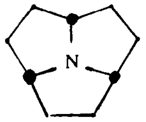
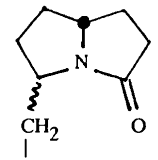
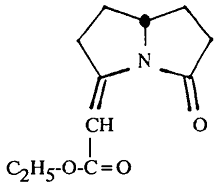
the N atom is *ca* 0·20 Å from the plane of its substituents, there is no pyramidalization at N1 [angle sum 359·8 (2)°]; in (5) and (6) the corresponding angle sums at N are 355·7 (2) and 358·9 (2)° respectively.


(1)



(2*a endo*)
(2*b exo*)



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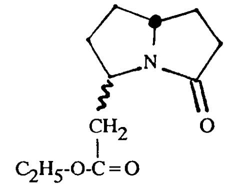

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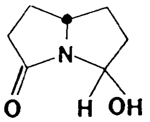

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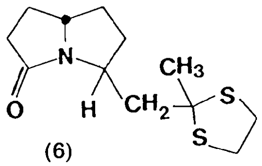
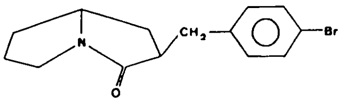


(6)



(7)

The molecular dimensions for (2*a*) are in accord with anticipated values (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987), and with the values found in (5) and in (6), with the same large external angle at C2—N1—C8 [131·6 (2)° in (2*a*), 128·0 (2)° in (5) and 130·7 (6)° in (6)]. The orientation of the —CH$_2$—C=O moiety at C8 is defined by the C8—C9—C10—O2 torsion angle (−33·0°) and is such that the carbonyl oxygen O2 is *cis* to the *exo* hydrogen at C8; such an orientation is well known for similar side chains (Mathieson, 1965). There are no unusual intermolecular contacts. Work is in progress on routes which may convert (2*a*) to (1).

We thank NSERC Canada for financial support through the award of an Operating Grant.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, G. A. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans,* 2, pp. S1–S19.

B. A. Frenz & Associates Inc. (1983). *SDP-Plus.* College Station, Texas 77840, USA, and Enraf–Nonius, Delft, The Netherlands.

Flippen-Anderson, J. L., D'Antonio, P. & Konnert, J. H. (1984). *J. Cryst. Spectrosc. Res.* **14**, 565–572.

Flitsch, W. & Muter, B. (1971). *Chem. Ber.* **104**, 2852–2855.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1982). *MULTAN*82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs., of York, England, and Louvain, Belgium.

Mathieson, A. McL. (1965). *Tetrahedron Lett.* pp. 4137–4140.

Winkler, F. K. (1979). *Cryst. Struct. Commun.* **8**, 553–558.

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Structure of *N*-(2,4-Dinitrophenyl)-4-(1-pyrrolyl)pyridinium Chloride Sesquihydrate

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Abstract. $C_{15}H_{11}N_4O_4^+.Cl^-.1\cdot5H_2O$, $M_r = 373\cdot8$, monoclinic, $C2/c$, $a = 14\cdot970\ (3)$, $b = 13\cdot301\ (3)$, $c = 17\cdot544\ (4)$ Å, $\beta = 103\cdot30\ (2)°$, $V = 3400\ (2)$ Å^3, $Z = 8$, $D_x = 1\cdot46$ g cm^{-3}, $\lambda(\mathrm{Mo}\ K\alpha) = 0\cdot71073$ Å, $\mu = 2\cdot6$ cm^{-1}, $F(000) = 1544$, $T = 294$ K, $R = 0\cdot043$ for 2059 observed reflections. In the cation, the pyrrolyl and pyridinium rings are almost coplanar and the bond lengths are consistent with there being conjugation between them. The phenyl ring is inclined at 59·5° to the pyridinium plane. The chloride ion and water molecules are linked by a network of O—H···Cl hydrogen bonds 3·296 (3) to 3·428 (3) Å.

