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1,5-Stereocontrol in tin(IV) halide promoted reactions of 2-alkoxy-1-(2-tributylstannylethylidene)cyclohexanes with aldehydes

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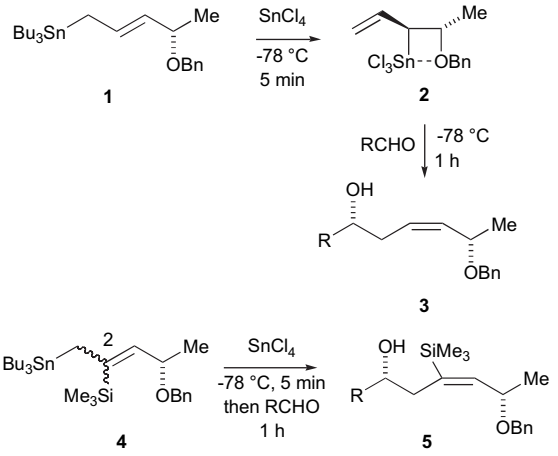
Abstract—2-Methoxy- and 2-(*p*-methoxybenzyloxy)-1-(2-tributylstannylethylidene)cyclohexanes **22** and **23** were prepared from 2-methoxy- and 2-(*p*-methoxybenzyloxy)cyclohexanones **12** and **13**. The allylstannane **22** was transmetallated stereoselectively with tin(IV) chloride at −78 °C to generate an allyltin trihalide, which reacted with aldehydes to give (*Z*)-(3-hydroxyalkylidene)-2-methoxycyclohexanes **24** with excellent 1,5-*syn*-stereocontrol. Similar reactions with aldehydes were observed for the 2-(*p*-methoxybenzyloxy) substituted allylstannane **23**. The structure of the product **24f** prepared from *p*-nitrobenzaldehyde was confirmed by an X-ray structure determination of its *p*-nitrobenzoate ester **27**.

1. Introduction

Alk-2-enylstannanes with heteroatom containing substituents at the 4-, 5- or 6-positions undergo stereoselective transmetallation on treatment with tin(IV) halides to generate allyltin trihalides, which react with aldehydes and imines with useful levels of 1,5-, 1,6- and 1,7-stereocontrol.[1] For example, transmetallation of 4-benzyloxypent-2-enylstannane **1** with tin(IV) chloride kinetically[2] generates allyltin trichloride **2**, with the methyl and ethenyl groups trans-disposed with respect to the four-membered ring, which reacts with aldehydes to give the (*Z*)-1,5-*syn*-products **3** with excellent stereoselectivity for formation of the (*Z*)-alkene and the 1,5-*syn*-stereoisomer.[3] This chemistry has been applied to complete syntheses of complex, biologically active, natural products.[4–6] Allylgermanes have been developed as alternatives to the alk-2-enylstannanes for these reactions[7] and allylic organobismuth reagents have been shown to react with aldehydes with complementary stereocontrol in favour of (*E*)-alk-3-enols.[8]

To delineate the scope of these reactions, it was necessary to establish whether this chemistry is compatible with additional substituents at the 2- and 3-positions of the alk-2-enylstannanes. It has been found that the stereoselectivity is not significantly affected by the presence of a substituent at the 2-position, if anything, it is slightly enhanced. For example, 2-trimethylsilylpent-2-enylstannane **4**, even as a mixture of (*E*)- and (*Z*)-isomers, is transmetallated stereoselectively to generate an allyltin trichloride, which reacts with aldehydes with excellent overall stereoselectivity in favour of the 1,5-*syn*-(*Z*)-stereoisomers **5**.[9]



However, the compatibility of this chemistry with an additional substituent at the 3-position of the alk-2-enylstannane is difficult to predict. This would generate a tertiary allyltin trichloride, for example, **7** from the alkenylstannane **6**, and the kinetic preference for the methyl substituent to be cis or trans with respect to the vinyl group may be small. Moreover, these intermediates may be very unstable and an elimination reaction may compete with the formation of homoallylic alcohols with aldehydes, cf. the formation of **8** or **9** from **7**.

To probe the effects of a substituent at the 3-position of an alk-2-enylstannane on the stereoselectivity of its transmetallation with tin(IV) halides and the reactivity of the allyltin trihalides so formed, it was decided first to study the reactions with aldehydes of allyltin trihalides generated by transmetallation of 2-alkoxy-1-(2-tributylstannylethylidene)cyclohexanes using tin(IV) chloride. The results of this study are described herein.[10]

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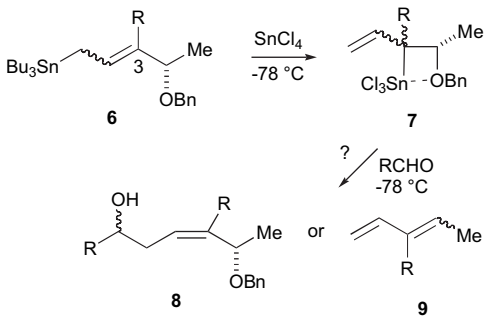
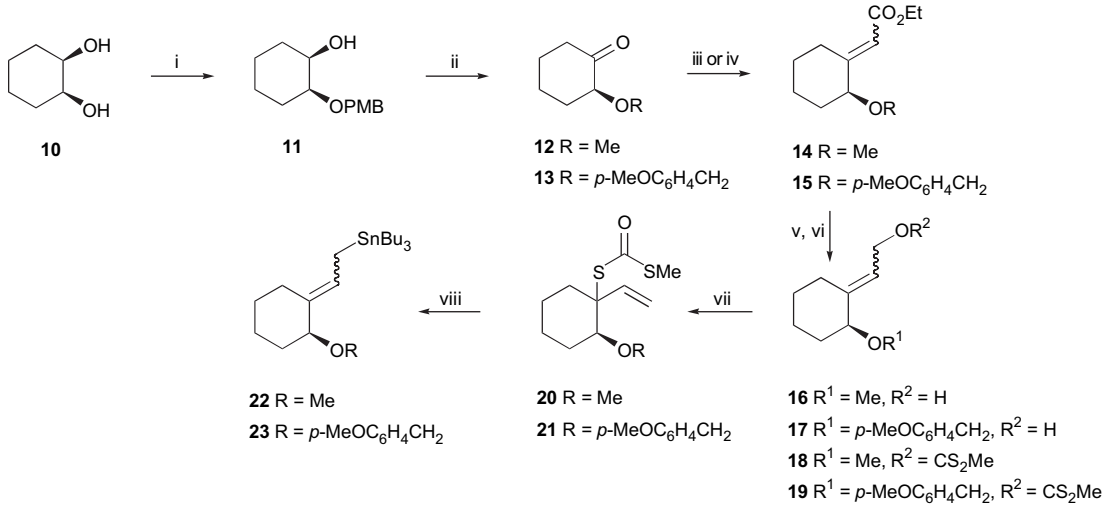


