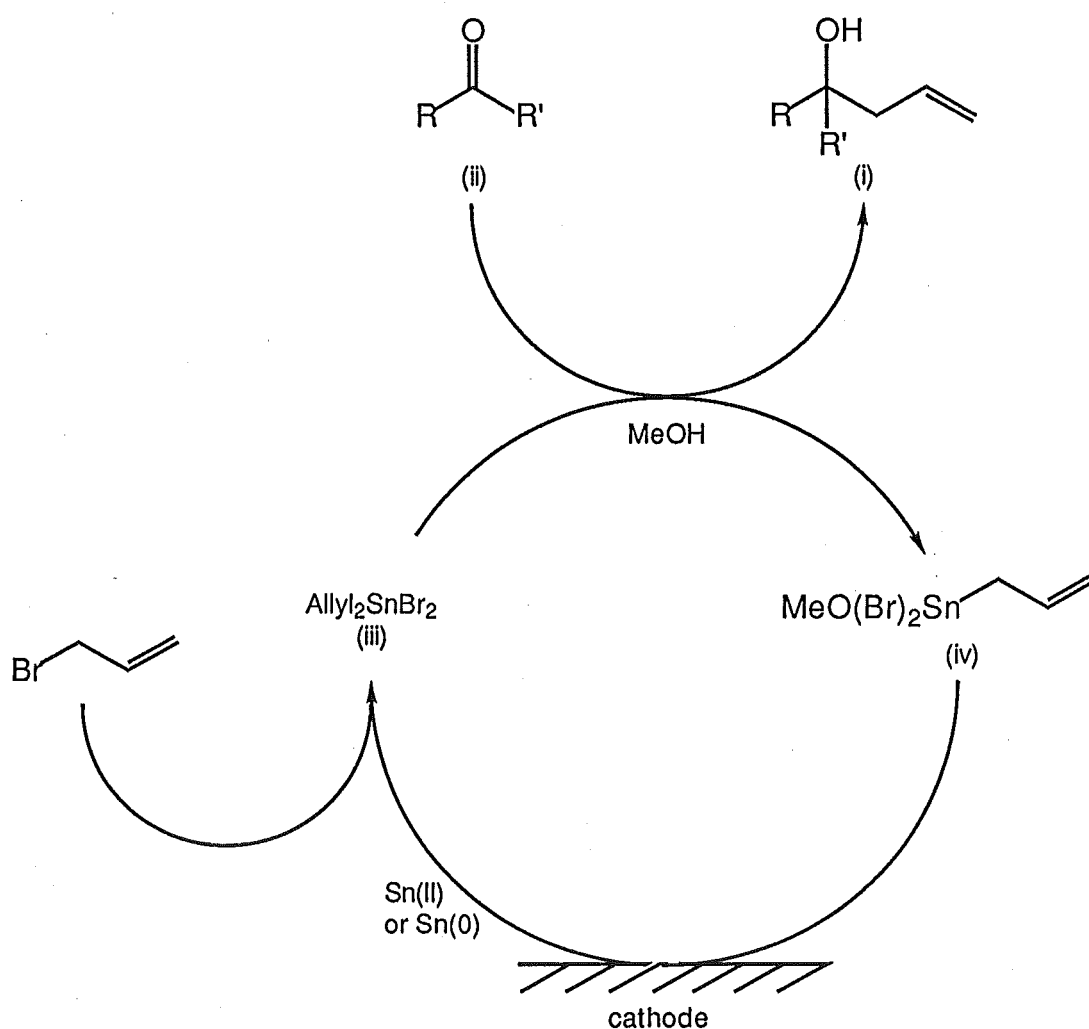
Torii found that allyl chloride was unreactive under these electrolysis conditions and so applied similar conditions to the tin-aluminium system of Nokami. Torii notes that aluminium is capable of reducing Sn(II) and Sn(IV) and carries out experiments using aluminium to reduce the tin salts rather than his electroreductive techniques. Using aluminium powder (2 equiv) and tin(II) chloride (0.1 equiv) in the MeOH-HOAc solvent system Torii had used for his previous electrochemical experiments he found no reaction occurred. Repeating the reaction with the addition of water lead to the formation of the homoallyl alcohol in 88% yield. Other solvent systems with a water co-solvent also gave good yields of the product. Since low

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product yields were obtained if either water or acetic acid were not present in the reaction mixture it is apparent that both play a part in the oxidative addition of allyl chloride to metallic tin rather than activation of the reduction process.

The absence of either aluminium or tin(II) chloride from the reaction mixture results in no homoallyl alcohol being produced and the use of metallic tin alone gives only low yields of the product. It becomes clear from these experiments that metallic (zero valent) tin together with aluminium is responsible for the allylation and the activity of this tin-aluminium system (however they are combined) affects the reaction rate and yield.

These experiments were repeated using active zero valent tin. Torii found that the Sn(II)-Al system enhances the rate of allylation as compared with a system of metallic tin and aluminium. Various tin reagents (SnSO$_4$, Sn(AcO)$_2$, SnO, SnCl$_2$) can be used as can Sn(IV)Cl$_4$ and at least 1 equivalent of aluminium is required for a complete conversion. Therefore, in this allylation system, [Sn(II)-Al-H$_2$O-HOAc-organic solvent], aluminium initially reduces Sn(II) to Sn(0) and an active Sn-Al combined metal is formed which oxidatively adds to allyl chloride. After the following allylation step Sn(IV) is again reduced by aluminium to Sn(0).

The Use of Other Metals in Diastereoselective Carbon-Carbon Bond-forming Reactions

It is impossible to include a comprehensive account of all research here but to obtain a more complete understanding of metal mediated carbon-carbon bond forming reactions it is important to have at least an overview of the diastereoselective and regioselective results of this reaction having been directed by a range of different metals. To this end a short discussion is presented here. In order to compare the reactions of tin (a group IVA

Introduction

element) with different classes of metals some results from reactions of chromium (a transition metal), zinc (a group II metal) and boron (a group IIIA metal) are briefly presented below.

Chromium

Tamejiro Hiyama et. al. established[77JA3179] the reaction of anhydrous chromic chloride with lithium aluminium hydride (presumably forming chromous chloride) and subsequent addition of aldehydes and allylic halides to form the corresponding homoallylic alcohols in reasonable (55 - 96%) yield. They report complete *threo* selectivity for the reaction of benzaldehyde and crotyl bromide. I have noted in the discussion that although in this case the *threo* selectivity is high a significant proportion (30%) of the linear isomer is also produced. This is in contrast to the reaction of cinnamyl chloride with benzaldehyde where I have found that the threo selectivity is not as high (17% erythro was found) but none of the linear isomer was formed. The similarity in results with commercial chromic chloride and the chromous chloride and lithium aluminium hydride mixture would imply that the reactive metal species in the latter case is the chromium(II) ion, although the identity of the species has not yet been established.

In a 1981 paper[81TL1037] Hiyama showed that both *trans*-crotyl bromide and *cis*-crotyl bromide with Cr(II) and aldehydes to give a *threo* preference (66-100%) although no mention of the linear isomer formation was made. The more hindered the aldehyde the less selective the reaction so that reaction of crotyl bromide with 2,2-dimethyl-propanal gave a 65% erythro bias.

In an important paper[82BJ0561] this effect is ascribed to the chair-like six-membered transition state. It is also shown that solvent does play a part in

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the reaction speed and to a lesser extent to its diastereoselective direction. Thus the more polar N,N-dimethylformamide (DMF) solvent gives better yields and but less definite *threo* selectivity. The lesser *threo* selectivity was attributed to the better solvating power of the DMF (cf THF) and the consequent increased bulkiness around the chromium metal to disfavour the chair transition state. It has been noted above that the solvent plays a noticeable role in yield and stereoselectivity in the various tin mediated reactions also. Generally the more substituted allylic carbon forms the new bond with the carbonyl carbon although in some cases significant reaction takes place at the less substituted allylic carbon to give the linear isomer. The reaction is very chemospecific; ketones are generally less reactive than aldehydes so that selective addition to aldehyde functions and not ketone functions can be achieved. Nitriles and carboxylates do not react under these conditions. Again this feature is common with the tin mediated reactions.

Zinc

Although many metals have been used previously to effect carbon carbon bond formation, alterations in the experimental conditions and newer experimental techniques have evolved to increase yields and limit the chemical side products of the reactions. An interest in the diastereo-selectivities of these reactions instead of only the regioselectivities has resulted in a renewed interest in many of these metal systems.

The allylation of aldehydes and ketones by zinc has been studied by Jean-Louis Luche et. al.[85JO0910] in a Barbier type reaction closely analogous to the tin-aluminium reaction. This reaction is activated using two different methods, both giving similar stereochemical results and again demonstrating that the method of activation of the allylation system does not generally have any effect on the direction of the reaction.

Introduction

Two experimental procedures are described; for example a mixture of benzaldehyde, allyl bromide and zinc powder in tetrahydrofuran and saturated aqueous ammonium chloride[82JO0751] was stirred 45 minutes and after workup yielded the alcohol in quantitative yield. Alternatively sonication of a similar reaction mixture in water:THF (5:1) for 45 minutes gave only a 23% yield. This should be compared with the unactivated reaction (no sonication, water:THF 1:1) which after 4 hours gave a 48% yield. Yields of the ammonium chloride activated system ranged from 48% to 100% depending on the allylic group and the aldehyde employed. Luche writes briefly on the mechanism "A reasonable mechanism cannot be proposed presently, but a classical organometallic process is quite improbable. Organozincs react violently with water and ammonium chloride is frequently used to quench organometallic reactions. To our knowledge, the only published organozinc reaction occurring in water is a Wurtz-type coupling of alkyl iodides.[64CZ0597] As the reactions depicted here are Barbier type reactions, the possibility of a free radical pair process occurring on the metallic surface, as suggested by Molle and Bauer[82JA3481] for the classical Barbier reaction, deserves consideration."

As in many of these metal directed reactions alkyl halides were not reactive under the conditions described. Also as is noted in the case of the tin mediated reactions and the chromium mediated reactions the reaction is chemoselective.[85TL1449] Intermolecular and intramolecular competition experiments between pairs of aldehyde and ketone functionalities convincingly showed that aldehydes undergo preferential allylation. This selectivity is likely due to kinetic control, the following experiment bears out this fact. Acetophenone is reacted with allyl bromide and zinc and after completion of the reaction 1 equivalent benzaldehyde is added to the

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reaction mixture. Analysis of the products reveals only the product derived from the ketone and unchanged benzaldehyde.

In a comparative study between the sonically activated tin reaction and the same zinc reaction[87JM0177] Luche reiterates his previous statement that the presence of water probably precludes the presence of an organometallic intermediate species and thus the cyclic or linear transition states which have been used to explain the diastereoselectivity of many metal mediated allylation reactions. While this is almost certainly true for the zinc reaction, organotins are in fact often quite stable to water. We must ask however, if the zinc mediated allylation takes place on the metal surface why should the tin mediated reaction also be a surface reaction.

Bismuth

A communication from Makoto Wada and Kin-ya Akiba[85TL4211] demonstrates another Barbier type and another Grignard type allylation reaction and suggests that this reaction can be generalized over a wide range of different metals. Allyl halide, aldehyde and bismuth metal were stirred in DMF using Barbier (all reactants added together) of Grignard (aldehyde added later in the reaction) conditions. Homoallylic alcohols resulted in 53-98% yield and it appeared the Grignard conditions gave the better yields. The reaction is chemoselective with aldehydes reacting faster than ketones (yield < 5%) and although allyl iodide and allyl bromide both reacted successfully with the aldehydes allyl chloride did not give the expected adduct. No diastereoselective reactions have been examined in this system to date.

Boron

Organoboranes play an important role in modern organic synthesis,[86SY0973] 1- or 2-alkenyl-9-borabicyclo[3.3.1]nonane (1- or 2-alkenyl-9-BBN) has been

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used to preferentially produce (Z)-2-alkenyl organotins and silanes[80JA4548] and in the allylation reaction of aldehydes to form the (Z)-linear isomer preferentially.[83TL3209] Yamamoto et. al.[83JO5408] found that a boron-selenium system could direct the reaction toward the linear alcohol ((E)-selectively) or the branched alcohol (*threo* selectively) depending on the reaction conditions.

Hoffmann has examined the allylation of aldehydes with boronates[79AC0306, 81JO1309] and he and others have continued this work to examine not only the diastereoselective direction of the reaction but also the enantioselective direction.[79TL4653, 81CB2786] This, however is beyond the scope of this discussion.

The important thing to note about the use of boron derivatives in this work is the extreme versatility of boron in directing the reaction. Slight changes in the reaction conditions can bring about impressive changes in the regio-diastereo- and enantioselectivity of the reactions.

Diastereofacial Selectivity

In the allylation reaction of an aldehyde or unsymmetrical ketone if the carbonyl has in addition to its prochiral face a chiral centre adjacent to the carbonyl carbon then relative asymmetric induction can be produced due to the diastereofacial selectivity. Cram,[52JA5828, 63JA1245] Karabatsos,[67JA1367] and Felkin[68TL2199] and others have proposed transition states to explain the 1,2-asymmetric induction encountered in nucleophilic additions to chiral carbonyl compounds. Cram's rule states that the carbonyl oxygen orients itself between the small and medium sized groups attached to the adjacent chiral centre (Figure 1.1 [i]). Karabatsos shows the transition state differently (Figure 1.1 [ii]) and Felkin considers the largest α-substituent is placed perpendicular to the carbonyl group and contrary to Cram's belief considers

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the carbonyl oxygen to have smaller steric bulk than the alkyl group (Figure
1.1 [iii]). In all cases the approaching nucleophile attacks preferentially on
the least hindered side of the plane. In addition to these three possible
transition states if the aldehyde is capable of chelating with the reagent (in
this case with the metal species) a fourth transition state may be preferred
(Figure 1.1 [iv]).

Figure 1.1

(i)

(ii)

(iii)

(iv)
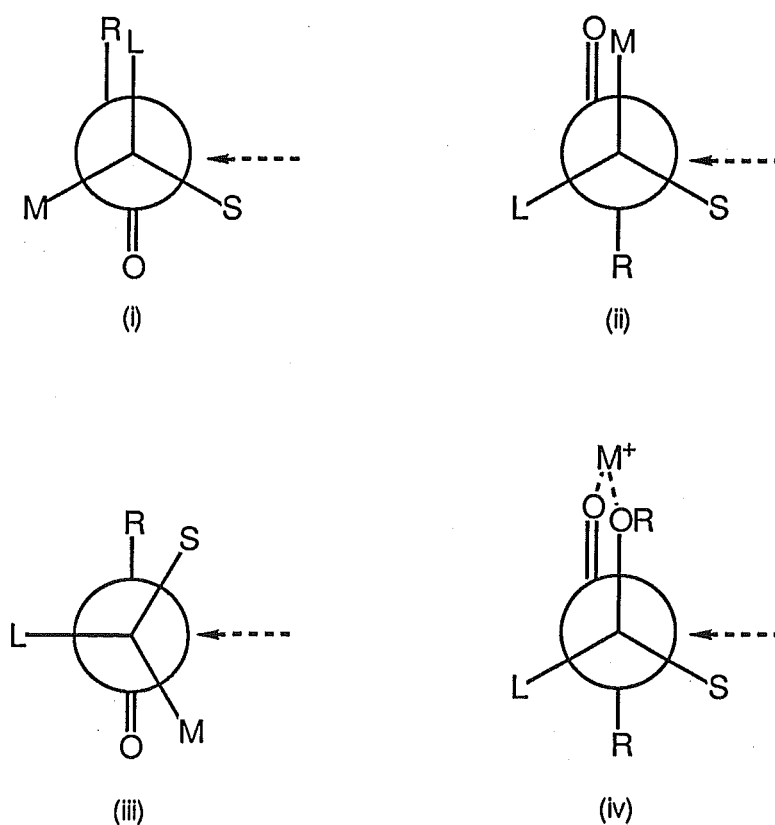
After these transition structures had been postulated theoretical calculations
and experimental systems were designed[77NC0061, 82JA7162, 87JA1580] to
determine which of these were closer to actuality. It would appear from the
results of these studies that the Felkin model comes closest to reality though
for different reasons. The antiperiplanar approach of the nucleophile allows
a n-σ^* interaction between the nucleophile electron pair and the σ^*
antibonding orbital of the antiperiplanar orbital of the C-L bond.[87JA1580]

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The diastereofacial selectivity of the allylation reaction has been probed for a number of metal systems including those above. Where a chelation mechanism is not able to operate it is generally found that the Cram isomer is formed predominantly, though the isomeric preference is somewhat low; often no better than 5:1 Cram selectivity; and generally dependent on the relative steric bulk of the aldehyde. This relatively low diastereofacial selectivity for many reactions is expected since the additional chirality is one bond further away from the reaction centre. Generally the *threo-erythro* selectivity is not affected by the formation of this third chiral centre.

A number of the investigators of the tin mediated allylation reaction have also probed the reaction for its efficacy as a diastereofacially selective system. Yamamoto[84TD2239] examines the Lewis acid catalysed reaction of allyl- and crotyl- trialkyl tins with 2-phenylpropanal and notes the reaction proceeds with Cram selectivity ranging from 2:1 to 7.3:1 depending on the Lewis acid used. Keck et. al.[84TL1879] examines the diastereofacial selectivity of the reaction of α-alkoxyaldehydes on addition to crotyl tributyl tin mediated by various Lewis acids. The three acids ZnI_2, $MgBr_2$ and $TiCl_4$ were used (they had previously shown these acids to be highly stereodirective) as well as boron triflouride etherate to catalyse the allylation of 2-benzyloxy-2-cyclohexyl ethanal with crotyl tributyltin. Analysis of the product mixture clearly showed a preference toward the antiCram isomer and a selectivity dependent on the Lewis acid employed. Thus boron triflouride exhibits only a moderate diastereofacial selectivity (antiCram:Cram 67:33) but a good diastereoselectivity (*erythro:threo* 92:8), in contrast zinc iodide provides excellent antiCram selectivity (98:2) but no diastereoselectivity. Titanium tetrachloride selectively produces the antiCram isomer close to 100% selectively but with only moderate *erythro* preference (63:37) and magnesium bromide provides the best of both worlds yielding excellent

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(>200:1 antiCram) diastereofacial selectivity and good (93:7 *erythro*) diastereoselectivity. Keck also noted the diastereofacial selectivity increases as expected as the steric bulk of the aldehyde increases.

Keck continued his studies on this reaction[84TL1883] and was ultimately able to selectively add crotyl tributyl stannane to either face of the aldehyde and still retain the *erythro* selectivity by proper choice of Lewis acid and hydroxyl protecting group. Thus almost total Cram selectivity was obtained with high *erythro* (95:5) diastereoselectivity by using a tertiary-butyl diphenylsilyl function as the hydroxyl protecting group and boron triflouride etherate as the catalyst. AntiCram diastereofacial selectivity is best obtained with magnesium bromide as the catalyst and the benzyl protecting group which gives 91:9 antiCram selectivity and a 89:11 *erythro* preference.

Diastereofacial selectivity in the tin-aluminium reaction is not outstanding. Reaction of cinnamyl chloride with various chiral aldehydes gives Cram diastereofacial selectivity depending on the steric bulk of the aldehyde, the *threo* diastereoselectivity of the reaction is retained. Thus 2-methylbutanal gives a 5:2 preference for the Cram-*threo* alcohol whereas 2-phenylpropanal produces the Cram alcohol as 75% of the product and 2,4,4-trimethylpentanal exhibits the same diastereofacial selectivity but produces the Cram-*threo* product as >90% of the yield.

Epoxidations

The epoxidation of alkenes is an important method of introducing a new chiral centre to the carbon skeleton being constructed. Epoxides are important intermediates in organic synthesis and the possibility of diastereoselective or even enantioselective control of this reaction has led to much effort in examining the epoxidation reaction. Although some highly diastereoselective epoxidations and enantioselective epoxidations are used

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today most diastereoselective epoxidations produce only moderate stereoselectivity.

Epoxidation of alkenes with peroxyacids has long been known.[09CB4811] Selective epoxidation of double bonds is often possible by varying the strength of the peroxyacid employed. One of the more well known peroxy-acids employed is m-chloroperoxybenzoic acid (MCBPA). MCPBA is a moderately strong epoxidising reagent which has found considerable favour amongst chemists due in a large part to its ease of use and the generally clean products produced. This peracid is commercially available in 60-85% purity (with the corresponding benzoic acid) and is used without purification. Typically 1.1 mole equivalents of 85% MCPBA in dichloromethane (to make a 0.4 - 0.5 molar solution). A 1 molar solution of the alkene (1 mole equivalent) is added and the mixture stirred for 1 - 5 hours or until completion of reaction. Cooling may be required to reduce formation of reaction byproducts. m-Chlorobenzoic acid may be removed from the organic solution by washing with 10% sodium hydroxide solution. Acid sensitive products that often rearrange under these conditions can be epoxidised with m-chloroperbenzoic acid in a dichloromethane - aqueous sodium bicarbonate two-phase system.[73JO2267]

The mechanism of the peracid epoxidation has been proposed by Bartlett[57RC0111] and has remained essentially accepted although some reports suggest an acid catalysis step is also an important consideration in the reaction (Scheme 1.8).

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Scheme **1.8**
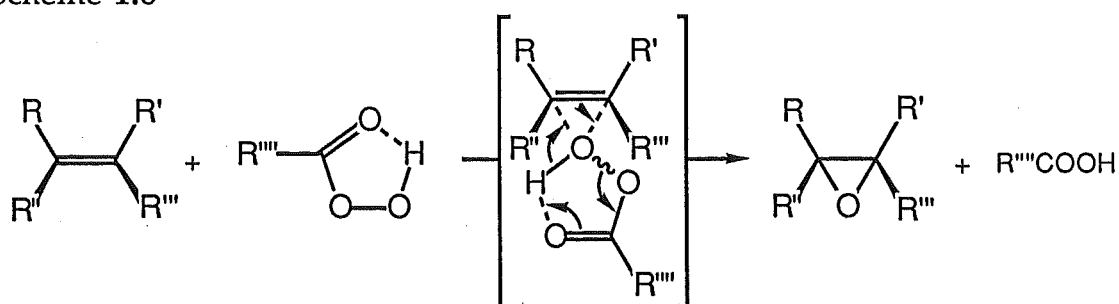
The origin of the diastereoselectivity of epoxidation reactions is often steric. Neighbouring and to a lesser extent remote functional groups cause the peracid to preferentially attack from the less hindered face of the double bond. In the case of certain groups (eg alcohol or carbonyl functionalities) weak electronic interactions cause the peracid to approach the reactive site from the same side as the participating neighbouring group (Figure **1.2**).

Figure **1.2**
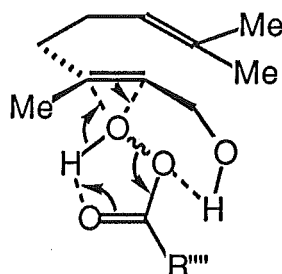
Transition metal complexes (Cr, Mo, Ti, V, Zr) can catalyse the alkyl peroxide epoxidation of alkenes. Vanadium has perhaps enjoyed especial success and has been used to regio- and stereospecifically catalyse the alkyl peroxide epoxidation of allylic and homoallylic alcohols.[65JO2074, 70JO1839] The alkyl peroxide used is very often *t*-butyl hydroperoxide. The epoxidation of (E)-geraniol[73JA6136] is demonstrative of this reactions synthetic utility. Tert-butyl hydroperoxide (17.6 g) was added dropwise to a refluxing mixture of (E)-geraniol (20 g) and vanadyl acetylacetonate (0.5 g) in benzene (150 ml). The reaction is completed in 4 hours and workup with aqueous bisulphite gives the epoxy alcohol in 98% yield. A number of mechanisms[77JO1587]

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have been proposed for this reaction amongst them a peroxymetal intermediate and an activated complex (Figure 1.3 i, ii). A tetrahedral vanadate ester transition state model (Figure 1.3 iii) has been proposed to explain the high asymmetric induction seen in the epoxidation of homoallylic alcohols.[79TL4729, 81JA7690]

Figure 1.3

(i)

(ii)

(iii)
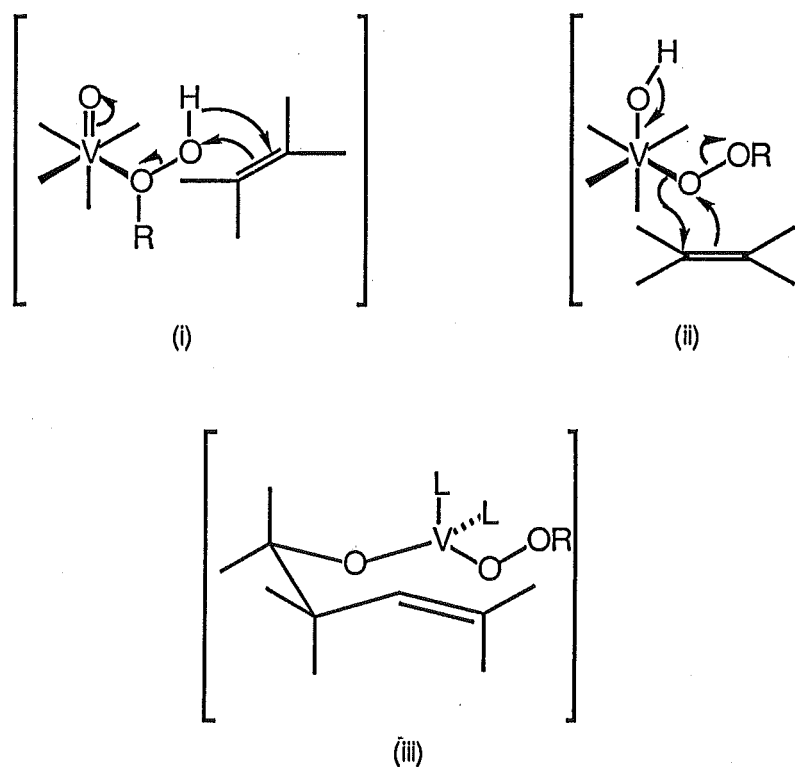
The Sharpless Epoxidation[80JA5974, 81JA6237, 84JO3707], so named after the discoverer is a special case of the metal catalysed alkyl peroxide epoxidation. A titanium complex (Ti(O-iPr)$_4$ with an optically pure enantiomer of diethyl tartrate catalyses the tert-butyl hydroperoxide epoxidation of allylic alcohols to yield the *erythro* epoxide in >90% enantiomeric excess. The enantiomer produced is dependent on the enantiomer of the diethyl tartrate used. The reaction is also sensitive to any chirality of the allylic alcohol substrate so that only one enantiomer of the alcohol forms the epoxide. The reaction is typically carried out by stirring 1 molar equivalent of Ti(O-iPr)$_4$, 1.2 molar

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equivalents of (+) or (-) tartrate and 1 molar equivalent of the allylic alcohol in dichloromethane (to make 0.1 M allylic alcohol solution) at -20°C. Tert-butyl hydroperoxide (0.6 molar equivalent as a 4-6 M dichloromethane solution) is added and the reaction maintained at -20°C until completion of the reaction. Sharpless went on to produce a rather complex mechanism and rate equation which adequately explains the selectivity of this reaction[83PA1823].

Since the epoxidation of homoallylic alcohols is so important in organic synthesis it was investigated to establish if this reaction could produce the same results for the epoxidation of homoallylic alcohols.[84JO3707] Though the enantiomeric excesses of the epoxidations were somewhat disappointing (23 - 55%) the reaction was shown to be of some potential synthetic usefulness by making GABOB (an antiepileptic and hypotensive drug) in high enantiomeric purity and 10% yield.

Epoxidations continue to be an important synthetic intermediate and research continues to be directed toward establishing successful epoxidation reactions which generate diastereo- and enantioselective products.

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Results and Discussion

Diastereoselectivity, Diastereofacial Selectivity and Regioselectivity

The reaction of (E)-cinnamyl magnesium chloride with benzaldehyde to give the homoallylic alcohols (8a) and (8b) under Barbier conditions[14] has recently been described[84AJ0065] and the product ratio was reported to be 70:30 respectively. In my hands this reaction gives a 50:50 mixture of diastereo-isomers ([1]H n.m.r., [13]C n.m.r., g.l.c). One diastereoisomer was separated by fractional crystallization and unambiguously identified as the *erythro* product (8a) by an X-ray structure determination of an epoxide derived from this alcohol namely (1RS, 2RS, 3RS)-3,4-epoxy-1,2-diphenyl-2-butanol. All attempts to purify the *threo* diastereoisomer (8b) were unsuccessful and a stereoselective synthesis of (8b) obviating the necessity for separation of the two diastereoisomers was attempted.

Ph
Ph
OH
(1RS, 2RS)-8a

Ph
Ph
OH
(1RS, 2SR)-8b

Ph
OH
8 c
Ph

Ph
Ph
O
9
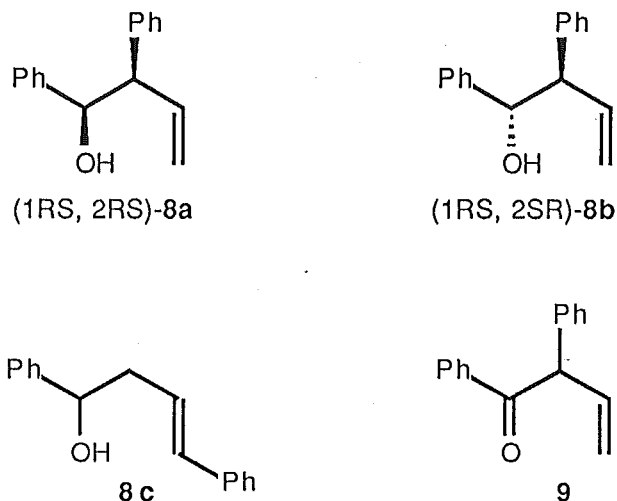
First attempts to synthesize (8b) involved stereoselective reductions[84TL2479] of the ketone (9). Reduction with lithium aluminium hydride gave a 9:2 mixture of (8a) and (8b) respectively while reduction with sodium boro-hydride in the presence of cerium chloride hexahydrate, a reagent mixture

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14   Barbier conditions: The concurrent addition of alkyl halide and carbonyl compound
      to magnesium in the presence of a catalytic quantity of the corresponding Grignard
      reagent.

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which has been reported[81JA5454] to effect stereoselective reductions, gave a 2:1 mixture of (8a) and (8b) respectively.

A second attempt at diastereoselective synthesize (8b) was made using a chromium (II) mediated method reported by Hiyama and co-workers. [77JA3179] Hiyama had reported that crotyl bromide in reaction with benzaldehyde in the presence of chromium (II) gave complete *threo*-selectivity (1b). Similar results have been reported using crotylzirconium [81TL2895] reagents. Reaction of cinnamyl chloride, benzaldehyde, chromium (III) chloride and lithium aluminium hydride gave alcohols (8a) and (8b) in a ratio 17:83, as determined by g.l.c. No linear isomer (8c) was found present in the product mixture. Initial difficulties with this reaction were overcome by carrying it out under nitrogen in the strict absence of moisture. Since the *threo* selectivity was rather less than reported for the reported reaction of crotyl bromide with benzaldehyde this reaction was repeated. No *erythro* homoallylic alcohol (1a) was in evidence from analysis of the [1]H n.m.r spectra (i.e. less than 5%) but the linear regioisomer (1c) was present as approximately 30% of the product mixture. Substitution of cinnamyl chloride in place of crotyl bromide gave a lesser *threo* selectivity but no linear isomer was found to be present.

The diastereoselectivity of the reaction of an allylic halide with an aldehyde or ketone when mediated by a metal atom (Scheme 2.1) can be understood if the energy of the transition state and the ground state energies of the products are known.[79IC0263, 78JM0037, 80JA7107, 82JM0149] The two most cited transition states are the cyclic chair transition state (Scheme 2.2) and the linear transition state (Scheme 2.3). These transition states both result in the diastereoselective formation of the γ-adducts (*threo*- and *erythro*-homo-allylic alcohols), and for any one reaction the predominant transition state is determined by several factors. So the required diastereomer might be

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obtained by altering the nature of the metal or in the case of Lewis acid catalysed reactions, the nature of the acid or even the order of mixing the reagents. These chair and linear transition states can be closely compared to analogous transition states for the metal mediated aldol condensation reaction. A brief description of these mechanisms is in order at this point.
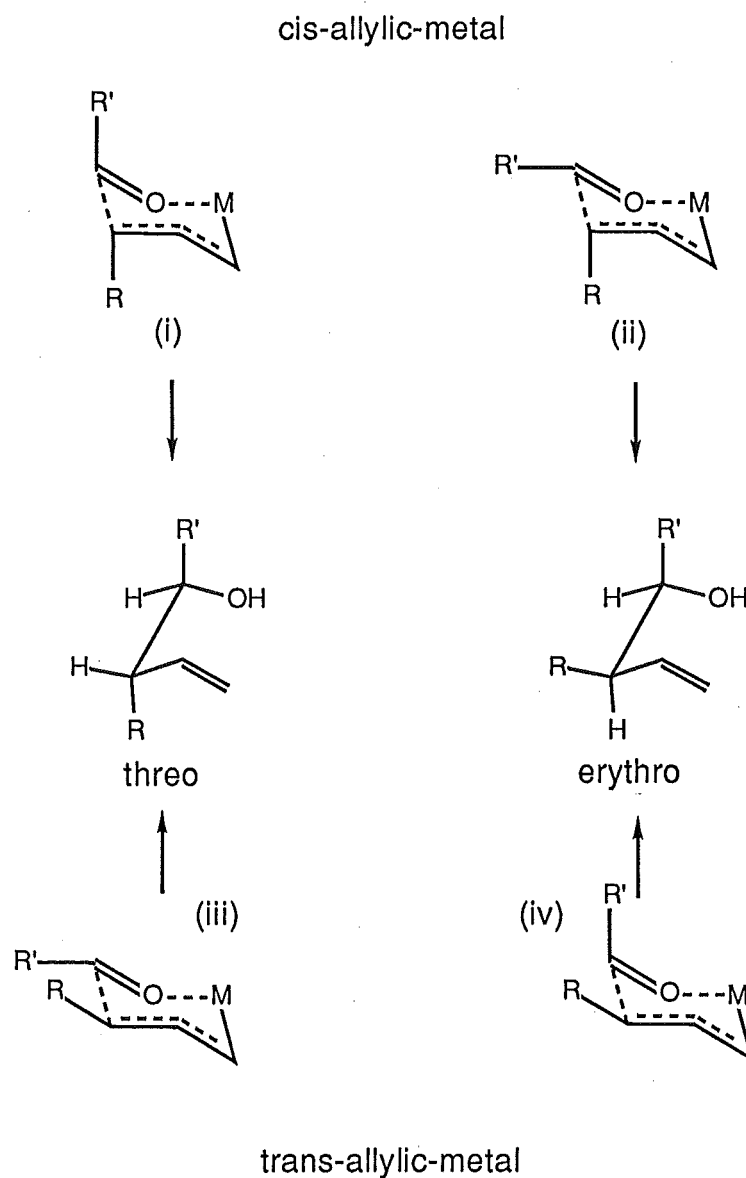
Scheme **2.1**
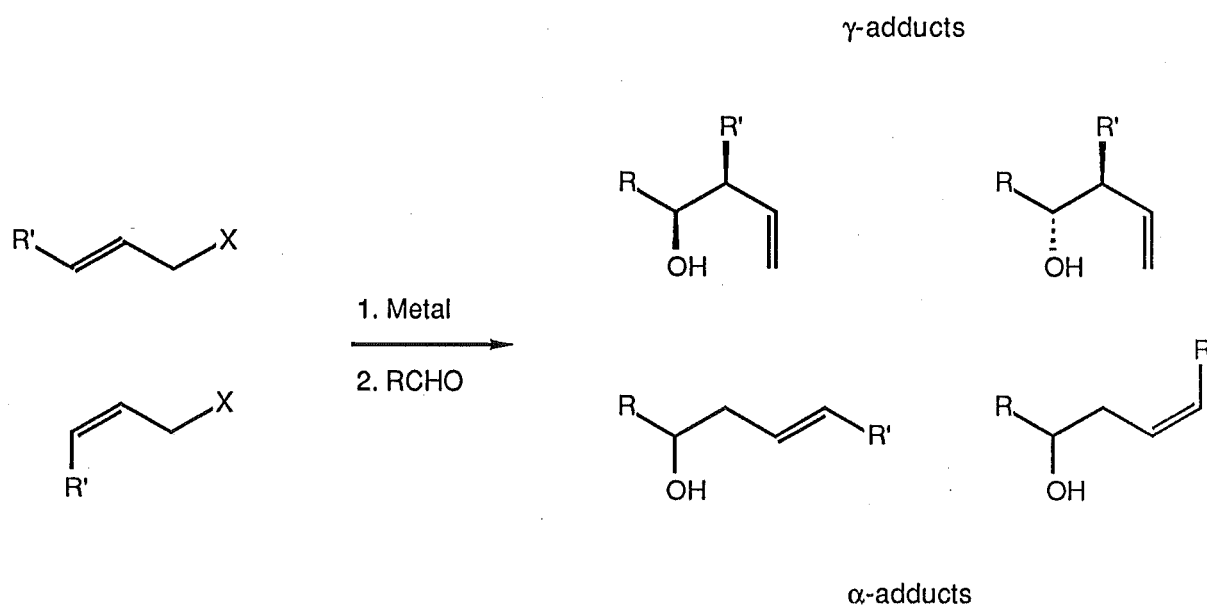
The cyclic mechanism (Scheme **2.2**) requires the metal (eg Cr[77JA3179, 81TL1037, 82BJ0561]) to be inserted between the halogen and the carbon of the allylic halide. This is followed by replacement of one of the ligands on the metal by the aldehyde (or ketone); bond formation followed by hydrolysis of the organometallic intermediate gives the product alcohol. Steric interactions in the 6-membered cyclic chair transition state can result in one or other of these transition states being formed and hence account for the observed stereoselectivity in the reaction.
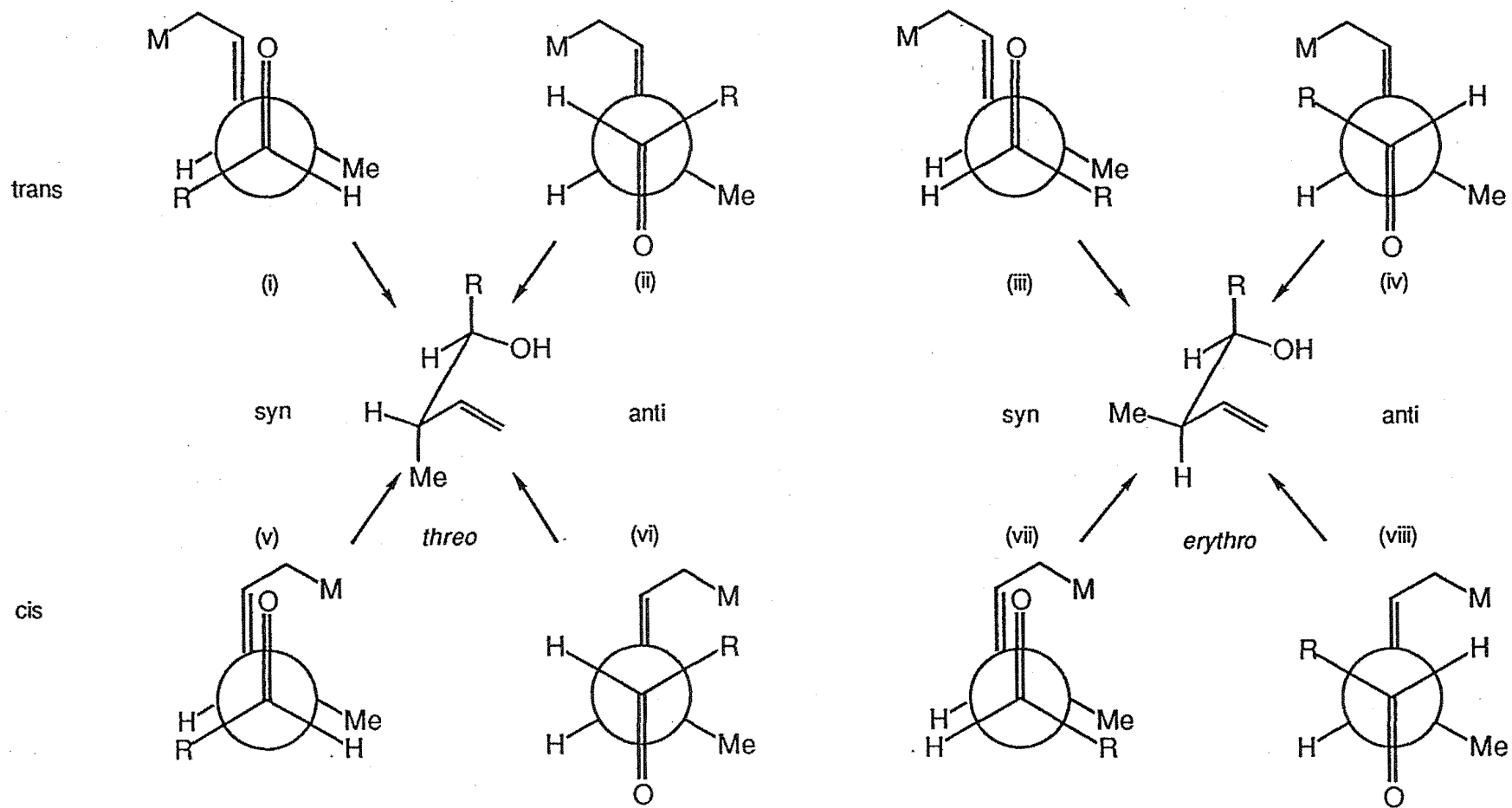
The procedure described by Nokami et. al.[83OM0191] using Sn and Al is *erythro*-selective for the reaction of crotyl bromide with aldehydes. We anticipated that it might be *threo*-selective for cinnamyl chloride since crotyl

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tri-n-butyltin has been shown to react with the opposite stereochemistry to that of cinnamyl tri-n-butyltin.[82CL1299] Reaction of cinnamyl chloride with benzaldehyde in the presence of tin and aluminium powders successfully gave the *threo* alcohol (8b) as the only detectable product (g.l.c., [1]H n.m.r., [13]C n.m.r.). No *erythro* homoallylic alcohol (8a) and no linear isomer (8c) was found.

Scheme **2.2**

<div align="center">cis-allylic-metal</div>

<div align="center">trans-allylic-metal</div>

Discussion

Scheme 2.3

trans

(i)

(ii)

syn

anti

threo

(v)

(vi)

cis

(iii)

(iv)

syn

anti

erythro

(vii)

(viii)

Since the structure of (8b) was not in question due to an earlier X-ray crystal structure of (1RS, 2RS, 3RS)-3,4-epoxy-1,2-diphenyl-2-butanol, and since no definitive proof was given for the structure of the products of the tin-aluminium catalysed crotyl bromide reaction the latter reaction was repeated in order to confirm the opposite diastereoselectivity of the crotyl bromide compared with cinnamyl chloride reactions. Thus reaction of crotyl bromide in the presence of tin and aluminium did indeed give alcohols (1a) and (1b) in the ratio 60:40 as previously reported. The structures of these alcohols have previously been established in this department by conversion to cyclic carbonate derivatives.[77AJ0835]

Me

Ph

OH

(1RS, 2SR)- 1 a

Me

Ph

OH

(1RS, 2RS)- 1 b

Ph

OH
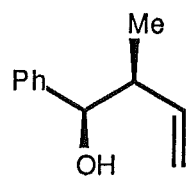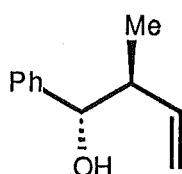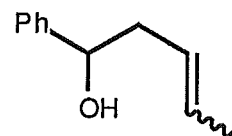
1 c

Apart from the diastereoselective properties of the tin and aluminium mediated reaction one of the major advantages of this reaction procedure is the ease with which the reaction is carried out. Neither an inert atmosphere nor the absence of water is required, indeed water is necessary to ensure good product yield.

Other metals (Zn,[85JO0910, 85TL1449, 87JM0177] Bi[85TL4211]) can also be used under similar reaction conditions and the diastereoselectivities of the described zinc reaction with both crotyl and cinnamyl halides were examined. The diastereoselectivity of this reaction, which is as easily carried out as the tin and aluminium reaction, has not previously been investigated. The diastereoselectivities were not as remarkable as in the tin and aluminium reaction. A mixture of the *threo* alcohol (1b) 57% and the *erythro* alcohol (1a) 43% were produced from the reaction of crotyl bromide with

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benzaldehyde under the described conditions. Also 75% of the *threo*

diastereoisomer **(8b)** and 25% of *erythro* diastereoisomer **(8a)** were

produced from the reaction of cinnamyl chloride with benzaldehyde under

the same conditions. No linear products **(1c, 8c)** were in evidence.

Table **2.1**
Barbier type reaction of allylic halides with benzaldehyde and reduction of
ketone **(9)** (see experimental section)

Method	Metal	Allylic halide	Percentage Erythro	Threo	Linear
a	Mg	cinnamyl chloride	50	50	
b	[H]	cinnamyl chloride	82	18	
c	[H]	cinnamyl chloride	67	33	
d	Cr(II)	cinnamyl chloride	17	83	
e	Sn-Al	cinnamyl chloride	0	100	
f	Zn	cinnamyl chloride	25	75	
a	Mg	crotyl bromide	50	50	
d	Cr(II)	crotyl bromide	0	70	30
e	Sn-Al	crotyl bromide	58	42	
f	Zn	crotyl bromide	43	57	

Methods
a: Barbier Grignard conditions;
b: Reduction of ketone **(9)** with lithium aluminium hydride;
c: Reduction of ketone **(9)** with sodium borohydride and cerium chloride;
d: Reaction mediated by chromic ion formed *in situ* by action of lithium
   aluminium hydride on chromous chloride;
e: Reaction mediated by tin-aluminium;
f: Reaction catalysed by zinc.

In view of the remarkably high diastereoselectivity in the tin and

aluminium promoted formation of **(8b)** the corresponding reaction with a

variety of selected aldehydes (RCHO; R = Ph, 4-MeOPh, 4-NCPh,

9-anthracenyl, Me, Et, iPr, $CH_3(CH_2)_5$, $PhCH_2$, $CH_3CH=CH$, $PhCH=CH$) was

examined. We have found that this wide range of aldehydes react with

cinnamyl chloride in this complex three or four phase system to produce in

all cases exclusively the *threo*-homoallylic alcohol, and neither electronic

nor steric effects of the aldehyde group affects the diastereoselectivity of the

reaction.

