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(3*R**,4*S**)-4-[(*S**)-2-Cyclohexyl-2-(*tert*-butyldimethylsiloxy)ethyl]-3-hexyl-3-(trimethylsilyl)oxetan-2-one

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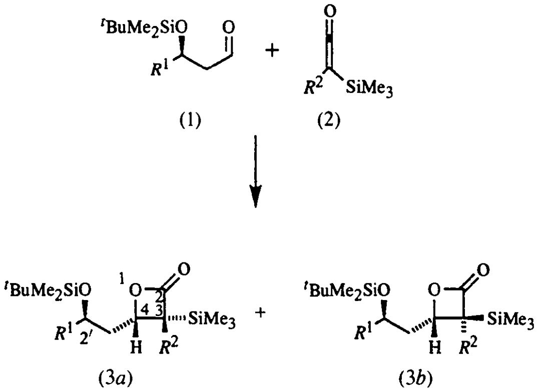
Abstract

The relative stereochemistry of the substituents of the oxetanone ring in the title compound, $C_{26}H_{52}O_3Si_2$, prepared by the highly diastereoselective [2+2] cycloaddition of a silylketene and a 3-alkoxy-substituted aldehyde, has been established.

Comment

In 1965, Shchukovskaya and co-workers (Shchukovskaya, Pal'chik & Lazarev, 1965) first prepared the remarkably stable (trimethylsilyl)ketene [(2), R^2 = H] and Zaitseva, Vinokurova & Baukov (1975) later showed that it undergoes [2+2] cycloaddition to benzaldehyde in the presence of boron trifluoride etherate to give 3-(trimethylsilyl)oxetanones (Pommier & Pons, 1993).



During a synthesis of the pancreatic lipase inhibitor tetrahydrolipstatin, Pommier, Pons, Kocienski & Wong (1994) found high 1,3-asymmetric induction in the analogous cycloaddition of *n*-hexyl(trimethylsilyl)ketene [(2), R^2 = C_6H_{13}] to the (*R*)-3-[(*tert*-butyldimethylsilyl)oxy]tetradecanal [(1), R^1 = $C_{11}H_{23}$]. Four diastereoisomers were generated in the ratio 80:10:8:2, in which the two major isomers having *S* stereochemistry at C-4 were assigned the structures (3*a*) (80%) and (3*b*) (10%). The relative stereochemistry at C-4 was determined from NMR experiments and chemical correlation, but the stereochemistry at C-3 could only be inferred from a sequence of subsequent transformations.

We now report that the [2+2] cycloaddition of the silylketene (2) (R^2 = C_6H_{13}) to the racemic aldehyde (1) (R^1 = C_6H_{11}), catalyzed by ethylaluminium dichloride, is also highly efficient and diastereoselective leading to only two diastereoisomers, *rac*-(3*a*) and *rac*-(3*b*) (9:1), according to high-field ^{1}H NMR analysis of the crude reaction mixture. The major isomer, *rac*-(3*a*), is crystalline (m.p. 359–361 K) and its relative stereochemistry was determined by X-ray crystallography. The structure (Fig. 1) was refined with anisotropic non-H atoms [isotropic for C(14)–C(19)] and shows the expected planar four-membered ring. As noted with related ring systems, the C—O bond adjacent to the C=O bond [1.381 (8) Å] is shorter than the other ring C—O distance [1.495 (7) Å]. The structure of (3*a*) confirms the sense of 1,3-asymmetric induction in the Lewis acid-catalyzed [2+2] cycloaddition of alkylsilylketenes to 3-alkoxy-substituted aldehydes (Pommier, Pons & Kocienski, 1995; Zemribo & Romo, 1995) and establishes for the first time the relative stereochemistry at C-3 of the oxetanone ring. In addition, we have shown that *n*-hexyl(trimethylsilyl)ketene [(2), $R^2 = C_6H_{13}$], like the parent (trimethylsilyl)ketene [(2), R^2 = H], exhibits a strong bias in favour of a *cis* orientation between the trimethylsilyl group and the aldehyde substituent in the oxetanone products. With the stereochemical ambiguity at C-3 now removed, further efforts are underway to establish the mechanism of the [2+2] cycloaddition.