2. Results and discussion

The racemic 2-methoxy- and 2-(*p*-methoxybenzyloxy)-1-(2-tributylstannylethylidene)cyclohexanes **22** and **23** were prepared as mixtures of (*E*)- and (*Z*)-isomers as outlined in Scheme 1. Racemic 2-methoxycyclohexanone **12** was converted into the unsaturated ester **14** using triethyl phosphonoacetate and via a Peterson reaction using ethyl trimethylsilylacetate. As reported in the literature,[11] these reactions gave very different stereoselectivities, with the phosphonate reagent giving more of the (*E*)-alkene (*E*)-**14**, (*E*)/(*Z*)=60:40, whereas the Peterson reaction gave more of the (*Z*)-isomer (*Z*)-**14**, (*E*)/(*Z*)=20:80. The configurations of these alkenes were assigned on the basis of ^{1}H NMR chemical shifts, for example, H(2) was considerably more deshielded for the (*Z*)-isomer, cf. δ 5.26 for the (*Z*)-isomer with δ 3.59 for the (*E*)-isomer, and were confirmed by NOE data, for example, significant NOE effects between H(2) and the vinylic proton for the (*E*)-isomer. The mixtures of the (*E*)- and (*Z*)-esters **14** were reduced to the alcohol **16**, which was converted into the xanthate **18**, still a mixture of (*E*)- and (*Z*)-isomers, by reaction with sodium hydride, carbon disulfide and methyl iodide. Initially, only low conversions, attributed to the low solubility of the initially formed sodium alkoxide of the alcohol **16**, were obtained for this reaction in hydrocarbon solvents such as toluene, and mixtures of products were obtained in tetrahydrofuran. However, better yields were obtained by adding the alcohol to a suspension of sodium hydride in toluene and then heating the mixture under reflux for 30 min before the addition of carbon disulfide. On heating under reflux in toluene, the xanthate **18** isomerised into the dithiocarbonate **20**, which was isolated as an 87:13 mixture of diastereoisomers, this ratio being independent of the (*E*)/(*Z*)-ratio of the xanthate, although the configurations of the dithiocarbonates were not established. Reaction of the mixture of dithiocarbonate epimers with tri-*n*-butyltin hydride under free-radical conditions[12] then gave the allylstannane **22**, as an 85:15 mixture of (*E*)- and (*Z*)-isomers, the double-bond configuration being assigned by ^{1}H NMR on the basis of significant NOE effects between H(2) and the vinylic proton for the major, but not for the minor, diastereoisomer. 2-(*p*-Methoxybenzyloxy)cyclohexanone **13**[13] was also prepared from cyclohexane-*cis*-1,2-diol **10** by reduction of 4-methoxybenzylidene acetal of the diol using diisobutylaluminium hydride (DIBAL-H) followed by oxidation of the alcohol **11** under Swern conditions, and taken through to the 2-*p*-methoxybenzyloxy substituted allylstannane **23** using the chemistry outlined for preparation of the 2-methoxy analogue **22**, see Scheme 1.

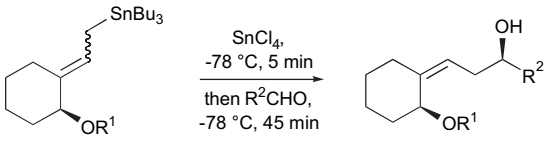
Reactions of the stannanes **22** and **23** with aldehydes were carried out at −78 °C by adding a cooled solution of tin(IV) chloride in dichloromethane to the stannane in dichloromethane, stirring for 5 min, and then adding a solution of the aldehyde. In all cases the reactions were highly stereoselective with only one product, identified as the (*Z*)-1,5-*syn*-isomer **24**, being detected by ^{1}H NMR (>98:2), see Table 1.

The products appeared to be single diastereoisomers, but to be sure of this it had to be demonstrated that the epimeric alcohols could be distinguished by ^{1}H NMR. Inversion of configuration of the products **24a** and **24c** prepared from benzaldehyde and butanal, respectively, was achieved using a Mitsunobu reaction followed by saponification to give the



Scheme 1. Reagents and conditions: (i) *p*-MeOC$_6$H$_4$CH(OMe)$_2$, *p*-TsOH (cat.), toluene, reflux, 1 h, then DIBAL-H in hexane, 0 °C, 2 h (95%); (ii) (COCl)$_2$, DMSO, CH_2Cl_2, Et_3N, −78 °C to rt (96%); (iii) (EtO)$_2$P(O)CH$_2$CO$_2$Et, NaH, THF, 0 °C to rt [**14**, 87%, (*E*)/(*Z*)=60:40]; (iv) $Me_3SiCH_2CO_2Et$, LDA, THF, −78 °C, 30 min [**14**, 47%, (*E*)/(*Z*)=20:80; **15**, 79%]; (v) DIBAL-H, THF, −78 °C to rt (**16**, 96%; **17**, 97%); (vi) NaH, toluene, reflux, 30 min, then CS_2, 0 °C to rt, 1 h followed by MeI, rt, 30 min (**18**, 88%); (vii) toluene, reflux (**20**, 100%, an 87:13 mixture of diastereoisomers; **21**, 72% from **17**); (viii) Bu_3SnH, AIBN (trace), benzene [**22**, 81%, (*E*)/(*Z*)=85:15; **23**, 78%].

Table 1. Tin(IV) chloride promoted reactions of 2-alkoxy-(2-tributylstannylethylidene)cyclohexanes with aldehydes



22 R = Me
23 R = *p*-MeOC$_6$H$_4$CH$_2$

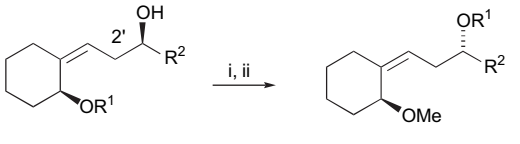
24

R^1	R^2	Product	Yield[a] (%)
Me	C_6H_5	**24a**	77
Me	*i*-Pr	**24b**	45
Me	*n*-Pr	**24c**	70
Me	$CH_3CH{=}CH$	**24d**	50
Me	2-Naphthyl	**24e**	62
Me	4-$O_2NC_6H_4$	**24f**	63
Me	4-BrC_6H_4	**24g**	61
PMB	C_6H_5	**24h**	32

[a] In all cases, no more than 2% of any other product was detected by ^{1}H NMR.

(*Z*)-1,5-*anti*-alcohols **26a** and **26c**, see Scheme 2. In both cases, although they were inseparable by TLC, the epimeric alcohols were clearly distinguishable by ^{1}H NMR; for example, H(2) was observed at δ 4.08 and δ 4.20 in ^{1}H NMR spectra of **24a** and its epimer **26a**, respectively. Examination of the product mixtures from tin(IV) chloride promoted reactions between the stannane **22** and benzaldehyde and butanal, and confirmed that less than 2% of the *anti*-epimers **26a** and **26c** had been formed. Examination of the ^{1}H NMR spectra of the products from the tin(IV) halide promoted reactions between stannanes **22** and **23** and other aldehydes indicated that these had also been highly stereoselective, ≥98:2 in all cases. The ^{1}H NMR data also indicated that 2-alkoxy substituents appeared to be axial in all compounds prepared during this work, perhaps to avoid steric interaction with the exocyclic alkylidene groups.

The geometry of the double bonds in the products **24** was established by NOE studies. For example, significant enhancement of the 2′-methylene group, but no enhancement of H(1′), was observed on irradiation of H(2) for **24a** and **24g**. Finally, the structure of the product **24f** from the reaction of allylstannane **22** with 4-nitrobenzaldehyde was confirmed by an X-ray crystal structure of its *p*-nitrobenzoate ester **27**. Figure 1 shows a projection of the ester **27** as determined by the X-ray structure, which confirms the configuration at



24

25a R^1 = *p*-$O_2NC_6H_4CO$, R^2 = Ph
25c R^1 = *p*-$O_2NC_6H_4CO$, R^2 = *n*-Pr
26a R^1 = H, R^2 = Ph
26c R^1 = H, R^2 = *n*-Pr

Scheme 2. Reagents and conditions: (i) Ph_3P, $EtO_2CN{=}NCO_2Et$, *p*-$O_2NC_6H_4CO_2H$, toluene, rt (**25a**, 51%; **25c**, 73%); (ii) NaOH, MeOH, rt (**26a**, 93%; **26c**, 77%).

