Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: LI1143). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Methyl 2,7,7-Trimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate and 3-Acetyl-2,7,7-trimethyl-4-phenyl-1,4,5,6,7,8-hexahydro-5-quinolone

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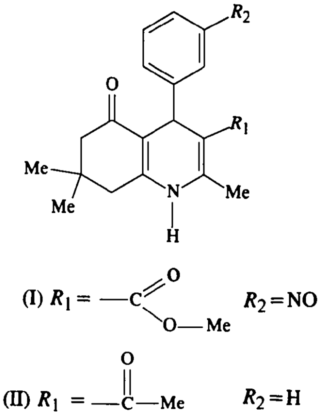
Abstract

The 1,4-dihydropyridine (1,4-DHP) ring and the cyclohexanone ring adopt similar conformations in both the title compounds, methyl 2,7,7-trimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate, $C_{20}H_{22}N_2O_5$, (I) and 3-acetyl-2,7,7-trimethyl-4-phenyl-1,4,5,6,7,8-hexahydro-5-quinolone, $C_{20}H_{23}NO_2$, (II). The 1,4-DHP rings have boat conformations with the aryl group occupying the pseudo-axial position and orthogonal to the plane through the 1,4-DHP ring. The cyclohexanone ring has an intermediate half-chair/sofa form. In both compounds, the carboxyl group is coplanar to the endocyclic double bond as a consequence of π conjugation. The molecules are linked by N—H···O hydrogen bonds but the packing is different in each case. In compound (I) a hydrogen bond is formed between the N—H and the carboxyl group while in compound (II), a hydrogen bond is formed between the N—H and the O atom of the cyclohexanone ring.

Comment

1,4-Dihydropyridines (1,4-DHP) such as nifedipine and other related structures are the most important calcium antagonists and are well established drugs for the treatment of cardiovascular diseases (Bosert & Vater, 1989; Martín-León & Seoane, 1990). In contrast to this, derivatives of 1,4-DHP which are closely related in structure can act as calcium agonists (Goldmann & Stoltefuss, 1991) whereby the 1,4-DHP agonist enhances Ca^{2+} influx across the cell membrane and thus produces quite the opposite pharmacological effect. It has been reported that the presence of fused five-membered lactones or cyclohexanone rings in the 1,4-DHP system leads to compounds which exhibit calcium agonist (Martín-León *et al.*, 1995; Goldmann & Stoltefuss, 1991), or similar effects (Rose & Dräguer, 1992). The crystal structure analyses of the title compounds (I) and (II) were carried out in order to investigate the conformational features of 1,4-DHP when fused with a cyclohexanone ring.



The 1,4-DHP ring and the cyclohexanone ring adopt similar conformations in both compounds. The 1,4-DHP ring has a boat conformation [Q_T = 0.257 (3) and 0.266 (5) Å for compounds (I) and (II), respectively] with two local pseudo-mirror planes, one running along N1···C4 and the other through the midpoints of the C2—C2 and C4a—C8a bonds. The aryl group occupies the pseudo-axial position in both compounds and is orthogonal to the mean plane through the 1,4-DHP ring. In compound (I), the nitro substituent on the phenyl ring is synperiplanar to the H atom H(4) of the 1,4-DHP ring. This is in agreement with the previously reported conformation of the 1,4-DHP moiety (Goldmann & Stoltefuss, 1991).

The cyclohexanone ring has an intermediate half-chair/sofa conformation [Q_T = 0.454 (4) and 0.479 (6) Å for compounds (I) and (II), respectively] with a local pseudo-twofold axis through the midpoints of the C6—C7 and C4a—C8a bonds, and a local pseudo-mirror plane along C7· · ·C4a.

The carboxyl group at C3 is coplanar with the endocyclic double bond in both compounds as a consequence of π conjugation. The molecules are linked by N—H· · ·O hydrogen bonds but the crystallographic packing is different in each case. In compound (I), a hydrogen bond is formed between the N—H group and atom O1 of the carboxyl group of an adjacent molecule, while in compound (II), a hydrogen bond is formed between the N—H group and the atom O2 of the cyclohexanone ring of an adjacent molecule.