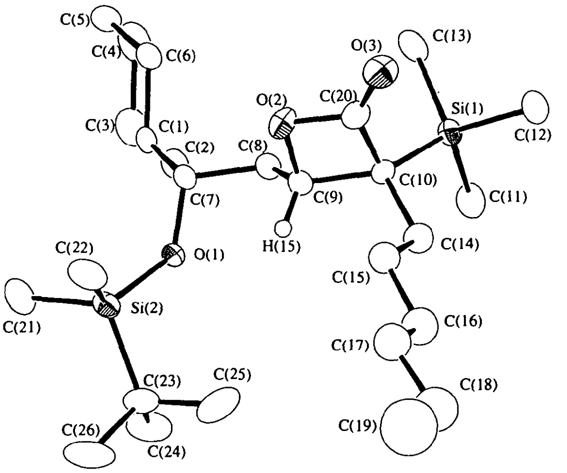


Fig. 1. The molecular structure of $C_{26}H_{52}O_3Si_2$ showing the atom-labelling scheme, with displacement ellipsoids drawn at the 40% probability level. H atoms, except for H(15), are excluded for clarity.

Experimental

A solution of racemic 3-[(*tert*-butyldimethylsilyl)oxy]-3-cyclohexylpropanal [*rac*-(1), $R^1 = C_6H_{11}$, 0.270 g, 1.0 mmol] in dry diethyl ether (20 ml) was cooled to 223 K under nitrogen. Ethylaluminium dichloride (1.3 ml of a 1 *M* solution in toluene) was added dropwise keeping the temperature below 233 K. The mixture was stirred for 5 min before adding *n*-hexyl(trimethylsilyl)ketene [(2), $R^2 = C_6H_{13}$, 0.257 g, 1.3 mmol] in diethyl ether (2 ml). The reaction mixture was allowed to warm gradually to 248 K over 1 h, whereupon the cooling bath was removed and water (10 ml) added with rapid stirring. The organic layer was separated, washed with water (2 × 10 ml) and dried over $MgSO_4$. After removing the solvents *in vacuo*, the residue was purified by column chromatography [silica gel, diethyl ether–hexanes eluent (1:99 *v*/*v*)] to give a mixture of *rac*-(3*a*) and *rac*-(3*b*) (0.380 g, 0.81 mmol, 81%) as a colourless oil. The major diastereoisomer, *rac*-(3*a*), crystallized from ethanol to give a solid (m.p. 359–361 K); IR (film): 1805 cm^{-1} (C=O); ^{1}H NMR (270 MHz, $CDCl_3$): δ 4.62 (1H, *dd*, J = 11.6, 1.9 Hz), 3.73–3.66 (1H, *m*), 1.95–1.05 (23H, *m*), 0.91 (9H, *s*), 0.89 (3H, distorted *t*, J = 6.8 Hz), 0.22 (*s*, 9H), 0.08 and 0.07 (3H each, *s*). Analysis found: C 66.44, H 11.15%; $C_{26}H_{52}O_3Si_2$ requires C 66.60, H 11.18%.

