

Structure of a Densely Oxygenated Carbocycle

KHALIL A. ABOUD,* ERIC J. ENHOLM AND ANTIGONE TRIVELLAS

Department of Chemistry, University of Florida, Gainesville, FL 32611, USA

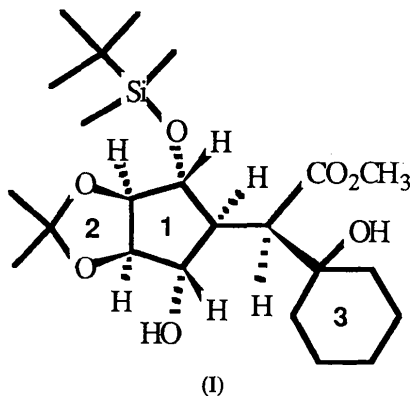
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Abstract. {3*aR*-[3*aα*,4*α*,5*β*(*R*^{*}),6*α*,6*α*]}-Methyl 4-[[1,1-dimethylethyl)dimethylsilyl]oxy}tetrahydro-6-hydroxy- α -(1-hydroxycyclohexyl)-2,2-dimethyl-4*H*-cyclopenta-1,3-dioxole-5-acetate, C₂₃H₄₂O₇Si, *M*_r = 458.75, monoclinic, *P*2₁, *a* = 11.537 (2), *b* = 8.552 (2), *c* = 13.916 (4) Å, β = 92.39 (2)°, *V* = 1371.8 (5) Å³, *Z* = 2, *D*_x = 1.11 g cm⁻³, Mo *Kα*, λ = 0.71069 Å, μ = 1.2 cm⁻¹, *F*(000) = 500, *T* = 298 K, *R* = 0.0564 and *wR* = 0.0638 for 1475 reflections [*I* ≥ 3 σ (*I*)]. Crystal chirality was assigned to correspond to the known chirality of the precursor compound. The cyclopentane ring exhibits an envelope conformation (*E*¹) where C(1) occupies the flap position [0.58 Å from the plane of C(2), C(3), C(5) and C(6)]. The dioxole ring is in an unusual planar conformation. This planarity may be partially attributed to the disorder of the C—(CH₃)₂ moiety at the C(4) position. The cyclohexyl ring exhibits a chair conformation (*₄C*¹) where atoms C(8) and C(11) are 0.61 Å and -0.66 Å, respectively, from the plane of atoms C(9), C(10), C(12) and C(13).

Experimental. The title compound, (I), (see scheme), was purified by flash chromatography over silica gel. This was followed by treatment of the colorless thick oil with hot pentane and subsequent cooling of the solution to 273 K to produce colorless rhombic needles. The crystals had m.p. 365–366.5 K (un-

corrected). Although only the relative stereochemistry is indicated in Fig. 1, the actual chirality was assigned on the basis of the carbohydrate D-(–)-arabinose which was used to prepare the crystals. Chiral centers C(2), C(3), and C(4) in D-(–)-arabinose are fixed in the densely oxygenated cyclopentane ring at C(3) and C(5) of the 1,3-dioxole ring fusion and at the carbon bearing the siloxy functionality, C(2). The crystal used in the X-ray analysis was obtained by slow evaporation from an *n*-hexane solution, cut from a colorless needle, of dimensions 0.18 × 0.20 × 0.29 mm. Data were collected, at 298 K, on a Siemens *R3m/E* diffractometer equipped with a graphite monochromator utilizing Mo *Kα* radiation (λ = 0.71069 Å). 25 reflections with 20° ≤ 2 θ ≤ 22° were used to refine the cell parameters. 5157 reflections were collected using the ω -scan method (*h*, -13 → 13; *k*, 0 → 10; *l*, -16 → 16), 2591 unique reflections, *R*_{int} = 0.0136; 2 θ range 3 → 50°, 1.2° ω -scan at 3–6° min⁻¹, depending upon intensity. Four reflections (20 $\bar{1}$, 02 $\bar{1}$, 020, 2 $\bar{1}$ 3) were measured every 96 reflections to monitor instrument and crystal stability (maximum correction on *I* was < 1.02%). Absorption corrections were not applied due to the crystal size and the low value of the absorption coefficient (μ = 1.2 cm⁻¹).

