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Crystal and Molecular Structures and the Absolute Configuration of O,Se-Dimethyl-N-(1-Phenylethyl)phosphoramidoselenoates

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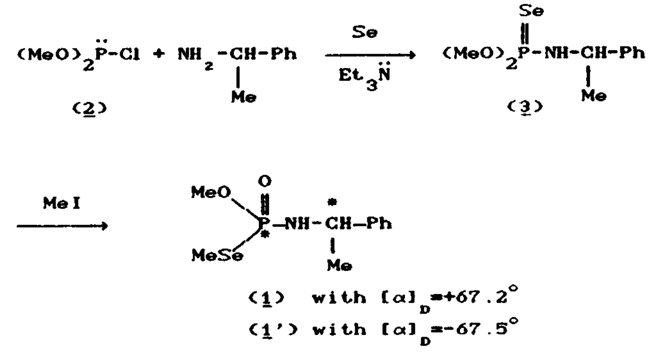
ABSTRACT

The structural investigation of two enantiomers of the phosphoroorganic selenium-containing compound [$(+)C_{10}H_{16}NO_2PSe$ (**1**) *and* $(-)C_{10}H_{16}NO_2PSe$ (**1**′)] *was carried out. The absolute configuration at the P and C3 atoms was found to be R for compound* **1** *and, respectively, S for compound* **1**′.

INTRODUCTION

Stereospecific transformations of optically active precursors into optically active products consist of one of the basic strategies leading to the synthesis of P-chiral optically active organophosphates. Therefore, the construction of P-chiral precursors possessing ligands that can undergo stereocontrolled replacement attracted the attention of several research groups aiming at the synthesis of optically active organophosphorus compounds. Stec and collaborators have focused their efforts on the construction of P-chiral N-substituted phosphoramidates, derivatives of easily available and cheap optically active primary amines, and separation of diastereoisomeric phosphoramidates, which, in consecutive steps, are in the process of PN→PX conversion transformed to P-epimeric phosphates, phosphorothioates, or phosphoroselenoates [1]. Extension of such strategy involves the introduction to P-chiral diastereoisomers of the second ligand undergoing easy stereodefined replacement. A representative example makes use of O,Se-dimethyl-N-(1-phenylethyl)phosphoramidoselenoate (**1**). Its synthesis involves condensation of O,O-dimethylphosphorchloridite (**2**) with optically active 1-phenylethylamine in the presence of dry selenium, with a subsequent Pischtshimuka-type rearrangement of O,O-dimethyl-N-(1-phenylethyl)-phosphoramidoselenoate (**3**) into **1** and separation of the diastereoisomers (Scheme 1) [4]. Replacement of the Se-Me group by any alkoxide takes place



SCHEME 1

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TABLE 1 Positional Parameters for the Nonhydrogen Atoms (and H1N Atom) in Structures **1** and **1′** with esd's in Parentheses

	Compound 1			*Compound 1′*		
	x	*y*	*z*	*x*	*y*	*z*
SE	0.1547(2)	0.2318(2)	0.89353(9)	0.1547(1)	0.2687(1)	0.89330(6)
P	−0.0277(3)	0.1966(3)	0.7976(2)	−0.0272(2)	0.3034(2)	0.7977(1)
O1	−0.103(1)	0.3332(8)	0.7861(6)	−0.1031(6)	0.1679(5)	0.7864(4)
O2	−0.1290(9)	0.0739(7)	0.8328(5)	−0.1307(6)	0.4254(5)	0.8334(3)
N	0.033(1)	0.1251(8)	0.7123(6)	0.0353(7)	0.3751(5)	0.7117(3)
C1	0.255(2)	0.051(2)	0.886(1)	0.260(1)	0.446(1)	0.8807(7)
C2	−0.219(2)	0.093(1)	0.9128(9)	−0.223(1)	0.4050(9)	0.9097(6)
C3	0.119(1)	0.206(1)	0.6467(6)	0.1190(8)	0.2934(7)	0.6478(4)
C4	0.048(1)	0.183(2)	0.5575(7)	0.048(1)	0.314(1)	0.5588(5)
C5	0.292(1)	0.166(1)	0.6483(7)	0.2914(8)	0.3323(7)	0.6491(4)
C6	0.339(1)	0.041(1)	0.6180(8)	0.3405(9)	0.4599(8)	0.6187(5)
C7	0.495(1)	0.002(1)	0.623(1)	0.4946(9)	0.498(1)	0.6241(6)
C8	0.596(1)	0.092(2)	0.660(1)	0.596(1)	0.407(1)	0.6596(6)
C9	0.550(1)	0.221(2)	0.6914(9)	0.548(1)	0.280(1)	0.6912(6)
C10	0.395(1)	0.259(1)	0.6855(8)	0.3960(9)	0.2402(9)	0.6849(5)
H1N	0.081(2)	0.028(2)	0.709(2)	0.084(2)	0.473(2)	0.708(2)

