

Structure of the Diastereoisomeric Salt of (–)-4-*o*-Chlorophenyl-2-hydroxy-2-oxo-1,3,2-dioxaphosphorinane-5-spirocyclohexane and (1*R*,2*S*)-(–)- α -[(1-Methylamino)ethyl]benzyl Alcohol

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Abstract. C₂₄H₃₃ClNO₅P, $M_r = 481.95$, orthorhombic, $P2_12_12_1$, $a = 8.026$ (2), $b = 16.103$ (6), $c = 19.169$ (5) Å, $V = 2478$ (2) Å³, $Z = 4$, $D_x = 1.29$ g cm⁻³, Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å, $\mu = 22.73$ cm⁻¹, $F(000) = 1024$, $R = 0.037$, $wR = 0.037$ for 3596 observed reflections and 391 variables. The structure was solved by automatic application of the vector-search orientation function and the *DIRDIF* structure expansion procedure. The structure contains phosphorinane anions and ephedrine cations which are linked in a three-dimensional network by N–H...O and O–H...O hydrogen bonds. The phosphorinane ring is in the chair conformation. The ephedrine is in the usual extended form. The structure of a diastereoisomer is reported by Kok, Wynberg, Garcia-Granda, Beurskens & Smit [*Acta Cryst.* (1988), C44, 2235–2237].

Experimental. The present compound (XINAM) was prepared from (–)-phosphorinane and (–)-ephedrine. Colourless crystals were recrystallized twice from ethanol. Melting point 516.1 K, solubility at 298 K in 100% ethanol: 1.7 g/100g solution.

Nearly all X-ray experiments and calculations were performed as described in a foregoing paper on a related compound INAM (Kok, Wynberg, Smits, Beurskens & Parthasarathi, 1987) and need not be repeated here. Relevant differences are: approximate crystal size 0.50 × 0.18 × 0.10 mm, θ range for cell dimensions: 20–31°, 15 430 reflections measured, $\theta < 70^\circ$, hkl limits (–4, –19, –23) and (9, 19, 23), drift: 0.99–1.15, absorption correction range: 0.88 to 1.00, $R_{int} = 0.035$, for 4700 unique reflections, 3596 observed with $I > 3\sigma(I)$.

The structure was solved by application of vector-search orientation functions, using the *ORIENT* option of the *DIRDIF* system (Beurskens, Beurskens, Strumpe & Nordman, 1987), to the PO₄ group of the related compound INAM. The orientation, position, and expansion to the complete structure were achieved in one run. DIFABS range: 0.900–1.366. The positional

parameters of all atoms, the anisotropic thermal parameters of the non-hydrogen atoms and the isotropic thermal parameters of the O and N hydrogen atoms were refined. The H atoms which were not bonded to O or N atoms had fixed isotropic temperature factors of 0.06 Å². Weights: $w = 1/[\sigma^2(F_o) + 0.00030F_o^2]$. $R = 0.037$, $wR = 0.037$ and $S = 1.5421$ for the 3596 observed reflections and 391 variables.

Table 1. Atomic parameters (with *e.s.d.*'s in parentheses)

