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(4*S*,6*S*,11*R*)-(+)-*trans*-4,6-Dimethyl-2-(1-phenylethylamino)-2-thio-1,3,2λ⁵-dioxa-phosphorinane

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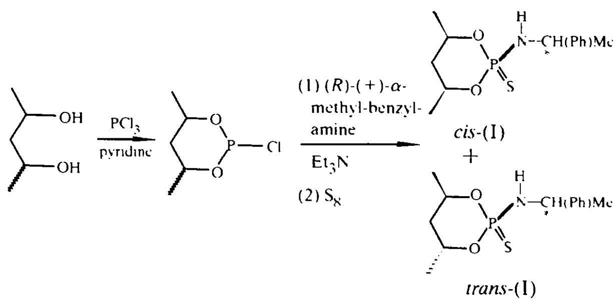
Abstract

The structure of the title compound, (4*S*,6*S*,11*R*)-(+)-*trans*-4,6-dimethyl-2-(1-phenylethylamino)-1,3,2λ⁵-dioxaphosphorinane-2-thione, $C_{13}H_{20}NO_2PS$, which crystallizes in the trigonal crystal system in the uncommon space group $P3_121$ (No. 152), has been determined from three-dimensional X-ray diffraction data.

Comment

Optically pure β-diols with C_2 symmetry, like 2,4-pentanediol in its *d* and *l* forms, are very useful chiral auxiliaries in asymmetric synthesis (Alexakis & Mangeney, 1990; Aitken & Kilenyi, 1992; Ojima, 1993; Noyori, 1994). A variety of methods of obtaining optically pure 1,3-polyols have been reported and are still under investigation (Oishi & Nakata, 1990; Chan & Nwe, 1992). Recently, for example, the asymmetric hydrogenation of β-hydroxy ketones or diketones in the presense of chiral catalysts has become popular (Ito *et al.*, 1980; Katamura *et al.*, 1988). Nevertheless, conventional resolution methods would represent, in some cases, advantageous strategies. The simple reduction of commercially available 2,4-pentanedione with $NaBH_4$ leads to a mixture of isomers (*meso*, *d*/*l*) in good yield (90%). Therefore, we devised an easy method for the separation of the isomer mixture and the resolution of the *d*/*l* enantiomers of 2,4-pentanediol based on the formation of phosphorus heterocycles, using (*R*)-(+)-α-methylbenzylamine as chiral agent as shown below (work in progress; for similar resolution methods, see Hoeve & Wynberg, 1985; Wang *et al.*, 1995).

In order to determine the configuration at the chiral C atoms of the diol subunit, a crystal structure determination of the least abundant *trans*-azathiophosphate, (I), was carried out. In the solid state, the molecule adopts a chair conformation with the amine group in the equatorial position [it is well documented that the more stable configuration of anancomeric 1,3,2-dioxaphosphorinanes is that wherein the amine group is equatorial; see, for example, Mosbo & Verkade (1973)] and the S atom in an axial orientation (Fig. 1). Remarkably, the molecule presents no severe ring flattening in the OPO region [torsion angles: C8—C6—O1—P2 −175.4 (3) and C7—C4—O3—P2 −78.2 (4)°]. Taking into account that the configuration at C11 is *R*, it is clear from the figure that the configuration at both C4 and C6 is *S*.



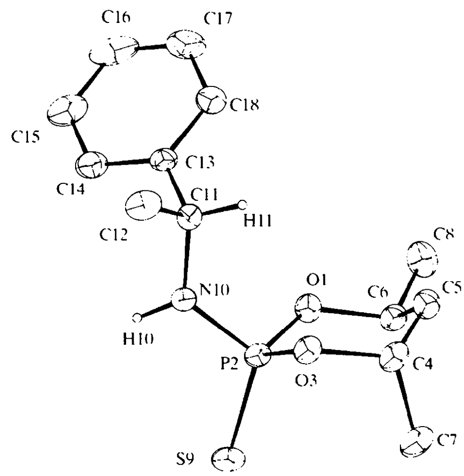


Fig. 1. The molecular structure of (I) with 20% probability ellipsoids for non-H atoms. Most of the H atoms have been omitted for clarity.