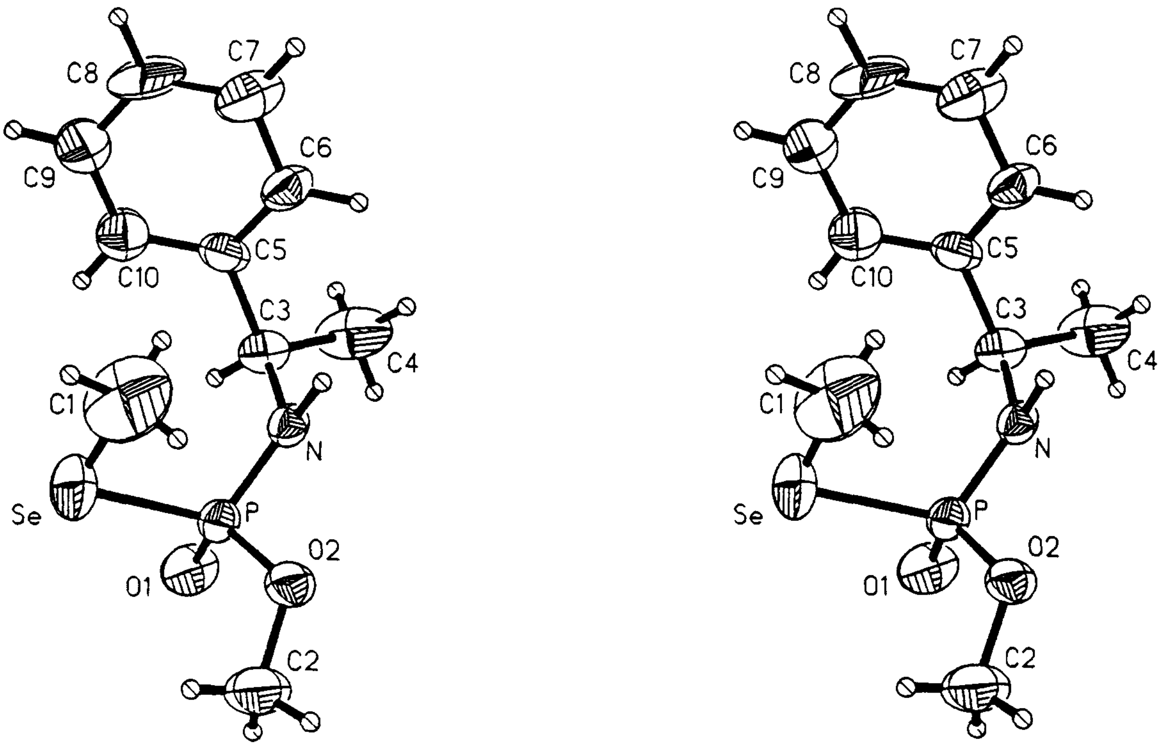

FIGURE 1 Thermal ellipsoidal (ORTEP) stereoview of the molecule of compound **1** with atom numbering.

