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(1*R,3*S**,4*R**)-4-*tert*-Butyldiphenylsilyloxy-6,7-dimethoxy-1-methyl-3-phenyl-1,2,3,4-tetrahydroisoquinoline**

MIREN KARMELE URTIAGA AND MARÍA ISABEL ARRIORTUA

Departamento de Mineralogía-Petrología, Universidad del País Vasco, Apartado 644, 48080 Bilbao, Spain

IMANOL TELLITU, DOLORES BADÍA AND ESTHER DOMÍNGUEZ

Departamento de Química Orgánica, Universidad del País Vasco, Apartado 644, 48080 Bilbao, Spain

LUIS OCHANDO AND JOSÉ MARÍA AMIGÓ

Departamento de Geología, Universidad de Valencia, Avda Dr Moliner 50, 46110 Burjassot, Valencia, Spain

TONY DEBAERDEMAEKER

Sektion für Röntgen- und Elektronenbeugung, Universität Ulm, 89081-Ulm, Germany

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Abstract

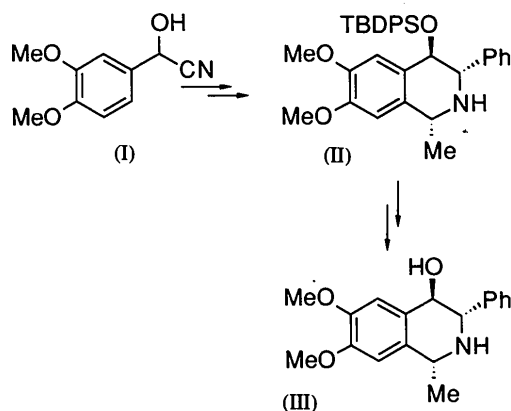
The crystal structure of the title compound, C₃₄H₃₉NO₃·Si, shows that the heterocyclic fragment of the molecule exhibits a half-chair conformation. The structural data also confirm the earlier configurational assignments and show that the solid-state conformation has the methyl and phenyl substituents in pseudoequatorial and equatorial positions, respectively, and that the group linked to C2 is in a *trans* configuration with respect to the phenyl substituent.

Comment

The potent pharmacological activity of simple 4-substituted tetrahydroisoquinolines has generated much interest in their synthesis and recently several new naturally occurring compounds of this type have been isolated (Ohta, Tachikawa, Makino, Tasaki & Hirobe, 1990). These facts, together with our continuous interest in this type of heterocyclic derivative, the isoquinolines, prompted us to undertake a novel synthesis of 4-hydroxy-1,2,3,4-tetrahydroisoquinoline (III), starting from the previously prepared cyanohydrin (I), which was achieved in good overall yield with high diastereomeric control (Badía, Domínguez & Tellitu, 1992).

(II) was purified by crystallization from MeOH and was shown by NMR to be a tetrahydrogenated isoquinolinic system containing methyl, phenyl and *tert*-

butyldiphenylsilyloxy substituents bonded to the three asymmetric C atoms, and two methoxy groups linked to the aromatic ring.



Although information obtained from spectroscopic data, supported by measurements of difference nuclear Overhauser effect (NOE) experiments (Kinns & Sanders, 1984), indicated the relative stereochemistry of the three chiral centres for both derivatives, (II) and (III), X-ray analysis performed on isoquinoline (II) supplied full and unambiguous information about the structure of the title compound, thus providing a substantial contribution to the study of structure–activity relationships.

A SCHAKAL88 diagram (Keller, 1988) of the molecule with atom-numbering scheme is shown in Fig. 1, and a view of the unit-cell packing in Fig. 2.

With the exception of C11 and N10, which deviate by 0.441 (5) and –0.335 (5) Å, respectively, the heterocyclic system is almost planar. These data, along with the torsion angle C2–C3–C8–C9, 1.4 (7)°, are in agreement with the sofa conformation reported for other tetrahydroisoquinoline derivatives (Plywaczyk, Tykarska, Jaskólski & Kosturkiewicz, 1984). In addition, both

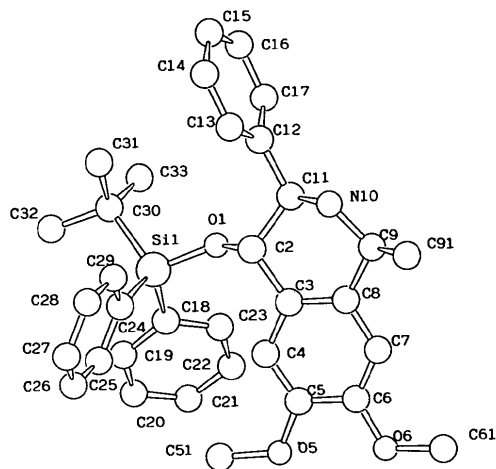


Fig. 1. View of title compound showing the labelling of atoms.