Experimental

Both *meso* and *d*,*l*-pentanediols were reacted with phosphorus trichloride and pyridine in dry ether under nitrogen at 273 K. The pyridinium salt was filtered off and the organic layer added to a flask containing (*R*)-(+)-α-methylbenzylamine and triethylamine in toluene. The resulting triethylammonium chloride was then filtered off and the filtrate added to a third flask containing elemental sulfur. The crude solution was chromatographed and the resulting four isomers (two *cis* and two *trans*; see scheme) were separated and characterized by ^1H, ^{13}C and ^{31}P NMR spectroscopy in $CDCl_3$ solution on a Jeol GSX-270 spectrometer. Single crystals of (4*S*,6*S*,11*R*)-(+)-2-(1-phenylethylamino)-2-thio-*trans*-4,6-dimethyl-1,3,2-dioxaphosphorinane suitable for crystallographic work were obtained from *n*-hexanes. M.p. 360–362 K. $[\alpha]_D^{24}$ +22.7° (*c*

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0.015, ethanol). ^{1}H (δ 1.12, *dd*, 3H; 1.42, *dd*, 3H; 1.51, *d*, 3H; 1.70, *m*, 1H; 1.83, *m*, 1H; 3.44, *dd*, 1H; 4.43, *m*, 1H; 4.54, *m*, 1H; 4.75, *m*, 1H; 7.3, *m*, 5H). ^{13}C (δ 21.32, *d*, 1C; 21.86, *d*, 1C; 24.64, *d*, 1C; 37.85, *d*, 1C; 51.40, *d*, 1C; 69.80, *d*, 1C; 74.70, *d*, 1C; 126.20, *s*, 2C; 127.06, *s*, 1C; 128.28, *s*, 2C; 144.11, *d*, 1C) and ^{31}P (δ 63.71, *s*). Calculated for $C_{13}H_{20}NO_2PS$: C 54.72, H 7.06%; found: C 54.78, H 7.14%.

Crystal data

$C_{13}H_{20}NO_2PS$
M_r = 285.33
Trigonal
$P3_121$
a = 9.921 (1) Å
c = 26.880 (5) Å
V = 2291.2 (5) Å^3
Z = 6
D_x = 1.24 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 24 reflections
θ = 11–12°
μ = 0.311 mm^{-1}
T = 293 (2) K
Equidimensional
0.36 × 0.30 × 0.30 mm
Colorless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: none
1626 measured reflections
1592 independent reflections
1208 reflections with $I > 2\sigma(I)$
R_{int} = 0.023

θ_{max} = 25°
$h = -11 \rightarrow 0$
$k = 0 \rightarrow 10$
$l = 0 \rightarrow 31$
3 standard reflections every 100 reflections frequency: 60 min intensity variation: ±2.4%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.112
S = 1.137
1592 reflections
172 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0558P)^2 + 0.0649P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.04 (19)

Table 1. *Selected geometric parameters (Å, °)*

P2—O3	1.583 (3)	C6—C8	1.513 (6)
P2—O1	1.589 (3)	C11—H11	0.95 (5)
P2—N10	1.609 (3)	C11—C12	1.510 (6)
P2—S9	1.930 (1)	C11—C13	1.514 (5)
N10—H10	0.78 (5)	C13—C18	1.374 (6)
N10—C11	1.481 (5)	C13—C14	1.380 (6)
O1—C6	1.464 (5)	C14—C15	1.370 (7)
O3—C4	1.474 (5)	C15—C16	1.343 (8)
C4—C5	1.502 (6)	C16—C17	1.359 (9)
C4—C7	1.528 (5)	C17—C18	1.396 (8)
C5—C6	1.516 (6)		
O3—P2—O1	103.4 (2)	O3—C4—C5	109.0 (3)
O3—P2—N10	104.7 (2)	O3—C4—C7	110.0 (4)
O1—P2—N10	103.5 (2)	C5—C4—C7	115.1 (4)
O3—P2—S9	115.5 (1)	C4—C5—C6	114.2 (4)
O1—P2—S9	115.7 (1)	O1—C6—C8	106.2 (3)
N10—P2—S9	112.7 (1)	O1—C6—C5	108.6 (3)
C11—N10—P2	124.1 (3)	C8—C6—C5	113.0 (4)
C6—O1—P2	120.6 (2)	N10—C11—C12	110.7 (4)
C4—O3—P2	122.4 (3)	N10—C11—C13	111.5 (3)
N10—P2—O1—C6	151.9 (3)	P2—O3—C4—C7	−78.2 (4)
S9—P2—O1—C6	−84.4 (3)	P2—O1—C6—C8	−175.4 (3)
N10—P2—O3—C4	−148.6 (3)	P2—N10—C11—C12	−123.6 (4)
S9—P2—O3—C4	86.9 (3)	P2—N10—C11—C13	111.9 (4)

The title structure was solved by direct methods and refined with the *SHELXL*93 software package (Sheldrick, 1993) in the uncommon space group $P3_121$ (only 40 crystal structures were reported in this space group before 1994; see Brock & Dunitz, 1994). Atoms H10 and H11 were located from a difference Fourier map and refined. All other H atoms were placed in calculated positions and refined using a riding model. In addition, in the refinement of the H atoms at C7, C8 and C12, only the rotation of the methyl groups was taken into consideration. The C11—H11 bond distance was determined to be 0.95 (5) Å, whereas N10—H10 was 0.78 (5) Å. No evidence of N—H···S intra- or intermolecular hydrogen bonding was found.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *MolEN* (Fair, 1990). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93. Molecular graphics: *XP* in *SHELXTL-Plus* (Sheldrick, 1991). Software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1328). Services for accessing these data are described at the back of the journal.

