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Acyclic Stereocontrol of Free Radical Reactions Involving Alkyl 2-(1-Hydroxyalkyl)propenoates*

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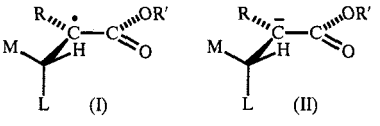
Abstract

The addition of cyclohexyl and t-butyl free radicals to silylated derivatives of alkyl 2-(1-hydroxyalkyl)propenoates was found to be stereoselective. In the case of the cyclohexyl radical the stereoselectivity was dependent upon the conditions used to generate the free radical and to quench the intermediate. Stereoselectivity in additions of the t-butyl radical was found to be temperature-dependent. In all cases stereoselectivity increased as the steric bulk of the group attached to the carbinol oxygen increased. A simple model which accounts for the stereoselectivity is proposed.

The control of stereoselectivity in intermolecular organic free radical reactions has only recently begun to be investigated systematically.[1] The stereocontrol elements which may be used will likely be similar to those used in other classes of reactions.[2] In the case of 1,2-stereoinduction, it has become apparent that stereochemical parallels exist between radical and ionic reactions.[3,4] The proposed preferred geometries for ester-subsituted radicals[5] and enolates[6–8] bearing an adjacent stereogenic centre are shown in (I) and (II) respectively. In both cases it is assumed that allylic strain[9] is the dominant factor in determining the preferred conformations.



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[2] Morrison, J. D., (Ed.), 'Asymmetric Synthesis' Vol. 3 (Academic Press: New York 1984).
[3] Erdmann, P., Schafer, J., Springer, R., Zeitz, H.-G., and Giese, B., *Helv. Chim. Acta*, 1992, **75**, 638.
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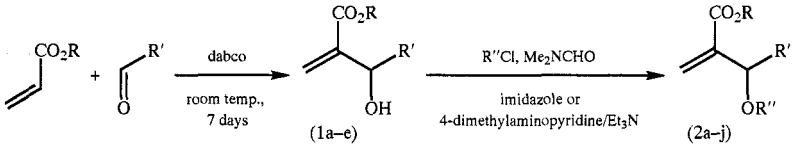
Table 1. Results of conjugate additions of cyclohexyl radical to alkenoates (1a–e) and (2a–j)

Entry No.	Alkene	R	R′	R″	Method	Product	Diastereoselectivity (*anti* to *syn*)	Isolated yield (%)
1	(1a)	Me	Me	H	*A*	(3a)	1:1	81
2	(1a)	Me	Me	H	*B*	(3a)	1:1	69
3	(1b)	Me	Pr^i	H	*A*	(3b)	1:1	76
4	(1b)	Me	Pr^i	H	*B*	(3b)	1:1	66
5	(1c)	Me	Ph	H	*A*	(3c)	1:1	97
6	(1c)	Me	Ph	H	*B*	(3c)	1:1	95
7	(1d)	Me	α-naphthyl	H	*A*	(3d)	2:1	91
8	(1d)	Me	α-naphthyl	H	*B*	(3d)	2:1	76
9	(1e)	Bu^t	Me	H	*A*	(3e)	1:1	78
10	(1e)	Bu^t	Me	H	*B*	(3e)	1:1	81
11	(2a)	Me	Me	Bu^tMe_2Si	*A*	(3k)	5:1	90
12	(2a)	Me	Me	Bu^tMe_2Si	*B*	(3k)	1:1	72
13	(2b)	Me	Pr^i	Bu^tMe_2Si	*A*	(3l)	6:1	79
14	(2b)	Me	Pr^i	Bu^tMe_2Si	*B*	(3l)	1:1	53
15	(2c)	Me	Ph	Bu^tMe_2Si	*A*	(3m)	4:1	89
16	(2c)	Me	Ph	Bu^tMe_2Si	*B*	(3m)	1:1	83
17	(2d)	Me	α-naphthyl	Bu^tMe_2Si	*A*	(3n)	3:1	97
18	(2d)	Me	α-naphthyl	Bu^tMe_2Si	*B*	(3n)	3:1	72
19	(2e)	Bu^t	Me	Bu^tMe_2Si	*A*	(3o)	3:1	78
20	(2e)	Bu^t	Me	Bu^tMe_2Si	*B*	(3o)	1:1	60
21	(2f)	Me	Me	Bu^tPh_2Si	*A*	(3f)	5:1	95
22	(2f)	Me	Me	Bu^tPh_2Si	*B*	(3f)	7:1	78
23	(2g)	Me	Pr^i	Bu^tPh_2Si	*A*	(3g)	7:1	78
24	(2h)	Me	Ph	Bu^tPh_2Si	*A*	(3h)	6:1	91
25	(2i)	Me	α-naphthyl	Bu^tPh_2Si	*A*	(3i)	2:1	85
26	(2j)	Bu^t	Me	Bu^tPh_2Si	*A*	(3j)	5:1	92

Recently, we have shown that conjugate additions of neutral[7] or anionic[10] nucleophiles to alkyl 2-(1-hydroxyalkyl)alkenoates are highly stereoselective. In this paper we show that reasonable levels of stereoselection can also be obtained in the addition of organic free radicals to these alkenoates. Also, we propose that, in support of previous suggestions, the stereoselectivity is due to hydrogen abstraction by (I) (where M is an alkyl or aryl group and L is a silyloxy group).

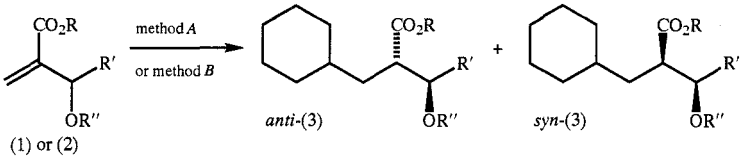
Results and Discussion

Two methods were used to generate the cyclohexyl free radical (Cy). The first (method *A*)[11] involved the use of iodocyclohexane, tributylstannane and an initiator, either ultraviolet light or azobis(isobutyronitrile). The second method (method *B*)[12] used the reductive decomposition of a cyclohexylmercury bromide by sodium borohydride to generate the organic free radical Cy. The alkyl 2-(1-hydroxyalkyl)propenoates (1a–e) (Table 1) were prepared as described earlier[13,14] and the corresponding t-butyldimethylsilyl (Bu^tMe_2Si) and t-butyldiphenylsilyl (Bu^tPh_2Si) ethers (2a–j) (Table 1) were prepared in the standard manner [equation *(1)*].[15,16]



(1)

The results obtained for the additions of the cyclohexyl radical to alkenoates (1a–e) and (2a–j) to give mixtures of diastereoisomers (3a–o) [equation *(2)*] are given in Table 1. These alkenoates were chosen as they provide the possibility for variation of the substituents R, R′ and R″ (see below for a discussion of their influence on stereocontrol).

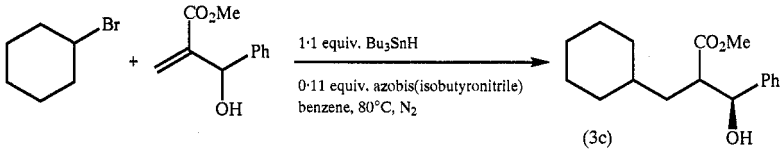


(2)

Method *A*: iodocyclohexane, Bu_3SnH, azobis(isobutyronitrile), benzene, 80°C.
Method *B*: cyclohexylmercury bromide, $NaBH_4$, CH_2Cl_2, 20°C.

[10] Lawrence, R. M., and Perlmutter, P., *Chem. Lett.*, 1992, 305.
[11] Giese, B., Dupuis, J., and Nix, M., *Org. Synth.*, 1987, **65**, 236.
[12] Giese, B., and Meixner, J., *Chem. Ber.*, 1981, **114**, 2138.
[13] Bayliss, A. B., and Hillman, M. E. D., Ger. Pat. 2155113, May 1972, (*Chem. Abstr.*, 1972, **77**, 34174q).
[14] Hoffman, H. M. R., and Rabe, J., *J. Org. Chem.*, 1985, **50**, 3849.
[15] Bu^tMe_2Si ethers: Chaudary, S. K., and Hernandez, O., *Tetrahedron Lett.*, 1979, 99.
[16] Bu^tPh_2Si ethers: Hanessian, S., and Lavallee, P., *Can. J. Chem.*, 1975, **53**, 2975.