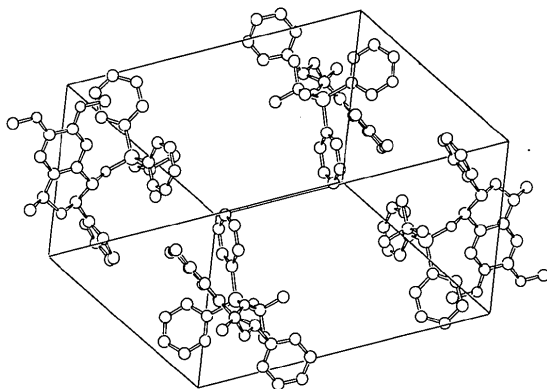


Fig. 2. Crystal packing of the title compound.

methoxy groups are coplanar with the aromatic ring described by the C3—C4—C5—C6—C7—C8 plane [C61 deviation: $-0.003(6)$ and C51 deviation: $-0.122(6)$ Å], as expected for this kind of substitution (Arrieta, Badía, Domínguez, Lete, Igartua, Germain, Vlasi & Debaerdemaeker, 1988).

On the other hand, the isoquinoline under study shows a *trans* configuration for the TBDPSO group bonded to C2 and the phenyl group bonded to C11 [torsion angle O1—C2—C11—C12, $63.3(5)^\circ$] and, as corroborated by NOE experiments, H2 and H11 have an antiperiplanar conformation [torsion angle H2—C2—C11—H11, $-177(2)^\circ$]. Therefore, the X-ray analysis confirms a pseudoequatorial and an equatorial conformation for the siloxy and phenyl groups, respectively, the latter group being in an orthogonal position with respect to the homoaromatic ring in the isoquinoline system [angle between planes $82.9(1)^\circ$]. In addition, the torsion angles for C11—N10—C9—C91, $-175.3(4)^\circ$, and C11—N10—C9—H9, $64(2)^\circ$, indicate a pseudoequatorial conformation for the methyl group at C9.

The remaining angles and bond distances are in agreement with the values reported for other compounds with a similar skeleton (Arrieta, Badía, Domínguez, Lete, Igartua, Germain, Vlasi & Debaerdemaeker, 1988; Arrieta, Badía, Domínguez, Lete, Martínez de Marigorta, Germain, Vlasi & Debaerdemaeker, 1988). Finally, both Si and N atoms show a typical sp^3 character as deduced from the sum of the valence angles around them (437 and 342° , respectively).

Experimental

Crystal data

$C_{34}H_{39}NO_3Si$
 $M_r = 537.773$
 Monoclinic
 $P2_1/n$
 $a = 13.747(9)$ Å
 $b = 21.08(4)$ Å
 $c = 10.30(1)$ Å
 $\beta = 98.97(6)^\circ$

Mo $K\alpha$ radiation
 $\lambda = 0.71073$ Å
 Cell parameters from 25 reflections
 $\theta = 1-25^\circ$
 $\mu = 0.109$ mm $^{-1}$
 $T = 295$ K
 Prismatic

$V = 2949(7)$ Å 3
 $Z = 4$
 $D_x = 1.21$ Mg m $^{-3}$

$0.10 \times 0.07 \times 0.05$ mm
 Colourless

Data collection

Philips PW1100 diffractometer
 $\omega/2\theta$ scans
 Absorption correction: none
 3904 measured reflections
 3759 independent reflections
 3125 observed reflections
 $[I > 3\sigma(I)]$

$R_{int} = 0.017$
 $\theta_{max} = 25^\circ$
 $h = -14 \rightarrow 14$
 $k = 0 \rightarrow 20$
 $l = 0 \rightarrow 10$
 3 standard reflections
 frequency: 60 min
 intensity decay: $<1.0\%$

Refinement

Refinement on F
 $R = 0.071$
 $wR = 0.094$
 $S = 1.115$
 3125 reflections
 509 parameters
 H atoms refined isotropically
 $w = 1/[\sigma^2(F) + 0.014141F^2]$

