Optical Resolution and Absolute Stereochemistry of *trans*-2,5-Dimethyl-1-phenyl-1-silacyclopentane

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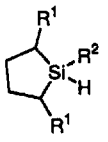
2,5-Dimethyl-1-phenyl-1-silacyclopentane (DMPSC) has been prepared in good yield, as a mixture of stereoisomers, by the reaction of 2,5-dibromohexane and dichlorophenylsilane with magnesium in tetrahydrofuran. The silane so prepared consists of a *ca.* 1:1:3 mixture of the *cis*-isomers **2**, **3** and the racemic *trans*-isomer **4** + **5**, respectively. Treatment of this product with copper(II) chloride in acetonitrile gives 1-chloro-DMPSC as a mixture of the *cis*-isomers **6**, **7** and the racemic *trans*-isomer **8** + **9** in the approximate ratio 1:6:12. Mono-*O*-silylation of dimethyl L-tartrate with this mixture of chlorosilanes gave the silyl ether **11** and the diastereoisomeric pair of *trans*-compounds **12** and **13** as crystalline solids. The molecular structure of the *cis*-silyl ether **11** has been determined by X-ray diffraction. Corresponding monosilylation of (2*S*)-1,1,2-triphenylethane-1,2-diol [(*S*)-TPED] occurs selectively at the less hindered secondary OH group; the stereoisomeric products were separated by a combination of recrystallisation and column chromatography and the molecular structure of the (2*S*,5*S*)-silyl ether was determined by single-crystal X-ray diffraction. Reduction of this diastereoisomer with $LiAlH_4$ afforded (2*S*,5*S*)-(+)-DMPSC, $[\alpha]_D^{22}$ +27.8 (*c* 2.16, cyclohexane), with an estimated enantiomeric excess of >98%. The (2*R*,5*R*)-(−)-enantiomer was prepared in a similar manner using (*R*)-TPED as the resolving agent, which was readily recovered in an optically-pure state and could be recycled.

In the course of our studies of enantioselective atom-transfer reactions,[1–3] we considered the possible applications of *trans*-2,5-dialkyl-1-silacyclopentane derivatives of the type **1** (R^1 substituents are *trans*) as chiral hydrogen-atom donors and sources of chiral triorganosilyl radicals. The silyl moiety could also serve as a chiral hydroxyl-protecting group and, more generally, as a chiral auxiliary in many types of reaction mediated by organosilanes and of importance in organic synthesis.[4,5] A major advantage of the *trans*-2,5-dialkylsilacyclopentyl residue in such applications is that the configuration of this group is unaffected by the stereochemical outcome of any reaction which takes place at the silicon centre and involves the exocyclic substituents.



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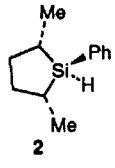
2,5-Dimethyl-1-phenyl-1-silacyclopentane **1** (R^1 = Me, R^2 = Ph) (DMPSC) has been prepared previously by Wells and Franke[6] in 24% yield, as a mixture of configurational isomers, by treatment of dichlorophenylsilane with the diGrignard reagent derived from 2,5-dibromohexane. 1,2,5-Trimethyl-1-silacyclopentane **1** (R^1 = R^2 = Me) was also prepared in low yield by a similar route from dichloromethylsilane.[6,7] The isomeric mixtures obtained for both cyclic silanes could be separated by GLC, but no attempt was made to resolve the racemic *trans*-isomers.

In this paper we report a high-yielding synthesis of DMPSC, the separation of the two (*meso*) *cis*-isomers, *r*-1,*t*-2,*t*-5-DMPSC **2** and *r*-1,*c*-2,*c*-5-DMPSC **3**, from the racemic mixture of *trans*-isomers, (*R*,*R*)-DMPSC **4** and (*S*,*S*)-DMPSC **5**, and the optical resolution of the racemate. Although *trans*-DMPSC obviously does not possess true C_2 symmetry, this silane, its derivatives and reactive intermediates containing three-coordinate silicon derived from these compounds would be expected to share some of the advantages for control of chirality which are exhibited by C_2-symmetric molecules.[8]



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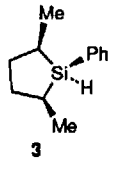

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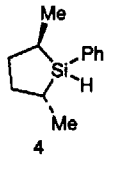

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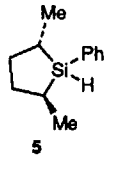

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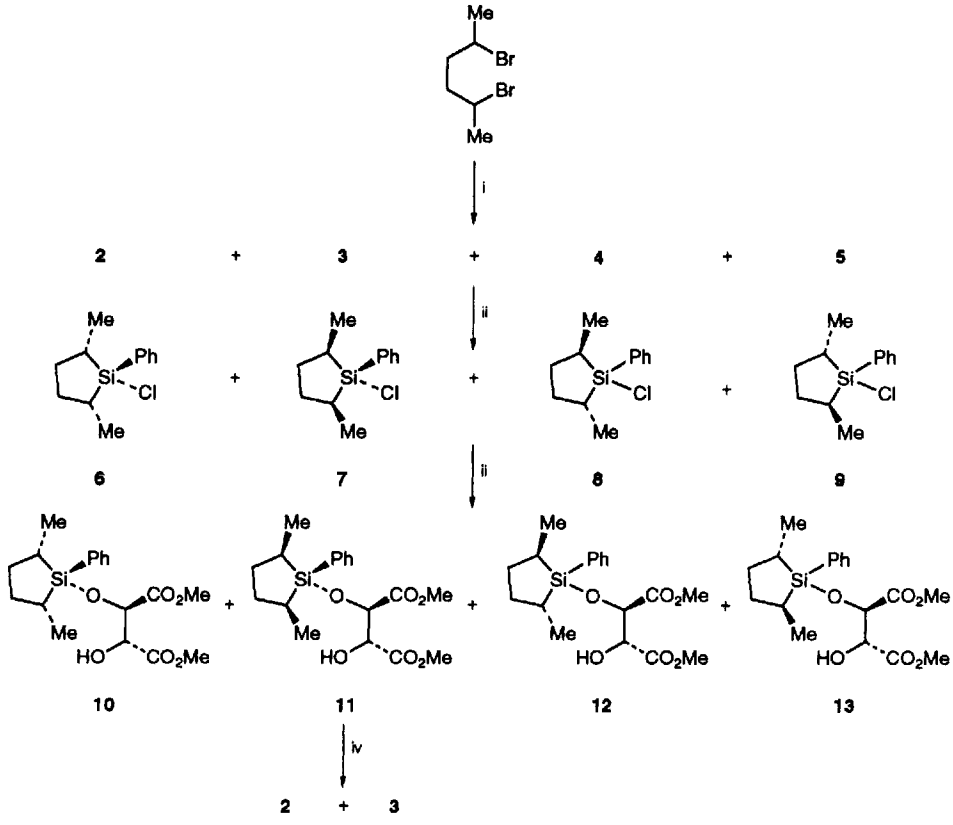
Results and Discussion