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* a_r a_r$$

	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq} (Å ² × 100)
P(2)	0.2757 (1)	0.27277 (4)	0.35133 (3)	3.67 (1)
Cl(1)	–0.1331 (1)	0.09025 (8)	0.18690 (6)	9.91 (5)
O(1)	0.2918 (3)	0.3419 (1)	0.29259 (8)	4.42 (6)
O(3)	0.2799 (3)	0.18843 (9)	0.30801 (8)	4.08 (6)
O(10)	0.3352 (3)	0.3225 (1)	0.6078 (1)	5.36 (8)
O(21)	0.4281 (3)	0.2774 (1)	0.39457 (9)	4.69 (7)
O(22)	0.1104 (3)	0.2806 (1)	0.38683 (9)	4.59 (7)
N(2)	0.0396 (3)	0.3401 (1)	0.5178 (1)	3.66 (8)
C(1)	0.3315 (4)	0.3721 (2)	0.5470 (1)	3.87 (9)
C(2)	0.1557 (4)	0.4077 (2)	0.5409 (1)	3.91 (9)
C(3)	0.0935 (5)	0.4465 (3)	0.6082 (2)	6.3 (1)
C(4)	0.1802 (4)	0.1811 (2)	0.2447 (1)	3.85 (9)
C(5)	0.2387 (3)	0.2492 (1)	0.1932 (1)	3.75 (8)
C(6)	0.1992 (5)	0.3315 (2)	0.2287 (1)	4.31 (9)
C(11)	0.4569 (4)	0.4417 (2)	0.5466 (1)	3.69 (8)
C(12)	0.4996 (4)	0.4775 (2)	0.4833 (2)	4.5 (1)
C(13)	0.6102 (4)	0.5434 (2)	0.4801 (2)	5.2 (1)
C(14)	0.6788 (4)	0.5735 (2)	0.5404 (2)	5.7 (1)
C(15)	0.6386 (4)	0.5393 (2)	0.6035 (2)	5.4 (1)
C(16)	0.5290 (4)	0.4730 (2)	0.6070 (2)	4.6 (1)
C(20)	–0.1326 (4)	0.3686 (2)	0.5017 (2)	4.7 (1)
C(41)	0.1974 (4)	0.0915 (2)	0.2212 (1)	4.5 (1)
C(42)	0.0651 (5)	0.0463 (2)	0.1943 (2)	6.0 (1)
C(43)	0.0830 (8)	–0.0363 (3)	0.1747 (2)	7.9 (2)
C(44)	0.2339 (8)	–0.0748 (2)	0.1816 (2)	8.7 (2)
C(45)	0.3637 (7)	–0.0320 (2)	0.2073 (2)	7.3 (2)
C(46)	0.3498 (5)	0.0508 (2)	0.2273 (1)	5.3 (1)
C(51)	0.4262 (4)	0.2405 (2)	0.1768 (2)	4.27 (9)
C(52)	0.4883 (5)	0.3031 (2)	0.1232 (2)	5.6 (1)
C(53)	0.3875 (5)	0.2979 (2)	0.0564 (2)	6.2 (1)
C(54)	0.2022 (5)	0.3081 (2)	0.0698 (2)	5.7 (1)
C(55)	0.1394 (4)	0.2457 (2)	0.1244 (1)	4.7 (1)
H(21)	0.081 (5)	0.313 (2)	0.474 (2)	8 (1)†
H(22)	0.464 (4)	0.701 (2)	0.049 (1)	4.2 (8)†
H(10)	0.080 (5)	0.707 (2)	0.113 (2)	7 (1)†

† U_{iso} .

Table 2. Selected bond lengths (Å) and angles (°)

O(1)—P(2)	1.588 (2)	C(11)—C(16)	1.390 (4)
O(1)—C(6)	1.443 (3)	C(12)—C(13)	1.385 (4)
P(2)—O(3)	1.592 (2)	C(13)—C(14)	1.370 (4)
P(2)—O(21)	1.480 (2)	C(14)—C(15)	1.366 (5)
P(2)—O(22)	1.496 (2)	C(15)—C(16)	1.385 (5)
O(3)—C(4)	1.459 (3)	C(41)—C(42)	1.387 (4)
Cl(1)—C(42)	1.747 (4)	C(41)—C(46)	1.393 (5)
O(10)—C(1)	1.413 (3)	C(42)—C(43)	1.389 (5)
C(1)—C(2)	1.527 (4)	C(43)—C(44)	1.367 (7)
C(1)—C(11)	1.506 (4)	C(44)—C(45)	1.344 (7)
C(2)—C(3)	1.519 (4)	C(45)—C(46)	1.391 (5)
C(2)—N(2)	1.500 (4)	C(51)—C(52)	1.523 (4)
C(4)—C(5)	1.549 (3)	C(52)—C(53)	1.517 (5)
C(4)—C(41)	1.517 (4)	C(53)—C(54)	1.518 (5)
C(5)—C(6)	1.523 (4)	C(54)—C(55)	1.536 (4)
C(5)—C(51)	1.543 (4)	N(2)—H(21)	1.01 (3)
C(5)—C(55)	1.542 (4)	N(2)—H(22)	0.89 (3)
N(2)—C(20)	1.489 (4)	O(10)—H(10)	0.83 (4)
C(11)—C(12)	1.386 (4)		