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Introduction. In connection with studies on the synthesis of certain heterocyclic derivatives, we required relatively large amounts of *N*-(2,4-dinitrophenyl)-4-(1-pyrrolyl)pyridinium chloride (1), whose preparation in the anhydrous form has been reported (Katritzky, Lewis, Musumarra & Ogretir, 1976). Our synthesis followed a route similar to that of Katritzky *et al.* (1976), *viz* preparation of 4-(1-pyrrolyl)pyridine (2) by condensation of 4-aminopyridine with 2,5-dimethoxytetrahydrofuran, followed by reaction of (2) with 1-chloro-2,4-dinitrobenzene. By modification of the reported procedures,* somewhat improved yields were obtained in both steps (78·1 and 85·8% respectively). Purification of the final product by recrystallization from water gave yellow cubes of the sesquihydrate [(1).1·5H_2O]. We undertook an X-ray analysis to determine the conformation in the solid state and the extent of conjugation between the rings.

Experimental. Accurate cell dimensions and crystal orientation matrix were determined on a CAD-4 diffractometer by a least-squares treatment of the setting angles of 25 reflections in the range $6 < \theta < 15°$. Crystal dimensions 0·38 × 0·40 × 0·42 mm; intensities of reflections with indices h −17 to 17, k 0 to 17, l 0 to 20, with $2 < 2\theta < 50°$ measured; ω–2θ scans, ω-scan width $(0·60 + 0·35\tan\theta)°$; graphite-monochromatized Mo $K\alpha$ radiation; intensities of three reflections measured every 2 h showed no evidence of crystal decay. 3296 reflections measured, 2988 unique, 2059 with $I > 3\sigma(I)$ labelled observed and used in structure solution and refinement, $R_{\rm int}$ = 0·019. Data were corrected for Lorentz and polarization effects. The systematic absences (hkl absent if $h + k = 2n + 1$, $h0l$ absent if $l = 2n + 1$) allow the space group to be either $C2/c$ or Cc, the former was assumed and confirmed by the successful analysis. The structure was solved with the aid of *MULTAN*82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982). One water molecule lies in a general position and the other has the O atom on a twofold crystallographic axis. Refinement was by full-matrix least-squares calculations, initially with isotropic and then with anisotropic thermal parameters. Difference maps showed maxima consistent with the anticipated locations of all H atoms. In the final rounds of calculations the H atoms were positioned on geometrical grounds (C—H, O—H 0·95 Å) and included (as riding atoms)

Table 1. *Positional and equivalent isotropic thermal parameters with their e.s.d.'s*

$$B_{\rm eq} = (4/3)[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)].$$

	x	y	z	$B_{\rm eq}$(Å^2)
Cl	0·16865 (5)	0·23181 (6)	0·34710 (5)	5·51 (2)
N1	0·4083 (1)	0·0303 (1)	0·0576 (1)	3·05 (4)
C2	0·3773 (2)	0·1178 (2)	0·0156 (2)	3·72 (6)
C3	0·2877 (2)	0·1058 (2)	−0·0173 (2)	4·26 (6)
C4	0·2611 (2)	0·0103 (2)	0·0023 (2)	4·25 (6)
C5	0·3340 (2)	−0·0346 (2)	0·0482 (2)	3·71 (6)
N6	0·6671 (1)	−0·0185 (2)	0·1972 (1)	2·98 (4)
C7	0·6507 (2)	0·0645 (2)	0·1516 (2)	3·28 (5)
C8	0·5664 (2)	0·0824 (2)	0·1055 (1)	3·18 (5)
C9	0·4950 (1)	0·0135 (2)	0·1033 (1)	2·91 (5)
C10	0·5152 (2)	−0·0737 (2)	0·1488 (2)	3·37 (5)
C11	0·6001 (2)	−0·0878 (2)	0·1949 (2)	3·38 (5)
C12	0·7564 (2)	−0·0374 (2)	0·2476 (1)	3·08 (5)
C13	0·7984 (2)	0·0259 (2)	0·3092 (1)	3·19 (5)
C14	0·8823 (2)	0·0031 (2)	0·3554 (2)	3·56 (5)
C15	0·9235 (2)	−0·0849 (2)	0·3412 (2)	3·39 (6)
C16	0·8848 (2)	−0·1486 (2)	0·2820 (2)	3·71 (6)
C17	0·8011 (2)	−0·1238 (2)	0·2349 (2)	3·56 (6)
N18	0·7544 (2)	0·1193 (2)	0·3281 (1)	4·14 (5)
O19	0·6719 (1)	0·1276 (2)	0·3070 (1)	5·12 (5)
O20	0·8053 (2)	0·1829 (2)	0·3653 (1)	5·92 (6)
N21	1·0128 (1)	−0·1107 (2)	0·3919 (2)	4·80 (6)
O22	1·0454 (2)	−0·0536 (2)	0·4450 (2)	8·09 (7)
O23	1·0502 (1)	−0·1874 (2)	0·3779 (1)	6·04 (6)
O*W*1	0·1267 (2)	0·2155 (2)	0·5250 (2)	7·56 (6)
O*W*2	0·0	0·0899 (3)	0·25	11·5 (2)