DMPSC was prepared in 80–90% yield by the addition of an equimolar mixture of 2,5-dibromohexane (±-+*meso*)[9] and dichlorophenylsilane to magnesium metal in tetrahydrofuran (THF); the yield represents a considerable improvement over that obtained by Wells and Franke.[6] Examination of the product by ^1H and ^{13}C NMR spectroscopy showed it to consist of approximately 20% of the *r*-1,*t*-2,*t*-5-isomer **2**, 20% of the *r*-1,*c*-2,*c*-5-isomer **3** and 60% of the racemic *trans*-silanes **4** + **5** (see Scheme 1). The spectroscopic assignments follow those of Wells and Franke[6] and the NMR parameters are collected in Table 1. The *cis*- and *trans*-isomers are easily distinguished because the former each possess a plane of symmetry, which passes through the silicon atom, while the latter do not. Nuclear Overhauser enhancement (NOE) studies confirmed the assignments for the *cis*-isomers. Thus, irradiation at the resonance frequency of the proton attached to silicon was associated with a significant enhancement of the signal from the *C*-methyl protons in the *r*-1,*t*-2,*t*-5-isomer **2**, but a negligible effect was



Scheme 1 *Reagents and conditions:* i, $PhSi(H)Cl_2$, Mg in THF; ii, $CuCl_2$ in MeCN, reflux; iii, L-DMT, imidazole in DMF, room temp.; iv, $LiAlH_4$ in THF, reflux

Table 1 ^1H and ^{13}C NMR spectroscopic parameters for the silacyclopentanes **2–5**

Isomer of DMPSC	^1H NMR (*J*)		^{13}C NMR[a]		
	2,5-Me	Si-*H*	2,5-Me	C-2, C-5	C-3, C-4
2 (*cis*)	1.21 (d, 7.12)	4.11 (t, 3.60)	17.5	20.1	35.1
3 (*cis*)	1.02 (d, 7.70)	4.43 (t, 3.75)	16.2	18.2	34.9
4 + **5** (*trans*)	0.90 (d, 7.30), 1.19 (d, 7.30)	4.22 (td,[b] 3.70 and 1.00)	15.7, 16.8	19.4, 20.6	35.7, 36.8

[a] Chemical shifts for aromatic carbons are given in the text. [b] Apparent triplet.

observed for the *r*-1,*c*-2,*c*-5-isomer **3**. It is noteworthy that shielding of the Si-H proton by the *C*-methyl groups increases as the number of proximate groups increases in the order **3** < **4** + **5** < **2**.[6,10]

The isomeric composition of the DMPSC was independent of the ±:*meso* ratio of the starting 2,5-dibromohexane, which could be varied by selective crystallisation of the *meso*-form from the mixture of dibromides obtained from the reaction of hexane-2,5-diol with PBr_3.[9] As reported previously,[6] the isomers of DMPSC could not be separated successfully by fractional distillation, which brought about only a small change in composition (the boiling points increased in the order **4** + **5** < **2** < **3**).

The mixture of isomers of DMPSC was converted in high yield to the corresponding chlorosilanes **6–9** by treatment with copper(II) chloride in acetonitrile (Scheme 1).[11,12] NMR spectroscopic examination of the product (see Table 2) showed that the relative amounts of the two *cis*-isomers of the chlorosilane were very different (*ca.* 6:1) from the relative amounts of the isomers **2** and **3** (*ca.* 1:1) in the starting DMPSC. Because of the absence of a proton attached to silicon,

Table 2 ^{13}C NMR spectroscopic parameters[a] for the chlorosilanes **6–9**

Isomer	2,5-Me	C-2, C-5	C-3, C-4
6 (*cis*)	17.7	23.9	33.8
7 (*cis*)	15.4	21.1	33.4
8 + **9** (*trans*)	14.5, 15.1	21.8, 25.2	34.2, 35.1

[a] Chemical shifts for the aromatic carbons (δ_C 120–140) were difficult to assign.

it is not possible to use simple NMR spectroscopic arguments[6] to identify the major *cis*-isomer of the chlorosilane. When the mixture of chlorosilanes obtained from DMPSC (in which the ratio **2**:**3**:**4** + **5** was 18:19:63) was reduced with lithium aluminium hydride in THF, DMPSC (in which the ratio **2**:**3**:**4** + **5** was 32:5:63) was produced in near-quantitative yield. Assuming that the reduction occurs stereospecifically with inversion at silicon,[10,13–15] the sample of chlorosilane must have consisted of an approximately 5:32:63 mixture of **6**, **7** and **8** + **9**, in which the *r*-1,*t*-2,*t*-5-isomer **7** predominates over the

r-1,*c*-2,*c*-5-isomer **6**. Replacement of H by Cl is thus not stereospecific.

Treatment of the isomeric mixture of 1-chloro-DMPSC with one molar equivalent of dimethyl L-tartrate* (L-DMT) in the presence of imidazole in dimethyl formamide (DMF) solvent afforded, after preliminary column chromatography, a mixture of three monosilylated tartrates (Scheme 1). Not more than trace amounts of the *r*-1,*c*-2,*c*-5-isomer **10** were present. The readily crystallisable *r*-1,*t*-2,*t*-5-isomer **11** was separated from the two *trans*-diastereoisomers **12** and **13** by column chromatography. The molecular structure of compound **11**, determined by single-crystal X-ray diffraction, is shown in Fig. 1. The crystal packing diagram revealed a short O(2)–O(4) contact (r_{O-O} = 2.89 Å) between adjacent molecules, corresponding to a C=O · · · HO hydrogen bond.