Discussion

Yamamoto et. al. have argued[84TD2239] that if the addition goes through a cyclic transition state then when a *cis*-allylic metal reacts with an aldehyde the sterically favoured transition state is with the aldehyde R group equatorial (Scheme **2.2**, [ii]) rather than axial (Scheme **2.2**, [i]). Compare the favoured transition state for the *trans*-allylic metal which has the R groups of the aldehyde positioned equatorially (Scheme **2.2**, [iii] cf Scheme **2.2**, [iv]). In this case the allylic R groups are also in an equatorial position. Thus the *trans*-allylic metal species gives the *threo*-homoallylic alcohol preferentially and for the *cis*-allylic metal species the *erythro*-product will mostly result.

The linear mechanism is important because it is considered to account for *erythro* selectivity regardless of the starting geometry of the double bond.[80JA7107] If the aldehyde is for any reason unable to replace a metal ligand (e.g. if a Lewis acid were coordinated to the aldehyde oxygen) then a linear mechanism is likely to operate. It is said by Yamamoto[80JA7107] to be apparent from Scheme **2.3** that the favoured transition state conformation for *trans*-allylic metals (Scheme **2.3**, [iv]) and for *cis*-allylic metals (Scheme **2.3**, [viii]) both result in the *erythro*-homoallylic alcohol. This will be discussed later.

It is the energy differences between different transition state conformations and the ground state conformations of the various reaction processes and competition between reaction processes that will determine the *threo* to *erythro* ratio in any one reaction of this type. In the light of this it can be argued the Cr(II) mediated reaction that has been investigated proceeds through the cyclic transition state so that the *threo*-homoallylic alcohol is produced predominantly in all cases. It is not clear why some linear alcohol is produced when crotyl bromide reacts with benzaldehyde under these conditions whereas no linear isomer is produced when cinnamyl chloride reacts with benzaldehyde. Nor is it clear why crotyl bromide reacts with

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benzaldehyde to produce only the *threo*-branched alcohol but cinnamyl chloride reacts with benzaldehyde to produce the *erythro*-isomer in minor but significant quantities. I propose that a number of different mechanisms operate (the linear mechanism, the cyclic mechanism and a further mechanism producing the linear isomer) and these mechanisms compete within the reaction mixture. Minor adjustments to the reactants or substrates or even reaction conditions can shift the balance through steric, electronic or other effects and so produce a preference (moderate or complete) toward one isomer. A complete understanding of how these factors operate may allow the precise production of the required isomer.

At this point a number of questions arise. It is likely that in the Sn-Al mediated reaction conditions the aluminium promotes the formation of the allylic tin by activating the tin and reduction of any tin salts formed. It is also probable that the water hydrolyses the tin carbinol thereby forcing the equilibrium toward the product homoallylic alcohol. The *erythro*-selectivity of the reactions of both *cis*- and *trans*-crotyl organotins reacting with aldehydes in the presence of boron triflouride etherate has been suggested to result from the removal of the availability of the carbonyl oxygen as a ligand to the tin metal centre and hence forcing a linear transition state for the reaction so determining the stereochemical outcome.[80JA7107, 84TD2239] Evidence supporting this explanation has recently been advanced by Reetz et. al.[86JA2405] who from an X-ray crystallographic study showed BF3 to be complexed *anti* to the benzaldehyde phenyl group. Heteronuclear Overhauser experiments confirm the *anti* conformation also holds for the benzaldehyde - boron triflouride complex in solution. This reasoning would suggest that the *erythro-* product preference in the reaction of crotyl bromide with aldehydes mediated by tin and aluminium is also due to the presence of a Lewis acid. No Lewis acid is known to be present and although
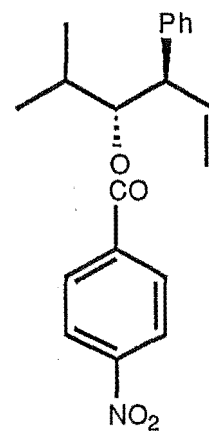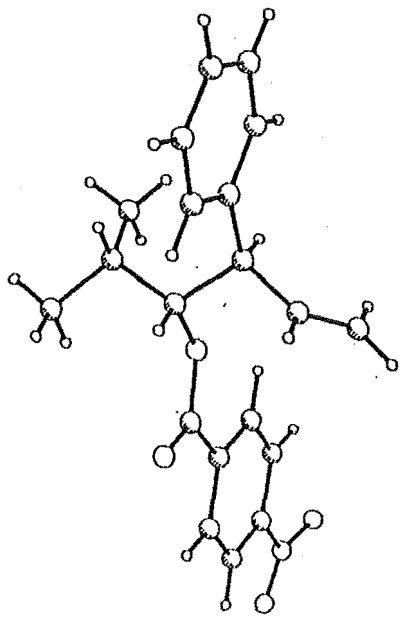
Discussion

SnCl$_4$ is a Lewis acid it is probably not present in this reaction mixture and if it were present the reaction would be expected to give poor product dia-stereoselectivity.[84TL3927] Hydrobromic acid is added in only catalytic quantities and is probably involved in generating an active metal site. The addition of hydrobromic acid is considered unlikely to effect the diastereo-selectivity of the reaction,[15] that is it does not play a role in the sterically controlled transition state. If there is no Lewis acid present then it may be reasonable to say that the Lewis acid (in the Lewis acid reaction) does not stop the formation of the cyclic mechanism by attaching itself to the carbonyl oxygen but rather promotes the formation of product via the linear mechanism.

Torii[86TL2395] also reports work, completed after our preliminary report[85TL6121] which he references, that Sn(II)-Al reacts with cinnamyl chloride and various aldehydes to give good yields (68% - 84%) and high threo diastereoselectivities. His work parallels our earlier studies.
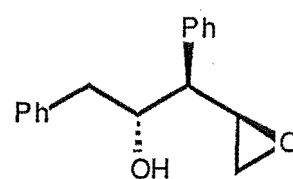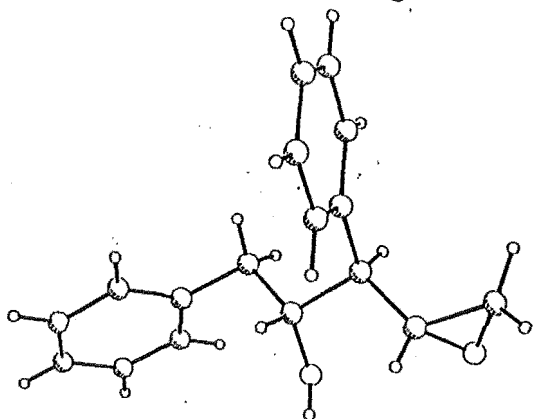
Since benzaldehyde and cinnamyl chloride give the *threo* diastereoisomer and because only one diastereoisomer was formed in these reactions it might be assumed that the diastereoisomer formed was the *threo* diastereo-isomer. This has been confirmed for (1RS, 2SR)-1-(9-anthracenyl)-2-phenyl-3-buten-1-ol (13b), (2RS, 3RS, 4SR)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol (7a), (2RS, 3SR, 4SR)-2,4-diphenyl-5-hexen-3-yl 3,5-dinitrobenzoate (25b) and (3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl 3,5-dinitrobenzoate (33b, R=iPr) by X-ray studies.[16]

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[15] See competition studies. The addition of large quantities of hydrobromic acid did not appear to effect the course of the reaction.

[16] 1-(4-Cyanophenyl)-2-phenyl-3-buten-1-ol (10b) has been crystallized and is waiting for an X-ray crystal structure analysis. A preliminary photographic study was performed on the crystalline 2-methyl-4-'phenyl-5-hexen-3-yl 4-nitrobenzoate (32b, R=iPr) and this indicated an orthorhombic unit cell of dimensions 6.09, 17.06, and 19.38 Å. Attempts to obtain this unit cell on the diffractometer were unsuccessful.
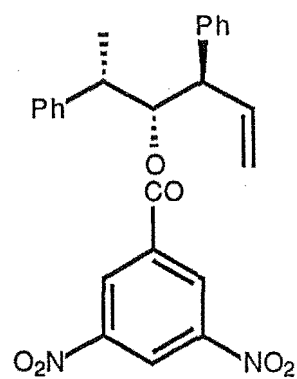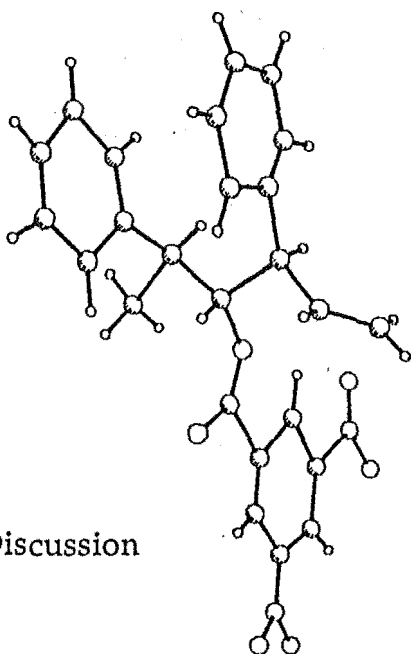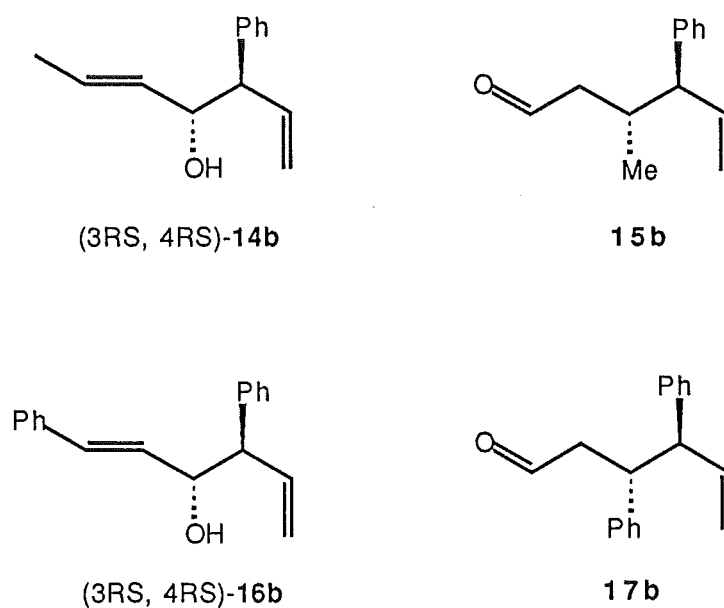
Discussion

32a, R=iPr

7a
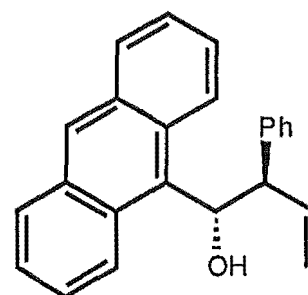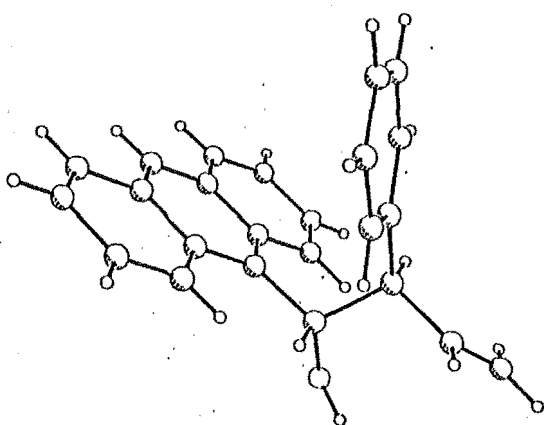
13b

33b, R=PhCH(CH₃)

Discussion

The reaction of acetophenone with cinnamyl chloride did not give the expected branched homoallylic alcohol. Pyridine-4-aldehyde and cinnamyl chloride in the presence of tin and aluminium powders was unreactive.

(3RS, 4RS)-14b

15b

(3RS, 4RS)-16b

17b

Elemental analyses of the products from these reactions which are generally oils, were difficult to obtain and since the homoallylic alcohols are somewhat unstable EI mass spectrometry tends to produce poor data. For almost all products CI mass spectra were obtained using the new standard poly-dimethylsiloxane[87AC0194] allowing for acquisition of an accurate mass; however due to repeated and extended periods of machine failure the time from synthesis to mass spectral data collection was often several months and prolonged storage of many of these compounds resulted in deterioration of samples. The crystal structures provide a definite proof of structure. A number of 4-nitrobenzoate and 3,5-nitrobenzoate derivatives of these alcohols have been made but in many cases while a derivative may be solid it does not easily form crystals suitable for X-ray crystallography.

Cinnamaldehyde and crotonaldehyde could as well as undergoing the 1,2-addition with allylic halides also undergo a 1,4-(Michael) addition to give
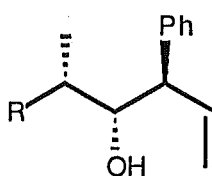
Discussion

the ketones **(17)** and **(15)** respectively. Reaction of both cinnamaldehyde and crotonaldehyde with cinnamyl chloride in tin and aluminium media gave only the 1,2-addition *threo* diastereoisomers **(16b)** and **(14b)** respectively. Thus this reaction occurs with both high regioselectivity and high diastereoselectivity. In contrast reaction of these aldehydes with cinnamyl chloride under Barbier-Grignard conditions gives a mixture of several products including both the *threo* and *erythro* products and 1,4-(Michael) addition products.

In view of the high selectivities found in the above reaction it was of interest to examine the possibility of extending this reaction to the synthesis of molecules containing more than two chiral centres. Firstly aldehydes containing a chiral centre adjacent to the carbonyl group were examined. In this case the products contain three contiguous chiral centres, i.e. four possible diastereomers (Figure **2.1**). The aldehydes chosen were 2-methyl-butanal, 2,4,4-trimethylpentanal **(20)** and 2-phenylpropanal **(24)** and these were synthesized as shown in Scheme **2.4**.
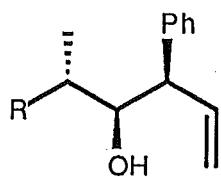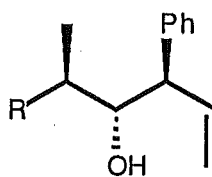
Figure **2.1**
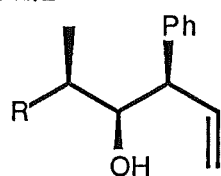
Erythro-Cram-**a**   Threo-Cram-**b**

Erythro-antiCram-**c**   Threo-antiCram-**d**

18 R=Et-

21 R=tBu-

25 R=Ph-

Discussion

Scheme 2.4

H$_2$SO$_4$

OH

19a

1. CrO$_2$Cl$_2$
2. Zn

20

19b

PhMgBr

Ph — OH

22

DMSO

Ph

23

1. CrO$_2$Cl$_2$
2. Zn

Ph — CHO

24
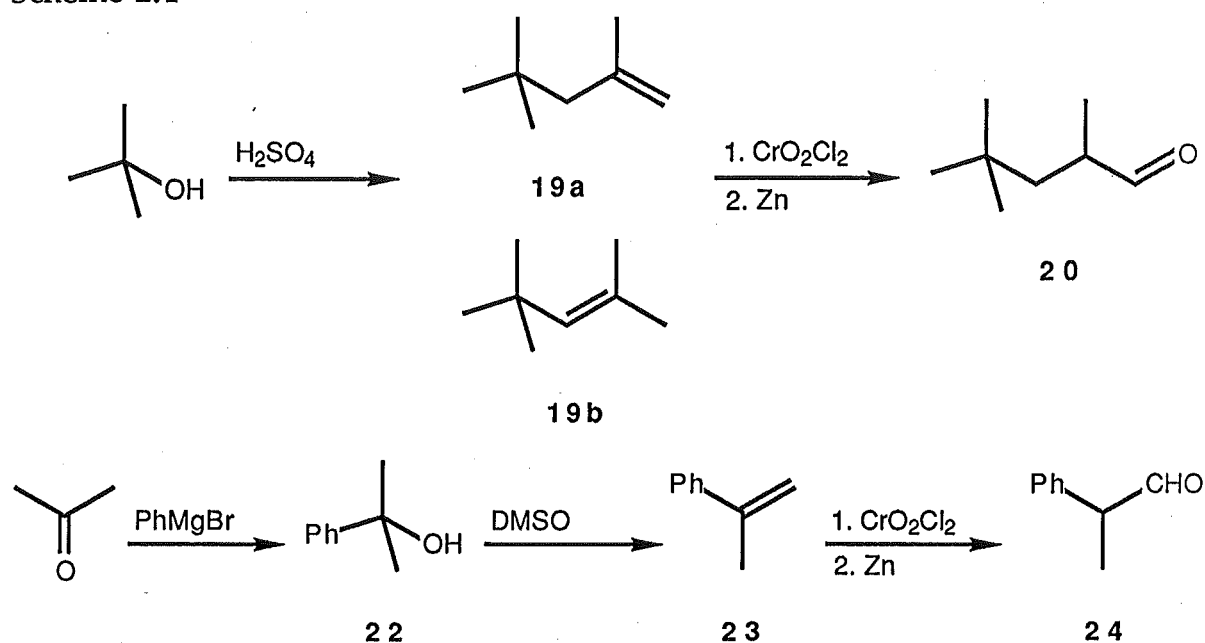
Reaction of 2-phenylpropanal with cinnamyl chloride, tin and aluminium gave two diastereoisomers one of which was present as greater than 90% yield. This diastereoisomer was determined to be the Cram-*threo* diastereoisomer (**25b**) by X-ray crystal structure analysis of the 3,5-dinitro-benzoate derivative. Thus the reaction occurs not only with diastereoselective carbon-carbon bond formation (*threo* selectivity), but also with selectivity between the enantiomeric faces of the carbonyl group (Cram selectivity).[17] 2-Methylbutanal and 2,4,4-trimethylpentanal also showed a diastereofacial preference, though not so marked, toward one

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[17] Cram's rule applied to reactions of this type states that the oxygen of the carbonyl orients itself between the small and medium sized groups attached to the adjacent asymmetric centre. The approaching group attacks preferentially on the least hindered side of the plane (see introduction).

L R

R'Z

M S

O

L

R R'

M S

OZ

L

R' R

M S

OZ

Major product   Minor product
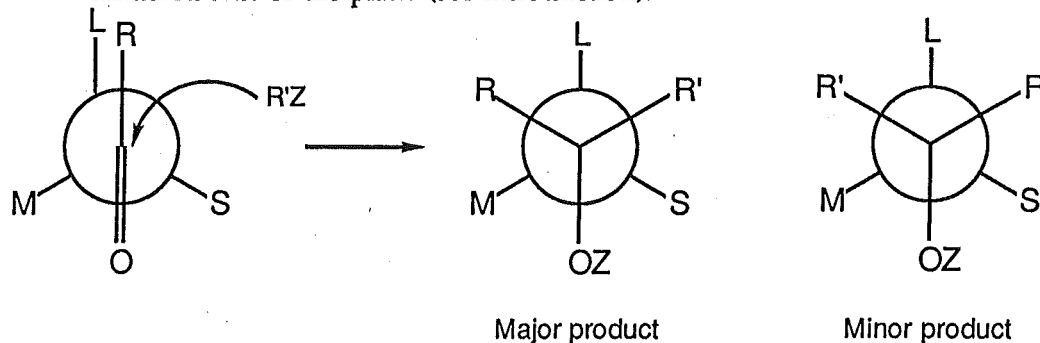
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diastereoisomer giving respectively a 2:5 and a 75:25 mixture of two of the four possible diastereoisomers. In each case the major diastereoisomer is (by analogy) *threo* Cram and the minor diastereoisomer *threo* anti-Cram.

The results are not as dramatic as for the simple diastereoselective (*erythro-threo*) system and the selectivity seems to be highly dependent on the steric bulk at the chiral centre of the aldehyde. The reduction in selectivity is expected because the chirality is one bond further away from the reaction centre.

Investigation of the diastereofacial selectivity of aldehydes capable of chelation with the tin centre has also been examined. Keck[84TL1879] for example found that α-alkoxyaldehydes on addition to crotyl tributyl tin catalysed with boron triflouride etherate gave a moderate preference for antiCram isomers. Ultimately, Keck was able to selectively add crotyl tributyl stannane to either face of the aldehyde[84TL1883] and still retain the *erythro*-selectivity by proper choice of Lewis acid and alkoxy group. In contrast Yamamoto[84TD2239] had found 2-phenylpropanal (not capable of chelation) gave the expected Cram isomer in moderate selectivity.

The reaction of glyceraldehyde with cinnamyl chloride was carried out in an attempt to form a triol diastereospecifically, however the resultant material was a mixture of several compounds, of sufficient complexity that the reaction was not pursued further. The chelation mechanism is very probably competing with the Cram mechanism and interfering with the *threo*-selective mechanism to produce up to eight different diastereomeric alcohols.

Reaction under Barbier-Grignard conditions were carried out for comparison purposes. 2-Phenylpropanal reacted with cinnamyl chloride to give a mixture of the four possible branched homoallylic alcohols (25a, 25b,

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25c, 25d) in the ratio 1:3:3:4 respectively. Crystals of the 3,5-dinitrobenzoate derivative of **(25d)** were obtained however these were of insufficient quality for X-ray crystal structure analysis.

Scheme 2.5
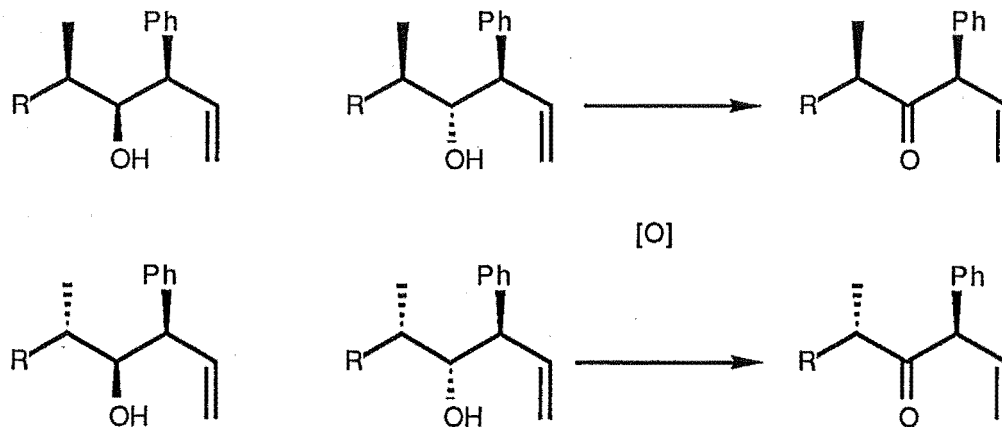
a: Oxidation of diastereomers produces two ketones
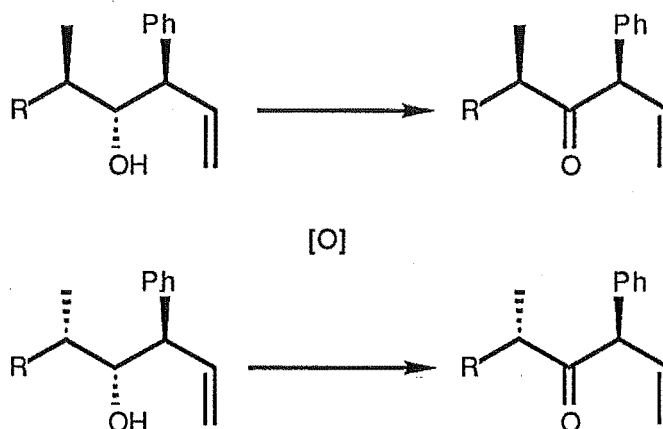
b: Oxidation of threo diastereomers produces two ketones

Oxidation of the product alcohols from the Grignard and tin-aluminium reactions support the evidence showing that the tin-aluminium reaction gives *threo* Cram and *threo* anti-Cram products. As can be seen in Scheme 2.5 reduction of a mixture of the four diastereoisomers produced in the Grignard reaction will give two ketones. It is also expected that both ketones would be formed after the reduction of the alcohol mixture

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produced in the tin-aluminium catalysed reaction, in this case one major ketone (from the *threo* Cram alcohol) and a minor ketone (from the *threo* antiCram alcohol). As predicted a 50:50 mixture of isomeric ketones resulted from oxidation of the four alcohols produced in the Grignard reaction and a 75:25 mixture of ketones was produced from the two *threo* alcohols obtained from the tin-aluminium reaction.

An attempt to extend the use of this reaction to the synthesis of molecules containing more than two chiral centres was made by studying the reaction of glyoxal (29) with cinnamyl chloride. 2,3-Dihydroxy-1,4-dioxane was also used but spectra indicated that this substance gave exactly the same product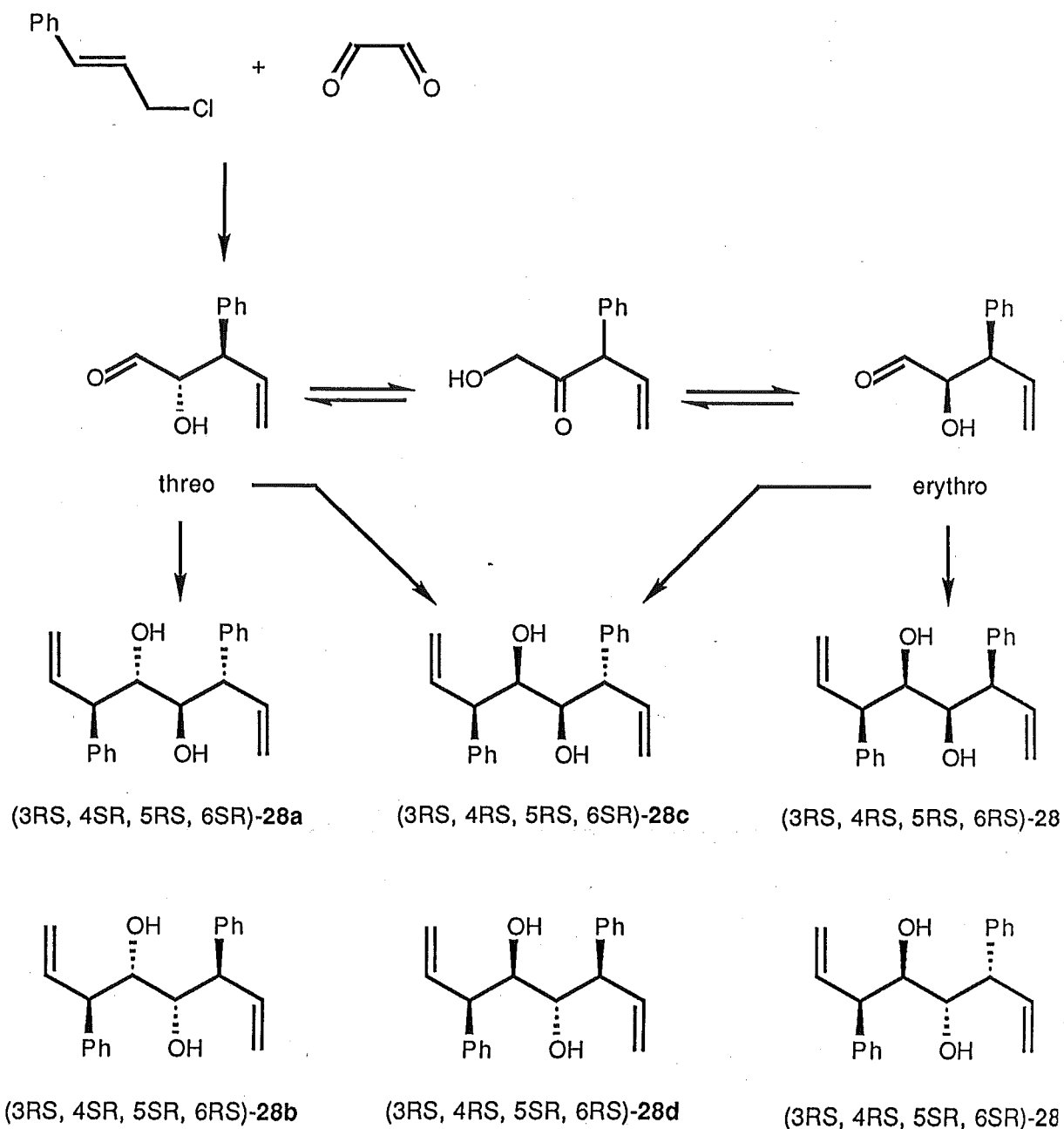s. The products contain four contiguous chiral centres and six diastereomers are possible (Scheme 2.6). Prediction of the product diastereoisomers is complicated by the fact that after addition of the first cinnamyl chloride to the carbonyl the intermediate may undergo tautomeric equilibration to form both the *erythro* and *threo* intermediate. Each of these two intermediates may further react with another molecule of cinnamyl chloride to form the product (28). It is most likely however that the second addition will occur with *threo* selectively and hence the two possible *erythro-erythro* products (28e, 28f) are unlikely to be produced. We would therefore expect four products; the symmetrical products (28a, 28b) and the unsymmetrical products (28c, 28d).

Analysis of the product mixture from the reaction with glyoxal was carried out by ^{13}C n.m.r. and ^{1}H n.m.r. spectroscopy. If all possible diastereoisomers (28a-f) had been obtained then each type of carbon would give rise to eight signals in the carbon spectrum since a symmetrical diastereoisomer gives one signal and an unsymmetrical diastereoisomer two signals for each type of carbon. If only the four diastereoisomers predicted above are obtained then each carbon should give up to six signals, in the absence of accidental

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overlap. The spectrum of the reaction mixture showed a maximum of four signals for any carbon, indicating some selectivity as predicted above. The [1]H n.m.r. spectrum was more informative. Resonance patterns for H2 and H7 were found centred at 5.8, 5.95, 5.99, 6.14, 6.25 in a ratio 60:60:100:100:15; indicative of the presence of at least three diastereoisomers and traces of another pattern hidden under larger peaks indicated the presence of a fourth diastereoisomer.

Scheme 2.6

| (3RS, 4SR, 5RS, 6SR)-28a | (3RS, 4RS, 5RS, 6SR)-28c | (3RS, 4RS, 5RS, 6RS)-28 |

| (3RS, 4SR, 5SR, 6RS)-28b | (3RS, 4RS, 5SR, 6RS)-28d | (3RS, 4RS, 5SR, 6SR)-28 |

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A successful separation of one diastereoisomer of (28) was accomplished by radial chromatography and identification of this diastereoisomer as (28a) was accomplished by preparation of the acetonide derivative (31). Since the separated diastereoisomer (28a) was symmetrical (^{13}C n.m.r.) and since (28e) and (28f) were already eliminated from consideration this diastereoisomer had to be either (28a) or (28b). The acetonide methyl groups of (31) were not equivalent (^{1}H n.m.r.) and therefore this established the acetonide had mirror symmetry (31a) corresponding to the alcohol (28a).

(3RS, 4SR, 5RS, 6SR)-31a   (3RS, 4SR, 5SR, 6RS)-31b
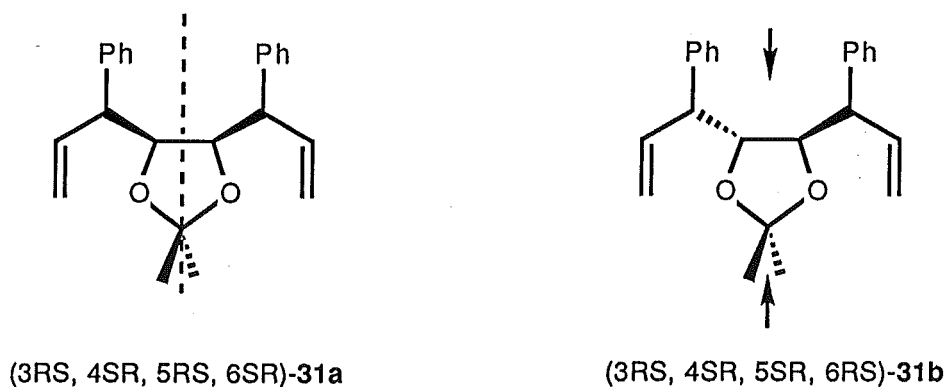
Secondly the reaction was carried out with terephthaldicarboxaldehyde. Six diastereoisomers are possible (27a, 27b, 27c, 27d, 27e, 27f). In this case however, a tautomeric equilibrium is not possible because the two carbonyls are separated. It is expected that both the carbonyls would add *threo* selectively and give only two symmetrical diastereoisomers (27a, 27b). Analysis of the product mixture from the reaction with terephthaldicarbox-aldehyde was carried out by ^{13}C n.m.r. A maximum of two signals was found for any carbon type indicating some selectivity as predicted above.

Discussion
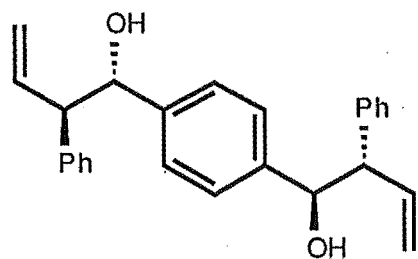
(1RS, 2SR, 1'SR, 2'RS)-**27a**
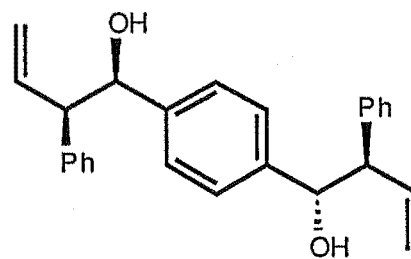
(1RS, 2RS, 1'RS, 2'SR)-**27d**
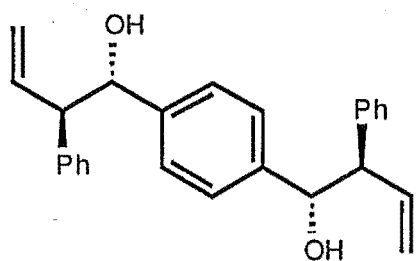
(1RS, 2SR, 1'RS, 2'SR)-**27b**
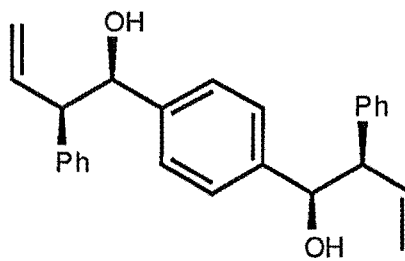
(1RS, 2RS, 1'RS, 2'RS)-**27e**
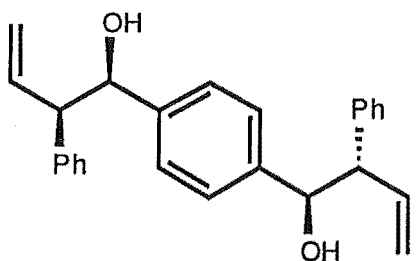
(1RS, 2RS, 1'SR, 2'RS)-**27c**
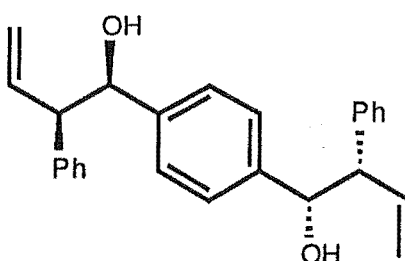
(1RS, 2RS, 1'SR, 2'SR)-**27f**

Mechanistic Generalizations

It is possible to generalize the results of my own studies and those of other authors. If the cyclic mechanism is operating in a reaction system then *trans*-crotyl trialkyltin will react with aldehydes to produce *threo*-homoallylic alcohols; *erythro*-homoallylic alcohols are produced from the reaction of *cis*-crotyl trialkyltin with aldehydes. On the other hand the linear transition state results in the formation of *erythro*-products both *trans*- and *cis*-crotyl trialkyltins.

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If steric interactions in these transition states were most important in determining the orientation of approach of the two reacting species and hence ultimately the stereochemistry of the product then we would expect similar diastereoselectivities for other allylic tins (and indeed other allylic metals). In order to be able to predict which mechanism is likely to take place in any one experimental system it is necessary to consider several factors, these include:

- the nature of the metal - carbon bond;

- whether transmetallation (Scheme 2.7) of the allylic system occurs and

- how added reagents (Lewis acids, additional metals) and solvents affect the mechanism.

It was considered important to determine whether tin and aluminium both played important roles in this reaction mechanism. Reaction of cinnamyl chloride with benzaldehyde in the presence of aluminium gave no product; and the same reactants in the presence of tin gave a very poor yield (i.e. less than 10%). When it is considered that the electrochemical potential of aluminium (Al^{+3} + 3e$^-$ $\leftrightarrow$ Al) is -1.706 V and the electrochemical potential of tin (Sn^{+2} + 2e$^-$ $\leftrightarrow$ Sn) is -0.1364 V then it would seem reasonable that the aluminium is present to reduce the tin salts produced in the course of the reaction back to active tin metal.

Scheme 2.7
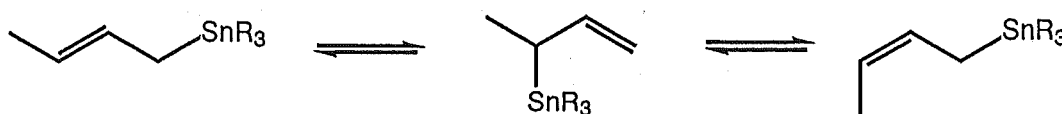
Koreeda and Tanaka[82CL1299] using the same Lewis acid conditions as Yamamoto[80JA7101, 84TD2239] found that *trans*-crotyl triphenyltin reacted with

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benzaldehyde to give 5:1 *erythro-* and *threo*-homoallylic alcohols but *trans-*cinnamyl triphenyltin reacted with benzaldehyde to give 1:99 *erythro-* and *threo*-homoallylic alcohols. They considered that these "observations may be accounted for in terms of the ionic property of the allylic carbon tin bond. Thus the allyl tin with a greater ionic contribution from the carbon tin bond increases the propensity for the cyclic transition state in its reactions with aldehydes."

In the case of cinnamyl trialkyltin the allylic species (anion or radical) is stabilized by conjugation with the phenyl ring. As a consequence of this stabilization the metal (in this case tin) is more electropositive and attracts the electron rich oxygen of the aldehyde to give a cyclic transition state. In contrast the crotyl system (anion or radical) of crotyl trialkyltin is not so well stabilized and the metal is less electropositive and does not attract the carbonyl oxygen and the *erythro* product is now formed via the linear mechanism.

They continue to write "...in this regard, the conjugated dienyltin, (E),(E)-2,4-hexadienyl-tri-n-butyltin exhibited intermediate property by providing a 5/3 ratio of the stereoisomers of the γ-adducts (stereochemistry unassigned) in addition to the ε-adducts in a 2/1 stereoisomeric mixture" (Scheme 2.8).

Scheme 2.8
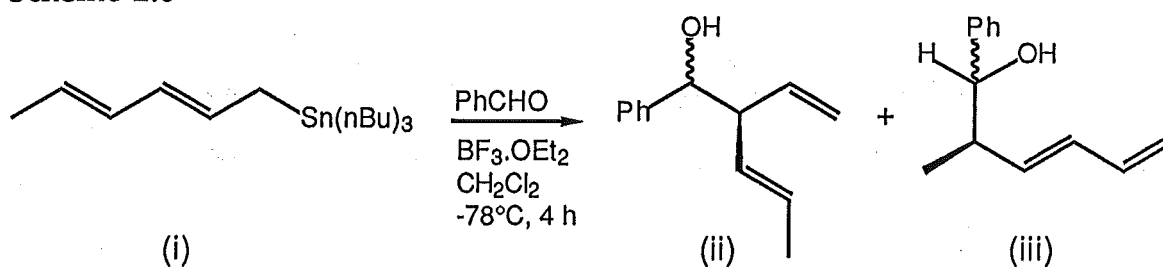
On examining the experiments of Koreeda and those of Yamamoto it is possible to infer that the two suggested mechanisms compete and it is this

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competition which results in the different *erythro:threo* ratios observed. The reaction of cinnamyl triphenyltin with benzaldehyde in the presence of $BF_3.OEt_2$ shows a 99 to 1 preference for producing *threo*-homoallylic alcohols whereas cinnamyl tributyltin reacting with benzaldehyde under the same conditions gives only a 9 to 1 preference for the *threo* alcohol. This lessened stereoselectivity indicates the ligand (phenyl or n-butyl) is also important to the reaction. The inductive effect of the phenyl ligands increasing the positive polarity on the tin centre relative to the butyl ligands inductive effect and thus increasing the role of the cyclic mechanism could account for these results. Further, when we consider *trans*-crotyl triphenyltin reacting with benzaldehyde gives a 5:1 mixture of *erythro*- to *threo*-homoallylic alcohols and the corresponding *trans*-crotyl tributyltin reaction gives 98:2 *erythro*- to *threo*-homoallylic alcohols it can again be suggested the phenyl ligands encourage reaction via a cyclic transition state; and taking these two sets of results it can be seen likely that the linear and cyclic mechanisms can both operate in any one system but compete to give mixtures of *erythro*-and *threo*-products.

In the same way, the organometallic species formed in the tin-aluminium reaction (probably diallylic tin dihalide) will be affected so that the cyclic transition state becomes more competitive to the point that it is only the *threo*-homoallylic alcohols produced on the reaction of cinnamyl chloride with alcohols. This is to be compared with the moderate *erythro*-selectivity of crotyl bromide reacting with aldehydes. In this case the cyclic mechanism has reduced in importance and the linear mechanism competes successfully and indeed dominate the reaction to give the *erythro* isomer in diastereomeric excess.

Tagliavini et. al.[80JM0045, 81JM0191] showed that the ability of compounds of the type $(RCH=CHCH_2)SnBu_{3-n}Cl_n$ (R = H, CH_3; n = 0,1,2,3) to bring about

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allylstannylation of ketones and aldehydes increases with the value of n. That is the reaction is faster on increasing the acceptor ability of the tin centre. The nucleophilic attack is clearly favoured by an increase in the number of halogens surrounding the tin centre. The pericyclic mechanism is supported by the complete rearrangement of the allylic group. It is also shown that the proposed pericyclic elimination reaction of homoallylic alcohols (Scheme 1.3) which occurs on reaction with $(Bu_3Sn)_2O$ and $(Bu_2SnCl)_2O$ produces *trans*-allyltins from *threo*-homoallyl alcohol and *cis*-allyltins from the *erythro*-isomer[78IC0041, 78JM0037, 79IC0263]. These results provide good evidence for the actuality of a cyclic transition state and support Koreeda and Tanakas' contention that the cyclic mechanism comes into play when the carbon tin bond is more polarized.

Bearing this in mind it was felt that the reaction of p-methoxycinnamyl bromide would exhibit reactive properties between those of cinnamyl chloride and crotyl bromide. The methoxy group in the *para* position should inhibit the resonance of the allylic tin thereby reducing the polarity of the carbon - tin bond so that the dominance of the cyclic mechanism in the system might be reduced and some *erythro* diastereoisomer be produced. Unfortunately while formation of this substrate does not pose many difficulties it is very unstable to the reaction conditions employed and makes a simple analysis of the reaction impossible.[18]

The presence of an optically active species or solvent has been known to affect reactions[86JA5919, 87JO5447] and result in a preference for one of two possible optical isomers. If this could be effected in the tin-aluminium-

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[18]   The only useful information to come out of this experiment was that the reaction to form p-methoxycinnamyl bromide (N-bromo-succinimide and anethole in carbon tetrachloride) appears to be very sensitive to the concentration of the reactants in solvent. An anethole concentration of 40 g.l^{-1} gives a mixture of both the allylic bromide and the vinyl bromide whereas the more dilute reaction conditions of 8.2 g.l^{-1} produced almost exclusively the allylic bromide.

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cinnamyl chloride reaction then not only would just *threo* alcohols be produced but also a preference for one (or the other) *threo* optical isomer would result. I tried a simple experiment using α-pinene and water as the solvent and although the yield continued to be reasonable and only the *threo* alcohol was produced no optical activity was seen after analysing the products by ORD.

When reacting aldehydes or ketones with allylic halides (under for instance Grignard conditions) it is important to reduce formation of 1,5-hexadienes from a competing reaction (Scheme 2.9). This is accomplished by using Barbier conditions and is appropriate and sufficient where diastereo-chemistry is unimportant. However, if the allylic system is active enough it is easier to carry out this reaction using the (already described) tin and aluminium conditions. Under these conditions no hexadienes are formed although in some cases a pinacol product from the aldehydes is produced (the formation of pinacols are catalysed by tin).

Scheme **2.9**
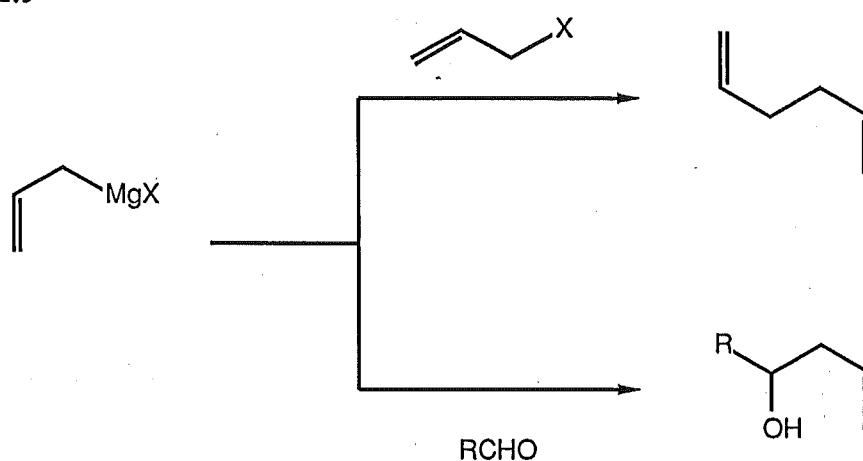
Exemplifying this is the formation of 4-phenyl-4-penten-2-ol (**34**) which was required to make 4,5-epoxy-4-phenyl-2-pentanone (**38**) for photochemical experiments. This has been reported to have been made in poor yield from 3-bromo-2-phenylpropene and acetaldehyde via a Grignard reaction[82JO3377],

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83TH0001 (even in THF which has a higher boiling point and better anion stabilizing properties). Dodge carried out the reaction with 1-bromo-2-phenylpropene impurity present. This reaction is difficult and only a poor yield of (34) is obtained. A number of different reaction products including the hexadienes were produced. It is thought that the halogenation of 2-phenylpropene with N-chlorosuccinimide or N-bromosuccinimide to form 3-bromo-2-phenylpropene[54JA2705] involves addition of Br_2 to the double bond and elimination of HBr, rather than allylic radical bromination.