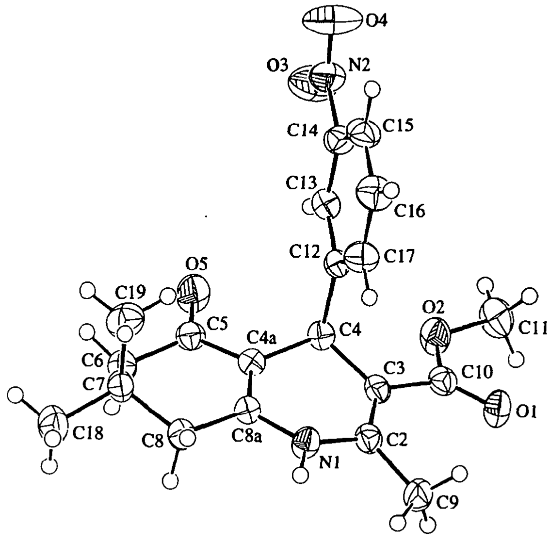


Fig. 1. A view of the molecule of (I) showing the labelling of the non-H atoms. Displacement ellipsoids are shown at the 30% probability level for non-H atoms, H atoms are represented by spheres of arbitrary radius.

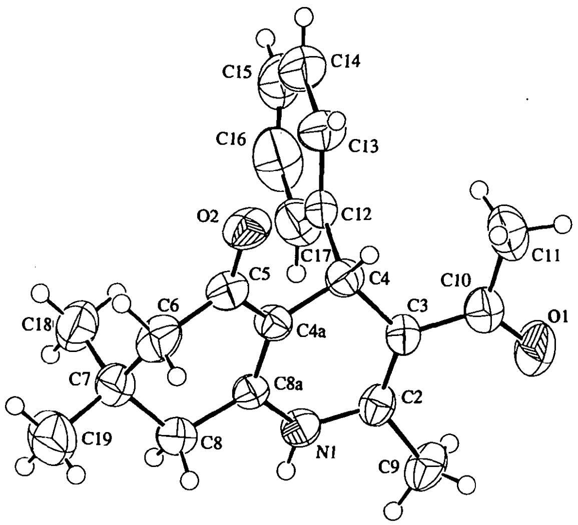


Fig. 2. A view of the molecule of (II) showing the labelling of the non-H atoms. Displacement ellipsoids are shown at the 30% probability level for non-H atoms, H atoms are represent by spheres of arbitrary radius.

Experimental

Compound (I) was prepared by mixing molecular amounts of dimedone, methyl β-aminocrotonate and 3-nitrobenzaldehyde. The mixture was refluxed for 1 h and then poured into iced water. The precipitated solid was collected by filtration. Further purification was accomplished by recrystallization from ethanol. Yield 80%, m.p. 496–497 K.

Compound (II) was prepared in the same way as the previous compound using dimedone, 4-amine-3-penten-2-one and benzaldehyde. Yield 60%, m.p. 485–487 K.

Crystals suitable for X-ray analysis were obtained by slow evaporation of an ethanol solution of each compound.

Compound (I)

Crystal data

$C_{20}H_{22}N_2O_5$
M_r = 370.40
Orthorhombic
Pbca
a = 11.130 (4) Å
b = 13.028 (4) Å
c = 24.74 (2) Å
V = 3587 (3) Å^3
Z = 8
D_x = 1.372 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 10–15°
μ = 0.099 mm^{-1}
T = 293 (2) K
Prismatic
0.3 × 0.2 × 0.2 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: none
3153 measured reflections
3153 independent reflections
1563 observed reflections [$I > 2\sigma(I)$]

$\theta_{\max}$ = 24.97°
$h = 0 \rightarrow 13$
$k = 0 \rightarrow 15$
$l = 0 \rightarrow 29$
3 standard reflections monitored every 200 reflections
frequency: 60 min
intensity decay: 3.9%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0502
$wR(F^2)$ = 0.1132
S = 1.167
3152 reflections
249 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0583P)^2 + 1.3535P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max}$ = 0.340 e Å^{-3}
$\Delta\rho_{\min}$ = −0.247 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