Formation of compound **11** thus takes place predominantly with apparent retention of configuration at silicon. However, the chemistry involved in the replacement of chlorine in 1-chloro-1-silacyclopentanes by an alkoxy group, using an alcohol in the presence of an amine, can be complex and the stereochemical outcome difficult to predict.[15] In particular, chlorosilanes can undergo epimerisation at silicon in the presence of amines *via* an intermediate adduct containing five-coordinate silicon.[15]

Reduction of the pure *r*-1,*t*-2,*t*-5-silyl ether **11** with excess $LiAlH_4$ gave a mixture of the *cis*-isomers of DMPSC in which the ratio of isomers **2**:**3** was 6:1. Hence, the reduction takes place with predominant inversion of configuration at silicon. Importantly, no trace of the *trans*-isomer of DMPSC was detected in the product, indicating that no epimerisation at C-2 or C-5 takes place under the basic conditions used for the reduction.

The diastereoisomeric *trans*-silyl ethers **12** and **13** could be separated only with considerable difficulty by column chromatography (although separation by HPLC was straightforward) and so the *O*- or the *N*-silyl derivatives of a number of other readily available homochiral alcohols and amines were prepared in the hope of finding a more easily separable pair of diastereoisomers.† The most successful resolving agent investigated so far is 1,1,2-triphenylethane-1,2-diol (TPED), both enantiomers of which are available commercially and also readily prepared by the reaction of phenylmagnesium bromide with methyl mandelate.[17–19]

Monosilylation of (*S*)-TPED with the isomeric mixture of 1-chloro-DMPSC (*vide supra*) in the presence of imidazole and a catalytic amount of 4-dimethylaminopyridine (DMAP) in DMF, takes place selectively at the less hindered secondary hydroxyl group to give, after preliminary chromatographic work-up, a mixture containing one *cis*-isomer and the two

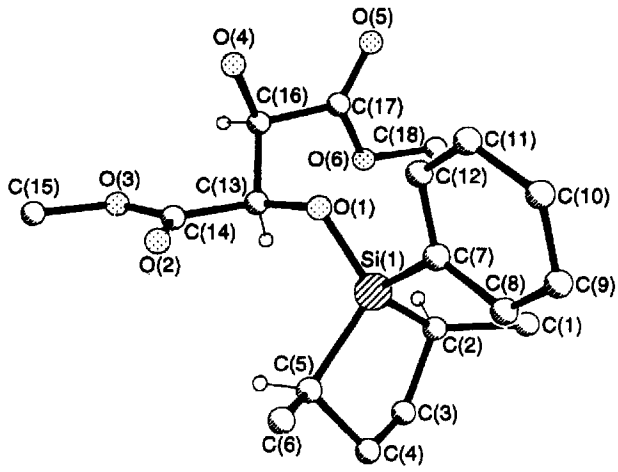


Fig. 1 Molecular structure of the *r*-1,*t*-2,*t*-5-silyl ether **11** derived from L-DMT (only selected hydrogen atoms are shown). Selected bond lengths (Å) and bond or torsion angles (°) are as follows: Si(1)–O(1) 1.653(2), Si(1)–C(2) 1.883(4), Si(1)–C(5) 1.882(3), Si(1)–C(7) 1.863(3), Si(1)–O(1)–C(13) 128.2(2), C(2)–Si(1)–C(5) 96.4(2), C(7)–Si(1)–O(1) 102.1(1), C(2)–C(3)–C(4)–C(5) 43.4.

trans-diastereoisomers **16** and **17** in a total yield of 85–90% (see Scheme 2). We assume that the *r*-1,*t*-2,*t*-5-isomer **15** is formed to the essential exclusion of the *r*-1,*c*-2,*c*-5-isomer **14**, by analogy with the results obtained from the silylation of L-DMT. Crystallisation of the silylation product from methanol yielded a mixture of compounds **15** and **17**, while the more soluble isomer **16** remained in solution. The compounds **15** and **17** could then be readily separated by column chromatography and, after final recrystallisation from methanol, the *trans*-silyl ether **17** was obtained with a diastereoisomeric excess (de) of >99%. The other *trans*-diastereoisomer **16** was less easy to obtain in a pure state and proved difficult to separate from traces of compound **15**.‡ The molecular structure of the silyl ether **17** was determined by single-crystal X-ray diffraction (see Fig. 2) and the absolute configuration of the DMPSC residue is established to be (2*S*,5*S*).

Reduction of the pure *r*-1,*t*-2,*t*-5-isomer **15** with $LiAlH_4$ in THF gave a 96% yield of *cis*-DMPSC in which the ratio of compounds **2**:**3** was *ca.* 7:1. Thus, as with the DMT derivative, the reduction proceeds with predominant inversion of configuration at silicon. Again, no trace of the *trans*-isomer was detected, confirming that deprotonation at C-2 and C-5 to give an α-silyl-stabilised carbanion[4] (which would result in epimerisation at these carbon centres), does not occur under the reaction conditions and indicates that the reduction of compound **17** should proceed with complete retention of configuration at C-2 and C-5.

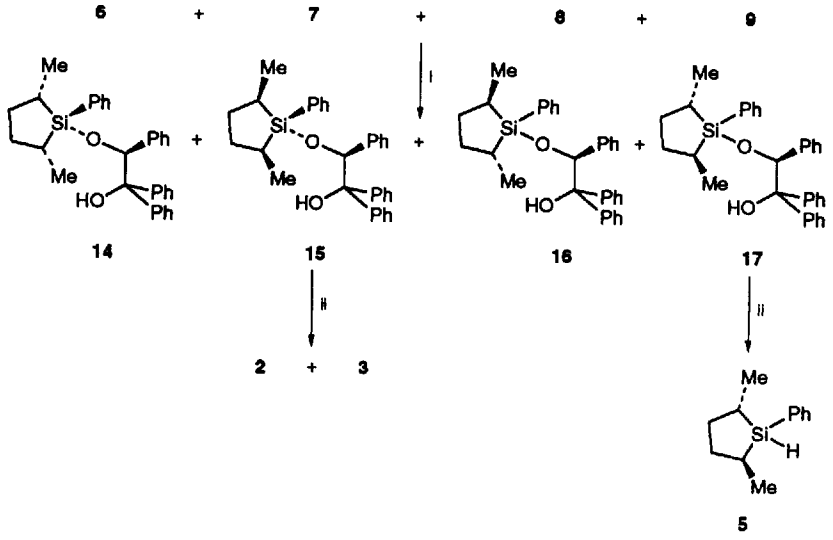
Reduction of the (*S*,*S*)-silyl ether **17** with $LiAlH_4$ in THF gave (*S*,*S*)-(+)-DMPSC **5** without any trace of the *cis*-isomers. Since the enantiomeric excess of the TPED resolving agent is probably >99% (see Experimental section) and the de of compound **17** was >99%, the ee of compound **5** should be >98%. The antipode of compound **17** was prepared in the same way using (*R*)-TPED as the resolving agent and was reduced to give (*R*,*R*)-(−)-DMPSC **4**, which showed a specific rotation of almost equal magnitude, but opposite in sign, to that measured for compound **5**.§ TPED could be recovered readily and

* Dimethyl (2*R*,3*R*)-tartate.