The structure was solved by direct methods in *SHELXTL* from which the locations of all non-H atoms were obtained. The structure was refined [*SHELX76* (Sheldrick, 1976)] using cascade-matrix least squares and the positions of all nonmethyl H atoms were determined from a difference Fourier map; the methyl H atoms were calculated in idealized positions. The non-H atoms were treated anisotropically, whereas the H atoms were refined with isotropic thermal parameters except the methyl H atoms, on C(16) to C(25), which had their isotropic thermal parameters fixed. The two methyl groups on C(4) are disordered and are both shown in Fig. 1 (as solid circles, for clarity). Both disordered units were refined as rigid groups riding on atom C(4) which appears with large thermal parameters and its disorder could not be resolved. Another disorder was observed in the position of the Si atom. This disorder could not be resolved but is clearly reflected by the



* Author for correspondence.

Table 1. Atomic coordinates ($\times 10^4$) and isotropic thermal parameters ($\text{\AA}^2 \times 10^3$)

| | x | y | z | U |
|--------|-----------|------------|----------|-----------|
| C(1) | 815 (5) | 7577 | 7782 (4) | 51 (2)* |
| C(2) | 1903 (5) | 7655 (7) | 7209 (4) | 57 (2)* |
| C(3) | 2333 (5) | 9325 (9) | 7345 (4) | 69 (2)* |
| C(5) | 1860 (5) | 9907 (8) | 8272 (4) | 59 (2)* |
| C(6) | 1132 (4) | 8576 (7) | 8663 (4) | 52 (2)* |
| C(7) | 352 (5) | 5889 (7) | 7901 (4) | 55 (2)* |
| C(8) | -846 (5) | 5700 (8) | 8351 (4) | 59 (2)* |
| C(9) | -1143 (6) | 3938 (8) | 8380 (4) | 74 (3)* |
| C(10) | -2406 (6) | 3662 (10) | 8696 (5) | 88 (3)* |
| C(11) | -3290 (6) | 4588 (11) | 8099 (5) | 104 (4)* |
| C(12) | -2985 (5) | 6296 (10) | 8131 (5) | 88 (3)* |
| C(13) | -1774 (5) | 6637 (10) | 7800 (5) | 74 (3)* |
| C(14) | 1286 (5) | 4834 (7) | 8311 (4) | 64 (2)* |
| C(15) | 2472 (6) | 4242 (9) | 9700 (5) | 87 (3)* |
| C(16) | 3116 (11) | 8695 (16) | 4898 (6) | 234 (8)* |
| C(17) | 4035 (7) | 5968 (20) | 6105 (7) | 215 (8)* |
| C(18) | 2067 (10) | 5487 (14) | 4624 (7) | 141 (5)* |
| C(19) | 925 (10) | 6136 (19) | 4222 (6) | 199 (7)* |
| C(20) | 2884 (9) | 5220 (15) | 3771 (6) | 205 (7)* |
| C(21) | 1955 (10) | 3883 (14) | 5108 (7) | 216 (7)* |
| C(4) | 3833 (5) | 10054 (10) | 8337 (6) | 108 (4)* |
| C(22) | 4565 | 11336 | 8384 | 129 (8)* |
| C(23) | 4295 | 8607 | 8981 | 181 (11)* |
| C(24) | 4049 | 11769 | 7920 | 194 (15)* |
| C(25) | 4930 | 9458 | 8724 | 237 (19)* |
| Si | 2724 (2) | 6811 (4) | 5487 (2) | 119 (1)* |
| O(2) | 1708 (3) | 7163 (6) | 6262 (2) | 76 (2)* |
| O(3) | 3549 (4) | 9457 (7) | 7466 (4) | 113 (2)* |
| O(4) | 2819 (3) | 10335 (6) | 8863 (3) | 80 (2)* |
| O(6) | 194 (3) | 9182 (5) | 9168 (3) | 67 (1)* |
| O(8) | -806 (3) | 6331 (4) | 9322 (2) | 51 (1)* |
| O(14a) | 1737 (5) | 3817 (6) | 7884 (3) | 111 (2)* |
| O(14b) | 1536 (3) | 5151 (5) | 9245 (3) | 69 (2)* |