Crystal data

$C_{26}H_{52}O_3Si_2$
M_r = 468.87
Orthorhombic
Pbca
a = 23.953 (3) Å
b = 22.097 (3) Å
c = 11.477 (4) Å
V = 6075 (2) Å^3
Z = 8
D_x = 1.025 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 20 reflections
θ = 19.0–20.7°
μ = 0.138 mm^{-1}
T = 150 K
Needle
0.80 × 0.25 × 0.10 mm
Colourless

Data collection

Rigaku AFC-7*S* diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North, Phillips & Mathews, 1968)
$T_{\min}$ = 0.910, $T_{\max}$ = 1.000
5941 measured reflections
5941 independent reflections

2020 observed reflections [$I > 3\sigma(I)$]
$\theta_{\max}$ = 25°
$h = 0 \rightarrow 28$
$k = 0 \rightarrow 26$
$l = -13 \rightarrow 0$
3 standard reflections monitored every 150 reflections
intensity decay: 0.99%

Refinement

Refinement on F
R = 0.0591
wR = 0.0510
S = 2.301
2020 reflections
250 parameters
H-atom parameters not refined
$w = 1/\sigma^2(F)$

$(\Delta/\sigma)_{\max}$ = 0.0325
$\Delta\rho_{\max}$ = 0.56 e Å^{-3}
$\Delta\rho_{\min}$ = −0.34 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)*

$U_{\rm iso}$ for C(14) to C(19); $U_{\rm eq} = (1/3)\Sigma_i\Sigma_jU_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$ for all others.

	x	y	z	$U_{\rm iso}/U_{\rm eq}$
Si(1)	0.31544 (8)	0.04592 (8)	0.7783 (2)	0.0293 (5)
Si(2)	0.56087 (8)	−0.12219 (8)	0.7294 (2)	0.0328 (6)
O(1)	0.5217 (2)	−0.0653 (2)	0.7721 (4)	0.030 (1)
O(2)	0.4083 (2)	−0.0060 (2)	0.5526 (4)	0.036 (2)
O(3)	0.3220 (2)	0.0184 (2)	0.4813 (4)	0.047 (2)
C(1)	0.5543 (2)	0.0390 (3)	0.7530 (6)	0.030 (2)
C(2)	0.5532 (3)	0.0528 (3)	0.8826 (6)	0.039 (2)
C(3)	0.5985 (3)	0.0983 (3)	0.9156 (6)	0.048 (3)
C(4)	0.5932 (3)	0.1561 (4)	0.8427 (8)	0.059 (3)
C(5)	0.5949 (3)	0.1420 (3)	0.7144 (8)	0.047 (3)
C(6)	0.5495 (3)	0.0968 (3)	0.6823 (6)	0.036 (2)
C(7)	0.5115 (3)	−0.0082 (3)	0.7163 (6)	0.028 (2)
C(8)	0.4512 (3)	0.0087 (3)	0.7456 (6)	0.032 (2)
C(9)	0.4100 (3)	−0.0278 (3)	0.6759 (6)	0.031 (2)
C(10)	0.3460 (3)	−0.0173 (3)	0.6846 (6)	0.028 (2)
C(11)	0.3196 (3)	0.0249 (3)	0.9343 (6)	0.048 (3)
C(12)	0.2411 (3)	0.0541 (3)	0.7343 (6)	0.042 (2)
C(13)	0.3510 (3)	0.1198 (3)	0.7520 (7)	0.047 (2)
C(14)	0.3122 (3)	−0.0764 (3)	0.7007 (6)	0.039 (2)
C(15)	0.3184 (3)	−0.1224 (3)	0.6026 (6)	0.043 (2)
C(16)	0.2855 (3)	−0.1808 (3)	0.6255 (7)	0.059 (2)
C(17)	0.2864 (3)	−0.2240 (3)	0.5245 (7)	0.060 (2)
C(18)	0.2485 (4)	−0.2803 (4)	0.5527 (8)	0.089 (3)
C(19)	0.2499 (5)	−0.3231 (5)	0.4603 (10)	0.143 (5)
C(20)	0.3510 (3)	0.0008 (3)	0.5576 (6)	0.033 (2)
C(21)	0.6362 (3)	−0.1052 (3)	0.7547 (7)	0.054 (3)
C(22)	0.5496 (3)	−0.1388 (3)	0.5732 (6)	0.051 (3)