† The following compounds were monosilylated (on oxygen or nitrogen, as appropriate) with 1-chloro-DMPSC under standard conditions:[16] (*R*)-pantolactone, (1*R*,2*R*,3*S*,5*R*)-pinane-2,3-diol, isosorbide, (2*S*)-1,1-diphenylpropane-1,2-diol, (+)-(4,6-*O*-benzylidene)methyl-α-D-glucopyranoside, 1,2:5,6-dicyclohexylidene-D-glucofuranose, (1*R*,2*S*)-ephedrine, (1*R*,2*S*)-*N*-methylephedrine, (1*S*,2*S*)-pseudoephedrine and methyl (*S*)-mandelate. Most reactions gave excellent yields, except the silylation of the glucopyranoside which gave a poor yield. The silylation products were reasonably moisture stable and could be chromatographed and/or recrystallised in air without hydrolysis. Most were viscous oils or glass-like materials, the stereoisomers of which were difficult to separate. The *cis*- and *trans*-isomers of the derivative from (2*S*)-1,1-diphenylpropane-1,2-diol were both highly crystalline, but could not be separated efficiently. The results demonstrate the possibilities of using *trans*-2,5-disubstituted silacyclopentyl groups as chiral protectors for OH and NH groups with a view to directing asymmetric synthesis. For such applications, 2,5-dialkyl substituents more bulky than methyl may be required, bearing in mind the relatively long Si–C bonds.

‡ In order to obtain a pure sample of (*R*,*R*)-DMPSC **4**, free from the *cis*-isomers, it was simpler to prepare the enantiomeric form of compound **17** starting from (*R*)-TPED and to reduce this with $LiAlH_4$ (*vide infra*).

§ The observed specific rotation of **4**, $[\alpha]_D^{22}$ −27.1 (*c* 2.60, cyclohexane), corresponds to an ee of *ca.* 96% by comparison with the specific rotation shown by (*S*,*S*)-(+)-DMPSC of ee >98%. This estimate accords with the ratio of the specific rotations for the enantiomeric silyl ether precursors **17** and *ent*-**17**.



Scheme 2 *Reagents and conditions:* i, (*S*)-TPED, imidazole, DMAP in DMF, room temp.; ii, $LiAlH_4$ in THF, room temp.

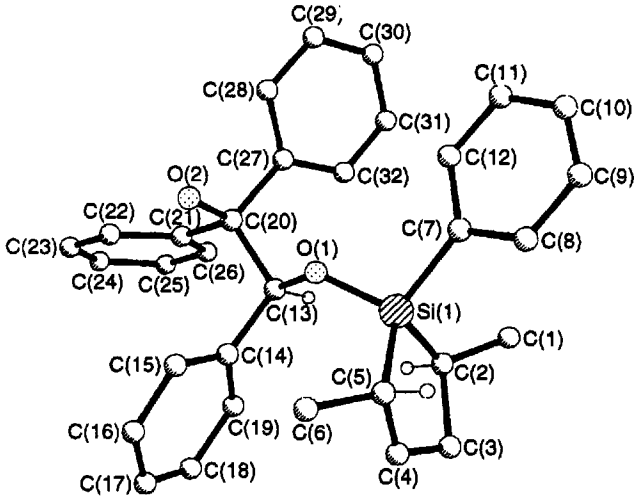


Fig. 2 Molecular structure of the (*S*,*S*)-silyl ether **17** derived from (*S*)-TPED (only selected hydrogen atoms are shown). Selected bond lengths (Å) and bond or torsion angles (°) are as follows: Si(1)–O(1) 1.649(4), Si(1)–C(2) 1.853(9), Si(1)–C(5) 1.884(14), Si(1)–C(7) 1.885(8), Si(1)–O(1)–C(13) 128.5(3), C(2)–Si(1)–C(5) 98.7(5), C(7)–Si(1)–O(1) 105.1(3), C(2)–C(3)–C(4)–C(5) 39.3.

essentially quantitatively after the reduction of the silyl ethers; it was still optically pure and was recycled.

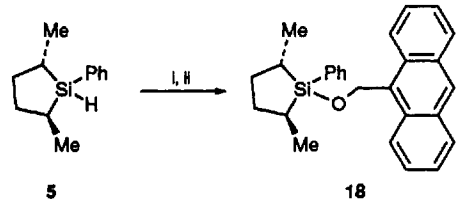
A sample of (*S*,*S*)-(+)-DMPSC was converted to the corresponding chlorosilane, by treatment with $CuCl_2$ in acetonitrile, and thence to the highly crystalline (*S*,*S*)-(+)-9-anthrylmethoxide **18** (see Scheme 3). This silyl ether represents a readily handled solid derivative of *trans*-DMPSC with an achiral alcohol and it should prove useful in future work.

Conclusion

trans-DMPSC has been prepared and resolved in good overall yield and its absolute configuration has been established. The applications in asymmetric synthesis of the optically active silyl moieties derived from this and related 2,5-disubstituted silacylopentanes remain to be explored.

Experimental

NMR spectra were recorded using a Varian VXR-400 instrument (400 MHz for ^1H). The solvent was $CDCl_3$ and chemical shifts are reported relative to Me_4Si; *J* values are



Scheme 3 *Reagents and conditions:* i, $CuCl_2$ in MeCN, reflux; ii, 9-anthrylmethanol, imidazole, DMAP in DMF, 40 °C

quoted in Hz. HPLC was performed using a Gilson 305 instrument, using UV or refractive index detectors, fitted with a 250 mm × 4.5 mm column packed with Kromasil 100 silica gel (particle size 5 μm). Column chromatography and TLC were carried out using Merck Kieselgel 60 (230–400 mesh) and Kieselgel 60 F_{254} aluminium-backed pre-coated plates, respectively. Optical rotations were determined at 589 nm (sodium D line) with an Optical Activity AA-10 automatic digital polarimeter, using a 1 dm pathlength cell, and are given in units of 10^{-1} deg cm^2 g^{-1}.

