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STEREOCHEMICAL STRUCTURES OF (8,8-ETHYLENEDIOXY-2-OXO-)- AND (8,8-ETHYLENEDIOXY-2-HYDROXY-)-6-PHENYLSULPHONYLBICYCLO[3·3·0]OCTANES

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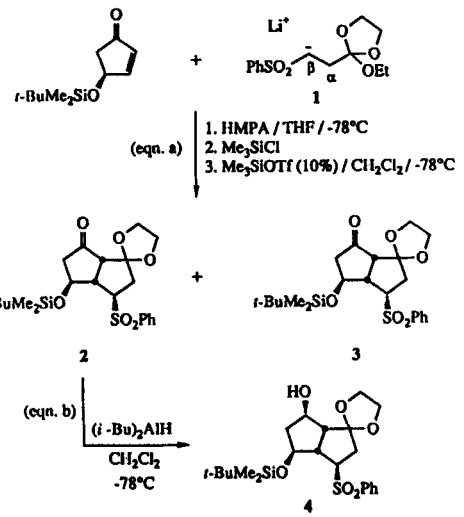
Cyclopentannulation of 4-*tert*-butyldimethylsilyloxy-2-cyclopenten-1-one from a β-metallated dioxolane-type orthoester affords 4-*tert*-butyldimethylsilyloxy-8,8-ethylenedioxy-6-phenylsulphonyl-2-oxobicyclo[3·3·0]octanes as a mixture of two diastereoisomers. Their stereochemical structures were established by NMR and x-ray analysis. The minor product possesses a *cis* ring fusion, the sulphonyl and the *tert*-butyldimethylsilyloxy groups being *endo* and *exo*, respectively. The major isomer also has a *cis* ring fusion but an *exo* position for both dimethylsilyloxy and sulphonyl groups. Both cyclopentannulation products result from an *anti* addition with respect to the 4-*tert*-butyldimethylsilyloxy group on the enone.

INTRODUCTION

Cyclopentannulation of 4-*tert*-butyldimethylsilyloxy-2-cyclopenten-1-one from the β-metallated dioxolane type orthoester **1** according to the previously reported[1] procedure affords 4-*tert*-butyldimethylsilyloxy-8,8-ethylenedioxy-6-phenylsulphonyl-2-oxobicyclo[3·3·0]octanes as a mixture of a major diastereoisomer **2** and a minor diastereoisomer **3** [Scheme 1, equation (a)]. These two diquinanes have been isolated by recrystallization and flash chromatography followed by recrystallization, respectively. Ketone diisobutylaluminum hydride reduction of **2** gives a single diastereoisomer **4** [Scheme 1, equation (b)].

In order to determine the stereochemical course of the reaction, we have undertaken high-field NMR and x-ray diffraction analysis of the resulting products.



Scheme 1

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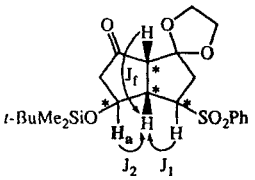
RESULTS AND DISCUSSION

NMR study of compounds 2 and 3

Products **2** and **3** are characterized by the ^3J(H,H) coupling constants reported in Figure 1. In particular we can determine without ambiguity that ring fusion ^3J(H,H) values of 10·0 and 8·2 Hz correspond to a synclinal relationship between the protons, implying a *cis* configuration. On the other hand, comparison between other typical ^3J(H,H) values for **2** and **3** cannot give stereochemical information; this is exemplified by the fact that ^3J(H,H) values between the protons adjacent to *t*-BuMe$_2$SiO and PhSO$_2$ and the vicinal proton at the fusion are nearly identical. A striking difference exists between the chemical shift δH_a of the proton adjacent to the silyloxy group for each diastereoisomer. Compared with **2**, the H_a proton in **3** is deshielded by 0·7 ppm in deuterochloroform. This is due to the important anisotropic effect of the sulphonyl group. It is likely that product **3** possesses proton H_a located close to this group. In contrast, this effect is absent for the major diastereoisomer **2**; the proton concerned resonates at the usual field. The ^{13}C chemical shifts do not differ by more than ±3 ppm between the two compounds. More information concerning the stereochemistry was obtained by x-ray analysis.