C(23)	0.5387 (3)	−0.1857 (3)	0.8237 (6)	0.044 (3)
C(24)	0.5538 (4)	−0.1733 (3)	0.9520 (7)	0.069 (3)
C(25)	0.4744 (4)	−0.1944 (4)	0.8144 (8)	0.086 (4)
C(26)	0.5668 (4)	−0.2455 (3)	0.7870 (7)	0.075 (3)

Table 2. *Selected geometric parameters (Å, °)*

Si(1)—C(10)	1.909 (7)	O(1)—C(7)	1.437 (7)
Si(1)—C(11)	1.852 (7)	O(2)—C(9)	1.495 (7)
Si(1)—C(12)	1.859 (7)	O(2)—C(20)	1.381 (8)
Si(1)—C(13)	1.867 (7)	O(3)—C(20)	1.184 (8)
Si(2)—O(1)	1.643 (4)	C(8)—C(9)	1.505 (9)
Si(2)—C(21)	1.866 (7)	C(9)—C(10)	1.554 (8)
Si(2)—C(22)	1.850 (7)	C(10)—C(14)	1.549 (8)
Si(2)—C(23)	1.850 (7)	C(10)—C(20)	1.517 (9)
Si(2)—O(1)—C(7)	129.6 (4)	Si(1)—C(10)—C(20)	112.3 (5)
C(9)—O(2)—C(20)	91.4 (5)	C(9)—C(10)—C(14)	113.4 (5)
O(2)—C(9)—C(8)	110.4 (5)	C(9)—C(10)—C(20)	84.3 (5)
O(2)—C(9)—C(10)	89.1 (5)	C(14)—C(10)—C(20)	112.2 (6)
C(8)—C(9)—C(10)	122.1 (5)	O(2)—C(20)—O(3)	126.1 (7)
Si(1)—C(10)—C(9)	121.7 (4)	O(2)—C(20)—C(10)	95.1 (6)
Si(1)—C(10)—C(14)	110.4 (4)	O(3)—C(20)—C(10)	138.7 (8)

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1995). Program(s) used to solve structure: direct methods using *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1256). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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1,3-Diphenyl-4-imidazoline-2-thione

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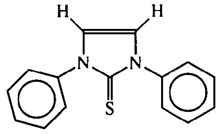
Abstract

In the title compound, 1,3-diphenyl-1,3-dihydro-2*H*-imidazole-2-thione, $C_{15}H_{12}N_2S$, the two phenyl rings are inclined at an angle of 71.9 (1)° with respect to one another.

Comment

The compounds methimazole (1-methyl-4-imidazoline-2-thione) and carbimazole (1-methyl-3-ethylcarboxylate-4-imidazoline-2-thione) are well known for their use in the treatment of hyperthyroidism (Reynolds, 1993). They block the production of thyroid hormones by inhibiting the enzyme thyroid peroxidase. In doing so, they become oxidized and these oxidized species are thought to be responsible for adverse effects observed in patients (Karkhanis & Field, 1985). 1,3-Diphenyl-4-imidazoline-2-thione, (I), is one of a series of compounds synthesized for the purpose of investigating the oxidation of thioimidazoles (Sohal, 1996).



(I)

In the molecule, the two phenyl rings are inclined at angles of 52.0 (1) and 61.6 (1)° with respect to the central ring, and at an angle of 71.9 (1)° with respect to one another. This conformation is also shown by the torsion angles about N1—C4 and N2—C10 (Table 2). The C2═C3 [1.332 (4) Å] and C1═S [1.671 (3) Å] double bonds are both normal. A search using *QUEST* (Allen & Kennard, 1993) on structures with *R* values less than 10% shows average S═C bond lengths of 1.67 (5) Å for over 5079 hits and 1.71 (3) Å for the 98 hits containing similar imidazole rings with exocyclic S═C bonds. In-plane bending is present at the C1 position, where the endocyclic valence angle is 103.8 (2)° and the two exocyclic angles are 127.5 (2)

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