Materials.—THF was freshly distilled from sodium–benzophenone before use. Dichloromethane and acetonitrile were distilled from calcium hydride and stored over activated molecular sieves (4 Å); dimethylformamide (DMF, HPLC grade, Aldrich) was stored over molecular sieves before use.

2,5-Dibromohexane was prepared by a literature method from hexane-2,5-diol.[9a] Dichlorophenylsilane was obtained commercially (Lancaster Synthesis) or was prepared by treatment of trichlorosilane (1.85 mol) with phenylmagnesium bromide [from magnesium (1.5 mol) and bromobenzene (1.4 mol) in diethyl ether] according to the published method;[20] the yield (150 g, 61%) was significantly higher than reported previously (38%).[20]

Dimethyl L-tartrate (L-DMT), $[\alpha]_D^{22}$ +21 (*c* 2.5, H_2O) (99% ee), was obtained commercially (Aldrich) and used as received.

1,1,2-*Triphenylethane*-1,2-*diol* (*TPED*).—(*S*)-(+)-Mandelic acid, $[\alpha]_D^{20}$ +154 (*c* 2.8, H_2O), 99% ee (Aldrich), was converted to methyl (*S*)-(+)-mandelate, $[\alpha]_D^{22}$ +146 (*c* 1.22, MeOH), as described in the literature.[17] The commercially-obtained ester, $[\alpha]_D^{20}$ +144 (*c* 1.0, MeOH), 98% ee (Aldrich) was also used (without purification). (*S*)-TPED was prepared by the reaction of the mandelate ester with phenylmagnesium bromide in diethyl ether as described previously,[17,18] and showed $[\alpha]_D^{22}$

−222 (*c* 1.25, 95% EtOH); no impurities were detected by ^{1}H NMR spectroscopy. Ref. 17 gives $[\alpha]_D^{25}$ +214–+215 (*c* 1, EtOH) for TPED prepared from methyl (*R*)-(−)-mandelate which showed $[\alpha]_D^{22}$ −130.5 (*c* 1.5, EtOH). Assuming that no epimerisation takes place at C-2 during conversion of the (*S*)-(+)-mandelate to (*S*)-TPED, the latter should have an ee of *ca.* 99%.* (*R*)-(+)-TPED was prepared by the same route, starting from methyl (*R*)-(−)-mandelate, and this showed $[\alpha]_D^{22}$ +220 (*c* 0.80, 95% EtOH). (*R*)-TPED, which showed $[\alpha]_D^{20}$ +210 (*c* 1.0, EtOH), as also obtained commercially (Aldrich) and the optical purity of the (2*R*,5*R*)-(−)-2,5-dimethyl-1-phenyl-1-silacyclopentane prepared using this diol was essentially the same as that derived from the (*R*)-TPED synthesised in this work.

2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentane* (*DMPSC*).—A mixture of dichlorophenylsilane (27.0 g, 0.15 mol) and 2,5-dibromohexane (36.0 g, 0.15 mol) in THF (160 cm^3) was added dropwise, with mechanical stirring under nitrogen, to THF (30 cm^3) containing magnesium turnings (8.0 g, 0.33 mol) which had been heated previously under a current of nitrogen. After the reaction had begun, the flask was cooled in an ice–water bath and the addition was complete in 2 h. The mixture was stirred for a further 2 h at room temperature, then hydrolysed with a 10% aqueous solution of ammonium chloride (100 cm^3). The aqueous layer was separated and extracted with diethyl ether (3 × 50 cm^3). THF was removed from the organic layer by evaporation and the residue was combined with the ethereal extracts. The solution was washed with saturated brine, dried ($MgSO_4$), the diethyl ether was removed by evaporation and the residue was distilled to give DMPSC (23–26 g, 80–90%), b.p. 58–65 °C/0.5 Torr (lit.,[6] b.p. 68–78 °C/1 Torr). The product consisted of a mixture of the *r*-1,*t*-2,*t*-5-isomer **2**, the *r*-1,*c*-2,*c*-5-isomer **3** and the racemic *trans*-isomers (**4** + **5**) of DMPSC in the approximate ratio 1 : 1 : 3, respectively, and this was independent of the ± : *meso* ratio of the starting 2,5-dibromohexane.[9] The NMR parameters for DMPSC are collected in Table 1. Irradiation at the Si-H resonance frequencies for the isomer **2** (δ 4.11) and for the isomer **3** (δ 4.43) caused a significant NOE for the *C*-methyl groups (δ 1.21) of compound **2**, but not for those of compound **3** (δ 1.02).

1-*Chloro*-2,5-*dimethyl*-1-*phenyl*-1-*silacyclopentane*.—Anhydrous copper(II) chloride (27.0 g, 0.20 mol) was flamed in a flask under reduced pressure (60 Torr) to remove traces of moisture and then allowed to cool under nitrogen. Dry acetonitrile (120 cm^3) and the isomeric mixture of DMPSC (17.0 g, 0.09 mol) were added and the resulting mixture was stirred and heated under gentle reflux for 2 h. The reaction mixture was allowed to cool to room temp. and the very dark homogenous solution was extracted with pentane (4 × 25 cm^3). The pentane was removed by evaporation and the residue was distilled to give 1-chloro-DMPSC (17.5 g, 85%), b.p. 69–76 °C/0.5 Torr, as a mixture of stereoisomers. The ^{1}H NMR spectrum of the mixture was complex, but the chemical shifts of the methyl protons and of the aliphatic and aromatic ring protons were similar to those for DMPSC; the ^{13}C NMR parameters are given in Table 2. (Found: C, 64.3; H, 7.8; Cl, 15.5. $C_{12}H_{17}ClSi$ requires C, 64.11; H, 7.62; Cl, 15.77%).

Reduction of 1-*Chloro-DMPSC*.—The chlorosilane (1.3 g, 5.8 mmol), prepared from DMPSC consisting of the stereoisomers **2**, **3** and **4** + **5** in the proportions 18 : 19 : 63, in THF (5 cm^3) was added dropwise with stirring to $LiAlH_4$ (1.0 g, 26 mmol) in THF (15 cm^3) cooled in an ice–water bath. The mixture was then stirred at room temp. for 10 h before being hydrolysed using the procedure described by Mićović and Mihailović,[21] in which the stirred mixture from *n* g of $LiAlH_4$ is treated at *ca.* 0 °C by successive dropwise addition of *n* cm^3 of water, *n* cm^3 of 15% aqueous sodium hydroxide solution and 3*n* cm^3 of water. The granular precipitate formed was removed by filtration, washed with diethyl ether and the solvents were removed by evaporation from the combined filtrates. The residue was chromatographed (pentane eluent) to give DMPSC (1.05 g, 95%) which consisted of the stereoisomers **2**, **3** and **4** + **5** in the proportions 32 : 5 : 63, respectively.