	δH_a	J_1	J_2	J_f
2	4,51	9,0	2,0	10,3
3	5,23	9,5	1,5	8,2

Figure 1. Coupling constants in **2** and **3**

X-ray analysis of compounds 3 and 4

The atomic parameters of **3** and **4** are given in Tables 1 and 2, respectively. Bond distances and bond angles are compared in Tables 3 and 4. Figures 2 and 3 are stereoscopic views of the molecules showing the numbering of the atoms; Figures 4 and 5 show the unit cell content for each structure (PLUTO program[2]).†

Table 1. Atomic coordinates ($\times 10^4$) of **3** and equivalent temperature factors $U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i a_j$ (Å^2)($\times 10^3$)

Atom	x	y	z	U_{eq}
C1	1661(3)	2547(2)	7712(2)	58(1)
C2	1742(4)	2307(3)	8848(3)	79(1)
C3	3045(5)	2553(4)	9173(3)	87(2)
C4	4163(3)	2200(3)	8012(3)	65(1)
C5	3161(3)	2653(2)	7244(2)	51(1)
C6	2613(3)	4120(2)	7321(2)	49(1)
C7	1018(3)	4892(2)	8216(2)	51(1)
C8	337(3)	3905(2)	7934(2)	52(1)
O9	−62(2)	3846(2)	6891(2)	69(1)
C10	−1399(4)	3623(4)	7022(3)	88(2)
C11	−2028(5)	3951(5)	8288(4)	100(2)
O12	−993(2)	4257(2)	8826(2)	64(1)
O13	4948(2)	774(2)	7473(2)	70(1)
Si14	6781(1)	−64(1)	7261(1)	58(1)
C15	7277(5)	629(4)	8602(4)	96(2)
C16	7898(6)	77(5)	5982(4)	118(3)
C17	7055(3)	−1812(3)	6989(3)	64(1)
C18	6600(5)	−2345(4)	5919(4)	100(2)
C19	8760(5)	−2701(4)	6752(6)	132(3)
C20	6065(7)	−1862(5)	8031(4)	125(3)
S21	3899(1)	4848(1)	7591(1)	55(1)
O22	3917(2)	5096(2)	8784(2)	71(1)
O23	5317(2)	4029(2)	6647(2)	76(1)
C24	3053(3)	6393(3)	7441(2)	55(1)
C25	2266(4)	7545(3)	8449(3)	69(1)
C26	1649(4)	8755(3)	8316(3)	82(2)
C27	1815(4)	8802(4)	7213(4)	84(2)
C28	2576(4)	7654(4)	6212(3)	81(2)
C29	3189(3)	6447(3)	6333(3)	67(1)
O30	923(4)	1946(3)	9364(3)	116(2)

Table 2. Atomic coordinates ($\times 10^4$) of **4** and equivalent temperature factors $U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i a_j$ (Å^2)($\times 10^3$)