Table 1 shows that the chemical yields of these free radical additions are good. From this work and other recent reports[17,18] it is becoming clear that efficient *intermolecular* free radical additons, using close to stoichiometric ratios of reactants, are possible. This is in contrast to earlier work where the use of a large excess of one of the reactants was common.[19] We examined different ratios of reactants in the following addition [equation *(3)*] and found that ratios of 1 : 2 through to 1 : 10 (cyclohexylbromide/alkene) gave acceptable yields (Table 2).



(3)

Table 2. Variation in yield of (3c) with different ratios of reactants in the addition of cyclohexyl radical to propenoate (1c) [equation *(3)*]

c-$C_6H_{11}Br$ to (1c)	Isolated yield (%) of (3c)
2 : 1	42
1 : 1	36
1 : 2	53
1 : 5	68
1 : 10	55

It can be seen from Table 1, however, that only with method *A* was any significant stereoselectivity observed. The best selectivity was found in additions to the t-butyldiphenylsilyl ethers (entries 21–26). The use of the less bulky protecting group Bu^tMe_2Si on the secondary alcohol led to lower selectivities. The best selectivities were of the order of 7 : 1.

Giese's group have reported the addition of the t-butyl radical to two of the alkenoates used in our study (2a,f).[5] They claimed stereoselectivity as high as 19 : 1 (*anti/syn*). In our hands it was found that an upper limit on the stereoselectivity was 13 : 1. Also, the stereoselectivity in these additions was quite temperature-dependent. As shown in Table 3 the selectivity varies from 13 : 1 at 18°C to *c.* 7 : 1 at 80°C.

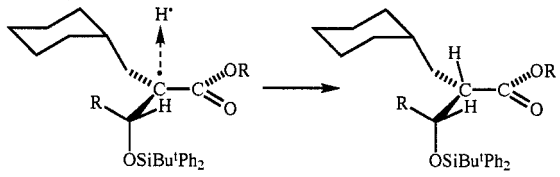
The simplest picture which accounts for the selection in favour of the *anti* diastereoisomer has hydrogen atom abstraction occurring from the conformation shown in Scheme 1 which is equivalent to conformation (I) described above.[5] In this conformation, reaction at one face of the free radical intermediate is sterically hindered by the bulky silyl group and therefore reaction occurs preferentially at the other face.

[17] Scott, D. M., McPhail, A. T., and Porter, N. A., *Tetrahedron Lett.*, 1990, **31**, 1679.
[18] Porter, N. A., Scott, D. M., Rosenstein, I. J., Giese, B., Veit, A., and Zeitz, H.-G., *J. Am. Chem. Soc.*, 1991, **113**, 1791.
[19] Giese, B., 'Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds' (Pergamon Press: Oxford 1986).

Table 3. Results of photo-initiated free radical additions to propenoates (1c) and (2c,f)

Entry No.	Radical[A]	Alkene	Bath temp. (°C)	Solvent	Yield (%)	*anti* to *syn*	Ref.
1	Cy	(1c)	−78	Et_2O	46	1:1	this work
2	Cy	(2c)	−78	Et_2O	36	78:22	this work
3	Cy	(2f)	18	toluene	78[B]	86:14	this work
4	Bu^t	(2f)	20[C]	toluene	97[B]	19:1	ref. 5
5	Bu^t	(2f)	23	toluene	56[B]	93:7	this work
6	Bu^t	(2f)	80	toluene	32[B]	87:13	this work

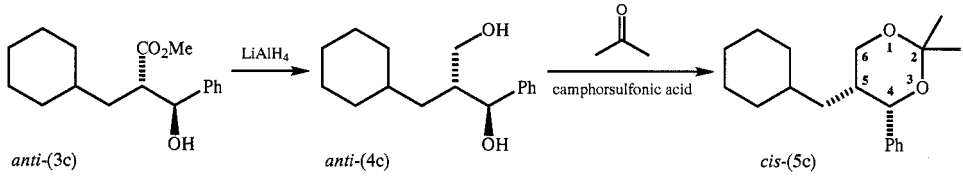
[A] Cy from iodocyclohexane; Bu^t from t-butyl iodide.
[B] Yields of isolated products.
[C] Method for temperature measurement not given.



Scheme 1

Proof of Relative Stereochemistry

In most cases the adducts were obtained as an inseparable mixture of diastereoisomers. However, the adducts (3c) from addition of cyclohexyl radical to (1c) were separable by preparative thin layer chromatography. One of these diastereoisomers was converted into the corresponding dioxan as shown in Scheme 2. For (5c), $J_{4,5}$ was found to be small (2·5 Hz) in the ^{1}H n.m.r. spectrum; this indicated that the C4 and C5 substituents are *cis* to each other in the ring. This, in turn, shows that the hydroxy ester has *anti* relative stereochemistry as shown.



anti-(3c) *anti*-(4c) *cis*-(5c)

Scheme 2

For the products from additions to (1a) and (2a,e,f,j) the stereochemical outcome was determined in the following way. Each mixture was reduced with lithium aluminium hydride to give a mixture of the corresponding diols (reduction was always accompanied by smooth desilylation during workup).

In each case the isomeric mixture of diols was converted into the corresponding mixture of dioxans. The isomeric ratio remained constant throughout these transformations. As for (5c), mentioned above, the major dioxan was the *cis* isomer which corresponded to the *anti* ester adduct. Comparisons of the ^{1}H n.m.r. spectra of this diol mixture (whose spectra had been assigned) with those

for each of the other diol mixtures indicated that the major diol in each case was derived from the corresponding *anti* ester adduct.

Similar correlations were carried out for the products of addition to (1d) and (2d,h,i). (Only in the isopropyl cases, (2b,g), were the relative stereochemistries assigned by analogy.)

Conclusion

The addition of cyclohexyl and t-butyl free radicals to *O*-silyl derivatives of alkyl 2-(1-hydroxyalkyl)propenoates was found to proceed with complete regioselectivity and good stereoselectivity. The best stereoselectivity was obtained where the largest silyl protecting group was employed. A simple model, based on steric control, accounts for the stereoselectivity observed.

Experimental

General

General conditions are as described previously.[20]

Additions to 2-(1-Hydroxyalkyl)propenoates

Methyl 2-(Cyclohexylmethyl)-3-hydroxybutanoate (3a)

Method A.[11]—A solution of tributylstannane (873 mg, 3·00 mmol) in benzene (0·5 ml) was added dropwise to a solution of methyl 3-hydroxy-2-methylenebutanoate (1a) (163 mg, 1·25 mmol), iodocyclohexane (525 mg, 2·50 mmol) and azobis(isobutyronitrile) (49 mg, 0·30 mmol) in benzene (2·5 ml) heated at reflux under an atmosphere of argon over a 1 h period. After the addition was complete the reaction mixture was heated at reflux for a further 3 h. The reaction mixture was allowed to cool to room temperature, the solvent was removed under vacuum and the residue was stirred vigorously for 1 h with ether (10 ml) and saturated aqueous potassium fluoride solution (10 ml). The reaction mixture was filtered, the ethereal layer was separated and the aqueous phase was extracted with ether (2×10 ml). The combined organic phases were dried (Na_2SO_4), and filtered and the solvent was removed under vacuum. G.l.c. analysis of the crude reaction mixture indicated the presence of both diastereoisomers of the title alcohol (3a) at R_t 6·62 and 6·70 min in a 1:1 ratio. Purification of the residue by preparative t.l.c. (70:30 light petroleum/ethyl acetate) gave the title alcohol mixture (3a) as a colourless liquid (218 mg) in 81% overall yield.