The Silyl Ethers **11–13** *derived from* L-*DMT*.—1-Chloro-DMPSC (**6** : **7** : **8** + **9** = 7 : 33 : 60) (5.0 g, 22 mmol) was added to a solution of L-DMT (5.0 g, 28 mmol) and imidazole (4.0 g, 59 mmol) in DMF (50 cm^3). The mixture was stirred at room temp. for 20 h and then poured into saturated brine (100 cm^3). The mixture was extracted with diethyl ether (5 × 20 cm^3), the combined organic phase was washed with saturated brine and then dried ($MgSO_4$). Evaporation of the solvent gave a viscious oil (7.5 g), which was dissolved in pentane (20 cm^3) and left to stand at −5–−10 °C to give *ca.* 3 g of crystalline material. This was recrystallised from pentane to give 2.5 g of colourless product which consisted of the stereoisomers **11**, **12** and **13** in the ratio of 5 : 5 : 1, respectively. Dimethyl 2-hydroxy-3-[(*r*-1,*t*-2,*t*-5-2,5-dimethyl-1-phenyl-1-silacyclopentyl)oxy]succinate **11** was separated by flash chromatography, using pentane–diethyl ether (96 : 4) eluent, and then recrystallised from pentane, m.p. 99–100 °C, $[\alpha]_D^{20}$ +30.9 (*c* 3.04, $CHCl_3$); δ_H 0.95 (3 H, d, *J* 7.41), 1.00 (3 H, d, *J* 7.70), 1.20 (2 H, m), 1.52 (2 H, m), 1.88 (2 H, m), 3.17 (1 H, d, *J* 9.48), 3.73 (3 H, s) 3.76 (3 H, s), 4.66 (1 H, dd, *J* 9.48 and 1.90), 4.72 (1 H, d, *J* 1.90, OH), 7.38 (3 H, m) and 7.58 (2 H, m); δ_C 15.5(5), 15.5(9), 19.2, 19.5, 33.6, 33.7, 52.5, 52.7, 73.2, 73.8, 127.6, 129.7, 132.2, 134.8, 170.6 and 171.8 (Found: C, 58.9; H, 7.1. $C_{18}H_{26}O_6Si$ requires C, 58.99; H, 7.15%).

It was difficult to separate the two diastereoisomers **12** and **13** on a large scale, but after repeated chromatographic purification small amounts of the pure compounds were obtained for characterisation. The configurations of the isomers **12** and **13** were assigned on the basis of the optical rotation of the *trans*-DMPSC† obtained from the $LiAlH_4$-reduction (as described below for the reduction of the isomer **11**) of a mixture containing compounds **12** and **13** (4 : 1).

Dimethyl 2-*hydroxy*-3-[(2R,5R-2,5-*dimethyl*-1-*phenyl*-1-*silacyclopentyl*)*oxy*]*succinate* **12** *derived from* L-*DMT*. M.p. 79–81 °C; $[\alpha]_D^{20}$ +23.3 (*c* 2.36, $CHCl_3$); δ_H 0.94 (3 H, d, *J* 7.80), 1.05 (3 H, d, *J* 6.67), 1.19 (2 H, m), 2.11 (4 H, m), 3.11 (1 H, d, *J* 10.15), 3.74 (3 H, s), 3.79 (3 H, s), 4.63 (1 H, dd, *J* 10.14 and 1.71), 4.85 (1 H, d, *J* 1.71, OH), 7.40 (3 H, m) and 7.65 (2 H, m); δ_C 14.1, 15.5, 20.6, 21.3, 34.7, 34.8, 52.5(5), 52.6(0), 73.1, 74.3, 127.7, 129.8, 133.9, 134.7, 170.8 and 171.6.

Dimethyl 2-*hydroxy*-3-[(2S,5S-2,5-*dimethyl*-1-*phenyl*-1-*silacyclopentyl*)*oxy*]*succinate* **13** *derived from* L-*DMT*. M.p. 55–57 °C, $[\alpha]_D^{20}$ −21.5 (*c* 2.18, $CHCl_3$); δ_H 1.12(9) (3 H, d, *J* 7.30), 1.13(2) (3 H, d, *J* 7.30), 1.33 (2 H, m), 2.10 (4 H, m), 3.09 (1 H, d, *J* 9.50), 3.68 (3 H, s), 3.78 (3 H, s), 4.55 (2 H, m), 7.39 (3 H, m) and 7.53 (2 H, m); δ_C 14.4, 15.8, 21.3, 22.1, 34.4, 34.8, 52.5, 52.7, 72.9, 74.1, 127.9, 129.9, 133.5, 134.6, 170.9 and 171.7.

Reduction of the Silyl Ether **11**.—A solution of compound **11** (1.5 g, 4.1 mmol) in THF (10 cm^3) was added dropwise with stirring to $LiAlH_4$ (1.5 g, 40 mmol) in THF (20 cm^3) cooled in

* It should be borne in mind that the optical purity of an incompletely resolved chiral compound can often be upgraded by simple recrystallisation.

† $[\alpha]_D^{22}$ −22.1 (*c* 2.05, cyclohexane), corresponding (*vide infra*) to an ee of *ca.* 80% in favour of (*R*,*R*)-(−)-DMPSC **4**.

an ice–water bath. The mixture was then heated under reflux for 4 h and stirred at room temp. for a further 4 h, before being hydrolysed as described for the reduction of 1-chloro-DMPSC. The precipitate formed was removed by filtration, washed with diethyl ether and the solvents were removed by evaporation from the combined filtrates. The residue was chromatographed (pentane eluent) to give a 6:1 mixture of compounds **2** and **3** (0.73 g, 94%).

r-1,t-2,t-5-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentane* **2**. δ_H 1.21 (6 H, d, *J* 7.12), 1.33 (2 H, m), 1.54 (2 H, m), 1.87 (2 H, m), 4.11 (1 H, t, *J* 3.60), 7.39 (3 H, m) and 7.57 (2 H, m); δ_C 17.5, 20.1, 35.1, 127.9, 129.4, 134.5 and 135.8.

r-1,c-2,c-5-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentane* **3**. δ_H 1.02, (6 H, d, *J* 7.70), 1.32 (2 H, m), 1.55 (2 H, m) 1.85 (2 H, m), 4.43 (1 H, t, *J* 3.75), 7.40 (3 H, m) and 7.55 (2 H, m); δ_C 16.2, 18.2, 34.9, 127.6, 129.6, 136.3 and 137.8.

