The crystal contains hydrophobic and hydrophilic zones running alternately, parallel to the *b* axis. The hydrophobic zones are alternate columns of pyrimidine and azido groups. The hydrophilic zones have hydrogen bonds and short contacts between waters *W*1 and *W*2 and O(2′) and O(3′) of the arabinose. The closest contact from the N(3′) atom of the azido group is to the N(1) and C(2) atoms of the neighboring molecules. No significant short contacts are seen between the azido groups themselves.

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Structure of Dimethyl 1,2-Dihydro-1,2,6-trimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylate

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Abstract. $C_{18}H_{20}N_2O_6$, $M_r = 360{\cdot}37$, monoclinic, $P2_1/n$, $a = 9{\cdot}537\ (2)$, $b = 16{\cdot}990\ (4)$, $c = 10{\cdot}909\ (2)$ Å, $\beta = 92{\cdot}48\ (2)°$, $V = 1766$ Å^3, $Z = 4$, $D_x = 1{\cdot}35$ Mg m^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71073$ Å, $\mu = 0{\cdot}096$ mm^{-1}, $F(000) = 760$, $T = 296$ K, $R = 0{\cdot}049$ for 1738 observed reflections. The structure determination of the title compound was undertaken to compare it to structures of 1,4-dihydropyridine analogues in view of the results from competitive binding studies and measurements of its calcium-channel antagonist activity. The major structural difference is the positioning of the aryl substituent relative to the mean plane of the dihydropyridine ring.

Introduction. The utility of 4-aryl-1,4-dihydropyridines related to nifedipine [dimethyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylate] as therapeutic agents in cardiovascular disorders (Janis & Triggle, 1983) has stimulated studies to investigate the geometrical requirements at the 1,4-dihydropyridine binding site. The solid-state conformation of several 1,4-dihydropyridine analogues indicated that the nature of the substituents at the C_3, C_4 and C_5 positions altered the conformation of the 1,4-dihydropyridine ring. In the solid state these compounds exist in a boat conformation where the plane of the C_4-substituted-phenyl ring is in a sterically favored orientation axial to the 1,4-dihydropyridine ring. Strain due to non-bonded interactions involving the C_3, C_4 and C_5 substituents is relieved predominantly by puckering of the 1,4-dihydropyridine ring and distortion of the bond angles about C_4 (Fossheim, 1986; Fossheim, Svarteng, Mostad, Romming, Shefter & Triggle, 1982; Triggle, Shefter & Triggle, 1980). Competitive [^{3}H]-nitrendipine [ethyl methyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylate] binding studies indicated that the receptor affinity for the novel 1,2-dihydropyridine compound (1) was much lower than expected from its calcium-channel antagonist activity (Soboleski, Li-Kwong-Ken, Wynn, Triggle,

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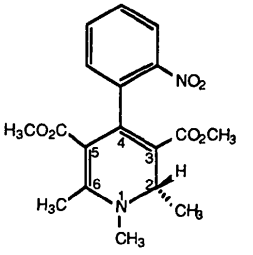
Wolowyk & Knaus, 1986). The conformation of compound (1) is expected to have a number of differences relative to the 1,4-dihydropyridine ring structures. The crystal structure of (1) was therefore investigated to determine its conformation and the structural requirements for the 1,2-dihydropyridine binding site.



(1)

Experimental. Sodium carbonate (10 mmol) was added to a solution of 3,5-bis(methoxycarbonyl)-1,2,6-trimethyl-4-(2-nitrophenyl)pyridinium perchlorate (1·98 mmol) in 98% ethanol (70 ml) and distilled water (7 ml) and the mixture was stirred at 273 K for 1 h. Sodium borohydride (2·8 mmol) was added and the reaction mixture was stirred at 298 K for 20 min. The reaction mixture was filtered and the solvents removed *in vacuo*. The residue obtained was extracted with diethyl ether, dried (Na_2SO_4), filtered and the solvent removed *in vacuo* to afford a white solid, m.p. 419 K (water:ethanol, 1:4 *v/v*).