Method B.[12]—A suspension of sodium borohydride (78 mg, 2·05 mmol) in deoxygenated water (0·5 ml) was added to a stirred solution of cyclohexylmercury bromide (372 mg, 1·03 mmol) and methyl 3-hydroxy-2-methylenebutanoate (1a) (67 mg, 0·52 mmol) in deoxygenated dichloromethane (1 ml) at room temperature under an atmosphere of argon. The reaction mixture was then stirred vigorously for 4 h. The reaction mixture was filtered to remove metallic mercury, then extracted with ether (3×20 ml). The combined ethereal extracts were dried (Na_2SO_4) and filtered and the solvent was removed under vacuum. G.l.c. analysis of the crude reaction mixture indicated the presence of both diastereoisomers of the title alcohol (3a) at R_t 6·68 and 6·77 min in a 1:1 ratio. Purification of the residue by preparative t.l.c. (70:30 light petroleum/ethyl acetate) gave the title alcohol mixture (3a) (60 mg), in 69% overall yield, as a colourless oil (Found: C, 67·4; H, 10·6. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·4%). F.t.i.r. ν_{max} (neat) 3448s(br), 1736s cm^{-1}. ^1H n.m.r. (200 MHz) δ 4·00, dq, *J* 5·0, 6·3 Hz, 0·5H, CHO**H**, diastereoisomer A; 3·87, p, *J* 6·3 Hz, 0·5H, C**H**OH, diastereoisomer B; 3·75, s, 1·5H, CO_2Me, A or B; 3·74, s, 1·5H, CO_2Me, A or B; 2·64–2·49, m, 1H, C**H**CO_2Me, A, B; 2·44, br s, 1H, OH, A, B; 2·08–1·55, m, 6H, 1·49–1·04, m, 5H, 1·03–0·77, m, 2H, c-$C_6H_{11}C\mathbf{H}_2$, A, B; 1·25, d, *J* 6·3 Hz, 1·5H, **Me**CH, A or B; 1·21, d, *J* 6·3 Hz, 1·5H, **Me**CH, A or B. Mass spectrum (methane c.i.) *m/z* 261 (M+1, 13%), 215

[20] Doyle, M. M., Jackson, W. R., and Perlmutter, P., *Aust. J. Chem.*, 1989, **42**, 1907.

(M, 100), 197 (33), 183 (28), 165 (71), 147 (10), 137 (42), 118 (10), 95 (28), 87 (94), 81 (24), 67 (18), 55 (47).

1,1-Dimethylethyl 2-(Cyclohexylmethyl)-3-hydroxybutanoate (3e)

Method *A*, as described above for (1a), gave, on reaction of (1e), (3e) as an inseparable 1:1 mixture of diastereoisomers in 78% yield. Method *B*, as described above for (1a), gave, on reaction of (1e), (3e), an inseparable 1:1 mixture of diastereoisomers in 81% yield as a colourless oil (Found: C, 70·2; H, 11·0. $C_{15}H_{28}O_3$ requires C, 70·3; H, 11·0%). F.t.i.r. ν_{max} (neat) 3438s(br), 1727s cm^{-1}. ^1H n.m.r. (200 MHz) δ 4·00–3·92, m, 0·5H, **CH**OH, diastereoisomer A; 3·87–3·77, m, 0·5H, **CH**OH, diastereoisomer B; 2·72, d, *J* 8·1 Hz, 0·5H, OH, A or B; 2·59, d, *J* 4·3 Hz, 0·5H, OH, A or B; 2·48–2·36, m, 1H, **CH**CO_2Bu^t; A, B; 1·91–1·57, m, 6H, 1·45–1·12 m, 5H, 1·03–0·83, m, 2H, c-$C_6H_{11}CH_2$, A, B; 1·51, s, 4·5H, CO_2Bu^t, A or B; 1·50, s, 4·5H, CO_2Bu^t, A or B; 1·25, d, *J* 6·3 Hz, 1·5H, **Me**CH, A or B; 1·20, d, *J* 6·3 Hz, 1·5H, **Me**CH, A or B. Mass spectrum (methane c.i.) *m/z* 257 (M+1, 100%), 201 (66), 183 (12), 97 (11), 73 (10), 57 (52).

Methyl 2-(Cyclohexylmethyl)-3-hydroxy-4-methylpentanoate (3b)

Method *A* gave, on reaction of (1b), (3b) as a 1:1 mixture of diastereoisomers in 76% yield. Method *B* gave (3b) again as a 1:1 mixture of diastereoisomers in 66% yield.

Diastereoisomer A.—Colourless oil (Found: C, 69·1; H, 11·0. $C_{14}H_{26}O_3$ requires C, 69·4; H, 10·8%). F.t.i.r. ν_{max} (neat) 3516s(br), 1781s cm^{-1}. ^1H n.m.r. (200 MHz) δ 3·73, s, 3H, CO_2Me; 3·36, br s, 1H, **CH**OH; 2·77, dt, *J* 5·3, 9·6 Hz, 1H, **CH**CO_2Me; 2·54, br s, 1H, OH; 1·88–1·54, m, 7H, 1·51–1·37, m, 1H, 1·32–1·11, m, 4H, 1·05–0·50, m, 2H, c-$C_6H_{11}CH_2$, **CH**Me_2; 0·98, d, *J* 3·5 Hz, 3H, **Me**CH; 0·92, d, *J* 3·5 Hz, 3H, **Me**CH. Mass spectrum (methane c.i.) *m/z* 243 (M+1, 6%), 211 (22), 199 (22), 193 (53), 165 (13), 95 (11), 87 (16), 83 (28), 73 (41), 71 (46), 57 (100).

Diastereoisomer B.—Colourless oil (Found: C, 69·0; H, 11·0. $C_{14}H_{26}O_3$ requires C, 69·4; H, 10·8%). F.t.i.r. ν_{max} (neat) 3504s(br), 1737s cm^{-1}. ^1H n.m.r. (200 MHz): δ 3·74, s, 3H, CO_2Me; 3·50, apparent dt, *J* 4·1, 6·7 Hz, 1H, **CH**OH; 2·73, ddd, *J* 3·4, 4·6, 11·4 Hz, 1H, **CH**CO_2Me; 2·41, d, *J* 3·9 Hz, OH; 1·90–1·64, m, 7H, 1·62–1·42, m, 1H, 1·39–1·11, m, 4H, 1·07–0·67, m, 2H, c-$C_6H_{11}CH_2$, **CH**Me_2; 1·01, d, *J* 6·7 Hz, 3H, **Me**CH; 0·92, d, *J* 6·7 Hz, 3H, **Me**CH. Mass spectrum (methane c.i.) *m/z* 243 (M+1, 7%), 225 (49), 211 (18), 193 (48), 165 (16), 143 (18), 141 (26), 109 (33), 95 (16), 87 (72), 71 (46), 57 (100).

Methyl 2-(Cyclohexylmethyl)-3-hydroxy-3-phenylpropanoate (3c)

Bromocyclohexane, tributylstannane and azobis(isobutyronitrile) were added to a stirred solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (1c) in benzene (1·4 ml) under an atmosphere of nitrogen, and the solution was then heated at reflux for 30 min. The mixture was allowed to cool to room temperature. Workup was as for (3a), method *A*. ^1H n.m.r. spectroscopic analysis of the crude reaction mixture indicated the presence of both diastereoisomers of the title alcohol (3c) in a 1:1 ratio. Purification of the residue by preparative t.l.c. (80:20 light petroleum/ether) gave *syn*-(3c) as a colourless crystalline solid (m.p. 62·5–64·5°) and *anti*-(3c) as a colourless liquid in varying yields as shown in the following tabulation.

Reaction	1	2	3	4	5
Alkyl bromide	1·43	0·71	0·71	0·71	0·71 mmol
Olefin	0·71	0·71	1·43	3·57	7·14 mmol
Stannane	1·57	0·79	0·79	0·79	0·79 mmol
Azobis(isobutyronitrile)	0·16	0·08	0·08	0·08	0·08 mmol
Ratio of *syn* to *anti*	1:1	1:1	1:1	1:1	1:1
Isolated yield	42	36	53	68	55%

Method *A* gave, on reaction of (1c), (3c) as a 1:1 mixture of diastereoisomers in 97% overall yield. Method *B*, and a reaction time of 4 h, gave (3c) as a 1:1 mixture of diastereoisomers in 95% yield. Reducing the reaction time to 1 h resulted in a reduced yield of 36%. Replacing cyclohexylmercury bromide with cyclohexylmercury acetate and using a reaction time of 1 h reduced the yield to 32%.