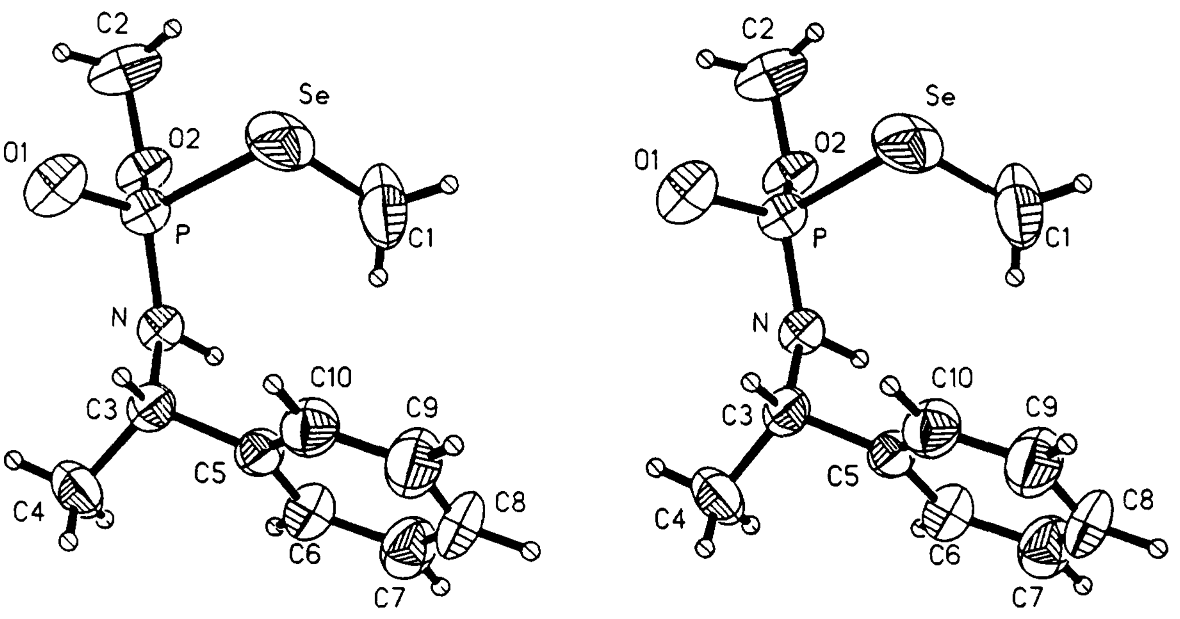

FIGURE 2 Thermal ellipsoidal (ORTEP) stereoview of the molecule of compound **1′** with atom numbering.

in a stereoinvertive manner if the alkoholysis is performed in the presence of mercurium trifluoroacetate [2].

Thus, **1** constitutes an interesting substrate for the family of O-methyl-O-alkyl-phosphoramidates which, under the action of NaH/CS_2, can be transformed into the enantiomeric O-methyl-O-alkyl-phosphorothioates [4].

TABLE 2 Selected Bond Lengths (Å) and Bond Angles (°) in **1** and **1′** with esd's in Parentheses

	Compound 1	*Compound 1′*
SE-P	2.216(3)	2.208(3)
SE-C1	1.95(2)	1.95(1)
P-O1	1.481(8)	1.470(5)
P-O2	1.574(8)	1.582(5)
P-N	1.591(9)	1.606(6)
N-C3	1.49(1)	1.466(8)
O2-C2	1.49(2)	1.45(2)
C3-C4	1.54(2)	1.54(1)
C3-C5	1.56(1)	1.55(1)
N-H1N	1.0(1)	1.0(1)
P-SE-C1	98.3(5)	98.1(3)
SE-P-O1	105.6(4)	105.8(2)
SE-P-O2	106.4(3)	106.6(3)
SE-P-N	113.1(3)	112.7(2)
P-O2-C2	120.1(7)	120.6(5)
P-N-C3	121.4(6)	120.8(4)
O1-P-O2	117.1(5)	116.0(3)
O1-P-N	115.5(5)	115.6(3)
O2-P-N	99.1(4)	100.0(3)
N-C3-C4	110.6(9)	110.3(6)
N-C3-C5	110.4(8)	110.3(5)
C4-C3-C5	111.6(9)	111.9(6)
P-N-H1N	125(1)	125(1)
C3-N-H1N	104(1)	104(1)

Since this last step is stereoretentive, the unambiguous assignment of the absolute configuration of **1** is a crucial condition step for the stereocontrolled synthesis of O-methyl-O-alkyl-phosphorothioates or the enantiomeric O-methyl-O-alkyl-[^{18}O]-phosphates [3].

In this report, we present the assignment of the absolute configuration of P-chiral O,Se-dimethyl-N-(1-phenylethyl)phosphoramidoselenoate, namely, [R_P, R_C]-(**1**), $[\alpha]_D = +67.2°$ (c 1.4; MeOH) mp 124–126°C and [S_P,S_C]-(**1′**), $[\alpha]_D = -67.5°$ (c 1.3; MeOH) mp 124–126°C.

Former tentative assignments of absolute configuration at phosphorus [4] have been fully confirmed by X-ray studies.

