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1,1-Dimethyl-5-phenyl-1,2,5-triazapentadienium Picrate

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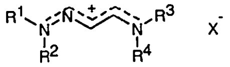
Abstract

The structure determination of 1,1-dimethyl-5-phenyl-1,2,5-triazapentadienium picrate, $C_{10}H_{14}N_3^+.C_6H_2N_3O_7^-$, illustrates the effects of two factors on the internal geometry of the 1,2,5-triazapentadienium system. The first is the presence at the 5 position of an aryl group, the second the existence of hydrogen bonding in the form of an N···O interionic contact of 2.784 (6) Å between the cation and the phenolic O atom of the picrate anion. The triazapentadienium system is planar and the phenyl ring is twisted relative to it by only 1.4°. Comparison is made with published structures containing the analogous cations with 1-aryl and 1,1,5,5-tetramethyl substituents.

Comment

The structure of the title compound, (1), was studied in order to estimate the effects an aryl group at the 5 position and potential hydrogen bonding may have on the structure of the 1,2,5-triazapentadienium conjugated system. The corresponding 1,1,5,5-tetramethyl derivative, (2) (Gould, McNab & Walkinshaw, 1983), and the 1-aryl derivative, (3) (Nagel & Allmann, 1981), have been reported.

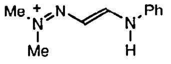


(1) $R^1 = R^2 = Me$, $R^3 = Ph$, $R^4 = H$, X = picrate

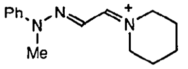
(2) $R^1 = R^2 = R^3 = R^4 = Me$, X = picrate

(3) $R^1 = Ph$, $R^2 = Me$, R^3-$R^4 = (CH_2)_5$, X = I

There is no significant difference between the bond lengths of the 1,2,5-triazapentadienium systems in (1) and (2). However, a comparison of (1) and (3) shows significant differences in the N1—N2, C3—C4 and C4—C5 (but not the N2—C3) distances. These results are generally in accord with an increase in the relative importance of the resonance structures (1*a*) and (3*a*), respectively, because the terminal aryl groups in these systems can interact conjugatively only by electron withdrawal from the N-atom lone pair. These observations are consistent with the results of ^{15}N NMR studies (Jones, McNab & Hanisch, 1978).



(1*a*)



(3*b*)

Comparing compounds (1) and (2), the bond angles at N1, N2 and C3 are very similar, but the angle at C4 is significantly more obtuse in (2), and that at N5 is significantly more obtuse in (1). These effects are presumably the result of non-bonded contacts between the *N*-methyl group and H3, and between the *N*-phenyl group and H4 in (2) and (1), respectively.

The triazapentadienium system in (1) is almost exactly planar (r.m.s. deviation of an atom from the least-squares plane is 0.009 Å) and the plane of the phenyl ring is twisted by just 1.4° with respect to this plane. This result is in contrast to the 1-aryl compound, (3), where the phenyl ring is twisted by about 22°. The phenyl ring is not significantly distorted from D_{3h} symmetry: C—C bond lengths range from 1.363 (6) to 1.388 (5) Å and C—C—C angles from 119.3 (4) to 120.8 (4)°.

The anion–cation association in the picrates (1) and (2) is quite distinct. In (2), the planes of the anions and cations are mutually perpendicular with the appropriate O atoms of the nitro groups in the picrate anion interacting with the N atoms of the triazapentadienium chain (Gould, McNab & Walkinshaw, 1983). In contrast, interionic contact in (1) is dominated by a hydrogen bond between H5 in the cation and O1′ (the phenolic O atom) of the picrate: the O···H distance is 1.931 (5) Å