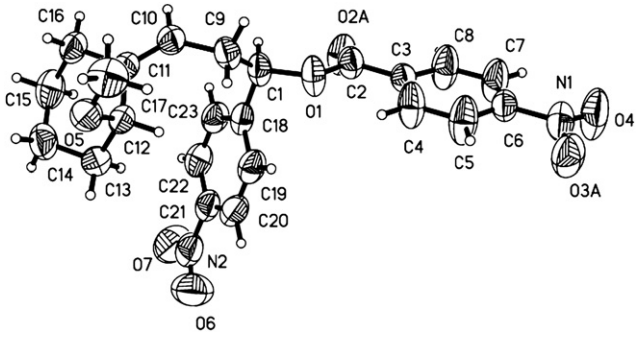
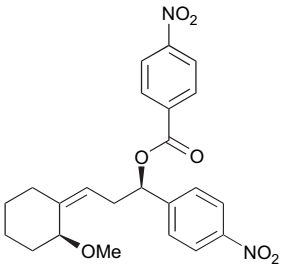


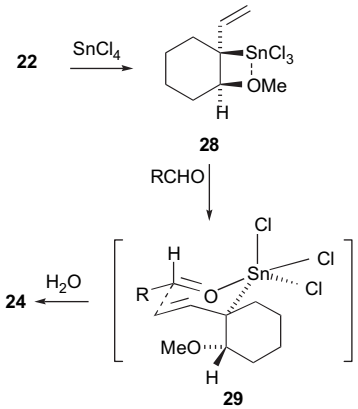
Figure 1. Projection of the structure of ester **27** as established by X-ray diffraction.

the hydroxyl bearing stereogenic centre and the geometry of the exocyclic double bond as depicted in structure **24f**. The structures of the other products were assigned by analogy.



27

The formation of the (*Z*)-1,5-*syn*-products **24** in the tin(IV) chloride promoted reactions of the allylstannane **22** with aldehydes is consistent with stereoselective transmetallation of the allylstannane to give the intermediate allyltin trichloride **28**, which reacts with aldehydes via a six-membered chair-like transition structure **29**.[1] Whether there is any residual bonding between the oxygen of the methoxy group and the electrophilic tin in this transition structure is not clear.[14] However, transition structure **29** shows the methoxy substituted carbon of the cyclohexane in the axial position so minimising steric and dipolar interactions with the apical chloride on the tin so setting up the observed (*Z*)-double bond geometry.[15] The preference of the R group of the aldehyde to adopt the equatorial position, then establishes the configuration at the hydroxyl bearing stereogenic centre. Similar processes are involved in the reactions of *p*-methoxybenzyloxy substituted allylstannane **23**.



3. Summary and conclusions

This work has shown that the 1,5-stereocontrol observed for open-chain allylstannanes **1** and **4** during tin(IV) halide promoted reactions with aldehydes is also observed for the analogous reactions of the allylstannanes **22** and **23**, which have two substituents at the 3-position of the allylstannane. In particular the second substituent at the 3-position does not disrupt the transmetallation using tin(IV) chloride of the 4-alkoxyalk-2-enylstannanes **22** and **23** and the allyltin trichloride so formed can react with aldehydes with excellent stereocontrol without elimination to form a diene being an evident problem. Further work may investigate the use of these products for the synthesis of fragments of natural products.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AC300 and Varian XL300 spectrometers in chloroform-d_1. Coupling constants are given in Hertz. Mass spectra were recorded on Kratos Concept and Fisons VG Trio 2000 mass spectrometers using electron impact (EI) or chemical ionisation (CI) mode. IR spectra were recorded on an ATI Matteson genesis FTIR spectrometer as evaporated films on sodium chloride plates unless otherwise stated. Flash column chromatography was carried out using Merck silica gel 60H (40–60 μ, 230–300 mesh) as the stationary phase. Melting points were recorded on a Kofler heated stage apparatus. Light petroleum refers to the fraction with bp 40–60 °C and was redistilled before use. Ether refers to diethyl ether. All solvents were distilled and purified by standard procedures. All products were obtained as colourless oils after chromatography unless otherwise stated.

4.2. *cis*-2-(*p*-Methoxybenzyloxy)cyclohexanol 11

p-Methoxybenzaldehyde dimethylacetal (1.0 cm^3, 5.98 mmol) and toluene *p*-sulfonic acid (34 mg) were added to a solution of *cis*-cyclohexane-1,2-diol (233 mg, 2 mmol) in toluene (10 cm^3) at room temperature under argon. The mixture was heated under reflux for 1 h, then cooled to room temperature and anhydrous potassium carbonate added. After stirring for a few minutes, the mixture was filtered and cooled to 0 °C. Diisobutylaluminium hydride (10 cm^3, 1.0 M in hexane) was added and the mixture stirred at 0 °C for 2 h. Methanol (2 cm^3) and saturated aqueous ammonium chloride were added, and the mixture filtered through Celite and extracted with ether. The combined organic layers were washed with water and brine, and then dried ($MgSO_4$). After concentration under reduced pressure, chromatography of the residue using light petroleum–ether (80:20) as an eluent gave the *title compound* **11** (450 mg, 95%) as a colourless oil (found: M$^+$, 236.1413. $C_{14}H_{20}O_3$ requires M, 236.1412); ν_{max} 3438, 1612, 1513, 1247, 1175, 1079 and 1034 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.38 and 6.92 (each 2H, br d, *J* 8.5, ArH), 4.58 and 4.50 (each 1H, d, *J* 11, HC*H*Ar), 3.9 (1H, m, 1-H), 3.85 (3H, s, OCH_3), 3.52 (1H, m, 2-H), 2.34 (1H, d, *J* 7, OH) and 1.9–1.2 (8H, m, 4×H_2); δ_C (75 MHz; $CDCl_3$) 159.1, 130.6, 129.0, 113.8, 77.8, 69.8, 68.6, 55.2, 30.4, 26.5, 22.1 and 21.1; *m*/*z* (CI) 254 (M$^+$+18, 25%) and 121 (100).

4.3. 2-(*p*-Methoxybenzyloxy)cyclohexanone 12[13]

Dimethyl sulfoxide (2.7 cm^3, 36.3 mmol) and dichloromethane (1 cm^3) were added to oxalyl chloride (1.6 cm^3, 18.5 mmol) in dichloromethane (2 cm^3) at −78 °C under argon. After 5 min, the alcohol **11** (3.99 g, 16.9 mmol) in dichloromethane (2 cm^3) was added and the solution stirred for 90 min at −78 °C. Triethylamine (11.7 cm^3, 84.5 mmol) was added and, after 5 min, the solution was warmed to room temperature. After 20 min, water (5 cm^3) was added and the mixture extracted with dichloromethane. The organic extracts were washed with brine and dried ($MgSO_4$), then concentrated under reduced pressure to give the *title compound* **12** (3.8 g, 96%) as a colourless oil (found: M$^+$, 234.1258. $C_{14}H_{18}O_3$ requires M, 234.1256); ν_{max} 1721, 1513, 1247, 1110 and 1035 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.3 and 6.9 (each 2H, br d, *J* 8.5, ArH), 4.70 and 4.48 (each 1H, d, *J* 11, HC*H*Ar), 3.91 (1H, dd, *J* 10, 6, 2-H), 3.82 (3H, s, OCH_3) and 2.64–1.6 (8H, m); δ_C (75 MHz; $CDCl_3$) 210.3, 159.2, 129.9, 129.4, 113.7, 81.3, 71.2, 55.2, 40.6, 34.5, 27.6 and 23.0; *m*/*z* (CI) 252 (M$^+$+18, 100%).