Atom	x	y	z	U_{eq}
C1	5992(1)	847(1)	1772(1)	42(1)
C2	5593(2)	1550(1)	2615(1)	56(1)
C3	4187(2)	917(1)	3693(1)	60(1)
C4	3278(1)	842(1)	3063(1)	45(1)
C5	4469(1)	382(1)	2068(1)	37(1)
C6	4717(1)	−1112(1)	2523(1)	38(1)
C7	6391(1)	−1339(1)	1845(1)	47(1)
C8	7081(1)	−381(1)	1969(1)	41(1)
O9	7138(1)	−965(1)	3176(1)	48(1)
C10	8674(2)	−1417(2)	3036(1)	69(1)
C11	9533(2)	−1000(2)	1688(2)	69(1)
O12	8564(1)	−75(1)	1133(1)	56(1)
O13	2721(1)	2132(1)	2480(1)	57(1)
Si14	1066(1)	2641(1)	2377(1)	44(1)
C15	−468(2)	1728(2)	3840(1)	67(1)
C16	1043(2)	2342(2)	1128(2)	81(2)
C17	933(2)	4438(1)	2033(2)	60(1)
C18	−636(2)	5026(2)	1991(2)	90(2)
C19	2195(2)	5140(2)	817(2)	102(2)
C20	1069(2)	4572(2)	3075(2)	89(1)
S21	3514(1)	−1799(1)	2289(1)	45(1)
O22	1982(1)	−1525(1)	3002(1)	61(1)
O23	3945(1)	−1401(1)	992(1)	69(1)
C24	3953(1)	−3497(1)	2958(1)	47(1)
C25	5018(2)	−4101(1)	2236(2)	64(1)
C26	5404(2)	−5429(2)	2790(2)	81(2)
C27	4700(2)	−6107(2)	4048(2)	83(2)
C28	3636(2)	−5491(2)	4757(2)	82(2)
C29	3238(2)	−4180(1)	4217(1)	63(1)
O30	6776(1)	1589(1)	2934(1)	76(1)

† Supplementary material is available from the senior author upon request.

As shown in Figure 2, the minor product **3** possesses a *cis* ring fusion. The sulphonyl and the *tert*-butyldimethylsilyloxy groups are located *endo* and *exo* respectively. The stereochemical structure of the major product **2** is deduced *a posteriori* from that of the alcohol **4**. The latter molecule has five stereocentres; it is characterized by a *cis* ring fusion,[3,4] an *exo* position of the *tert*-butyldimethylsilyloxy and sulphonyl substituents, as for **2**, and by an *endo* position of the alcoholic function (Figure 3). With regard of the *exo* position of the *tert*-butyldimethylsilyloxy group, we can assume that *cis* ring junction[5] cyclopentannulation products **2** and **3** both result from an *anti* addition to 4-*tert*-butyldimethylsilyloxy group on the enone.

It is worth making some brief comments about the conformations of compounds **3** and **4**. They are different, as shown by the comparison of the endocyclic torsion angles listed in Table 5. In molecule **3**, the cyclopentanone is a half-chair with the diad axis

Table 3. Bond distances (Å)

Bond	3	4
C2—C1	1·525(4)	1·534(2)
C5—C1	1·545(4)	1·543(2)
C8—C1	1·553(3)	1·540(2)
C3—C2	1·503(6)	1·506(2)
O30—C2	1·198(4)	1·420(2)
C4—C3	1·498(5)	1·506(2)
C5—C4	1·550(3)	1·539(2)
O13—C4	1·434(3)	1·417(2)
C6—C5	1·555(3)	1·533(2)
C7—C6	1·523(3)	1·514(2)
S21—C6	1·778(2)	1·775(1)
C8—C7	1·509(3)	1·536(2)
O9—C8	1·411(3)	1·435(2)
O12—C8	1·399(3)	1·395(2)
C10—O9	1·416(3)	1·430(2)
C11—C10	1·469(5)	1·481(2)
O12—C11	1·404(4)	1·403(2)
Si14—O13	1·642(2)	1·633(1)
C15—Si14	1·865(4)	1·855(1)
C16—Si14	1·848(4)	1·849(2)
C17—Si14	1·863(3)	1·887(2)
C18—C17	1·516(5)	1·540(2)
C19—C17	1·542(5)	1·518(2)
C20—C17	1·503(5)	1·521(3)
O22—S21	1·435(2)	1·432(1)
O23—S21	1·440(2)	1·431(1)
C24—S21	1·762(3)	1·763(1)
C25—C24	1·390(4)	1·367(2)
C29—C24	1·382(4)	1·380(2)
C26—C25	1·382(5)	1·392(2)
C27—C26	1·372(5)	1·377(2)
C28—C27	1·382(5)	1·366(2)
C29—C28	1·373(5)	1·377(2)