Method C.—Iodocyclohexane (146 mg, 0·71 mmol) and tributylstannane (277 mg, 0·79 mmol) were added to a solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (1c) (137 mg, 0·71 mmol) in dry, de-oxygenated ether (1·4 ml) under an atmosphere of argon. The resulting solution was transferred to the quartz reaction vessel which had previously been flushed with argon, cooled to −78° (dry ice/acetone) and irradiated for 4·5 h with ultraviolet light (254 nm). The reaction mixture was allowed to warm to room temperature. Workup was as for (3a), method *A*. ^{1}H n.m.r. spectroscopic analysis of the crude reaction mixture after workup indicated the presence of both diastereoisomers of the title alcohol in a 1:1 ratio. An isolated yield was not obtained; however, the ^{1}H n.m.r. spectroscopic analysis indicated a 46% yield.

syn-*(3c)*.—Colourless crystals, m.p. 62·5–64·5° (Found: C, 74·0; H, 8·8. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·8%). F.t.i.r. ν_{max} (Nujol) 3335s(br), 1734s cm^{-1}. ^{1}H n.m.r. (200 MHz) δ 7·35, m, 5H, Ph; 4·74, d, *J* 7·8 Hz, 1H, C**H**OH; 3·69, s, 3H, CO_2Me; 2·96–2·84, ddd, *J* 4·2, 7·8, 10·6 Hz, 1H, C**H**CO_2Me; 2·96–3·50, br s, 1H, OH; 1·78–1·38, m, 6H, 1·27–1·03, m, 5H, 1·02–0·63, m, 2H, c-$C_6H_{11}CH_2$. Mass spectrum (methane c.i.) *m/z* 277 (M+1, 0·5%), 276 (M, 2), 259 (59), 227 (100), 199 (19), 197 (19), 171 (21), 170 (53), 121 (15), 107 (63), 97 (28), 87 (82), 83 (13), 79 (33), 55 (17).

anti-*(3c)*.—Colourless oil (Found: C, 74·1; H, 8·8. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·8%). F.t.i.r. ν_{max} (neat) 3471s(br), 1733s, 1604w cm^{-1}. ^{1}H n.m.r. (300 MHz) δ 7·35, m, 5H, Ph; 4·93, dd, *J* 2·9, 5·3 Hz, 1H, C**H**OH; 3·60, s, 3H, CO_2Me; 2·87–2·81, ddd, *J* 3·6, 5·3, 10·9 Hz, 1H, C**H**CO_2Me; 2·79, d, *J* 2·9 Hz, 1H, OH; 1·74–1·58, m, 6H, 1·46–1·25, m, 1H, 1·24–1·04, m, 4H, 0·92–0·81, m, 1H, 0·80–0·61, m, 1H, c-$C_6H_{11}CH_2$. Mass spectrum (methane c.i.) *m/z* 276 (M, 2%), 259 (100), 227 (52), 197 (7), 170 (30), 121 (10), 107 (38), 97 (21), 87 (90), 79 (29), 55 (19).

Methyl 2-(Cyclohexylmethyl)-3-hydroxy-3-(1-naphthyl)propanoate (3d)

Method *A* gave, on reaction of (1d), (3d) as a separable 1:1 mixture of diastereoisomers in 78% yield. Method *B* gave (3d) as a separable 1:1 mixture of diastereoisomers in 81% yield.

syn-*(3d)*.—Colourless oil (Found: C, 77·2; H, 8·3. $C_{21}H_{26}O_3$ requires C, 72·3; H, 8·0%). F.t.i.r. ν_{max} (neat) 3467s(br), 1732s, 1598w cm^{-1}. ^{1}H n.m.r. (200 MHz) δ 8·21–8·16, m, 1H, 7·95–7·77, m, 2H, 7·63–7·46, m, 4H, naphthyl ring protons; 5·56, t, *J* 6·5 Hz, 1H, C**H**OH; 3·70, s, 3H, CO_2Me; 3·27, ddd, *J* 4·0, 6·5, 10·6 Hz, 1H, C**H**CO_2Me; 3·19, d, *J* 6·5 Hz, 1H, OH; 1·81–1·42, m, 6H, 1·31–1·00, m, 5H, 0·89–0·60, m, 2H, c-$C_6H_{11}CH_2$. Mass spectrum (methane c.i.) *m/z* 327 (M+1, 1%), 326 (M, 4%), 309 (31), 277 (73), 247 (14), 199 (11), 170 (28), 157 (100), 129 (39), 97 (17), 87 (59), 55 (34).

anti-*(3d)*.—Colourless oil (Found: C, 77·0; H, 8·3. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·0%). F.t.i.r. ν_{max} (neat) 3416 s(br), 1733s, 1598w cm^{-1}. ^{1}H n.m.r. (200 MHz) δ 8·08–7·94, m, 1H, 7·93–7·74, m, 3H, 7·61–7·45, m, 3H, naphthyl ring; 5·83, d, *J* 3·6 Hz, 1H, C**H**OH; 3·72, s, 3H, CO_2Me; 3·12, dt, *J* 3·6, 10·7 Hz, 1H, C**H**CO_2Me; 3·03, br s, 1H, OH; 1·83, ddd, *J* 4·4, 10·7, 13·8 Hz, 1H, c-C_6H_{11}C**H**; 1·65–1·25, m, 5H, 1·15–0·73, m, 5H, 0·56–0·38, m, 2H, c-C_6H_{11}CH. Mass spectrum (methane c.i.) *m/z* 327 (M+1, 7%), 326 (M, 22), 309 (100), 277 (44), 199 (10), 170 (28), 157 (65), 129 (31), 97 (15), 87 (59), 55 (33).

Additions to the 2-[((1,1-Dimethylethyl)dimethylsilyloxy)alkyl]propenoate Systems

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)butanoate (3k)

Method *A* gave, on reaction of (2a), (3k) as a separable 1:1 mixture of diastereoisomers in 90% yield. Method *B* gave (3k) as a separable 1:1 mixture of diastereoisomers in 66% yield.

syn-*(3k)*.—Colourless oil (Found: C, 65·5; H, 11·1. $C_{18}H_{36}O_3Si$ requires C, 65·8; H, 11·0%). F.t.i.r. ν_{max} (neat) 1741s cm^{-1}. ^{1}H n.m.r. (200 MHz) δ 3·95, dq, *J* 6·1, 7·7 Hz, 1H, CHOSi; 3·69, s, 3H, CO_2Me; 2·55, ddd, *J* 3·5, 7·7, 11·1 Hz, 1H, C**H**CO_2Me; 1·89–1·43, m, 6H, 1·30–1·12, m, 5H, 0·94–0·59, m, 2H, c-$C_6H_{11}CH_2$; 1·17, d, *J* 6·1 Hz, 3H, **Me**CH; 0·89, s, 9H, Bu^{t}Si; 0·08, s, 3H, MeSi; 0·05, s, 3H, MeSi. Mass spectrum (methane c.i.) *m/z* 329 (M+1, 15%), 313 (M − 15, 12), 271 (M − 57, 100), 159 (35), 89 (17), 73 (10), 55 (11).

anti-*(3k)*.—Colourless oil (Found: C, 65·6; H, 11·3. $C_{18}H_{36}O_3Si$ requires C, 65·8; H, 11·0%). F.t.i.r. ν_{max} (neat) 1739s cm^{-1}. ^{1}H n.m.r. (200 MHz) δ 3·90, dq, *J* 6·2, 7·1 Hz, 1H, CHOSi; 3·70, s, 3H, CO_2Me; 2·52, ddd, *J* 4·5, 7·1, 10·1 Hz, 1H, C**H**CO_2Me; 1·84–1·35,

m, 7H, 1·29–1·03, m, 4H, 1·01–0·79, m, 2H, c-$C_6H_{11}CH_2$; 1·16, d, *J* 6·2 Hz 3H, **Me**CH; 0·91, s, 9H, Bu^tSi; 0·08, s, 6H, Me_2Si. Mass spectrum (methane c.i.) *m/z* 329 (M+1, 15%), 313 (M − 15, 14), 271 (M − 57, 100), 159 (44), 133 (15), 115 (12), 89 (25), 73 (13), 57 (14).

1,1-Dimethylethyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)butanoate (3o)

Method *A* gave, on reaction of (2e), (3o) as an inseparable 3:1 (*anti/syn*) mixture of diastereoisomers in 78% yield. Method *B* gave (3o), an inseparable 1:1 mixture of diastereoisomers in 60% yield, as a colourless oil (Found: C, 67·8; H, 11·8. $C_{21}H_{42}O_3Si$ requires C, 68·1; H, 11·4%). F.t.i.r. ν_{max} (neat) 1729s cm^{-1}. ^1H n.m.r. (200 MHz) δ 4·01, p, *J* 6·2 Hz, 0·5H, CHOSi, diastereoisomer B (*syn*); 3·81, dq, *J* 6·1, 7·8 Hz, 0·5H, CHOSi, diastereoisomer A (*anti*); 2·59–2·34, m, 1H, **CH**CO_2Bu^t, A, B; 1·92–1·57, m, 6H, 1·31–1·02, m, 5H, 1·01–0·60, m, 2H, c-$C_6H_{11}CH_2$, A, B; 1·48, s, 4·5H, CO_2Bu^t, B; 1·47, s, 4·5H, CO_2Bu^t, A; 1·18, d, *J* 6·1 Hz, 1·5H, **Me**CH, A; 1·14, d, *J* 6·2 Hz, 1·5H, **Me**CH B; 0·92, s, 4·5H, Bu^tSi, A; 0·91, s, 4·5H, Bu^tSi, B; 0·09, s, 3H, Me_2Si, A or B; 0·08, s, 3H, Me_2Si, A or B. Mass spectrum (methane c.i.) *m/z* 371 (M+1, 50%), 315 (100), 297 (38), 257 (53), 159 (93), 119 (26), 115 (48), 95 (14), 75 (44), 57 (78).