Ideally the formation of (34) should be accompanied with a minimum of side reactions and have a high yield. Also, since the formation of 3-bromo-2-phenylpropene (55a) is normally accompanied with the formation of 1-bromo-2-phenylpropene (55b) and these are difficult to separate (spinning band distillation, b.p. (55b) 63°C 2 mmHg; b.p. (55a) 76°C 2 mmHg) it is preferable to be able to perform this reaction cleanly with the vinyl bromide impurity present in the reaction mixture and produce an easily separable mixture of vinyl bromide and homoallylic alcohol. The reaction of 3-bromo-2-phenylpropene (55a) with acetaldehyde in the presence of tin and aluminium contrasts the corresponding Grignard reaction. The procedure is more simple and gives a cleaner product. Pinacol byproducts were found to be easily removed by chromatography or distillation under vacuum. Reaction of aldehydes with crotyl and cinnamyl halides catalysed by tin and aluminium did not produce pinacols in noticeable yield, ([13]C n.m.r.) possibly because these allylic reactants are more reactive than 3-halo-2-phenyl-propene and the pinacol reaction is less successful in competition with the carbon carbon bond forming reaction. It is known that tin metal catalyses the formation of pinacols. As in the Grignard reaction it is not necessary to purify the mixture of 3-halo-2-phenylpropene from 1-halo-2-phenylpropene

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because under tin and aluminium conditions only the allylic halide and not the vinylic halide is sufficiently active to react with aldehydes.

Competition studies

The relative rates of reaction of aryl aldehydes with cinnamyl chloride or crotyl bromide in the presence of various catalysts have been measured. Three different reaction systems were studied; tin and aluminium metals; allylic organometals thermally activated and allylic organometals catalysed with boron triflouride diethyletherate. Preparation of crotyl tributyl tin and cinnamyl tributyl tin was accomplished using standard methods[70JM0675, 74JM0395, 80JA3774] and the reaction of these allylic stannanes with the various aldehydes studied. The effects of electron withdrawing and electron donating groups on the aromatic aldehyde were compared and the differences between cinnamyl and crotyl nucleophiles were established. A summary of the results is shown in Table 2.2.

The results in Table 2.2 for the tin-aluminium mediated reactions (A) show that methyl and methoxy groups reduce the reactivity of the carbonyl while the nitrile group increases reactivity. The addition of large amounts of hydrobromic acid (24 drops instead of the normal 3 drops) does not cause any change in the ratio of products produced indicating the acid does not take any significant part in the rate determining step of the reaction and is considered a catalyst to the formation of the likely organometallic intermediate. These same reaction conditions for crotyl bromide show similar trends. A preference toward *erythro* products is observed with typically 60:40 *erythro:threo* homoallylic alcohol mixtures being observed.

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Table **2.2**
Relative rates of reaction of various aldehydes with allylic functions under different conditions

Competing Aldehydes (RCHO/R'CHO)

Method	Allylic function	Ph/MeOPh	Ph/NCPh	MeOPh/NCPh	Ph/MePh
		e:t / e:t	e:t / e:t	e:t / e:t	e:t / e:t
a	cinnamyl	00:63/00:37	00:34/00:66	0038/00:62	00:61/00:39
b	cinnamyl	00:70/00:30			
a	crotyl	46:32/10:11	16:12/43:27		43:33/14:10
b	crotyl	70:00/30:00			67:00/33:00
c	crotyl	35:25/20:20			32:23/26:19

e = erythro; t=threo.

Method
a: Reaction mediated by tin-aluminium;
b: Reaction of allylic tributyl tin with aldehydes catalysed with $BF_3.OEt_2$;
c: Reaction of allylic tributyl tin with aldehydes heated 200°C. ·

The same relative rate observations were established for boron triflouride catalysed reaction of cinnamyl tributyl tin with aryl aldehydes. Benzaldehyde reacted faster than p-methylbenzaldehyde. The boron triflouride catalysed reaction of crotyl tributyl tin with benzaldehyde was faster than with p-methylbenzaldehyde and p-methoxybenzaldehyde (see Table **2.2**). The thermal reaction of cinnamyl organotins with aldehydes does not appear to proceed under the conditions employed (no solvent, 200°C) and this is thought to result from the cinnamyl moiety stabilizing the organometal by virtue of its ability to accept electrons. The same thermal reaction using crotyl tributyl tin gives *erythro* and *threo* mixtures of homoallylic alcohols with low diastereoselectivity and only small rate differences were observed with varying substituted aryl aldehydes. The lack of selectivity may result from the high temperature employed in these reactions.

Reaction of either cinnamyl chloride or crotyl bromide with p-nitrobenzaldehyde in competition with benzaldehyde and when catalysed by tin

Discussion

and aluminium produces no homoallylic product. Not only does the p-nitrobenzaldehyde not react with the allylic group to form the alcohol but it also does not allow the reaction of benzaldehyde with the allylic group.

The *erythro* product is likely to be formed from reaction involving a linear transition state while the *threo* product is more likely to result from a cyclic transition state. The relative rate of reaction of the various aldehydes with allylic metals can therefore differ depending on how substituents effect the linear and cyclic transition states. The relative importance of each mechanism from a particular allylic substrate is assumed to be independent of the aldehyde structure. Competition experiments therefore should reflect the effect of substituents on the linear or cyclic transition states and their effect may be different for these two processes. From examination of the table it would appear that the Sn-Al mediated reaction of cinnamyl chloride with aldehydes has similarities to the Lewis acid mediated reaction of cinnamyl organotin with aldehydes. In contrast the Sn-Al mediated reaction of crotyl bromide gives very different results to the Lewis acid mediated reaction of crotyl organotins with aldehydes but similar results to the thermal addition of crotyl organotins to aldehydes. The thermal addition of cinnamyl organotins to aldehydes is dissimilar to both the Sn-Al mediated and the Lewis acid mediated additions of cinnamyl moiety to aldehydes. The same competitive trends are observed in both the *erythro* selective mechanism for crotyl and in the *threo* selective mechanism for cinnamyl indicating that even if the mechanisms are different the relative reactivities toward substituted aryl aldehydes are similar. The order of substituted aryl aldehyde reactivity with crotyl bromide and with cinnamyl chloride is NCPhCHO > PhCHO > MePhCHO >= MeOPhCHO. These results are also discussed in the light of molecular orbital calculations later in this thesis.

Discussion

Preparation of Epoxy Ketones

Certain β,γ-epoxyketones have proved difficult to synthesize from the corresponding homoallylic alcohols. Hii[77AJ0161, 77AJ0835] and Dodge[83TH0001] have prepared 1,3-diphenyl-3,4-epoxy-1-butanone, 3,4-epoxy-3-methyl-1-phenyl-1-butanone, 3,4-epoxy-2,2-dimethyl-1-phenyl-1-butanone and others by epoxidation and oxidation reactions but low yields and difficulty in epoxidation limits these reactions. For example Dodge when attempting to epoxidise 1,3-diphenyl-3-buten-1-one **(45)** using meta-chloroperbenzoic acid in dry ether obtained a complex product mixture containing no epoxyketone **(44)**. This problem was eventually partially overcome by epoxidising 1,3-diphenyl-3-buten-1-one **(45)** in a two-phase reaction system[19] but poor yields and a number of side-products were still obtained. The continuing problem of instability of β,γ-epoxyalcohols, β,γ-epoxyketones and the sensitivity of the epoxidation reaction to experimental conditions prompted our continued investigation of these reactions. The two products 1,3-diphenyl-3,4-epoxy-1-butanone **(44)** and 3,4-epoxy-3-methyl-1-phenyl-1-butanone **(50)** had already been made and a third, 4,5-epoxy-4-phenyl-2-pentanone **(38)**, was also used to test these altered procedures.

| **3 8** | **4 4** | **4 5** | **5 0** |
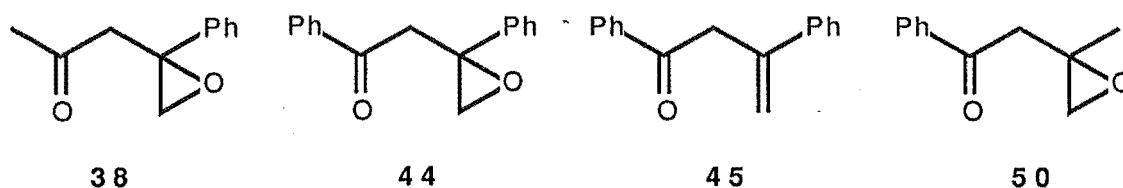
Epoxidation of 4,5-epoxy-4-phenyl-2-pentanone with meta-chloroperbenzoic acid in an ether solvent system was fraught with complicated side reactions and seldom gave epoxide product (60 Hz ^{1}H n.m.r.). Epoxidation of the ketone gave very poor results with cyclic furan being formed[71JO3011] (see Scheme). Various reaction conditions were attempted including a chloroform - water - tetrabutylammonium hydroxide phase transfer meta-

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[19] The ketone was epoxidised with MCPBA in a chloroform-water two phase system and tetrabutylammonium hydroxide as a phase transfer reagent.

Discussion

chloroperbenzoic acid epoxidation method. Although these conditions improved the yields of epoxide it was felt the improvement was insufficient for obtaining useful quantities of epoxyketones.
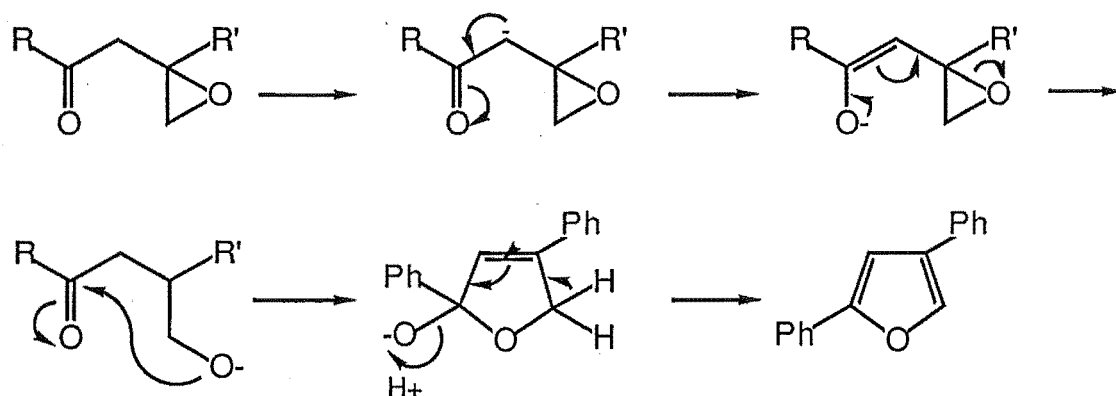
Because of these initial difficulties it was decided to acetylate the alcohol functional group and then epoxidise the acetate in the hope that the epoxy-acetate was more stable than the respective epoxy alcohol. This epoxy acetate could be hydrolysed and the resultant epoxy alcohol oxidized using pyridinium chlorochromate to give the epoxy ketone. Very much cleaner reaction mixtures from epoxidation were obtained and in excellent yields. Thus in the preparation of 4,5-epoxy-4-phenyl-2-pentanone (38) (Scheme 2.6), acetylation of 4-phenyl-4-penten-2-ol (34) gave an 83% yield (49% after purification by silica gel radial chromatography) of 2-acetoxy-4-phenyl-4-pentene (35). Subsequent epoxidation with the meta-chloroperbenzoic acid reagent yielded 100% (70% after chromatographic purification) 2-acetoxy-4,5-epoxy-4-phenyl pentane (36) as a mixture of two isomers. Although epoxidations with this reagent have been reported to give good diastereoselectivities in some cases[67JA4435] in this instance only moderate stereoselectivity was observed. The major and more polar isomer was present as 54% of the mixture with the minor and less polar isomer making up the balance. These ratios were determined from the integrals of the acetyl hydrogens in the ^{1}H n.m.r. spectrum, and confirmed by g.l.c. Two

Discussion

decoupling experiments were performed to partly characterize the two isomers from the mixture. Irradiation at C2 (δ_H 5.0) caused the doublet of doublets (δ_H 2.67, 1.74) to collapse to a solitary doublet and the AB quartet of doublets (δ_H 2.19, 2.32) to collapse to an AB quartet. This allowed for resolution between the methylene and epoxide protons which have sufficiently similar chemical shifts that straight forward assignment was impossible.

The two isomers were successfully separated by careful radial chromatography using 0 - 10% ether - petroleum ether mixtures. On another occasion the same reaction produced a third product in addition to the two diastereomeric acetates in a reversed diastereomeric ratio (most to least polar 33:67%). The ^{13}C n.m.r. resonance at 119.5 ppm suggested this was an ortho-ester and subsequent analysis of ^1H n.m.r. spectra determined the product to be (1RS, 3SR, 5SR)-1,3-dimethyl-5-phenyl-2,7,8-trioxabicyclo[3,2,1]octane (40). This ortho-ester is produced by the action of base (present during the alkaline workup procedure) on the product epoxy acetates. The stereochemistry of the ester was determined by analysis of the ^1H n.m.r. spectra. The 2 Hz coupling between the two *exo* hydrogens (H6$_{exo}$, H4$_{exo}$) allowed their assignment in the ^1H n.m.r. spectra (δ_H 1.772 H4$_{exo}$, 3.772, H6$_{exo}$). The 11.8 Hz coupling constant between H4$_{exo}$ and H3 determined the antiperiplanar (and not gauche) relationship between H3 and H4$_{exo}$ (and not H4$_{endo}$). The H4$_{endo}$, H3 coupling of 4.05 Hz is consistent with a gauche interaction. Combining this data with the examination of models enabled the chair conformation be designated to the six membered ring system and the relative stereochemistry of the ortho ester to be determined.

The most polar epoxy-acetate (36a) was formed predominantly in the epoxidation reaction where no ortho-ester was produced; comparatively when the ortho-ester was found to be present in the product mixture the

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least polar isomer predominated. This indicates that the more polar isomer (36a) rearranges to the ortho-ester (40). Separate hydrolysis of each isomer confirms this; the more polar isomer (36a) when treated with an alcoholic solution of sodium hydroxide gave large quantities of the ortho-ester after workup. No ortho-ester was in evidence in the product mixture when the less polar epoxy-acetate (36b) was treated similarly.
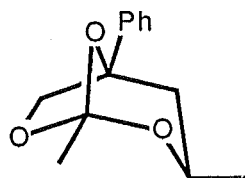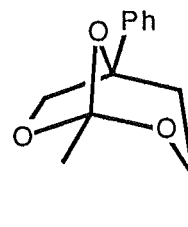
(1RS, 3SR, 5SR)-40   (1RS, 3RS, 5SR)-40

These results can be rationalized from an examination of the mechanism of this reaction. The ortho-ester can be formed form either carbonyl oxygen attack on C4 (Scheme 2.5 [i]) or attack on C5 (Scheme 2.5 [ii,iii,iv,v,vi]) displacing the respective C-O epoxide bonds which then attacks the carbonyl carbon. Attack on C5 can potentially occur with inversion (Scheme 2.5 [iii,v]) or retention (Scheme 2.5 [iv,vi]) of configuration. Studies by Coxon et. al.[73AJ2521, 74JO1142] indicate by labeling the carbonyl oxygen on the acetate function that attack occurs at C4, i.e. the non-terminal carbon of the epoxide function, giving rise to a 6-membered transition structure. Further consideration of the steric requirements indicate that the reaction would occur with inversion of configuration. Since the (1RS, 3SR, 5SR)-ortho-ester (40) and not the (1RS, 3RS, 5SR)-ortho-ester is produced only one possibility (Scheme 2.5 [iii]) of the six shown is viable. This also indicates the stereo-chemistry of the epoxy acetate, and thus the stereochemistry of the epoxy-alcohol.

Discussion

Scheme **2.5**

(i)

(ii)

(iii)   inversion

(iv)   retention

(v)   inversion

(vi)   retention
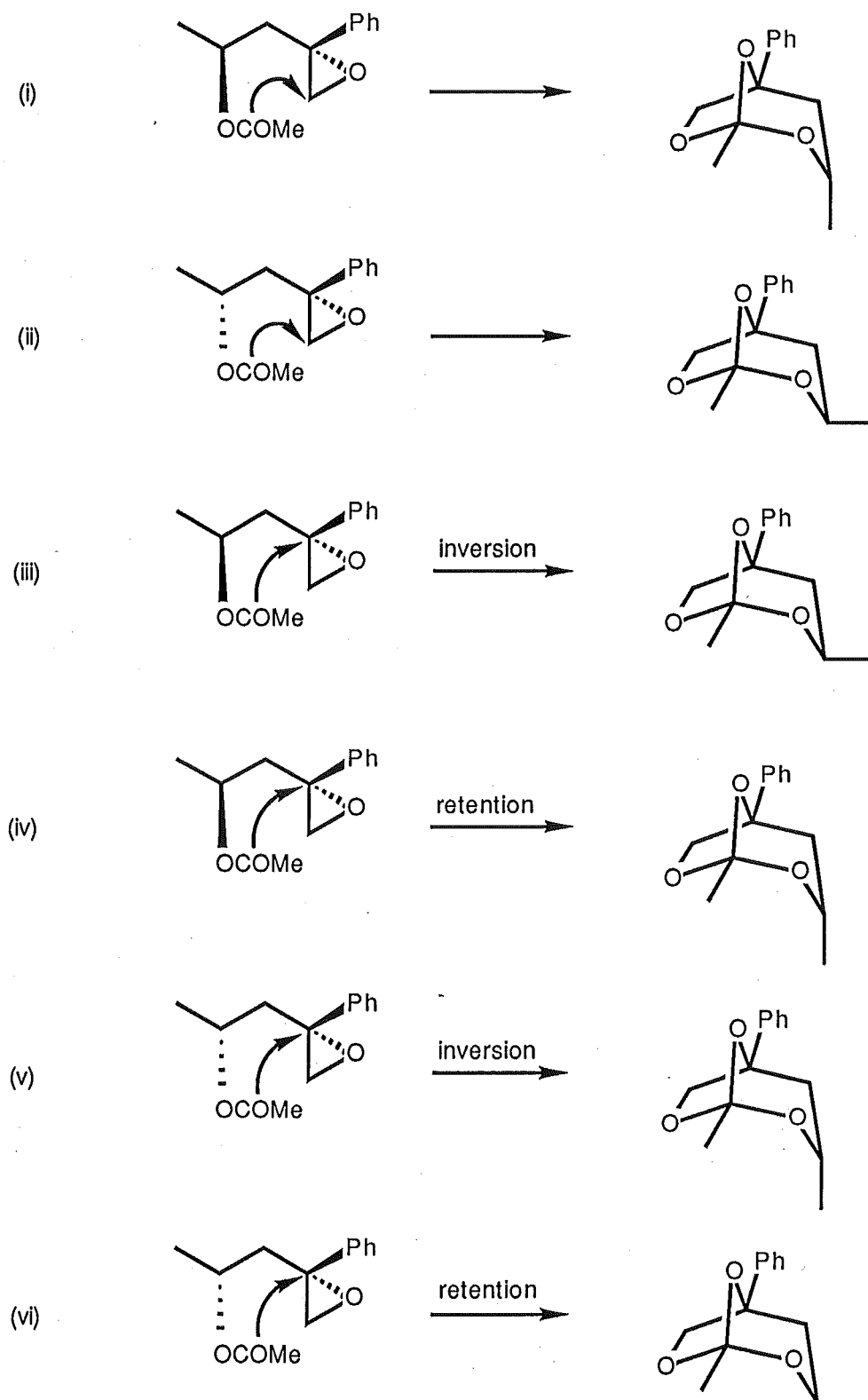
Hydrolysis of the isomeric mixture of epoxy-acetates (36) gave a 95% yield of identifiable products including an 83% yield of the required epoxy-alcohols (37) and an 12% yield of the ortho-ester (40). From hydrolysis of the separate

Discussion

isomers above it was clear that the alcohol (37a) corresponded to the acetate (36a) and (37b) corresponded to (36b). These isomers are easily identified in the ^1H n.m.r. spectra by their characteristic methylene chemical shifts. The more polar 2-acetoxy-4,5-epoxy-4-phenyl pentane (36a) has the two methylene proton resonances at δ_H 2.19 and 2.32. The less polar isomer (36b) methylene resonances occur at δ_H 1.74 and 2.32. It is interesting to consider why the prochiral hydrogens of this isomer have such different chemical shifts. Correspondingly the alcohol corresponding to (36a), 4,5-epoxy-4-phenyl-2-pentanol (37a) has its methylene proton resonances widely separated (δ_H 1.70, 2.49) and (37b) corresponding to (36b) has the resonances closely spaced (δ_H 2.15, 2.30). The final step in this reaction sequence, oxidation of 4,5-epoxy-4-phenyl-2-pentanol (37) with pyridinium chloro-chromate yielded a 48% of 4,5-epoxy-4-phenyl-2-pentanone (38). All attempts to purify the ketone met with limited success as the product reacted or rearranged on the alumina and silica columns or radial plates and only small yields of the epoxy ketone were recovered.

(2RS, 4SR)-36a   (2RS,4RS)-37a   (1RS, 3SR, 5SR)-40

(2RS, 4RS)-36b   (2RS, 4SR)-37b

Discussion

Scheme 2.6

Scheme 2.7

PhCHO +

Me

Cl

Sn/Al

Ph

OH

46

acetic anhydride
in pyridine
95% yield

Ph

OAc

47

MCPBA
NaOAc
82% yield

Ph

OAc

O

48 (57:43 isomeric mixture)

alcoholic
NaOH (5%)
95% yield

Ph

OH

O

PCC
NaOAc
90% yield

Ph

O

O

50

PCC
NaOAc
88% yield

Ph

O

51

MCPBA
NaOAc

this reaction
had not gone
to completion
after 1 week

Ph

O

O

50

MCPBA
NaOAc
76% yield

Ph

OH

O

49 (2:1 isomeric mixture)

PCC
NaOAc
90% yield

radial
chromatography

Ph

O

O

50

Discussion

A similar reaction sequence (Scheme 2.7) was used to ultimately produce 3,4-epoxy-3-methyl-1-phenyl-1-butanone (50) from 3-methyl-1-phenyl-3-buten-1-ol (46). Acetylation of the β,γ-unsaturated alcohol gave 1-acetoxy-3-methyl-1-phenyl-3-butene (47) (95%) and this was epoxidised without further purification to give an 82% yield of a 57:43 mixture of isomeric 1-acetoxy-3,4-epoxy-3-methyl-1-phenyl butanes (48); no ortho-ester was formed. Hydrolysis of the epoxy-acetates gave a 95% yield of isomeric 3,4-epoxy-3-methyl-1-phenyl-1-butanols (49) in the same ratio. The two alcohols were partly characterized by ^{1}H n.m.r. by irradiation of C$\underline{H}$OH resonances (δ_H 4.95 and 4.74) and examining the subsequent collapse of the CH$_2$ resonances (δ_H 1.88, 2.02; 2.01). Subsequent oxidation gave 3,4-epoxy-3-methyl-1-phenyl-1-butanone (50) (90%) but attempts to purify the ketone by distillation or chromatography on silica or alumina tended to destroy the product. Dry column silica gel chromatography and elution with 10% ether - benzene gave satisfactory (though not excellent) purification with minimum destruction of the product.

The use of radial or column silica gel chromatography afforded pure samples of epoxy ketones but only in low yields. While this method was successful in producing the required products and although some interesting information was gained from these studies it involved a large number of experimental steps and the final purification procedure resulted in a large loss of material. When a small modification to the MCPBA procedure for epoxidation of the homoallylic alcohol or equivalent ketone was effected and resulted in very good yields and a very clean product studies on the epoxidation of the acetylated alcohol were not pursued further.

The addition of two equivalents of anhydrous sodium acetate to the epoxidation reaction mixture resulted in epoxidations of the homoallylic

Discussion

alcohols and the β,γ-unsaturated ketone being clean and easily carried out. The sodium acetate acts as a buffer in the reaction and thereby inhibits the formation of reaction by-products. Both epoxidation followed by oxidation and oxidation followed by epoxidation procedures can be pursued. Both synthetic pathways were carried out on a small scale without intermediate purification of the epoxy-alcohol or ketone (as the case may be). Although the oxidation - epoxidation procedure generally gave a cleaner product and better yields a problem was encountered in that epoxidation of the ketone could not be completed. Workup of the reaction mixture followed by re-epoxidation with a new batch of metachloroperbenzoic acid could not force the reaction to completion. It is therefore established that epoxidation followed by oxidation is the best route to formation of these epoxy ketones.

Thus (Scheme 2.6) epoxidation of 4-phenyl-4-penten-2-ol (34) with meta-chloroperbenzoic acid and anhydrous sodium acetate gave a 76% yield (64% after chromatographic purification) of a 2:1 isomeric mixture of 4,5-epoxy-4-phenylpentan-2-ols (37). Interestingly the same reaction but without sodium acetate has given on one occasion the same yield of the same isomeric mixture. It should be emphasized that these results are not repeatable whereas the acetate buffered reaction mixture gives reproduceable results. Note also that the stereochemical preference of the alcohol resulting from this epoxidation reaction is opposite to the stereochemical preference of the epoxidation of the acetate described above. This may be due to hydroxyl participation in the transition state or it may be due to the different stable steric conformations of the homoallylic alcohol and acetate. Oxidation of this alcohol and the difficulties and loss of yield encountered in the purification procedures has been described above.

The alternative (Scheme 2.6) oxidation and epoxidation method gave 4-phenyl-4-penten-2-one (39) in 73% yield and after epoxidation a mixture of

Discussion

this ketone (39) and 4,5-epoxy-4-phenyl-2-pentanone (38) in 85% yield. Even after re-epoxidation considerable quantities of unreacted ketone remained and this synthetic procedure was deemed unsuitable for further examination.

Similar problems were encountered in the preparation of both 3,4-epoxy-3-methyl-1-phenyl-1-butanone (50) and 3,4-epoxy-1,3-diphenyl-1-butanone (44) (Scheme 2.7, 2.8).

Scheme 2.8
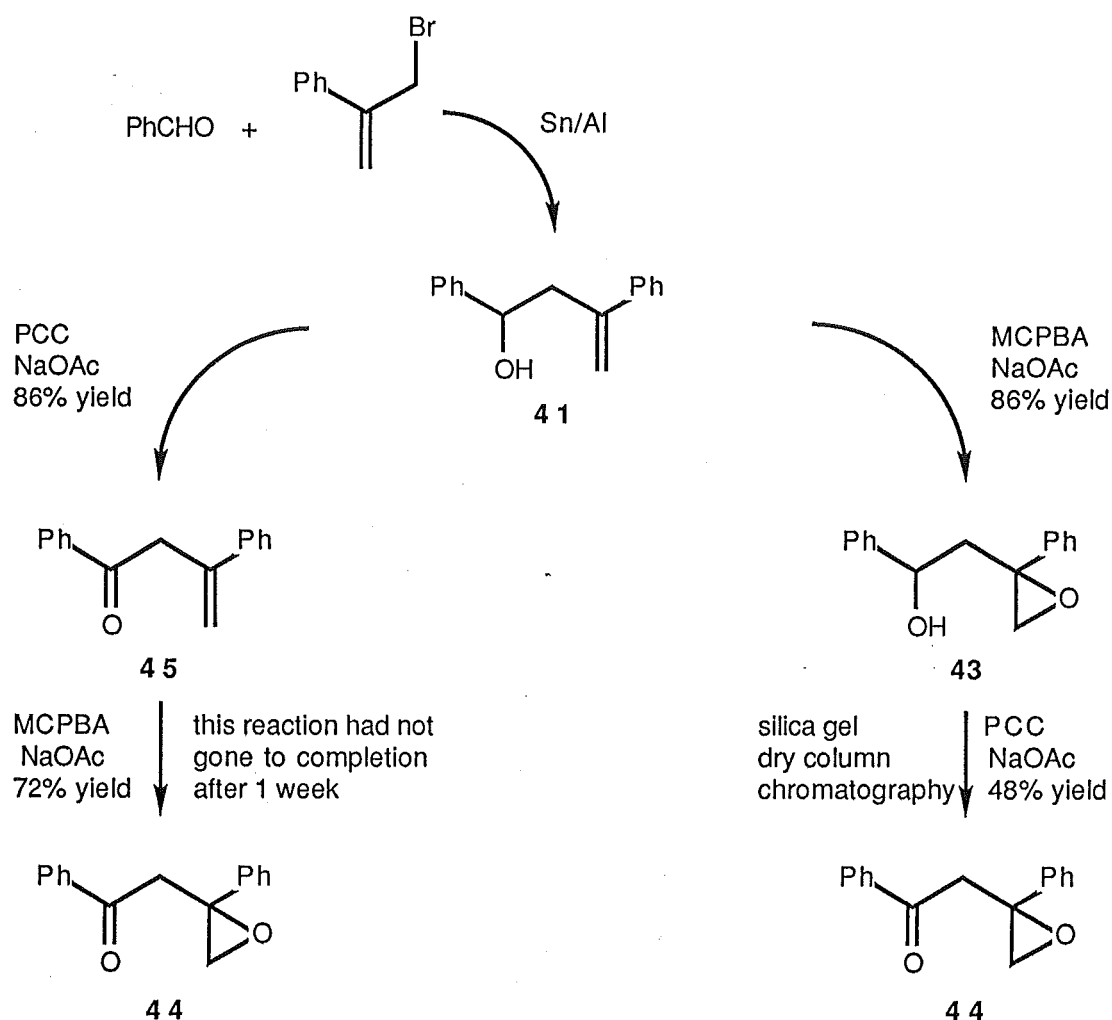
In order to obtain a relatively pure product the final step must be some form of purification; and unfortunately this purification step is difficult to carry out without a large loss of product. Impurities were formed during the

Discussion

epoxidation step and therefore purification at this stage is carried out with the more stable epoxide not being affected by the purification procedure. Subsequent oxidation produces a comparatively clean product which can be rapidly purified on dry column silica. Because the chromatographic step is so fast reaction on the silica media is minimized and a product suitable for photolysis is obtained. Thus medium yields of high purity were obtained.

Discussion

Conformation and Frontier Molecular Orbital Calculations

Conformational Analysis

It has been proposed that *erythro* selective reactions of allylic compounds with aldehydes proceed through an acyclic transition state.[80JA7107] In the same way that cyclohexane conformational analysis has been applied to the cyclic transition state, so acyclic conformational analysis can be applied to the linear transition state.[82TL4891]

Calculations of the steric MM-energies for rotamers of the methyl ethers of homoallylic alcohols were carried out in an attempt to explain the *erythro* diastereoselectivity of the linear mechanism. First the steric energies, heats of formation and total energies of a number of rotamers of the methyl ethers of *erythro* and *threo* 2-methyl-1-phenyl-3-buten-1-ol (Figures 3.1, 3.2) were calculated and are tabulated in tables 3.1 to 3.4.

Calculations were carried out on these product-like structures in the supposition that the steric requirements of the products might reflect and so model something of the steric requirements of the transition state. This approach has limitations; the Hammond postulate requires that for an exothermic reaction the transition state is more reactant-like than product-like; but there is good evidence that steric factors which dictate energy of the various conformations of the products will also influence the various transition states involved in their formation.[82JA7162] In the reaction of an allylic anion with an aldehyde either face of the anion may attack either face of the aldehyde. Thus the reacting species may approach each other in four possible ways giving rise to two possible transition state topicities. Each table (3.1 - 3.4) represents one of these transition states topicities for either (E)- or (Z)-crotyl anion and as is easily seen in the associated figures each transition state may have several rotameric isomers. The methyl ether of the

Conformation...

aldehydes was used to mimic the steric bulk BF₃ might cause in the transition state.

The staggered structure of ethane was input and minimized using MODEL.[20] Modifications to the minimized ethane structure were made to provide a single conformer of each of the methyl ethers of *erythro* and *threo* 2-methyl-1-phenyl-3-buten-1-ol. Because of the danger in these calculations of falling into a local minima the ethereal methyl group was drawn *anti* to the phenyl group and the phenyl group was drawn in the same plane as the C1-O bond. Boron triflouride is thought to be complexed *anti* to the R-group of the aldehyde in the transition state, but because B-F and B-O bond parameters were unknown for the MMX program BF₃ could not be used in the model of the transition state. Each diastereoisomer was again minimized by MODEL. The two resulting structures were converted to a MMX[21] readable files and submitted to MMX and driven 0° to 300° in 60° increments around the C1-C2 bond that would be formed in the equivalent transition state. In addition the Me-CH-CH=CH₂ dihedral angle was set at 0° and 180° to simulate (E)- and (Z)-crotyl functions.

Figure **3.1** shows the *erythro* 2-methyl-1-phenyl-3-buten-1-ol methyl ether rotamers. Table **3.1** tabulates the results of the calculations on these rotamers when the Me-CH-CH=CH₂ angle was set at 0° to simulate the addition of (Z)-crotyl nucleophile to benzaldehyde and Table **3.2** shows rotamers of the same ether with the Me-CH-CH=CH₂ angle set at 180° to simulate the addition of (E)-crotyl nucleophile to benzaldehyde. Figure 3.2 is of *threo* 2-methyl-1-phenyl-3-buten-1-ol methyl ether rotamers. Table **3.5** tabulates the results of the calculations on these rotamers when the

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20 MODEL is a graphical input/MM2 optimisation program developed by Kosta Steliou; University of Montreal.
21 MMX is derived from MM2 with MMP1 PI subroutines incorporated for localised π electron systems.

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Me-CH-CH=CH$_2$ dihedral angle set at 0° and Table 3.6 shows the *threo* ether with the dihedral angle set at 180°.

If steric requirements of the transition state entirely govern the diastereo-selectivity of the reaction then taking the lowest energy conformers from each table should provide some information on the reaction pathway. Thus a comparison of Tables 3.1, (vi) and 3.5, (ii) should predict the diastereo-selectivity of the reaction of (Z)-crotyl anion with benzaldehyde and a comparison of Tables 3.2, (vi) and 3.6, (ii) may be used to suggest the reaction course of (E)-crotyl anion with benzaldehyde. Since 3.5, (ii) is lower in energy than 3.1, (vi) such an argument predicts the *threo* homoallylic alcohol is produced from (Z)-crotyl anion and since 3.2, (vi) is lower in energy than 3.6, (ii) that (E)-crotyl anion will give the *erythro* homoallylic alcohol. At this point it should be noted that this is contrary to the experimental results which predict that both (E)- and (Z)-crotyl anions produce the *erythro* alcohol.

It has been suggested that for this linear mechanism to occur successfully the reacting species must approach each other with the double bonds (allylic and carbonyl) *anti* to one another. In this case Table 3.5, (vi) has higher energy than Table 3.1, (iv) suggesting that (Z)-crotyl anions react to form *erythro* homoallylic alcohol and Table 3.6, (vi) is lower in energy than Table 3.2, (iv) suggesting that (E)-crotyl anions also react to form *threo* alcohols. Again these predictions are at odds with experimental results.

In the each of the above calculations however two bonds have been restricted to a defined angle. Thus the energies calculated would not represent the exact local minimum (or maximum) of the ether in this approximate conformation. It is not reasonable to assume that in the linear transition state (that these systems are modelling) the reactants approach

Conformation...

each other in convenient 60° orientations. Nor is it reasonable to assume that the allylic double bond remains planar (or near planar) during the course of the reaction. Therefore each of the conformers generated were minimized with the dihedral angle constraints removed. The energies thus produced represent the true local minimum of each staggered conformation and it is these minima that may better reflect the importance of steric effects in the transition state.

If steric constraints of the transition state alone govern the product diastereoselectivity then an examination of these results indicates that for both (E)- and (Z)-crotyl anions reacting with benzaldehyde the *threo* alcohol will be produced (Table **3.3**, (ii) cf Table **3.7**, (vi) and Table **3.4**, (ii) cf Table **3.8**, (vi)). If as has been suggested is the case the double bonds approach each other in an *anti* conformation then for both (E)- and (Z)-crotyl anions the *erythro* alcohol will be produced (Table **3.3**, (vi) cf Table **3.7**, (iv) and Table **3.4**, (vi) cf Table **3.8**, (iv)). The *erythro* preference can only be accounted for if some non-steric factor requires the double bonds *anti* to one another.

Conformation...

Figure 3.1

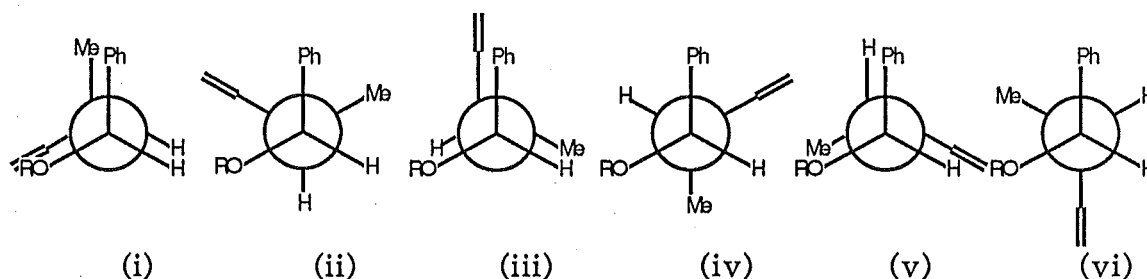Rotational Conformers of *Erythro* 2-Methyl-1-phenyl-3-buten-1-ol Methyl Ether

| | (i) | (ii) | (iii) | (iv) | (v) | (vi) |

Table 3.1

Energies of Figure 3.1 Conformers with Me-C2-C3-C4 Dihedral angle set at 0°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	18.075	15.080	19.959	14.864	16.896	12.892
ΔH_f	-10.567	-13.548	-8.661	-13.764	-11.758	-15.704
Total	23.9449	20.9501	25.8289	20.7335	22.7655	18.7621

Table 3.2

Energies of Figure 3.1 Conformers with Me-C2-C3-C4 Dihedral angle set at 180°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	19.293	15.873	21.908	16.452	16.729	12.710
ΔH_f	-9.338	-12.756	-6.685	-12.180	-11.923	-15.909
Total	25.1631	21.7430	27.7779	22.3223	22.5989	18.5797

Table 3.3

Energies of Table 3.1 Conformers Minimized (ie no constraints on dihedral angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	14.573	14.587	14.048	14.049	12.412	12.395
ΔH_f	-14.061	-14.053	-14.589	-14.588	-16.235	-16.240
Total	20.4435	20.4574	19.9183	19.9192	18.2816	18.2651

Table 3.4

Energies of Table 3.2 Conformers Minimized (ie no constraints on dihedral angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	14.103	14.119	13.602	13.606	11.820	11.811
ΔH_f	-14.532	-14.514	-15.039	-15.039	-16.818	-16.822
Total	19.9727	19.9893	19.4721	19.4756	17.6896	17.6813

Conformation...

Figure 3.2
Rotational Conformers of *Threo* 2-Methyl-1-phenyl-3-buten-1-ol Methyl
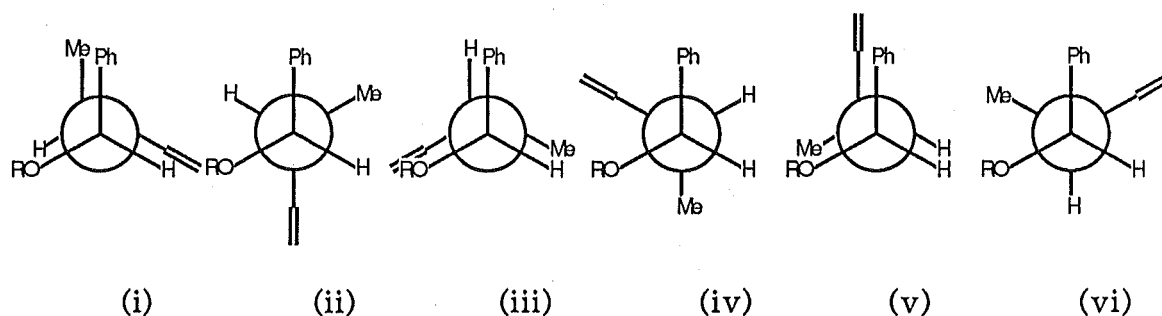Ether

(i)   (ii)   (iii)   (iv)   (v)   (vi)

Table 3.5

Energies of Figure 3.2 Conformers with Me-C2-C3-C4 Dihedral angle set at 0°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	17.685	11.924	16.718	15.453	20.880	15.507
ΔH_f	-10.943	-16.719	-11.938	-13.150	-7.737	-13.118
Total	23.5551	17.7936	22.5840	21.3228	26.7501	21.3772

Table 3.6

Energies of Figure 3.2 Conformers with Me-C2-C3-C4 Dihedral angle set at
180°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	17.353	13.040	17.454	17.766	22.121	15.678
ΔH_f	-11.295	-15.617	-11.178	-10.831	-16.505	-12.955
Total	23.2235	18.9104	23.3239	23.6355	27.9906	21.5478

Table 3.7

Energies of Table 3.5 Conformers Minimized (ie no constraints on dihedral
angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	11.217	11.207	11.211	14.465	15.195	15.195
ΔH_f	-17.437	-17.443	-17.441	-14.173	-13.444	-13.436
Total	17.0873	17.0773	17.0811	20.3351	21.0653	21.0645

Table 3.8

Energies of Table 3.6 Conformers Minimized (ie no constraints on dihedral
angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	10.814	10.815	10.818	13.886	14.552	14.552
ΔH_f	-17.836	-17.840	-17.825	-14.750	-14.082	-14.081
Total	16.6839	16.6852	16.6881	19.7559	20.4220	20.4220

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The same analysis can be imposed on the reaction of cinnamyl substrates and aldehydes. Figures 3.3 and 3.4 and Tables 3.9 to 3.16 model the rotamers and topicities of the proposed transition state of this reaction. Tables 3.3, 3.4, 3.7, 3.8 list energies for each rotamer where the driven dihedral angles have been fixed. These would indicate that if the transition state conformation is governed by steric effects then (E)-cinnamyl anion would give *erythro* 1,2-diphenyl-3-buten-1-ol (Tables 3.10, (vi) and 3.14, (ii)) and (Z)-cinnamyl anion would also give *erythro* alcohols (Tables 3.9, (iv) and 3.13, (ii)). If the linear transition state also requires the *anti* conformation of double bonds then again for both (E)- and (Z)-cinnamyl anions on reaction with benzaldehyde the *erythro* homoallylic alcohol is predicted (Tables 3.9, (iv) cf 3.13, (vi) and Tables 3.10, (iv) cf 3.14, (vi)).

Tables 3.11, 3.12, 3.15, 3.16 remove the dihedral angle constraint. As has been mentioned in the case of crotyl anion on reaction with aldehydes, it is believed that this situation more accurately mimics the steric factors in the actual transition state. It can be seen from an examination of the energies of each conformer that for both the sterically directed transition state and the *anti* directed transition state we would expect *erythro* selectivity for (Z)- and (E)-cinnamyl moieties.

My experiments and those of Koreeda have shown that cinnamyl substrates produce the *threo* isomer preferentially. These calculation confirm that the reaction of cinnamyl organotins with aldehydes catalysed by BF_3 to give *threo* homoallylic alcohols do not go through the linear transition state.

Conformation...

Figure **3.3**

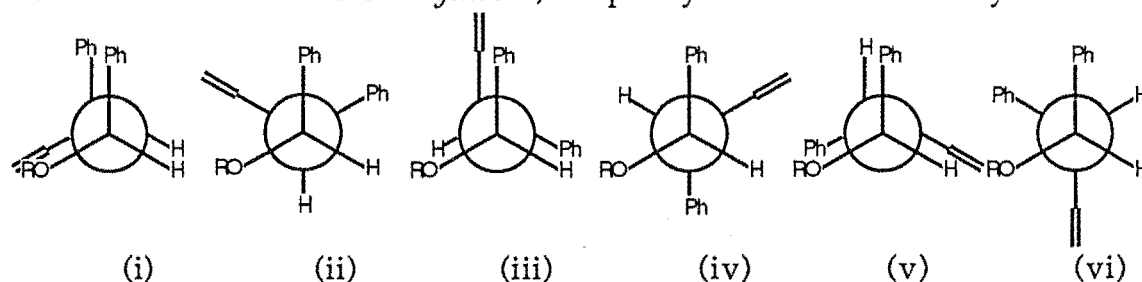Rotational Conformers of *Erythro* 1,2-Diphenyl-3-buten-1-ol Methyl Ether

(i) (ii) (iii) (iv) (v) (vi)

Table **3.9**

Energies of Figure **3.3** Conformers with Ph-C2-C3-C4 Dihedral Angle set at 0°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	33.519	28.824	30.591	24.048	28.446	25.925
ΔH_f	26.375	22.069	23.888	17.357	21.734	18.958
Total	38.6493	33.9536	35.7206	29.1782	33.5764	31.0550

Table **3.10**

Energies of Figure **3.3** Conformers with Ph-C2-C3-C4 Dihedral Angle set at 180°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	33.554	28.677	32.155	25.124	27.152	24.770
ΔH_f	26.189	21.837	25.496	18.450	20.444	17.819
Total	38.6844	33.8067	37.2854	30.2538	32.2818	29.9000

Table **3.11**

Energies of Table **3.9** Conformers Minimized (ie no constraints on dihedral angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	27.296	27.171	22.630	22.435	23.665	23.644
ΔH_f	20.401	20.328	15.903	15.725	16.855	16.787
Total	32.4260	32.3009	27.7595	27.5649	28.7951	28.7737

Table **3.12**

Energies of Table **3.10** Conformers Minimized (ie no constraints on dihedral angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Strain	27.298	27.211	22.713	22.413	23.735	23.693
ΔH_f	20.386	20.403	15.974	15.712	16.932	16.840
Total	32.4280	32.3411	27.8425	27.5426	28.8651	28.8227

Conformation...