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

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

	x	y	z	U_{eq}
N1	0.1731 (3)	0.8641 (2)	0.31419 (12)	0.0335 (7)
C2	0.1738 (3)	0.7618 (3)	0.29830 (12)	0.0311 (8)
C3	0.0867 (3)	0.6979 (2)	0.31661 (12)	0.0293 (8)
C4	−0.0077 (3)	0.7347 (2)	0.35685 (12)	0.0295 (8)
C4a	−0.0187 (3)	0.8509 (2)	0.35470 (13)	0.0299 (8)
C5	−0.1305 (3)	0.8980 (3)	0.37088 (13)	0.0333 (8)
C6	−0.1396 (3)	1.0131 (3)	0.36613 (15)	0.0405 (9)
C7	−0.0211 (3)	1.0703 (2)	0.37600 (14)	0.0351 (8)
C8	0.0746 (3)	1.0242 (2)	0.33878 (14)	0.0360 (9)
C8a	0.0737 (3)	0.9092 (3)	0.33724 (13)	0.0307 (8)
C9	0.2736 (3)	0.7383 (3)	0.25927 (13)	0.0406 (9)
C10	0.0840 (3)	0.5883 (3)	0.30197 (13)	0.0326 (8)
O1	0.1612 (2)	0.5386 (2)	0.27901 (10)	0.0439 (6)
O2	−0.0196 (2)	0.5454 (2)	0.31794 (10)	0.0441 (7)
C11	−0.0308 (4)	0.4353 (3)	0.3108 (2)	0.0522 (11)
C12	0.0185 (3)	0.6993 (2)	0.41442 (13)	0.0287 (8)
C13	−0.0736 (3)	0.6621 (2)	0.44640 (13)	0.0341 (8)
C14	−0.0496 (3)	0.6323 (3)	0.49869 (14)	0.0364 (9)
C15	0.0631 (4)	0.6370 (3)	0.52096 (14)	0.0425 (10)
C16	0.1548 (4)	0.6734 (3)	0.48907 (15)	0.0458 (10)
C17	0.1324 (3)	0.7042 (3)	0.43663 (14)	0.0408 (9)
N2	−0.1503 (3)	0.5931 (2)	0.53163 (13)	0.0499 (9)
O3	−0.2461 (3)	0.5781 (2)	0.51023 (12)	0.0705 (9)
O4	−0.1326 (3)	0.5761 (3)	0.57949 (12)	0.0886 (11)
O5	−0.2172 (2)	0.8464 (2)	0.38520 (11)	0.0486 (7)
C18	−0.0367 (4)	1.1843 (3)	0.3626 (2)	0.0518 (11)
C19	0.0170 (4)	1.0592 (3)	0.43530 (14)	0.0547 (11)

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

N1—C8a	1.376 (4)	C7—C19	1.534 (5)
N1—C2	1.390 (4)	C8—C8a	1.499 (5)
C2—C3	1.356 (4)	C10—O1	1.217 (4)
C2—C9	1.503 (4)	C10—O2	1.341 (4)
C3—C10	1.474 (5)	O2—C11	1.450 (4)
C3—C4	1.524 (4)	C12—C13	1.382 (5)
C4—C4a	1.520 (5)	C12—C17	1.384 (4)
C4—C12	1.525 (4)	C13—C14	1.377 (5)
C4a—C8a	1.349 (4)	C14—C15	1.371 (5)
C4a—C5	1.444 (5)	C14—N2	1.477 (5)
C5—O5	1.229 (4)	C15—C16	1.375 (5)
C5—C6	1.508 (5)	C16—C17	1.381 (5)
C6—C7	1.535 (5)	N2—O3	1.206 (4)
C7—C18	1.531 (5)	N2—O4	1.220 (4)
C7—C8	1.531 (5)		
C8a—N1—C2	122.1 (3)	C4a—C8a—N1	120.4 (3)
C3—C2—N1	119.3 (3)	C4a—C8a—C8	124.0 (3)
C2—C3—C4	121.2 (3)	O1—C10—O2	121.5 (3)
C4a—C4—C3	110.2 (3)	C13—C12—C17	117.9 (3)
C8a—C4a—C5	120.5 (3)	C14—C13—C12	119.5 (3)
C8a—C4a—C4	120.7 (3)	C15—C14—C13	122.9 (3)
C4a—C5—C6	117.3 (3)	C14—C15—C16	117.6 (3)
C5—C6—C7	114.3 (3)	C15—C16—C17	120.4 (3)
C8—C7—C6	108.2 (3)	C16—C17—C12	121.7 (3)
C8a—C8—C7	113.8 (3)	O3—N2—O4	122.6 (4)
C8a—N1—C2—C3	−15.5 (5)	C6—C7—C8—C8a	−44.5 (4)
C9—C2—C3—C10	4.2 (5)	C4—C4a—C8a—N1	8.9 (5)
N1—C2—C3—C4	−3.6 (5)	C5—C4a—C8a—C8	7.0 (5)
C2—C3—C4—C4a	21.9 (4)	C2—N1—C8a—C4a	12.8 (5)
C3—C4—C4a—C8a	−24.6 (4)	C7—C8—C8a—C4a	16.5 (5)
C8a—C4a—C5—C6	1.4 (5)	C2—C3—C10—O1	9.9 (5)
C4a—C5—C6—C7	−32.8 (4)	C4a—C4—C12—C13	99.6 (4)
C5—C6—C7—C8	53.2 (4)	C4a—C4—C12—C17	−79.5 (4)