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)-4-methylpentanoate (3l)

Method *A* gave, on reaction of (2b), (3l) as an inseparable 6:1 (*anti/syn*) mixture of diastereoisomers in 79% yield. Method B gave (3l), an inseparable 1:1 mixture of diastereoisomers in 53% yield, as a colourless oil (Found: C, 67·3; H, 11·4. $C_{20}H_{40}O_3Si$ requires C, 67·4; H, 11·3%). F.t.i.r. ν_{max} (neat) 1723s cm^{-1}. ^1H n.m.r. (200 MHz) δ 3·69, dd, *J* 3·8, 6·9 Hz, 0·5H, CHOSi, diastereoisomer B (*syn*); 3·65–3·60, m, 0·5H, CHOSi, diastereoisomer A (*anti*); 3·65, s, 1·5H, CO_2Me, A or B; 3·64, s, 1·5H, CO_2Me, A or B; 2·72–2·55, m, 1H, **CH**CO_2Me, A, B; 1·82–1·45, m, 8H, 1·33–1·04, m, 5H, 0·98–0·63, m, 1H, c-$C_6H_{11}CH_2$, **CH**Me_2, A, B; 0·90, d, *J* 6·7 Hz, 3H, Me_2CH, A or B; 0·89, s, 4·5H, Bu^tSi, A or B; 0·87, s, 4·5H, Bu^tSi, A or B; 0·84, d, *J* 6·7 Hz, 3H, Me_2CH, A or B; 0·03, s, 4·5H, Me_2Si, A, MeSi, B; −0·01, s, 1·5H, MeSi, B. Mass spectrum (methane c.i.) *m/z* 357 (M+1, 1%), 341 (M − 15, 11), 313 (11), 299 (M − 57, 100), 187 (65), 175 (12), 161 (15), 145 (20), 121 (20), 115 (20), 89 (67), 73 (71), 55 (25).

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)-3-phenylpropanoate (3m)

Method *A* gave, on reaction of (2c), (3m) as a separable 4:1 (*anti/syn*) mixture of diastereoisomers in 89% yield. The same isomer ratio but a lower yield (36%) were obtained when this reaction was run in diethyl ether at −78°C. Method *B* gave (3m) as a separable 1:1 mixture of diastereoisomers in 83% yield.

syn-*(3m)*.—Colourless oil (Found: C, 70·5; H, 9·5. $C_{23}H_{38}O_3Si$ requires C, 70·7; H, 9·8%). F.t.i.r. ν_{max} (neat) 1738s, 1602w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·29, m, 5H, Ph; 4·65, d, *J* 9·5 Hz, 1H, CHOSi; 3·72, s, 3H, CO_2Me; 2·77–2·90, ddd, *J* 3·5, 9·5, 11·7 Hz, 1H, **CH**CO_2Me; 1·72–1·21, m, 6H, 1·17–0·88, m, 4H, 0·76–0·41, m, 3H, c-$C_6H_{11}CH_2$; 0·79, s, 9H, Bu^tSi; −0·04, s, 3H, MeSi; −0·34, s, 3H, MeSi. Mass spectrum *m/z* 333 (M − 57, 57%), 221 (36), 195 (11), 145 (23), 121 (11), 89 (100), 73 (50), 59 (19).

anti-*(3m)*.—Colourless oil (Found: C, 70·6; H, 9·7. $C_{23}H_{38}O_3Si$ requires C, 70·7; H, 9·8%). F.t.i.r. ν_{max} (neat) 1736s, 1603w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·35, m, 5H, Ph; 4·77, d, *J* 7·7 Hz, 1H, CHOSi; 3·46, s, 3H, CO_2Me; 2·81–2·71, m, 1H, **CH**CO_2Me; 1·80–1·40, m, 7H, 1·29–1·02, m, 4H, 0·90–0·60, m, 2H, c-$C_6H_{11}CH_2$; 0·92, s, 9H, Bu^tSi; 0·07, s, 3H, MeSi; −0·20, s, 3H, MeSi. Mass spectrum *m/z* 375 (M − 15, 1%), 333 (M − 57, 83), 221 (53), 195 (19), 145 (23), 121 (14), 115 (10), 89 (100), 73 (59), 55 (17).

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)-3-(1-naphthyl)propanoate (3n)

Method *A* gave, on reaction of (2d), (3n) as an inseparable 3:1 (*anti/syn*) mixture of diastereoisomers in 97% yield. Method *B* gave (3n), an inseparable 3:1 (*anti/syn*) mixture of diastereoisomers in 72% yield, as a colourless oil (Found: C, 73·6; H, 9·5. $C_{27}H_{40}O_3Si$ requires C, 73·6; H, 9·2%). F.t.i.r. ν_{max} (neat) 1736s, 1598w cm^{-1}. ^1H n.m.r. (300 MHz,

−48°) [A denotes major rotamer of *anti*-(3n), A′ denotes minor rotamer of *anti*-(3n), B denotes major rotamer of *syn*-(3n) and B′ denotes minor rotamer of *syn*-(3n)] δ 8·64, d, *J* 9·4 Hz, 0·26H, 8·08, d, *J* 8·4 Hz, 0·74H, 7·90–7·68, m, 3H, 7·60–7·45, m, 2·40H, 7·31–7·13, m, 0·60H, naphthyl rings, A, A′, B, B′; 5·89, d, *J* 2·8 Hz, 0·69H, CHOSi, A; d, *J* 8·9 Hz, 0·05H, CHOSi, A′; 4·97, d, *J* 10·3 Hz, 0·03H, CHOSi, B′; 4·87, d, *J* 10·2 Hz, 0·23H, CHOSi, B; 3·65, s, 2·22H, CO_2Me, A, A′; 3·51–3·40, m, 0·26H, $CHCO_2Me$, B, B′; 3·10, s, 0·78H, CO_2Me, B, B′; 2·88–2·84, m, 0·74H, $CHCO_2Me$, A, A′; 1·93–1·73, m, 1H, 1·68–1·33, m, 5H, 1·26–0·21, m, 7H, c-$C_6H_{11}CH_2$, A, A′, B, B′; 0·91, s, 6·66H, Bu^tSi, A, A′; 0·80, s, 2·34H, Bu^tSi, B, B′; 0·08, s, 0·81H, MeSi, B, A′ or B′; −0·02, s, 2·19H, MeSi, A, A′ or B′; −0·10, s, 0·12H, MeSi, A′ or B′; −0·28, s, 2·07H, MeSi, A; −0·50, s, 0·69H, MeSi, B; −0·63, s, 0·12H, MeSi, A′ or B′. Mass spectrum *m/z* 425 (M − 15, 1%), 383 (M − 57, 99), 271 (95), 245 (15), 213 (31), 141 (25), 121 (12), 89 (96), 73 (100), 55 (19).

Additions to the 2-[((1,1-Dimethylethyl)diphenylsilyloxy)alkyl]propenoate Systems

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)butanoate (3f)

Method *A* gave, on reaction of (2f), (3f) as an inseparable 5:1 (*anti/syn*) mixture of diastereoisomers in 95% yield. Method *B* gave (3f), an inseparable 7:1 (*anti/syn*) mixture of diastereoisomers in 78% yield, as a colourless oil (Found: C, 74·5; H, 9·2. $C_{28}H_{40}O_3Si$ requires C, 74·3; H, 8·9%). F.t.i.r. ν_{max} (neat) 1738s, 1590w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·73–7·61, m, 4H, 7·48–7·35, m, 6H, 2×Ph, diastereoisomers A (*anti*) and B (*syn*); 4·09–4·01, m, 0·17H, CHOSi, B; 3·92, p, *J* 6·2 Hz, 0·83H, CHOSi, A; 3·64, s, 2·49H, CO_2Me, A; 3·63, s, 0·51H, CO_2Me, B; 2·68–2·54, m, 1H, $CHCO_2Me$, A, B; 1·86–1·48, m, 6H, 1·47–0·88, m, 5·51H, 0·86–0·68, m, 2H, c-$C_6H_{11}CH_2$, A, B, **Me**CH, B; 1·07, d, *J* 6·2 Hz, 2·49H, **Me**CH, A; 1·04, s, 7·47H, Bu^tSi, A; 1·01, s, 1·53H, Bu^tSi, B. Mass spectrum *m/z* 437 (M − 15, 0·3%), 395 (M − 57, 59), 257 (11), 213 (100), 199 (19), 183 (33), 153 (39), 135 (26), 105 (11), 55 (14).