4.4. 1-(Ethoxycarbonylmethylidene)-2-methoxycyclohexane 14

4.4.1. Using a Horner–Wadsworth–Emmons olefination. Triethyl phosphonoacetate (17.5 g, 78.0 mmol) in tetrahydrofuran (50 cm^3) was added dropwise to a suspension of sodium hydride (60% dispersion in mineral oil, 3.12 g, 78.0 mmol) in tetrahydrofuran (100 cm^3) at 0 °C. The mixture was allowed to warm to ambient temperature and stirred for 30 min. After cooling to 0 °C, 2-methoxycyclohexanone **12** (10.0 g, 78.0 mmol) in tetrahydrofuran (50 cm^3) was added. The mixture was allowed to warm to ambient temperature and left to stir for 1 h before being poured into water (200 cm^3) and extracted with ether (3×100 cm^3). The organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:10) as an eluent, afforded the *title compound* **14** [13.38 g, 87%, (*E*)/(*Z*)=60:40] as a colourless oil with partial separation of the stereoisomers. (*E*)-**14**: R_f [ether–light petroleum (1:10)] 0.28 (found: M$^+$, 198.1254. $C_{11}H_{18}O_3$ requires M, 198.1256); ν_{max} (neat) 1714, 1655, 1447, 1382, 1294, 1270, 1218, 1197, 1162, 1099, 1036, 942 and 875 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 5.85 (1H, s, 1′-H), 4.19 (2H, q, *J* 7, OCH_2CH_3), 3.59 (1H, dd, *J* 7.5, 3, 2-H), 3.33 (3H, s, OCH_3), 3.09 (1H, m, 6-H), 2.61 (1H, m, 6-H′), 2.00–1.43 (6H, m, 3-H_2, 4-H_2 and 5-H_2) and 1.31 (3H, t, *J* 7.1, OCH_2CH_3); δ_C (75 MHz; $CDCl_3$) 166.6, 160.9, 112.7, 82.4, 59.6, 56.5, 34.6, 27.7, 27.1, 22.6 and 14.2; *m*/*z* (CI) 216 (M$^+$+18, 88%) and 199 (M$^+$+1, 100). (*Z*)-**14**: R_f [ether–light petroleum (1:10)] 0.29 (found: M$^+$, 198.1253. $C_{11}H_{18}O_3$ requires M, 198.1256); ν_{max} (neat) 1715, 1650, 1446, 1436, 1380, 1334, 1264, 1223, 1161, 1094, 1037, 946, 863 and 805 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 5.79 (1H, d, *J* 1, 1′-H), 5.26 (1H, m, 2-H), 4.16 (2H, q, *J* 7, OCH_2CH_3), 3.27 (3H, s, OCH_3), 2.53 (1H, m, 6-H), 2.14–1.96 (2H, m, 3-H and 6-H′), 1.96–1.70 (2H, m, 4-H and 5-H), 1.57–1.33 (3H, m, 3-H′, 4-H′ and 5-H′) and 1.29 (3H, t, *J* 7, OCH_2CH_3); δ_C (75 MHz; $CDCl_3$) 166.0, 160.8,

116.4, 72.4, 59.7, 55.6, 32.8, 32.7, 28.4, 20.0 and 14.1; *m/z* (CI) 199 (M^++1, 100%).

4.4.2. Using Peterson olefination. *n*-Butyllithium (4.6 cm^3, 1.68 M in hexanes, 7.8 mmol) was added to diisopropylamine (790 mg, 7.8 mmol) in tetrahydrofuran (10 cm^3) at 0 °C, the mixture stirred for 15 min, then cooled to −78 °C and ethyl trimethylsilylacetate (1.25 g, 7.8 mmol) in tetrahydrofuran (5 cm^3) added. After 30 min, 2-methoxycyclohexanone (1.0 g, 7.8 mmol) in tetrahydrofuran (5 cm^3) was added and the mixture stirred for 2 h at −78 °C. After allowing the mixture to warm to room temperature, saturated aqueous ammonium chloride (20 cm^3) was added and the mixture was poured into water (50 cm^3) and extracted with ether (3×50 cm^3). The organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:10) as an eluent, afforded the title compound **14** [0.73 g, 47%, (*E*)/(*Z*)=20:80)] as a colourless oil.

4.5. 1-(Ethoxycarbonylmethylidene)-2-*p*-methoxybenzyloxycyclohexane 15

Following the procedure outlined for the synthesis of the unsaturated ester **14** using the Peterson reaction, 2-*p*-methoxybenzyloxycyclohexanone **13** (4 g, 17 mmol) gave, after chromatography using light petroleum–ethyl acetate (10:1) as an eluent, the *title compound* **15** (4.09 g, 79%) as a mixture of diastereoisomers (*E*)/(*Z*)=20:80. (Found: M^++H, 305.1746. $C_{18}H_{25}O_4$ requires M, 305.1753); ν_{max} 1713, 1513, 1247, 1224, 1164 and 1035 cm^{-1}; δ_H (300 MHz; $CDCl_3$) major (*Z*)-isomer: 7.12 and 6.72 (each 2H, d, *J* 8, ArH), 5.68 (1H, s, 1′-H), 5.31 (1H, m, 2-H), 4.22 (2H, s, OCH_2Ar), 4.02 (2H, q, *J* 7, CH_2CH_3), 3.64 (3H, s, OCH_3), 2.50 (1H, m, 6-H), 1.96 (2H, m), 1.75 (2H, m), 1.5–1.2 (3H, m) and 1.18 (3H, t, *J* 7, CH_2CH_3); distinctive peaks for the minor (*E*)-isomer: 5.76 (1H, s, 1-H), 4.38 and 4.22 (each 1H, d, *J* 11, HCHAr), 3.62 (3H, s, OCH_3) and 3.63 (1H, m, 2-H); δ_C (75 MHz; $CDCl_3$) major (*Z*)-isomer: 166.1, 161.2, 158.9, 131.1, 129.0, 116.2, 113.6, 70.9, 69.6, 59.8, 55.2, 33.1, 28.5, 20.2 and 14.2; *m/z* (CI) 322 (M^++18, 100%) and 305 (45).

4.6. 1-(2-Hydroxyethylidene)-2-methoxycyclohexane 16

Diisobutylaluminium hydride (163 cm^3, 1.0 M in hexanes, 163 mmol) was added to the α,β-unsaturated ester **14** (12.9 g, 65 mmol) in tetrahydrofuran (130 cm^3) at −78 °C. The mixture was stirred for 2 h, then allowed to warm to 0 °C, stirred for 30 min, and then water (30 cm^3) added cautiously. Saturated aqueous potassium sodium tartrate (150 cm^3) followed by ether (150 cm^3) were added. The mixture was agitated rapidly at 0 °C until a gel had formed, then allowed to warm to ambient temperature and stirred rapidly until the gel had completely dispersed (ca. 2 h). The aqueous layer was extracted with ether (2×100 cm^3) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (50:50) as an eluent gave the *title compound* **16** [9.77 g, 96%, (*E*)/(*Z*)=60:40] as a colourless oil (found: M^+, 156.1151. $C_9H_{16}O_2$ requires M, 156.1150); ν_{max} (neat) 3368, 1670, 1445, 1320, 1195, 1139, 1094, 997, 943, 872 and 804 cm^{-1}; δ_H (300 MHz; $CDCl_3$) (*E*)-isomer: 5.55 (1H, t, *J* 7, 1′-H), 4.21 (2H, m, 2′-H_2), 3.57 (1H, m, 2-H), 3.26 (3H, s, OCH_3) and 2.23–1.25 (9H, m); (*Z*)-isomer: 5.59 (1H, td, *J* 7, 1.5, 1′-H), 4.21 (2H, m, 2′-H_2), 4.16 (1H, m, 2-H), 3.22 (3H, s, OCH_3), 2.31 (1H, m, 6-H) and 2.23–1.25 (8H, m); δ_C (75 MHz; $CDCl_3$; (*E*)/(*Z*)-mixture) 141.50, 141.45, 124.9, 122.9, 82.4, 74.1, 58.2, 57.7, 55.7, 55.2, 33.5, 32.6, 32.4, 27.8, 27.3, 25.4, 21.8 and 20.8; *m/z* (CI) 174 (M^++18, 53%), 156 (M^+, 53), 142 (49), 139 (M^+−17, 100), 125 (M^+−31, 25), 124 (19) and 107 (29).