The Silyl Ethers **15–17** *derived from* (S)-*TPED*.—1-Chloro-DMPSC (**6**:**7**:**8** + **9** = 7:33:60) (10.5 g, 47 mmol) was added to a solution of (*S*)-TPED (16.0 g, 55 mmol), imidazole (7.0 g, 0.1 mol) and 4-dimethylaminopyridine (DMAP) (1.0 g) in DMF (100 cm^3). The mixture was stirred at room temp. for 24 h, then heated at 60 °C (bath temperature) for a further 4 h. After the mixture had cooled to room temp., it was poured into a mixture of water (100 cm^3) and diethyl ether (100 cm^3) and shaken. The organic layer was separated, the aqueous layer was extracted with diethyl ether (3 × 30 cm^3), the combined organic phase was washed with saturated brine and then dried ($MgSO_4$). The solvent was removed by evaporation to give a viscous oil (20.2 g, 90%) which was crystallised from methanol to give 10.6 g of crystalline material. The methanol was removed from the mother liquor by evaporation and the residue was purified by chromatography, using pentane–diethyl ether (98:2) eluent, followed by recrystallisation from methanol to give a second crop (2.5 g). The combined product was recrystallised from methanol to give the silyl ether (10.5 g), which consisted of approximately equal amounts of compounds **15** and **17**, along with a trace of compound **16**. The silyl ethers showed HPLC retention times which increased in the order **17** < **16** < **15** with hexane–ethyl acetate (98:2) as the mobile phase. The (2*R*,5*R*)-silyl ether **16** was formed as a viscous oil, which was removed by further recrystallisation from methanol. A mixture of compounds **15** and **17** (4 g) was separated chromatographically using *ca.* 60 g of silica gel in a 20 cm × 32 mm column. Flash elution with pentane (600 cm^3) was followed by elution with pentane–diethyl ether (98:2), during which fractions (10 cm^3) were collected and analysed by HPLC. The involatile residue from combined fractions was recrystallised from methanol and, by this method, *ca.* 1 g each of the pure compounds **15** and **17** could be isolated.

2S-2-[(r-1,c-2,c-5-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentyl*)-*oxy*]-1,1,2-*triphenylethanol* **15** *derived from* (S)-*TPED*. Purity > 99% by NMR spectroscopy, m.p. 108–109 °C, $[\alpha]_D^{22}$ −128 (*c* 1.32, $CHCl_3$); δ_H 0.79 (3 H, br s), 0.85 (3 H, d, *J* 7.71), 1.2–1.9 (6 H, m), 3.52 (1 H, s, OH), 5.64 (1 H, s) and 7.0–7.7 (20 H, m); δ_C 15.3, 15.8, 18.3, 20.1, 33.4, 33.6, 80.1, 81.1 and 126–146 (16 peaks) (Found: C, 80.25; H, 7.2. $C_{32}H_{34}O_2Si$ requires C, 80.29; H, 7.16%).

2S-2-[(2R,5R-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentyl*)*oxy*]-1,1,2-*triphenylethanol* **16** *derived from* (S)-*TPED*. δ_H 0.81 (3 H, d, *J* 6.90), 0.86 (3 H, d, *J* 6.90), 0.90–1.20 (4 H, m), 1.85 (2 H, m), 3.67 (1 H, s, OH), 5.61 (1 H, s) and 6.9–7.8 (20 H, m); δ_C 14.5, 15.5, 20.1, 21.7, 34.3, 34.5, 80.2 and 125–148 (16 peaks).

2S-2-[(2S,5S-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentyl*)*oxy*]-1,1,2-*triphenylethanol* **17** *derived from* (S)-*TPED*. Purity > 99% by NMR spectroscopy, m.p. 97–98 °C, $[\alpha]_D^{22}$ −83.1 (*c* 1.54, $CHCl_3$); δ_H 0.69 (3 H, d, *J* 7.36), 0.70 (3 H, d, *J* 7.17), 0.85–1.20 (4 H, m), 1.85 (2 H, m), 3.50 (1 H, s, OH), 5.44 (1 H, s) and 6.9–7.5 (20 H, m); δ_C 15.3(0), 15.3(4), 20.1, 21.8, 34.3, 34.5, 79.8, 81.1 and 126–146 (16 peaks) (Found: C, 80.2; H, 7.1. $C_{32}H_{34}O_2Si$ requires C, 80.29; H, 7.16%).

The combined residue (11 g) from the above separations consisted of compounds **15**, **16** and **17** in a ratio of 1:2:1, respectively, and this was reduced with $LiAlH_4$ to give DMPSC rich in the (2*R*,5*R*)-form **4** which could be used to prepare optically pure samples of this enantiomer *via* the silyl ether derived from (*R*)-TPED. Thus, the same procedure, starting from (*R*)-TPED as the resolving agent, afforded *ent*-**15** (isomeric purity 99%) m.p. 107–109 °C, $[\alpha]_D^{22}$ +125 (*c* 2.38, $CHCl_3$) and *ent*-**17** (isomeric purity 98.5%), m.p. 96–97 °C, $[\alpha]_D^{22}$ +81.2 (*c* 1.91, $CHCl_3$).

(2S,5S)-(+)-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentane* **5**.—A solution of the (2*S*,5*S*)-silyl ether **17** (3.0 g, 6.3 mmol) in THF (30 cm^3) was added dropwise over 1 h to a suspension of $LiAlH_4$ (2.0 g, 53 mmol) in THF (30 cm^3) cooled in an ice–water bath. The mixture was then stirred at room temp. for 6 h before being hydrolysed as described above for the reduction of 1-chloro-DMPSC. The precipitate formed was removed by filtration through Celite, washed with diethyl ether and the solvents were removed by evaporation from the combined filtrates. The residue was chromatographed (pentane eluent) to give compound **5** (1.15 g, 96%) with an estimated (NMR) chemical purity of > 99%, $[\alpha]_D^{22}$ +27.8 (*c* 2.16, cyclohexane); δ_H 0.90 (3 H, d, *J* 7.30), 1.19 (3 H, d, *J* 7.30), 1.25 (2 H, m), 1.37 (2 H, m), 2.05 (2 H, m), 4.22 (1 H, td, *J* 3.70 and 1.00), 7.36 (3 H, m) and 7.52 (2 H, m); δ_C 15.7, 16.8, 19.4, 20.6, 35.7, 36.8, 127.8, 129.3, 134.0 and 135.4.