Figure 3.4
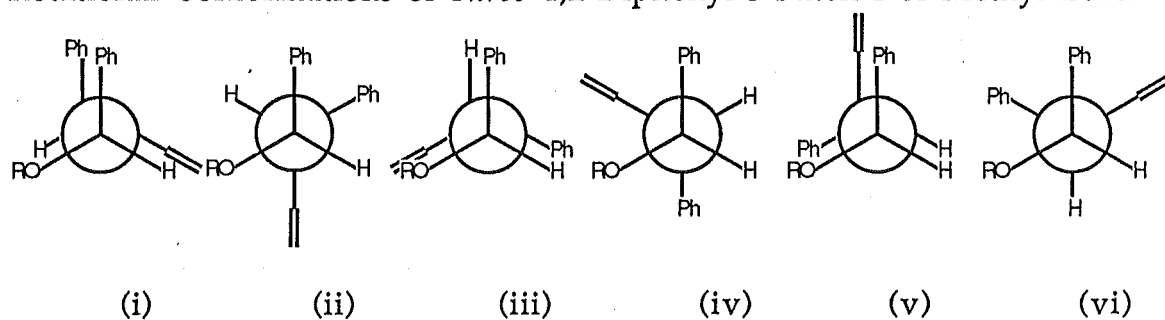Rotational Conformations of *Threo* 1,2-Diphenyl-3-buten-1-ol Methyl Ether

| (i) | (ii) | (iii) | (iv) | (v) | (vi) |

Table 3.13
Energies of Figure 3.4 Conformers with Ph-C2-C3-C4 Dihedral Angle set at 0°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	33.374	25.562	28.672	27.140	32.313	30.264
ΔH_f	26.316	18.516	21.966	20.503	25.633	23.444
Total	38.5044	30.6923	33.8021	32.2704	37.4427	35.3936

Table 3.14
Energies of Figure 3.4 Conformers with Ph-C2-C3-C4 Dihedral Angle set at 180°

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	31.866	25.941	28.386	28.167	32.798	29.037
ΔH_f	24.685	18.866	21.681	21.531	26.125	22.101
Total	36.9958	31.0706	33.5160	39.2975	37.9279	34.1670

Table 3.15
Energies of Table 3.13 Conformers Minimized (ie no constraints on dihedral angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	23.755	23.720	24.304	24.256	32.074	27.839
ΔH_f	16.797	16.752	17.613	17.575	25.383	21.020
Total	28.8849	28.8497	29.4338	29.3865	37.2036	32.9690

Table 3.16
Energies of Table 3.14 Conformers Minimized (ie no constraints on dihedral angles)

	(i)	(ii)	(iii)	(iv)	(v)	(vi)
Steric	23.738	23.716	24.322	24.273	30.379	27.836
ΔH_f	16.759	16.769	17.641	17.598	23.701	21.028
Total	28.8681	28.8465	29.4520	29.4030	35.5090	32.9659

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The approach so far has considered only steric interactions, and additional effects such as solvents, counter-ions and electronic effects are neglected. However, the following conclusions can tentatively be made :

- if the linear mechanism is operating and if the double bonds of the reactant species are oriented *anti* to one another then complete *erythro* selectivity should be established

- since experimental results prove crotyl n-butyltin reacting with aldehydes catalysed by boron triflouride etherate to be totally *erythro* selective it is reasonable to assume the transition state of this reaction is linear and in the *anti* conformation

- experimental results show the reaction of cinnamyl triphenyltin with aldehydes catalysed by boron triflouride etherate to be totally *threo* selective. It is therefore concluded that the linear mechanism does not operates.

Orbital Calculations

I have investigated the competition experiments discussed earlier by examination of the molecular orbitals of the reacting species. The molecular orbitals of (E)-cinnamyl and (E)-crotyl anions and of (E)-cinnamyl and (E)-crotyl trimethyltins were calculated. Also calculated were the molecular orbitals of a number of substituted aryl aldehydes and the same aryl aldehydes complexed with boron triflouride *anti* to the phenyl ring (see Tables **3.17,3.18**). The orbitals were calculated using parametrized methods MNDO[77AJ4899, 77JA4907] and AM1[85JA3902] both of which are available from the AMPAC[22] package of computer software, and also by the *ab initio* method Gaussian 82[23] using the STO-3G basis set. The p_z components of the

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22   AMPAC is a general purpose semi-empirical molecular orbital package for the study
      of chemical reactions. The semi-empirical Hamiltonians MNDO, MINDO/3 and AM1
      are implemented and calculations of vibrational spectra, thermodynamic quantities,
      isotopic substitution effects and force constants for molecules, radicals, ions and
      polymers are combined in a fully integrated package.
23   Gaussian 82 is available from QCPE.

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π-orbitals are tabulated below and the MNDO results in particular are shown diagrammatically as an aid to the present discussion. Also tabulated is a list of the HOMO-LUMO energy differences between reacting species, as a guide to the more favoured interactions.

Frontier Molecular Orbital theory states that provided appropriate orbital overlap can occur then the nearer in energy the frontier orbitals of the two reacting species are the greater the energy gain and hence the more favourable the HOMO-LUMO interaction. Since orbitals with coefficients of similar magnitude overlap with greater efficiency than orbitals of dissimilar magnitude then a faster reaction will occur where the coefficients of the orbitals at the reacting centres are most alike provided that the energy differences between the orbitals are the same. The gain in stabilization energy as the orbitals interact is energy available to help offset normal steric, torsional and other related energy requirements associated with molecular change in going to the transition state. The HOMO-LUMO or frontier molecular orbital approach is therefore considered to be appropriate for understanding the viability of a reaction pathway, since it comments specifically on orbital transition state energy.

Since the MNDO parameters for tin are only provisional it was decided to consider the orbitals of the allylic anions preliminary to a goal of a full investigation. The orbital calculations on the allylic anions using the improved AM1 parametrization set and an *ab initio* method are presented for comparison purposes with the MNDO calculations. As a first step in this analysis the correlation between HOMO-LUMO interactions and the relative reactivity of crotyl and cinnamyl substrates with the variously substituted aryl aldehydes was investigated. For both allylic anions the energy differences between the HOMO of the allylic anion and the LUMO of each aldehyde is less than that between the LUMO of the allylic group and the

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HOMO of the aldehydes. This is consistent with the known nucleophilic character of reaction between an anion and an electrophilic centre.

The HOMO π-orbital coefficient for C4 of the crotyl anion (0.661) is closer in magnitude than C2 (0.722) to the LUMO π-orbital coefficient for C7 of benzaldehyde (0.319). Hence most favourable overlap would be obtained for a bond formed between the carbonyl carbon of benzaldehyde and the terminal allylic carbon of the crotyl anion. Thus the linear isomer rather than the branched isomer of the homoallylic alcohol should be produced. Parallel conclusions can be drawn between the crotyl anion and each other aldehydes shown and also between the cinnamyl anion and each aldehyde. This however contrasts with experimental observations for the tin mediated reactions where the linear isomer is not formed. In the presence of tin, crotyl and cinnamyl halides will react with aldehydes give the more substituted homoallylic alcohol (branched isomer).

The difference in π-orbital energies between the HOMO orbital of the allylic anions and the LUMO orbitals of the aldehydes (Table 3.18) indicates that the rates of reaction of the substituted aryl aldehydes with the allylic anions might be for each substituent CN>>Me>=H>=MeO. Competition experiments indicate that NCPhCHO does indeed react significantly faster than the other substituted aldehydes but that PhCHO reacts faster than MePhCHO and MeOPhCHO which react at comparable rates.

The course of reaction of allylic anion synthons with carbonyls is known to be dependent on the metal associated with the allylic synthon. For example when the associated metal is Cr the linear isomer is formed in addition to the more substituted product.

The calculations have been extended by considering the effect of BF$_3$ coordinated to the aldehydes. The boron triflouride was complexed *anti* to

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the aromatic ring.[86JA2405] The orbitals of crotyl and cinnamyl trimethyltin were also calculated. It was anticipated that tin would alter the coefficient of the crotyl HOMO C2 and C4 lobes and the cinnamyl HOMO C7 and C9 lobes.

These calculations are more consistent with the observed experimental results. The presence of tin lowers the HOMO π-orbital coefficients on C4 of the crotyl group and C9 of the cinnamyl group so that a bond is unlikely to form between these carbons and the aldehyde carbonyl carbons and is consistent with the absence of the linear isomer for these reactions. For crotyl trimethyltin C2 (0.560) and any BF₃-complexed aldehyde (C7 = 0.490, 0.566, 0.546, 0.566; RPhCHO.BF₃: R=NC, H, MeO, Me respectively) favourable overlap exists for formation of the branched alcohol since the appropriate orbitals have similar coefficients. Overlap with the BF₃-complexed aldehydes and C7 (0.268) of cinnamyl trimethyltin is not as favourable as for reaction with uncomplexed aldehydes (C7 = 0.246, 0.319, 0.302, 0.303; RPhCHO: R=NC, H, MeO, Me respectively). The difference in orbital energies of the complexed aldehydes$_{LUMO}$ and the cinnamyl trimethyltin$_{HOMO}$ is more than the difference between uncomplexed aldehydes$_{LUMO}$ and cinnamyl trimethyltin$_{HOMO}$ and therefore compensates for the poorer overlap. This can account for the fact that cinnamyl organotins react with aldehydes in the presence of BF₃ via the cyclic mechanism. The poor overlap integral for orbitals of the linear mechanism enables the cyclic mechanism to compete successfully so that *threo* homoallylic alcohols are produced.

The efficiency of the orbital overlap between cinnamyl trimethyltin and BF₃ complexed aldehydes predicts the relative rates of reaction to be in the order NC>MeO>=Me>=H while the energy differences between the HOMO and LUMO orbitals favour a different order; NC>Me>=H>MeO. It is notable that NCPhCHO is still clearly the most competitive substituted aryl aldehyde for

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reaction of cinnamyl trimethyltin in the presence of BF_3. The efficiency of the orbital overlap between crotyl trimethyltin and BF_3 complexed aldehydes predicts the relative rates of reaction to be in the order H>Me>=MeO>NC while the energy differences between HOMO and LUMO orbitals favour a different order; NC>Me>=H>=MeO. These two factors must interplay in such a way as to produce the relative reaction rates noted in the competition experiments; NC>H>Me=MeO.

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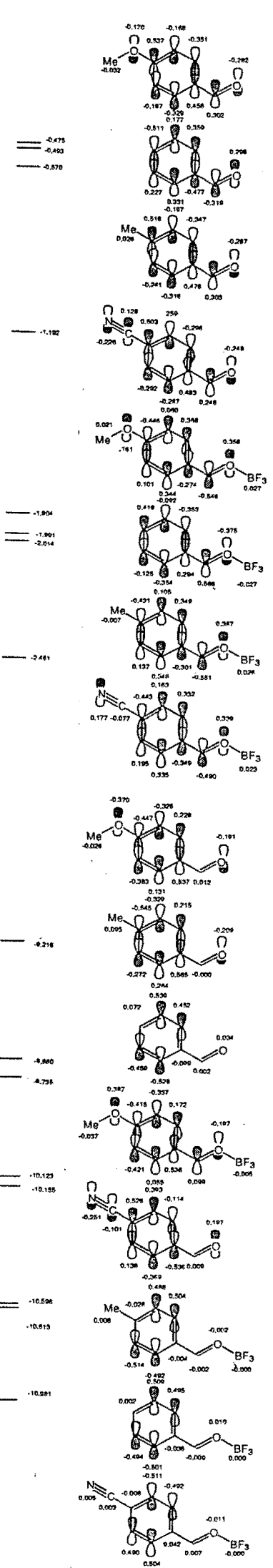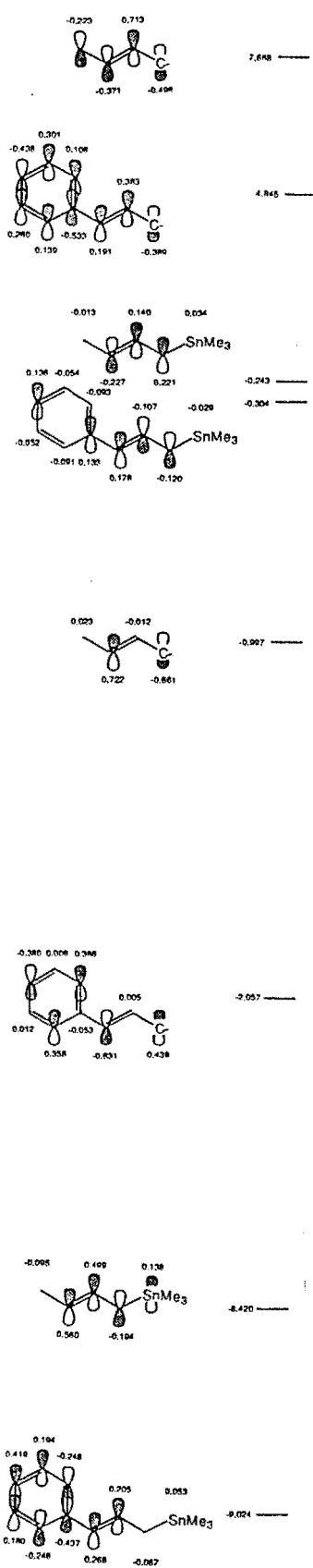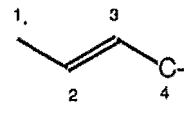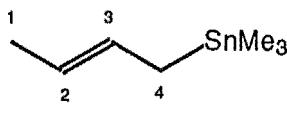
Figure 3.5
Diagrammatic representation of HOMO and LUMO π-Orbital coefficients

Table **3.17**
HOMO and LUMO π-Orbital eigenvalues and coefficients

	Crotyl anion			Crotyl trimethyltin	
	Ampac[24]		Gaussian 82[25,26]		Ampac
	AM1	MNDO	STO-3G	MNDO	
LUMO E	7.958	7.668	0.648	-0.243	
C1	0.215	-0.223	0.162	-0.013	
C2	0.383	-0.371	0.533	-0.227	
C3	-0.707	0.713	-0.857	0.140	
C4	0.486	-0.498	0.591	0.221	
Sn				0.034	
HOMO E	-0.893	-0.997	0.135	-9.420	
C1	-0.016	0.023	0.010	-0.095	
C2	0.711	0.722	-0.720	0.560	
C3	0.008	-0.012	-0.007	0.499	
C4	-0.665	-0.661	0.694	-0.194	
Sn				0.138	

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24   units of eigen values (E) are electron volts.
25   units of eigenvalues (E) are atomic units.
26   1 a.u. = 27.2107 eV.

Conformation...
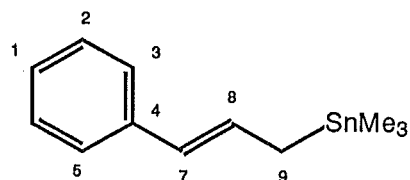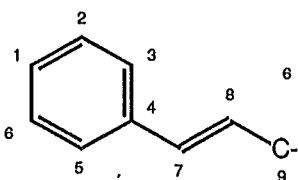
| | Cinnamyl anion | | | Cinnamyl trimethyltin |
| | Ampac | | Gaussian 82 | Ampac |
	AM1	MNDO	STO-3G	MNDO
LUMO E	5.004	4.845	0.463[27]	-0.304
C1	0.455	-0.438	-0.561	0.136
C2	-0.313	0.301	0.377	-0.054
C3	-0.107	0.108	0.145	-0.093
C4	0.528	-0.533	-0.587	0.133
C5	-0.145	0.139	0.224	-0.091
C6	-0.268	0.260	0.301	-0.052
C7	-0.179	0.191	0.168	0.178
C8	-0.371	0.383	0.393	-0.107
C9	0.377	-0.389	-0.417	-0.120
Sn				-0.029
HOMO E	-2.058	-2.057	0.091	-9.024
C1	-0.367	-0.380	0.366	0.419
C2	0.008	0.006	0.016	0.194
C3	0.353	0.366	0.328	-0.248
C4	-0.050	-0.053	-0.048	-0.437
C5	0.349	0.358	0.324	-0.246
C6	0.012	0.012	0.014	0.180
C7	-0.632	-0.631	-0.673	0.268
C8	0.004	0.005	0.001	0.205
C9	0.466	0.438	0.515	-0.067
Sn				0.053

---

[27] also calculated E=.451; C1, -0.038; C2, -0.545; C3; 0.587; C4, -0.035; C5, -0.561; C6, 0.587; C7, 0.004; C8, 0.031; C9, -0.035.

Conformation...
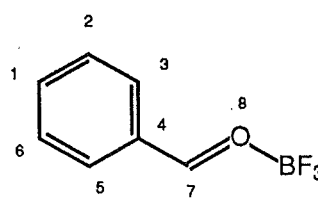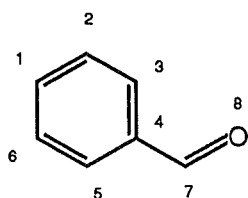
	PhCHO			PhCHO.BF$_3$	
	Ampac AM1	MNDO	Gaussian 82 STO-3G	Ampac MNDO	Gaussian 82 STO-3G
LUMO E	-0.434	-0.493	0.211	-1.991	-0.160
C1	0.489	-0.511	-0.498	0.419	0.435
C2	-0.162	0.177	0.197	-0.092	-0.139
C3	-0.357	0.359	0.342	-0.353	-0.342
C4	0.443	-0.477	-0.457	0.294	0.346
C5	-0.324	0.331	0.344	-0.354	-0.343
C6	-0.213	0.227	0.192	-0.125	-0.134
C7	0.379	-0.319	-0.433	0.566	0.567
O8	-0.340	0.298	0.510	-0.375	-0.540
B9				-0.027	-0.027
HOMO E	-10.003	-9.735	-0.293[28]	-10.613	-0.315
C1	-0.290	0.072	0.042	0.002	0.209
C2	-0.575	0.539	0.480	0.509	-0.306
C3	-0.273	0.452	0.440	0.495	-0.518
C4	0.323	-0.099	-0.035	-0.036	-0.226
C5	0.559	-0.528	-0.478	-0.501	0.318
C6	0.273	-0.459	-0.437	-0.494	0.526
C7	-0.001	-0.002	0.008	-0.009	0.017
O8	-0.140	0.034	0.021	0.010	0.124
B9				0.000	-0.001

---

[28] also calculated E = -0.285; C1, 0.498; C2, 0.207; C3, -0.297; C4, -0.509; C5, -0.230; C6, 0.281; C7, 0.114; O8, 0.297.

Conformation...
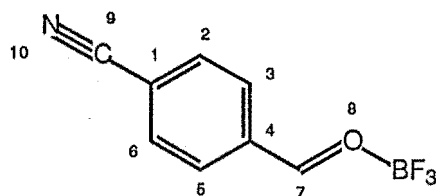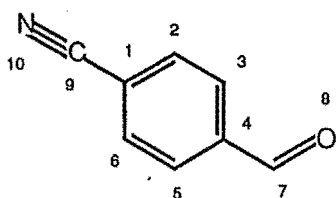
| | NCPhCHO | | | NCPhCHO.BF₃ | |
| | Ampac | | Gaussian 82 | Ampac | Gaussian 82 |
	AM1	MNDO	STO-3G	MNDO	STO-3G
LUMO E	-1.145	-1.192	0.171	-2.461	0.133
C1	0.484	0.503	-0.495	-0.443	-0.457
C2	-0.245	-0.259	0.279	0.163	0.222
C3	-0.298	-0.296	0.290	0.332	0.312
C4	0.456	0.483	-0.481	-0.349	-0.406
C5	-0.282	-0.287	0.289	0.335	0.311
C6	-0.278	-0.292	0.277	0.195	0.219
C7	0.296	0.246	-0.324	-0.490	0.461
O8	-0.286	-0.248	0.422	0.339	0.477
C9	0.144	0.128	-0.171	-0.077	-0.127
N10	-0.248	-0.226	0.303	0.177	0.258
B11				0.023	0.020
HOMO E	-10.342	-10.155	-0.301	-10.981	-0.336[29]
C1	0.531	0.526	-0.480	-0.008	-0.027
C2	0.332	0.393	-0.217	-0.511	-0.476
C3	-0.190	-0.114	0.259	-0.492	-0.450
C4	-0.536	-0.536	0.472	0.042	0.018
C5	-0.295	-0.369	0.232	0.504	0.467
C6	0.217	0.138	-0.251	0.490	0.445
C7	0.007	0.009	-0.109	0.007	-0.001
O8	0.232	0.197	-0.274	-0.011	-0.009
C9	-0.121	-0.101	0.162	0.003	0.012
N10	-0.287	-0.251	0.311	0.005	-0.020
B11				-0.000	0.000

[29] also calculated E=-0.326; C1, -0.475; C2, -0.229; C3, 0.236; C4, 0.476; C5, 0.194; C6, -0.278; C7, -0.043; O8, -0.258; C9, 0.188; N10, 0.330; B11, 0.001.

Conformation...
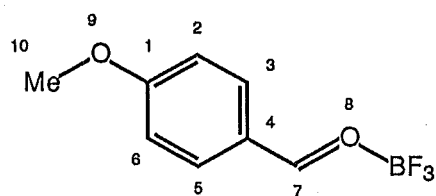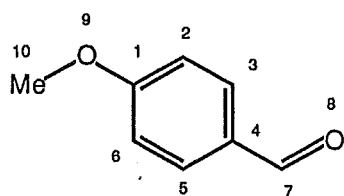
| | MeOPhCHO | | MeOPhCHO.BF$_3$ |
| | AMPAC | | AMPAC |
	AM1	MNDO	MNDO
LUMO E	-0.378	-0.475	-1.904
C1	0.505	0.537	-0.446
C2	-0.131	-0.168	0.060
C3	-0.371	-0.351	0.368
C4	0.424	0.456	-0.274
C5	-0.315	-0.329	0.344
C6	-0.189	-0.197	0.101
C7	0.370	0.302	-0.546
O8	-0.329	-0.282	0.358
O9	-0.161	-0.170	0.161
C10	-0.020	-0.032	0.021
B11			0.027
HOMO E	-9.374	-9.216	-10.123
C1	-0.433	-0.447	-0.415
C2	-0.326	-0.325	-0.337
C3	0.223	0.228	0.172
C4	0.525	0.537	0.536
C5	0.132	0.131	0.055
C6	-0.371	-0.383	-0.421
C7	0.017	0.012	0.099
O8	-0.216	-0.191	-0.197
O9	0.398	0.370	0.387
C10	-0.052	-0.026	-0.037
B11			-0.005

Conformation...
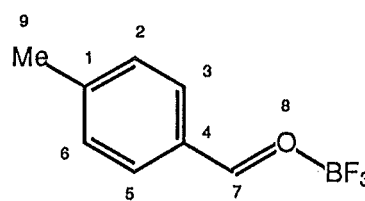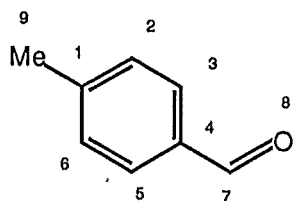
| | MePhCHO | | | MePhCHO.BF$_3$ | |
| | AMPAC | | Gaussian 82 | AMPAC | Gaussian 82 |
	AM1	MNDO	STO-3G	MNDO	STO-3G
LUMO E	-0.430	-0.570	-0.214	-2.014	0.162
C1	0.497	0.516	-0.500	-0.431	0.435
C2	-0.165	-0.197	0.190	0.105	-0.128
C3	-0.355	-0.347	0.342	0.349	-0.342
C4	0.438	0.476	-0.449	-0.301	0.334
C5	-0.312	-0.316	0.344	0.348	-0.344
C6	-0.219	-0.241	0.185	0.137	-0.123
C7	0.368	0.303	-0.433	-0.551	0.572
O8	-0.331	-0.287	0.508	0.367	-0.539
C9	0.007	0.026	-0.020	-0.007	0.008
B10				0.026	-0.027
HOMO E	-9.700	-9.660	-0.274	-10.596	-0.314[30]
C1	0.522	-0.545	-0.492	-0.028	0.032
C2	0.327	-0.329	-0.249	0.488	0.479
C3	-0.215	0.215	0.259	0.504	0.448
C4	-0.548	0.565	0.506	-0.004	-0.024
C5	-0.231	0.264	0.233	-0.492	-0.470
C6	0.296	-0.272	-0.283	-0.514	-0.440
C7	-0.006	-0.000	0.101	-0.002	-0.001
O8	0.232	-0.209	-0.287	-0.002	0.013
C9	-0.162	0.095	0.090	0.008	-0.007
B10				-0.000	-0.000

[30] also calculated E=-0.305; C1, 0.491; C2, 0.258; C3, -0.238; C4, -0.515; C5, -0.189; C6, 0.315; C7, 0.025; C8, 0.279; C9, -0.100; B10, -0.001.

Conformation...

Table 3.18

π-Orbital Eigenvalue Differences

R	NC-	H-	Me-	MeO
Cinnamyl anion$_{HOMO}$ - RPhCHO$_{LUMO}$	0.865	1.564	1.487	1.582
Cinnamyl anion$_{HOMO}$ - RPhCHO.BF$_3$ $_{LUMO}$	0.404	0.066	0.043	0.153
Cinnamyl anion$_{LUMO}$ - RPhCHO$_{HOMO}$	15.000	14.580	14.505	14.061
Cinnamyl anion$_{LUMO}$ - RPhCHO.BF$_3$ $_{HOMO}$	15.826	15.458	15.441	14.968
Cinnamyl SnMe$_3$ $_{HOMO}$ - RPhCHO$_{LUMO}$	7.832	8.531	8.454	8.549
Cinnamyl SnMe$_3$ $_{HOMO}$ - RPhCHO.BF$_3$ $_{LUMO}$	6.563	7.033	7.010	7.120
Cinnamyl SnMe$_3$ $_{LUMO}$ - RPhCHO$_{HOMO}$	9.851	9.431	9.356	8.912
Cinnamyl SnMe$_3$ $_{LUMO}$ - RPhCHO.BF$_3$ $_{HOMO}$	10.677	10.309	10.292	9.819
Crotyl anion$_{HOMO}$ - RPhCHO$_{LUMO}$	0.195	0.504	0.427	0.522
Crotyl anion$_{HOMO}$ - RPhCHO.BF$_3$ $_{LUMO}$	1.464	0.994	1.017	0.907
Crotyl anion$_{LUMO}$ - RPHCHO$_{HOMO}$	17.823	17.403	17.328	16.884
Crotyl anion$_{LUMO}$ - RPhCHO.BF$_3$ $_{HOMO}$	18.649	18.281	18.264	17.791
Crotyl SnMe$_3$ $_{HOMO}$ - RPhCHO$_{LUMO}$	8.228	8.927	8.850	8.945
Crotyl SnMe$_3$ $_{HOMO}$ - RPhCHO.BF$_3$ $_{LUMO}$	6.959	7.429	7.406	7.516
Crotyl SnMe$_3$ $_{LUMO}$ - RPhCHO$_{HOMO}$	9.912	9.492	9.417	8.973
Crotyl SnMe$_3$ $_{LUMO}$ - RPhCHO.BF$_3$ $_{HOMO}$	10.738	10.370	10.353	9.880

Conformation...

Crystallography

Structure solutions and refinements

Table **4.1** lists the crystal data and X-ray experimental details for the four structure determinations. Intensity data were collected with a Nicolet R3m four circle diffractometer by using monochromatized Mo Kα radiation (λ 0.71069 Å). Cell parameters were determined by least squares refinement, the setting angles of 25 accurately centered high angle reflections being used. Throughout data collections the intensities of three standard reflections were monitored at regular intervals and this indicated no significant crystal decomposition. The intensities were corrected for Lorentz and polarization effects but no corrections were deemed necessary for absorption. Reflections with intensities $I > 3\ \sigma(I)$ were used for structure solution and refinement.

All structures were solved by direct methods and refined by blocked-cascade least squares procedures. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included in calculated positions with isotropic thermal parameters equal to the isotropic equivalent of their carrier atoms. The function minimized was $\Sigma \underline{w}(\,|\,F_o\,|\,-\,|\,F_c\,|\,)^2$, with $\underline{w} = [s^2(F_o)+gF_o{}^2]^{-1}$.

All calculations (including diagrams) were performed on a Nova 4X computer using SHELXTL. (G M Sheldrick, SHELXTL User Manual, Nicolet XRD Corporation.) The scattering factors used were taken from reference J A Ibers and W C Hamilton, (Eds) 'International Tables for X-Ray Crystallography', Vol. 4 (Kynoch: Birmingham, 1974).

Discussion of the Structures

Figure **4.1** shows a perspective view and atom labelling of the structure of (1RS, 2RS)-1-(9-anthracenyl)-2-phenyl-3-buten-1-ol (**13b**) which confirms the structure as the threo product. Tables **4.2-4.4** list atomic coordinates, bond

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lengths and bond angles respectively. The anthracenyl ring is planar to within 0.02 Å. Figure 4.2 shows a projection of the unit cell contents viewed down the c-axis. The four molecules related by the four-fold axis are hydrogen bonded in a cyclic manner with an O-H···O distance of 2.733 Å.

An X-ray structure determination was attempted on 2,4-diphenyl-5-hexen-3-yl-3,5-dinitrobenzoate. Although the data was collected and the structure solved the paucity of observed data and poor crystal quality precluded a full refinement of the structure. However isotropic refinement of the non-hydrogen atoms was carried out and the structure unambiguously determined to be the Cram threo product (2RS, 3SR, 4SR)-2,4-diphenyl-5-hexen-3-yl-3,5-dinitrobenzoate.
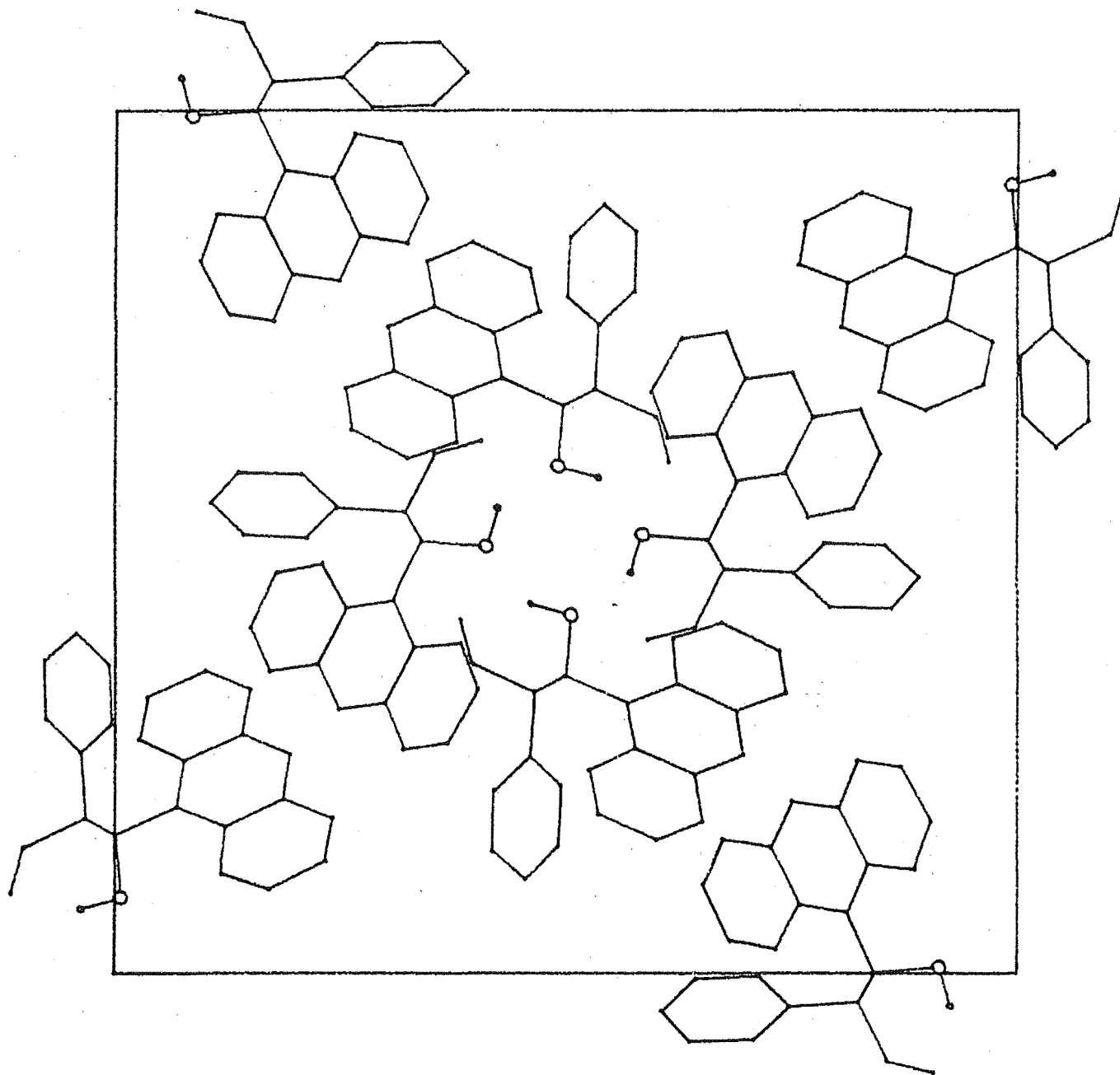
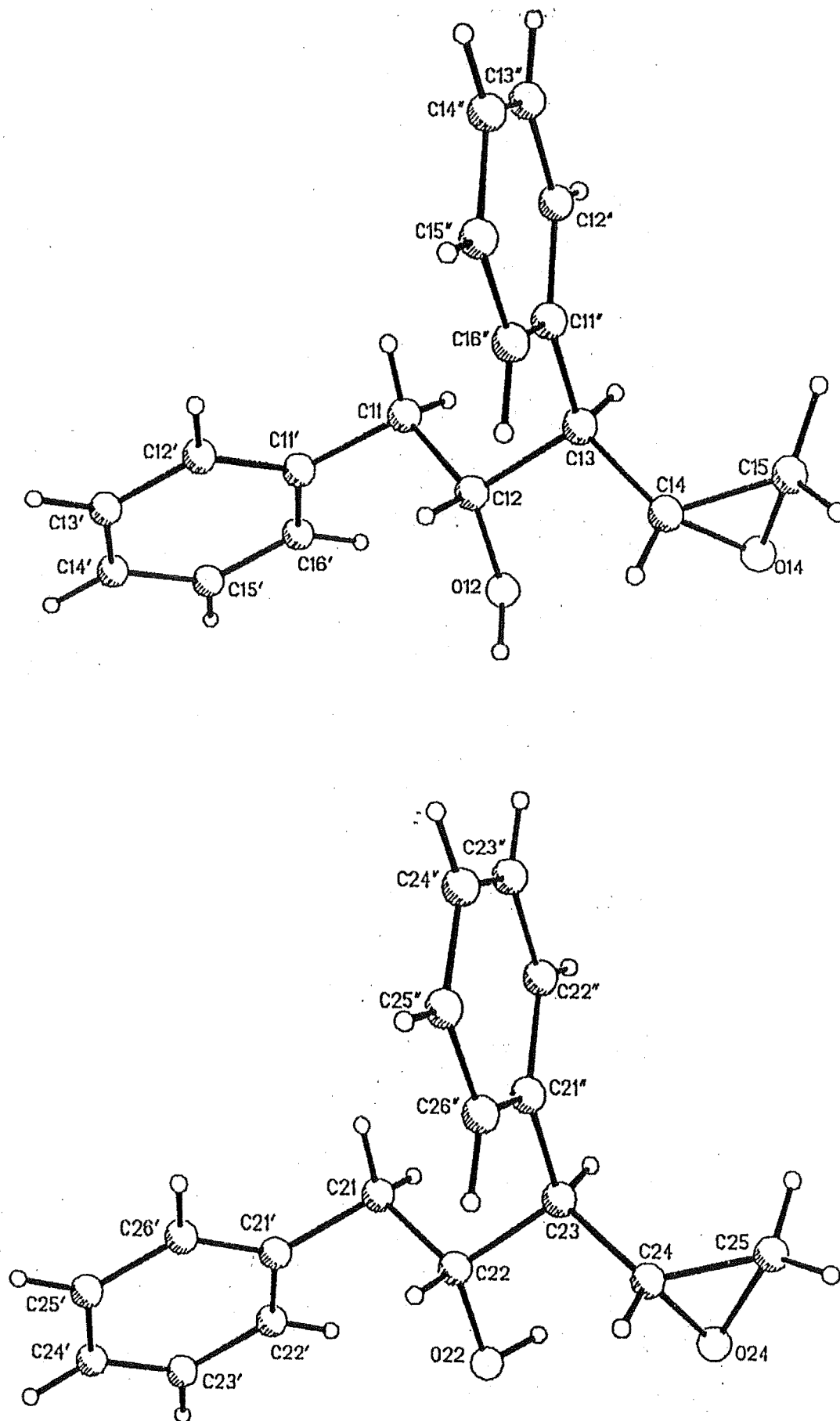Figure 4.3 shows perspective views and atom labelling of the two independent molecules of (2RS, 3RS, 4SR)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol (7a) in the asymmetric unit. The structure is thus confirmed as the threo product and the relative stereochemistry of the epoxide ring is determined. Tables 4.5-4.7 list atomic coordinates, bond lengths and bond angles respectively. The two independent molecules have similar bonding geometries and exist in similar conformations except for small torsional differences. For example the mean planes through the two phenyl rings of molecule one are mutually inclined at an angle of 66.3° while the corresponding value for molecule two is 59.4°. All four independent phenyl rings are planar to within 0.006 Å. As shown in figure 4.4 the crystal packing is determined by a network of hydrogen bonding wherein the hydroxyl groups form hydrogen bonded chains with two independent O-H···O distances of 2.877 Å and 2.845 Å.

Crystallography

Figure 4.1
Perspective view and atom labelling of (1RS, 2RS)-1-(9-anthracenyl)-
2-phenyl-3-buten-1-ol (13b)

Crystallography
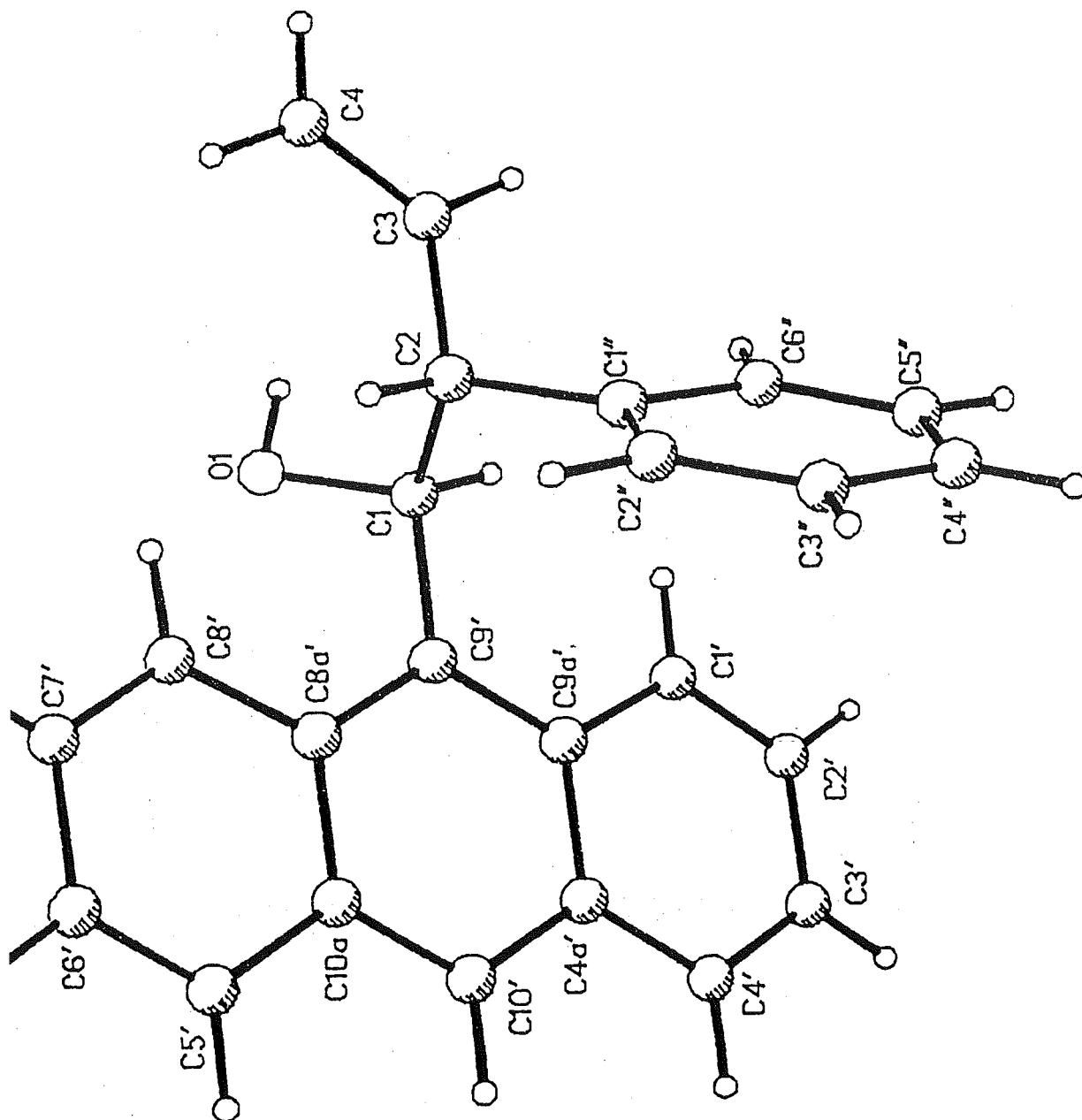
Figure 4.2
Projection of the unit cell contents for (1RS, 2RS)-1-(9-anthracenyl)-
2-phenyl-3-buten-1-ol (**13b**) viewed down the c-axis

Crystallography

Figure 4.3
Perspective view and atom labelling of the two independent molecules of
(2RS, 3RS, 4SR)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol (7a)

Figure 4.4
Packing diagram for (2RS, 3RS, 4SR)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol
(7a) showing hydrogen bonds as dotted lines

Crystallography
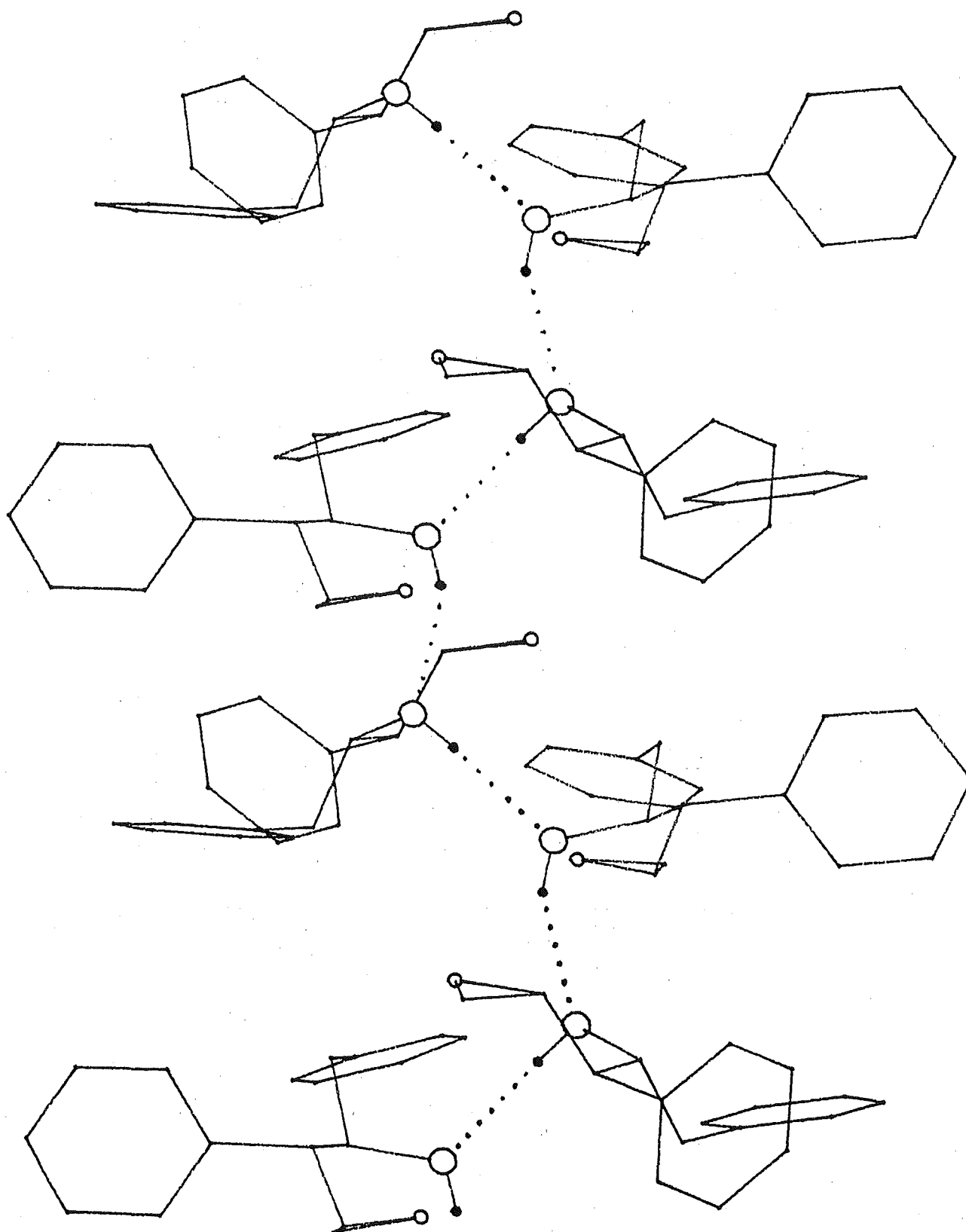
Figure **4.5** shows a perspective view and atom labelling of the structure of (3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl 3,5-dinitrobenzoate (**33b**, R=iPr) which again confirms the structure as the threo product. Tables **4.8-4.10** list atomic coordinates, bond lengths and bond angles respectively. Both phenyl rings are planar to within 0.008 Å and are inclined to one another at 5.9° and with the carbonyl group lying in the plane of the nitrophenyl ring. No short intermolecular contacts (< 3.1 Å) exist. However as shown in figure 4.6 (a projection down the *b*-axis) the molecules pack in layers with the nitrophenyl groups closely stacked down the *c*-axis and the unsubstituted phenyl rings slightly staggered.