4.7. 1-(2-Hydroxyethylidene)-2-*p*-methoxybenzyloxycyclohexane 17

Following the procedure outlined for the synthesis of the alcohol **16**, the ester **15** (3.65 g, 12 mmol) in dichloromethane (50 cm^3) gave the *title compound* **17** (3.05 g, 97%) as a mixture of diastereoisomers (found: M^++NH_4, 280.1905. $C_{16}H_{26}NO_3$ requires M, 280.1912); ν_{max} 3408, 1612, 1513, 1247, 1067, 1034 and 819 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.12 and 6.88 (each 2H, d, *J* 8, ArH), 5.55 (1H, m, 1′-H), 4.5–4.0 (5H, m), 3.78 (3H, s, OCH_3), 3.74 (1H, m, 2-H) and 2.44–1.18 (8H, m); δ_C (75 MHz; $CDCl_3$) 159.0, 142.2, 130.9, 129.0, 128.9, 124.6, 122.6, 113.7, 113.6, 99.9, 79.7, 71.4, 69.3, 68.8, 58.4, 57.9, 55.2, 33.9, 33.0, 32.7, 28.0, 27.5, 25.7, 22.0 and 20.9; *m/z* (CI) 280 (M^++18, 30%), 263 (M^++1, 10), 245 (30) and 121 (100).

4.8. 2-Methoxy-(2-methyldithiocarbonyloxyethylidene)-cyclohexane 18

The allylic alcohol **16** (6.5 g, 41.67 mmol) in toluene (40 cm^3) was added to a suspension of sodium hydride (60% dispersion in mineral oil, 2.5 g dispersion, 62.50 mmol) in toluene (40 cm^3) at ambient temperature. The mixture was heated under reflux for 30 min, allowed to cool to ambient temperature and further cooled to 0 °C. Carbon disulfide (5.0 cm^3, 83.33 mmol) in toluene (40 cm^3) was added and the mixture stirred for 1 h at ambient temperature. Iodomethane (5.2 cm^3, 83.33 mmol) in tetrahydrofuran (40 cm^3) was added and the mixture stirred for 30 min before the cautious addition of water (20 cm^3), then poured into water (300 cm^3) and extracted with ether (3×100 cm^3). The organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography of the residue using ether–light petroleum (1:20) as an eluent gave the *title compound* **18** [9.0 g, 88%, (*E*)/(*Z*)=60:40) as a pale yellow oil with partial separation of the geometrical isomers. (*E*)-**18**: R_f [ether–light petroleum (1:20)] 0.3 (found: M^+, 246.0748. $C_{11}H_{18}O_2S_2$ requires M, 246.0748); ν_{max} (neat) 1669, 1639, 1446, 1216, 1140, 1093, 1063, 1051, 966, 908 and 852 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 5.65 (1H, t, *J* 7, 1′-H), 5.21 (2H, d, *J* 7, 2′-H_2), 3.62 (1H, m, 2-H), 3.29 (3H, s, OCH_3), 2.59 (3H, s, SCH_3), 2.25 (2H, m, 6-H_2) and 1.90–1.40 (6H, m); δ_C (75 MHz; $CDCl_3$) 215.5, 146.1, 115.9, 82.1, 69.5, 55.9, 33.6, 27.3, 26.1, 21.9 and 19.0; *m/z* (CI) 264 (M^++18, 5%), 247 (M^++1, 13), 215 (M^+−31, 21), 156 (18), 155 (32) and 139 (100). (*Z*)-**18**: R_f [ether–light petroleum (1:20)] 0.4 (found: M^+, 246.0750. $C_{11}H_{18}O_2S_2$ requires M, 246.0748); ν_{max} (neat) 1665, 1638, 1446, 1434, 1263, 1215, 1087, 1063, 1052, 963, 946, 910 and 853 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 5.69 (1H, td, *J* 7.5, 1.5, 1′-H), 5.22 (2H, d, *J* 7.5, 2′-H_2), 4.21 (1H,

m, 2-H), 3.25 (3H, s, OCH_3), 2.60 (3H, s, SCH_3), 2.39 (1H, m, 6-H), 2.06 (2H, m, 6-H′ and 3-H), 1.80 (2H, m, 4-H and 5-H) and 1.60–1.30 (3H, m, 3-H′, 4-H′ and 5-H′); δ_C (75 MHz; $CDCl_3$) 215.5, 146.2, 118.3, 74.0, 68.9, 55.4, 32.8, 32.4, 27.9, 20.6 and 19.0; *m/z* (CI) 247 (M^++1, 14%), 215 (M^+−31, 19), 156 (17), 155 (33) and 139 (100).

4.9. 1-Ethenyl-2-methoxy-l-thiomethylcarbonylthiocyclohexane 20

A solution of the allylic xanthate **18** (8.5 g, 34.55 mmol) in toluene (50 cm^3) was heated under reflux for 4 h. After being allowed to cool to ambient temperature, concentration under reduced pressure gave the *title compound* **20** (8.5 g, 100%), a mixture of diastereoisomers, in the ratio of 87:13, as a pale yellow oil and used without further purification, R_f [ether–light petroleum (1:20)] 0.4 (found: M^+, 246.0753. $C_{11}H_{18}O_2S_2$ requires M, 246.0748); ν_{max} (neat) 1715, 1638, 1449, 1411, 1365, 1310, 1196, 1159, 1145, 1101, 964, 921, 851 and 813 cm^{-1}; δ_H (300 MHz; $CDCl_3$) major diastereoisomer: 6.17 (1H, dd, *J* 17.5, 11, 1′-H), 5.40 (1H, d, *J* 17.5, 2′-H), 5.34 (1H, d, *J* 11, 2′-H′), 3.70 (1H, dd, *J* 9, 3.5, 2-H), 3.41 (3H, s, OCH_3), 2.60–1.26 (8H, m) and 2.37 (3H, s, SCH_3); δ_C (75 MHz; $CDCl_3$) major diastereoisomer: 188.8, 136.1, 117.2, 81.5, 62.7, 57.6, 32.9, 26.7, 22.8, 22.2 and 12.8; *m/z* (CI) 247 (M^++1, 100%), 215 (M^+−31, 12), 155 (22) and 139 (74).

4.10. 2-Methoxy-l-(2-tributylstannylethylidene)-cyclohexane 22

The dithiocarbonate **18** (8.3 g, 33.74 mmol), tri-*n*-butyltin hydride (13.6 cm^3, 50.61 mmol) and azobisisobutyronitrile (554 mg, 3.37 mmol) were combined together in benzene (80 cm^3) and the resulting mixture degassed for 15 min using argon. The mixture was then heated under reflux for 1 h before being allowed to cool to ambient temperature. The mixture was concentrated under reduced pressure. Flash column chromatography of the residue, eluting with ether–light petroleum–triethylamine (1:50:0.5), afforded the *title compound* **22** [11.76 g, 81%, (*E*)/(*Z*)=85:15] as a colourless oil, R_f [ether–light petroleum (1:50)] 0.3; ν_{max} (neat) 1654, 1462, 1417, 1376, 1346, 1319, 1194, 1141, 1095, 1040, 1025, 941, 868 and 718 cm^{-1}; δ_H (300 MHz; C_6D_6) (*E*)-isomer: 5.62 (1H, t, *J* 9, 1′-H), 3.58 (1H, m, 2-H), 3.25 (3H, s, OCH_3) and 2.44–0.86 (37H, m, 2′-H_2, 3-H_2, 4-H_2, 5-H_2, 6-H_2 and $SnBu_3$); δ_C (75 MHz; C_6D_6) (*E*)-isomer: 133.5, 124.8, 84.2, 55.9, 35.1, 30.3, 28.5, 28.3, 25.4, 22.8, 14.6, 10.8 and 10.3; *m/z* (ES+) 350 (10%), 332 (100), 291 (70), 276 (17) and 235 (7).