1,1-Dimethylethyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)butanoate (3j)

Method *A* gave, on reaction of (2j), (3j), an inseparable 5:1 (*anti/syn*) mixture of diastereoisomers in 92% yield, as a colourless oil (Found: C, 75·4; H, 9·8. $C_{31}H_{46}O_3Si$ requires C, 75·3; H, 9·4%). F.t.i.r. ν_{max} (neat) 1726s, 1590w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·74–7·61, m, 4H, 7·43–7·32, m, 6H, 2×Ph, diastereoisomers A (*anti*) and B (*syn*); 4·13–4·07, m, 0·17H, CHOSi, B; 3·83, p, *J* 6·2 Hz, 0·83H, CHOSi, A; 2·52, ddd, *J* 4·3, 6·2, 10·5 Hz, 0·83H, $CHCO_2Bu^t$, A; 3·90–2·42, m, 0·17H, $CHCO_2Bu^t$; B; 1·86–1·49, m, 5H, 1·48–1·01, m, 12·06H, 1·00–0·66, m, 2H, c-$C_6H_{11}CH_2$, **Me**CH, A, B, CO_2Bu^t, Bu^tSi, B; 1·44, s, 7·47H, CO_2Bu^t, A; 1·05, s, 7·47H, Bu^tSi, A. Mass spectrum *m/z* 381 (24), 303 (11), 199 (100), 181 (31), 139 (73), 77 (13), 57 (29).

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)-4-methylpentanoate (3g)

Method *A* gave, on reaction of (2g), an inseparable 7:1 (*anti/syn*) mixture of diastereoisomers in 92% yield, as a colourless oil (Found: C, 75·3; H, 9·6. $C_{30}H_{44}O_3Si$ requires C, 75·0; H, 9·2%). F.t.i.r. ν_{max} (neat) 1736s, 1590w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·74–7·61, m, 4H, 7·43–7·32, m, 6H, 2×Ph, diastereoisomers A (*anti*) and B (*syn*); 3·83, dd, *J* 3·7, 6·1 Hz, 0·12H, CHOSi, B; 3·74, dd, *J* 3·1, 6·4 Hz, 0·88H, CHOSi, A; 3·55, s, 2·64H, CO_2Me, A; 3·49, s, 0·36H, CO_2Me, B; 2·78–2·72, m, 0·12H, $CHCO_2Me$, B; 2·64, ddd, *J* 4·1, 6·4, 10·5 Hz, 0·88H, $CHCO_2Me$, A; 1·77–1·48, m, 5H, 1·44–1·28, m, 3H, 1·26–0·54, m, 6·72H, c-$C_6H_{11}CH_2$, $CHMe_2$, A, B, Me_2CH, B; 1·05, s, 7·92H, Bu^tSi, A; 1·04, s, 1·08H, Bu^tSi, B; 0·88, d, *J* 6·9 Hz, 3·64H, **Me**CH, A; 0·79, d, *J* 6·9 Hz, 3·64H, **Me**CH, A. Mass spectrum *m/z* 465 (M − 15, 0·1%), 423 (M − 57, 55) 285 (12), 213 (100), 199 (15), 183 (23), 153 (15), 135 (31), 55 (10).

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)-3-phenylpropanoate (3h)

Method *A* gave, on reaction of (2h), (3h), an inseparable 6:1 (*anti/syn*) mixture of diastereoisomers in 92% yield, as a white solid (Found: C, 76·8; H, 8·3. $C_{33}H_{42}O_3Si$

requires C, 77·0; H, 8·2%). F.t.i.r. ν_{max} (Nujol) 1732s, 1588w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·70–7·53, m, 2H, 7·47–7·28, m, 6H, 7·23–6·98, m, 7H, 3×Ph, diastereoisomers A (*anti*) and B (*syn*); 4·75, d, *J* 9·2 Hz, 0·14H, CHOSi, B; 4·69, d, *J* 7·6 Hz, 0·86H, CHOSi, A; 3·57, s, 0·42H, CO_2Me, B; 3·31, s, 2·58H, CO_2Me, A; 3·06–2·94, m, 0·14H, C**H**CO_2Me, B; 2·83, ddd, *J* 3·6, 7·6, 11·1 Hz, 0·86H, C**H**CO_2Me, A; 1·68–1·36, m, 6H, 1·33–0·88, m, 5H, 0·82–0·62 m, 2H, c-$C_6H_{11}CH_2$, A, B; 1·00, s, 7·74H, Bu^tSi, A; 0·92, s, 1·26H, Bu^tSi, B. Mass spectrum *m/z* 457 (M − 57, 3%), 213 (100), 183 (18), 167 (34), 135 (14), 121 (11), 91 (11), 77 (10), 55 (26).

Methyl 2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)-3-(1-naphthyl)propanoate (3i)

Method *A* gave, on reaction of (2i), (3i), an inseparable 2:1 (*anti/syn*) mixture of diastereoisomers in 85% yield, as a colourless oil (Found: C, 78·3; H, 8·2. $C_{37}H_{44}O_3Si$ requires C, 78·7; H, 7·9%). F.t.i.r. ν_{max} (neat) 1736s, 1590w cm^{-1}. ^1H n.m.r. (300 MHz, −48°) δ 8·82, d, *J* 8·6 Hz, 0·34H, 7·86–7·83, m, 1H; 7·80–7·56, m, 3·32H; 7·54–7·31, m, 7H; 7·28–7·22, m, 1H; 7·18–7·00, m, 3H, 6·82, d, *J* 6·6 Hz, 0·34H, naphthyl rings, 2×Ph, diastereoisomers A (*anti*) and B (*syn*); 5·93, d, *J* 4·3 Hz, 0·66H, CHOSi, A; 4·80, d, *J* 9·8 Hz, 0·34H, CHOSi, B; 3·54, t, *J* 9·8 Hz, 0·34H, C**H**CO_2Me, B; 3·15, s, 1·98H, CO_2Me, A; 3·01, s, 1·02H, CO_2Me, B; 2·85–2·81, m, 0·66H, C**H**CO_2Me, A; 1·83–1·72, m, 1H, 1·70–1·34, m, 5H, 1·32–0·30, m, 7H, c-$C_6H_{11}CH_2$, A, B; 1·01, s, 5·94H, Bu^tSi, A; 0·93, s, 3·06H, Bu^tSi, B. Mass spectrum *m/z* 507 (M − 57, 40%), 395 (11), 337 (11), 213 (100), 183 (12), 135 (27), 55 (13).

Methyl 4,4-Dimethyl-2-(1-((1,1-dimethylethyl)diphenylsilyloxy)ethyl)pentanoate

A solution of tributylstannane (301 mg, 1·03 mmol) in toluene (2 ml) was added dropwise over a 2 h period to a solution of methyl 3-((1,1-dimethylethyl)diphenylsilyloxy)-2-methylenebutanoate (2f) (173 mg, 0·47 mmol) and 2-iodo-2-methylpropane (579 mg, 3·15 mmol) in toluene (3 ml) in a water bath at 23° under irradiation from a tungsten lamp (100 W) under an atmosphere of argon. Workup was as for (3a), method *A*. ^1H n.m.r. spectroscopic analysis of the crude reaction mixture indicated the presence of both diastereoisomers of the title silyl ether in a 7:93 (*syn/anti*) ratio. Purification of the residue by preparative t.l.c. (95:5 light petroleum/ethyl acetate) gave the title silyl ether as a colourless liquid (94 mg) in 61% overall yield. F.t.i.r. ν_{max} (neat) 1737s cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·74–7·64, m, 4H, 7·47–7·32, m, 6H, 2×Ph, diastereoisomers A (*anti*) and B (*syn*); 4·05–3·99, m, 0·07H, CHOSi, B; 3·87, p, *J* 6·0 Hz, 0·93H, CHOSi, A; 3·64, s, 2·79H, CO_2Me, A; 3·63, s, 0·21H, CO_2Me, B; 2·63–2·51, m, 0·07H, C**H**CO_2Me, B; 2·55, ddd, *J* 1·5, 6·0, 10·5 Hz, 0·93H, C**H**CO_2Me, A; 1·75, dd, *J* 10·8, 13·9 Hz, 0·07H, CH_2, B; 1·66, dd, *J* 10·5, 13·9 Hz, 0·93H, CH_2, A; 1·40–0·96, m, 3·70H, CH_2, B, Bu^tSi, B, MeCH, A, B; 1·21, dd, *J* 1·5, 13·9 Hz, 0·93H, CH_2, A; 1·05, s, 8·37H, Bu^tSi, A; 0·84, s, 0·63H, **Bu**^{t}CH_2, B; 0·76, s, 8·37H, **Bu**^{t}CH, A. Mass spectrum *m/z* 425 (M − 1, 0·3%), 396 (M − 57, 34), 257 (10), 213 (100), 199 (23), 183 (32), 181 (18), 155 (10), 153 (25), 135 (19), 105 (15), 77 (13), 57 (26). Repeating this reaction at 80° instead of 23° gave a 13:87 (*syn/anti*) ratio according to ^1H n.m.r. spectroscopic analysis of the crude reaction mixture. Purification of the residue by preparative t.l.c. (95:5 light petroleum/ethyl acetate) gave the title silyl ethers as a colourless liquid (55 mg) in 32% overall yield.

