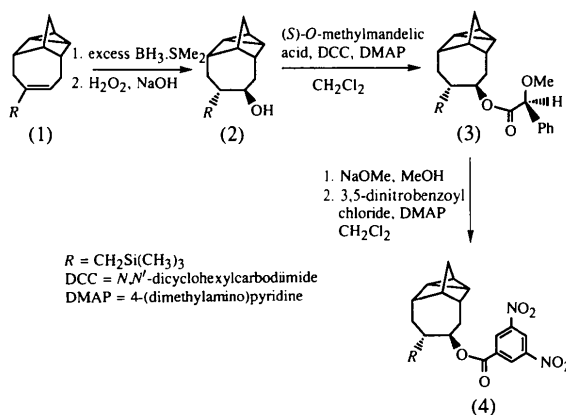Garcia, J. G. & McLaughlin, M. L. (1991). *Tetrahedron Lett.* **32**, 3292–3296.

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preparation and NMR analysis of Mosher's esters (Dale, Dull & Mosher, 1969; Dale & Mosher, 1973) and mandelic esters (Dale & Mosher, 1968; Bonner, 1951), for racemic and enantiomerically enriched materials. We have already established the absolute stereochemistry of 5-phenyldeltacylene by the X-ray structural analysis of its Mosher's ester derivative (Lautens, Lautens & Lough, 1991). In this case we were unable to grow suitable single crystals of the Mosher's ester derivative (3). We therefore carried out the determination of the structure of the corresponding 3,5-dinitrobenzoate (4) and used the X-ray data to confirm the absolute stereochemistry.

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4-[(Trimethylsilyl)methyl]tetracyclo-[5.4.0.0^{6,10}.0^{9,11}]undec-3-yl 3,5-Dinitro-benzoate

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Abstract

The absolute stereochemistry of the title compound, $C_{22}H_{28}N_2O_6Si$, has been confirmed. The bond lengths and angles of the deltacyclane moiety are affected by strain.

Comment

The reaction between norbornadiene and a 2-substituted butadiene yields a substituted deltacyclene (1). Recently, we reported that a cobalt complex in the presence of catalytic quantities of a chiral bidentate phosphine promotes this higher order [4 + 2 + 2] cycloaddition with an enantiomeric excess greater than 70% (Lautens, Tam & Sood, 1993). The assignment of the absolute stereochemistry of the deltacyclene (1) was made on the basis of a well known empirical method, the
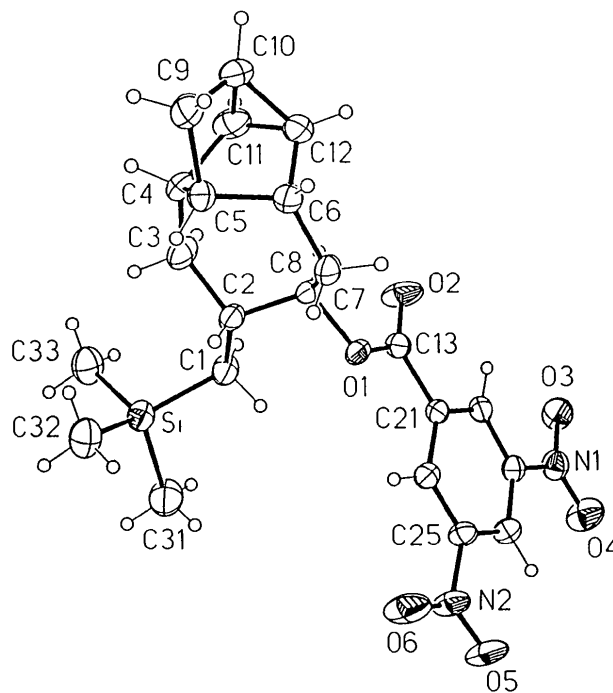

Fig. 1. View of the molecule with the crystallographic numbering scheme. Displacement ellipsoids are drawn at the 25% probability level and H atoms are shown as spheres of arbitrary radii for clarity.