4.11. 2-*p*-Methoxybenzyloxy-l-(2-tributylstannylethylidene)cyclohexane 23

The alcohol **17** (3 g, 11.45 mmol) in anhydrous benzene (4 cm^3) was added to a suspension of sodium hydride (550 mg, 13.7 mmol) in benzene (10 cm^3) at 0 °C and the mixture stirred at room temperature for 1 h. After cooling to 0 °C, carbon disulfide (2.8 cm^3, 45.8 mmol) was added and the mixture stirred at room temperature for 3 h, then cooled to 0 °C. Methyl iodide (2.8 cm^3, 48.5 mmol) was added and the mixture stirred for 16 h at room temperature. The mixture was then filtered through Celite and extracted with dichloromethane. The extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the xanthate **19**, which was used without further purification. Small samples of the two diastereoisomers were separated by chromatography using ether–light petroleum as an eluent: data for the minor, less polar (*E*)-isomer (*E*)-**19**: (found: M^+, 352.1164. $C_{18}H_{24}O_3S_2$ requires M, 352.1167); δ_H (300 MHz; $CDCl_3$) 7.31 and 6.92 (each 2H, br d, *J* 8, ArH), 5.71 (1H, t, *J* 7.5, 1′-H), 5.23 (2H, d, *J* 7.5, 2′-H_2), 4.47 and 4.35 (each 1H, d, *J* 11, HC*H*Ph), 3.86 (3H, s, OCH_3), 3.8 (1H, m, 2-H), 2.61 (3H, s, SCH_3) and 2.40–1.20 (8H, m); *m/z* (CI) 370 (M^++18, 2%), 353 (M^++1, 1), 293 (9), 215 (10) and 121 (100): data for the more polar, major (*Z*)-isomer (*Z*)-**19**: (found: M^+, 352.1166. $C_{18}H_{24}O_3S_2$ requires M, 352.1167); δ_H (300 MHz; $CDCl_3$) 7.28 and 6.92 (each 2H, br d, *J* 9, ArH), 5.68 (1H, t, *J* 8, 1′-H), 5.12 (2H, d, *J* 7.5, 2′-H_2), 4.49 (1H, d, *J* 11, HCHAr), 4.38 (1H, m, 2-H), 4.34 (1H, d, *J* 11, HC*H*Ph), 3.86 (3H, s, OCH_3), 2.61 (3H, s, SCH_3) and 2.54–1.28 (8H, m); *m/z* (CI) 370 (M^++18, 10%), 353 (M^++1, 1), 293 (16), 215 (25) and 121 (100).

A solution of this xanthate in toluene (20 cm^3) was heated under reflux overnight and then concentrated under reduced pressure. Chromatography of the residue using light petroleum–ethyl acetate (10:1) gave the dithiocarbonate **21** (2.87 g, 72%) (found: M^+, 352.1171. $C_{18}H_{24}O_3S_2$ requires M, 352.1167); ν_{max} 1637, 1513, 1247, 1036 and 853 cm^{-1}; δ_H (300 MHz; $CDCl_3$) major isomer: 7.28 and 6.92 (each 2H, d, *J* 8, ArH), 6.22 (1H, dd, *J* 17, 10, 1′-H), 5.4 (2H, m, 2′-H_2), 4.58 and 4.53 (each 1H, d, *J* 11, HC*H*Ar), 4.0 (1H, dd, *J* 9, 3, 2-H), 3.82 (3H, s, OCH_3), 2.37 (3H, s, SCH_3) and 2.6–1.3 (8H, m); *m*/z (CI) 353 (M^++1, 1%), 310 (7) and 293 (15).

Following the procedure outlined for the synthesis of the stannane **22** but with heating under reflux overnight, the dithiocarbonate **19** (2.85 g, 8.09 mmol) gave the *title compound* **23** (3.39 g, 78%) as a mixture of diastereoisomers; ν_{max} 1613, 1513, 1460, 1247, 1174, 1075 and 1040 cm^{-1}; δ_H (300 MHz; $CDCl_3$) major (*E*)-diastereoisomer: 7.32 and 6.92 (each 2H, d, *J* 8, ArH), 5.52 (1H, t, *J* 8, 1′-H), 4.44 and 4.22 (each 1H, d, *J* 11, HC*H*Ar), 3.84 (3H, s, OCH_3), 3.78 (1H, m, 2-H), 2.4–1.22 (28H, m), 0.98 (9H, t, *J* 7, 3×CH_3); *m/z* (CI) 308 (5%), 306 (4) and 304 (3).

4.12. General procedure for allylstannane–aldehyde reactions

4.12.1. (*Z*)-(2*SR*,3′*RS*)-1-(3-Hydroxy-3-phenylpropylidene)-2-methoxycyclohexane 24a. A cooled solution of tin(IV) chloride (4.7 cm^3, 4.69 mmol) in dichloromethane was added dropwise to a solution of the stannane **22** (1.08 g, 3.9 mmol) in dichloromethane under argon at −78 °C. After 5 min, a cooled solution of benzaldehyde (0.6 cm^3, 6 mmol) in dichloromethane (5 cm^3) was added and the mixture stirred at −78 °C for 1 h. Saturated aqueous sodium bicarbonate (2 cm^3) was added and the mixture allowed to warm to room temperature. Dichloromethane and water were added and the organic extracts washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (3:1) as an eluent gave the *title compound* **24a**

(0.74 g, 77%) (found: M^++NH_4, 264.1969. $C_{16}H_{26}NO_2$ requires M, 264.1963); ν_{max} 3400, 1602, 1493, 1447, 1197, 1143, 1088, 944, 762 and 700 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.41–7.26 (5H, m, ArH), 5.41 (1H, td, *J* 7.5, 1.5, 1′-H), 4.71 (1H, t, *J* 7, 3′-H), 4.08 (1H, m, 2-H), 3.23 (3H, s, OCH_3), 2.58 (3H, m, 2′-H_2 and OH) and 2.31 (1H, m, 6-H), 1.95 (2H, m, 6-H′ and 3-H), 1.70 (2H, m, 4-H and 5-H), 1.42 (1H, m, 4-H′), 1.23 (1H, m, 5-H′) and 1.07 (1H, m 3-H′); δ_C (75 MHz; $CDCl_3$) 144.0, 141.2, 128.3, 127.4, 125.9, 121.3, 74.1, 73.7, 55.0, 37.0, 32.6, 31.8 and 27.9, 20.6; *m/z* (CI) 264 (M^++18, 6%), 247 (M^++1, 5), 246 (M^+, 8), 232 (100), 215 (27) and 197 (51).

4.12.2. (*Z*)-(2*SR*,3′*RS*)-1-(3-Hydroxy-4-methylpentylidene)-2-methoxycyclohexane 24b. Yield (45%) 79 mg (found: M^++NH_4, 230.2107. $C_{13}H_{28}NO_2$ requires M, 230.212); ν_{max} 3435, 1465, 1446, 1197, 1142, 1096, 1085, 1000, 945 and 874 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 5.42 (1H, t, *J* 8, 1′-H), 4.22 (1H, m, 2-H), 3.41 (1H, m, 3′-H), 3.24 (3H, s, OCH_3), 2.62–1.4 (12H, m) and 0.98 and 0.96 (each 3H, d, *J* 7, CH_3); δ_C (75 MHz; $CDCl_3$) 141.0, 122.3, 76.5, 73.8, 55.1, 32.9, 32.7, 32.0, 31.7, 28.0, 20.7, 18.8 and 17.2; *m/z* (CI) 230 (M^++18, 16%), 213 (M^++1, 18), 198 (65), 181 (71) and 163 (100).