$(\Delta/\sigma)_{max} = 0.15$
 $\Delta\rho_{max} = 0.28$ e Å $^{-3}$
 $\Delta\rho_{min} = -0.50$ e Å $^{-3}$
 Extinction correction: none
 Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (Å 2)

$$B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^*a_i\cdot a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq}
Si1	0.3785 (1)	0.3159 (1)	0.9110 (1)	2.90 (3)
C3	0.5957 (2)	0.3795 (2)	1.1067 (3)	2.39 (9)
O1	0.4249 (2)	0.3749 (1)	1.0019 (2)	2.80 (6)
O6	0.8831 (2)	0.3769 (1)	1.0347 (3)	4.23 (8)
N10	0.5363 (2)	0.4502 (2)	1.2998 (3)	3.41 (9)
C5	0.7235 (3)	0.3365 (2)	0.9985 (3)	2.77 (10)
C18	0.4344 (3)	0.3213 (2)	0.7600 (4)	3.28 (10)
C20	0.4662 (3)	0.2790 (2)	0.5526 (4)	4.64 (13)
C17	0.3006 (3)	0.4961 (2)	1.1595 (4)	4.09 (13)
C2	0.4880 (2)	0.3805 (2)	1.1228 (3)	2.47 (10)
C23	0.4945 (3)	0.3724 (2)	0.7384 (4)	3.57 (10)
C12	0.3634 (2)	0.4487 (2)	1.2157 (3)	2.74 (10)
C4	0.6278 (2)	0.3366 (2)	1.0198 (3)	2.63 (10)
C9	0.6338 (3)	0.4649 (2)	1.2754 (4)	3.69 (11)
O5	0.7599 (2)	0.2973 (1)	0.9135 (3)	4.21 (8)
C8	0.6625 (3)	0.4204 (2)	1.1791 (3)	2.81 (9)
C6	0.7902 (2)	0.3789 (2)	1.0660 (3)	3.06 (10)
C91	0.7031 (3)	0.4653 (3)	1.4020 (4)	6.49 (18)
C30	0.2414 (3)	0.3275 (2)	0.8699 (4)	3.47 (11)
C13	0.3327 (3)	0.4105 (2)	1.3079 (4)	3.67 (11)
C19	0.4207 (3)	0.2752 (2)	0.6609 (4)	3.74 (10)
C51	0.6947 (3)	0.2509 (2)	0.8509 (5)	5.55 (15)
C7	0.7599 (3)	0.4188 (2)	1.1540 (4)	3.36 (10)
C11	0.4657 (2)	0.4437 (2)	1.1834 (3)	2.88 (10)
C22	0.5412 (3)	0.3763 (2)	0.6319 (4)	4.55 (13)
C21	0.5260 (3)	0.3301 (2)	0.5382 (4)	4.60 (13)
C61	0.9544 (3)	0.4162 (3)	1.1079 (5)	6.16 (17)
C24	0.4099 (3)	0.2385 (2)	0.9966 (3)	3.33 (10)
C14	0.2412 (3)	0.4186 (2)	1.3445 (4)	4.35 (12)
C15	0.1790 (3)	0.4657 (2)	1.2867 (4)	4.61 (13)
C25	0.4536 (3)	0.1890 (2)	0.9392 (4)	4.55 (13)
C26	0.4745 (4)	0.1317 (2)	1.0070 (5)	5.98 (17)
C27	0.4481 (4)	0.1220 (2)	1.1255 (5)	5.46 (17)
C28	0.4040 (4)	0.1708 (2)	1.1822 (5)	5.23 (14)
C16	0.2093 (3)	0.5040 (3)	1.1967 (5)	5.06 (14)
C29	0.3854 (3)	0.2275 (2)	1.1189 (5)	4.70 (13)
C31	0.1921 (4)	0.3248 (4)	0.9937 (6)	6.08 (19)
C32	0.1948 (4)	0.2752 (3)	0.7800 (7)	5.85 (19)
C33	0.2207 (4)	0.3919 (3)	0.8071 (6)	5.84 (15)

Table 2. Selected geometric parameters (Å, °)