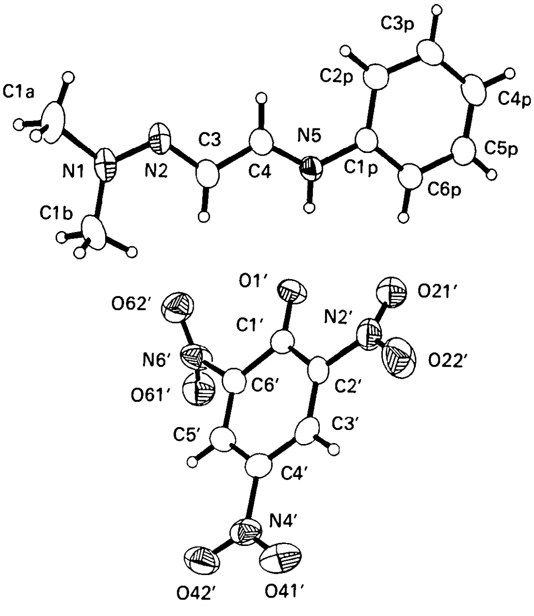


Fig. 1. A view of one cation–anion pair with atom-numbering scheme. Displacement ellipsoids enclose 50% probability surfaces.

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and the N5—H5···O1′ and C1′–O1′···H5 angles are 171.1 (5) and 139.7 (6)°, respectively. The interplanar angle between the phenyl ring of the picrate and the triazapentadienium system in the cation is 70.6°.

Experimental

The title compound was produced from the reaction of $Me_2N—N{=}CH—CHO$ with anilinium picrate in aqueous acetone. Crystals were grown from acetonitrile solution (McNab, 1978).

Crystal data

$C_{10}H_{14}N_3^+.C_6H_2N_3O_7^-$
$M_r = 404.35$
Triclinic
$P\overline{1}$
$a = 12.7783$ (15) Å
$b = 9.5867$ (12) Å
$c = 8.2046$ (12) Å
$\alpha = 80.066$ (6)°
$\beta = 108.617$ (9)°
$\gamma = 95.533$ (8)°
$V = 937.3$ (2) Å^3
$Z = 2$
$D_x = 1.433$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 36 reflections
$\theta = 12–14°$
$\mu = 0.115$ mm^{-1}
$T = 295$ (2) K
Column
0.66 × 0.18 × 0.12 mm
Yellow

Data collection

Stoe Stadi-4 diffractometer
$\omega–2\theta$ scans
2932 measured reflections
2458 independent reflections
1679 observed reflections
[$I > 2\sigma(I)$]
$R_{\rm int} = 0.0371$

$\theta_{\rm max} = 22.49°$
$h = 0 \rightarrow 13$
$k = -10 \rightarrow 10$
$l = -8 \rightarrow 8$
3 standard reflections
frequency: 120 min
intensity variation: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0656$
$wR(F^2) = 0.1871$
$S = 1.170$
2456 reflections
263 parameters
Calculated weights
$w = 1/[\sigma^2(F_o^2) + (0.1178P)^2 + 0.6363P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.234$

$\Delta\rho_{\rm max} = 0.487$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.312$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0039 (47)
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)