Table 3. *Hydrogen-bonding geometry (Å, °) for (I)*

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1^{i}	0.86 (4)	2.21 (4)	3.054 (4)	165 (3)

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

Compound (II)

Crystal data

$C_{20}H_{23}NO_2$
$M_r = 309.41$
Monoclinic
$P2_1/n$
$a = 11.046$ (5) Å
$b = 12.7318$ (8) Å
$c = 12.944$ (5) Å
$\beta = 106.68$ (3)°
$V = 1743.7$ (10) Å^3
$Z = 4$
$D_x = 1.184$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 10$–15°
$\mu = 0.071$ mm^{-1}
$T = 293$ (2) K
Prismatic
0.3 × 0.2 × 0.2 mm
Yellow

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: none
3191 measured reflections
3037 independent reflections
859 observed reflections [$I > 2\sigma(I)$]
$R_{int} = 0.1212$

$\theta_{max} = 24.97°$
$h = -13 \rightarrow 12$
$k = 0 \rightarrow 15$
$l = 0 \rightarrow 15$
3 standard reflections monitored every 200 reflections frequency: 60 min intensity decay: 3.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0591$
$wR(F^2) = 0.1172$
$S = 1.232$
3037 reflections
213 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0579P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.204$ e Å^{-3}
$\Delta\rho_{min} = -0.225$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 4. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2) for (II)*

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

	x	y	z	U_{eq}
N1	0.5489 (4)	0.1999 (4)	0.5766 (4)	0.0498 (14)
C2	0.4921 (5)	0.1169 (4)	0.6129 (4)	0.045 (2)
C3	0.3751 (5)	0.0828 (4)	0.5542 (4)	0.0421 (15)
C4	0.3033 (5)	0.1435 (4)	0.4532 (4)	0.044 (2)
C4a	0.3935 (5)	0.2046 (4)	0.4084 (4)	0.0402 (14)
C5	0.3578 (5)	0.2288 (4)	0.2939 (4)	0.045 (2)
C6	0.4523 (5)	0.2863 (5)	0.2524 (4)	0.061 (2)
C7	0.5348 (5)	0.3665 (5)	0.3329 (5)	0.056 (2)
C8	0.5975 (5)	0.3054 (4)	0.4363 (4)	0.054 (2)
C8a	0.5071 (5)	0.2371 (4)	0.4723 (4)	0.0415 (15)
C9	0.5744 (5)	0.0695 (5)	0.7175 (4)	0.061 (2)
C10	0.3147 (6)	−0.0062 (5)	0.5889 (5)	0.052 (2)
C11	0.1872 (6)	−0.0421 (5)	0.5170 (5)	0.085 (2)
C12	0.2004 (5)	0.2151 (5)	0.4710 (5)	0.049 (2)
C13	0.0787 (6)	0.2140 (5)	0.4000 (5)	0.068 (2)
C14	−0.0134 (7)	0.2771 (6)	0.4160 (8)	0.093 (3)
C15	0.0103 (9)	0.3443 (7)	0.5010 (9)	0.098 (3)
C16	0.1305 (8)	0.3474 (6)	0.5735 (7)	0.090 (3)
C17	0.2251 (6)	0.2835 (5)	0.5575 (6)	0.068 (2)

C18	0.4513 (5)	0.4552 (5)	0.3522 (5)	0.072 (2)
C19	0.6364 (6)	0.4106 (5)	0.2859 (5)	0.091 (2)
O1	0.3601 (4)	−0.0575 (4)	0.6711 (4)	0.086 (2)
O2	0.2555 (3)	0.1988 (3)	0.2318 (3)	0.0597 (12)