4.12.3. (*Z*)-(2*RS*,3′*RS*)-1-(3-Hydroxyhexylidene)-2-methoxycyclohexane 24c. Yield (70%) 275 mg (found: M^++NH_4, 230.2119. $C_{13}H_{28}NO_2$ requires M, 230.2120); ν_{max} 3409, 1446, 1379, 1197, 1141, 1085, 1025 and 945 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 5.42 (1H, t, *J* 7.5, 1′-H), 4.2 (1H, m, 2-H), 3.48 (1H, m, 3′-H), 3.28 (3H, s, OCH_3) and 2.42–0.98 (18H, m); δ_C (75 MHz; $CDCl_3$) 141.0, 121.9, 73.7, 71.4, 55.1, 39.0, 34.9, 32.7, 32.1, 28.1, 20.7, 18.8 and 14.0; *m/z* (CI) 230 (M^++18, 100%) and 213 (M^++1, 88).

4.12.4. (*Z*)-(2*SR*,3′*RS*,4′*E*)-1-(3-Hydroxyhex-4-enylidene)-2-methoxycyclohexane 24d. Yield (50%) 67 mg (found: M^++H, 211.1693. $C_{13}H_{23}O_2$ requires M, 211.1697); δ_H (300 MHz; $CDCl_3$) 5.6 (1H, dq, *J* 16, 7, 5′-H), 5.44 (1H, ddd, *J* 16, 8, 1, 4′-H), 5.28 (1H, t, *J* 7, 1′-H), 4.32 (1H, m, 2-H), 3.98 (1H, q, *J* 7, 3′-H), 3.18 (3H, s, OCH_3), 2.22 and 1.92 (each 3H, m), 1.64 (3H, d, *J* 8, 6′-H_3) and 1.27 (4H, m); δ_C (75 MHz; $CDCl_3$) 140.6, 133.5, 126.8, 121.5, 73.7, 72.6, 55.0, 34.9, 32.6, 32.1, 28.1, 20.7 and 17.6; *m/z* (CI) 211 (M^++1, 8%) and 161 (100).

4.12.5. (*Z*)-(2*SR*,3′*RS*)-1-[3-(2-Naphthyl)propylidene]-2-methoxycyclohexane 24e. Yield (62%) 85 mg, colourless viscous oil (found: M^+, 296.1767. $C_{20}H_{24}O_2$ requires M, 296.1776); ν_{max} (neat) 3399, 1632, 1601, 1508, 1444, 1318, 1197, 1143, 1086, 1071, 944, 856, 819 and 748 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.83 (4H, m, ArH), 7.48 (3H, m, ArH), 5.40 (1H, td, *J* 7.5, 1.5, 1′-H), 4.84 (1H, t, *J* 6.5, 3′-H), 4.09 (1H, m, 2-H), 3.21 (3H, s, OCH_3), 2.63 (2H, m, 2′-H_2), 2.28 (1H, m, 6-H) and 2.01–0.94 (7H, m); δ_C (75 MHz; $CDCl_3$) 141.4, 141.3, 133.2, 132.9, 128.1, 127.8, 127.6, 126.0, 125.7, 124.6, 124.0, 121.3, 74.2, 73.8, 55.1, 36.9, 32.6, 31.8, 27.9 and 20.6; *m/z* (CI) 282 (13%), 279 (M^+−17, 17), 247 (53), 171 (78), 125 (67) and 108 (100).

4.12.6. (*Z*)-(2*SR*,3′*RS*)-1-(3-Hydroxy-3-*p*-nitrophenylpropylidene)-2-methoxycyclohexane 24f. Yield (63%) 85 mg, pale yellow oil (found: M^+, 291.1467. $C_{16}H_{21}NO_4$ requires M, 291.1471); ν_{max} (neat) 3386, 1604, 1522, 1445, 1346, 1085, 1070, 942, 911, 853, 733 and 701 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 8.19 and 7.53 (each 2H, br d, *J* 8.5, ArH), 5.33 (1H, td, *J* 7.5, 1.5, 1′-H), 4.78 (1H, dd, *J* 7, 5.5, 3′-H), 4.04 (1H, m, 2-H), 3.20 (3H, s, OCH_3), 2.70 (1H, br s, OH), 2.53 (2H, m, 2′-H_2), 2.29 (1H, m, 6-H) and 2.04–1.05 (7H, m); δ_C (75 MHz; $CDCl_3$) 151.4, 147.0, 142.5, 126.4, 123.4, 120.0, 73.8, 72.7, 55.0, 37.0, 32.7, 31.3, 27.6 and 20.5; *m/z* (EI) 277 (10%), 260 (M^+−31, 15), 242 (21), 212 (13), 164 (9), 150 (9), 139 (29), 122 (26) and 108 (100).

4.12.7. (*Z*)-(2*SR*,3′*RS*)-1-(3-*p*-Bromophenyl-3-hydroxypropylidene)-2-methoxycyclohexane 24g. Yield (61%) 93 mg, colourless oil (found: M^++NH_4, 342.1060. $C_{16}H_{25}{}^{79}BrNO_2$ requires M, 342.1068); ν_{max} (neat) 3399, 1592, 1486, 1444, 1403, 1196, 1143, 1070, 1010, 943 and 823 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.50 and 7.25 (each 2H, br d, *J* 8.5, ArH), 5.36 (1H, br t, *J* 7.5, 1′-H), 4.66 (1H, t, *J* 7, 3′-H), 4.06 (1H, m, 2-H), 3.22 (3H, s, OCH_3), 2.53 (3H, m, 2′-H_2 and OH), 2.30 (1H, m, 6-H), 1.97 (2H, m, 6-H′ and 3-H) and 1.82–1.06 (5H, m, 3-H′, 4-H_2 and 5-H_2); δ_C (75 MHz; $CDCl_3$) 143.1, 141.7, 131.3, 127.6, 121.1, 120.8, 73.8, 73.3, 55.1, 37.0, 32.7, 31.7, 27.9 and 20.6; *m/z* (CI) 344 (M^++18, 12%), 342 (M^++18, 15), 312 (96), 310 (96), 295 (17), 293 (23), 277 (37), 275 (40), 201 (44) and 199 (53).

4.12.8. (Z)-(2*SR*,3*RS*)-1-(3-Hydroxy-3-phenylpropylidene)-2-*p*-methoxybenzyloxycyclohexane 24h. Yield (32%) 158 mg; ν_{max} 3432, 1612, 1513, 1452, 1301, 1247, 1175, 1037 and 821 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.4 (7H, m, ArH), 6.9 (2H, d, *J* 8, ArH), 5.42 (1H, t, *J* 6.5, 1′-H), 4.64 (1H, t, *J* 6, 3′-H), 4.42 (1H, d, *J* 11, HC*H*Ar), 4.27 (2H, m, HC*H*Ar and 2-H), 3.8 (3H, s, OCH_3) and 2.6–1.0 (10H, overlapping m); δ_C (75 MHz; $CDCl_3$) 158.9, 144.1, 141.3, 131.2, 129.1, 128.2, 127.4, 125.9, 121.4, 113.7, 74.1, 71.4, 68.6, 55.2, 37.0, 32.9, 32.2, 28.2 and 20.9; *m/z* (CI) 370 (M^++18, 1%), 352 (M^+, 2) and 121 (100).