Table 2. *Molecular dimensions*

(*a*) Bond lengths (Å)

N1	C2	1·399 (3)	C12	C17	1·374 (4)
N1	C5	1·387 (3)	C13	C14	1·362 (3)
N1	C9	1·378 (3)	C13	N18	1·479 (3)
C2	C3	1·343 (4)	C14	C15	1·372 (4)
C3	C4	1·397 (4)	C15	C16	1·362 (3)
C4	C5	1·339 (3)	C15	N21	1·467 (3)
N6	C7	1·352 (3)	C16	C17	1·373 (3)
N6	C11	1·356 (3)	N18	O19	1·210 (3)
N6	C12	1·445 (3)	N18	O20	1·221 (3)
C7	C8	1·354 (3)	N21	O22	1·213 (4)
C8	C9	1·401 (3)	N21	O23	1·215 (3)
C9	C10	1·400 (3)	Cl···O*W*1		3·329 (3)
C10	C11	1·354 (3)	Cl···O*W*1$^{\rm i}$		3·428 (3)
C12	C13	1·400 (3)	Cl···O*W*2		3·296 (3)

(*b*) Bond angles (°)

C2	N1	C5	107·2 (2)	C12	C13	N18	122·3 (2)
C2	N1	C9	126·5 (2)	C14	C13	N18	116·8 (2)
C5	N1	C9	126·2 (2)	C13	C14	C15	118·3 (2)
N1	C2	C3	107·7 (2)	C14	C15	C16	122·6 (2)
C2	C3	C4	108·4 (2)	C14	C15	N21	118·3 (2)
C3	C4	C5	108·4 (2)	C16	C15	N21	119·0 (2)
N1	C5	C4	108·3 (2)	C15	C16	C17	118·6 (2)
C7	N6	C11	120·3 (2)	C12	C17	C16	121·0 (2)
C7	N6	C12	121·4 (2)	C13	N18	O19	118·9 (2)
C11	N6	C12	118·2 (2)	C13	N18	O20	116·5 (2)
N6	C7	C8	120·9 (2)	O19	N18	O20	124·6 (2)
C7	C8	C9	120·1 (2)	C15	N21	O22	117·9 (2)
N1	C9	C8	121·4 (2)	C15	N21	O23	118·1 (2)
N1	C9	C10	121·1 (2)	O22	N21	O23	123·9 (2)
C8	C9	C10	117·5 (2)	O*W*1···Cl···O*W*1$^{\rm i}$			74·5 (1)
C9	C10	C11	120·3 (2)	O*W*1···Cl···O*W*2			99·2 (1)
N6	C11	C10	120·6 (2)	O*W*1$^{\rm i}$···Cl···O*W*2			156·7 (8)
N6	C12	C13	123·8 (2)	Cl···O*W*1···Cl$^{\rm i}$			105·5 (1)
N6	C12	C17	117·6 (2)	Cl···O*W*2···Cl$^{\rm ii}$			110·1 (1)
C13	C12	C17	118·6 (2)				
C12	C13	C14	120·9 (2)				

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

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* Full details of the synthetic procedures and tables of calculated hydrogen coordinates, anisotropic thermal parameters, mean plane data and lists of structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52655 (27 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

in the structure-factor calculations with an overall $B_{\rm iso}$ of 6·0 Å^2 for the water H atoms and 3·5 Å^2 for the remainder. An extinction correction was also refined (final value $3{\cdot}0 \times 10^{-6}$). The final cycle of refinement included 232 variable parameters, R = 0·043, wR = 0·060, goodness-of-fit 2·16 $w = 1/[\sigma^2(F_o) + 0{\cdot}04(F_o)^2]$, $w(\Delta F)^2$ minimized. Max. shift/e.s.d. in final refinement cycle < 0·005; density in final difference map ±0·48 e Å^{-3}; there were no chemically significant features. Scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974). All calculations were performed on a PDP11/73 computer using *SDP-Plus* (Frenz, 1983). Atomic coordinates* and details of molecular geometry are given in Tables 1 and 2. Fig. 1 is a view of the molecule prepared using *ORTEP*II (Johnson, 1976).