Reduction with Lithium Aluminium Hydride

2-(Cyclohexylmethyl)butane-1,3-diol (4a)

A solution of a diastereoisomeric mixture (18:82, *syn/anti*) of methyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)butanoate (3k) (363 mg, 1·11 mmol) in anhydrous ether (5ml) was added dropwise to a stirred suspension of lithium aluminium hydride (420 mg, 11·1 mmol) in anhydrous ether (15 ml) under an atmosphere of argon. The reaction mixture was heated at reflux for 2 h and cooled (ice bath), and ice (420 mg), aqueous sodium hydroxide solution (15% w/w, 420 mg) and ice (1·26 g) were added successively. The resulting suspension was stirred until a white granular powder formed. The reaction mixture was filtered, the

granular powder was washed with ethyl acetate (4×30 ml), and then the combined organic phase was washed with water (20 ml). The organic phase was separated, dried (Na_2SO_4), and filtered, and the solvent was removed under vacuum. Purification of the residual liquid by preparative t.l.c. (70:30 light petroleum/ethyl acetate) gave the title diol mixture (4a) as a colourless liquid (167 mg, 87%). The mixture became a colourless crystalline *solid* (m.p. 30–55°) on standing (Found: C, 71·0; H, 11·8. $C_{11}H_{22}O_2$ requires C, 70·9; H, 11·9%). F.t.i.r. ν_{max} (neat) 3346s(br) cm^{-1}. ^1H n.m.r. (200 MHz): δ 4·02, dq, J 2·9, 6·4 Hz, 0·82H, **CH**OH, diastereoisomer A (*syn*); 3·90–3·51, m, 0·54H, **CH**OH, CH_aH_b, diastereoisomer B (*anti*); 3·73, dd, J 7·6, 10·8 Hz, 0·82H, CH_a or CH_b, A; 3·64, dd, J 4·1, 10·8 Hz, 0·82H, CH_a or CH_b, A; 3·24, br s, 2H, 2×OH, A, B; 1·89–1·44, m, 6H, 1·38–0·94, m, 6H, 0·91–0·68, m, 2H, c-$C_6H_{11}CH_2CH$, A, B; 1·22, d, J 6·3 Hz, 0·54H, **Me**CH, B; 1·16, d, J 6·4 Hz, 2·46H, **Me**CH, A. Mass spectrum m/z 169 (M − 17, 1%), 124 (54), 96 (40), 83 (100), 82 (99), 81 (61), 79 (18), 67 (74), 63 (14), 57 (19), 55 (100).

In a similar manner a diastereoisomeric mixture (1:3, *syn/anti*) of 1,1-dimethylethyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)butanoate (3o) gave diol (4a) as a 1:3 mixture of diastereoisomers in 93% yield.

In a similar manner a diastereoisomeric mixture (1:5, *syn/anti*) of methyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)butanoate (3f) gave diol (4a) as a 1:5 mixture of diastereoisomers in 85% yield.

In a similar manner a diastereoisomeric mixture (1:5, *syn/anti*) of 1,1-dimethylethyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)butanoate (3j) gave diol (4a) as a 1:5 mixture of diastereoisomers in 84% yield.

anti-*2-(Cyclohexylmethyl)-1-phenylpropane-1,3-diol (4c)*

Reduction of methyl *anti*-2-(cyclohexylmethyl)-3-hydroxy-3-phenylpropanoate [*anti*-(3c)] in a manner similar to that for (3k) gave *anti*-(4c) as a white solid in 46% yield, m.p. 93–94·5° (Found: C, 77·7; H, 9·4. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%). F.t.i.r. ν_{max} (Nujol) 3322s(br), 1601w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·35, m, 5H, Ph; 5·00, d, J 3·4 Hz, 1H, **CH**OH; 3·69, d, J 5·0 Hz, 2H, CH_2OH; 3·13, br s, 1H, OH; 2·59, br s, 1H, OH; 2·15–2·01, m, 1H, **CH**CH_2OH; 1·90–1·41, m, 5H, 1·38–1·01, m, 6H, 0·98–0·73, m, 1H, 0·71–0·59, m, 1H, c-$C_6H_{11}CH_2$. Mass spectrum m/z 248 (M, 0·2%), 124 (32), 107 (100), 105 (12), 83 (28), 79 (43), 77 (28), 67 (16), 55 (47).

2-(Cyclohexylmethyl)-1-phenylpropane-1,3-diol (4c)

In a manner similar to that for *anti*-(3k) a diastereoisomeric mixture (1:6, *syn/anti*) of methyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)-3-phenylpropanoate (3k) was reduced to give diol (4c) as a diastereoisomeric mixture (1:6) in 85% yield, and as a white solid, m.p. 87–98° (Found: C, 77·2; H, 9·6. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%). F.t.i.r. ν_{max} (Nujol) 3328s(br), 1601w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·39–7·21, m, 5H, Ph, diastereoisomers A (*anti*) and B (*syn*); 4·99, d, J 3·4 Hz, 0·88H, **CH**OH, A; 4·62, d, J 7·1 Hz, 0·12H, **CH**OH, B; 3·81–3·52, m, 0·24H, CH_2OH, B; 3·67, d, J 5·2 Hz, 1·76H, CH_2OH, A; 3·36, br s, 1H, OH, A, B; 2·84, br s, 1H, OH, A, B; 2·14–1·85, m, 1H, **CH**CH_2OH, A, B; 1·63–1·59, m, 5H, 1·38–0·97, m, 6H, 0·94–0·52, m, 2H, c-$C_6H_{11}CH_2$, A, B. Mass spectrum m/z 248 (M, 0·2%), 124 (39), 107 (100), 105 (11), 83 (20), 79 (25), 77 (15), 55 (21).

anti-*2-(Cyclohexylmethyl)-1-(1-naphthyl)propane-1,3-diol (4d)*

In a manner similar to that for *anti*-(3k), methyl *anti*-2-(cyclohexylmethyl)-3-hydroxy-3-(1-naphthyl)propanoate [*anti*-(3d)] was reduced to give diol (4d) as a white solid in 96% yield, m.p. 102·5–104° (Found: C, 80·4; H, 8·6. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%). F.t.i.r. ν_{max} (Nujol) 3384s(br), 1598w cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·98–7·81, m, 2H, 7·78–7·68, m, 2H, 7·53–7·41, m, 3H, naphthyl ring; 5·89, br s, 1H, **CH**OH; 3·98–3·81, m, 2H, **CH**OH; 2·76, d, J 2·7 Hz, CHO**H**; 2·38, m, 1H, CH_2O**H**; 2·18–2·03, m, 1H, **CH**CH_2OH; 1·57–0·65, m, 12H, 0·36–0·18, m, 1H, c-$C_6H_{11}CH_2$. Mass spectrum (methane c.i.) m/z 298 (M, 1%), 167 (23), 156 (100), 141 (12), 129 (39), 55 (23).