The remaining material on the column was eluted with pentane–diethyl ether–CH_2Cl_2 (8:1:1) to give (*S*)-TPED (1.8 g, 98%), which was recrystallised from methanol and dried at 60 °C under reduced pressure (60 Torr), m.p. 127–128 °C, $[\alpha]_D^{22}$ −225 (*c* 0.51, 95% EtOH).

(2R,5R)-(−)-2,5-*Dimethyl*-1-*phenyl*-1-*silacyclopentane* **4**.—Reduction of *ent*-**17** (1.0 g, 2.1 mmol) with $LiAlH_4$ in THF, as described for the preparation of compound **5**, gave the title compound **4** (0.38 g, 95%); $[\alpha]_D^{22}$ −27.1 (*c* 2.60, cyclohexane) and (*R*)-TPED (0.58 g, 95%); $[\alpha]_D^{22}$ +224 (*c* 0.53, 95% EtOH).

Reduction of the Silyl Ether **15**.—The isomerically pure silyl ether (4.0 g, 8.4 mmol) was treated with $LiAlH_4$ (3.5 g, 92 mmol) in THF as described above to give DMPSC as an isomeric mixture containing the *cis*-dimethyl isomers **2** (87%) and **3** (13%) (1.5 g, 94%).

(2S,5S)-1-(9-*Anthrylmethoxy*)-2,5-*dimethyl*-1-*phenyl*-1-*silacyclopentane* **18**.—(2*S*,5*S*)-DMPSC **5** (0.5 g, 2.6 mmol) was added to a suspension of anhydrous copper(II) chloride (2.0 g, 14 mmol) in acetonitrile (10 cm^3) and the mixture was stirred and heated under reflux for 1 h. The mixture was stirred at room temp. for a further 1 h and then extracted with pentane (3 × 10 cm^3). The solvent was removed from the combined extracts and the crude (2*S*,5*S*)-1-chloro-DMPSC **9** was treated with 9-anthrylmethanol (0.7 g, 3 mmol), imidazole (0.5 g, 7 mmol) and DMAP (50 mg) in DMF (10 cm^3), with stirring at 40 °C for 10 h. The reaction mixture was poured into a mixture of water (10 cm^3) and diethyl ether (10 cm^3) and shaken; the organic layer was separated, the aqueous layer was extracted with diethyl ether (3 × 10 cm^3) and the combined organic phase was washed with saturated brine and dried ($MgSO_4$). The solvent was removed by evaporation and the residue was recrystallised from methanol to give the silyl ether **18** (0.82 g, 79% overall yield

from DMPSC), m.p. 68 °C; $[\alpha]_D^{22}$ +19.2 (*c* 1.04, $CHCl_3$); δ_H 0.93 (3 H, d, *J* 7.40), 1.12 (1 H, m), 1.20 (3 H, d, *J* 6.77), 1.31 (3 H, m), 2.05 (2 H, m), 5.72 and 5.77 (2 H, ABq, *J* 11.80), 7.3–7.5 (7 H, m), 7.62 (2 H, m), 8.01 (2 H, dd, *J* 9.61 and 2.09), 8.31 (2 H, d, *J* 8.58) and 8.45 (1 H, s); δ_C 14.9, 15.6, 20.6, 20.9, 34.7, 35.0, 58.4 and 124–135 (12 peaks) (Found: C, 81.5; H, 7.1. $C_{27}H_{28}OSi$ requires C, 81.77; H, 7.12%).

X-Ray Crystallography.—Data were collected on a Nicolet R3mV diffractometer at 20 °C using graphite monochromated Mo-Kα radiation (λ = 0.710 73 Å). Three standard reflections monitored throughout the data collection showed no loss in intensity with time. The data were corrected for Lorentz and polarisation effects. The structures were solved by direct methods and developed using alternating cycles of least-squares refinement and difference-Fourier synthesis. Non-hydrogen atoms were refined anisotropically while hydrogens were placed in idealised positions (r_{C-H} = 0.96 Å) and assigned a common isotropic thermal parameter (U = 0.08 Å^2). All calculations were performed with the SHELXTL PLUS program package [22] on a MicroVax II computer. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre (see Instructions for Authors, Issue No. 1).

Crystal data for compound **11**. $C_{18}H_{26}O_6Si$, M = 366.49, Orthorhombic, space group $P2_12_12_1$, a = 7.611(1), b = 11.720(3), c = 21.826(5), V = 1929 Å^3 (by least-squares refinement of diffractometer angles for 27 reflections in the range $14 \leq 2\theta \leq 28°$), Z = 4, $F(000)$ = 784, D_c = 1.26 g cm^{-3}, μ(Mo-Kα) = 1.44 cm^{-1}. Colourless block 0.78 × 0.38 × 0.34 mm. Full-matrix least-squares refinement of 226 parameters gave R = 0.0481 (R_w = 0.0509) for 2897 independent reflections [$I \geq 3\sigma(I)$] in the range $5 \leq 2\theta \leq 52°$. The final electron difference map was featureless with the largest peak 0.56 e Å^{-3}.

Crystal data for compound **17**. $C_{32}H_{34}O_2Si$, M = 478.71, Monoclinic, space group $P2_1$, a = 10.389(4), b = 8.327(2), c = 16.184(5), β = 97.24(3) Å, V = 1389 Å^3 (by least-squares refinement of diffractometer angles for 30 reflections in the range $16 \leq 2\theta \leq 25°$), Z = 2, $F(000)$ = 512, D_c = 1.14 g cm^{-3}, μ(Mo-Kα) = 1.05 cm^{-1}. Colourless block 0.74 × 0.68 × 0.46 mm. Full-matrix least-squares refinement of 315 parameters gave R = 0.0683 (R_w = 0.0697) for 2002 independent reflections [$I \geq 2\sigma(I)$] in the range $5 \leq 2\theta \leq 52°$. The final electron difference map was featureless with the largest peak 0.22 e Å^{-3}.

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