P(2)—O(1)—C(6)	118.6 (2)	O(1)—P(2)—O(21)	107.1 (1)
O(1)—P(2)—O(22)	109.6 (1)	O(1)—P(2)—O(3)	103.1 (1)
O(21)—P(2)—O(22)	118.3 (1)	O(3)—P(2)—O(21)	108.5 (1)
O(3)—P(2)—O(22)	109.1 (1)	P(2)—O(3)—C(4)	119.5 (2)
C(2)—N(2)—C(20)	114.4 (2)	C(2)—C(1)—C(11)	109.7 (2)
O(10)—C(1)—C(11)	114.2 (2)	O(10)—C(1)—C(2)	107.2 (2)
C(1)—C(2)—C(3)	113.1 (3)	C(1)—C(2)—N(2)	108.9 (2)
C(3)—C(2)—N(2)	110.2 (3)	C(5)—C(4)—C(41)	117.2 (2)
O(3)—C(4)—C(41)	105.9 (2)	O(3)—C(4)—C(5)	107.8 (2)
C(4)—C(5)—C(51)	111.2 (2)	C(4)—C(5)—C(55)	111.2 (2)
C(4)—C(5)—C(6)	105.6 (2)	C(51)—C(5)—C(55)	109.1 (2)
C(6)—C(5)—C(51)	111.9 (2)	C(6)—C(5)—C(55)	107.8 (2)
O(1)—C(6)—C(5)	111.8 (2)	C(1)—C(11)—C(12)	118.6 (2)
C(1)—C(11)—C(16)	122.9 (3)	C(12)—C(11)—C(16)	118.4 (3)
C(11)—C(12)—C(13)	121.1 (3)	C(12)—C(13)—C(14)	119.4 (3)
C(13)—C(14)—C(15)	120.6 (3)	C(14)—C(15)—C(16)	120.3 (3)
C(11)—C(16)—C(15)	120.2 (3)	C(4)—C(41)—C(42)	122.7 (3)
C(4)—C(41)—C(46)	120.2 (3)	C(42)—C(41)—C(46)	117.1 (3)
C(41)—C(42)—C(43)	121.6 (4)	Cl(1)—C(42)—C(41)	121.0 (3)
Cl(1)—C(42)—C(43)	117.4 (3)	C(42)—C(43)—C(44)	120.0 (4)
C(43)—C(44)—C(45)	119.3 (4)	C(44)—C(45)—C(46)	122.1 (4)
C(41)—C(46)—C(45)	119.9 (4)	C(5)—C(51)—C(52)	113.4 (3)
C(51)—C(52)—C(53)	111.0 (3)	C(52)—C(53)—C(54)	111.9 (3)
C(53)—C(54)—C(55)	111.5 (3)	C(5)—C(55)—C(54)	112.8 (3)
C(2)—N(2)—H(21)	111 (2)	C(2)—N(2)—H(22)	112 (2)
C(20)—N(2)—H(21)	106 (2)	C(20)—N(2)—H(22)	110 (2)
H(21)—N(2)—H(22)	103 (3)	C(1)—O(10)—H(10)	116 (2)

Hydrogen bonds

(1—2...3)	(1—2)	(2—3)	(1—3)	(1—2—3)
N(2)—H(21)...O(22)	1.01 (3)	1.77 (3)	2.746 (3)	164 (3)
N(2)—H(22)...O(21 ^b)	0.89 (3)	1.86 (3)	2.684 (3)	154 (3)
O(10)—H(10)...O(21 ^b)	0.84 (4)	1.93 (4)	2.765 (3)	173 (3)

Symmetry code: (i) $-\frac{1}{2} + x, -y, 1 - z$; (ii) $\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$.

Final maximum shift-over-e.s.d. ratio: 0.05 for the non-hydrogen and 0.09 for the H atoms. The final difference Fourier map showed no peaks higher nor deeper than $\pm 0.3 \text{ e } \text{Å}^{-3}$. The absolute configuration was checked with the *BIJVOET* program: $B = 0.941 (2)$ for 185 pairs.

Final parameters are given in Table 1.* Geometry calculations (Table 2) were performed with *PARST* (Nardelli, 1983). Fig. 1 shows the molecular configuration and the crystallographic numbering. The

* Lists of structure factors, anisotropic thermal parameters, H atoms not involved in hydrogen bonds, selected torsion angles and angles between least-squares planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51242 (23 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