RESULTS AND DISCUSSION

The investigated compounds **1** and **1′** (see Figures 1 and 2) differ only by the sign of the optical rotation value. This suggests that they might be enantiomers with opposite configuration at P and C3 asymmetric atoms. Structural investigations have confirmed that assumption, establishing the R configuration at P and C3 in **1** and, respectively, S in **1′**. The absolute configurations were assigned on the basis of the Hamilton test and by calculations of the ETA (η) parameters (for **1**, $\mathfrak{R}$-ratio = 1.0012, $\alpha < 0.1$, and ETA = 1.129; for **1′**, $\mathfrak{R}$-ratio = 1.0051, $\alpha < 0.001$, and ETA = 0.906) [5,6].

In Table 2, selected bond lengths and bond angles for structures **1** and **1′** are presented. The P–Se bond lengths show some interesting features. In the literature, the P–Se bond length varies between 2.22(1) Å and 2.30(1) Å [7,8]. The larger values are usually quoted in articles published before 1980 when the measurements were made using photographic methods which were less accurate. The sum of the covalent radii for a single P–Se bond is equal to 2.27 Å [11]. That bond in the investigated compounds is somewhat shorter (P=Se double bond = 2.03–2.17 Å [7,11]).

The projections of the ligands around the P and C3 atoms on the plane perpendicular to the P-C3 line for both compounds are shown in Figures 3 and 4. The large phenyl substituent located at the C3 atom approaches the synclinal one in the connection to the biggest ligand (selenium) at the P atom. The difference between **1** and **1′** is the opposite orientation of that arrangement (opposite torsional angles). In both compounds, a contact indicating the presence of hydrogen bonding 01 . . . H1N–N is observed (in **1**, the 01 . . . H1N distance equals 1.886(9) Å, bond length H1N–N = 1.02(1) Å, and 01 . . . H1N–N angle = 160.9(4)°; in **1′**, 01 . . . H1N distance = 1.877(9) Å, H1N–N bond length = 1.04(1) Å, and 01 . . . H1N–N angle = 159.9(6)°).

EXPERIMENTAL

Crystal and molecular structures of **1** and **1′** were determined using data collected on a CAD4 diffractometer. Both compounds formed crystals in the orthorhombic system, space group $P2_12_12_1$. Crystal data and experimental details are shown in Table 3. Intensity data for both compounds were collected at room temperature using a diffractometer with graphite monochromatized radiation. Lattice constants were refined by a least-squares fit of 25 reflections in the θ range 9.7–14.1° for **1** and 9.8–14.3° for **1′**. The decline in intensities of three standard reflections for **1** (4,3,-1; 5,3,1; 1,1,-7) was 0.5% during 27.4 hours of exposure, and, for **1′** (2,3,-7; 2,3,-8; 2,2,-6), the decline was 0.6% during 27.7 hours. For **1** and **1′**, absorption corrections were applied by the EAC program [9] (see Table 3). A total of 1332 observed reflections for **1** and 1389 for **1′** [with $I \geq 3\sigma(I)$] were used to solve the structures by direct methods (SHELXS program) [10]. Structures were refined on the SDP computing package [9] by full matrix least squares using *F*'s. For both compounds, all H atoms were placed geometrically at idealized positions (except the H1N atom which was found from a difference Fourier map) and refined as riding with fixed isotropic thermal parameters. Anisotropic thermal parameters were refined for all nonhydrogen atoms in both structures. The final refinement converged to $R = 0.067$ with unit weight for **1** and to $R = 0.049$ with unit weight for **1′**. The largest shift/error parameter in the last cycle was 0.01 for **1** and 0.03 for **1′**. The largest residual peak in the final difference Fourier map was 0.933 $e\text{Å}^{-3}$ for **1** and 0.489 $e\text{Å}^{-3}$ for **1′**. All calculations were carried out with the Enraf-Nonius SDP crystallographic computing package [9], except for direct methods which were applied with the SHELXS program [10]. Scattering factors were taken from the *International Tables for X-ray Crystallography* [12]. Atom coordinates, bond lengths, bond and torsional angles, temperature factors of all atoms, and F_{obs}/F_{calc} val-