Table 4. Bond angles (°)

Bonds	3	4
C5—C1—C2	105·1(2)	104·7(1)
C8—C1—C2	112·3(2)	117·2(1)
C8—C1—C5	106·1(2)	106·5(1)
C3—C2—C1	108·3(3)	104·0(1)
O30—C2—C1	125·0(4)	116·3(1)
O30—C2—C3	126·7(4)	115·2(1)
C4—C3—C2	104·0(3)	102·3(1)
C5—C4—C3	105·0(2)	103·3(1)
O13—C4—C3	107·9(3)	107·6(1)
O13—C4—C5	106·2(2)	109·2(1)
C4—C5—C1	105·2(2)	105·6(1)
C6—C5—C1	103·9(2)	104·3(1)
C6—C5—C4	118·5(2)	113·9(1)
C7—C6—C5	106·3(2)	104·5(1)
S21—C6—C5	115·4(2)	112·3(1)
S21—C6—C7	114·2(2)	114·3(1)
C8—C7—C6	101·8(2)	101·4(1)
C7—C8—C1	104·2(2)	103·7(1)
O9—C8—C1	109·0(2)	112·8(1)
O9—C8—C7	110·0(2)	108·9(1)
O12—C8—C1	114·1(2)	111·2(1)
O12—C8—C7	112·2(2)	114·6(1)
O12—C8—O9	107·3(2)	105·9(1)
C10—O9—C8	107·1(2)	107·3(1)
C11—C12—C8	107·7(2)	107·3(1)
O12—C11—C10	107·0(3)	105·3(1)
C11—C10—O9	105·6(3)	105·5(1)
Si14—O13—C4	123·2(2)	129·5(1)
C15—Si14—O13	109·6(1)	111·0(1)
C16—Si14—O13	108·9(2)	108·4(1)
C16—Si14—C15	110·1(3)	108·3(1)
C17—Si14—O13	104·9(1)	103·3(1)
C17—Si14—C15	111·2(2)	112·2(1)
C17—Si14—C16	112·1(2)	113·5(1)
C18—C17—Si14	110·5(2)	108·7(1)
C19—C17—Si14	109·3(2)	110·0(1)
C19—C17—C18	108·2(3)	111·2(1)
C20—C17—Si14	110·0(2)	109·1(1)
C20—C17—C18	108·0(4)	108·1(1)
C20—C17—C19	110·9(4)	109·7(2)
O22—S21—C6	109·6(1)	107·6(1)
O23—S21—C6	106·9(1)	109·6(1)
O23—S21—O22	119·0(1)	118·7(1)
C24—S21—C6	103·5(1)	102·8(1)
C24—S21—O22	108·4(1)	108·7(1)
C24—S21—O23	108·4(1)	108·3(1)
C25—C24—S21	119·0(2)	119·9(1)
C29—C24—S21	119·9(2)	118·6(1)
C29—C24—C25	121·0(3)	121·4(1)
C26—C25—C24	118·4(3)	119·1(1)
C27—C26—C25	120·3(3)	119·4(1)
C28—C27—C26	121·4(3)	120·9(1)
C29—C28—C27	118·8(3)	120·2(1)
C28—C29—C24	120·1(3)	119·0(1)

through C1 ($\Delta C2 = 1^\circ$), the cyclopentane an envelope with C7 at the flap ($\Delta Cs = 5{\cdot}8^\circ$) and the dioxolane ring an envelope with C8 at the flap ($\Delta Cs = 5{\cdot}1^\circ$).[6] For compound **4**, both cyclopentane rings adopt envelope conformations; that with the hydroxyl substituent has C3 at the flap ($\Delta Cs = 0^\circ$) and the other has C7 at the flap, i.e. the same conformation as in **3** ($\Delta Cs = 6{\cdot}3^\circ$). Curiously, the dioxolane ring here adopts a different envelope conformation as it is now atom O12 which is at the flap ($\Delta Cs = 4{\cdot}5^\circ$).