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

slightly large thermal parameters of the Si atom. As a result of the disorder in the position of the Si atom, all groups bonded to it [namely atoms C(16) through C(21)] have large thermal parameters. 349 parameters were refined and $\sum w(|F_o| - |F_c|)^2$ was minimized; $w = 1/(\sigma|F_o|)^2$, $\sigma(F_o) = 0.5kI^{-1/2}\{[\sigma(I)]^2 + (0.02I)^2\}^{1/2}$, $I(\text{intensity}) = (I_{\text{peak}} - I_{\text{background}})/(\text{scan rate})$, and $\sigma(I) = (I_{\text{peak}} + I_{\text{background}})^{1/2}(\text{scan rate})$, k is the correction due to decay and Lp effects, 0.02 is a factor used to downweight intense reflections and to account for instrument instability. Final $R = 0.0564$, $wR = 0.0638$ ($R_{\text{all}} = 0.0972$, $wR_{\text{all}} = 0.0729$) for 1475 reflections having $I \geq 3\sigma(I)$, and goodness-of-fit = 2.13. Maximum $\Delta/\sigma = 0.03$ in the final refinement cycle and the minimum and maximum peaks in the ΔF map were -0.18 and 0.37 e \AA^{-3} , respectively. The linear absorption coefficient was calculated using values from *International Tables for X-ray Crystallography* (1974, Vol. IV, p. 55). Scattering factors for non-H atoms were taken from Cromer & Mann (1968) with anomalous-dispersion corrections from Cromer & Liberman (1970), while those of H atoms were from Stewart, Davidson & Simpson (1965). The positional parameters and the equivalent isotropic thermal parameters of the non-H atoms are

Table 2. Bond lengths (\AA) and angles ($^\circ$)