Table 4.1.
Crystal Data and X-Ray Experimental Details

	(13b)	(33)	(7a)	(32)
Formula	$C_{24}H_{20}O$	$C_{25}H_{22}N_2O_6$	$C_{17}H_{18}O_2$	$C_{20}H_{21}NO_4$
Molecular Weight	342.4	446.5	254.3	339.4
Crystal System	tetragonal	triclinic	monoclinic	monoclinic
Space Group	$P4_22_12$	$P\bar{1}$	$P2_1/n$	$P2_1/c$
a (Å)	19.920(4)	10.172(4)	15.243(4)	19.521(6)
b (Å)	19.920(4)	10.494(4)	9.736(2)	6.014(2)
c (Å)	9.095(2)	12.378(5)	19.066(4)	15.454(5)
α (°)	90	83.6(3)	90	90
β (°)	90	70.29(3)	103.03(2)	96.78(3)
γ (°)	90	62.66(3)	90	90
V (Å^3)	3609(2)	1103(1)	2757(1)	1802(1)
Dc (g cm^{-3})	1.19	1.34	1.23	1.25
Z	8	2	8	4
F (000)	1376	468	1088	720
μ (cm^{-1})	0.8	1.1	0.7	0.8
Radiation	Mo Kα	Mo Kα	Mo Kα	Mo Kα
Wavelength (Å)	0.7107	0.7107	0.7107	0.7107
Temperature (°C)	20	-100	-120	-100
Scan mode	$\theta/2\theta$	ω	$\theta/2\theta$	ω
2θ range (°)	3 - 55	3 - 40	3 - 50	3 - 48
Unique reflections	2421	2046	4882	2758
Observed reflections (I>3σ(I))	1756	814	2339	1182
Number of parameters	226	133	367	226
g	0.00045	0.0038	0.0007	0.0007
R (%)	4.6	16.1	4.7	4.4
wR (%)	5.9	20.6	5.2	5.0

Crystallography

Figure 4.5
Perspective view and atom labelling of (3RS, 4RS)-2-methyl-
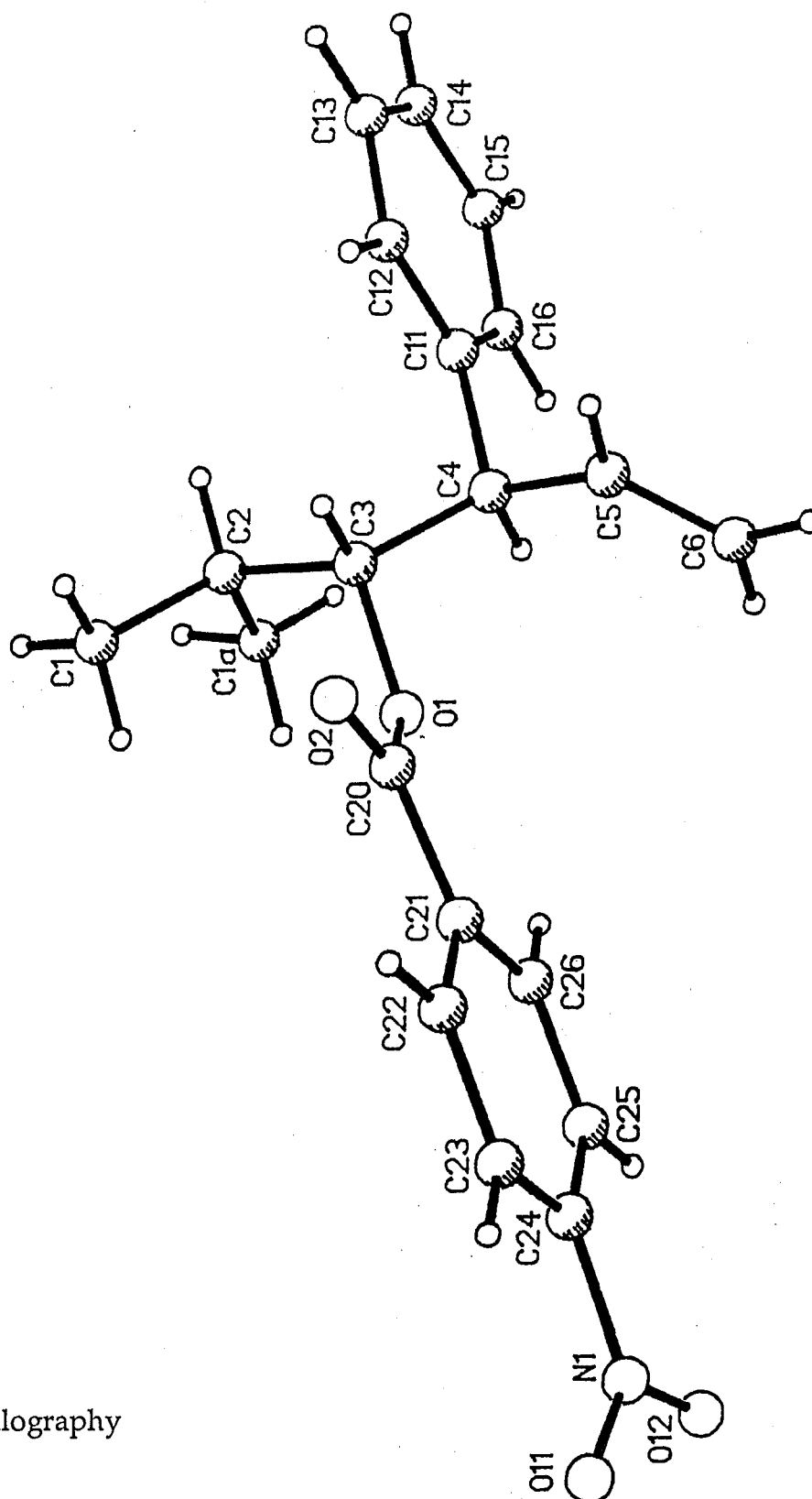4-phenyl-5-hexen-3-yl 3,5-dinitrobenzoate (33b, R=iPr)

Crystallography

Figure 4.6
Projection of the unit cell contents for (3RS, 4RS)-2-methyl-
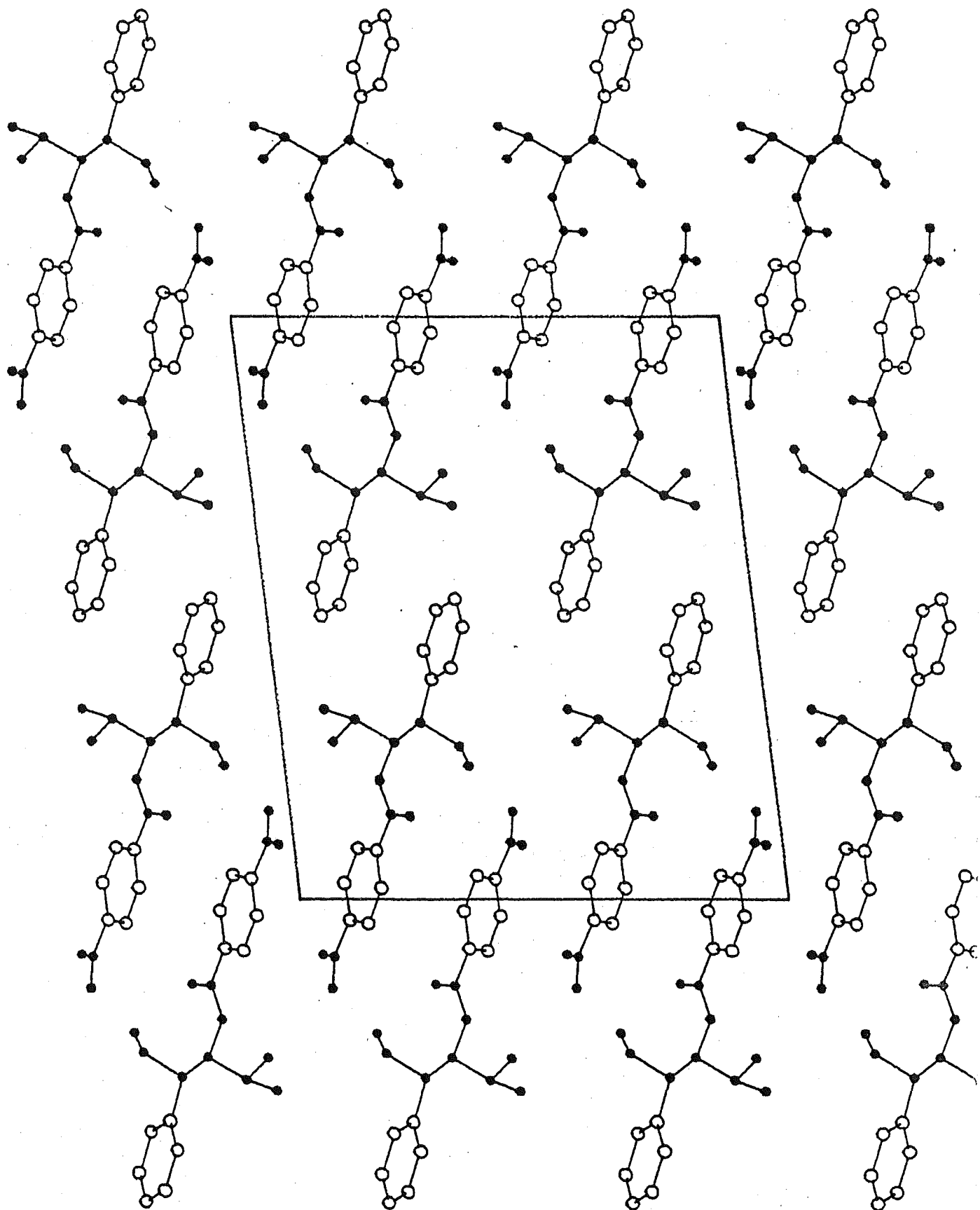4-phenyl-5-hexen-3-yl 3,5-dinitrobenzoate (33b, R=iPr) viewed
down the *b*-axis

Table 4.2.
Atom coordinates (x10^4) and temperature factors ($\mathring{A}^2$ x 10^3) for
(1RS, 2RS)-1-(9-anthracenyl)-2-phenyl-3-buten-1-ol

atom	x	y	z	U_{eq}^*
O(1)	867(1)	-69(1)	666(2)	45(1)
C(1)	1578(1)	-8(1)	807(3)	39(1)
C(2)	1768(1)	338(1)	2295(3)	39(1)
C(3)	1436(1)	1014(1)	2398(3)	47(1)
C(4)	914(2)	1155(2)	3217(4)	73(1)
C(1')	2677(2)	-271(2)	-1328(3)	48(1)
C(2')	3178(2)	-378(2)	-2313(3)	57(1)
C(3')	3481(2)	-1019(2)	-2438(4)	61(1)
C(4')	3261(2)	-1529(2)	-1575(4)	58(1)
C(4a')	2733(1)	-1438(1)	-543(3)	47(1)
C(5')	1778(2)	-2436(2)	2237(4)	57(1)
C(6')	1288(2)	-2360(2)	3256(4)	60(1)
C(7')	958(2)	-1733(2)	3395(3)	55(1)
C(8')	1138(1)	-1198(1)	2546(3)	48(1)
C(8a')	1674(1)	-1245(1)	1497(3)	41(1)
C(9')	1899(1)	-698(1)	637(3)	38(1)
C(9a')	2425(1)	-786(1)	-391(3)	42(1)
C(10')	2505(2)	-1965(1)	318(3)	51(1)
C(10a)	1989(1)	-1890(1)	1331(3)	46(1)
C(1")	2522(1)	386(1)	2467(3)	38(1)
C(2")	2854(1)	36(1)	3570(3)	44(1)
C(3")	3546(2)	67(2)	3715(3)	53(1)
C(4")	3919(2)	439(2)	2745(4)	60(1)
C(5")	3603(2)	792(2)	1639(4)	57(1)
C(6")	2912(2)	772(1)	1509(3)	48(1)

*   Equivalent isotropic U defined as one third of the trace of
the orthogonalises U_{ij} tensor

Table 4.3.
Bond lengths (Å) for
(1RS, 2RS)-1-(9-anthracenyl)-2-phenyl-3-buten-1-ol

O(1)-C(1)	1.428(3)	C(1)-C(2)	1.564(4)
C(1)-C(9')	1.524(4)	C(2)-C(3)	1.503(4)
C(2)-C(1")	1.514(4)	C(3)-C(4)	1.310(5)
C(1')-C(2')	1.358(4)	C(1')-C(9a')	1.425(4)
C(2')-C(3')	1.416(5)	C(3')-C(4')	1.356(5)
C(4')-C(4a')	1.421(4)	C(4a')-C(9a')	1.444(4)
C(4a')-C(10')	1.387(4)	C(5')-C(6')	1.354(5)
C(5')-C(10a)	1.429(4)	C(6')-C(7')	1.416(5)
C(7')-C(8')	1.364(4)	C(8')-C(8a')	1.434(4)
C(8a')-C(9')	1.413(4)	C(8a')-C(10a)	1.438(4)
C(9')-C(9a')	1.415(4)	C(10')-C(10a)	1.389(4)
C(1")-C(2")	1.390(4)	C(1")-C(6")	1.397(4)
C(2")-C(3")	1.386(4)	C(3")-C(4")	1.371(5)
C(4")-C(5")	1.380(5)	C(5")-C(6")	1.382(4)

Table 4.4.
Bond angles (°) for
(1RS, 2RS)-1-(9-anthracenyl)-2-phenyl-3-buten-1-ol

O(1)-C(1)-C(2)	110.8(2)	O(1)-C(1)-C(9')	109.2(2)
C(2)-C(1)-C(9')	112.6(2)	C(1)-C(2)-C(3)	110.0(2)
C(1)-C(2)-C(1")	110.9(2)	C(3)-C(2)-C(1")	111.9(2)
C(2)-C(3)-C(4)	125.2(3)	C(2')-C(1')-C(9a')	122.7(3)
C(1')-C(2')-C(3')	120.5(3)	C(2')-C(3')-C(4')	119.4(3)
C(3')-C(4')-C(4a')	121.7(3)	C(4')-C(4a')-C(9a')	119.6(3)
C(4')-C(4a')-C(10')	121.3(3)	C(9a')-C(4a')-C(10')	119.2(3)
C(6')-C(5')-C(10a)	121.4(3)	C(5')-C(6')-C(7')	119.7(3)
C(6')-C(7')-C(8')	121.1(3)	C(7')-C(8')-C(8a')	121.4(3)
C(8')-C(8a')-C(9')	123.6(2)	C(8')-C(8a')-C(10a)	116.9(2)
C(9')-C(8a')-C(10a)	119.5(2)	C(1)-C(9')-C(8a')	120.4(2)
C(1)-C(9')-C(9a')	119.2(2)	C(8a')-C(9')-C(9a')	120.4(2)
C(1')-C(9a')-C(4a')	116.1(2)	C(1')-C(9a')-C(9')	124.6(3)
C(4a')-C(9a')-C(9')	119.3(2)	C(4a')-C(10')-C(10a)	122.4(3)
C(5')-C(10a)-C(8a')	119.5(3)	C(5')-C(10a)-C(10')	121.2(3)
C(8a')-C(10a)-C(10')	119.3(2)	C(2)-C(1")-C(2")	121.0(2)
C(2)-C(1")-C(6")	121.5(2)	C(2")-C(1")-C(6")	117.5(3)
C(1")-C(2")-C(3")	121.3(3)	C(2")-C(3")-C(4")	120.1(3)
C(3")-C(4")-C(5")	119.8(3)	C(4")-C(5")-C(6")	120.2(3)
C(1")-C(6")-C(5")	121.0(3)		

Crystallography

Table 4.5.
Atomic coordinates (x10^4) and isotropic thermal parameters
(Å^{2}x10^3) for (2RS, 3RS, 4RS)-4,5-epoxy-1,3-diphenyl-
4-penten-2-ol

atom	x	y	z	U$_{eq}$*
O(12)	7736(1)	5555(2)	2123(1)	26(1)
O(14)	6049(1)	4960(3)	813(1)	37(1)
C(11)	8754(2)	7169(3)	1793(2)	29(1)
C(12)	8226(2)	5845(3)	1582(2)	23(1)
C(13)	7581(2)	5961(3)	837(2)	22(1)
C(14)	6942(2)	4755(3)	693(2)	26(1)
C(15)	6170(2)	4793(4)	92(2)	33(1)
C(11')	9471(2)	7044(3)	2482(2)	26(1)
C(12')	10337(2)	6616(4)	2471(2)	31(1)
C(13')	10981(2)	6447(4)	3101(2)	36(1)
C(14')	10778(2)	6703(4)	3755(2)	33(1)
C(15')	9927(2)	7148(3)	3779(2)	31(1)
C(16')	9277(2)	7313(3)	3149(2)	27(1)
C(11")	8098(2)	6067(3)	248(2)	24(1)
C(12")	8151(2)	7300(4)	-108(2)	29(1)
C(13")	8612(2)	7370(4)	-653(2)	39(1)
C(14")	9033(2)	6226(4)	-849(2)	43(1)
C(15")	8988(2)	4996(4)	-501(2)	39(1)
C(16")	8522(2)	4912(4)	43(2)	32(1)
O(22)	6968(2)	7669(2)	2854(1)	27(1)
O(24)	6377(2)	8623(2)	1382(1)	36(1)
C(21)	6107(2)	5808(3)	3226(2)	31(1)
C(22)	6071(2)	7182(3)	2836(2)	25(1)
C(23)	5520(2)	7105(3)	2057(2)	23(1)
C(24)	5582(2)	8424(4)	1663(2)	30(1)
C(25)	5520(2)	8442(4)	887(2)	36(1)
C(21')	6521(2)	5905(3)	4021(2)	27(1)
C(22')	7442(2)	5878(4)	4275(2)	41(1)
C(23')	7806(3)	6013(5)	5001(3)	69(2)
C(24')	7295(4)	6161(5)	5483(3)	87(2)
C(25')	6379(4)	6163(4)	5243(2)	74(2)
C(26')	5992(3)	6046(4)	4512(2)	48(2)
C(21")	4548(2)	6754(3)	2026(2)	24(1)
C(22")	4188(2)	5510(3)	1745(2)	29(1)
C(23")	3302(2)	5171(4)	1720(2)	37(1)
C(24")	2759(2)	6070(4)	1992(2)	37(1)
C(25")	3103(2)	7301(4)	2281(2)	34(1)
C(26")	3988(2)	7647(4)	2292(2)	29(1)

*   Equivalent isotropic U defined as one third of the trace of
the orthoganalised U$_{ij}$ tensor

Crystallography

Table **4.6.**
Bond lengths (Å) for
(2RS, 3RS, 4RS)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol

molecule:	1	2		1	2
O(12)-C(12)	1.432(4)	1.441(4)	O(14)-C(14)	1.443(4)	1.443(4)
O(14)-C(15)	1.437(4)	1.439(4)	C(11)-C(12)	1.524(4)	1.525(5)
C(11)-C(11')	1.513(4)	1.508(4)	C(12)-C(13)	1.538(4)	1.535(4)
C(13)-C(14)	1.511(4)	1.502(5)	C(13)-C(11")	1.514(5)	1.509(4)
C(14)-C(15)	1.447(4)	1.460(5)	C(11')-C(12')	1.390(5)	1.377(5)
C(11')-C(16')	1.393(5)	1.372(6)	C(12')-C(13')	1.378(4)	1.377(6)
C(13')-C(14')	1.374(5)	1.340(8)	C(14')-C(15')	1.379(5)	1.368(8)
C(15')-C(16')	1.383(4)	1.391(5)	C(11")-C(12")	1.390(5)	1.386(4)
C(11")-C(16")	1.397(5)	1.391(5)	C(12")-C(13")	1.381(5)	1.381(5)
C(13")-C(14")	1.378(6)	1.384(5)	C(14")-C(15")	1.379(6)	1.373(5)
C(15")-C(16")	1.384(5)	1.386(5)			

Table **4.7.**
Bond angles (°) for
(2RS, 3RS, 4RS)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol

	molecule 1	molecule 2
C(14)-O(14)-C(15)	60.3(2)	60.8(2)
C(12)-C(11)-C(11')	113.3(3)	113.3(3)
O(12)-C(12)-C(11)	107.9(2)	110.3(2)
O(12)-C(12)-C(13)	110.5(2)	110.3(3)
C(11)-C(12)-C(13)	111.8(3)	112.4(3)
C(12)-C(13)-C(14)	111.2(3)	111.1(3)
C(12)-C(13)-C(11")	111.0(2)	111.5(3)
C(14)-C(13)-C(11")	110.0(3)	110.3(2)
O(14)-C(14)-C(13)	117.2(3)	116.9(3)
O(14)-C(14)-C(15)	59.6(2)	59.4(2)
C(13)-C(14)-C(15)	120.0(3)	121.3(3)
O(14)-C(15)-C(14)	60.0(2)	59.7(2)
C(11)-C(11')-C(12')	120.9(3)	120.9(3)
C(11)-C(11')-C(16')	121.2(3)	120.9(3)
C(12')-C(11')-C(16')	117.9(3)	118.1(3)
C(11')-C(12')-C(13')	120.9(3)	119.9(4)
C(12')-C(13')-C(14')	120.6(3)	122.3(4)
C(13')-C(14')-C(15')	119.5(3)	118.6(4)
C(14')-C(15')-C(16')	120.2(3)	120.3(5)
C(11')-C(16')-C(15')	120.9(3)	120.7(4)
C(13)-C(11")-C(12")	121.2(3)	120.8(3)
C(13)-C(11")-C(16")	120.3(3)	121.5(3)
C(12")-C(11")-C(16")	118.5(3)	117.8(3)
C(11")-C(12")-C(13")	120.4(3)	121.3(3)
C(12")-C(13")-C(14")	120.7(4)	120.0(3)
C(13")-C(14")-C(15")	119.7(4)	119.7(3)
C(14")-C(15")-C(16")	120.1(4)	120.0(3)
C(11")-C(16")-C(15")	120.7(3)	121.1(3)

Crystallography

Table **4.8**.
Atomic coordinates ($\times 10^4$) and isotropic thermal parameters
($\text{Å}^2 \times 10^3$) for (3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl-
4-nitrobenzoate

atom	x	y	z	U_{eq}*
C(1)	2706(2)	9888(8)	1050(3)	51(2)
C(1a)	3262(2)	6163(8)	937(3)	51(2)
C(2)	3086(2)	8005(7)	1546(3)	40(2)
C(3)	2694(2)	7182(7)	2288(3)	35(1)
C(4)	3035(2)	5329(7)	2871(3)	35(1)
C(5)	2625(2)	4938(8)	3616(3)	38(2)
C(6)	2283(2)	3137(8)	3757(3)	53(2)
C(11)	3781(2)	5820(8)	3210(3)	39(2)
C(12)	3977(2)	7782(8)	3634(3)	50(2)
C(13)	4663(3)	8119(11)	3974(3)	73(2)
C(14)	5145(3)	6516(11)	3887(3)	85(3)
C(15)	4953(2)	4554(10)	3475(4)	81(2)
C(16)	4274(2)	4230(9)	3127(3)	57(2)
O(1)	2038(1)	6240(5)	1896(2)	35(1)
O(2)	1430(1)	9001(5)	2429(2)	57(1)
C(20)	1457(2)	7273(7)	2048(3)	37(2)
C(21)	833(2)	6002(7)	1668(2)	30(1)
C(22)	190(2)	7005(7)	1686(2)	32(1)
C(23)	-403(2)	5962(7)	1330(2)	33(2)
C(24)	-346(2)	3920(7)	964(2)	31(1)
C(25)	279(2)	2843(7)	939(2)	33(1)
C(26)	873(2)	3928(7)	1296(2)	35(1)
N(1)	-976(2)	2789(6)	556(2)	40(1)
O(11)	-1511(1)	3856(5)	448(2)	51(1)
O(12)	-935(1)	844(5)	333(2)	58(1)

*   Equivalent isotropic U defined as one third of the trace of the
orthogonalised U_{ij} tensor

Table 4.9.
Bond lengths (Å) for
(3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl-4-nitrobenzoate

C(1)-C(2)	1.512(6)	C(1a)-C(2)	1.518(6)
C(2)-C(3)	1.536(6)	C(3)-C(4)	1.535(6)
C(3)-O(1)	1.463(4)	C(4)-C(5)	1.496(6)
C(4)-C(11)	1.518(5)	C(5)-C(6)	1.304(7)
C(11)-C(12)	1.382(6)	C(11)-C(16)	1.374(6)
C(12)-C(13)	1.393(6)	C(13)-C(14)	1.366(8)
C(14)-C(15)	1.372(8)	C(15)-C(16)	1.384(6)
O(1)-C(20)	1.339(5)	O(2)-C(20)	1.198(5)
C(20)-C(21)	1.499(5)	C(21)-C(22)	1.395(5)
C(21)-C(26)	1.380(6)	C(22)-C(23)	1.374(5)
C(23)-C(24)	1.362(6)	C(24)-C(25)	1.385(5)
C(24)-N(1)	1.480(5)	C(25)-C(26)	1.387(5)
N(1)-O(11)	1.219(4)	N(1)-O(12)	1.225(4)

Table 4.10.
Bond angles (°) for
(3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl-4-nitrobenzoate

C(1)-C(2)-C(1a)	111.5(3)	C(1)-C(2)-C(3)	111.2(3)
C(1a)-C(2)-C(3)	113.4(4)	C(2)-C(3)-C(4)	116.9(3)
C(2)-C(3)-O(1)	107.7(3)	C(4)-C(3)-O(1)	105.0(3)
C(3)-C(4)-C(5)	109.4(3)	C(3)-C(4)-C(11)	113.2(3)
C(5)-C(4)-C(11)	110.1(3)	C(4)-C(5)-C(6)	126.1(4)
C(4)-C(11)-C(12)	122.1(4)	C(4)-C(11)-C(16)	119.2(4)
C(12)-C(11)-C(16)	118.7(4)	C(11)-C(12)-C(13)	120.2(4)
C(12)-C(13)-C(14)	120.2(5)	C(13)-C(14)-C(15)	119.9(5)
C(14)-C(15)-C(16)	119.9(5)	C(11)-C(16)-C(15)	121.0(5)
C(3)-O(1)-C(20)	117.7(3)	O(1)-C(20)-O(2)	125.1(3)
O(1)-C(20)-C(21)	111.2(3)	O(2)-C(20)-C(21)	123.7(3)
C(20)-C(21)-C(22)	117.6(3)	C(20)-C(21)-C(26)	122.8(3)
C(22)-C(21)-C(26)	119.7(3)	C(21)-C(22)-C(23)	120.8(4)
C(22)-C(23)-C(24)	118.1(3)	C(23)-C(24)-C(25)	123.3(3)
C(23)-C(24)-N(1)	119.1(3)	C(25)-C(24)-N(1)	117.6(4)
C(24)-C(25)-C(26)	117.8(4)	C(21)-C(26)-C(25)	120.3(3)
C(24)-N(1)-O(11)	118.1(3)	C(24)-N(1)-O(12)	118.7(3)
O(11)-N(1)-O(12)	123.2(3)		

Crystallography

Conclusions

We have examined in some detail the reactions of cinnamyl chloride with various aldehydes catalysed by Sn-Al and for comparison purposes we have studied selected metal allylic systems in an attempt to understand the regiochemistry and stereoselection observed in these important reactions. We have found that cinnamyl chloride reacts with aldehydes and Sn-Al to give complete *threo* selectivity; crotyl bromide and aldehydes under the same conditions gives only moderate *erythro* selectivity. In contrast cinnamyl organotins react with aldehydes catalysed with $BF_3.OEt_2$ to give the same *threo* selectivity but crotyl organotins show complete *erythro* selectivity.

The linear and the cyclic mechanisms for product formation in these reactions have been discussed and we have concluded that the reactions occur by competition of these mechanisms. For tin catalysed allylation of aldehydes (Sn-Al, or allylic organotins either BF_3 catalysed of catalysed by heat) the linear mechanism has been shown from our computational studies to favour the formation of the *erythro* isomer for both (E)- and (Z)-allylic systems whereas the cyclic mechanism favours the *threo* homoallylic alcohol for (E)-allylic isomers and the *erythro* alcohol for (Z)-allylic isomers. Where the diastereoselectivity of a reaction is not complete both the linear and the cyclic mechanism may operate to produce both isomers. Alternatively (E)-(Z) isomerization of the allylic metal can lower the diastereoselectivity of the cyclic mechanism.

Increasing the positive polarity at the tin centre by changing the nature of the allylic and other ligands should increase the propensity of the cyclic transition state to form since carbonyl coordination to tin is thereby increased and this should be and is reflected by an increase in the *threo*

Conclusions

product alcohol formed, consistent with the linear and cyclic mechanisms being in competition.

Molecular modelling calculations (MM2 and MMX) show the energy difference of product-like models of the *threo* and *erythro* producing linear transition states in an *anti* conformation to be in the order of 3 kcal.mol^{-1}. This steric interaction is sufficient to account for the observed *erythro* diastereoselectivity.

Conformational calculations have confirmed the linear mechanism must occur with *anti* addition of the allylic and carbonyl reactants if this mechanism is to explain *erythro* selectivity of both (Z)- and (E)-crotyl tins to aldehydes.

Molecular Orbital calculations indicate that complexing of aldehydes with BF$_3$ will reduce the reactivity of cinnamyl trimethyltin with the aldehydes by the linear transition state and the cyclic mechanism is therefore more able to compete with the linear mechanism. This accounts for the change in selectivity from *erythro* selectivity for the crotyl organotins to *threo* selectivity for (E)-cinnamyl organotins.

The epoxidation and oxidation reactions of the so prepared homoallylic alcohols were examined and preparative routes to several β,γ-epoxy ketones established.

Conclusions

Experimental

General

Infrared spectra were recorded on a Shimadzu IR27G or Pye Unicam SP3-300 spectrophotometer. Mass spectra were recorded on an A.E.I. MS902 or Kratos MS80RFA spectrometer. Radial chromatography was performed on a Chromatotron (Harrison and Harrison) using Merck type 60 P.F. 254 silica gel. [1]H n.m.r. spectra were recorded on a Varian T60 or XL-300 spectrometer, and [13]C n.m.r. were recorded on a Varian CFT20 or XL-300 spectrometer, for $CDCl_3$ solutions with $(CH_3)_4Si$ as an internal standard. Melting points were determined using an Electrothermal melting point apparatus and are uncorrected.

PREPARATION OF HOMOALLYLIC ALCOHOLS BY REDUCTION OF HOMOALLYLIC KETONES.

Reduction of 1,2-diphenyl-3-buten-1-one

(i) *with lithium aluminium hydride*

1,2-Diphenyl-3-buten-1-one[31] **(9)** (111 mg, 0.05 mmol) was dissolved in dry ether (5 ml) and added dropwise to a stirred suspension of lithium aluminium hydride (111 mg) in dry ether (2 ml) and the resulting mixture refluxed for 5 hours under nitrogen. Excess lithium aluminium hydride was destroyed with sodium sulphate decahydrate and the mixture diluted

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31   *Preparation of 1,2-Diphenyl-3-buten-1-one*
A mixture of (1RS, 2RS)- and (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol **(8b, 8a)** (2 g) in dichloromethane (4 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (7.84 g), anhydrous sodium acetate (0.41 g) and dichloromethane (50 ml). After six hours ether (50 ml) was added with stirring and the mixture decanted from the tarry residue and washed with ether (3 * 50 ml). The combined organic solutions were filtered through Florosil, dried with magnesium sulphate and after removal of solvent gave a pale yellow solid which was recrystallised from pentane to give 1,2-diphenyl-3-buten-1-one[84AJ0065, 71JO0036] **(9)** (1.2 g), m.p. 70°C. [1]H n.m.r. (CCl_4) δ_H 4.93, $J_{3,4\,cis}$ 11 Hz, $J_{4,4}$ 2 Hz, (H4)$_{anti}$; 5.10, $W_{h/2}$ 10 Hz, (H4)$_{syn}$, H2; 6.32, $J_{3,4\,trans}$ 15 Hz, $J_{3,4\,cis}$ 11 Hz, $J_{2,3}$ 7 Hz, H3; 7.22, $W_{h/2}$ 3 Hz, o, m, p; 7.37, $W_{h/2}$ 4 Hz, m', p'; 7.90, $W_{h/2}$ 12 Hz, o'.

Experimental

with 1% sulphuric acid, extracted with ether, washed with water, and dried with sodium sulphate. The solvent was removed by distillation to give a mixture, 9:2 (ratio determined by integration of peaks at δ_H 7.16 and 7.06 of ^{1}H n.m.r. spectrum) of (1RS, 2RS)- and (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol[84AJ0065] (8a, 8b). ^{1}H n.m.r. (CCl$_4$) δ_H 3.17 - 3.67, H2; 4.6 - 5.1, H1, (H4)$_2$; 5.6 - 6.3, H3; 7.07, (8b)-ArH; 7.16, (8a)-ArH.

(ii) with cerium chloride hexahydrate-sodium borohydride[81JA5454]

1,2-Diphenyl-3-buten-1-one (9) (1 mmol, 221 mg) and cerium chloride hexahydrate (1 mmol, 355 mg) was dissolved in methanol (2.5 ml). Sodium borohydride (1 mmol, 38 mg) was added in one portion with stirring. Vigorous gas evolution occurred and the temperature rose. Stirring was continued for a few minutes and the pH adjusted to neutrality by controlled addition of dilute aqueous hydrochloric acid. The mixture was extracted with ether, dried with sodium sulphate and after removal of solvent gave a mixture, 2:1 (ratio determined by integration of peaks at δ_H 7.17 and 7.1 of the ^{1}H n.m.r. spectrum) of (1RS, 2RS)- and (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol[84AJ0065] (8a, 8b) (0.21 g). ^{1}H n.m.r. (CCl$_4$) δ_H 1.67, W$_h$/2 8 Hz, OH; 3.17 - 3.63, H2; 4.63 - 5.3, H1, (H4)$_2$; 5.6 - 6.2, H3; 7.1, W$_h$/2 3 Hz, (8b)-ArH; 7.17, W$_h$/2 2 Hz, (8a)-ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 58.4, 59.0, C2; 77.1, 77.4, C1; 117.1, 118.2, C4; 137.7, 137.8, C3; 127.0, 127.1, 128.0, 128.6, 128.8, 140.3, 141.9, phenyl carbons.

CHROMIC CHLORIDE AND LITHIUM ALUMINIUM HYDRIDE MEDIATED ADDITION OF ALLYLIC HALIDES TO ALDEHYDES.

2-Methyl-1-phenyl-3-buten-1-ols

Lithium aluminium hydride (418 mg, 11 mmol) was added portionwise to anhydrous chromic chloride[57IO0153] (3.49 g, 22 mmol) and stirred in

Experimental

anhydrous tetrahydrofuran (30 ml) at 0°C in a nitrogen atmosphere[32]. After

5 minutes at 0°C and 20 minutes at room temperature a tan suspension was

obtained. The suspension was cooled to 0°C and benzaldehyde (834 mg,

7.9 mmol) in anhydrous tetrahydrofuran (5 ml) added. (E)-1-Bromo-

2-butene (1.49 g, 11 mmol) in anhydrous tetrahydrofuran (30 ml) was added

dropwise over 15 minutes. Aliquots of the reaction mixture were taken at

intervals and the course of the reaction monitored by ^{1}H n.m.r. After 3

hours the reaction was poured into water and ether and the organic layer

washed with water, dried with sodium sulphate and after removal of

solvent gave (1RS, 2RS)-2-methyl-1-phenyl-3-buten-1-ol[77AJ0835, 80JM0137,

82OM0149] (1b) and 1-phenyl-3-penten-1-ol[74CA0496] (1c) as an oil (0.84 g). (1b)

^{1}H n.m.r. (CCl$_4$) δ_H 0.86, J$_{2,5}$ 7 Hz, Me; 2.47, J$_{2,5}$ 7 Hz, J$_{2,3}$ 7 Hz, H2; 4.34, J$_{1,2}$ 7.8

Hz, H1; 5.14 - 5.21, (H4)$_2$; 5.8, J$_{2,3}$ 8.1 Hz, J$_{3,4a}$ 10.3 Hz, J$_{3,4b}$ 17.1 Hz, H3; 7.2 - 7.4,

ArH; ^{13}C n.m.r. (CDCl$_3$) δ_C 16.5, C2-Me; 46.1, C2; 77.8, C1; 116.5, C4; 140.4, C3.

(1c) ^{1}H n.m.r. (CCl$_4$) δ_H 1.67, J$_{3,5}$ 1.2 Hz, J$_{4,5}$ 5 Hz, (H5)$_3$; 2.41, (H2)$_2$; 4.63 - 4.67,

H1; 5.35 - 5.47, 5.52 - 5.65, H3, H4; 7.2 - 7.4, ArH; ^{13}C n.m.r. (CDCl$_3$) δ_C 18.0, C5;

42.7, C2; 73.4, C1; 142.6, 144.2, C3, C4; (1b, 1c) ^{13}C n.m.r. (CDCl$_3$) δ_C (phenyl

carbons) 125.8, 126.8, 127.3, 127.5, 128.1, 128.3, 129.1. (1RS, 2SR)-2-methyl-

2-phenyl-3-buten-1-ol (1a) was not seen in the ^{1}H n.m.r. or ^{13}C n.m.r. spectra.

1,2-Diphenyl-3-buten-1-ols

Lithium aluminium hydride (445 mg, 12 mmol), anhydrous chromic

chloride (3.26 g, 21 mmol), anhydrous tetrahydrofuran (30 ml) and

benzaldehyde (863 mg, 8.1 mmol) in anhydrous tetrahydrofuran (5 ml) was

reacted with (E)-3-chloro-1-phenylpropene (1.61 g, 11 mmol) in anhydrous

tetrahydrofuran (30 ml). Aliquots of the reaction mixture were taken at

intervals and the course of the reaction monitored by ^{1}H n.m.r. After 23

hours the reaction was poured into water and ether and the organic layer

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[32]   Note: It is important that this reaction is carried out in absolutely dry conditions.

Experimental

washed with water, dried with sodium sulphate and after removal of solvent gave an oil (0.72 g); shown by g.l.c. to be a mixture (83:17) of (1RS, 2SR)- and (1RS, 2RS)-1,2-diphenyl-3-buten-1-ols[84AJ0065] **(8b, 8a)**.

^{1}H n.m.r. (CCl$_4$) δ_H **(8b)** 2.3, W$_h$/2 8 Hz, OH; 3.43, J$_{1,2}$ 7 Hz, J$_{2,3}$ 7 Hz, H2; 4.6 - 5.1, H1, (H4)$_2$; 7.1, W$_h$/2 4 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C **(8a, 8b)** 57.9, 59.0, C2; 77.2, C1; 117.1, 118.2, C4; 137.9, C3; 126.6, 127.3, 127.8, 128.4, 128.5, 140.7, phenyl carbons.

TIN AND ALUMINIUM MEDIATED ADDITION OF ALLYLIC HALIDES TO ALDEHYDES.

A number of homoallylic alcohols were prepared using a mixture of tin and aluminium metal to direct carbon - carbon bond formation in a stereospecific manner.[83OS0191] The preparation of the 2-methyl-1-phenyl-3-buten-1-ols is representative of the procedure.

2-Methyl-1-phenyl-3-buten-1-ols

A mixture of (E)-1-bromo-2-butene (2.82 g, 20 mmol) and benzaldehyde (2.32 g, 22 mmol) was dissolved in ether (5 ml) and water (3 ml). Tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were added. The mixture was stirred for 24 hours at room temperature, filtered, the solid washed with ether (2 * 100 ml), and the filtrate washed with water (2 * 50 ml), dried with sodium sulphate and after removal of solvent gave an oil (2.08 g) shown to be a mixture, (58:42, g.l.c., 2% carbowax 20M on chromosorb W, column temperature 90°C) of (1RS, 2SR)- and (1RS, 2RS)-2-methyl-1-phenyl-3-buten-1-ols[77AJ0835, 82OM0149] **(1a, 1b)**. ^{1}H n.m.r. (CCl$_4$) δ_H **(1a)** 1.0, J$_{2,5}$ 7 Hz, Me; 4.40, J$_{1,2}$ 6 Hz, H1; **(1b)** 0.87, J$_{2,5}$ 8 Hz, Me; 4.28, J$_{1,2}$ 8 Hz, H1; the following signals coincide 2.2 - 2.6, H2; 4.6 - 5.2, (H4)$_2$; 5.3 - 6.0, H3; 7.30, W$_h$/2 4 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C **(1a)** 14.2, Me; 44.6, C2; 77.3, C1; 115.3, C4; 140.4, C3; **(1b)** 16.5, Me; 46.1, C2; 77.9, C1;

Experimental

116.6, C4; 140.6, C3; **(1a, 1b)** 126.6, 126.8, 127.3, 127.6, 128.0, 128.2, 142.5, 142.7, phenyl carbons.

3-Phenyl-4-penten-2-ol

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), acetaldehyde (2 g, 50 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as above to give an oil (3.2 g), purified by radial chromatography on a 2 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give (2RS, 3RS)-3-phenyl-4-penten-2-ol **(2b)**. Elution was effected with 10% - 30% ether - petroleum ether mixtures. (Found CIMS (C_4H_{10}): M+H$^+$-H$_2$O = 145.1013; $C_{11}H_{14}O$ requires 162.10453). υ_{max} 3425, 760, 705 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.16, $J_{1,2}$ 6 Hz, (H1)$_3$; 2.06, $W_h/_2$ 6 Hz, OH; 3.23, $J_{2,3}$ 8 Hz, $J_{3,4}$ 8 Hz, H3; 4.03, $J_{1,2}$ 6 Hz, $J_{2,3}$ 8 Hz, H2; 5.03 - 5.43, (H5)$_2$; 5.9 - 6.66, H4; 7.33, $W_h/_2$ 5 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 20.7, C1; 59.0, C3; 70.2, C2; 117.7, C5; 126.7, p; 128.0, 128.6, o, m; 138.5, C4; 141.6, i.

4-Phenyl-5-hexen-3-ol

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), propanal (1.16 g, 20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as above to give an oil (3.2 g), purified by radial chromatography on a 2 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give (3RS, 4RS)-4-phenyl-5-hexen-3-ol **(3b)**. Elution was effected with 10% - 30% ether - petroleum ether mixtures. (Found CIMS (C_4H_{10}): M+H$^+$-H$_2$O = 159.1165; $C_{12}H_{16}O$ requires 176.12019). υ_{max} 3430, 1460, 710 cm^{-1}. ^{1}H n.m.r. (CCl$_4$) δ_H 0.7 - 1.5, (H1)$_3$, (H2)$_2$; 1.8, $W_h/_2$ 14 Hz, OH; 3.17, $J_{3,4}$ 8 Hz, $J_{4,5}$ 8 Hz, H4; 3.57, $J_{3,4}$ 8 Hz, $J_{2,3}$ 7 Hz, H3; 4.9 - 5.4, (H6)$_2$; 5.88 - 6.4, H5; 7.18, $W_h/_2$ 3 Hz, ArH. ^{13}C n.m.r.

Experimental

(CDCl$_3$) δ_C 10.0, C1; 27.3, C2; 56.9, C4; 75.4, C3; 117.6, C6; 126.6, p; 128.0, 128.7, o, m; 138.4, C5; 141.8, i.

2-Methyl-4-phenyl-5-hexen-3-ol and derivatives

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 2-methylpropanal (1.47 g, 20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as above to give an oil (3.6 g), purified by radial chromatography on a 2 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate to give (3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-ol (4b). Elution was effected with 10% - 30% ether - petroleum ether mixtures. (Found CIMS (C$_4$H$_{10}$): M+H$^+$-H$_2$O = 173.1314; C$_{13}$H$_{18}$O requires 190.13585). υ_{max} 3450, 705 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 0.93, W$_{h/2}$ 12 Hz, (H1)$_3$, H2-Me; 1.33 - 1.83, H2; 1.76, W$_{h/2}$ 3 Hz, OH; 3.23 - 3.78, H3, H4; 5.0 - 5.4, (H6)$_2$; 5.9 - 6.6, H5; 7.3, W$_{h/2}$ 3 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 15.8, 20.1, C1, C2-Me; 29.8, C2; 54.6, C4; 78.5, C3; 117.4, C6; 126.5, p; 128.0, 128.7, o, m; 138.8, C5; 142.1, i.

(3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl-4-nitrobenzoate. (3RS, 4RS)-2-Methyl-4-phenyl-5-hexen-3-ol (4b) (140 mg) and 4-nitrobenzoylchloride (140 mg) were dissolved in dry pyridine (2 ml) and allowed to stand overnight. Water (5 ml) and sulphuric acid (2 drops) were added and the mixture shaken. The solid was collected and shaken with sodium hydroxide (5 ml, 2%) to remove nitrobenzoic acid, filtered, washed with cold water, and recrystallized from ethanol to give crystals of (3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl-4-nitrobenzoate. (32b, R=(CH$_3$)$_2$CH) M.p. 107 - 9°C. ^{13}C n.m.r. (CDCl$_3$) δ_C 15.9, 20.0, C1, C2-Me; 29.2, C2; 53.3, C4; 81.4, C3; 117.0, C6; 138.2, C5; 123.6, 127.0, 127.9, 128.9, 130.6, 140.6, phenyl carbons. ^{1}H n.m.r. (CDCl$_3$) δ_H 0.92, J$_{1,2}$ 7 Hz, 0.99 J$_{1,2}$ 7 Hz, (H1)$_3$, C2-Me; 1.8, H2; 3.67, J$_{3,4}$ 9 Hz, J$_{4,5}$ 9 Hz, H4; 5.0, J$_{5,6a}$ 10 Hz, H6a; 5.07, J$_{5,6b}$ 17 Hz, H6b; 5.46, H3; 6.06, J$_{4,5}$ 9 Hz, J$_{5,6a}$ 10 Hz, J$_{5,6b}$ 17 Hz, H5; 7.2 - 7.35, 8.18 - 8.33, ArH. *(3RS, 4RS)-2-methyl-4-phenyl-*

Experimental

5-hexen-3-yl-3,5-dinitrobenzoate. (3RS, 4RS)-2-Methyl-4-phenyl-

5-hexen-3-ol **(4b)** (300 mg) and 3,5-dinitrobenzoylchloride[33] (450 mg) were

dissolved in dry pyridine (10 ml) and stirred overnight. Water (10 ml) and

sulphuric acid (2 drops) were added and the mixture shaken, filtered and the

reaction product washed with sodium hydroxide (5 ml, 2%) to remove

nitrobenzoic acid, then water (5 ml) and recrystallized from ethanol to give

crystals of (3RS, 4RS)-2-methyl-4-phenyl-5-hexen-3-yl 3,5-dinitrobenzoate.

(33b, R=(CH$_3$)$_2$CH) M.p. 128 - 30°C. ^{13}C n.m.r. (CDCl$_3$) δ_C 15.9, 20.0, C1, C2-Me;

29.1, C2; 53.3, C4; 82.8, C3; 117.4, C6; 138.0, C5; 162.3, C=O; 122.3, 127.2, 127.9,

129.0, 129.3, 140.3, phenyl carbons. ^{1}H n.m.r. (CDCl$_3$) δ_H 0.95, J$_{1,2}$ 7 Hz, 1.1, J$_{1,2}$

8 Hz, (H1)$_3$, C2-Me; 1.86, H2; 3.75, J$_{4,5}$ 9 Hz, J$_{3,4}$ 9 Hz, H4; 5.03, J$_{5,6a}$ 10 Hz, H6a;

5.04, J$_{5,6b}$ 17 Hz, H6b; 5.53, J$_{3,4}$ 9 Hz, J$_{2,3}$ 4 Hz, H3; 6.07, J$_{4,5}$ 9 Hz, J$_{5,6a}$ 10 Hz, J$_{5,6b}$

17 Hz, H5; 7.18 - 7.35, 9.1 - 9.2, ArH.

3-Phenyl-2-decen-4-ol

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), heptanal (2.28 g, 20 mmol),

tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium

powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as

above to give an oil (4.5 g), purified by radial chromatography on a 2 mm

silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate. Elution was effected with

10% - 30% ether - petroleum ether mixtures to give (3RS, 4RS)-3-phenyl-

2-decen-4-ol **(5b)**. (Found CIMS(C$_4$H$_{10}$): M+H$^+$-H$_2$O = 215.1801; C$_{16}$H$_{24}$O

requires 232.1827). υ_{max} 3450, 2950, 1070, 710 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H

0.7 - 1.4, (H5)$_2$, (H6)$_2$, (H7)$_2$, (H8)$_2$, (H9)$_2$, (H10)$_3$; 1.75, W$_{h/2}$ 8 Hz, OH; 3.2, J$_{2,3}$

8 Hz, J$_{3,4}$ 8 Hz, H3; 3.8, W$_{h/2}$ 14 Hz, H4; 5.0 - 5.4, H12; 5.8 - 6.6, H2; 7.3, W$_{h/2}$

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[33] *Preparation of 3,5-Dinitrobenzoylchloride*
3,5-Dinitrobenzoic acid (5 g) was heated under reflux with thionyl chloride (150 ml)
for 2 hours. The thionyl chloride was removed by distillation and the resulting solid
recrystallized from carbon tetrachloride. Recrystallization from petroleum ether
gave a more pure sample of 3,5-dinitrobenzoylchloride. M.p. 73 - 74°C[81CRCHCP].