Table 5. *Selected geometric parameters (Å, °) for (II)*

N1—C2	1.379 (6)	C7—C18	1.523 (7)
N1—C8a	1.379 (6)	C7—C19	1.529 (7)
C2—C3	1.369 (6)	C7—C8	1.531 (7)
C2—C9	1.522 (6)	C8—C8a	1.496 (6)
C3—C10	1.450 (7)	C10—O1	1.227 (6)
C3—C4	1.530 (6)	C10—C11	1.519 (7)
C4—C4a	1.504 (7)	C12—C17	1.382 (7)
C4—C12	1.526 (7)	C12—C13	1.394 (7)
C4a—C8a	1.355 (6)	C13—C14	1.357 (8)
C4a—C5	1.453 (7)	C14—C15	1.359 (10)
C5—O2	1.244 (5)	C15—C16	1.388 (9)
C5—C6	1.495 (7)	C16—C17	1.386 (8)
C6—C7	1.553 (7)		
C2—N1—C8a	122.7 (5)	C4a—C8a—N1	118.9 (5)
C3—C2—N1	120.2 (5)	C4a—C8a—C8	124.9 (5)
C2—C3—C4	119.3 (5)	O1—C10—C11	116.6 (6)
C4a—C4—C3	110.6 (4)	C17—C12—C13	118.0 (6)
C8a—C4a—C5	119.4 (5)	C14—C13—C12	121.1 (7)
C8a—C4a—C4	121.5 (5)	C13—C14—C15	121.1 (8)
C4a—C5—C6	117.2 (5)	C14—C15—C16	119.3 (8)
C5—C6—C7	114.6 (5)	C17—C16—C15	119.9 (8)
C8—C7—C6	106.5 (5)	C12—C17—C16	120.6 (7)
C8a—C8—C7	113.1 (5)		
C8a—N1—C2—C3	−14.5 (8)	C6—C7—C8—C8a	−47.2 (6)
C9—C2—C3—C10	0.6 (8)	C4—C4a—C8a—N1	10.1 (8)
N1—C2—C3—C4	−5.2 (8)	C5—C4a—C8a—C8	5.4 (8)
C2—C3—C4—C4a	23.8 (7)	C2—N1—C8a—C4a	12.2 (8)
C3—C4—C4a—C8a	−26.6 (7)	C7—C8—C8a—C4a	19.8 (8)
C8a—C4a—C5—C6	2.0 (8)	C2—C3—C10—O1	0.4 (9)
C4a—C5—C6—C7	−34.1 (7)	C4a—C4—C12—C17	−75.9 (7)
C5—C6—C7—C8	55.6 (6)	C4a—C4—C12—C13	103.6 (6)

Table 6. *Hydrogen-bonding geometry (Å, °) for (II)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O2^{i}	0.83 (5)	2.07 (5)	2.864 (8)	160 (5)

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

The structures were solved by direct methods and Fourier synthesis. Non-H atoms were refined anisotropically by full-matrix least-squares techniques. H atoms were calculated geometrically and were refined riding with common isotropic displacement parameters, except for H(1) which was refined isotropically in both structures.

Data collection: *CAD*-4 *Software* (Enraf-Nonius, 1994). Cell refinement: *CRYSDA* (*DIRDIF*; Beurskens *et al.*, 1992). Data reduction: *REFLEX* (local program). Program used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program used to refined structure: *SHELXL*93 (Sheldrick, 1993). Geometrical calculations: *PARST* (Nardelli, 1983). Molecular graphics: *EUCLID* (Spek, 1982). Software used to prepare material for publication: *SHELXL*93.

We would like to acknowledge financial support of the Ministry of Science and Education of Spain for the sabbatical leave to ADM (sab95-0182).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1225). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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The Anhydrous Racemate of the Carcinostatic Agent Cyclophosphamide and the Bicyclic Degradation Product 1-(2-Chloroethyl)tetrahydro-1*H*,5*H*-1,3,2-diazaphospholo[2,1-*b*][1,3,2]oxazaphosphorine 9-Oxide

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Abstract

Anhydrous racemic cyclophosphamide, [(±)-*N*,*N*-bis(2-chloroethyl)-tetrahydro-2*H*-1,3,2-oxazaphosphorin-2-amine 2-oxide, $C_7H_{15}Cl_2N_2O_2P$, (1)], displays a chair conformation with an axial phosphoryl O atom and approximately planar geometry at the N atoms. The molecules are linked by N—H···O═P hydrogen bonds into chains. One chloroethyl side chain is extended, the other is *gauche*. The C—Cl bond lengths are Cl1—C5 1.789 (2) and Cl2—C7 1.791 (2) Å. The bicyclic degradation product, 1-(2-chloroethyl)tetrahydro-1*H*,5*H*-1,3,2-diazaphospholo[2,1-*b*][1,3,2]oxazaphosphorine 9-

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