The title molecule has a rigid deltacyclane-type skeleton with a seven-membered ring and a three-membered ring, as shown in Fig. 1. The internal angles of the seven-membered ring range from 104.8 (3)° for C4—C5—C6 to 120.6 (3)° for C3—C4—C5 and the C$_{sp^3}$—C$_{sp^3}$ bond lengths in the deltacylane group range from 1.481 (5) to 1.543 (5) Å, indicating significant strain in this part of the molecule. The steric interaction of the trimethylsilyl group and the deltacyclane group appears to have an effect on the C2—C1—Si angle, which is unusually large at 120.3 (2)°.

Experimental

Hydroboration–oxidation of (1) followed by esterification of the product alcohol (2) with (S)-O-methylmandelic acid afforded two diastereomers of the mandelate (3). These diastereomers were separated by flash column chromatography and the major diastereomer of the mandelate (3) was hydrolyzed and esterified to give the corresponding enantiomerically pure benzoate (4). Crystals were obtained from a methanol/pentane (1:1) mixture.

Crystal data

C$_{22}$H$_{28}$N$_2$O$_6$Si	Mo *Kα* radiation
$M_r = 444.55$	$\lambda = 0.71073$ Å
Orthorhombic	Cell parameters from 22
$P2_12_12_1$	reflections
$a = 11.408$ (2) Å	$\theta = 20.0–26.5°$
$b = 11.495$ (2) Å	$\mu = 0.141$ mm^{-1}
$c = 17.672$ (4) Å	$T = 293$ (2) K
$V = 2317.4$ (8) Å^3	Plate
$Z = 4$	$0.35 \times 0.30 \times 0.12$ mm
$D_x = 1.274$ Mg m^{-3}	Colourless

Data collection

Enraf–Nonius CAD-4	$R_{int} = 0.0247$
diffractometer	$\theta_{max} = 26.0°$
ω–2θ scans	$h = -14 \rightarrow 14$
Absorption correction:	$k = 0 \rightarrow 14$
none	$l = 0 \rightarrow 21$
5019 measured reflections	3 standard reflections
4552 independent reflections	frequency: 120 min
2909 observed reflections	intensity decay: <3%
[$I > 2\sigma(I)$]	

Refinement

Refinement on F^2	Extinction correction:
$R[F^2 > 2\sigma(F^2)] = 0.0483$	SHELXL93 (Sheldrick,
$wR(F^2) = 0.1092$	1993)
$S = 1.113$	Extinction coefficient:
4551 reflections	0.0026 (10)
282 parameters	Atomic scattering factors
$w = 1/[\sigma^2(F_o^2) + (0.0581P)^2$	from *International Tables*
$+ 0.3272P]$	*for Crystallography* (1992,
where $P = (F_o^2 + 2F_c^2)/3$	Vol. C, Tables 4.2.6.8 and
$(\Delta/\sigma)_{max} = 0.024$	6.1.1.4)
$\Delta\rho_{max} = 0.187$ e Å^{-3}	Absolute configuration:
$\Delta\rho_{min} = -0.144$ e Å^{-3}	Flack (1983)