Crystal size 0·31 × 0·11 × 0·28 mm. CAD-4 diffractometer. Lattice parameters determined using 25 reflections with $9 < 2\theta < 24°$. Data corrected for Lorentz–polarization and background effects. No absorption correction. Intensity measurements in range $0 < 2\theta < 55°$ (index limits: h 12; k 22; $l \pm 14$). Intensity standards: 032, 150, 404; min. max. and mean change (%) in intensity standards: 0·1, −0·9, −0·4. 4438 reflections measured, 4047 unique, 1738 observed [$I > 3\sigma(I)$], $R_{int} = 0·026$. Solved by direct methods using *MULTAN*11/82 (Main *et al.*, 1982). Full-matrix least-squares refinement using F magnitudes. All H atoms located in a difference Fourier synthesis and used to calculate idealized coordinates (C–H 0·95 Å). H-atom positional parameters were constrained to 'ride' with the appropriate C atom and the thermal parameters were kept fixed at values 20% greater than those of the attached C atom. Positional and anisotropic thermal parameters for all non-H atoms were refined. $R = 0·049$, $wR = 0·059$, $S = 1·74$. Weights of $1/\sigma^2(F)$ with $\sigma(F)$ defined by Stout & Jensen (1968) with instability factor 0·04. $(\Delta/\sigma)_{max} = 0·03$. Max. peak height in final difference Fourier map 0·34 (5) e Å^{-3}. No secondary-extinction correction. Atomic scattering factors, f' and f'' values from *International Tables for X-ray Crystallography* (1974). Computer programs used include the Enraf–Nonius (1983) *SDP* and *ORTEP* (Johnson, 1976). Positional and equivalent isotropic thermal parameters are listed in Table 1.*

Table 1. *Positional* (×10⁴) *and equivalent isotropic thermal* (×10²) *parameters*

	x	y	z	U_{eq}(Å²)
O1	6593 (2)	1111 (2)	6139 (2)	6·9 (1)
O2	8908 (2)	1285 (1)	6252 (2)	5·10 (8)
O3	9664 (3)	1272 (2)	348 (2)	7·9 (1)
O4	11048 (3)	1536 (2)	1930 (2)	7·4 (1)
O5	9120 (3)	2849 (2)	3369 (2)	7·30 (9)
O6	10210 (3)	3474 (1)	4823 (3)	8·0 (1)
N1	6516 (3)	577 (2)	2592 (2)	4·39 (9)
N2	9993 (3)	2879 (2)	4200 (3)	4·85 (9)
C1	8924 (3)	1265 (2)	3614 (3)	3·16 (9)
C2	8797 (3)	1068 (2)	2324 (3)	3·50 (9)
C3	7639 (3)	616 (2)	1911 (3)	4·1 (1)
C4	6370 (3)	1139 (2)	3598 (3)	4·4 (1)
C5	7763 (3)	1214 (2)	4295 (3)	3·44 (9)
C6	7686 (3)	1203 (2)	5628 (3)	3·9 (1)
C7	8876 (4)	1201 (3)	7566 (3)	7·1 (1)
C8	5824 (4)	1929 (2)	3121 (3)	6·0 (1)
C9	5300 (4)	78 (2)	2299 (4)	6·7 (1)
C10	7640 (4)	114 (2)	785 (4)	6·3 (1)
C11	9846 (3)	1281 (2)	1442 (3)	4·0 (1)
C12	12104 (4)	1792 (3)	1141 (4)	6·9 (1)
C13	10337 (3)	1434 (2)	4201 (3)	3·12 (9)
C14	10844 (3)	2176 (2)	4511 (3)	3·57 (9)
C15	12139 (3)	2304 (2)	5091 (3)	4·7 (1)
C16	12991 (3)	1667 (2)	5358 (3)	5·4 (1)
C17	12533 (3)	920 (2)	5057 (3)	5·2 (1)
C18	11232 (3)	807 (2)	4484 (3)	4·3 (1)

$U_{eq} = \frac{1}{3}\sum r_i^2$ where r_i are the root-mean-square amplitudes of vibration.

Discussion. Although many crystal structures of various substituted 1,4-dihydropyridines have been reported (Fossheim *et al.*, 1982; Triggle *et al.*, 1980; Tacke, Bentlage, Sheldrick, Ernst, Towart & Stoepel, 1982), 1,2-dihydropyridines have undergone very little investigation. We are aware of a few $Cr(CO)_3$ complexes (Bear & Trotter, 1973; Trotter & Mak, 1980) but of only one other structure of an uncomplexed compound (Krow, Raghavachari, Siatkowski & Chodosh, 1986). A drawing of the title compound is shown in Fig. 1 along with the arbitrary atomic-labeling scheme. Bond distances and angles are presented in Table 2.

Although the compound is a 1,2-dihydropyridine (1,2-DHP) derivative it is obvious from the bond distances that strict localization of the double bonds, particularly at the C_5–C_6† site, does not occur. The

* Lists of observed and calculated structure factors, anisotropic thermal parameters, H positional parameters, torsion angles and least-squares planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43974 (28 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

† Reference to the positions of the DHP ring in (1) is by a subscripted C. Reference to the atoms in the crystal structure is made with unsubscripted labels.