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Three Intermediates in the Synthesis of Chrysanthemic Acid

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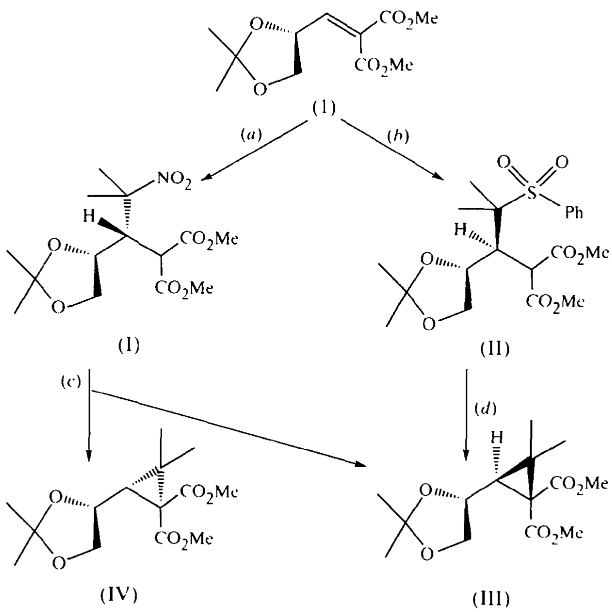
Abstract

The structures of three compounds, namely, dimethyl 2-{(1*S*)-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-methyl-2-nitropropyl}malonate [$C_{14}H_{23}NO_8$, (I)], dimethyl 2-{(1*S*)-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-methyl-2-(phenylsulfonyl)propyl}malonate [$C_{20}H_{28}O_8S$, (II)] and dimethyl (3*S*)-2,2-dimethyl-3-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]cyclopropane-1,1-dicarboxylate [$C_{14}H_{22}O_6$, (III)], which are intermediates in the synthesis of chrysanthemic acid, are presented and discussed.

Comment

Some esters of chrysanthemic acid are powerful insecticides (Elliott & Janes, 1978) and significant efforts have been made to design synthetic routes which produce them in high yield and with high enantiomeric purity. Dimethyl 2,2-dimethyl-3-(2,2-dimethyl-1,3-dioxolan-4-yl)cyclopropane-1,1-dicarboxylate, (III), is a valuable intermediate of chrysanthemic acid and we have studied a new diastereoselective synthesis (see scheme below) of this compound (Froidbize, 1997; Krief *et al.*, 1998). This synthesis uses the enantiomerically pure alkylidene malonate (1) (produced from D-mannitol) as the starting compound. During this study, it was necessary to unambiguously establish the relative stereochemistry of intermediate malonates (I) and (II), as well as the target molecule (III), and so their structures were determined by single-crystal X-ray diffraction.



(*a*) $LiC(CH_3)_2NO_2$, DMSO, 293 K, 24 h;
(*b*) $LiC(CH_3)_2SO_2Ph$, THF, 273 K, 2 h;
(*c*) Cs_2CO_3, DMSO, 353 K, 24 h;
(*d*) Cs_2CO_3, DMSO, 353 K, 8 h.

Compound (I) (Fig. 1) was obtained in 72% yield by a diastereoselective Michael addition of 2-lithio-2-nitropropane on alkylidene malonate (1). The absolute configuration of compound (1) being known, it was possible to establish the configuration of (I) to be (3*S*,4*S*). The dioxolane ring (C4–C6, O5, O6) is in the so-called 'envelope' conformation (Dunitz, 1979), with the O5 atom out of the plane defined by the other four atoms. The conformation around the C1—C3 single bond is energetically-disfavoured 'eclipsed', with the H1—C1 and C3—C2 bonds facing each other (Table 1). In contrast, the conformation around the C3—C2 single bond is 'staggered', the nitro group and the C1 atom being in *anti* positions. Consequently, the H1 atom, which is close to the two methyl groups of the nitropropyl substituent, is in a crowded environment.

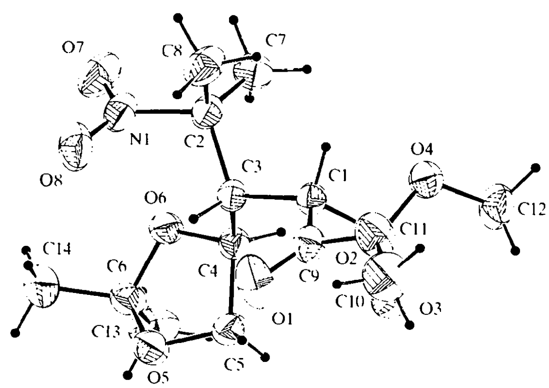


Fig. 1. The molecular structure of compound (I). Displacement ellipsoids are drawn at the 50% probability level and the H1 atom is linked to C1.