| | | | |
|---------------------|------------|---------------------|------------|
| C(1)—C(2) | 1.517 (8) | C(1)—C(6) | 1.526 (7) |
| C(1)—C(7) | 1.551 (6) | C(2)—C(3) | 1.521 (10) |
| C(2)—O(2) | 1.393 (7) | C(3)—C(5) | 1.506 (9) |
| C(3)—O(3) | 1.410 (8) | C(5)—C(6) | 1.528 (9) |
| C(5)—O(4) | 1.399 (7) | C(6)—O(6) | 1.414 (6) |
| C(7)—C(8) | 1.550 (8) | C(7)—C(14) | 1.499 (8) |
| C(8)—C(9) | 1.546 (9) | C(8)—C(13) | 1.518 (9) |
| C(8)—O(8) | 1.454 (6) | C(9)—C(10) | 1.558 (10) |
| C(10)—C(11) | 1.512 (11) | C(11)—C(12) | 1.503 (12) |
| C(12)—C(13) | 1.517 (9) | C(14)—O(14a) | 1.186 (8) |
| C(14)—O(14b) | 1.348 (8) | C(15)—O(14b) | 1.454 (8) |
| C(16)—Si | 1.871 (13) | C(17)—Si | 1.854 (11) |
| C(18)—C(19) | 1.515 (16) | C(18)—C(20) | 1.563 (14) |
| C(18)—C(21) | 1.543 (16) | C(18)—Si | 1.795 (11) |
| C(4)—C(22) | 1.384 (1) | C(4)—C(23) | 1.605 (1) |
| C(4)—C(24) | 1.601 (1) | C(4)—C(25) | 1.448 (1) |
| C(4)—O(3) | 1.343 (9) | C(4)—O(4) | 1.426 (8) |
| Si—O(2) | 1.653 (4) | | |
| | | | |
| C(2)—C(1)—C(7) | 113.1 (4) | C(2)—C(1)—C(6) | 102.8 (4) |
| C(1)—C(2)—C(3) | 104.4 (4) | C(6)—C(1)—C(7) | 120.5 (4) |
| C(3)—C(2)—O(2) | 116.1 (5) | C(1)—C(2)—O(2) | 112.3 (4) |
| C(2)—C(3)—O(3) | 114.0 (6) | C(2)—C(3)—C(5) | 106.8 (5) |
| C(3)—C(5)—C(6) | 106.4 (5) | C(5)—C(3)—O(3) | 105.4 (5) |
| C(6)—C(5)—O(4) | 114.8 (5) | C(3)—C(5)—O(4) | 106.5 (5) |
| C(1)—C(6)—O(6) | 116.3 (4) | C(1)—C(6)—C(5) | 104.4 (4) |
| C(5)—C(6)—O(6) | 110.3 (5) | C(1)—C(7)—C(8) | 110.9 (5) |
| C(1)—C(7)—C(8) | 117.2 (5) | C(7)—C(8)—C(9) | 108.3 (5) |
| C(8)—C(7)—C(14) | 115.0 (5) | C(9)—C(8)—C(13) | 112.1 (5) |
| C(7)—C(8)—C(13) | 111.3 (5) | C(9)—C(8)—O(8) | 109.6 (4) |
| C(7)—C(8)—O(8) | 110.0 (4) | C(8)—C(9)—C(10) | 111.5 (6) |
| C(13)—C(8)—O(8) | 105.6 (5) | C(10)—C(11)—C(12) | 109.9 (6) |
| C(9)—C(10)—C(11) | 112.5 (6) | C(8)—C(13)—C(12) | 112.6 (6) |
| C(11)—C(12)—C(13) | 113.3 (6) | C(7)—C(14)—O(14b) | 111.6 (5) |
| C(7)—C(14)—O(14a) | 125.0 (6) | O(14a)—C(14)—O(14b) | 123.4 (6) |
| O(14a)—C(14)—O(14b) | 123.4 (6) | C(19)—C(18)—C(20) | 108.4 (8) |
| C(19)—C(18)—C(21) | 111.5 (10) | C(20)—C(18)—C(21) | 106.8 (9) |
| C(19)—C(18)—Si | 110.7 (9) | C(20)—C(18)—Si | 110.5 (8) |
| C(21)—C(18)—Si | 109.0 (7) | C(22)—C(4)—C(23) | 113.4 (1) |
| C(24)—C(4)—C(25) | 108.1 (1) | C(22)—C(4)—O(3) | 118.0 (4) |
| C(23)—C(4)—O(3) | 105.8 (4) | C(24)—C(4)—O(3) | 93.2 (4) |
| C(25)—C(4)—O(3) | 112.3 (4) | C(22)—C(4)—O(4) | 110.8 (4) |
| C(23)—C(4)—O(4) | 96.0 (4) | C(24)—C(4)—O(4) | 100.1 (4) |
| C(25)—C(4)—O(4) | 126.3 (3) | O(3)—C(4)—O(4) | 110.6 (5) |
| C(16)—Si—C(17) | 109.3 (6) | C(16)—Si—C(18) | 110.7 (5) |
| C(17)—Si—C(18) | 112.2 (6) | C(16)—Si—O(2) | 108.7 (4) |
| C(17)—Si—O(2) | 110.8 (3) | C(18)—Si—O(2) | 105.1 (4) |
| C(2)—O(2)—Si | 125.5 (3) | C(3)—O(3)—C(4) | 110.1 (5) |
| C(5)—O(4)—C(4) | 107.5 (5) | C(14)—O(14b)—C(15) | 115.9 (5) |