There is an intramolecular hydrogen bond in molecule **4**, between the hydroxyl hydrogen and O9 of the dioxolane ring; the geometry is O30···O9 = 2·760(2) Å, H30···O9 = 2·32(4) Å and O—H···O = 135(2)°.

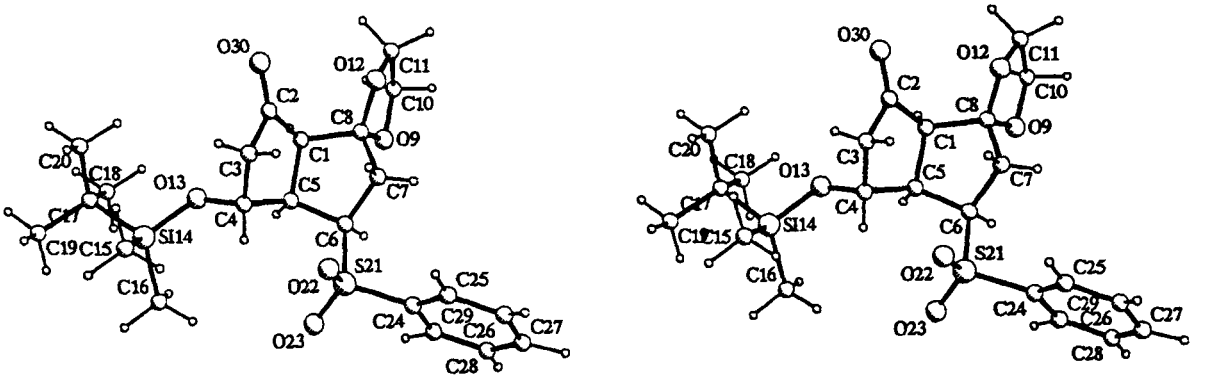


Figure 2. Stereoscopic view of **3**

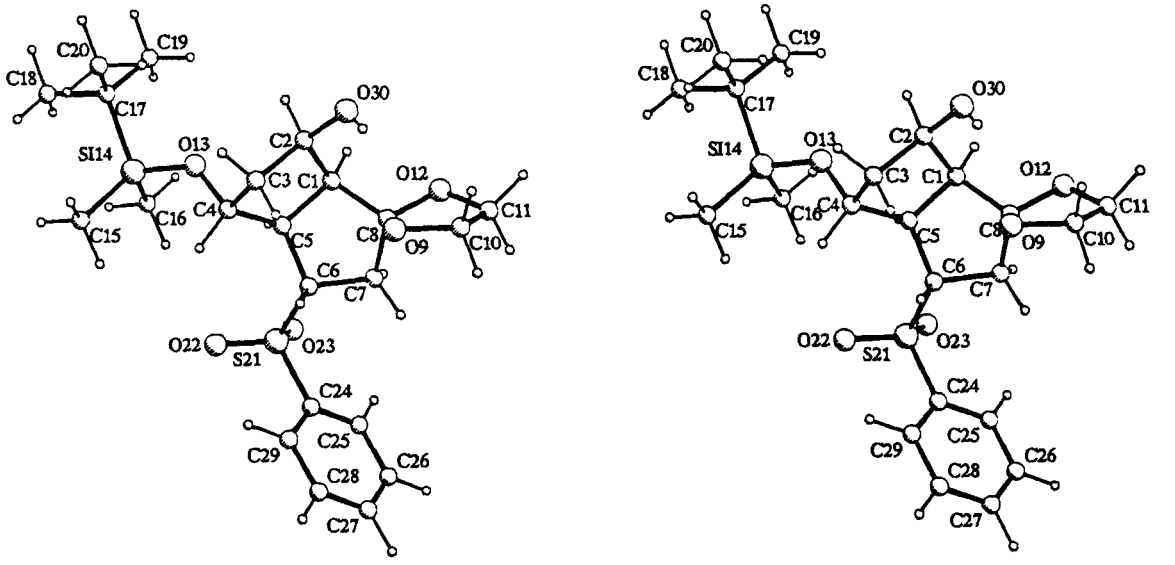


Figure 3. Stereoscopic view of **4**

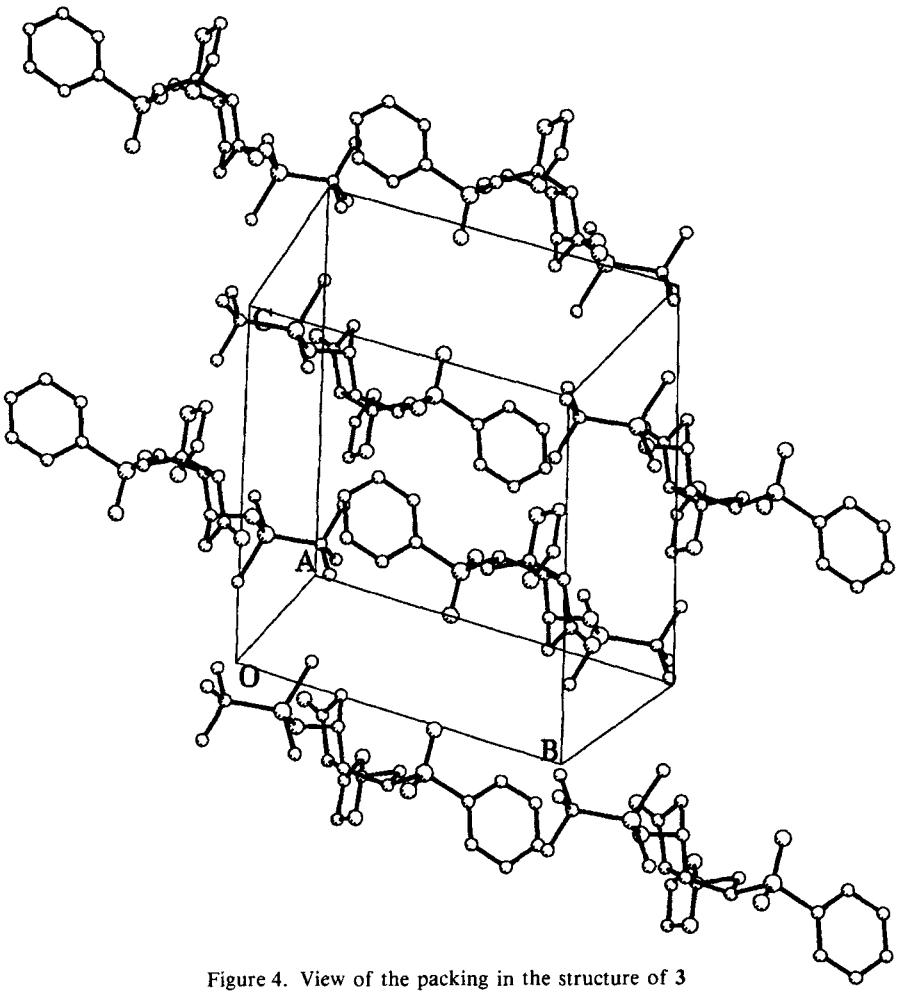


Figure 4. View of the packing in the structure of 3

Table 5. Endocyclic torsion angles (°) ($\sigma = 1°$)

Bonds	3	4
C5—C1—C2—C3	11	26
C1—C2—C3—C4	−30	−43
C2—C3—C4—C5	36	43
C3—C4—C5—C1	−29	−26
C2—C1—C5—C4	10	0
C8—C1—C5—C6	4	4
C1—C5—C6—C7	21	−30
C5—C6—C7—C8	−39	44
C6—C7—C8—C1	41	−40
C5—C1—C8—C7	−29	22
O12—C8—O9—C10	−23	−20
C8—O9—C10—C11	17	3
O9—C10—C11—O12	4	14
C10—C11—O12—C8	−10	−28
O9—C8—O12—C10	21	30