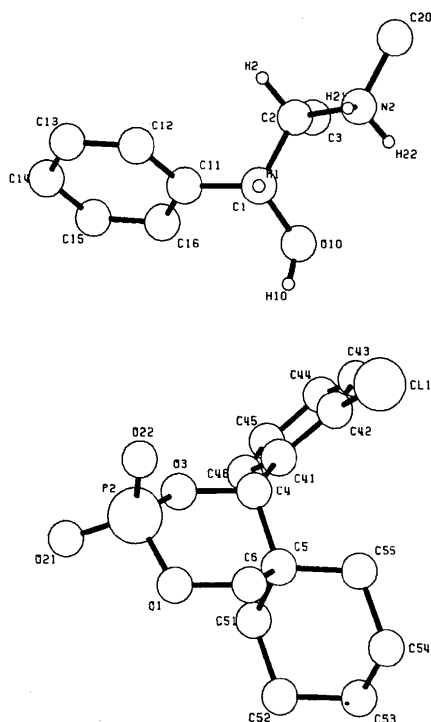


Fig. 1. Projections of the ions with crystallographic atomic numbering scheme. The ephedrine part is given as a projection along H(1)—C(1).

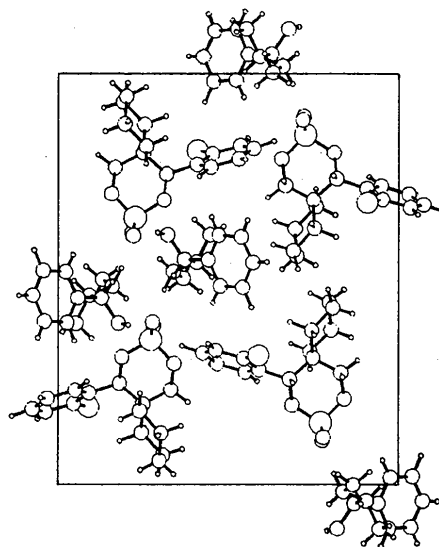


Fig. 2. Molecular packing viewed along the *a* axis.

ephedrine is given in a projection along H(1)—C(1). The molecular packing is shown in Fig. 2.

Related literature. The synthesis of the dioxaphosphorinane, a novel chiral acidic resolving agent, has been described by ten Hoeve & Wynberg (1985). The

present structure, denoted XINAM, is part of a series of structure determinations of phosphorinane and ephedrine salts, performed in order to discover significantly different structural features, as an aid in a resolution protocol. For a more general introduction and reference to related literature we refer to the first paper of this series, INAM (Kok, Wynberg, Smits, Beurskens & Parthasarathi, 1987) and the fourth, CLINAP (Kok, Wynberg, Parthasarathi, Smits & Beurskens, 1987). The present compound, XINAM, is one of a pair of diastereoisomers. The second, denoted XINAP, is presented in the following paper (Kok, Wynberg, García-Granda, Beurskens & Smits, 1988).

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Acta Cryst. (1988). **C44**, 2235–2237

Structure of the Diastereoisomeric Salt of (–)-4-*o*-Chlorophenyl-2-hydroxy-2-oxo-1,3,2-dioxaphosphorinane-5-spirocyclohexane and (1*S*,2*R*)-(+)- α -[(1-Methylamino)ethyl]benzyl Alcohol Monohydrate

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Abstract. $C_{24}H_{33}ClNO_5P.H_2O$, $M_r = 499.97$, orthorhombic, $P2_12_12_1$, $a = 7.927$ (6), $b = 17.744$ (1), $c = 18.697$ (2) Å, $V = 2627.7$ (4) Å³, $Z = 4$, $D_x = 1.26$ g cm⁻³, Cu $K\alpha$ radiation, $\lambda = 1.54184$ Å, $\mu = 21.88$ cm⁻¹, $F(000) = 1064$, $R = 0.042$, $wR = 0.042$ for 3130 observed reflections and 400 variables. The structure was solved by automatic application of the vector-search orientation function and the *DIRDIF* structure expansion procedure. The structure contains phosphorinane anions, ephedrine cations and water molecules, which are linked in a three-dimensional network by N–H...O and O–H...O hydrogen bonds. The phosphorinane ring is in the chair conformation. The ephedrine is in the usual extended form. The

structure of a diastereoisomer is reported by García-Granda, Beurskens, Smits, Kok & Wynberg [*Acta Cryst.* (1988), **C44**, 2233–2235].

Experimental. The title compound was prepared from (–)-phosphorinane and (+)-ephedrine. The colourless crystals were recrystallized twice from ethanol before use. Melting point 490.8 K, solubility at 298 K in 100% ethanol: 16.9 g/100 g solution.

Nearly all X-ray experiments and calculations were performed as described in a foregoing paper on a related compound (INAM; Kok, Wynberg, Smits, Beurskens & Parthasarathi, 1987) and need not be repeated here. Relevant differences are: approximate