4.13. (*Z*)-(2*SR*,3′*SR*)-2-Methoxy-l-(3-*p*-nitrobenzoyloxy-3-phenylpropylidene)cyclohexane 25a

Diethyl azodicarboxylate (87 mg, 0.5 mmol) was added dropwise to the alcohol **24a** (114 mg, 0.46 mmol), *p*-nitrobenzoic acid (92 mg, 0.55 mmol) and triphenylphosphine (145 mg, 0.55 mmol) in toluene at room temperature under an argon atmosphere. After 4 h, the solution was diluted with ether and washed with water. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (10:1) as an eluent gave the *title compound* **25a** (93 mg, 51%) (found: M^++NH_4, 413.2075. $C_{23}H_{29}N_2O_5$ requires M, 413.2076); δ_H (300 MHz; $CDCl_3$) 8.36 and 8.30 (each 2H, d, *J* 8, ArH), 7.4 (5H, m, ArH), 6.08 (1H, t, *J* 7, 3′-H), 5.4 (1H, t, *J* 8, 1′-H), 4.2 (1H, m, 2-H), 3.18 (3H, s, OCH_3), 2.97 and 2.78 (each 1H, dt, *J* 16, 8, 2′-H), 2.29 (1H, m, 6-H), 1.97 and 1.72 (each 2H, m), 1.46 (1H, m) and 1.22 (2H, m); δ_C (75 MHz; $CDCl_3$) 163.8, 150.5, 141.5, 139.4, 135.7, 130.7, 128.6, 128.3, 126.4, 123.5, 119.9, 77.5, 73.6, 54.9, 34.0, 32.7, 32.5, 28.0 and 20.7; *m/z* (CI) 413 (M^++18, 100%), 381 (10) and 364 (38).

4.14. (*Z*)-(2*RS*,3*RS*)-1-(3-Hydroxy-3-phenylpropylidene)-2-methoxycyclohexane 26a

The ester **25a** (0.187 mmol, 74 mg) in methanol (0.5 cm^3) was added dropwise to sodium hydroxide (8 mg, 0.20 mmol) in methanol (3 cm^3) at room temperature. After 2 h, ether was added and the mixture washed with water. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (70:1) as an eluent gave the *title compound* **26a** (43 mg, 93%) (found: M^++NH_4, 264.1966. $C_{16}H_{26}NO_2$ requires M, 264.1963); δ_H (300 MHz; $CDCl_3$) 7.3 (5H, m, ArH), 5.43 (1H, t, *J* 8, 1′-H), 4.76 (1H, m, 3′-H), 4.20 (1H, m, 2-H), 3.17 (3H, s, OCH_3) 2.68 and 2.56 (each 1H, dt, *J* 14, 7, 2′-H), 2.32 (1H, m, 6-H) and 2.2–1.2 (8H, m); *m*/*z* (CI) 264 (M^++18, 20%), 247 (M^++1, 22) and 232 (100).

4.15. (*Z*)-(2*SR*,3*RS*)-1-(3-Hydroxyhexylidene)-2-methoxycyclohexane 26c

Following the procedure outlined for the synthesis of *p*-nitrobenzoate **25a**, the alcohol **24c** (127 mg, 0.59 mmol), *p*-nitrobenzoic acid (120 mg, 0.71 mmol) and triphenylphosphine (188 mg, 0.71 mmol) in toluene gave, after chromatography using light petroleum–ether (0.8:1) as an eluent, the ester **25c** (157 mg, 73%); δ_H (300 MHz; $CDCl_3$) 8.33 and 8.27 (each 2H, d, *J* 8, ArH), 5.42 (1H, t, *J* 8, 1′-H), 5.22 (1H, q, *J* 6, 3′-H), 4.22 (1H, m, 2-H), 3.22 (3H, s, OCH_3), 2.60 and 2.49 (each 1H, dt, *J* 15, 7.5, 2′-H), 2.29 (1H, m, 6-H), 2.10–1.10 (11H, m) and 0.98 (3H, t, *J* 7, 6′-H_3); δ_C (75 MHz; $CDCl_3$) 164.2, 150.4, 140.9, 136.0, 130.5, 123.4, 120.4, 75.8, 73.6, 55.0, 35.8, 32.7, 32.5, 31.7, 28.1, 20.7, 18.6 and 13.8; *m*/*z* (CI) 379 (M^++18, 4%), 330 (5), 300 (12) and 163 (100).

Following the procedure outlined for the synthesis of the alcohol **26a**, the ester **25c** (125 mg, 0.34 mmol) gave, after chromatography using light petroleum–ether (10:1), the *title compound* **26c** (57 mg, 77%) (found: M^++NH_4, 230.2115. $C_{13}H_{28}NO_2$ requires M, 230.2120); δ_H (300 MHz; $CDCl_3$) 5.44 (1H, t, *J* 8, 1′-H), 4.24 (1H, m, 2-H), 3.68 (1H, m, 3′-H), 3.24 (3H, s, OCH_3), 2.4–1.24 (14H, m) and 0.98 (3H, t, *J* 7, 6′-H_3); δ_C (75 MHz; $CDCl_3$) 141.1, 121.9, 73.7, 71.1, 55.0, 38.9, 34.9, 32.6, 32.5, 28.2, 20.7, 18.9 and 14.0; *m*/*z* (CI) 230 (M^++18, 100%) and 213 (M^++1, 68).

4.16. (*Z*)-(2*SR*,3′*RS*)-2-Methoxy-1-(3-*p*-nitrophenyl-3-*p*-nitrophenylcarbonyloxypropylidene)cyclohexane 27

p-Nitrobenzoyl chloride (124 mg, 0.668 mmol) was added to the homoallylic alcohol **24f** (65 mg, 0.223 mmol) and triethylamine (155 μl, 1.112 mmol) in dichloromethane (5 cm^3) at ambient temperature. The resulting mixture was stirred for 18 h then poured into water (10 cm^3) and extracted with dichloromethane (2×10 cm^3). The organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Flash column chromatography of the residue, eluting with ether–light petroleum (1:2), afforded the *title compound* **27** (72 mg, 73%) as a yellow solid. An analytical sample was recrystallised from ether to give pale yellow needles, mp 117–119 °C (found: C, 62.3; H, 5.5; N, 6.4%; M^+, 440.1582. $C_{23}H_{24}N_2O_7$ requires C, 62.7; H, 5.5; N, 6.4%; M, 440.1583); ν_{max} (Nujol) 1721, 1608, 1529, 1460, 1350, 1269, 1116, 1098, 853 and 716 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 8.41–8.14 (6H, m, ArH), 7.59 (2H, d, *J* 8, ArH), 6.04 (1H, t, *J* 7, 3′-H), 5.28 (1H, br t, *J* 7, 1′-H), 4.01 (1H, m, 2-H), 3.17 (3H, s, OCH_3), 2.86 (2H, m, 2′-H_2), 2.25 (1H, m, 6-H) and 1.97–0.81 (7H, m); δ_C (75 MHz; $CDCl_3$) 163.7, 150.7, 147.7, 146.4, 142.8, 135.0, 130.7, 127.4, 123.8, 123.6, 118.2, 76.4, 73.8, 55.1, 33.7, 32.7, 32.3, 28.0 and 20.5; *m*/*z* (CI) 458 (M^++18, 6%), 409 (12), 379 (13), 242 (77), 212 (32), 155 (27) and 59 (100).

4.17. Crystallographic data for ester 27

$C_{23}H_{24}N_2O_7$, *M*=440.45, triclinic *P*-1, *a*=8.869 Å, *b*=20.469 Å, *c*=6.201 Å, *α*=93.582°, *β*=99.109°, *γ*=81.589°, *V*=1098.7 $Å^3$, *Z*=2, *T*=296 K, *λ*=1.5418. A tabular crystal, 0.35×0.25×0.17 mm^3, was used to measure 4738 reflections on a Rigaku AFC5R (R_{int}=0.02, 4445 unique). The structure was solved by direct methods and refined anisotropically on F^2. Hydrogen atoms were located geometrically. The final agreement indices are: *R*=0.054, *wR*=0.147 ($I>2\sigma(I)$, 3102 reflections), R_{all}=0.083. The structure is deposited at the Cambridge Crystallographic Data Centre as CCDC no. 632903.

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