Si1—O1	1.626 (3)	C23—C22	1.357 (6)
Si1—C18	1.843 (5)	C12—C13	1.362 (6)
Si1—C30	1.882 (4)	C12—C11	1.498 (4)
Si1—C24	1.873 (5)	C9—C8	1.464 (6)
C3—C2	1.515 (4)	C9—C91	1.490 (6)
C3—C4	1.392 (5)	O5—C51	1.413 (5)
C3—C8	1.389 (5)	C8—C7	1.403 (6)
O1—C2	1.408 (4)	C6—C7	1.349 (6)
O6—C6	1.366 (4)	C30—C31	1.536 (8)
O6—C61	1.409 (6)	C30—C32	1.516 (8)
N10—C9	1.436 (5)	C30—C33	1.512 (8)
N10—C11	1.427 (4)	C13—C14	1.379 (6)
C5—C4	1.367 (5)	C22—C21	1.364 (6)
C5—O5	1.355 (5)	C24—C25	1.382 (6)
C5—C6	1.387 (5)	C24—C29	1.374 (6)
C18—C23	1.396 (6)	C14—C15	1.383 (6)
C18—C19	1.401 (6)	C15—C16	1.344 (7)
C20—C19	1.364 (6)	C25—C26	1.402 (6)
C20—C21	1.377 (6)	C26—C27	1.342 (8)
C17—C12	1.387 (6)	C27—C28	1.370 (7)
C17—C16	1.378 (6)	C28—C29	1.366 (6)
C2—C11	1.523 (6)		
C30—Si1—C24	111.6 (3)	C5—O5—C51	116.4 (4)
C18—Si1—C24	110.8 (3)	C3—C8—C9	122.4 (4)
C18—Si1—C30	109.7 (3)	C9—C8—C7	120.4 (4)
O1—Si1—C24	110.7 (2)	C3—C8—C7	117.1 (4)
O1—Si1—C30	108.6 (3)	O6—C6—C5	115.5 (4)
O1—Si1—C18	105.1 (3)	C5—C6—C7	119.3 (4)
C4—C3—C8	120.0 (4)	O6—C6—C7	125.2 (4)
C2—C3—C8	120.5 (4)	Si1—C30—C33	109.2 (4)
C2—C3—C4	119.5 (4)	Si1—C30—C32	110.8 (4)
Si1—O1—C2	134.9 (4)	Si1—C30—C31	111.4 (4)
C6—O6—C61	117.0 (4)	C32—C30—C33	111.0 (5)
C9—N10—C11	113.9 (4)	C31—C30—C33	108.1 (5)
O5—C5—C6	115.8 (4)	C31—C30—C32	106.3 (5)
C4—C5—C6	119.7 (4)	C12—C13—C14	120.8 (5)
C4—C5—O5	124.5 (4)	C18—C19—C20	121.9 (5)
Si1—C18—C19	123.1 (4)	C8—C7—C6	122.8 (4)
Si1—C18—C23	121.1 (4)	C2—C11—C12	114.1 (4)
C23—C18—C19	115.8 (4)	N10—C11—C12	110.2 (3)
C19—C20—C21	119.4 (5)	N10—C11—C2	105.9 (4)
C12—C17—C16	120.4 (5)	C23—C22—C21	119.3 (5)
C3—C2—O1	112.3 (3)	C20—C21—C22	120.7 (5)
O1—C2—C11	107.5 (3)	Si1—C24—C29	120.5 (4)
C3—C2—C11	108.6 (4)	Si1—C24—C25	122.7 (3)
C18—C23—C22	122.8 (5)	C25—C24—C29	116.8 (5)
C17—C12—C11	120.2 (4)	C24—C25—C26	120.4 (4)
C17—C12—C13	118.5 (4)	C25—C26—C27	121.4 (5)
C13—C12—C11	121.1 (4)	C26—C27—C28	118.3 (5)
C3—C4—C5	120.9 (4)	C27—C28—C29	121.0 (5)
N10—C9—C91	109.6 (4)	C17—C16—C15	120.9 (5)
N10—C9—C8	109.8 (4)	C24—C29—C28	122.1 (5)
C8—C9—C91	113.2 (4)	C13—C14—C15	120.0 (5)
C14—C15—C16	119.4 (5)		

Due to the poor quality of the crystal the data could be measured up to an angle $\theta = 25^\circ$. This explains the poor relative number of parameters, number of reflections, the resulting high *R* value, and the large standard deviations.

Structure solution: *MULTAN87* (Debaerdemaeker, Germain, Main, Tate & Woolfson, 1987). Structure refinement: *SHELX76* (Sheldrick, 1976). Molecular graphics: *SCHAKAL88* (Keller, 1988). Preparation of material for publication: *PARST* (Nardelli, 1983).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and bond distances and angles involving H atoms have been deposited with the IUCr (Reference: NA1106). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Five Salts of Berberine

BENSON M. KARIUKI

*Department of Chemistry, University of Liverpool,
PO Box 147, Liverpool L69 3BX, England*

WILLIAM JONES

*Department of Chemistry, University of Cambridge,
Lensfield Road, Cambridge CB2 1EW, England*

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Abstract

Structures of berberine chloride tetrahydrate, C₂₀H₁₈-NO₄⁺.Cl⁻.4H₂O (I), berberine chloride ethanol solvate hemihydrate, C₂₀H₁₈NO₄⁺.Cl⁻.C₂H₅OH.0.5H₂O (II), berberine bromide dihydrate, C₂₀H₁₈NO₄⁺.Br⁻.2H₂O (III), berberine iodide, C₂₀H₁₈NO₄⁺.I⁻ (IV) and bis(berberine) sulfate heptahydrate, 2C₂₀H₁₈NO₄⁺.SO₄²⁻.7H₂O (V) are reported. In all the salts, the cations pack in antiparallel pairs.