C1—C5 distance of 1·362 (3) Å indicates conjugation with the $-CO_2Me$ substituent on C5 as does the shortening of C5—C6 [1·459 (3) Å *vs* approximately 1·50 Å for a Csp^2–Csp^2 single bond]. The observed torsion angle for C1—C5—C6—O1 of −175·7 (3)° is also consistent with conjugation amongst these atoms. The other 'double bond' between C2 and C3 shows an even greater lengthening to 1·404 (3) Å and appears to be partially conjugated with the $-CO_2Me$ group on C2 [C2—C11 1·464 (3) Å; C3—C2—C11—O3 18·8 (5)°] and strongly conjugated with the lone pair on the N atom because the Csp^2–N distance [N1—C3 1·330 (3) Å] is much shorter than the expected single-bond value of 1·4 Å. The N1—C4 and N1—C9 distances, both N—Csp^2, are normal at 1·466 (3) and 1·461 (3) Å, respectively.

Overall the DHP ring adopts a distorted 'boat'-type conformation in which C4 is twisted well out of the mean plane formed by the other five atoms of the ring. The alkyl and ester substituents on the ring, with the exception of the methyl group on C4, are all disposed equatorially to the ring. The methyl substituent on C4 is oriented axially to the 1,2-DHP ring putting the sterically smaller H atom in the plane of the ester and alkyl substituents on the neighboring C5 and N1 atoms. The closest non-bonding distance to this methyl group is 2·91 Å between H2C8 and O5 of the aryl nitro group.

Both carbonyl groups of the two ester substituents are oriented in the same direction with respect to the DHP ring, thus making a synperiplanar and anti-periplanar configuration with respect to the nominal positions for the double bonds in the ring. Both symmetrical (as in this structure) and unsymmetrical orientations of these carbonyls are seen in related 1,4-DHP compounds (Fossheim *et al.*, 1982; Triggle *et al.*, 1980; Fossheim, 1986; Tacke *et al.*, 1982) and presumably only minor structural differences will result in one orientation being preferred to the other.

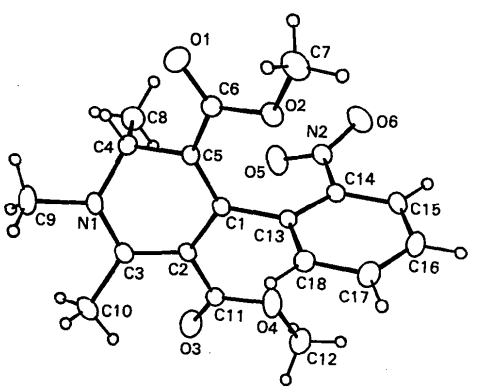


Fig. 1. Perspective view of the molecule showing the atomic-labeling scheme. Atoms are drawn at the 20% probability level except for the H atoms which are an arbitrary size.

Table 2. *Bond distances* (Å) *and angles* (°)

O1	C6	1·214 (3)		C1	C13	1·494 (3)	
O2	C6	1·331 (3)		C2	C3	1·404 (3)	
O2	C7	1·442 (3)		C2	C11	1·464 (3)	
O3	C11	1·198 (3)		C3	C10	1·496 (4)	
O4	C11	1·317 (3)		C4	C5	1·508 (3)	
O4	C12	1·420 (3)		C4	C8	1·523 (4)	
O5	N2	1·206 (3)		C5	C6	1·459 (3)	
O6	N2	1·230 (3)		C13	C14	1·388 (3)	
N1	C3	1·330 (3)		C13	C18	1·391 (3)	
N1	C4	1·466 (3)		C14	C15	1·380 (3)	
N1	C9	1·461 (3)		C15	C16	1·377 (4)	
N2	C14	1·475 (3)		C16	C17	1·377 (4)	
C1	C2	1·446 (3)		C17	C18	1·378 (3)	
C1	C5	1·362 (3)					
C6	O2	C7	116·3 (2)	C1	C5	C4	116·7 (2)
C11	O4	C12	118·9 (2)	C1	C5	C6	128·4 (2)
C3	N1	C4	119·4 (2)	C4	C5	C6	114·9 (2)
C3	N1	C9	123·8 (2)	O1	C6	O2	121·9 (2)
C4	N1	C9	116·2 (2)	O1	C6	C5	122·7 (2)
O5	N2	O6	123·0 (3)	O2	C6	C5	115·3 (2)
O5	N2	C14	119·5 (2)	O3	C11	O4	119·6 (2)
O6	N2	C14	117·4 (2)	O3	C11	C2	125·3 (2)
C2	C1	C5	118·7 (2)	O4	C11	C2	115·0 (2)
C2	C1	C13	119·8 (2)	C1	C13	C14	125·2 (2)
C5	C1	C13	121·2 (2)	C1	C13	C18	118·8 (2)
C1	C2	C3	118·1 (2)	C14	C13	C18	116·0 (2)
C1	C2	C11	123·5 (2)	N2	C14	C13	119·9 (2)
C3	C2	C11	118·3 (2)	N2	C14	C15	116·8 (2)
N1	C3	C2	119·2 (2)	C13	C14	C15	123·4 (2)
N1	C3	C10	117·4 (2)	C14	C15	C16	118·8 (3)
C2	C3	C10	123·2 (2)	C15	C16	C17	119·7 (2)
N1	C4	C5	108·8 (2)	C16	C17	C18	120·4 (3)
N1	C4	C8	111·1 (2)	C13	C18	C17	121·7 (2)
C5	C4	C8	112·2 (2)				