Experimental

2 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 14.1, C10; 22.6, C9; 25.7, C6; 29.3, C7; 31.8, C8; 34.5, C5; 57.5, C3; 74.1, C4; 117.8, C1; 126.6, p; 128.7, o, m; 138.5, C2; 141.8, i.

1,3-Diphenyl-4-penten-2-ol and epoxide derivative

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 1-phenylethanal (2.4 g, 20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as above to give (2RS, 3RS)-1,3-diphenyl-4-penten-2-ol (6b) as an oil (4.5 g). (Found CIMS (C$_4$H$_{10}$): M+H$^+$-H$_2$O = 221.1314; C$_{17}$H$_{18}$O requires 238.13585). υ_{max} 3440, 750, 700 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 2.6, J$_{1,2}$ 6 Hz, (H1)$_2$; 3.3, J$_{2,3}$ 7 Hz, J$_{3,4}$ 7 Hz, H3; 3.83 - 4.16, H2; 4.96 - 5.36, (H5)$_2$; 5.83 - 6.63, H4; 7.23, W$_{h/2}$ 2 Hz, 7.33, W$_{h/2}$ 2 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 41.2, C1; 56.4, C3; 75.1, C2; 117.8, C5; 138.1, C4; 126.3, 126.7, 128.1, 128.4, 128.7, 129.4, 138.8, 141.7, phenyl carbons.

Epoxidation of (2RS, 3RS)-1,3-Diphenyl-4-penten-2-ol. To (2RS, 3RS)-1,3-diphenyl-4-penten-2-ol (6b) (200 mg) in dry ether (10 ml) was added metachloroperbenzoic acid (400 mg) and the solution kept at room temperature 72 hours. The solution was washed with saturated aqueous sodium bisulphite (10 ml), saturated aqueous sodium bicarbonate (10 ml) and water (10 ml) and dried with sodium sulphate. Removal of solvent gave an oil which was purified by radial chromatography on a 1 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate. Elution was effected with 10% - 50% ether - petroleum ether mixtures to give pure fractions of (2RS, 3RS, 4RS)- and (2RS, 3RS, 4SR)4,5-epoxy-1,3-diphenyl-4-penten-2-ol (7b, 7a). υ_{max} 3425 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 2.33 - 2.93, (H1)$_2$, H3, (H5)$_2$; 3.27 - 3.6, H4; 3.93 - 4.37, H2; 7.0 - 7.57, ArH. (2RS, 3RS, 4RS)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol (7b); (Found CIMS(C$_4$H$_{10}$): M+H$^+$-H$_2$O = 237.1309; C$_{17}$H$_{18}$O$_2$ requires 254.1308). ^{13}C n.m.r. (CDCl$_3$) δ_C 41.6, C1; 45.6, C5; 53.7, C4; 54.5, C3; 75.8, C2; 126.4, 127.3, 128.4, 128.8, 129.5, 138.4, 139.3, phenyl carbons.

Experimental

(2RS, 3RS, 4SR)-4,5-epoxy-1,3-diphenyl-4-penten-2-ol (**7a**); (Found

CIMS(C_4H_{10}): M+H$^+$-H_2O = 237.1248; $C_{17}H_{18}O_2$ requires 254.1308). ^{13}C n.m.r.

(CDCl$_3$) δ_C 41.9, C1; 46.8, C5; 53.0, C4; 53.5, C3; 74.2, C2; 126.5, 127.3, 128.5, 128.7,

128.8, 129.4, 129.5, 138.3, phenyl carbons.

1,2-Diphenyl-3-buten-1-ol

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), benzaldehyde (2.12 g,

20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol),

aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were

reacted as above to give (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol[84AJ0065] (**8b**) as

an oil (3.2 g). ^1H n.m.r. (CCl$_4$) δ_H 3.43, $J_{1,2}$ 7 Hz, H2; 4.73, $J_{1,2}$ 7 Hz, H1;

4.83 - 5.27, (H4)$_2$; 6.2, $J_{2,3}$ 8 Hz, $J_{3,4 \text{ cis}}$ 10 Hz, $J_{3,4 \text{ trans}}$ 16 Hz, H3; 7.1, $W_{h/2}$ 3 Hz,

ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 59.0, C2; 77.2, C1; 118.1, C4; 137.9, C3; 126.5, 126.6,

127.3, 127.9, 128.2, 128.3, 140.7, 142.0 phenyl carbons.

1-(4-Cyanophenyl)-2-phenyl-3-buten-1-ol and derivative

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 4-cyanobenzaldehyde (2.62 g,

20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol),

aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were

reacted as above to produce a solid, recrystallised from carbon tetrachloride

to give (1RS, 2SR)-1-(4-cyanophenyl)-2-phenyl-3-buten-1-ol (**10b**) (3.6 g). M.p.

93 - 94°C. (Found: C, 81.4; H, 6.0; N, 5.3%; $C_{17}H_{15}NO$ requires C, 81.9; H, 6.1;

N, 5.6%). (Found CIMS(C_4H_{10}): M+H$^+$ = 250.1222; $C_{17}H_{15}NO$ requires

249.1154). υ_{max} 3425, 2250, 1055, 760, 710 cm^{-1}. ^1H n.m.r. (CDCl$_3$) δ_H 2.63,

$W_{h/2}$ 7 Hz, OH; 3.41, $J_{1,2}$ 8 Hz, $J_{2,3}$ 8 Hz, H2; 4.85, $J_{1,2}$ 8 Hz, H1; 4.96 - 5.35,

(H4)$_2$; 6.18, $J_{2,3}$ 8 Hz, $J_{3,4 \text{ trans}}$ 16 Hz, $J_{3,4 \text{ cis}}$ 10 Hz, H3; 7.23, $W_{h/2}$ 20 Hz, ArH.

^{13}C n.m.r. (CDCl$_3$) δ_C 59.2, C2; 76.5, C1; 110.9, p'; 119.0, C4; 127.0, p, 127.3, 128.2,

128.6, m, o', o; 131.6, m'; 136.9, C3; 139.8, i; 147.4, i'; CN not observed.

(1RS, 2SR)-1-(4-cyanophenyl)-2-phenyl-3-buten-1-yl-3,5-dinitrobenzoate.

Experimental

(1RS, 2SR)-1-(4-Cyanophenyl)-2-phenyl-3-buten-1-ol (**10b**) (200 mg) and 3,5-dinitrobenzoyl chloride (330 mg) was dissolved in dry pyridine (10 ml) and stirred 24 hours. Water (10 ml) and sulphuric acid (2 drops) were added and the mixture shaken, filtered and the reaction product washed with sodium hydroxide (2%, 5 ml) and water (5 ml) and recrystallized from ethanol to give a solid, (1RS, 2SR)-1-(4-cyanophenyl)-2-phenyl-3-buten-1-yl-3,5-dinitrobenzoate. (**33b, R=4-cyanophenyl**) υ_{max} 1730 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 3.98, $J_{1,2}$ 9 Hz, $J_{2,3}$ 9 Hz, H2; 5.24, $J_{4a,5}$ 10 Hz, H4a; 5.31, $J_{3,4b}$ 17 Hz, H4b; 6.21, $J_{2,3}$ 9 Hz, $J_{3,4a}$ 10 Hz, $J_{3,4b}$ 17 Hz, H3; 6.29, $J_{1,2}$ 9 Hz, H1; 7.1 - 7.6, 9.1 - 9.23, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 56.4, C2; 80.0, C1; 118.7, C4; 136.5, C3; 161.6, C=O; 112.4, 122.8, 127.6, 128.0, 128.4, 128.9, 129.4, 132.1, 138.0, 142.6, 148.8, 149.0, phenyl carbons.

1-(4-Methoxyphenyl)-2-phenyl-3-buten-1-ol and derivative

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 4-methoxybenzaldehyde (2.72 g, 20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid. Standard workup gave an oil (3.87 g). A portion of the oil was purified by radial chromatography on a 2 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate. Elution was effected with 10% - 20% ether - petroleum ether mixtures to give (1RS, 2SR)-1-(4-methoxyphenyl)-2-phenyl-3-buten-1-ol (**11b**). (Found CIMS(C$_4$H$_{10}$): M+H$^+$ = 255.1394; C$_{17}$H$_{18}$O$_2$ requires 254.1307). υ_{max} 3450, 1520, 1240, 1035, 765, 710 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 2.25, W$_{h/2}$ 8 Hz, OH; 3.5, $J_{1,2}$ 8 Hz, $J_{2,3}$ 8 Hz, H2; 3.83, W$_{h/2}$ 2 Hz, OCH$_3$; 4.9, $J_{1,2}$ 8 Hz, H1; 5.06 - 5.46, (H4)$_2$; 6.06 - 6.66, H3; 6.73 - 7.5, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 55.1, OMe; 59.2, C2; 76.8, C1; 113.3, m'; 118.1, C4; 126.5, p; 127.8, 18.3, 128.4, o, m, o'; 134.1, i'; 138.2, C3; 140.8, i; 158.8, p'.

(1RS, 2SR)-1-(4-methoxyphenyl)-2-phenyl-3-buten-1-yl 3,5-dinitrobenzoate.

(1RS, 2SR)-1-(4-Methoxyphenyl)-2-phenyl-3-buten-1-ol (**11b**) (1 g) and

Experimental

3,5-dinitrobenzoyl chloride (0.82 g) was dissolved in dry pyridine (50 ml) and stirred 24 hours. Water (50 ml) and sulphuric acid (10 drops) were added and the mixture shaken, filtered and the reaction product washed with sodium hydroxide (2%, 25 ml) and water (25 ml) and purified by radial chromatography to give a solid (0.6 g) 1-(4-methoxyphenyl)-2-phenyl-3-buten-1-yl 3,5-dinitrobenzoate. **(33b, R=4-methoxyphenyl)** υ_{max} 1730, 710 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 3.7, OMe; 4.1, J$_{1,2}$ 8 Hz, H1; 5.03 - 5.47, (H4)$_2$; 5.93 - 6.67, H3; 6.7 - 7.4, 9 - 9.2, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 55.2, OMe; 56.4, C2; 80.6, C1; 117.8, C4; 137.6, C3; 113.7, 122.3, 127.1, 128.4, 128.5, 128.6, 128.8, 129.4, phenyl carbons.

1-(9-Anthracenyl)-2-phenyl-3-buten-1-ol

(E)-3-Chloro-1-phenylpropene (1.6 g, 10 mmol), 9-anthraldehyde (93%, 2.25 g, 6.6 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were reacted as above to give a solid (3.52 g), recrystallised from benzene to give (1RS, 2RS)-1-(9-anthracenyl)-2-phenyl-3-buten-1-ol. **(13b)** M.p. 153 - 4°C. (Found: C, 89.1; H, 6.4%. C$_{24}$H$_{20}$O requires C, 88.9; H, 6.2%). (Found: M$^+$-OH = 307.1488; C$_{24}$H$_{20}$O requires 324.1514). ^{1}H n.m.r. (CDCl$_3$) δ_H 2.73, W$_{h/2}$ 12 Hz, OH; 4.46, J$_{1,2}$ 9 Hz, J$_{2,3}$ 9 Hz, H2; 5.25 - 5.52, (H4)$_2$; 6.25, J$_{1,2}$ 9 Hz, H1, H3; 6.77, W$_{h/2}$ 4 Hz, ArH; 7.17 - 7.5, 7.73 - 8.0, 8.2 - 8.67, Anthracenyl H. ^{13}C n.m.r. (CDCl$_3$) d$_C$ 57.0, C2; 73.3, C1; 118.3, C4; 138.5, C3; 124.4, 125.1, 126.2, 127.7, 128.3, 129.0, 129.9, 131.3, 132.1, phenyl and anthracenyl carbons.

3-Phenylhept-1,5-dien-4-ol

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), (E)-2-butenal (1.4 g, 20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as

Experimental

above to give (3RS, 4RS)-(E)-3-phenylhept-1,5-dien-4-ol (14b) as an oil (4.8 g).

(Found CIMS (C_4H_{10}): M+H$^+$ = 189.1283; $C_{13}H_{16}O$ requires 188.12019). υ_{max}

3425 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.56, $J_{6,7}$ 5 Hz, (H7)$_3$; 3.3, $J_{2,3}$ 8 Hz, $J_{3,4}$ 8 Hz,

H3; 4.26, $J_{3,4}$ 6 Hz, $J_{4,5}$ 6 Hz, H4; 5.0 - 5.4, H2; 5.1 - 5.7, H5, H6; 5.8 - 6.6, (H1)$_2$;

7.26, $W_{h/2}$ 4 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 17.7, C7; 57.3, C3; 75.2, C4; 117.7,

C1; 126.6, p; 127.9, C6; 128.4, o, m; 131.4, C5, 138.2, C2; 141.0, i.

1,4-Diphenylhexa-1,5-dien-3-ol

(E)-3-chloro-1-phenylpropene (3 g, 20 mmol), (E)-1-phenylpropenal (2.64 g,

20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol),

aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were

reacted as above to give an oil (4.38 g), purified by radial chromatography on

a 2 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate. Elution was effected

with 10% - 20% ether - petroleum ether mixtures to give (3RS, 4RS)-

(E)-1,4-diphenylhexa-1,5-dien-3-ol (16b). (Found CIMS (C_4H_{10}): M+H$^+$-H$_2$O =

233.1349; $C_{18}H_{18}O$ requires 250.1358). υ_{max} 3450, 1500, 1455, 755, 705 cm^{-1}.

^{1}H n.m.r. (CDCl$_3$) δ_H 2.08, $W_{h/2}$ 12 Hz, OH; 3.53, $J_{4,5}$ 7 Hz, $J_{3,4}$ 7 Hz, H4; 4.6, $J_{2,3}$

7 Hz, $J_{3,4}$ 7 Hz, H3; 5.1 - 5.46, H5, H1, H2; 7.36, $W_{h/2}$ 4 Hz, ArH. ^{13}C n.m.r.

(CDCl$_3$) δ_C 57.4, C4; 75.0, C3; 118.0, C6; 129.8, 131.0, C1, C2; 137.8, C5; 126.5,

126.8, 127.5, 128.5, 128.6, 140.6, phenyl carbons.

5-Methyl-3-phenyl-1-hepten-4-ols

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 2-methylbutanal (1.7 g,

20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol),

aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were

reacted as above to give an oil (1.27 g) a mixture, 2:5 (ratio estimated by

inspection of peaks at δ_C 53.9 and 55.0 of ^{13}C n.m.r. spectrum) of

(3RS, 4RS, 5RS)- and (3RS, 4RS, 5SR)-3-phenyl-5-methyl-1-hepten-4-ol (18d,

18b). (Found CIMS (C_4H_{10}): M+H$^+$-H$_2$O = 187.1494; $C_{14}H_{20}O$ requires

Experimental

204.15151). ν_{max} 3425, 1710, 700 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 0.79 - 0.94, (H7)$_3$,

C5-Me; 1.0 - 1.7, (H6)$_2$, H5; 3.36, J$_{3,4}$ 7 Hz, J$_{4,5}$ 7 Hz, **(18b)-H4;** 3,47, J$_{3,4}$ 6.5 Hz, J$_{4,5}$

9 Hz, **(18d)-H4;** 3.61, J$_{3,4}$ 6.5 Hz, J$_{2,3}$ 5.3 Hz, **(18d)-H3;** 3.78, J$_{3,4}$ 7 Hz, J$_{2,3}$ 2.8 Hz,

(18b)-H3; 5.16 - 5.23, (H1)$_2$; 6.09, J=9.5 Hz, J=9.5 Hz, J=17.5 Hz, **(18b)-H2;** 6.16,

J=9 Hz, J=10.2 Hz, J=17 Hz, **(18d)-H2;** 7.15 - 7.35, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C

(18d) 11.5, 16.1, C7, C5-Me; 23.2, C6; 36.7, C5; 53.9, C3; 78.5, C4; 117.6, C1; 138.1,

C2. **(18b)** 11.7, 12.3, C7, C5-Me; 27.0, C6; 35.8, C5; 55.0, C3; 75.8, C4; 117.3, C1;

139.7, C2. (Both stereoisomers) 126.5, 127.9, 128.0, 128.1, 128.7, 141.7, phenyl

carbons.

5,7,7-Trimethyl-3-phenyl-1-octen-4-ols and derivatives

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 2,4,4-trimethylpentanal[34] **(20)**

(2.56 g, 20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder

(1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of

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[34] *Preparation of 2,4,4-Trimethyl-1-pentene*
A mixture of 50% sulphuric acid (250 ml) and t-butanol (175 ml) was swirled to obtain a homogenous solution and heated on a steam bath for 45 minutes with occasional swirling. The lower acid layer was discarded and the product washed with aqueous sodium bicarbonate and dried with sodium sulphate. The product was distilled to give a mixture, 80:20 (ratio determined by integration of peaks at δ_H 0.93 and 1.06 of ^{1}H n.m.r. spectrum) of 2,4,4-trimethyl-1-pentene[76OR0426] and 2,4,4-tri-methyl-2-pentene **(19b)** (83 g). ^{1}H n.m.r. (CCl$_4$) δ_H **(19b)** 0.93, C4-Me$_2$, (H5)$_3$; 1.76, C2-Me; 1.9, (H3)$_2$; 4.6, 4.8, H1$_{syn}$, H1$_{anti}$. **(19a)** 1.06, C4-Me$_2$, (H5)$_3$; 1.67, W$_{h/2}$ 10 Hz, C2-Me, H1; 5.1, H3. ^{13}C n.m.r. (CDCl$_3$) δ_C **(19a)** 25.23, C6; 30.13, C5; 31.37, C4; 51.86, C3; 113.83, C1; 143.88, C2; **(19b)** 18.76, C6; 27.98, C1; 31.24, C5; 32.17, C4; 130.04, C2; 135.20, C3.
Preparation of 2,4,4-Trimethylpentanal[71OS0004]
In a three necked flask fitted with thermometer, mechanical stirrer and dropping funnel equipped with a calcium chloride drying tube was placed a mixture (80:20) of freshly distilled 2,4,4-trimethyl-1-pentene **(19a)** and 2,4,4-trimethyl-2-pentene **(19b)** (14 g, 0.1 mol) and freshly distilled dichloromethane (100 ml) cooled to 0 - 5°C. A solution of chromyl chloride (16 g, 0.102 mol) in dichloromethane (20 ml) was added dropwise with stirring to maintain the temperature at 0 - 5°C. The reaction mixture was stirred for 15 minutes and zinc dust (18.4 g, technical grade) was added. The mixture was stirred a further 5 minutes and ice-water (100 ml) and ice (40 g) were added as rapidly as possible and the mixture stirred an additional 15 minutes. After removal of dichloromethane by distillation the residue was steam distilled until the distillate gave a negative test with 2,4-dinitrophenylhydrazine reagent. The organic layer of the distillate was taken and the aqueous layer extracted with dichloro-methane (3 * 50 ml). The combined organic layers were dried and the solvent removed by distillation to give 2,4,4-trimethylpentanal[73JO2136] **(20)** (14.5 g). ν_{max} 1725 cm^{-1}. ^{13}C n.m.r. (CDCl$_3$) δ_C 20.2, C2-Me; 26.2, C4; 29.4, C5, C4a, C4b; 36.2, C3; 47.6, C2; 184.6, C1.

Experimental

hydrobromic acid were reacted as above to give an oil (5.13 g) a mixture, >90:10 (ratio estimated by inspection of peaks at δ_C 49.2 and 44.7 of ^{13}C n.m.r. spectrum) of (3RS, 4RS, 5SR)- and (3RS, 4RS, 5RS)-5,7,7-trimethyl-3-phenyl-1-octen-4-ol (21b, 21d). This oil was purified by radial chromatography on a 2 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give the same mixture. Elution was effected with 10% - 30% ether - petroleum ether mixtures. (Found CIMS (C_4H_{10}): $M+H^+-H_2O = 229.1933$; $C_{17}H_{26}O$ requires 246.19849). υ_{max} 3450, 3000, 1710, 705 cm^{-1}. ^1H n.m.r. (CDCl$_3$) δ_H (21b) 0.7, $W_{h/2}$ 2 Hz, C7-Me$_2$, (H8)$_3$; 0.7 - 1.66, H5, C5-Me, (H6)$_2$; 3.16, J$_{2,3}$ 8 Hz, J$_{3,4}$ 8 Hz, H3; 3.56, J$_{3,4}$ 8 Hz, J$_{4,5}$ 2 Hz, H4; 4.9 - 5.26, (H1)$_2$; 5.7 - 6.46, H2; 7.1, $W_{h/2}$ 3 Hz, ArH. (21d) peaks hidden under (21b) spectrum. ^{13}C n.m.r. (CDCl$_3$) (21b) δ_C 14.6, C5-Me; 29.6, C7-Me$_2$, C8; 30.2, C6; 31.1, C7; 49.2, C5; 55.4, C3; 78.5, C4; 117.3, C1; 140.0, C2; 126.6, 127.9, 128.7, 141.5, phenyl carbons. Partial assignment was possible for (21d) 20.3, C5-Me; 44.7, C5; 53.9, C3; 79.5, C4; 117.5, C1.

5,7,7-Trimethyl-3-phenyl-1-octen-4-yl 4-nitrobenzoate. A mixture (>9:1) of (3RS, 4RS, 5SR)- and (3RS, 4RS, 5RS)-5,7,7-trimethyl-3-phenyl-1-octen-4-ol (19b, 19d) (200 mg) and 4-nitrobenzoylchloride (500 mg) was dissolved in dry pyridine (10 ml) and stirred 48 hours. The mixture was poured into water (50 ml), extracted with benzene (2 * 50 ml) and the organic extracts washed with water (10 * 100 ml), dried with sodium sulphate and after removal of solvent gave 5,7,7-trimethyl-3-phenyl-1-octen-4-yl 4-nitrobenzoate (32, R=(CH$_3$)$_3$CH$_2$CH(CH$_3$)) as an oil. υ_{max} 720, 1260, 1530, 1730 cm^{-1}. ^1H n.m.r. (CDCl$_3$) δ_H 0.66 - 1.55, C7-Me$_2$, (H8)$_3$, H5, C5-Me$_2$, (H6)$_2$; 3.63, J$_{2,3}$ 9 Hz, J$_{3,4}$ 9 Hz, H3; 4.88 - 5.57, (H1)$_2$, H4; 5.94 - 6.09, H2; 7.2 - 7.5, 8.2 - 8.4, ArH.

^{13}C n.m.r. (CDCl$_3$) δ_C 15.8, C5-Me; 29.5, C7-Me$_2$, C8; 30.2, C6; 31.1, C7; 48.4, C5; 54.0, C3; 82.1, C4; 116.6, C1; 138.9, C2; 123.6, 128.0, 128.5, 128.7, 129.0, 130.7, 130.8, phenyl carbons.

(3RS, 4RS, 5SR)-5,7,7-Trimethyl-3-phenyl-1-octen-en-4-yl 3,5-dinitro-

Experimental

benzoate. 3,5-Dinitrobenzoic acid (500 mg) was dissolved in thionyl chloride (5 ml) and refluxed for 40 minutes. The condenser was removed and the thionyl chloride removed by distillation. A mixture (>9:1) of (3RS, 4RS, 5SR)- and (3RS, 4RS, 5RS)-5,7,7-trimethyl-3-phenyl-2-octen-4-ol **(19b, 19d)** (200 mg) was added with dry pyridine (20 ml) and stirred overnight. The mixture was poured into water (50 ml), extracted with benzene (2 * 50 ml) and the organic extracts washed with water (10 * 100 ml), dried with sodium sulphate and after removal of solvent gave a gummy reaction product which was recrystallised from ethanol to give a solid, (3RS, 4RS, 5SR)-5,7,7-trimethyl-3-phenyl-1-octen-en-4-yl 3,5-dinitrobenzoate. **(33, R=(CH₃)₃CH₂CH(CH₃))** υ_{max} 1730 cm^{-1}. ^{1}H n.m.r. (CDCl₃) δ_H 1.0 - 1.5, C7-Me$_2$, (H8)$_3$, H5, C5-Me$_2$, (H6)$_2$; 3.06, J$_{2,3}$ 8 Hz, J$_{3,4}$ 8 Hz, H3; 3.6, J$_{3,4}$ 8 Hz, H4; 4.8 - 5.3, (H1)$_2$; 5.6 - 6.4, H2; 7.23, W$_{h/2}$ 4 Hz, 8.9 - 9.3, ArH. ^{13}C n.m.r (CDCl₃) δ_C 5.9, C5-Me; 29.5, C7-Me$_2$, C8; 30.0, C6; 31.1, C7; 48.5, C5; 54.0, C3; 83.5, C4; 116.9, C1; 138.8, C2; 122.3, 127.3, 129.1, 129.4, 140.1, phenyl carbons.

Experimental

2,4-Diphenyl-5-hexen-3-ols and derivatives

(E)-3-Chloro-1-phenylpropene (1.5 g, 10 mmol), 2-phenylpropanal[35] (1.34 g,

10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g,

4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of

hydrobromic acid. Standard workup gave an oil (1.93 g), a mixture, 75:25

(ratio estimated by inspection of peaks at δ_C 53.6 and 54.0 of ^{13}C n.m.r.

spectrum) of (2RS, 3SR, 4SR)- and (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-ol

(25b, 25d) respectively. A portion of the oil was purified by radial

chromatography on a 2 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to

give the same mixture. Elution was effected with 10% - 30% ether -

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[35]   *Preparation of 2-Phenyl-2-propanol*[01CO0685]
To a stirred mixture of magnesium turnings (12.2 g) in dry ether (100 ml) was added
bromobenzene (78.6 g) in dry ether (100 ml) and the mixture maintained at a gentle
reflux. After 30 minutes the mixture was cooled to 0°C and acetone (26.2 g) in dry
ether (50 ml) was added dropwise. The solution was stirred overnight at room
temperature and carefully poured onto crushed ice (100 g). Hydrochloric acid (5 M)
was added slowly until the mixture was acidic. The ether layer was separated and the
aqueous layer extracted with ether (2 * 30 ml). The combined ether fractions were
washed with brine (20 ml), saturated sodium bicarbonate (until basic), brine (2 *
20 ml), dried with magnesium sulphate and after removal of solvent gave 2-phenyl-
propan-2-ol[53JC4106] (22) (70 g). ^{1}H n.m.r. (CCl$_4$) δ_H 1.58, (H1)$_3$, (H3)$_3$; 2.6, W$_{h/2}$ 14 Hz,
OH; 3.93, W$_{h/2}$ 18 Hz, ArH.
Preparation of 2-Phenylpropene[62JO2377]
A solution of 2-phenylpropan-2-ol (22) (20 g) and dry dimethylsulphoxide (100 ml)
was heated on an oil bath at 160 - 185°C for 24 hours. The solution was cooled and ice
water (100 ml) slowly added. The organic layer was separated and the aqueous layer
extracted with petroleum ether (3 * 100 ml). The combined petroleum ether
fractions were washed with brine (2 * 20 ml), dried with magnesium sulphate and
after removal of solvent gave 2-phenylpropene[69JA5286, 65CJ0510] (23) (14 g) as an oil.
^{1}H n.m.r. (CCl$_4$) δ_H 2.13, (H3)$_3$; 5.0, H1$_{anti}$; 5.26, H1$_{syn}$; 7.2, W$_{h/2}$ 16 Hz, ArH.
Preparation of 2-Phenylpropanal
In a three necked flask fitted with thermometer, mechanical stirrer and dropping
funnel equipped with a calcium chloride drying tube was placed a mixture of freshly
distilled 2—phenylpropene (23) (5 g, 0.05 mol) and freshly distilled dichloromethane
(50 ml) cooled to 0 - 5°C. A solution of chromyl chloride (8 g, 0.051 mol) in
dichloromethane (10 ml) was added dropwise with stirring to maintain the
temperature at 0 - 5°C. The reaction mixture was stirred for 15 minutes and zinc dust
(9.2 g, technical grade) added. The mixture was stirred a further 5 minutes and ice
water (50 ml) and ice (20 g) added as rapidly as possible and the mixture stirred an
additional 15 minutes. After removal of dichloromethane by distillation the residue
was steam distilled until the distillate gave a negative test with 2,4-dinitrophenyl-
hydrazine reagent. The organic layer of the distillate was taken and the aqueous
layer extracted with dichloromethane (3 * 50 ml). The combined organic layers were
dried and the solvent removed by distillation to give 2-phenylpropanal[71OS0004] (24)
(3 g). ν_{max} 710, 1600, 1725 cm^{-1}. ^{1}H n.m.r. (CCl$_4$) δ_H 1.53, J$_{2,3}$ 7 Hz, (H3)$_3$; 1.8, J$_{2,3}$ 7 Hz,
H2; 7.2, W$_{h/2}$ 8 Hz, 7.83, W$_{h/2}$ 8 Hz, ArH; 9.43, H1.

Experimental

petroleum ether mixtures. (Found CIMS(C_4H_{10}): M+H$^+$-H$_2$O = 235.1471; $C_{18}H_{20}O$ requires 252.1515). υ_{max} 3475, 1495, 1455, 705 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.07 - 1.43, (H1)$_3$; 1.82, W$_{h/2}$ 6 Hz, OH; 2.75, J$_{3,4}$ 6 Hz, H4; 3.42, J$_{1,2}$ 7 Hz, J$_{2,3}$ 7 Hz, H2; 3.93, J$_{2,3}$ 7 Hz, J$_{3,4}$ 6 Hz, H3; 5.03 - 5.37, H6; 5.83 - 6.63, (H5)$_2$; 7.27, W$_{h/2}$ 4 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C (25b) 15.2, C1; 42.0, C2; 53.6, C4; 78.6, C3; 117.8, C6; 137.7, C5; and (25d) 19.2, C1; 42.5, C2; 54.0, C4; 78.1, C3; 117.5, C6; 138.0, C5; and phenyl carbons (25b, 25d) 126.3, 126.6, 127.8, 127.9, 128.3, 128.4, 128.5, 128.7, 142.3, 145.1.

2,4-Diphenyl-5-hexen-3-yl 4-nitrobenzoates. A mixture (75:25) of (2RS, 3SR, 4SR)- and (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-ols (25b, 25d) (190 mg) and 4-nitrobenzoylchloride (380 mg) was dissolved in dry pyridine (10 ml) and stirred 48 hours. The mixture was poured into water (50 ml), extracted with benzene (2 * 50 ml) and the organic extracts washed with water (10 * 100 ml), dried with sodium sulphate and after removal of solvent gave a mixture, 75:25 (ratio estimated by inspection of peaks at δ_C 52.5 and 53.4 of ^{13}C n.m.r. spectrum) of (2RS, 3SR, 4SR)- and (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-yl 4-nitrobenzoate (32, R=PhCH(CH$_3$)) as an oil. υ_{max} 1735, 1725 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.28 - 1.35, (H1)$_3$; 2.98 - 3.12, H2; 3.45 - 3.6, H4; 4.9 - 5.2, H6; 5.7 - 5.82, H3; 6.0 - 6.25, H5; 7.1 - 7.4, 8.1 - 8.3, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C (32b, R=PhCH(CH$_3$)) 16.0, C1; 41.3, C2; 53.4, C4; 81.4, C3; 118.2, C6; 132.5, C5; 163.9, C=O; and (32d, R=PhCH(CH$_3$)) 19.2, C1; 42.0, C2; 52.5, C4; 80.5, C3; 117.2, C6; 137.2, C5; and phenyl carbons (32b, 32d, R=PhCH(CH$_3$)) 123.6, 126.8, 126.9, 127.6, 127.7, 128.6, 128.8, 130.5, 140.9, 143.2, 150.5.

2,4-Diphenyl-5-hexen-3-yl 3,5-dinitrobenzoates. A mixture (75:25) of (2RS, 3SR, 4SR)- and (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-ols (25b, 25d) (200 mg) and 3,5-dinitrobenzoylchloride (340 mg) was dissolved in dry pyridine (10 ml) and stirred 48 hours. Water (10 ml) and sulphuric acid (2 drops) were added and the mixture shaken, filtered and the reaction

Experimental

product washed with sodium hydroxide (2%, 5 ml) and water (5 ml) to give a

wax, a mixture, 80:20 (ratio estimated by inspection of peaks δ_C 52.5 and 53.3

of ^{13}C n.m.r. spectrum) of (2RS, 3RS, 4RS)- and (2RS, 3SR, 4SR)-2,4-diphenyl-

5-hexen-3-yl 3,5-dinitrobenzoate. (33, R=PhCH(CH$_3$)) υ_{max} 1730 cm^{-1}.

^{1}H n.m.r. (CDCl$_3$) δ_H 1.37, $J_{1,2}$ 7 Hz, (H1)$_3$; 3.1, $J_{3,4}$ 7 Hz, H2; 3.43 - 3.8, H4;

4.87 - 5.27, H6; 5.8, $J_{2,3}$ 6 Hz, $J_{3,4}$ 6 Hz, H3; 7.27, W$_{h/2}$ 4 Hz, 8.9 - 9.2, ArH.

^{13}C n.m.r. (CDCl$_3$) δ_C (33b, R=PhCH(CH$_3$)) 15.6, C1; 40.9, C2; 53.3, C4; 82.7, C3;

118.5, C6; 132.5, C5; 161.8, C=O. (33d, R=PhCH(CH$_3$)) 19.0, C1; 41.2, C2; 52.5, C4;

81.9, C3; 117.7, C6; 137.2, C5; and phenyl carbons (33b, 33d, R=PhCH(CH$_3$))

122.3, 127.0, 127.1, 127.6, 127.7, 128.2, 128.4, 128.7, 129.0, 129.2, 140.5, 142.8,

148.7. This solid was recrystallised from ethanol to give crystals of

(2RS, 3SR, 4SR)-2,4-diphenyl-5-hexen-3-yl 3,5-dinitrobenzoate m.p. 126 - 7°C.

^{13}C n.m.r. δ_C 15.6, 40.9, 52.5, 82.8.

(2RS, 3RS, 4RS)-2,4-Diphenyl-5-hexen-3-yl 3,5-dinitrobenzoate.

(2RS, 3RS, 4RS)-2,4-Diphenyl-5-hexen-3-ol (25d) and 3,5-dinitrobenzoyl-

chloride were dissolved in dry pyridine (10 ml) and stirred 48 hours. Water

(10 ml) and sulphuric acid (4 drops) were added and the mixture shaken,

filtered and the reaction product washed with sodium hydroxide (5%, 10 ml)

and water (10 ml) to give a solid which was recrystallized from ethanol to

give (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-yl 3,5-dinitrobenzoate (33d,

R=PhCH(CH$_3$)) ^{1}H n.m.r. (CDCl$_3$) δ_H 1.39, $J_{1,2}$ 7 Hz, (H1)$_3$; 3.25, $J_{1,2}$ 7 Hz, $J_{2,3}$

5.4 Hz, H2; 3.64, $J_{4,5}$ 8 Hz, $J_{3,4}$ 8 Hz, H4; 5.1 - 5.24, (H6)$_2$; 5.78, $J_{2,3}$ 5.4 Hz, $J_{3,4}$

8 Hz, H3; 6.10, $J_{5,6a}$ 16 Hz, $J_{5,6b}$ 10 Hz, $J_{4,5}$ 8 Hz, H5; 7.1 - 7.4, ArH. ^{13}C n.m.r.

(CDCl$_3$) δ_C 19.1, C1; 41.7, C2; 52.6, C4; 81.8, C3; 118.1, C6; 137.2, C5; 122.0, 127.0,

128.3, 128.4, 128.5, 128.9, 129.3, 138.4, 141.2, C=O, phenyl carbons.

4-Phenyl-5-hexen-1,2,3-triols

(E)-3-Chloro-1-phenylpropene (1.5 g, 10 mmol), glyceraldehyde (0.9 g,

10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g,

Experimental

4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were reacted as above to give an oil (1.47 g). The product mixture of impure 4-phenyl-5-hexen-1,2,3-triols (26) was not purified further. (Found CIMS (C_4H_{10}): 208.1089; $C_{12}H_{16}O_3$ requires 208.11001). ^1H n.m.r. (CDCl$_3$) 3.3 - 3.9, m; 4.3, d; 4.65, d; 5.0 - 5.4, 5.9 - 6.7, 7.0 - 7.5.

1,4-Di-(2-phenyl-3-buten-1-ol)-benzenes

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), terephthaldicarboxaldehyde (1.34 g, 10 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as above to give 1,4-di-(2-phenyl-3-buten-1-ol)-benzene (27) as an oil (3 g). (Found CIMS(C_4H_{10}): M+H$^+$-H$_2$O = 353.1860, M-PhCHCH=CH$_2$ = 253.1232, M-PhCHCH=CH$_2$-H$_2$O = 235.1133; $C_{26}H_{26}O_2$ requires 370.1933). υ_{max} 3425, 1060, 915, 740, 705 cm^{-1}. ^1H n.m.r. (CDCl$_3$) δ_H 2.36, W$_{h/2}$ 10 Hz, OH; 3.4 - 3.51, H2, H2'; 4.73 - 4.84, H1, H1'; 5.13 - 5.25, (H4)$_2$; 6.12 - 6.26, H3, H3'; 6.92 - 7.38, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 59.0, 59.3, C2, C2'; 76.9, C1, C1'; 118.1, 118.2, C4, C4'; 137.5, 137.6, C3, C3'; 125.97, 126.02, 126.3, 128.1, 128.3, 128.4, 140.2, 140.7, phenyl carbons.

3,6-Diphenylocta-1,7-dien-4,5-diols

(i) From glyoxal

(E)-3-chloro-1-phenylpropene (6 g, 40 mmol), 40% w/w solution of glyoxal (29) in water (2.9 g, 20 mmol), tetrahydrofuran (10 ml), water (4.2 ml), tin powder (2 g, 16.8 mmol), aluminium powder (1 g, 37 mmol) and 3 drops of hydrobromic acid were reacted as above to give an oil (2.2 g) shown to be a mixture of four stereoisomers, (3RS, 4SR, 5RS, 6SR)-, (3RS, 4SR, 5SR, 6RS)-, (3RS, 4RS, 5RS, 6SR)- and (3RS, 4RS, 5SR, 6RS)-3,6-diphenylocta-1,7-dien-4,5-diol (30a, 30b, 30c, 30d). υ_{max} 3450, 705 cm^{-1}. ^1H n.m.r. (CDCl$_3$) δ_H crude 3.4 - 3.7, 3.9 - 4.1, H3, H4, H5, H6; 5.0 - 5.3, H1, H8; 5.80, J=17.1 Hz, J=10.2 Hz,

Experimental

J=8.8 Hz, 5.95, J=17.7 Hz, J=9.6 Hz, J=8.6 Hz, 5.99, J=17 Hz, J=10.1 Hz, J=9 Hz, 6.14, J=16.5 Hz, J=10.6 Hz, J=8.8 Hz, 6.25, J=17 Hz, J=10 Hz, J=9 Hz, H2, H7; 6.9 - 7.5 ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C crude 53.8, 54.0, C3, C6; 72.0, 72.1, 72.5, 72.7, C4, C5; 117.1, 117.3, 117.4, 117.5, C1, C8; 138.0, 138.2, 139.3, C2, C7; 126.4, 126.7, 126.8, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 140.7, 140.9, 141.1, phenyl carbons. A portion of the oil was purified by radial chromatography on a 2 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate. Elution was effected with 10% - 20% ether - petroleum ether mixtures. Two fractions of 3,6-diphenylocta-1,7-dien-4,5-diol were obtained. The first fraction was a mixture of isomers: (Found CIMS (NH$_3$): M+NH$_4^+$ = 312.2006; C$_{20}$H$_{24}$O$_2$ requires 294.1621). ^{1}H n.m.r. (CDCl$_3$) δ_H 2.27, W$_{h/2}$ 18 Hz, OH; 3.41 - 3.66, 3.94 - 4.06, H3, H4, H5, H6; 5.08 - 5.22, H1, H8; 5.74 - 6.61, H2, H7; 6.95 - 7.37, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 53.9, 54.2, C3, C6; 72.0, 72.1, 72.6, C4, C5; 117.1, 117.2, 117.3, 117.5, C1, C8; 138.0, 139.3, C2, C7; 126.8, 128.2, 128.3, 128.7, 128.8, 140.7, 140.9, phenyl carbons. The second fraction was the pure diastereomer: (3RS, 4SR, 5SR, 6RS)-(30b). ^{1}H n.m.r. (CDCl$_3$) δ_H 2.17, W$_{h/2}$ 10 Hz, OH; 3.33 - 3.83, H3, H4, H5, H6; 4.92 - 5.33, H1, H8; 5.5 - 6.75, H2, H7; 7.33, W$_{h/2}$ 10 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 54.2, C3, C6; 72.0, C4, C5; 117.4, C1, C8; 139.3, C2, C7; 126.7, 128.1, 128.4, 128.5, 128.7, 128.9, 140.6, phenyl carbons.

(ii) From 2,3-dihydroxy-1,4-dioxane

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), 2,3-dihydroxy-1,4-dioxane (28) (1.2 g, 10 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol), aluminium powder (0.5 g, 18.5 mmol) and 3 drops of hydrobromic acid were reacted as above to give an oil (2.59 g) shown by ^{13}C n.m.r. to be a mixture of four stereoisomers, (3RS, 4SR, 5RS, 6SR)-, (3RS, 4SR, 5SR, 6RS)-, (3RS, 4RS, 5RS, 6SR)- and (3RS, 4RS, 5SR, 6RS)- 3,6-diphenylocta-1,7-dien-4,5-diol (30a, 30b, 30c, 30d). ν_{max} 3450, 705 cm^{-1}. ^{1}H n.m.r. (CCl$_4$) δ_H 3.17 - 3.83, H3, H4, H5, H6; 4.67 - 5.17, H1, H8; 5.33 - 6.5, H2,

Experimental

H7; 7.17, $W_{h/2}$ 10 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) d_C 53.8, 54.0, 54.1, C3, C6; 72.0, 72.1, 72.5, 72.7, C4; C5; 117.1, 117.3, 117.4, C1, C8; 138.0, 138.1, 139.3, C2, C7; 126.3, 126.4, 126.7, 126.8, 127.5, 127.6, 127.8, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 140.6, 140.9, 141.1, phenyl carbons.

Preparation of 3,6-Diphenylocta-1,7-dien-4,5-diol acetonides[83JE1084]

(i) From a mixture of diols. A solution of crude 3,6-diphenylocta-1,7-dien-4,5-diols **(30)** (200 mg) and anhydrous ferric chloride (60 mg) in anhydrous acetone (10 ml) was refluxed for 30 minutes. The mixture was cooled and aqueous potassium carbonate (2 ml, 10%) and water (10 ml) was added. The mixture was extracted with dichloromethane (3 * 10 ml) and the combined organic extracts washed with water (10 ml), dried with sodium sulphate and the solvent evaporated to give a mixture of 3,6-diphenylocta-1,7-dien-4,5-diol acetonides **(31)** as an oil (190 mg). (Found (C$_4$H$_{10}$): M$^+$-PhCHCH=CH$_2$ = 217.1290; C$_{23}$H$_{26}$O$_2$ requires 334.1934). ^{1}H n.m.r. (CDCl$_3$) δ_H 1.23, $W_{h/2}$ 3 Hz, 1.43, $W_{h/2}$ 3 Hz, (H9)$_3$, (H10)$_3$; 4.7 - 5.3, (H1)$_2$, (H8)$_2$; 5.6 - 6.6, H2, H7; 7.27, $W_{h/2}$ 8 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 27.4, 29.3, C9, C10; 52.5, 52.9, 53.2, 53.7, C3, C6; 81.0, 81.1, 81.9, 82.3, C4, C5; 116.0, 116.4, 116.9, C8, C1; 137.6, 137.8, 138.8, 139.0, C2, C7; 126.7, 127.0, 128.1, 128.3, 128.4, 128.5, 128.6, 129.2, phenyl carbons.

(ii) From (3RS, 4SR, 5RS, 6SR)-3,6-diphenylocta-1,7-dien-4,5-diol. A solution of a (3RS, 4SR, 5RS, 6SR)-3,6-diphenylocta-1,7-dien-4,-diol **(30b)** (24 mg) and anhydrous ferric chloride (20 mg) in anhydrous acetone (5 ml) was refluxed for 30 minutes. The mixture was cooled and aqueous potassium carbonate (1 ml, 10%) and water (5 ml) was added. The mixture was extracted with dichloromethane (3 * 10 ml) and the combined organic extracts washed with water (10 ml), dried with sodium sulphate and the solvent evaporated to give 3,6-diphenylocta-1,7-dien-4,5-diol acetonide **(31b)** as an oil (27 mg). (Found: M$^+$ = 334.192170; C$_{23}$H$_{26}$O$_2$ requires 334.1934). ^{1}H n.m.r. (CDCl$_3$) δ_H 1.23, $W_{h/2}$ 2 Hz, 1.43, $W_{h/2}$ 2 Hz, (H9)$_3$, (H10)$_3$; 2.75 - 2.85,

Experimental

H3, H6; 4.0 - 4.2, H4, H5; 4.73 - 5.3, (H1)$_2$, (H8)$_2$; 6.15, J$_{7,8a}$ 16.8 Hz, J$_{7,8b}$ 9.8 Hz,

J$_{6,7}$ 7.8 Hz, H2, H7; 7.23, W$_{h/2}$ 12 Hz, ArH. ^{13}C n.m.r. (CDCl$_3$) δ$_C$ 27.4, C9, C10;

53.0, C3, C6; 81.9, C4, C5; 108.7, C11; 116.9, C8, C1; 126.8, p; 128.4, 128.6, o, m;

137.6, C2, C7; 141.0, i.

Reaction of (E)-3-Bromo-1-(4-methoxyphenyl)-propene with benzaldehyde

(E)-3-Bromo-1-(4-methoxyphenyl)-propene[36] (4.54 g), benzaldehyde (2.12 g),

tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g), aluminium powder

(0.5 g) and three drops hydrobromic acid were reacted as above to give a

mixture (4.95 g) which could not be separated into components and

identified.

Preparation of 4-Phenyl-4-penten-2-ol

(i) 3-Chloro-2-phenylpropene (3 g, 20 mmol), excess acetaldehyde (3 g),

tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g), aluminium powder

(0.5 g) and 3 drops of hydrobromic acid were reacted as above to give an oil.