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

	x	y	z	$U_{\rm eq}$
N1	0.2565 (3)	0.0357 (3)	0.0862 (4)	0.0633 (10)
C1*A*	0.2850 (5)	−0.0584 (4)	−0.0128 (6)	0.0820 (15)
C1*B*	0.1615 (4)	0.0007 (5)	0.1480 (8)	0.0854 (15)
N2	0.3181 (3)	0.1503 (3)	0.1099 (4)	0.0582 (9)
C3	0.2955 (3)	0.2439 (4)	0.1952 (5)	0.0560 (10)
C4	0.3667 (3)	0.3629 (4)	0.2124 (5)	0.0539 (10)
N5	0.3553 (2)	0.4680 (3)	0.2881 (4)	0.0513 (8)
C1P	0.4228 (3)	0.5940 (4)	0.3076 (5)	0.0480 (9)
C2P	0.5120 (3)	0.6218 (4)	0.2454 (6)	0.0621 (11)
C3P	0.5746 (4)	0.7459 (5)	0.2705 (6)	0.0694 (12)
C4P	0.5481 (4)	0.8430 (5)	0.3540 (6)	0.0702 (12)
C5P	0.4608 (4)	0.8142 (4)	0.4176 (6)	0.0689 (12)
C6P	0.3969 (3)	0.6893 (4)	0.3948 (5)	0.0589 (11)
C1′	0.0777 (3)	0.3944 (4)	0.3772 (5)	0.0509 (10)
O1′	0.1805 (2)	0.4089 (3)	0.4264 (4)	0.0670 (9)
C2′	0.0024 (3)	0.4927 (4)	0.2506 (5)	0.0506 (10)
N2′	0.0448 (3)	0.6161 (4)	0.1558 (5)	0.0678 (10)
O21′	0.1412 (7)	0.6587 (12)	0.2326 (20)	0.074 (5)
O21″	0.1426 (4)	0.6252 (7)	0.1600 (11)	0.076 (3)
O22′	−0.0186 (3)	0.6907 (4)	0.0427 (6)	0.1083 (14)
C3′	−0.1110 (3)	0.4747 (4)	0.2074 (5)	0.0559 (10)
C4′	−0.1584 (3)	0.3571 (4)	0.2838 (5)	0.0534 (10)
N4′	−0.2769 (3)	0.3378 (5)	0.2349 (5)	0.0671 (10)
O41′	−0.3328 (3)	0.4292 (4)	0.1295 (5)	0.0960 (11)
O42′	−0.3165 (3)	0.2298 (4)	0.3020 (5)	0.0877 (11)
C5′	−0.0930 (3)	0.2555 (4)	0.4033 (5)	0.0552 (10)
C6′	0.0188 (3)	0.2731 (4)	0.4439 (5)	0.0523 (10)
N6′	0.0846 (3)	0.1616 (4)	0.5628 (5)	0.0765 (11)
O61′	0.0666 (10)	0.1429 (19)	0.7106 (19)	0.103 (5)
O61″	0.0453 (6)	0.0797 (12)	0.6652 (11)	0.089 (4)
O62′	0.1608 (3)	0.1189 (4)	0.5336 (5)	0.0966 (12)

Table 2. *Selected geometric parameters* (Å, °) *for* (1) *and some corresponding parameters for* (2) *and* (3)

Parameters for (2) are taken from Gould, McNab & Walkinshaw (1983), and those for (3) from Nagel & Allmann (1981).

	(1)	(2)	(3)
N1—N2	1.294 (4)	1.289 (6)	1.332 (12)
N1—C1*A*	1.453 (6)	–	–
N1—C1*B*	1.448 (6)	–	–
N2—C3	1.331 (5)	1.316 (5)	1.334 (12)
C3—C4	1.387 (5)	1.381 (7)	1.440 (12)
C4—N5	1.313 (5)	1.290 (5)	1.262 (12)
N5—C1P	1.417 (4)	–	–
N2—N1—C1*A*	116.5 (4)	117.2 (4)	116.6†
N2—N1—C1*B*	123.6 (4)	123.4 (3)	118.8†
C1*A*—N1—C1*B*	119.9 (4)	119.1 (4)	124.4†
N1—N2—C3	120.1 (4)	121.4 (3)	122.4†
N2—C3—C4	115.0 (4)	114.8 (4)	114.8†
N5—C4—C3	123.5 (4)	127.2 (4)	126.3†
C4—N5—C1P	126.9 (3)	120.8 (3)	–
C6P—C1P—N5	117.1 (3)	–	–
C2P—C1P—N5	122.6 (3)	–	–

† No e.s.d.'s given, but uncertainty is probably of the order of one degree.