Numbers in parentheses are e.s.d.'s in the least-significant digits.

In discussions of the structures of 1,4-DHP compounds (Fossheim *et al.*, 1982; Triggle *et al.*, 1980; Fossheim, 1986) much attention is paid to the flatness of the DHP ring as this appears to correlate with the degree of biological activity of these compounds as Ca^{2+} antagonists. In the present compound the puckering of the DHP ring, as measured by the sum of the absolute values of the torsion angles for the ring atoms, is quite large (153°) when compared to the range of values seen in several 1,4-DHP compounds (52·1–112·5°). This large value arises mostly from the high degree of out-of-plane bending of C4 since the other five atoms comprise a reasonably planar grouping.

With position C_4 of the 1,4-DHP ring being sp^3 in nature, as opposed to sp^2 for 1,2-DHP, the position of the aryl substituent at this site is much different in the 1,2-DHP structure than the 1,4-DHP analogues. The aryl ring in the 1,4-DHP molecules universally adopts an axial orientation with respect to the DHP ring. This puts the centroid of the aryl ring over the DHP ring and steric constraints force an orientation such that the plane normal is approximately perpendicular to that of the DHP ring. With 1,2-DHP, however, C_4 is an sp^2 carbon which constrains the aryl substituent to lie in the plane of the atoms C1—C2—C5. Thus, in contrast to the 1,4-DHP case, the centroid of the aryl ring is

approximately in the plane of the DHP ring. Steric considerations still require that the normals for the aryl and DHP rings be approximately perpendicular, however. The phenyl ring may adopt an orientation which puts the *ortho*-NO_2 substitutent either above or below the plane formed by C1–C2–C5. Since the DHP ring is neither flat nor symmetrically substituted these two orientations will be of different energies. The orientation observed is the one in which the NO_2 group is on the same side of the ring as the methyl group C8.

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Structure of *N*-(*N*-Isopropyl-*N*-propylaminoethyl)phenothiazine Hydrochloride

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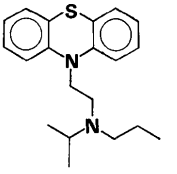
(*Received* 4 *June* 1986; *accepted* 10 *April* 1987)

Abstract. $C_{20}H_{27}N_2S^+.Cl^-$, $M_r = 362{\cdot}9$, monoclinic, $P2_1/c$, $a = 12{\cdot}204\ (2)$, $b = 12{\cdot}032\ (2)$, $c = 13{\cdot}643\ (3)$ Å, $\beta = 103{\cdot}21\ (2)°$, $V = 1950{\cdot}4$ Å^3, $Z = 4$, $D_x = 1{\cdot}236$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}70930$ Å, $\mu = 3{\cdot}0$ cm^{-1}, $F(000) = 776$, $T = 100\ (2)$ K, final $R = 0{\cdot}051$ for 2469 reflections. The title compound crystallizes with a 'butterfly' fold angle of 134·7° between the two benzo rings. The N atom in the side chain is protonated and there is a hydrogen bond between it and the chloride ion. There are no unusual intramolecular distances or angles.

Introduction. Phenothiazine derivatives form a class of drugs which can be used as neuroleptics, sedatives, analgesics, anti-emetics and antihistamines. Although the pharmacological activity of the title compound has not been fully tested, the substituent bound to the phenothiazine skeleton causes this compound to be structurally similar to compounds that are known to possess anti-parkinsonian activity (diethazine and isothiazine) and antihistaminic activity (promethazine and thiazinamium methyl sulfate) (Tollenaere, Moereels & Raymaekers, 1979). In order better to understand the varied pharmacological activity of these compounds, we have been studying the structural characteristics of a series of phenothiazine derivatives (Klein, Conrad & Morris, 1985; Klein & Conrad, 1986; Southall, Malmstrom & Klein, 1987).



Experimental. Colorless crystal, approximate dimensions 0·30 × 0·25 × 0·40 mm recrystallized from a dichloromethane, hexane, 2-propanol (5:3:1) solution. Enraf–Nonius CAD-4 diffractometer with graphite-

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