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[36]   *Preparation of (E)-3-Bromo-1-(4-methoxyphenyl)-propene*
Anethole (4.1 g) and N-bromosuccinamide (5 g) were dissolved in carbon
tetrachloride (500 ml) and refluxed under an infra-red lamp for 2.5 hours. The
reaction mixture was cooled to precipitate succinamide and filtered and the filtrate
evaporated to give a yellow solid (E)-3-bromo-1-(4-methoxyphenyl)-propene (54a)
was obtained. ^{1}H n.m.r. (CDCl$_3$) δ$_H$ 3.8, MeO; 4.17, J$_{2,3}$ 7 Hz, (H3)$_2$; 6 - 6.5, H1, H2; 6.7 -
7.5, ArH.
Preparation of (E)-3-Chloro-1-(4-methoxyphenyl)-propene
p-Methoxycinnamic acid (1 g) was dissolved in methanol (50 ml) and concentrated
sulphuric acid (1 ml) added. The mixture was stirred and refluxed gently for 3 hours
and poured into water (50 ml), extracted with ether (2 x 100 ml), dried with sodium
sulphate and after removal of solvent gave the methyl ester (0.99 g) as a crystalline
solid. This solid was dissolved in dichloromethane (25 ml) and lithium aluminium
hydride (0.5 g) was added and the solution refluxed 3 hours. Excess lithium
aluminium hydride was destroyed with sodium sulphate decahydrate and the
mixture diluted with sulphuric acid (1%) and extracted with ether (200 ml). The
solvent was removed to give 3-(4-methoxyphenyl)-2-propen-1-ol (840 mg) as a solid.
To a solution of 3-(4-methoxyphenyl)-2-propen-1-ol (320 mg, 2 mmol) and carbon
tetrachloride (2 ml) was added triphenylphosphine (682 mg, 2.6 mmol) and the
reaction heated and stirred 1 hour. Pentane (5 ml) was added and the mixture stirred
an additional 5 minutes, filtered, the solid washed with pentane (2 ml) and the
solvent removed to give (E)-3-chloro-1-(4-methoxyphenyl)-propene (54b) (200 mg).
^{1}H n.m.r. (CDCl$_3$) δ$_H$ 3.8, OMe; 4.23, J$_{1,2}$ 7.6 Hz, (H1)$_2$; 6.15, J$_{1,2}$ 7.6 Hz, H2; 6.6, J$_{2,3}$
15.6 Hz, H3; 6.8 - 6.9, 7.3 - 7.4, ArH. ^{13}C n.m.r. (CDCl$_3$) δ$_C$ 45.9, C1; 55.3, OMe; 122.6,
133.8, C2, C3; 114.0, m; 127.9, o; 159.7, p.

Experimental

Analysis of this oil by ^{1}H n.m.r. indicated both 4-phenyl-4-penten-2-ol **(34)**

and butan-2,3-diol (^{1}H n.m.r. (CDCl$_3$) δ_H 1.06, J$_{1,2}$ 6 Hz, (H2)$_3$; 5.03, J$_{1,2}$ 6 Hz,

H1. ^{13}C n.m.r. (CDCl$_3$) δ_C 20.6, 98.5) were present. Removal of the butan-

2,3-diol by distillation under reduced pressure gave 4-phenyl-

4-penten-2-ol[82JO3377] **(34)** (3.72 g) as an oil. (Found CIMS (C$_4$H$_{10}$): M+H$^+$-H$_2$O

= 145.1013; C$_{11}$H$_{14}$O requires 162.10453) ^{1}H n.m.r. (CDCl$_3$) δ_H 1.20, J$_{1,2}$ 6.2 Hz,

(H1)$_3$; 1.76, OH; 2.58, J$_{3a,3b}$ 14 Hz, J$_{2,3a}$ 8.4 Hz, J$_{3a,5a}$ 1.4 Hz, H3a; 2.72, J$_{3a,3b}$

14 Hz, J$_{2,3b}$ 4.7 Hz, J$_{3b,5a}$ 1.5 Hz, H3b; 3.8 - 3.9, H2; 5.16, H5a; 5.4, H5b; 7.24 - 7.42,

ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 22.9, C1; 45.5, C3; 65.8, C2; 115.1, C5; 126.2, 128.4, o,

m; 127.7, p; 140.6, C4; 145.5, i.

(ii) Crude 3-bromo-2-phenylpropene[37] (13 g), excess acetaldehyde (10 ml),

tetrahydrofuran (20 ml), water (12 ml), tin powder (4 g), aluminium powder

(2 g) and 3 drops of hydrobromic acid were reacted as above to give an oil

(9.4 g). This oil was purified by radial chromatography on a silica gel P.F. 254

with CaSO$_4$.^{1}/$_2$H$_2$O plate eluted with ether - petroleum ether mixtures to

give 4-phenyl-4-penten-2-ol[82JO3377] **(34)** (2.9 g).

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[37]   *Preparation of 3-Bromo-2-phenylpropene*
        A mixture of 2-phenylpropene **(23)** (50 g) and N-bromosuccinimide (30 g) in carbon
        tetrachloride (20 ml) was refluxed at 160 - 170°C until completion of reaction and the
        mixture then allowed to cool slowly. The precipitate succinimide was separated by
        filtration and after distillation at reduced pressure a mixture (25:75) of 1-bromo-
        2-phenylpropene **(56b)** and 3-bromo-2-phenylpropene[65JO3258] **(56a)** was recovered.
        ^{1}H n.m.r. (CCl$_4$) δ_H 4.2, (H3)$_2$; 5.4, H1$_{anti}$; 5.5, H1$_{syn}$; 7.0 - 7.5, ArH.

Experimental

Preparation of 1,3-Diphenyl-3-buten-1-ol and derivative

(i) 3-Chloro-2-phenylpropene[38] (1 g, 7 mmol), benzaldehyde (0.7 g, 7 mmol), tetrahydrofuran (2 ml), water (1 ml), tin powder (0.33 g), aluminium powder (0.17 g) and 2 drops of hydrobromic acid were reacted as above to give an oil (1.33 g). The oil was purified by radial chromatography on a 4 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give white crystals of 1,4-diphenyl-3-buten-1-ol[73CF0618, 83MSDodg] (41) (0.476 g). Elution was effected with petroleum ether and 10% ether - petroleum ether. υ_{max} 3450 cm^{-1}. M.p 47 - 48°C. (Found C, 85.45; H, 7.14%; $C_{16}H_{16}O$ requires C, 85.68; H, 7.19%).

(Found EIMS: M^+ = 224.118640, $C_{16}H_{16}O$ requires 224.1201. ^1H n.m.r. (CDCl$_3$) δ_H 2.09, OH; 2.78, $J_{2,2}$ 14 Hz, $J_{1,2a}$ 9 Hz, $J_{2a,4}$ 2 Hz, H2a; 3.05, $J_{2,2}$ 14 Hz, $J_{1,2b}$ 4 Hz, $J_{2b,4}$ 1 Hz, H2b; 4.71, $J_{1,2a}$ 9 Hz, $J_{1,2b}$ 4 Hz, H1; 5.15, $J_{2,4}$ 1.7 Hz, H4; 5.40, $J_{2,4}$ 1.5 Hz, H4; 7.23 - 7.45, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 46.0, C2; 72.1, C1; 115.7, C4; 125.7, 126.2, 128.3, 128.4, o, m, o', m'; 127.5, 127.7, p, p'; 140.2, 143.8, 144.9, C3, i, i'.

(ii) 3-Bromo-2-phenylpropene (with 1-bromo-2-phenylpropene impurity) (13 ml), benzaldehyde (9 g), tetrahydrofuran (20 ml), water (12 ml), tin powder (4 g), aluminium powder (2 g) and a few drops of hydrobromic acid were reacted as above to give an oil (21 g) which on standing gave some crystals of 1,2-diphenyl-1,2-ethanediol. Radial chromatography on a 4 mm silica gel P.F.254 with $CaSO_4.^1/_2H_2O$ plate eluted with 0 - 25% ether - petroleum ether mixtures gave 1,3-diphenyl-3-buten-1-ol[73CF0618, 83MSDodg]

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[38]   *Preparation of 3-Chloro-2-phenylpropene*
A mixture of 2-phenylpropene (23) (100 g) and N-chlorosuccinimide (68 g) in carbon tetrachloride (50 ml) was refluxed at 160 - 170°C. These conditions were maintained until the N-chlorosuccinimide had completely dissolved at which point the mixture was allowed to cool slowly over the next 3 hours. The precipitated succinimide was separated by filtration and the carbon tetrachloride was removed by distillation under reduced pressure. Distillation under reduced pressure yielded a mixture of 3-chloro-2-phenylpropene (55a) and 1-chloro-2-phenylpropene[65JO3258] (55b). Separation of the chlorides was accomplished by fractional distillation on a spinning band column to give 1-chloro-2-phenylpropene (55b) (4 g, 63°C, 2 mmHg) (^1H n.m.r. (CCl$_4$) δ_H 2.2, (H3)$_3$; 6.2, H1; 7.3, ArH) and 3-chloro-2-phenylpropene (55a) (12 g, 76°C, 2 mmHg). ^1H n.m.r. (CCl$_4$) δ_H 4.47, (H3)$_2$; 5.47, H1$_{anti}$; 5.57, H1$_{syn}$; 7.17 - 7.63, ArH.

Experimental

(41) (3.37 g) as a solid. ^{1}H n.m.r. (CDCl$_3$) δ_H 2.85, J$_{2a,2b}$ 14 Hz, J$_{1,2a}$ 4.3 Hz, J$_{2a,4}$ 1.3 Hz, H2a; 3.01, J$_{2a,2b}$ 14 Hz, J$_{1,2b}$ 9 Hz, H2b; 4.73, J$_{1,2b}$ 9 Hz, J$_{1,2a}$ 4.3 Hz, H1; 5.17, H4a; 5.41, H4b; 7.21 - 7.49, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 46.0, C2; 72.1, C1; 115.7, C4; 125.7, 126.2, 128.3, 128.4, o, m, o', m'; 127.5, 127.7, p, p'; 140.2, 143.8, 144.9, C3, i, i'.

1-Acetoxy-1,3-diphenyl-3-butene. 1,3-Diphenyl-1,3-buten-1-ol (41) (240 mg) was added to a solution of acetic anhydride (0.5 ml) and pyridine (10 ml) and stirred overnight. The mixture was poured into ether (150 ml) and washed with sodium bicarbonate (4 * 20 ml), dilute sulphuric acid (10 * 20 ml) and water (20 ml) and dried with sodium sulphate. The solvent was removed under reduced pressure to give 1-acetoxy-1,3-diphenyl-3-butene (42) (270 mg) as an oil. v_{max} 690, 1010, 1200, 1720 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.95, OCOMe; 2.92, J$_{1,2b}$ 6 Hz, J$_{2a,2b}$ 13 Hz, H2b; 3.14, J$_{1,2a}$ 8 Hz, J$_{2a,2b}$ 13 Hz, H2a; 4.99, H4a; 5.27, H4b; 5.83, J$_{1,2a}$ 8 Hz, J$_{1,2b}$ 6 Hz, H1; 7.24 - 7.40, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 21.1, Me; 42.6, C2; 74.7, C1; 115.6, C4; 169.9, C=O; 126.2, 126.4, 127.5, 127.8, 128.2, 128.3, 140.1, 140.6, 144.0, C3, phenyl carbons.

Preparation of 3-Methyl-1-phenyl-3-buten-1-ol

3-Chloro-2-methylpropene (9.05 g, 0.1 mol), benzaldehyde (9.2 g, 0.1 mol), tetrahydrofuran (20 ml), water (12 ml), tin powder (4 g), aluminium powder (2 g) and 3 drops of hydrobromic acid were reacted as above to give an oil (15 g) which on standing gave some crystals. These crystals were identified as 1,2-diphenylethan-1,2-diol. M.p. 128 - 30°C. (Found C, 78.46; H, 6.55%. C$_{14}$H$_{14}$O$_2$ requires C, 78.48; H, 6.59%). ^{1}H n.m.r. (CDCl$_3$) δ_H 2.26, OH; 4.81, H1, H2; 7.21 - 7.34, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 78.1, C1, C2; 127.0, 128.0, 128.1, 139.6, phenyl carbons. The remaining oil was purified by radial chromatography on a 4 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate to give 3-methyl-1-phenyl-3-buten-1-ol (4.68 g) as an oil. Elution was effected with petroleum ether and ether mixtures to give 3-methyl-1-phenyl-

Experimental

3-buten-1-ol.[85JO1373, 83MSDodg] (46) υ_{max} 3350, 1640, 990 cm^{-1}. ^{1}H n.m.r.

(CDCl$_3$) δ_H 1.78, C3-Me; 2.21, OH; 2.42, J$_{1,2}$ 7 Hz, (H2)$_2$; 4.8, J$_{1,2}$ 7 Hz, H1; 4.85,

H4a; 4.91, H4b; 7.23 - 7.39, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 22.4, C3-Me; 48.3, C2;

71.4, C1; 113.9, C4; 142.2, C3; 125.6, 127.3, 128.3, phenyl carbons; 143.9, i.

Reaction of (E)-3-chloro-1-phenylpropene with acetophenone

(E)-3-Chloro-1-phenylpropene (3 g, 20 mmol), acetophenone (2.4 g,

20 mmol), tetrahydrofuran (5 ml), water (3 ml), tin powder (1 g, 8.4 mmol),

aluminium powder (0.5 g, 18.5 mmol) and 3 drops hydrobromic acid were

reacted as above to give an oil (3.4 g) which contained no starting materials.

υ_{max} 3430 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.4 - 1.5; 2.1 - 2.3; 2.5; 6.2 - 6.6; 7.0 - 7.2.

^{13}C n.m.r. (CDCl$_3$) δ_C 24.8, 25.0, 26.5, 78.6, 115.0, 126.4, 126.8, 127.0, 127.2, 127.4,

127.5, 127.7, 128.3, 128.5, 133.1.

ZINC MEDIATED ADDITION OF ALLYLIC HALIDES TO ALDEHYDES.

2-Methyl-1-phenyl-3-buten-1-ols

A mixture of (E)-1-bromo-2-butene (2.6 g, 20 mmol) and benzaldehyde (2.2 g,

20 mmol) was dissolved in tetrahydrofuran (1 ml) and saturated aqueous

ammonium chloride (5 ml). Zinc powder (1.3 g, 20 mmol) was added and

the mixture stirred for 1 hour at room temperature, filtered, the solid

washed with ether (2 * 100 ml), and the filtrate washed with water (50 ml),

dried with sodium sulphate and after removal of solvent gave an oil (3.1 g),

shown to be a mixture 57:43 (ratio determined by integration of peaks at δ_H

1.0 and 0.86 of ^{1}H n.m.r. spectrum) of (1RS, 2RS)- and (1RS, 2SR)-2-methyl-

1-phenyl-3-buten-1-ol[77AJ0835, 80JM0137, 82OM0149] (1a, 1b). υ_{max} 3440, 1455,

1190, 700 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 0.86, J$_{2,5}$ 6.9 Hz, 1.0, J$_{2,5}$ 7 Hz, Me; 2.26,

OH; 2.47, J$_{2,2-Me}$ 7 Hz, 2.56, J$_{2,2-Me}$ 6.9 Hz, H2; 4.35, J$_{1,2}$ 7.8 Hz, 4.58 J$_{1,2}$ 5.55 Hz,

H1; 5.00 - 5.06, 5.15 - 5.21, (H4)$_2$; 5.68 - 5.86, H3; 7.24 - 7.35, ArH. ^{13}C n.m.r.

Experimental

(CDCl$_3$) δ_C 14.1, 16.5, Me; 44.6, 46.1, C2; 77.2, 77.7, C1; 115.3, 116.5, C4; 134.2, 140.1, C3; 126.3, 126.6, 127.1, 127.4, 127.8, 128.0, 142.2, 142.4, phenyl carbons.

1,2-Diphenyl-3-buten-1-ols

(E)-Chloro-1-phenylpropene (3 g, 20 mmol), benzaldehyde (2.2 g, 20 mmol), tetrahydrofuran (1 ml), saturated aqueous ammonium chloride (5 ml), zinc powder (1.3 g, 20 mmol) were reacted as above to give an oil (3.9 g), a mixture, 3:1 (ratio estimated by inspection of peaks δ_C 58.4 and 58.9 of ^{13}C n.m.r. spectrum) of (1RS, 2SR)- and (1RS, 2RS)-1,2-diphenyl-3-buten-1-ol[84AJ0065] (8b, 8a). ^{1}H n.m.r. (CDCl$_3$) δ_H 2.23, W$_{h/2}$ 8 Hz, OH; 3.2 - 3.67, H2; 4.7 - 5.3, H1, (H4)$_2$; 5.77 - 6.57, H3; 7.13, 7.17, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 58.4, 58.9, C2; 77.1, 77.3, C1; 116.9, 117.9, C4; 137.9, C3; 126.0, 126.4, 126.6, 127.2, 127.8, 128.2, 128.4, 128.9, 129.6, phenyl carbons.

GRIGNARD PREPARATIONS OF HOMOALLYLIC ALCOHOLS.

A number of homoallylic alcohols were prepared using Barbier Grignard conditions[84AJ0065]. The preparation of the 1,2-diphenyl-3-buten-1-ols is representative of the procedure.

1,2-Diphenyl-3-buten-1-ols

(E)-3-Chloro-1-phenylpropene (0.1 ml) and a crystal of iodine were added to magnesium turnings (1.8 g) and dry ether (10 ml) and the mixture vigorously stirred and heated to initiate reaction. A solution of (E)-3-chloro-1-phenylpropene (2 g, 13 mmol) and benzaldehyde (1.2 g, 11 mmol) in dry ether (10 ml) was added at such a rate as to maintain a gentle reflux (30 min). The mixture was stirred and kept under reflux for a further 3 hours, cooled and poured into ice-cold saturated aqueous ammonium chloride solution (20 ml). The ether layer was separated and the aqueous layer extracted several times with ether. The combined ether extracts were washed with

Experimental

water, dried over magnesium sulphate and after removal of solvent gave a yellow oil (3 g); shown by g.l.c. to be a mixture, 1:1 of (1RS, 2SR)- and (1RS,2RS)-1,2-diphenyl-3-buten-1-ol[84AJ0065] (8b, 8a). υ_{max} 3450, 920, 760, 700 cm^{-1}. [1]H n.m.r. (CCl$_4$) δ_H 1.87, $W_{h/2}$ 9 Hz, OH; 2.18, $W_{h/2}$ 7 Hz, OH; 3.3 - 3.65, H2; 4.6 - 5.3, H1, (H4)$_2$; 5.6 - 6.5, H3; 7.10, 7.17, ArH. [13]C n.m.r. (CDCl$_3$) δ_C 58.4, 59.0, C2; 77.2, 77.4, C1; 117.1, 118.2, C4; 137.7, 137.8, C3; 126.5, 126.6, 127.0, 127.3, 127.7, 127.9, 128.1,128.3, 128.6, 128.7, 128.8, 140.3, 140.7, 141.9, phenyl carbons. The oil crystallized to give crystals of (1RS, 2RS)-1,2-diphenyl-3-buten-1-ol (8a) which were collected and recrystallized from dichloromethane : pentane; m.p. 76°C. [1]H n.m.r. (CCl$_4$) δ_H 1.62 $W_{h/2}$ 8 Hz, OH; 3.47 $J_{1,2}$ 7 Hz, H2; 4.6 - 5.1, H1, (H4)$_2$; 5.87 $J_{3,4}$ cis 10 Hz, $J_{3,4}$ trans 16 Hz, $J_{2,3}$ 7 Hz, H3; 7.17, $W_{h/2}$ 2 Hz, ArH. [13]C n.m.r. (CDCl$_3$) δ_C 58.4, C2; 77.4, C1; 117.1, C4; 137.7, C3; 127.0, 127.7, 127.9, 128.1, 128.6, 128.8, 140.3, 141.9 phenyl carbons.

3-Phenylhept-1,5-dien-4-ol

(E)-3-Chloro-1-phenylpropene (0.1 ml), magnesium turnings (0.48 g), dry ether (10 ml), (E)-3-chloro-1-phenylpropene (0.55 g, 3.7 mmol) and (E)-2-butenal (0.26 g, 3.7 mmol) in dry ether (10 ml) were reacted as above to give an oil (0.65 g) shown by [13]C n.m.r. to be a mixture of at least three compounds. [1]H n.m.r. (CDCl$_3$) δ_C 1.5 - 1.9, 2.5 - 2.8, 3.3 - 3.6, 4.2 - 5.3, 6.0 - 6.8, 7.0 - 7.6, 9.5 - 10. [13]C n.m.r. (CDCl$_3$) δ_C (14a) 57.0, C3; 117.1, C1; (14b) 17.7, C7; 57.3, C3; 75.5, C4; 117.7, C1; 131.4, C5; 138.2, C2; (unaccounted possibly 15a, 15b) 32.9, 32.0, 50.0, 114.6, 115.8, 135.9, 141.5; (phenyl carbons) 126.0, 126.3, 126.6, 126.9,127.7, 127.9, 128.4, 128.6.

1,4-Diphenylhexa-1,5-dien-3-ol

(E)-3-Chloro-1-phenylpropene (0.1 ml), magnesium turnings (1.8 g), dry ether (10 ml), (E)-3-chloro-1-phenylpropene (3 g, 20 mmol) and (E)-1-phenyl-propenal (2.64 g, 20 mmol) in dry ether (10 ml) were reacted as above to give

Experimental

an oil (2.37 g) shown by ^{13}C n.m.r. to be a mixture of several compounds.

υ_{max} 3425, 1680 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.85 - 1.88, 2.60 - 2.67, 3.37 - 3.54, 4.27 - 4.30, 4.47 - 4.56, 5.04 - 5.28, 6.03 - 6.75, 7.03 - 7.48, 9.66, 10.0. ^{13}C n.m.r. (CDCl$_3$) δ_C 39.1, 40.3, 50.0, 57.1, 57.2, 57.5, 61.9, 63.6, 75.0, 75.3, 76.5, 114.5, 115.7, 117.6, 117.7, 118.0, 118.1, 126.3, 126.4, 126.7, 126.9, 127.4, 127.6, 128.2, 128.3, 128.4, 128.5, 128.6, 129.7, 130.9, 131.0, 131.2, 131.3, 131.5, 136.6, 136.7, 137.4, 137.7, 140.1, 140.4, 141.3.

2,4-Diphenyl-5-hexen-3-ol

(E)-3-Chloro-1-phenylpropene (0.1 ml), magnesium turnings (0.48 g), dry ether (10 ml), (E)-3-chloro-1-phenylpropene (0.55 g, 3.6 mmol) and 2-phenyl-propanal (0.5 g, 3.7 mmol) in dry ether (10 ml) were reacted as above to give an oil (0.8 g), a mixture, approx. 1:3:3:4 (ratio estimated by inspection of ^{13}C n.m.r. spectrum) of four isomers of 2,4-diphenyl-5-hexen-3-ol (**25a, 25b, 25c, 25d**). υ_{max} 3475, 1500, 1460 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.29 - 1.60, (H1)$_3$; 2.38 - 2.40, 2.56 - 2.95, 3.26 - 3.41, 3.59 - 3.70, 3.93 - 4.05, C3, C4; 4.90 - 5.23, C6; 6.03 - 6.47, C5; 7.19 - 7.33, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 14.5, 15.1, 17.6, 19.2, C1; 40.2, 41.9, 42.1, 42.6, C2; 53.7, 54.0, 54.1, C4; 78.1, 78.6, C3; 116.3, 117.5, 117.9, C6; 137.4, 137.7, 138.0, 139.2, C5. Radial chromatography on a 2 mm silica gel 60 P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate eluted with 10% - 30% ether - petroleum ether mixtures successfully afforded (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-ol (**25d**). ^{1}H n.m.r. (CDCl$_3$) δ_H 1.36, J$_{1,2}$ 7 Hz, (H1)$_3$; 2.85, J$_{1,2}$ 7 Hz, J$_{2,3}$ 6.4 Hz, H2; 3.31, J$_{3,4}$ 7.4 Hz, J$_{4,5}$ 8 Hz, H4; 4.01, J$_{2,3}$ 6.4 Hz, J$_{3,4}$ 7.4 Hz, H3; 5.04, J$_{5,6a}$ 17 Hz, J$_{6a,6b}$ 2.5 Hz, J$_{4,6a}$ 1.5 Hz, H6a; 5.13, J$_{5,6b}$ 10 Hz, J$_{6a,6b}$ 2.5 Hz, H6b; 6.12, J$_{4,5}$ 8 Hz, J$_{5,6a}$ 17 Hz, J$_{5,6b}$ 10 Hz, H5; 7.23 - 7.32, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 19.4, C1; 42.6, C2; 54.1, C4; 78.3, C3; 116.4, C6; 139.6, C5; 126.5, 126.7, 128.2, 128.43, 128.46, 128.53, 128.7, 128.9, phenyl carbons. A further fraction was obtained containing a mixture of isomers. ^{13}C n.m.r. (CDCl$_3$) δ_C 14.5,

Experimental

15.1, 19.2, C1; 41.9, 42.1, 42.6, C2; 53.7, 54.0, 54.1, C3; 117.5, 117.8, 117.9, C6; 137.6, 137.8, 139.0, C5.

COMPETITION STUDIES

Cinnamyl chloride and aldehydes: Tin and aluminium mediated

(i) (E)-3-Chloro-1-phenylpropene (1.53 g, 10 mmol), benzaldehyde (1.06 g, 10 mmol), anisaldehyde (1.36 g, 10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were stirred for 24 hours at room temperature and after standard workup gave a mixture (3.7 g) of (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol (8b) (63%) and (1RS, 2SR)-1-(4-methoxyphenyl)-2-phenyl-3-buten-1-ol (11b) (37%). The ratio was determined by integration of peaks 4.83, $J_{1,2}$ 7.7 Hz, H1 and 4.79, $J_{1,2}$ 7.95 Hz, H1 respectively of ^{1}H n.m.r. spectra.

This reaction was repeated and stirred for 2 hours to give a mixture of (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol (8b) (69%) and (1RS, 2SR)-1-(4-methoxyphenyl)-2-phenyl-3-buten-1-ol (11b) (31%) and starting materials. The reaction was again repeated using 24 drops hydrobromic acid and gave no significant difference in product ratio.

(ii) (E)-3-Chloro-1-phenylpropene (1.53 g, 10 mmol), benzaldehyde (1.06 g, 10 mmol), 4-cyanobenzaldehyde (1.31 g, 10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were stirred for 24 hours at room temperature and after standard workup gave a mixture (3.26 g) of (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol (8b) (34%) and (1RS, 2SR)-1-(4-cyanophenyl)-2-phenyl-3-buten-1-ol (10b) (66%). The ratio was determined by integration

Experimental

of peaks 4.83, $J_{1,2}$ 7.7 Hz, H1 and 4.86, $J_{1,2}$ 7.7 Hz, H1 respectively of [1]H n.m.r. spectra.

(iii) (E)-3-Chloro-1-phenylpropene (1.53 g, 10 mmol), anisaldehyde (1.36 g, 10 mmol), 4-cyanobenzaldehyde (1.31 g, 10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were stirred for 24 hours at room temperature and after standard workup gave a mixture (4.14 g) of (1RS, 2SR)-1-(4-methoxyphenyl)-2-phenyl-3-buten-1-ol **(11b)** (38%) and (1RS, 2SR)-1-(4-cyanophenyl)-2-phenyl-3-buten-1-ol **(10b)** (62%). The ratio was determined by integration of peaks 4.79, $J_{1,2}$ 7.95 Hz, H1 and 4.86, $J_{1,2}$ 7.7 Hz, H1 respectively of [1]H n.m.r. spectra.

(iv) (E)-3-Chloro-1-phenylpropene (1.53 g, 10 mmol), benzaldehyde (1.06 g, 10 mmol), 4-nitrobenzaldehyde (1.51 g, 10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid. The mixture was stirred for 24 hours at room temperature and after standard workup [1]H n.m.r. indicated starting materials remained and neither benzaldehyde nor 4-nitro-benzaldehyde reacted with (E)-3-chloro-1-phenylpropene to give the homo-allylic alcohols.

(v) (E)-3-Chloro-1-phenylpropene (1.53 g, 10 mmol), benzaldehyde (1.06 g, 10 mmol), 4-methylbenzaldehyde (1.20 g, 10 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were stirred for 24 hours at room temperature and after standard workup gave a mixture (3.65 g) of (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol **(8b)** (61%) and (1RS, 2SR)-1-(4-methyl-phenyl)-2-phenyl-3-buten-1-ol **(12b)** (39%). The ratio was determined by

Experimental

integration of peaks 4.83, $J_{1,2}$ 7.7 Hz, H1 and 4.80, $J_{1,2}$ 6.5 Hz, H1 respectively of ^{1}H n.m.r. spectra.

Crotyl bromide and aldehydes: Tin and aluminium mediated

(vi) (E)-1-Bromo-2-butene (1.35 g, 10 mmol), benzaldehyde (2.12 g, 20 mmol), anisaldehyde (2.72 g, 20 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were stirred for 1 hour at room temperature and after standard workup gave a mixture (4.4 g) of (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol **(1a)** (46%) and (1RS, 2RS)-2-methyl-1-phenyl-3-buten-1-ol **(1b)** (32%) and (1RS, 2SR)-1-(4-methoxyphenyl)-2-methyl-3-buten-1-ol (10%) and (1RS, 2RS)-1-(4-methoxyphenyl)-2-methyl-3-buten-1-ol (11%). The ratio was determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1; and 4.37, $J_{1,2}$ 7.8 Hz, H1; and 4.54, $J_{1,2}$ 5.9 Hz, H1; and 4.31, $J_{1,2}$ 8.06 Hz, H1 respectively of ^{1}H n.m.r. spectra.

(vii) (E)-1-Bromo-2-butene (1.35 g, 10 mmol), benzaldehyde (2.12 g, 20 mmol), p-nitrobenzaldehyde (3.02 g, 20 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.5 g, 4.2 mmol), aluminium powder (0.25 g, 9.3 mmol) and 3 drops of hydrobromic acid were stirred for 1 hour at room temperature and after standard workup ^{1}H n.m.r. indicated starting materials remained and neither benzaldehyde nor 4-nitrobenzaldehyde reacted with (E)-1-bromo-2-butene to give the homoallylic alcohols.

(viii) (E)-1-Bromo-2-butene (0.405 g, 3 mmol), benzaldehyde (0.5 g, 5 mmol), p-cyanobenzaldehyde (0.660 g, 5 mmol), tetrahydrofuran (2.5 ml), water (1.5 ml), tin powder (0.16 g), aluminium powder (0.08 g) and 3 drops of hydrobromic acid were stirred for 2 hours at room temperature and after standard workup gave a mixture (1.45 g) of (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol **(1a)** (16%) and (1RS, 2RS)-2-methyl-1-phenyl-3-buten-1-ol **(1b)**

Experimental

(12%) and (1RS, 2SR)-1-(4-cyanophenyl)-2-methyl-3-buten-1-ol (43%) and

(1RS, 2RS)-1-(4-cyanophenyl)-2-methyl-3-buten-1-ol (27%). The ratio was

determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1 and 4.37, $J_{1,2}$ 7.8 Hz,

H1 and 4.71, $J_{1,2}$ 5.17 Hz, H1 and 4.475, $J_{1,2}$ 7.22 Hz, H1 respectively of

^{1}H n.m.r. spectra.

(ix) (E)-1-Bromo-2-butene (0.405 g, 3 mmol), benzaldehyde (0.5 g, 5 mmol),

4-methylbenzaldehyde (0.6 g, 5 mmol), tetrahydrofuran (2.5 ml), water

(1.5 ml), tin powder (0.16 g), aluminium powder (0.08 g) and 3 drops of

hydrobromic acid. The mixture was stirred for 2 hours at room temperature

and after standard workup gave a mixture (1.45 g) of (1RS, 2SR)-2-methyl-

1-phenyl-3-buten-1-ol (1a) (43%) and (1RS, 2RS)-2-methyl-1-phenyl-

3-buten-1-ol (1b) (33%) and (1RS, 2SR)-1-(4-methylphenyl)-2-methyl-

3-buten-1-ol (14%) and (1RS, 2RS)-1-(4-methylphenyl)-2-methyl-3-buten-1-ol

(10%). The ratio was determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1

and 4.37, $J_{1,2}$ 7.8 Hz, H1 and 4.56, $J_{1,2}$ 5.8 Hz, H1 and 4.32, $J_{1,2}$ 7.8 Hz, H1

respectively of ^{1}H n.m.r. spectra.

Cinnamyl tri-n-butyltin and aldehydes: with boron triflouride[80JA7109, 40TD2239]

(x) To a solution of benzaldehyde (4 mmol, 0.424 g) and 4-methyl-

benzaldehyde (4 mmol, 0.475 g) in dry dichloromethane (5 ml) was added

boron triflouride etherate (10 mmol) at -78°C under a nitrogen atmosphere.

Subsequently cinnamyl tri-n-butyltin[39] (2 mmol, 0.81 g) was added and the

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[39] *Preparation of Cinnamyltributyltin*
(E)-3-Chloro-1-phenyl-propene (0.1 ml, 3 drops) and a crystal of iodine were added to magnesium turnings (1.8 g) and dry tetrahydrofuran (10 ml) and the mixture vigorously stirred and heated to initiate reaction. A solution of (E)-3-chloro-1-phenyl-propene (4 g) and tributyltin chloride (8.74 g) in dry tetrahydrofuran (12 ml) was added at such a rate as to maintain a gentle reflux. The mixture was stirred and kept under reflux overnight, cooled and poured into ice-cold aqueous ammonium chloride solution (30 ml). The organic layer was separated and the aqueous layer extracted several times with ether. The combined organic layers were washed with water, dried with sodium sulphate and after removal of solvent gave cinnamyltri-butyltin as an oil. ^{1}H n.m.r.[102JA3774] (CDCl$_3$) δ_H 0.8 - 1.6, nBu$_3$; 1.95, J=7.5 Hz, CH$_2$;

Experimental

reaction mixture was allowed to warm to room temperature. The reaction was quenched with water and the organic phase was separated dried and the solvent removed to give an oil (1.5 g) a mixture of (1RS, 2SR)-1,2-diphenyl-3-buten-1-ol **(8b)** (70%) and (1RS, 2SR)-1-(4-methylphenyl)-2-phenyl-3-buten-1-ol **(12b)** (30%). The ratio was determined by integration of peaks 4.83, $J_{1,2}$ 7.7 Hz, H1 and 4.80, $J_{1,2}$ 6.5 Hz, H1 respectively of ^{1}H n.m.r. spectra.

(xi) To a solution of benzaldehyde (4 mmol, 0.424 g) and anisaldehyde (4 mmol, 0.544 g) in dry dichloromethane (5 ml) was added boron triflouride etherate (10 mmol) at -78°C under a nitrogen atmosphere. Subsequently cinnamyl tri-n-butyltin* (2 mmol, 0.81 g) was added and the reaction mixture was allowed to warm to room temperature. The reaction was quenched with water and the organic phase was separated dried and the solvent removed to give an oil (1.55 g). Although some reaction had taken place no homoallylic alcohols were evident in ^{1}H n.m.r. or ^{13}C n.m.r.

Crotyl tri-n-butyltin and aldehydes: with boron triflouride[80JA7109, 40TD2239]

(xii) To a solution of benzaldehyde (8 mmol, 0.848 g) and p-methyl-benzaldehyde (8 mmol, 0.980 g) in dry dichloromethane (10 ml) was added boron triflouride etherate (20 mmol) at -78°C under a nitrogen atmosphere. Subsequently crotyltri-n-butyltin[40] (4 mmol, 1.38 g) was added and the reaction mixture was allowed to warm to room temperature. The reaction was quenched with water and the organic phase was separated dried and the

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6.15 - 6.5, CH=CH; 7.1 - 7.4, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 9.5, 13.7, 27.3, 29.1, nBu$_3$; 30.6, CH$_2$; 124.9, 125.2, 125.7, 128.5, 131.2, CH=CH, phenyl carbons.

40   *Preparation of Crotyltributyltin;*
Crotyl bromide (0.1 ml, 3 drops) and a crystal of iodine were added to magnesium turnings (3.6 g) and dry tetrahydrofuran (20 ml) and the mixture vigorously stirred and heated to initiate reaction. A solution of crotyl bromide (7.5 g) and tributyltin chloride (17.4 g) in dry tetrahydrofuran (24 ml) was added at such a rate as to maintain a gentle reflux. The mixture was stirred and kept under reflux overnight, cooled and poured into ice-cold aqueous ammonium chloride solution (30 ml). The organic layer was separated and the aqueous layer extracted several times with ether. The combined organic layers were washed with water, dried with sodium sulphate and after removal of solvent gave crotyltributyltin (18.42 g) as an oil.

Experimental

solvent removed to give an oil (3.8 g) a mixture of (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol **(1a)** (67%) and (1RS, 2SR)-1-(4-methylphenyl)-2-methyl-3-buten-1-ol (33%). The ratio was determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1 and 4.56, $J_{1,2}$ 5.8 Hz, H1 respectively of ^{1}H n.m.r. spectra.

(xiii) To a solution of benzaldehyde (8 mmol, 0.848 g) and anisaldehyde (8 mmol, 1.088 g) in dry dichloromethane (10 ml) was added boron triflouride etherate (20 mmol) at -78°C under a nitrogen atmosphere. Subsequently crotyltri-n-butyltin** (4 mmol, 1.38 g) was added and the reaction mixture was allowed to warm to room temperature. The reaction was quenched with water and the organic phase was separated dried and the solvent removed to give an oil (4 g) a mixture of (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol **(1a)** (70%) and (1RS, 2SR)-1-(4-methoxyphenyl)-2-methyl-3-buten-1-ol (30%). The ratio was determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1 and 4.54, $J_{1,2}$ 5.9 Hz, H1 respectively of ^{1}H n.m.r. spectra.

Cinnamyl tri-n-butyltin and aldehydes: thermal reaction

(xiv) A solvent free mixture of cinnamyl tri-n-butyltin (4 mmol, 1.6 g) and benzaldehyde (8 mmol, 0.848 g) and 4-methylbenzaldehyde (8 mmol, 0.950 g) was stirred at 200°C for 5 hours. The reaction was worked up with saturated aqueous ammonium chloride (10 ml), extracted with ether (200 ml), dried with sodium sulphate and the solvent removed to give an oil (3.57 g). ^{1}H n.m.r. and ^{13}C n.m.r. indicated that although the aldehydes and cinnamyl tri-n-butyltin had reacted or decomposed, no homoallylic alcohol had been formed.

Experimental

Cinnamyl triphenyltin and aldehydes: thermal reaction

(xv) A solvent free mixture of cinnamyl triphenyltin (4 mmol, 1.6 g) and benzaldehyde (8 mmol, 0.848 g) and anisaldehyde (8 mmol, 1.088 g) was stirred at 200°C for 5 hours. The reaction was worked up with saturated aqueous ammonium chloride (10 ml), extracted with ether (200 ml), dried with sodium sulphate and the solvent removed to give an oil (3.57 g). ^{1}H n.m.r. and ^{13}C n.m.r. indicated that although the aldehydes and cinnamyl triphenyltin had reacted or decomposed, no homoallylic alcohol had been formed.

(xvi) A solvent free mixture of cinnamyl triphenyltin (4 mmol, 1.6 g) and benzaldehyde (8 mmol, 0.848 g) and 4-methylbenzaldehyde (8 mmol, 0.950 g) was stirred at 200°C for 5 hours. The reaction was worked up with saturated aqueous ammonium chloride (10 ml), extracted with ether (200 ml), dried with sodium sulphate and the solvent removed to give an oil (3.57 g). ^{1}H n.m.r. and ^{13}C n.m.r. indicated that although the aldehydes and cinnamyl triphenyltin had reacted or decomposed, no homoallylic alcohol had been formed.

Crotyl tributyltin and aldehydes: thermal reaction[79IC0263]

(xvii) A solvent free mixture of crotyltributyltin (4 mmol, 1.38 g) and benzaldehyde (8 mmol, 0.848 g) and anisaldehyde (8 mmol, 1.088 g) was stirred 3 hours at 200°C. The reaction was worked up with saturated aqueous ammonium chloride (10 ml), extracted with ether (200 ml), dried with sodium sulphate and the solvent removed to give an oil (3.29 g) a mixture of (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol (1a) (35%) and (1RS, 2RS)-2-methyl-1-phenyl-3-buten-1-ol (1b) (25%) and (1RS, 2SR)-1-(4-methoxyphenyl)-2-methyl-3-buten-1-ol (20%) and (1RS, 2RS)-1-(4-methoxyphenyl)-2-methyl-3-buten-1-ol (20%). The ratio was

Experimental

determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1 and 4.37, $J_{1,2}$ 7.8 Hz, H1 and 4.54, $J_{1,2}$ 5.9 Hz, H1; and 4.31, $J_{1,2}$ 8.06 Hz, H1 respectively of ^{1}H n.m.r. spectra.

(xviii) A solvent free mixture of crotyltributyltin (4 mmol, 1.38 g) and benzaldehyde (8 mmol, 0.848 g) and 4-methylbenzaldehyde (8 mmol, 0.950 g) was stirred 3 hours at 200°C. The reaction was worked up with saturated aqueous ammonium chloride (10 ml), extracted with ether (200 ml), dried with sodium sulphate and the solvent removed to give an oil (3.29 g) a mixture of (1RS, 2SR)-2-methyl-1-phenyl-3-buten-1-ol **(1a)** (32%) and (1RS, 2RS)-2-methyl-1-phenyl-3-buten-1-ol **(1b)** (23%) and (1RS, 2SR)-1-(4-methylphenyl)-2-methyl-3-buten-1-ol (26%) and (1RS, 2RS)-1-(4-methylphenyl)-2-methyl-3-buten-1-ol (19%). The ratio was determined by integration of peaks 4.62, $J_{1,2}$ 5.5 Hz, H1 and 4.37, $J_{1,2}$ 7.8 Hz, H1 and 4.56, $J_{1,2}$ 5.8 Hz, H1 and 4.32, $J_{1,2}$ 7.8 Hz, H1 respectively of ^{1}H n.m.r. spectra.

OXIDATIONS OF HOMOALLYLIC ALCOHOLS.

Preparation of 5,7,7-Trimethyl-3-phenyl-1-octen-4-one

A mixture (>9:1) of (3RS, 4RS, 5SR)- and (3RS, 4RS, 5RS)-5,7,7-trimethyl-3-phenyl-1-octen-4-ols **(21b, 21d)** (500 mg) obtained via tin and aluminium reaction conditions, in dichloromethane (4 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (1.96 g), anhydrous sodium acetate (0.11 g) and dichloromethane (25 ml). After six hours ether (50 ml) was added with stirring and the mixture was decanted from the tarry residue and washed with ether (3 * 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave (3RS, 5SR)-5,7,7-trimethyl-3-phenyl-1-octen-4-one **(52a)** (330 mg) as an oil. (Found CIMS (NH$_3$): M+H$^+$ = 245.1927; C$_{17}$H$_{24}$O requires 244.18283). υ_{max} 2950, 1705, 700 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 0.67 - 1.4, 1.8 - 1.95,

Experimental

(H8)$_3$, C7-Me$_2$, (H6)$_2$; 2.7 - 2.8, H5; 4.5, J$_{2,3}$ 8 Hz, H3; 5.0 - 5.3, (H1)$_2$; 6.2 - 6.4, H2; 7.2 - 7.7, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C (20a) 19.9, C5a; 29.5, C7-(Me)$_2$, C8; 61.6, C3; 116.9, C1; 136.8, C2. (Unaccounted) 29.4, 29.6, 29.8, 29.85, 29.9, 42.0, 45.4, 116.7, 117.1, 192.1, 193.5, 211.6.

Preparation of 2,4-Diphenyl-5-hexen-3-one

(i) A mixture of all four diastereoisomers of 2,4-diphenyl-5-hexen-3-ol (25) (150 mg), prepared from reaction of (E)-3-chloro-1-phenylpropene and 2-phenylpropanal under Grignard conditions, in dichloromethane (4 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (1 g), anhydrous sodium acetate (0.11 g) and dichloromethane (50 ml). After six hours ether (50 ml) was added with stirring and the mixture was decanted from the tarry residue and washed with ether (3 * 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave a mixture 50:50 (ratio estimated by inspection of peaks at δ_C 61.3, 60.6 of ^{13}C n.m.r. spectrum) of (2RS, 4SR)- and (2RS, 4RS)-2,4-diphenyl-5-hexen-3-one (53a, 53b) as an oil (0.17 g). (Found CIMS (NH$_3$): M+H$^+$ = 251.1417; C$_{18}$H$_{13}$O requires 250.13585). υ_{max} 1700 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.17 - 1.53, (H1)$_3$; 3.96, J$_{1,2}$ 7 Hz, H2; 4.53, J$_{4,5}$ 8 Hz, H4; 4.93 - 5.37, (H6)$_2$; 5.76 - 6.67, H5; 6.83 - 8.17, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C (53b) 18.0, C1; 52.1, C2; 61.3, C4; 117.8, C6; 129.0, C5; 183.7, C3; and (53a) 26.5, C1; 51.4, C2; 60.6, C4; 116.7, C6; 136.6, C5; and phenyl carbons (53a, 53b) 126.9, 127.2, 128.1, 128.3, 128.5, 128.7, 129.0.

(ii) A mixture (75:25) of (2RS, 3SR, 4SR)- and (2RS, 3RS, 4RS)-2,4-diphenyl-5-hexen-3-ols (25b, 25d) (500 mg), prepared from reaction of (E)-3-chloro-1-phenylpropene and 2-phenylpropanal in the presence of tin and aluminium, in dichloromethane (4 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (1.96 g), anhydrous sodium acetate

Experimental

(0.11 g) and dichloromethane (50 ml). After six hours ether (50 ml) was added with stirring and the mixture was decanted from the tarry residue and washed with ether (3 * 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave a mixture 75:25 (ratio estimated by inspection of peaks at δ_C 61.3, 60.6 of [13]C n.m.r. spectrum) of (2RS, 4SR)- and (2RS, 4RS)-2,4-diphenyl-5-hexen-3-one (53a, 53b) as an oil (450 mg). υ_{max} 1700 cm^{-1}. [1]H n.m.r. (CDCl$_3$) δ_H 1.17 - 1.53, (H1)$_3$; 3.96, J$_{1,2}$ 7 Hz, H2; 4.53, J$_{4,5}$ 8 Hz, H4; 4.93 - 5.37, (H6)$_2$; 5.76 - 6.67, H5; 6.83 - 8.17, ArH. [13]C n.m.r. (CDCl$_3$) δ_C (53a) 18.0, C1; 52.1, C2; 61.3, C4; 117.8, C6; 129.0, C5; 183.7, C3; and (53b) 26.5, C1; 51.4, C2; 60.6, C4; 116.7, C6; 136.6, C5; and phenyl carbons (53a, 53b) 126.9, 127.2, 128.1, 128.3, 128.5, 128.7, 129.0, 137.8, 139.8.