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

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
Si	0.87003 (10)	0.79301 (9)	0.02493 (5)	0.0595 (3)
N1	0.9005 (3)	0.0838 (3)	0.1916 (2)	0.0665 (8)
N2	1.2294 (3)	0.3515 (3)	0.1588 (2)	0.0736 (9)
O1	0.9614 (2)	0.4334 (2)	−0.05923 (12)	0.0543 (6)
O2	0.8018 (2)	0.3231 (3)	−0.0420 (2)	0.0938 (10)
O3	0.8048 (2)	0.0522 (2)	0.1712 (2)	0.0835 (9)
O4	0.9515 (3)	0.0436 (3)	0.2462 (2)	0.1035 (11)
O5	1.2752 (2)	0.3051 (3)	0.2130 (2)	0.0932 (10)
O6	1.2702 (3)	0.4325 (3)	0.1250 (2)	0.1171 (14)
C1	0.8682 (3)	0.6432 (3)	−0.0165 (2)	0.0620 (9)
C2	0.8955 (3)	0.6247 (3)	−0.1003 (2)	0.0513 (8)
C3	0.8033 (3)	0.6845 (4)	−0.1500 (2)	0.0719 (11)
C4	0.8121 (3)	0.6754 (3)	−0.2369 (2)	0.0606 (9)
C5	0.9293 (3)	0.6535 (3)	−0.2750 (2)	0.0582 (9)
C6	0.9514 (3)	0.5237 (3)	−0.2647 (2)	0.0591 (9)
C7	0.9909 (3)	0.4767 (3)	−0.1882 (2)	0.0618 (10)
C8	0.9088 (3)	0.4973 (3)	−0.1230 (2)	0.0538 (8)
C9	0.8921 (4)	0.6573 (3)	−0.3580 (2)	0.0775 (12)
C10	0.7978 (4)	0.5671 (4)	−0.3524 (2)	0.0787 (12)
C11	0.7490 (3)	0.5763 (4)	−0.2740 (2)	0.0759 (11)
C12	0.8354 (4)	0.4831 (4)	−0.2915 (2)	0.0751 (12)
C13	0.8987 (3)	0.3540 (3)	−0.0241 (2)	0.0513 (8)
C21	0.9606 (3)	0.3052 (3)	0.0432 (2)	0.0449 (7)
C22	0.9065 (3)	0.2175 (3)	0.0832 (2)	0.0508 (8)
C23	0.9605 (3)	0.1755 (3)	0.1476 (2)	0.0479 (8)
C24	1.0663 (3)	0.2160 (3)	0.1732 (2)	0.0529 (8)
C25	1.1163 (3)	0.3036 (3)	0.1324 (2)	0.0507 (8)
C26	1.0669 (3)	0.3499 (3)	0.0679 (2)	0.0488 (8)
C31	0.9106 (5)	0.7725 (4)	0.1255 (2)	0.105 (2)
C32	0.9790 (4)	0.8891 (4)	−0.0201 (3)	0.0883 (13)
C33	0.7253 (4)	0.8637 (4)	0.0199 (3)	0.0900 (13)

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

O1—C8	1.472 (4)	C5—C9	1.527 (5)
C1—C2	1.529 (4)	C6—C12	1.481 (5)
C2—C8	1.525 (4)	C6—C7	1.524 (5)
C2—C3	1.533 (4)	C7—C8	1.504 (5)
C3—C4	1.543 (5)	C9—C10	1.498 (6)
C4—C11	1.498 (5)	C10—C11	1.496 (6)
C4—C5	1.518 (5)	C10—C12	1.508 (5)
C5—C6	1.525 (5)	C11—C12	1.488 (6)
C2—C1—Si	120.3 (2)	C8—C7—C6	116.1 (3)
C8—C2—C1	114.1 (3)	O1—C8—C7	104.7 (2)
C8—C2—C3	110.4 (3)	O1—C8—C2	108.6 (2)
C1—C2—C3	110.6 (3)	C7—C8—C2	114.5 (3)
C2—C3—C4	119.7 (3)	C10—C9—C5	96.7 (3)
C11—C4—C5	95.9 (3)	C11—C10—C9	106.2 (3)
C11—C4—C3	117.2 (3)	C11—C10—C12	59.4 (3)
C5—C4—C3	120.6 (3)	C9—C10—C12	106.6 (3)
C4—C5—C6	104.8 (3)	C12—C11—C10	60.7 (3)
C4—C5—C9	100.2 (3)	C12—C11—C4	108.7 (3)
C6—C5—C9	100.8 (3)	C10—C11—C4	106.3 (3)
C12—C6—C7	115.8 (3)	C6—C12—C11	107.4 (3)
C12—C6—C5	97.0 (3)	C6—C12—C10	106.3 (3)
C7—C6—C5	120.1 (3)	C11—C12—C10	59.9 (3)