2-(Cyclohexylmethyl)-1-(1-naphthyl)propane-1,3-diol (4d)

In a manner similar to that for *anti*-(3k), a diastereoisomeric mixture (1 : 3, *syn/anti*) of methyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)dimethylsilyloxy)-3-(1-naphthyl)propanoate (3d) was reduced to give diol (4d), a 1 : 3 mixture of diastereoisomers in 77% yield, as a colourless oil, m.p. 102·5–104° (Found: C, 80·5; H, 8·8. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%). F.t.i.r. ν_{max} (neat): 3362s(br), 1598w cm^{-1}. ^1H n.m.r. (200 MHz): δ 8·01–7·80, m, 2H, 7·76–7·62, m, 2H, 7·49–7·40, m, 3H, naphthyl ring protons, diastereoisomers A (*anti*) and B (*syn*); 5·86, d, J 2·4 Hz, 0·75H, C**H**OH, A; 5·46, d, J 6·4 Hz, 0·25H, C**H**OH, B; 3·94–3·64, m, 2H, C**H**$_2$OH, A, B; 3·29, br s, 1H, OH, A, B; 2·99, br s, 1H, OH, A, B; 2·14–2·02, m, 1H, C**H**CH$_2$OH, A, B; 1·56–1·27, m, 4H, 1·26–1·00, m, 3H, 0·95–0·61, m, 5H, 0·32–0·13, m, 1H, c-$C_6H_{11}CH_2$, A, B. Mass spectrum *m/z* 298 (M, 2%), 157 (35), 156 (100), 155 (18), 129 (30), 128 (28), 127 (17), 55 (16).

In a manner similar to that for (3k), a diastereoisomeric mixture (34:66, *syn/anti*) of methyl 2-(cyclohexylmethyl)-3-((1,1-dimethylethyl)diphenylsilyloxy)-3-(1-naphthyl)propanoate (3i) was reduced to give (4d) as a diastereoisomeric mixture of identical ratio in 89% yield.

Preparation of Dioxans (5)

5-(Cyclohexylmethyl)-2,2,4-trimethyl-1,3-dioxan (5a)

D-Camphor-10-sulfonic acid (27 mg, 0·120 mmol) was added to a stirred solution of 2-(cyclohexylmethyl)butane-1,3-diol (82 : 18, *anti/syn*) (4a) (130 mg, 0·700 mmol) in dry acetone (41 ml) under an atmosphere of argon. The resulting solution was allowed to stand at room temperature overnight. The solvent was removed under vacuum, and the residue was dissolved in ether (20 ml), washed with aqueous sodium hydrogen carbonate solution (10% w/w, 2×10 ml) and then with water (10 ml). The organic layer was separated, dried (Na_2SO_4) and filtered, and the solvent was removed under vacuum. G.l.c. analysis of the crude reaction mixture indicated the presence of both diastereoisomers of the title dioxan (5a) at R_t 7·06 and 7·24 min in a 83 : 17 (*cis/trans*) ratio respectively. Purification of the residue by preparative t.l.c. (90 : 10 light petroleum/ethyl acetate) gave the title dioxan mixture (5a) as a colourless oil (90 mg, 77%) (Found: C, 74·0; H, 11·3. $C_{14}H_{26}O_2$ requires C, 74·3; H, 11·6%). F.t.i.r. ν_{max} (neat) 1198s cm^{-1}. ^1H n.m.r. (200 MHz) δ 4·14, dq, J 2·5, 6·5 Hz, 0·83H, C**H**OCMe$_2$, diastereoisomer A (*cis*); 3·94, ddd, J 1·1, 2·7, 11·6 Hz, 0·83H, CH$_a$ or CH$_b$, A; 3·76, dd, J 5·1, 11·5 Hz, 0·17H, CH$_a$ or CH$_b$, diastereoisomer B (*trans*); 3·69, dd, J 1·6, 11·6 Hz, 0·83H, CH$_a$ or CH$_b$, A; 3·58, dq, J 5·9, 9·8 Hz, 0·17H, CHOCMe$_2$, B; 3·46, t, J 11·5 Hz, 0·17H, CH$_a$ or CH$_b$, B; 1·79–1·49, m, 6H, 1·48–0·64, m. 9·02H, c-$C_6H_{11}CH_2CH$, A, B, Me$_2$C, B; 1·41, s, 2·49H, MeC, A; 1·35, s, 2·49H, MeC, A; 1·12, d, J 5·9 Hz, 0·51H, **Me**CH, B; 1·07, d, J 6·5 Hz, 2·49H, **Me**CH, A. Mass spectrum *m/z* 211 (M − 15, 17%), 124 (19), 109 (14), 95 (50), 83 (39), 67 (26), 59 (100).

cis-*5-(Cyclohexylmethyl)-2,2-dimethyl-4-phenyl-1,3-dioxan (5c)*

In a manner similar to that for (4a), *anti*-2-(cyclohexylmethyl)-3-phenyl-propane-1,3-diol was cyclized to give dioxan *cis*-(5c) in 79% yield, as a colourless oil (Found: C, 79·0; H, 10·0. $C_{19}H_{28}O_2$ requires C, 79·1; H, 9·8%). F.t.i.r. ν_{max} (neat) 1606w, 1196s cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·35, m, 5H, Ph; 5·19, d, J 2·5 Hz, 1H, C**H**OCMe$_2$; 4·23–4·15, ddd, J 1·2, 2·2, 11·6 Hz, 1H, CH$_a$ or CH$_b$; 3·86–3·80, dd, J 1·4, 11·6 Hz, 1H, CH$_a$ or CH$_b$; 1·85–1·25, m, 13H, 1·17–0·84, m, 4H, 0·79–0·67, m, 2H, 0·55–0·45, m, 1H, c-$C_6H_{11}CH_2CH$, OCMe$_2$O. Mass spectrum *m/z* 288 (M, 0·1%), 124 (40), 117 (10), 107 (100), 91 (10), 83 (28), 67 (10), 59 (49), 55 (32).

cis-*5-(Cyclohexylmethyl)-2,2-dimethyl-4-(1-naphthyl)-1,3-dioxan (5d)*

In a manner similar to that for (4a), *anti*-2-(cyclohexylmethyl)-1-naphthylpropane-1,3-diol *anti*-(4d) was cyclized to given dioxan *cis*-(5d) in 88% yield, as a colourless oil (Found: C, 81·8; H, 9·1. $C_{23}H_{30}O_2$ requires C, 81·6; H, 8·9%). F.t.i.r. ν_{max} (neat) 1598w, 1197s cm^{-1}. ^1H n.m.r. (200 MHz) δ 7·93–7·83, m, 2H, 7·78–7·65, m, 2H, 7·53,–7·41, m, 3H, naphthyl ring; 5·89, d, J 2·6 Hz, 1H, C**H**OCMe$_2$; 4·34, dd, J 2·0, 11·6 Hz, 1H, CH$_a$ or CH$_b$; 3·82, dd, J 1·8, 11·6 Hz, 1H, CH$_a$ or CH$_b$; 2·01–1·96, m, 1H, C**H**CHOCMe$_2$; 1·63, s, 3H, MeC;

1·58, s, 3H, MeC; 1·53–1·06, m, 5H, 1·01–0·52, m, 7H, 0·28–0·08, m, 1H, c-$C_6H_{11}CH_2$. Mass spectrum *m/z* 338 (M, 0·3%), 156 (100), 128 (15), 59 (17).

Preparation of Methyl *anti*- and *syn*-2-(Cyclohexylmethyl)-3-((1,1-dimethylethyl)-dimethylsilyloxy)-3-phenylpropanoate (3m)

Chloro(1,1-dimethylethyl)dimethylsilane (278 mg, 1·85 mmol) and imidazole (185 mg, 2·71 mmol) were added to stirred solution of methyl *anti*-2-(cyclohexylmethyl)-3-hydroxy-3-phenylpropanoate [*anti*-(3c)] (170 mg, 0·670 mmol) in dimethylformamide (0·9 ml) under an atmosphere of argon. The reaction mixture was stirred at room temperature for 12 h, then dissolved in ether (40 ml) and washed with water (2×10 ml). The organic layer was separated, dried (Na_2SO_4) and filtered, and the solvent was removed under vacuum. Purification of the residual liquid by preparative t.l.c. (80:20 light petroleum/ether) gave the title silyl ether *anti*-(3m) as a colourless oil (131 mg, 56%). This product was identical in all respects to that obtained from the free radical addition to (2c) described above.

In a similar manner methyl *syn*-2-(cyclohexylmethyl)-3-hydroxy-3-phenylpropanoate [*syn*-(3c)] gave silyl ether *syn*-(3m) as a colourless oil in 92% yield. This product was identical in all respects to that obtained from the free radical addition to (2c) described above.

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