Discussion. In the cation (Fig. 1), the pyrrolyl and pyridinium rings are almost coplanar (interplanar angle 6·4°). Intramolecular overcrowding associated with the 2-nitro group causes the pyridinium and phenyl rings to be rotated about the N6—C12 bond through 59·5° from planarity. There is thus little possibility of the phenyl ring being in conjugation with the pyrrolylpyridinium system. Examination of the bond lengths (Table 2) reveals that there is considerable conjugation between the pyrrolyl and pyridinium rings, consistent with a significant contribution from a canonical form such as shown in (1*a*) to the ground-state structure of the cation. Thus, the N(pyrrolyl)—C(pyridinium) bond [N1—C9 1·378 (3) Å] is 0·067 Å shorter than the N(pyridinium)—C(phenyl) bond [N6—C12 1·445 Å], consistent with significant double-bond character for the former. In the pyridinium ring, the C7—C8 and C10—C11 bonds [both 1·354 (3) Å] are shorter, and the C8—C9 and C9—C10 bonds are longer [mean C—C 1·401 (3) Å] than values found for the corresponding bonds in 151 pyridinium cations (1·373 and 1·383 Å respectively; Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987); the C—N distance is also longer [mean 1·354 (3) Å] than that found in pyridines (1·337 Å, Allen *et al.*, 1987). In the cyanoborane adduct of 4-(dimethylamino)pyridine (3) a formulation similar to that inferred for (1) was found with three localized double bonds (Ferguson, Kaitner, Myers & Spalding, 1990). The bonds in the pyrrole ring also show an alternation consistent with formulation (1*a*), with the mean ring distances [C—N 1·393 (3), C=C 1·341 (3), C—C 1·397 (4) Å]; in unconjugated pyrroles (Allen *et al.*, 1987) the distances found for these bonds are C—N 1·372, C=C 1·375, C—C 1·412 Å. The remaining bond lengths in (1) are in accord with anticipated values.

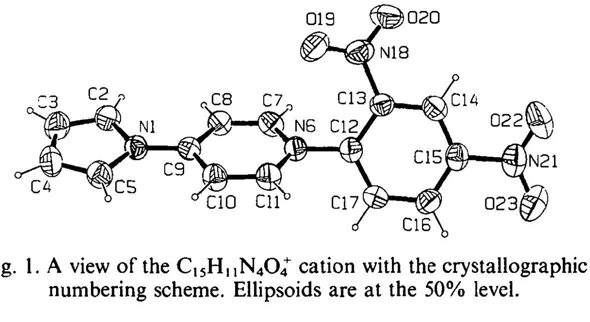
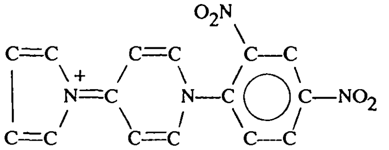
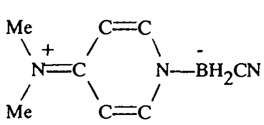


Fig. 1. A view of the $C_{15}H_{11}N_4O_4^+$ cation with the crystallographic numbering scheme. Ellipsoids are at the 50% level.



(1*a*)



(3)

Overcrowding with the adjacent pyridinium ring results in the 2-nitro group (at C13) being rotated 22·5° from the phenyl plane about the exocyclic C—N bond and also causes the N6—C12—C13 angle [123·8 (2)°] to be enlarged over N6—C12—C17 [117·6 (2)°] The remote 4-nitro group (at C15) is essentially coplanar with the phenyl ring (interplanar angle 1·2°).

In the crystal lattice the oxygen of one water molecule (O2) lies on a twofold crystallographic axis and the other is in a general position. The chloride ion takes part (with the water O—H groups) in three O···H···Cl hydrogen bonds (Table 2), with O···Cl 3·296 (3) to 3·428 (3) Å. In this way eight-membered centrosymmetric hydrogen-bonded rings are formed; these rings are then linked to form infinite chains by the hydrogen bonds involving the water molecule on the twofold axis as shown schematically in Fig. 2.

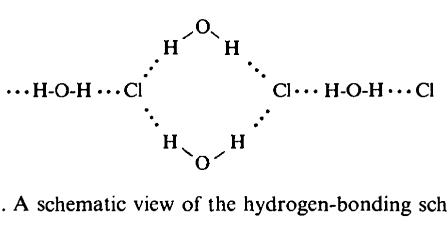


Fig. 2. A schematic view of the hydrogen-bonding scheme.