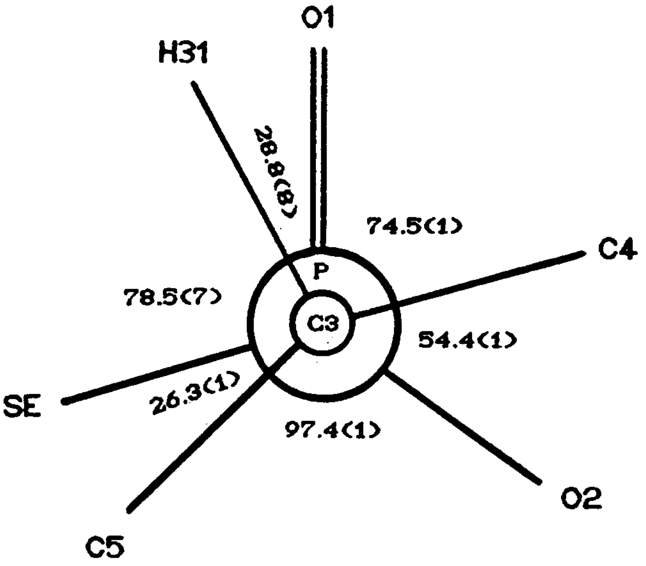

FIGURE 3 Projection perpendicular to the P-C3 line in compound **1**.

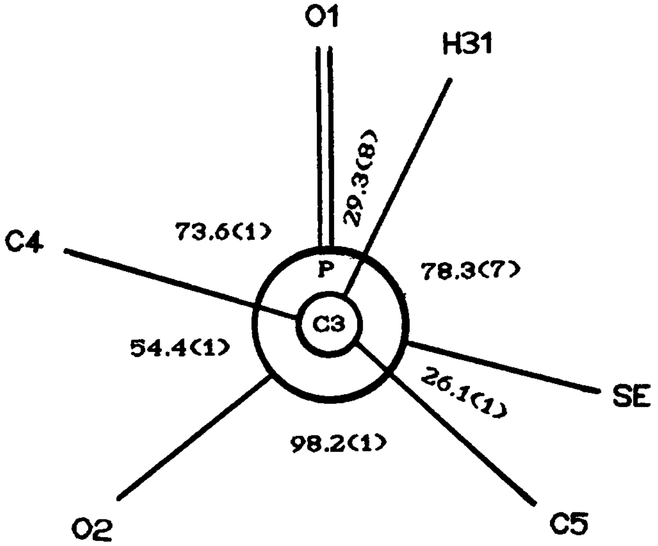

FIGURE 4 Projection perpendicular to the P-C3 line in compound **1′**.

TABLE 3 Crystal Data and Experimental Details

	Compound 1	*Compound 1′*
Molecular formula	$C_{10}H_{16}NO_2PSe$	$C_{10}H_{16}NO_2PSe$
$[\alpha]_D$ (°)	+67.2	−67.5
Crystallization solvent	acetone	acetone
Space group	$P2_12_12_1$	$P2_12_12_1$
a (Å)	8.740(1)	8.742(1)
b (Å)	9.614(2)	9.597(3)
c (Å)	15.631(2)	15.640(2)
V (Å^3)	1313.5(1)	1312.0(5)
Z	4	4
μ (cm^{-1})	29.3	29.3
D_c (g/cm^3)	1.477(2)	1.479(2)
Crystal dimensions (mm)	0.20, 0.22, 0.35	0.14, 0.20, 0.40
Maximum 2θ (°)	60	60
Radiation, λ (Å)	MoK$_\alpha$, 0.70930	MoK$_\alpha$, 0.70930
Scan mode	$\omega/2\theta$	$\omega/2\theta$
Scan width	0.90 ± 0.35 tan θ	0.92 ± 0.35 tan θ
hkl ranges	h = 0 12 k = 0 13 l = 0 22	h = 0 12 k = 0 13 l = 0 22
EAC correction:		
correction factors:		
minimum:	0.9186	0.7721
maximum:	0.9988	0.9989
average:	0.9667	0.9145
transmission (%):		
minimum:	84.38	59.61
maximum:	99.77	99.77
average:	93.45	83.64
Number of reflections measured:		
total:	2206	2203
with I ≥ 3σ(I):	1332	1389
Number of parameters refined:	136	136
R	0.067	0.049

ues (for **1** and **1**′)[**] are deposited at the Cambridge Crystallographic Data Centre [13].

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[**] These tables are standard computer listings, in which standard deviations of data concerned with H atoms are estimated in the same range as esd's in corresponding C, N atoms, to which these H's are bonded. Correctly, it is necessary to treate esd's in data concerned with H atoms as one range less than those in corresponding C, N atoms.