EXPERIMENTAL

All NMR spectra were acquired with a Bruker AM500 spectrometer (^{1}H at 500·13 MHz, ^{13}C at 125·77 MHz). Assignments of the ^{13}C NMR resonances were obtained by using two-dimensional ^{1}H–^{13}C NMR shift correlation spectroscopy (HCCORR).[7] Two-dimensional double-quantum filtered correlation spectroscopy (DQF-COSY)[7] gave all the ^{1}H–^{1}H connectivities. DQF-COSY spectra were measured using the time-proportional phase incrementation method (TPPI) and transformed in the phase-sensitive mode.[7,8] Chloroform was chosen as an external reference.

Suitable crystals were obtained by slow evaporation at room temperature of a solution in methyl acetate for **3** and a solution in diethyl ether for **4**. The crystal data, the data collection and the refinement parameters are summarized in Table 6. The lattice parameters were

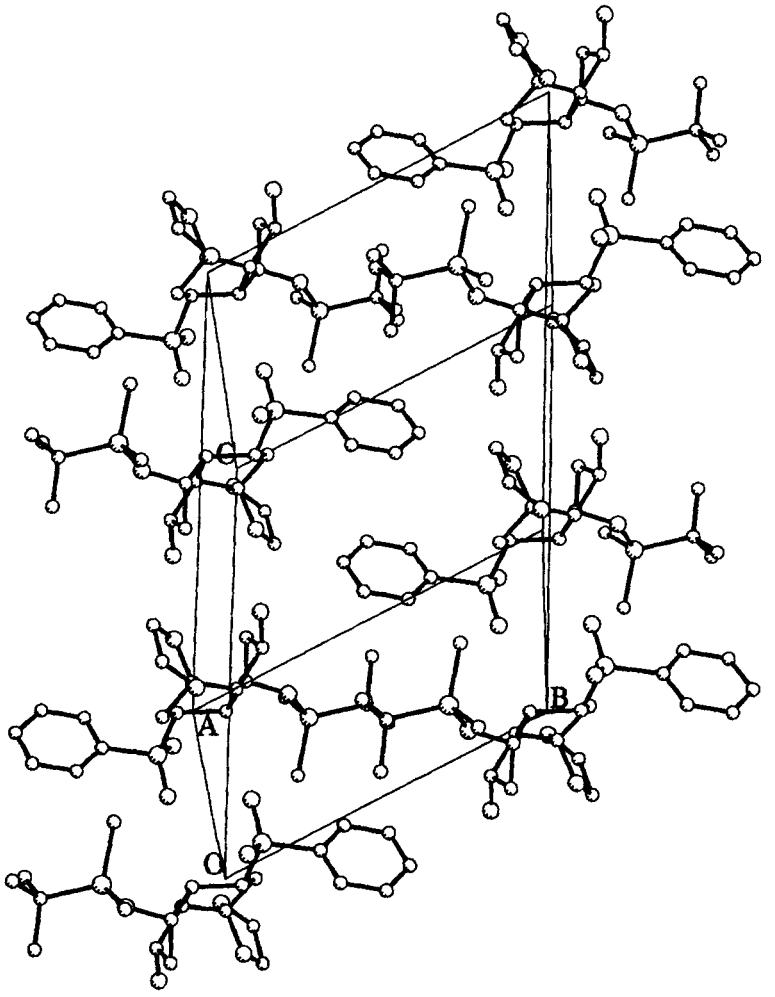


Figure 5. View of the packing in the structure of **4**

refined using 16 reflections for **3** and 22 for **4** in the range $20^\circ < 2\theta < 60^\circ$. A Huber four-circle diffractometer equipped with monochromatized Cu Kα radiation was used for both data collections. One standard reflection was checked every 50 measurements; no significant intensity decrease was observed. Both structures were solved by direct methods using the SHELXS86 program[9] and refined with SHELX76[10] using F values. All the H atoms were computed riding on their C atoms (C—H = 1·08 Å, H—C—H = 109.5°) except the H of the hydroxyl in **4** and those which are not methyl in **3** which were located from Fourier difference synthesis. The H atoms were included in the refinement with common refined isotropic temperature factor ($U = 0{\cdot}12\,\text{Å}^2$ for **3** and $0{\cdot}10\,\text{Å}^2$ for **4**). The full list of atomic coordinates including H atoms and the anisotropic thermal parameters have been deposited as supplementary material. Atomic scattering factors were taken from the *International Tables*.[11]