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* See previous footnote.

There are no hydrogen bonds between water molecules. The shortest inter-ion contact is 3·173 (3) Å between pyrrolyl nitrogen N1 (which would have a formal positive charge in canonical form 1*a*) and nitro oxygen O19 of a symmetry-related cation (at $1 - x, y, \frac{1}{2} - z$).

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References

ALLEN, F. H., KENNARD, O., WATSON, D. G., BRAMMER, L., ORPEN, G. A. & TAYLOR, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–S19.

FERGUSON, G., KAITNER, B., MYERS, M. & SPALDING, T. R. (1990). *Acta Cryst.* C46, 125–126.

FRENZ, B. A. (1983). *SDP-Plus Structure Determination Package*, College Station, Texas, USA, and Enraf–Nonius, Delft, The Netherlands.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

KATRITZKY, A. R., LEWIS, J., MUSUMARRA, G. & OGRETIR, C. (1976). *Chim. Acta Turc.* **4**, 71–80.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN82. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

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Structures of Leukotriene Antagonists: Racemic 2-Hydroxy-3-[2-(8-phenyloctyl)phenyl]-4-thiaheptanedioic Acid, SK&F 103944

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Abstract. $C_{26}H_{34}O_5S$, $M_r = 458{\cdot}62$, monoclinic, $C2/c$, $a = 26{\cdot}686$ (7), $b = 16{\cdot}479$ (4), $c = 11{\cdot}988$ (5) Å, $\beta = 105{\cdot}37$ (3)°, $V = 5083{\cdot}1$ (10) Å^3, $Z = 8$, D_m (flotation in aqueous $ZnCl_2$) = 1·20 (2), $D_x = 1{\cdot}198$ g cm^{-3}, λ(Mo $K\overline{\alpha}$) = 0·71073 Å, $\mu = 1{\cdot}516$ cm^{-1}, $F(000) = 1968$, $T = 293$ K, $R = 0{\cdot}048$, $wR = 0{\cdot}054$ for 2726 observations, $I \geq 3\sigma(I)$. The 2-hydroxy-3-[2-(8-phenyloctyl)phenyl]-4-thiaheptanedioic acid molecule, a member of a novel class of selective leukotriene receptor antagonists, has its all-*trans* phenyloctyl and mercaptopropionate chains each fully extended. In the hydroxyacetate chain both the carboxylic and hydroxyl groups are *gauche* to the phenyl ring. The interphenyl dihedral angle is 67·3 (3)°. Hydrophobic and hydrophilic groups are segregated by the molecular packing. Lipophilic chains pack in a head-to-tail fashion. There are three intermolecular, and possibly two intramolecular, hydrogen bonds clustered in a channel parallel to **c**. The molecular conformation resembles that which we reported for a prototype of the related dithia class of antagonists.

Introduction. Leukotrienes LTC_4, D_4 and E_4 are released upon antigenic challenge of sensitized human lung tissue and are known to be causative agents of bronchoconstriction (Dahlen, Hedquist, Hammarstrom & Samuelsson, 1980), mucous production (Marom, Shelhamer, Bach, Morton & Kaliner, 1982) and microvascular permeability (Peck, Piper & Williams, 1981; Woodward, Weichman, Gill & Wasserman, 1983). These substances are involved in the pathophysiology of allergic asthma and are implicated in certain non-immunologically driven diseases (Lefer, 1986; Feuerstein, 1985). Leukotrienes exert their pharmacological effects *via* receptor-mediated events. The identification of LTD_4-specific binding sites in human and animal tissues (Lewis, Mong, Vessella & Crooke, 1985; Mong, Wu, Hogaboom, Clark & Crooke, 1984; Pong & DeHaven, 1983) has spurred considerable research efforts toward the design and synthesis of high-affinity peptidoleukotriene receptor antagonists (Gleason *et al.*, 1983; Gleason *et al.*, 1987; Perchonock *et al.*, 1985*a*; Ku, McCarthy, Weichman & Gleason 1985; Perchonock *et al.*, 1985*b*). These efforts have resulted in the identification of a series of [(phenyloctyl)phenyl]-propionic acids as novel, potent, specific, high-affinity leukotriene receptor antagonists. We report

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