H atoms were included in calculated positions (C—H 0.96 Å) and included in the refinement as riding atoms with a general isotropic displacement parameter which refined to 0.091 (2) Å^2. The certainty of the assignment of the absolute stereochemistry is based on the value of the final Flack parameter (Flack, 1983) of 0.08 (19) [compared to 0.93 (19) for the inverted structure] and is completely supported by the NMR data (Lautens, Tam & Sood, 1993) for the Mosher's ester derivative.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *XCAD4* (Siemens, 1993). Program(s) used to solve structure:

SHELXTL/PC (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *SHELXTL/PC*. Software used to prepare material for publication: *SHELXL93*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and bond distances and angles involving non-H atoms have been deposited with the IUCr (Reference: FG1035). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Comment

The title compound is an immunomodulant drug active on CD4 + T-lymphocyte functions (Pugliese, Biglino, Uslenghi, Marinelli, Forno & Girardello, 1992). It induces maturation and activation of T-lymphocytes and stimulates polymorphonuclear granulocytes, macrophages and natural killer-cell activity. NMR studies in solution and conformational calculations on its conjugate base (probably the bioactive form of the molecule) indicate the existence of *trans* and *cis* conformers around the peptide bond with a very close conformational population (55 and 45%, respectively) (Villani, Pucciariello, Crimella & Stradi, 1993).

trans (55%)   *cis* (45%)

This study proves that the conformation of the acidic form of the molecule in the solid state is *cis*. Although only the relative stereochemistry of the molecule is shown in Fig. 1, its absolute (2S,4S) configuration is assigned on the basis of the chemical pathway followed during the preparation of the compound [the chirality of the molecule originates from the absolute configuration of (S)-pyroglutamic acid and (S)-thiazolidine-4-carboxylic acid employed in its preparation].

The molecular structure with the atom-numbering scheme is illustrated as an *ORTEP* (Johnson, 1976) plot in Fig. 1.

The thiazolidine and prolyl rings are rotated by 98.95°, and the thiazolidine moiety is present in two conformations (envelope and quasiplanar) due

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3-(5-Oxo-L-prolyl)-L-thiazolidine-4-carboxylic Acid

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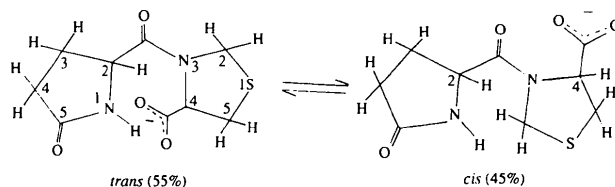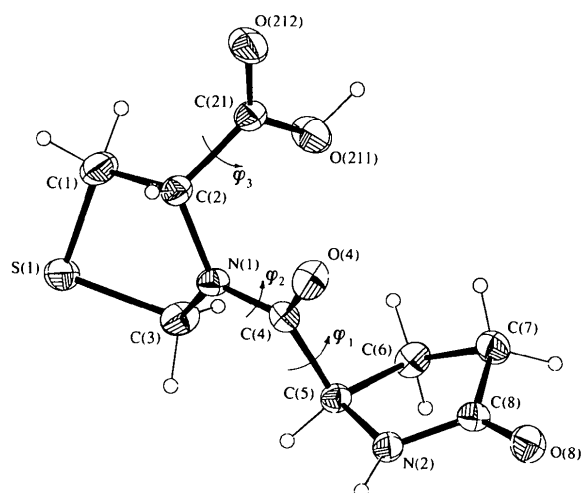
Abstract

The molecular structure of the title compound, $C_9H_{12}N_2O_4S$, with (2S,4S) absolute configuration, is characterized by the *cisoid* geometry of the carboxylic acid residue and by the presence of two different disordered conformations of the thiazolidine moiety.

Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the title compound illustrating the stereochemistry and the atomic labelling (displacement elipsoids are drawn at the 40% probability level). The H atoms are drawn as spheres with fixed radii.