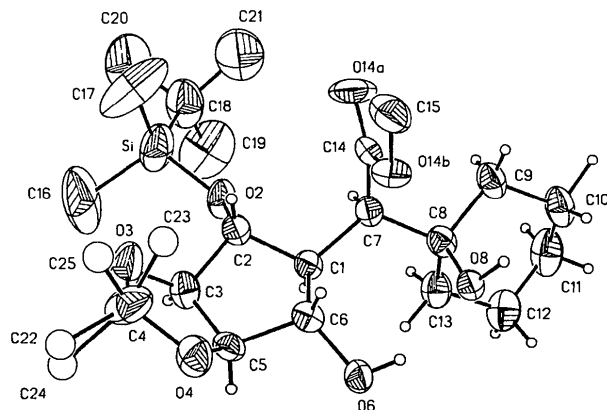


Fig. 1. Molecular structure of (I), with 50% probability ellipsoids, showing the atom-numbering scheme [the disordered methyl groups on C(4) are shown as solid circles].

listed in Table 1,* bond lengths and angles are in Table 2. The thermal ellipsoids drawing (*SHELXTL*; Sheldrick, 1986) of the molecule with the atom-labelling scheme is given in Fig. 1.

Related literature. Similar densely oxygenated cyclopentane rings have been prepared by treatment of an acyclic carbohydrate template with SmI₂ (Enholm & Trivellas, 1989). These highly functionalized rings have also been applied to natural products synthesis (Enholm, Satici & Trivellas, 1989).

* Tables of the crystallographic data, anisotropic thermal parameters, H-atom positional parameters and bond lengths and angles, and the structure-factor amplitudes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54543 (23 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: ST0530]

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Structures of a Pair of Diastereomeric Salts of Ephedrine and Bromo-Substituted Cyclic Phosphoric Acid

BY HILBERT J. BRUINS SLOT* AND FRANK J. J. LEUSEN

CAOS/CAMM Center, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

A. D. VAN DER HAEST

Organic Chemistry Department, University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands

AND JAN M. M. SMITS

Crystallography Laboratory, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands

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Abstract. (1) (*R*)-(+)-4-*ortho*-Bromophenyl-2-hydroxy-5,5-dimethyl-1,3,2-dioxaphosphorinane 2-oxide (1*R*,2*S*)-(–)- α -[(1-methylamino)ethyl]benzyl alcohol, (–)C₁₀H₁₆NO⁺·(+)-C₁₁H₁₃BrO₄P[–], *M_r* = 486.341, monoclinic, *P*2₁, *a* = 13.3540 (3), *b* = 8.1671 (2), *c* = 10.4791 (3) Å, β = 91.331 (7)°, *V* = 1142.58 (5) Å³, *Z* = 2, *D_x* = 1.414 Mg m^{–3}, Cu *K* α radiation (graphite monochromator), λ = 1.54184 Å, μ (Cu *K* α) = 33.910 cm^{–1}, *F*(000) = 504, *T* = 293 K, final *R* = 0.045, *wR* = 0.054, for 4155 observed unique reflections and 237 variables. (2) (*S*)-(–)-4-*ortho*-Bromophenyl-2-hydroxy-5,5-dimethyl-1,3,2-

dioxaphosphorinane 2-oxide (1*R*,2*S*)-(–)- α -[(1-methylamino)ethyl]benzyl alcohol dihydrate, (–)-C₁₀H₁₆NO⁺·(–)C₁₁H₁₃BrO₄P[–]·2H₂O, *M_r* = 522.372, monoclinic, *C*2, *a* = 20.9469 (9), *b* = 7.7456 (3), *c* = 15.7571 (5) Å, β = 102.013 (5)°, *V* = 2500.5 (2) Å³, *Z* = 4, *D_x* = 1.388 Mg m^{–3}, Cu *K* α radiation (graphite monochromator), λ = 1.54184 Å, μ (Cu *K* α) = 31.931 cm^{–1}, *F*(000) = 1088, *T* = 293 K, final *R* = 0.052, *wR* = 0.063, for 4253 observed unique reflections and 276 variables. For both (1) and (2), the phosphorinane ring is in the usual chair conformation and ephedrine is in the usual extended form. The crystal packing of (1) can be regarded as a chain parallel to the *b* axis of phosphorinane cations

* Author for correspondence.