Attempted epoxidation of 1,2-Diphenyl-3-buten-1-ol via an iodo carbonate[82JO4626]

To a solution of 1,2-diphenyl-3-buten-1-ol (8) (1 g, 4.46 mmol) in dry tetrahydrofuran (30 ml) under nitrogen atmosphere at room temperature was added phenyl lithium (5 ml of a 1 M solution, 5.1 mmol) and the mixture stirred for 1 hour at room temperature. Carbon dioxide was then bubbled into the solution at 0°C and the mixture allowed to stand at room temperature for 1 hour under a carbon dioxide stream. To the carbonate so obtained was added iodine (2.49 g, 9.812 mmol) dissolved in tetrahydrofuran (10 ml) and the mixture stirred for 12 hours. Ethyl acetate (40 ml) was then added and the organic phase washed with sodium thiosulphate solution until the iodine colour disappeared. After normal workup spectra indicated that starting materials had been recovered. (yield 1.984 g).

Experimental

PREPARATION OF 4,5-EPOXY-4-PHENYL-2-PENTANONE

(i) by a sequence involving acetylation, epoxidation, hydrolysis, oxidation

4-Phenyl-4-penten-2-ol (34) (1.7 g, 10.5 mmol) was added to a solution of acetic anhydride (3 ml) in pyridine (75 ml) and stirred overnight. The mixture was poured into ether (600 ml) and washed with sodium bicarbonate (4 * 100 ml), dilute sulphuric acid (10 * 100 ml) and water (100 ml) and dried with sodium sulphate. The solvent was removed under reduced pressure to give an oil (1.77 g) which was purified by radial chromatography on a 4 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate. Elution was effected with 0% - 10% ether - petroleum ether mixtures to give 2-acetoxy-4-phenyl-4-pentene (35) (1.04 g). ^1H n.m.r. (CDCl$_3$) δ_H 1.20, $J_{1,2}$ 6 Hz, (H1)$_3$; 1.91, OCOMe; 2.61, $J_{3a,3b}$ 14 Hz, $J_{2,3a}$ 7.5 Hz, $J_{3a,5}$ 1 Hz, H3a; 2.90, $J_{3a,3b}$ 14 Hz, $J_{2,3b}$ 6.5 Hz, $J_{3b,5}$ 1 Hz, H3b; 4.98, $J_{1,2}$ 6 Hz, H2; 5.10, $J_{5a,5b}$ 2 Hz, $J_{3,5a}$ 1 Hz, H5a; 5.33, $J_{5a,5b}$ 2 Hz, H5b; 7.24 - 7.42, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 19.5, C1; 21.1, Me; 41.7, C3; 69.6, C2; 115.2, C5; 126.2, 127.5, 128.3, phenyl carbons; 140.6, C4; 170.4, C=O.

To 2-acetoxy-4-phenyl-4-pentene (35) (200 mg, 0.98 mmol) in dry ether (20 ml) was added meta-chloroperbenzoic acid (400 mg) and the reaction kept at room temperature and followed by thin layer chromatography. After 2 weeks a reaction appeared to have occurred. The reaction mixture was poured into ether (100 ml) and washed with sodium hydroxide (5%, 3 * 50 ml) and water (50 ml) and dried with sodium sulphate. Removal of solvent gave a mixture, 54:46 (ratio determined by integration of peaks at δ_H 1.91 and 1.83 of ^1H n.m.r. spectrum) of both possible diastereomeric isomers of 2-acetoxy-4,5-epoxy-4-phenyl pentane (36) (0.22 g) as an oil. υ_{max} 1735, 1225, 760, 700 cm^{-1}. This oil was carefully purified by radial chromatography on a 1 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give each isomer in a pure form. Elution was effected with 0 - 10% ether - petroleum ether.

Experimental

Major isomer, most polar fraction (36a); ^{1}H n.m.r. (CDCl$_3$) δ_H 1.225, $J_{1,2}$

6.6 Hz, (H1)$_3$; 1.91, OCOMe; 2.19, $J_{3a,3b}$ 14.2 Hz, $J_{2,3a}$ 8.1 Hz, H3a; 2.32, $J_{3a,3b}$

14.2 Hz, $J_{2,3b}$ 4.4 Hz, H3b; 2.74, $J_{5a,5b}$ 4.8 Hz, H5a; 2.94, $J_{5a,5b}$ 5 Hz, H5b; 4.95, $J_{1,2}$

6.6 Hz, $J_{2,3a}$ 8.1 Hz, $J_{2,3b}$ 4.4 Hz, H2; 7.26 - 7.4, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 20.8,

C1; 21.3, Me; 41.5, C3; 54.3, C5; 58.4, C4; 68.0, C2; 170.1, C=O; 125.8, 127.5, 128.3,

139.5, phenyl carbons. Minor isomer (36b); ^{1}H n.m.r. (CDCl$_3$) δ_H 1.232, $J_{1,2}$

6.6 Hz, (H1)$_3$; 1.742, $J_{3a,3b}$ 14 Hz, $J_{2,3a}$ 5.68 Hz, H3a; 1.83, OCOMe; 2.672, $J_{3a,3b}$

14 Hz, $J_{2,3b}$ 7.7 Hz, H3b; 2.70, $J_{5a,5b}$ 5.5 Hz, H5a; 2.93, $J_{5a,5b}$ 5.5 Hz, H5b; 4.99, $J_{1,2}$

6.6 Hz, $J_{2,3a}$ 5.68 Hz, $J_{2,3b}$ 7.7 Hz, H2; 7.26 - 7.41, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C

20.3, C1; 21.0, Me; 41.6, C3; 55.6, C5; 58.1, C4; 68.4, C2; 170.1, C=O; 125.7, 127.4,

128.2, 136.9, phenyl carbons.

On a subsequent epoxidation large quantities of an ortho ester (40), least

polar fraction, were found to be present, presumably formed during the

alkaline workup procedure. Further the major and minor isomer ratios

were reversed, (36b):(36a) 2:1. (1RS, 3SR, 5SR)-5-phenyl-2,7,8-trioxa-

bicyclo[3,2,1]octane (40) (Found CIMS (C$_4$H$_{10}$): M-Ac = 177.1278, M-OAc =

161.1170, M - C$_6$H$_5$ = 143.0530; C$_{13}$H$_{16}$O$_3$ requires 220.11001); ^{1}H n.m.r. (CDCl$_3$)

δ_H 1.26, $J_{3,3\text{-Me}}$ 6.7 Hz, 3-Me; 1.72, 1-Me; 1.77, $J_{4\,exo,4\,endo}$ 13.6 Hz, $J_{4\,exo,3}$

11.8 Hz, $J_{4\,exo,6\,exo}$ 2 Hz, H4$_{exo}$; 1.97, $J_{4\,exo,4\,endo}$ 13.6 Hz, $J_{3,4\,endo}$ 4.1 Hz,

H4$_{endo}$; 3.77, $J_{6\,exo,6\,endo}$ 7 Hz, $J_{4\,exo,6\,exo}$ 2 Hz, H6$_{exo}$; 4.322, $J_{6\,exo,6\,endo}$ 7 Hz,

H6$_{endo}$; 4.327, $J_{2,3\text{-Me}}$ 6.7 Hz, $J_{3,4\,exo}$ 11.8 Hz, $J_{3,4\,endo}$ 4.1 Hz, H3; 7.3 - 7.4, ArH.

^{13}C n.m.r. (CDCl$_3$) δ_H 21.1, C3-Me; 22.4, C1-Me; 42.3, C4; 65.0, C6; 74.0, C3; 82.0,

C5; 119.5, C1; 124.0, 127.7, 128.4, 140.1, phenyl carbons.

2-Acetoxy-4,5-epoxy-4-phenyl-pentane (200 mg, 0.91 mmol) was added to a

water : methanol solution (1:3, 10 ml) of sodium hydroxide (5%) and stirred

at -20°C. After 1 hour sodium bicarbonate (1.1 g) and cold ether (50 ml) were

added and the mixture stirred a further 15 minutes, filtered, dried with

sodium sulphate and the solvent removed to give an oil (153 mg) consisting

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of a mixture, 47%, 40% (percentage composition determined by integration of peaks at δ_H 1.169 and 1.206 of ^{1}H n.m.r. spectrum) of both isomers of 4,5-epoxy-4-phenyl-2-pentanols (37a, 37b) and (1RS, 3SR, 5SR)-5-phenyl-2,7,8-trioxabicyclo[3,2,1]octane (40), 12% (percentage determined by integration of peak at δ_H 1.978 of ^{1}H n.m.r. spectrum). This oil was carefully purified by radial chromatography on a 1 mm silica gel 60 P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give each isomer in a pure form. Elution was effected with 0 - 30% ether - petroleum ether. Major isomer; (37a) corresponding to (36a) ^{1}H n.m.r. (CDCl$_3$) δ_H 1.17, $J_{1,2}$ 6.22 Hz, (H1)$_3$; 1.70, $J_{3a,3b}$ 14.6 Hz, $J_{2,3a}$ 9.5 Hz, H3a; 2.49, $J_{3a,3b}$ 14.6 Hz, $J_{2,3b}$ 2.7 Hz, H3b; 2.58, OH; 2.72, $J_{5a,5b}$ 5 Hz, H5a; 3.00, $J_{5a,5b}$ 5 Hz, H5b; 3.76 - 4.00, H2; 7.25 - 7.41, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 23.7, C1; 44.0, C3; 55.6, C5; 65.3, C2; 125.6, 127.7, 128.5, 140.3, phenyl carbons. Minor isomer; (37b) corresponding to (36b) ^{1}H n.m.r. (CDCl$_3$) δ_H 1.21, $J_{1,2}$ 6.3 Hz, (H1)$_3$; 2.15, $J_{3a,3b}$ 14.5 Hz, $J_{2,3a}$ 3.7 Hz, H3a; 2.30, $J_{3a,3b}$ 14.5 Hz, $J_{2,3b}$ 8.8 Hz, H3b; 2.81, $J_{5a,5b}$ 4.7 Hz, H5a; 3.22, $J_{5a,5b}$ 4.7 Hz, H5b; 3.76 - 4.00, H2; 7.25 - 7.41, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 23.3, C1; 42.6, C3; 54.3, C5; 64.6, C2; 125.8, 127.8, 128.5, 141.2, phenyl carbons. (1RS, 3SR, 5SR)-5-phenyl-2,7,8-trioxabicyclo[3,2,1]octane (40); ^{1}H n.m.r. (CDCl$_3$) δ_H 1.26, $J_{3,3\text{-Me}}$ 6.7 Hz, 3-Me; 1.72, 1-Me; 1.77, $J_{4\text{ exo,4 endo}}$ 13.6 Hz, $J_{4\text{ exo,3}}$ 11.8 Hz, $J_{4\text{ exo,6 exo}}$ 2 Hz, H4exo; 1.97 $J_{4\text{ exo,4 endo}}$ 13.6 Hz, $J_{3,4\text{ endo}}$ 4.1 Hz, H4endo; 3.77, $J_{6\text{ exo,6 endo}}$ 7 Hz, $J_{4\text{ exo,6 exo}}$ 2 Hz, H6exo; 4.322, $J_{6\text{ exo,6 endo}}$ 7 Hz, H6endo; 4.327, $J_{3,3\text{-Me}}$ 6.7 Hz, $J_{3,4\text{ exo}}$ 11.8 Hz, $J_{3,4\text{ endo}}$ 4.1 Hz, H3; 7.3 - 7.4, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 21.1, C3-Me; 22.4, C1-Me; 42.3, C4; 65.0, C6; 74.0, C3; 82.0, C5; 119.5, C1; 124.0, 127.7, 128.4, 140.1, phenyl carbons.

A single isomer of 2-acetoxy-4,5-epoxy-4-phenyl-pentane (36a) (50 mg) was added to a water : methanol solution (1:3, 10 ml) of sodium hydroxide (5%) and stirred at -20°C. After 1 hour sodium bicarbonate (1.1 g) and cold ether (50 ml) were added and the mixture stirred a further 15 minutes, filtered,

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dried with sodium sulphate and the solvent removed to give an oil (42 mg) consisting of 4,5-epoxy-4-phenylpentan-2-ol (37a) and (1RS, 3SR, 5SR)-5-phenyl-2,7,8-trioxabicyclo[3,2,1]octane (40).

The other isomer 2-acetoxy-4,5-epoxy-4-phenyl-pentane (36b) (70 mg) was similarly treated to give 4,5-epoxy-4-phenylpentan-2-ol (37b). No (1RS, 3SR, 5SR)-5-phenyl-2,7,8-trioxabicyclo[3,2,1]octane (40) was present in the product mixture.

A mixture of both isomers of 4,5-epoxy-4-phenyl-2-pentanol (37) (84 mg) in dichloromethane (5 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (300 mg), anhydrous sodium acetate (80 mg) and dichloromethane (15 ml). After six hours ether (20 ml) was added with stirring and the mixture decanted from the tarry residue and washed with ether (3 x 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave an oil (41 mg) 4,5-epoxy-4-phenyl-2-pentanone (38). (Found CIMS (NH3): M+NH4+-OH- = 177.1159; $C_{11}H_{12}O_2$ requires 176.08378.) υ_{max} 1710 cm^{-1}.

^{1}H n.m.r. (CDCl3) δ_H 2.15, (H1)3; 2.87, J5a,5b 5.1 Hz, H5b; 2.95, J3a,3b 16 Hz, H3b; 3.05, J5a,5b 5.1 Hz, H5a; 3.23, J3a,3b 16 Hz, H3a; 7.26 - 7.47, ArH. ^{13}C n.m.r. (CDCl3) δ_C 21.9, C3-Me; 46.4, C2; 53.9, C4; 54.6, C3; 128.1, 128.2, 128.6, 133.3, phenyl carbons; 197.0, C1. This oil was partially purified on a silica gel dry column using 10% ether - benzene as an eluant.

(ii) by a sequence involving epoxidation, oxidation

To 4-phenyl-4-penten-2-ol (34) (100 mg) in dry ether (10 ml) was added metachloroperbenzoic acid (200 mg) and anhydrous sodium acetate (200 mg) and the reaction kept at room temperature for 2 days. The reaction mixture was poured into ether (50 ml) and washed with sodium hydroxide (5%, 4 * 20 ml) and water (20 ml) and dried with sodium sulphate. Removal of

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solvent gave an oil (84 mg). This oil was purified by radial chromatography on a silica gel P.F. 254 with $CaSO_4.^1/_2H_2O$ plate to give a mixture, 2:1 (ratio determined by integration of peaks at δ_H 2.72, 2.81 of ^1H n.m.r. spectrum) of both diastereomeric isomers of 4,5-epoxy-4-phenylpentan-2-ol (37) (70 mg). ^1H n.m.r. $(CDCl_3)$ δ_H (major isomer) 1.16, $J_{1,2}$ 6.22 Hz, $(H1)_3$; 1.72, $J_{3a,3b}$ 14.7 Hz, $J_{2,3a}$ 9.5 Hz, H3a; 2.46, $J_{3a,3b}$ 14.7 Hz, $J_{2,3b}$ 2.6 Hz, H3b; 2.71, $J_{5a,5b}$ 5.3 Hz, H5b; 3.92 - 3.99, H2; 7.24 - 7.49, ArH. (minor isomer) 1.20, $J_{1,2}$ 6.29 Hz, $(H1)_3$; 2.12, $J_{3a,3b}$ 14.8 Hz, $J_{2,3a}$ 3.8 Hz, H3a; 2.29, $J_{3a,3b}$ 14.8 Hz, $J_{2,3b}$ 8.7 Hz, H3b; 2.80, $J_{5a,5b}$ 4.8 Hz, H5a; 3.19, $J_{5a,5b}$ 4.8 Hz, H5b; 3.85 - 3.92, H2; 7.24 - 7.49, ArH. ^{13}C n.m.r. $(CDCl_3)$ δ_C (Major isomer) 23.7, C1; 43.9, C3; 55.4, C5; 59.7, C4; 65.1, C2. (Minor isomer) 23.3, C1; 42.7, C3; 54.3, C5; 59.6, C4; 64.6, C2. (Phenyl carbons) 125.5, 125.6, 127.5, 127.6, 128.3, 139.1, 140.0.

Oxidation of 4,5-epoxy-4-phenyl-2-pentanol as above gave 4,5-epoxy-4-phenyl-2-pentanone.

(iii) by a sequence involving oxidation and epoxidation

A solution of 4-phenyl-4-penten-2-ol (34) (100 mg) in dichloromethane (5 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (300 mg), anhydrous sodium acetate (80 mg) and dichloromethane (15 ml). The mixture was stirred for 6 hours and ether (20 ml) added with stirring. The liquid was decanted from the tarry residue; this was subsequently washed with ether (3 * 50 ml). The combined organic solutions were filtered through Florosil, and after removal of solvent gave 4-phenyl-4-penten-2-one (39) (72 mg) as an oil. ^1H n.m.r. $(CDCl_3)$ δ_H 2.12, $(H1)_3$; 3.58, $(H3)_2$; 5.21, H5anti; 5.60, H5syn; 7.25 - 7.41, ArH. ^{13}C n.m.r. $(CDCl_3)$ δ_C 28.9, C1; 51.0, C3; 116.6, C5; 206.8, C2; 139.6, 141.5, C4, i; 125.8, 128.5, 127.9, phenyl carbons.

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To 4-phenyl-4-penten-2-one (39) (72 mg) in dry ether was added metachloro-perbenzoic acid (200 mg) and anhydrous sodium acetate (200 mg) and the reaction kept at room temperature 2 days. The reaction mixture was poured into ether (50 ml) and washed with sodium hydroxide (5%, 4 x 20 ml) and water (20 ml) and dried with sodium sulphate. Removal of solvent gave an oil (67 mg) shown by [1]H n.m.r. and [13]C n.m.r. to be a mixture of 4,5-epoxy-4-phenyl-2-pentanone (38) and the starting material 4-phenyl-4-penten-2-one (39). This mixture was again epoxidized and large quantities of unreacted 4-phenyl-4-penten-2-one still remained.

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PREPARATION OF 3,4-EPOXY-1,3-DIPHENYL-1-BUTANONE

(i) by a sequence involving epoxidation and oxidation

To 1,3-diphenyl-3-buten-1-ol (41) (92 mg) in dry ether (10 ml) was added metachloroperbenzoic acid (200 mg) and anhydrous sodium acetate (200 mg) and the reaction kept at room temperature for 2 days. The reaction mixture was poured into ether (50 ml) and washed with sodium hydroxide (5%, 4 * 20 ml) and water (20 ml) and dried with sodium sulphate. Removal of solvent gave a mixture, 3:1 (ratio determined by integration of peaks at δ_H 2.04, 2.4 of ^1H n.m.r. spectrum) of both diastereomeric isomers of 3,4-epoxy-1,3-diphenyl-1-butanol (43) as an oil (85 mg). ^1H n.m.r. (major isomer) (CDCl$_3$) δ_H 2.04, $J_{2a,2b}$ 15 Hz, $J_{1,2a}$ 10 Hz, H2a; 2.69, $J_{2a,2b}$ 15 Hz, $J_{1,2b}$ 2.5 Hz, H2b; 2.73, $J_{4a,4b}$ 5.17 Hz, H5a; 2.96, OH; 3.01, $J_{4a,4b}$ 5.17 Hz, H5b; 4.83, $J_{1,2a}$, 10 Hz, $J_{1,2b}$, 2.5 Hz, H1; 7.22 - 7.45, ArH. (Minor isomer) (CDCl$_3$) δ_H 2.45 - 2.49, (H2)$_2$; 2.89, $J_{4a,4b}$ 4.73 Hz, H4a; 3.1, OH; 3.33, $J_{4a,4b}$ 4.73 Hz, H4b; 4.78, $J_{1,2a}$ 4.2 Hz, $J_{1,2b}$ 8.8 Hz, H1; 7.22 - 7.45, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C (major isomer) 44.8, C2; 55.4, C4; 71.4, C1; (minor isomer) 43.5, C2; 54.3, C4; 71.0, C1; (phenyl carbons) 125.7, 125.8, 127.4, 127.5, 127.7, 128.3, 128.4, 128.5, 138.9, 140.0, 143.5, 144.0.

3,4-Epoxy-1,3-diphenylbutan-1-ol (43) (85 mg) in dichloromethane (5 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (0.3 g), anhydrous sodium acetate (0.08 g) and dichloromethane (15 ml). After 6 hours ether (20 ml) was added with stirring and the mixture decanted from the tarry residue and washed with ether (3 * 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave an oil (40 mg). ^1H n.m.r. and ^{13}C n.m.r. showed this reaction to be very messy but that 3,4-epoxy-1,3-diphenyl-1-butanone[83MSDodg] (44) was produced. ^1H n.m.r. (CDCl$_3$) δ_H 2.97, $J_{4a,4b}$ 5 Hz,

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H4a; 3.12, $J_{4a,4b}$ 5 Hz, H4b; 3.59, $J_{2a,2b}$ 16 Hz, H2a; 3.78, $J_{2a,2b}$ 16 Hz, H2b; 7.23 -

7.6, 7.7 - 8.0, ArH. [13]C n.m.r. (CDCl$_3$) δ_C 45.4, C2; 55.3, C4; 196.3, C1; 125.7,

127.7, 128.2, 128.3, 128.5, 133.3, 136.7, 139.5, phenyl carbons.

(ii) by a sequence involving oxidation and epoxidation

1,3-Diphenyl-3-buten-1-ol (41) (100 mg) in dichloromethane (5 ml) was

added to a vigorously stirred mixture of pyridinium chlorochromate (0.3 g),

anhydrous sodium acetate (0.08 g) and dichloromethane (15 ml). After

6 hours ether (20 ml) was added with stirring and the mixture decanted from

the tarry residue and washed with ether (3 * 50 ml). The combined organic

solutions were filtered through Florosil, dried with sodium sulphate and

after removal of solvent gave crude 1,3-diphenyl-3-buten-1-one[83MSDodg] (45)

as an oil (85 mg). [1]H n.m.r. (CDCl$_3$) δ_H 4.15, (H2)$_2$; 5.17, H4a; 5.59, H4b; 7.15 -

7.61, 7.84 - 8.01, ArH. [13]C n.m.r. (CDCl$_3$) δ_C 45.3, C2; 116.4, C4; 141.7, C3; 125.7,

127.6, 128.3, 128.4, 133.0, 136.5, 140.1, phenyl carbons; 197.4, C=O.

To crude 1,3-diphenyl-3-buten-1-one (45) (85 mg) in dry ether (10 ml) was

added metachloroperbenzoic acid (170 mg) and anhydrous sodium acetate

(170 mg) and the reaction stirred at room temperature for two days. The

reaction mixture was poured into ether (50 ml) and washed with sodium

hydroxide (5%, 4 * 20 ml) and water (20 ml) and dried with sodium sulphate.

Removal of solvent gave an oil (66 mg) shown by [1]H n.m.r. to include

unreacted 1,3-diphenyl-3-buten-1-one (45) and 1,3-diphenyl-3,4-epoxy-

1-butanone (44). 1,3-Diphenyl-3,4-epoxy-1-butanone[83MSDodg] [1]H n.m.r.

(CDCl$_3$) δ_H 2.97, $J_{4a,4b}$ 5 Hz, H4a; 3.11, $J_{4a,4b}$ 5 Hz, H4b; 3.59, $J_{2a,2b}$ 16.6 Hz, H2a;

3.77, $J_{2a,2b}$ 16.6 Hz, H2b; 7.16 - 7.64, 7.92 - 8.05, ArH. [13]C n.m.r. (CDCl$_3$) δ_C 45.4,

C2; 55.3, C4; 57.1, C3; 125.7, 127.6, 128.1$_7$, 128.2$_9$, 128.3$_7$, 128.4$_7$, 128.5$_1$, 133.3,

136.6, 139.5, phenyl carbons, 196.3, C=O. Radial chromatography on a silica

gel P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate eluted with ether - petroleum ether

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mixtures caused large amounts of decomposition of 1,3-diphenyl-3,4-epoxy-1-butanone. Column chromatography on 10% deactivated alumina eluted with petroleum ether - chloroform mixtures also caused partial decomposition of the product.

PREPARATION OF 3,4-EPOXY-3-METHYL-1-PHENYL-1-BUTANONE

(i) by a sequence involving acetylation, epoxidation, hydrolysis, oxidation

3-Methyl-1-phenyl-3-buten-1-ol (46) (500 mg) was added to a solution of acetic anhydride (2 ml) in pyridine (20 ml) and stirred overnight. The mixture was poured into ether (300 ml) and washed with sodium bicarbonate (4 * 50 ml), dilute sulphuric acid (10 * 50 ml) and water (50 ml) and dried with sodium sulphate. The solvent was removed under reduced pressure to give 1-acetoxy-3-methyl-1-phenyl-3-butene (47) (600 mg) as an oil. v_{max} 700, 1220, 1740 cm^{-1}. ^{1}H n.m.r. (CDCl$_3$) δ_H 1.74, C3-Me; 2.05, OCOMe; 2.42, $J_{1,2a}$ 5.4 Hz, $J_{2a,2b}$ 14 Hz, H2a; 2.64, $J_{1,2b}$ 7.6 Hz, $J_{2a,2b}$ 14 Hz, H2b; 4.71, H4a; 4.79, H4b; 5.93, $J_{1,2a}$ 5.4 Hz, $J_{1,2b}$ 7.6 Hz, H1; 7.25 - 7.88, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 21.1, 22.5, C3-Me, OCOMe; 44.8, C2; 73.9, C1; 113.5, C4; 169.9, C=O; 126.3, 127.7, 128.2, 140.3, 140.9, C3, phenyl carbons.

To 1-acetoxy-3-methyl-1-phenyl-3-butene (47) (500 mg) in dry ether (40 ml) was added metachloroperbenzoic acid (1 g) and anhydrous sodium acetate (1 g) and the reaction mixture kept at room temperature for 1 week. The reaction was poured into ether (150 ml) and washed with sodium hydroxide (5%, 4 * 50 ml) and water (50 ml) and dried with sodium sulphate. Removal of solvent gave a mixture, 57:43 (ratio estimated by inspection of peaks at δ_C 44.0 and 43.6 of ^{13}C n.m.r. spectrum) of both isomers of 1-acetoxy-3,4-epoxy-3-methyl-1-phenylbutane (48) (440 mg) as an oil . v_{max} 1740, 1240 cm^{-1}. (Found CIMS (NH$_3$): M+NH$_4^+$ = 238.1444; C$_{13}$H$_{16}$O$_3$ requires 220.11001) ^{1}H n.m.r. (CDCl$_3$) δ_H 1.36, 1.38, C3-Me; 1.92, $J_{1,2a}$ 6 Hz, $J_{2a,2b}$ 14 Hz, H2a; 2.01,

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$J_{1,2a}$ 5 Hz, $J_{2a,2b}$ 14.5 Hz, H2a; 2.07, 2.08, OCOMe; 2.16, $J_{1,2b}$ 4 Hz, $J_{2a,2b}$ 14.5 Hz, H2b; 2.31, $J_{1,2b}$ 9 Hz, $J_{2a,2b}$ 14 Hz, H2b; 2.42, J=4.5 Hz, J=11.5 Hz, (H4)$_2$; 2.62, J=5 Hz, J=22 Hz, (H4)$_2$; 5.87 - 6.0, H1; 7.26 - 7.35, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 21.2$_3$, 21.2$_7$, 21.3$_6$, 21.4$_2$, C3-Me, OCOMe; 43.6, 44.0, C2; 53.3, 53.9, C4; 54.6, 54.8, C3; 73.0, 73.1, C1; 126.2, 126.3, 126.4, 128.1, 128.3, 128.5, phenyl carbons.

1-Acetoxy-3,4-epoxy-3-methyl-1-phenyl-butane (48) (200 mg) was added to a water : methanol solution (1:3, 10 ml) of sodium hydroxide (5%) and stirred at -20°C. After 1 hour sodium bicarbonate (1.1 g) and cold ether (50 ml) were added and the mixture stirred a further 15 minutes, filtered, dried with sodium sulphate and the solvent removed to give a mixture, 57:43 (ratio estimated by inspection of peaks δ_C 21.3 and 22.7 of ^{13}C n.m.r. spectrum) of both isomers of 3,4-epoxy-3-methyl-1-phenyl-1-butanols[83MSDodg] (49) as an oil (153 mg). The two isomers were differentiated by irradiation of CHOH peaks and examining the effects on the CH$_2$ peaks. ^{1}H n.m.r. (CDCl$_3$) δ_H (isomer A) 1.88, $J_{1,2a}$ 9.4 Hz, $J_{2a,2b}$ 14.51 Hz, H2a; 2.02, $J_{1,2b}$ 3.7 Hz, $J_{2a,2b}$ 14.51 Hz, H2b; 4.95, $J_{1,2b}$ 3.7 Hz, $J_{1,2a}$ 9.4 Hz, H1. (isomer B) 2.01, $J_{1,2a}$ 9.5 Hz, $J_{2a,2b}$ 14.9 Hz, H2b; 4.74, $J_{1,2a}$ 9.5 Hz, $J_{1,2b}$ 3.45 Hz, H1. (also) 1.39, 1.43, Me, Me; 2.57, $J_{4a,4b}$ 4.7 Hz, 2.61, $J_{4a,4b}$ 4.7 Hz, H4a, H4b; 2.70, $J_{4a,4b}$ 4.2 Hz, 3.01, $J_{4a,4b}$ 4.2 Hz, H4a, H4b; 7.24 - 7.34, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 21.3, 22.7, C3-Me; 44.0, 45.5, C2; 53.0, 53.9, C4; 56.2, 57.0, C3; 71.1, 71.5, C1; 125.5, 127.4$_0$, 127.4$_4$, 128.3$_0$, 128.3$_3$, 143.7, 144.1, phenyl carbons.

3,4-Epoxy-3-methyl-1-phenyl-1-butanol (49) (89 mg) in dichloromethane (5 ml) was added to a vigorously stirred mixture of pyridinium chlorochromate (0.3 g), anhydrous sodium acetate (0.08 g) and dichloromethane (15 ml). After 6 hours ether (20 ml) was added with stirring and the mixture decanted from the tarry residue and washed with ether (3 x 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave

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3,4-epoxy-3-methyl-1-phenyl-1-butanone[83MSDodg] (50) (79 mg) as an oil.
Purification by radial chromatography gave the pure product; v_{max}
1725 cm^{-1}. (Found CIMS(NH$_3$): M-OH+NH$_4^+$; C$_{11}$H$_{12}$O$_2$ requires
176.08378).^{1}H n.m.r. (CDCl$_3$) δ_H 1.46, CH$_3$; 2.73, J$_{4a,4b}$ 4.6 Hz, H4a; 2.76, J$_{4a,4b}$
4.6 Hz, J$_{4b,2a}$ 1.1 Hz, H4b; 3.03, J$_{2a,2b}$ 16 Hz, H2b; 3.45, J$_{2a,2b}$ 16.5 Hz, J$_{4b,2a}$
1.1 Hz, H2a; 7.43 - 7.60, 7.93 - 7.97, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 21.8, Me; 46.3,
C2; 53.8, C4; 54.5, C3; 128.1, 128.5, 133.2, 136.6, phenyl carbons; 196.9, C=O.

(ii) by a sequence involving epoxidation, oxidation

To 3-methyl-1-phenyl-3-buten-1-ol (46) (108 mg) in dry ether (10 ml) was
added metachloroperbenzoic acid (200 mg) and anhydrous sodium acetate
(200 mg) and the reaction kept at room temperature for 3 days. The reaction
mixture was poured into ether (50 ml) and washed with sodium hydroxide
(5%, 4 x 20 ml) and water (20 ml) and dried with sodium sulphate. Removal
of solvent gave an oil (95 mg). This oil was purified by radial
chromatography on a silica gel P.F. 254 with CaSO$_4$.^{1}/$_2$H$_2$O plate eluted with
petroleum ether - ether mixtures to give 3,4-epoxy-3-methyl-1-phenyl-
1-butanols (49) (90 mg). ^{1}H n.m.r. (CDCl$_3$) δ_H (isomer A) 1.88, J$_{1,2a}$ 9.4 Hz,
J$_{2a,2b}$ 14.51 Hz, H2a; 2.02, J$_{1,2b}$ 3.7 Hz, J$_{2a,2b}$ 14.51 Hz, H2b; 4.95, J$_{1,2b}$ 3.7 Hz, J$_{1,2a}$
9.4 Hz, H1. (isomer B) 2.01, J$_{1,2a}$ 9.5 Hz, J$_{2a,2b}$ 14.9 Hz, H2b; 4.74, J$_{1,2a}$ 9.5 Hz,
J$_{1,2b}$ 3.45 Hz, H1. (also) 1.39, 1.43, Me, Me; 2.57, J$_{4a,4b}$ 4.7 Hz, 2.61, J$_{4a,4b}$ 4.7 Hz,
H4a, H4b; 2.70, J$_{4a,4b}$ 4.2 Hz, 3.01, J$_{4a,4b}$ 4.2 Hz, H4a, H4b; 7.24 - 7.34, ArH.

Oxidation of 3,4-epoxy-3-methyl-1-phenyl-1-butanol as above gave 3,4-epoxy-
3-methyl-1-phenyl-1-butanone.

(iii) by a sequence involving oxidation and epoxidation

3-Methyl-1-phenyl-3-buten-1-ol (46) (100 mg) in dichloromethane (5 ml) was
added to a vigorously stirred mixture of pyridinium chlorochromate (0.3 g),

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anhydrous sodium acetate (0.08 g) and dichloromethane (15 ml). After 6 hours ether (20 ml) was added with stirring and the mixture decanted from the tarry residue and washed with ether (3 x 50 ml). The combined organic solutions were filtered through Florosil, dried with sodium sulphate and after removal of solvent gave 3-methyl-1-phenyl-3-buten-1-one as an oil (51) (87 mg). ^{1}H n.m.r. (CDCl$_3$) δ_H 1.86, CH$_3$; 3.72, (H2)$_2$; 4.89, 5.01, (H4)$_2$; 7.30 - 7.62, 7.89 - 8.04, ArH. ^{13}C n.m.r. (CDCl$_3$) δ_C 22.8, Me; 47.6, C2; 114.8, C4; 128.2, 128.4, 132.9, 136.6, phenyl carbons; 140.3, C3; 197.7, C=O.

To 3-methyl-1-phenyl-3-buten-1-one (51) (77 mg) in dry ether (10 ml) was added metachloroperbenzoic acid (160 mg) and anhydrous sodium acetate (160 mg) and the reaction kept at room temperature for three days. The reaction mixture was poured into ether (50 ml) and washed with sodium hydroxide (5%, 4 x 20 ml) and water (20 ml) and dried with sodium sulphate. Removal of solvent gave an oil (77 mg) shown by ^{1}H n.m.r. and ^{13}C n.m.r. to be 3,4-epoxy-3-methyl-1-phenyl-1-butanone[83MSDodg] (50) and the starting material 3-methyl-1-phenyl-3-buten-1-one (51).

Experimental

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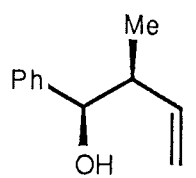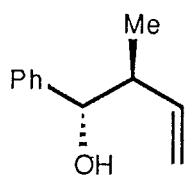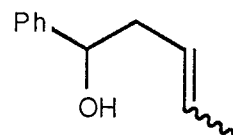
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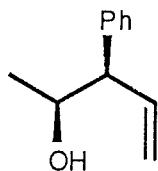
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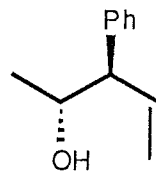
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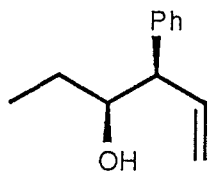
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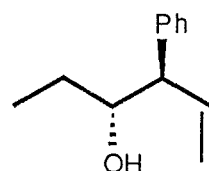
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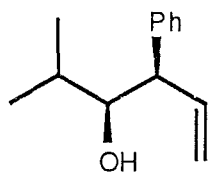
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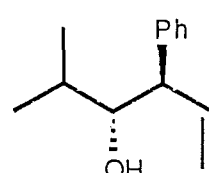
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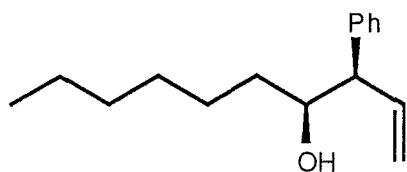
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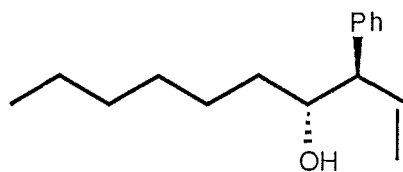
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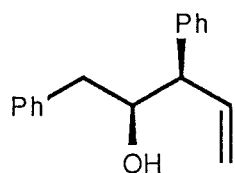
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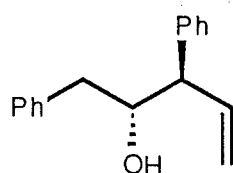
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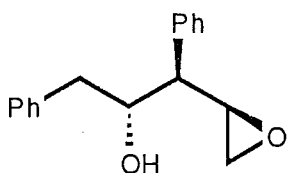
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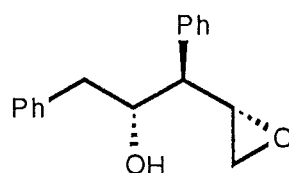
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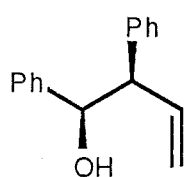
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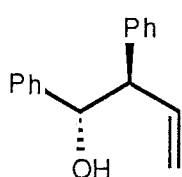
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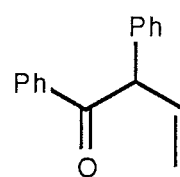
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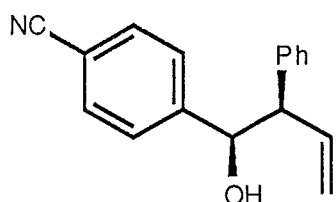
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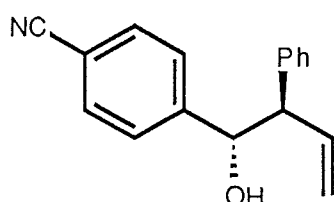
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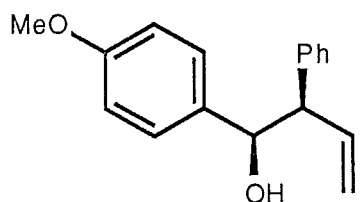
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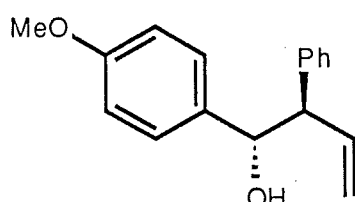
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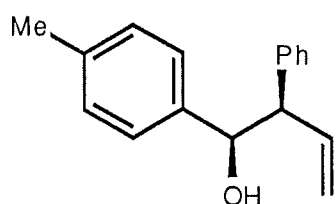
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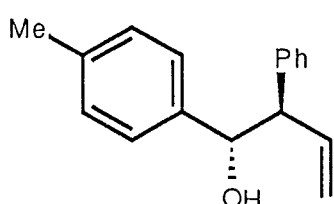
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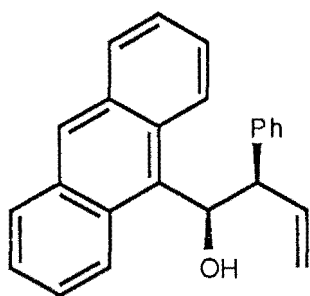
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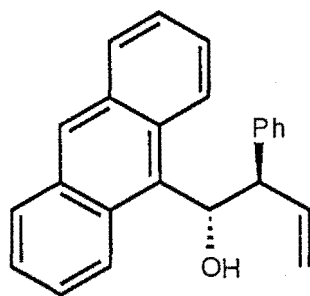
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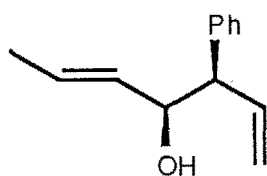
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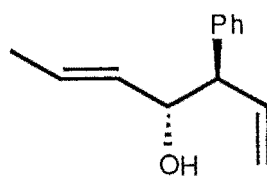
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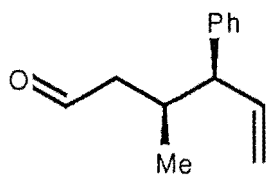
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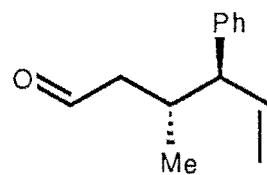
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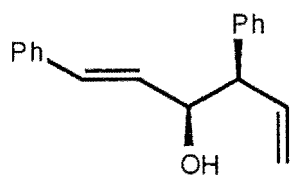
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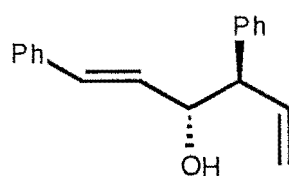
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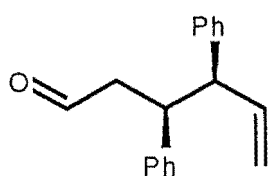
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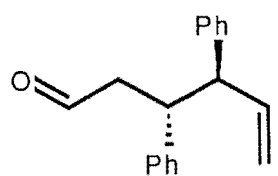
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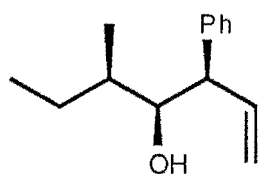
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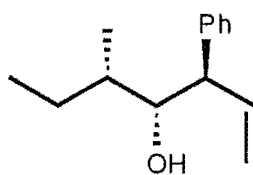
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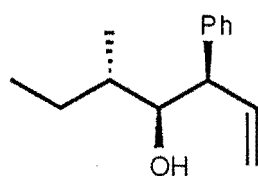
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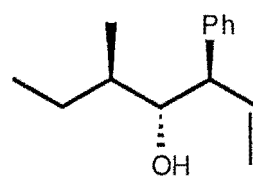
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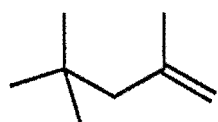
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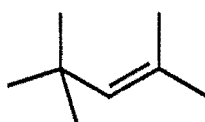
19b
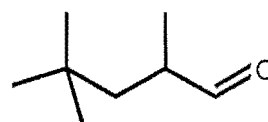
20
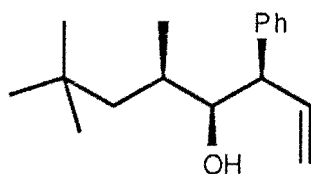
(3RS, 4SR, 5RS)-**21a**
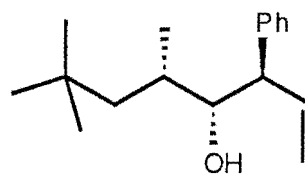
(3RS, 4SR, 5SR)-**21b**
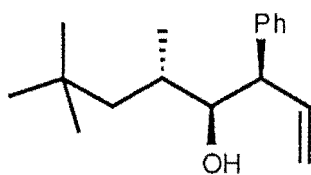
(3RS, 4RS, 5SR)-**21c**
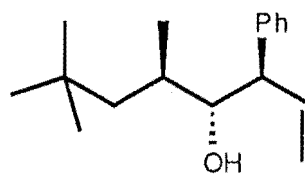
(3RS, 4RS, 5RS)-**21d**
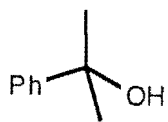
22
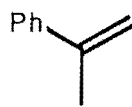
23
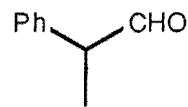
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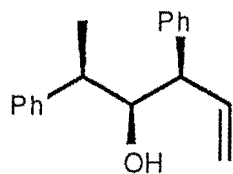
(2RS, 3SR,4RS)-**25a**
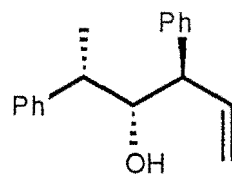
(2RS, 3SR, 4SR)-**25b**
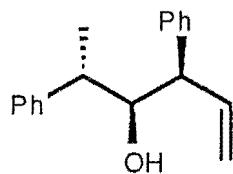
(2RS, 3RS, 4SR)-**25c**
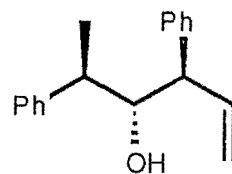
(2RS, 3RS, 4RS)-**25d**
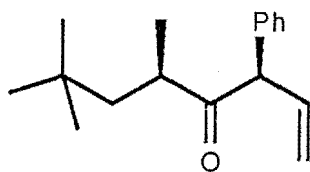
(3RS, 5RS)-**52a**
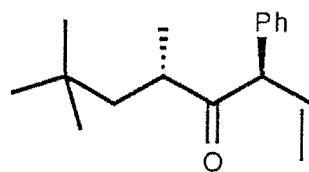
(3RS, 5SR)-**52b**
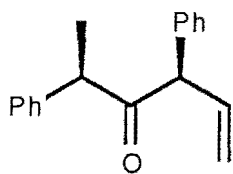
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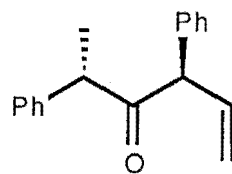
(2RS, 4SR)-**53b**
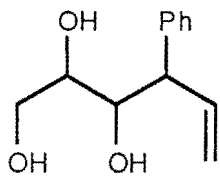
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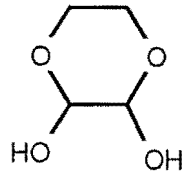
28

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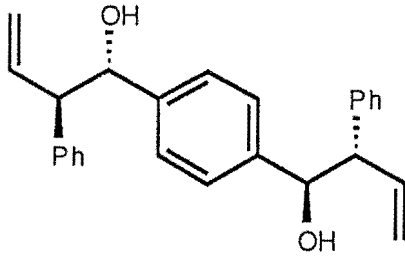
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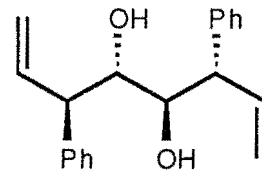
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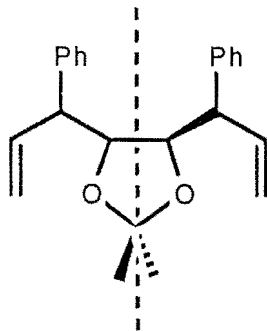
(3RS, 4SR, 5RS, 6SR)-**31a**
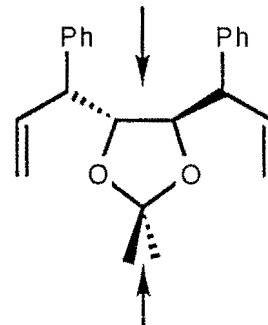
(3RS, 4SR, 5SR, 6RS)-**31b**

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