Table 6. Data collection and refinement parameters

Parameter	3	4
Formula	$C_{22}H_{32}O_6SSi$	$C_{22}H_{34}O_6SSi$
Dimensions (mm)	0·32 × 0·20 × 0·20	0·20 × 0·28 × 0·40
M_r	452·64	454·66
System	Triclinic	Triclinic
Space group	$P-1$	$P-1$
a (Å)	9·820(1)	9·852(3)
b (Å)	11·563(1)	11·547(3)
c (Å)	12·439(2)	13·224(3)
α (°)	106·25(2)	62·14(3)
β (°)	79·77(2)	63·77(3)
γ (°)	69·18(1)	75·56(3)
V (Å^3)	1205·6(2)	1191·3(5)
D_x (g cm^{-3})	1·25	1·27
Z	2	2
λ	1·54178	1·54178
$F(000)$	484	488
μ (cm^{-1})	19·0	19·3
Collection range:		
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0·60	0·60
Range of hkl	$-11 < h < 11$	$-10 < h < 11$
	$-13 < k < 12$	$-12 < k < 13$
	$0 < l < 14$	$0 < l < 15$
Indices of standard reflections	1 5 −3	−3 2 1
No. of measured reflections	4338	4284
No. of observed reflections [$I \geqslant 2·5(I)$]	3587	4004
No. of parameters	311	275
R =	0·049	0·053
wR =	0·064	0·082
$w = 1/(\sigma^2 + gF^2)$: g =	0·00626	0·03212
S	1·03	0·69
(Δ/σ)	0·47	0·22
$\rho_{(max,min)}$ (e Å^{-3})	0·29, −0·34	0·36, −0·52

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REFERENCES

1. S. De Lombaert, I. Nemery, B. Roekens, J. C. Carretero, T. Kimmel and L. Ghosez, *Tetrahedron Lett.* **27**, 5099 (1986).
2. W. D. S. Motherwell and W. Clegg, *PLUTO Program for Plotting Molecular and Crystal Structures.* University of Cambridge, Cambridge (1978).
3. J. P. Declercq, J. C. Carretero and I. Nemery, *Acta Crystallogr., Sect. C* **43**, 2146 (1987).
4. B. Tinant, J. P. Declercq and M. Demillequand, *Bull. Soc. Chim. Belg.* **98**, 83 (1989).
5. For an example of *trans* ring fusion, see B. Tinant, J. P. Declercq and M. Demillequand, *Bull. Soc. Chim. Belg.* **102**, 53 (1993).
6. W. L. Duax, C. M. Weeks and D. C. Roher, *Top. Stereochem.* **9**, 271 (1976).
7. A. E. Derome, *Modern NMR Techniques for Chemistry Research.* Pergamon Press, Oxford (1987).
8. D. Marion and K. Wüthrich, *Biochem. Biophys. Res. Commun.* **113**, 967 (1983).
9. G. M. Sheldrick, in *Crystallographic Computing 3*, edited by G. M. Sheldrick, C. Kruger and R. Goddard, pp. 175–189. Oxford University Press, London (1985).
10. G. M. Sheldrick, *SHELX76 Program for Crystal Structure Determination.* University of Cambridge, Cambridge (1976).
11. International Tables for X-Ray Crystallography, Vol. IV. 1974. Birmingham: Kynoch Press (Present distributor D. Reidel, Dordrecht).