Data collection employed on-line profile fitting (Clegg, 1981). The accurate values of 2θ used in cell refinement were obtained at $\pm\omega$. Disorder identified in two of the nitro groups of the picrate anion was modelled by allowing two alternative positions for one O atom in each. H atoms were placed in calculated positions with $U_{\rm iso} = 1.2U_{\rm eq}$ of the corresponding non-H atom. Data collection and cell refinement: *DIF*4 (Stoe & Cie, 1988*a*). Data reduction: *REDU*4 (Stoe & Cie, 1988*b*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SHELXTL/PC* (Sheldrick, 1992).

We thank the SERC for the provision of a four-circle diffractometer.

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: HA1111). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Structure and Absolute Configuration of (–)-(3*S*,4*R*)-4-Carboxy-1-[4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenylpiperidinium Bromide (Levocabastine Hydrobromide)†

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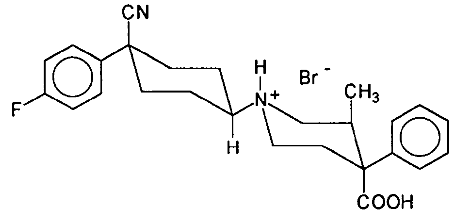
Abstract

Levocabastine is a potent H_1 antihistamine agent. Both the piperidine and cyclohexane rings in the title compound, $C_{26}H_{30}FN_2O_2^+.Br^-$, have conformations close to an ideal chair. The piperidine and fluorophenyl rings are positioned equatorially on the cyclohexane ring, while the cyano group is oriented axially, resulting in a *cis* configuration. The phenyl moiety on the piperidine ring is in an equatorial orientation while the methyl and carboxyl substituents are placed axially. This corresponds to a *trans* configuration. The molecules are linked together in the **c** direction by N—H···Br···H—O hydrogen bonds.

Comment

The title compound (I) contains a 1,4-substituted cyclohexane ring and a 3,4-substituted piperidine ring. As such substituted rings give rise to *cis* and *trans* isomers and, moreover, 3,4-substituted piperidines are chiral, eight isomers are possible. The geometry of the four racemates was derived from the NMR spectra of the benzyl esters (Stokbroekx *et al.*, 1986). Here we report the structure of levocabastine, the most potent histamine H_1 antagonist of the series.



(I)

The absolute configuration is (3*S*,4*R*). The bond distances and angles lie within the expected ranges. The cyclohexane and piperidine rings have confromations close to an ideal chair. The fluorophenyl and phenyl substituents are placed equatorially, while the cyano, methyl and carboxyl groups are oriented axially. The conformation of the cyclohexane–piperidine connection is staggered. The carboxyl substituent is almost perpendicular to the phenyl ring [80.2 (2)°], while the fluorophenyl moiety is nearly coplanar with it [9.8 (2)°]. The molecules are linked together by N15—H15···Br [N15···Br 3.248 (4), H15···Br 2.272 Å, N15—H15···Br 145.7°] and O23^i—H23^i···Br [O23^i···Br 3.118 (4), H23^i···Br 2.070 Å, O23^i—H23^i···Br 148.4°; symmetry code: (i) $\frac{3}{2} - x, -y, \frac{1}{2} + z$] hydrogen bonds, forming infinite chains in the **c** direction.

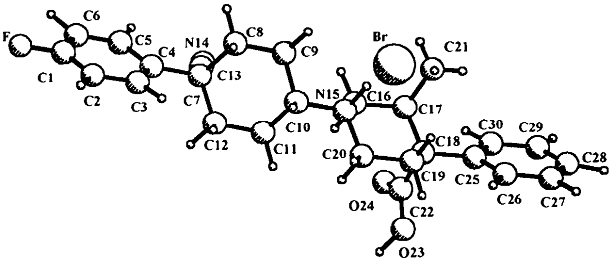


Fig. 1. *PLUTO* (Motherwell & Clegg, 1978) diagram of the molecule showing the atomic numbering scheme.

Experimental

Crystal data

$C_{26}H_{30}FN_2O_2^+.Br^-$
$M_r = 501.44$

Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å

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† Internal code of the Janssen Research Foundation: R53474.