ORGANIC COMPOUNDS

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DL-Pheniramine Hydrogen Maleate

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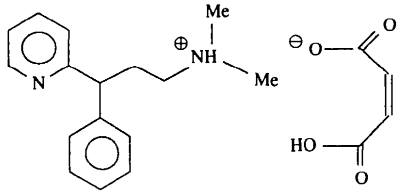
Abstract

The structure of the title compound, *N*,*N*-dimethyl-γ-phenyl-2-pyridinepropanaminium hydrogen maleate, $C_{16}H_{21}N_2^+.C_4H_3O_4^-$, a potent anti-allergic drug, is composed of hydrogen-bonded pheniraminium cations and maleate anions, the latter forming a seven-membered ring through an intramolecular hydrogen bond.

Comment

Continuing our interest in the studies of anti-allergic drugs effective on H1-receptors, we have solved the crystal structure of DL-pheniramine hydrogen maleate, (1). In this paper, we wish to report the result of our analysis and a comparison of the conformation of (1) with those of its derivatives, DL-brompheniramine (2) (James & Williams, 1971), DL-chlorpheniramine (3) (Parvez, 1990) and D-chlorpheniramine (4) (James & Williams, 1974).



(1)

An *ORTEP*II (Johnson, 1976) drawing (Fig. 1) shows the hydrogen-bonded structure of the pheniraminium cation and maleate anion with atomic numbering scheme. The molecular dimensions in (1) are normal, with the following average bond distances in the cation: C_{sp^3}—C_{sp^3} 1.530 (9), C_{sp^3}—C_{sp^2} 1.513 (9), C—C_{aromatic} 1.372 (9), N—C_{sp^3} 1.495 (8), N—C_{sp^2} 1.349 (19) Å, and in the anion: C═O 1.233 (7), C—O 1.285 (10), C═C 1.325 (9) and C_{sp^2}—C_{sp^2} 1.490 (8) Å. The cation and the anion are hydrogen bonded with an N1···O1 separation of 2.714 (7) Å and N—H···O angle of 165°. The maleate anion, which is essentially planar, forms a seven-membered ring through an intramolecular hydrogen bond with O2···O3 2.433 (6) Å and a linear O—H···O angle (180°). The angles at the C_{sp^2} atoms C18 and C19 in the anion are much larger than the ideal 120° value [131.1 (7) and 130.3 (7)°, respectively] and are in accordance with the values observed in the maleate anions in the crystal structures of (2), (3) and (4).

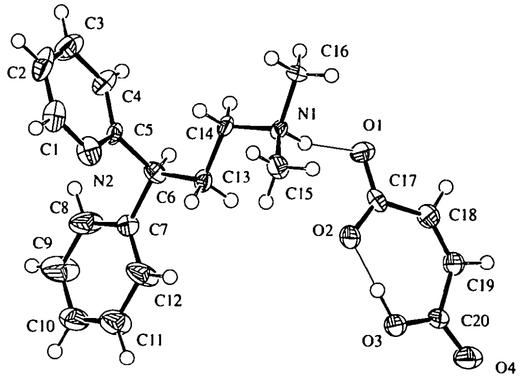


Fig. 1. An *ORTEP*II (Johnson, 1976) drawing showing the intramolecular hydrogen bond between the pheniraminium and maleate ions and the intramolecular hydrogen bond within the maleate anion. The non-H atoms have been plotted as displacement ellipsoids at the 50% probability level.

A comparison of the conformation of (1) with the conformations of (2), (3) and (4) shows significant differences in the angles between least-squares planes; the conformations of (2) and (3) are somewhat identical. The six-membered rings in (1) are inclined at 92.9 (2)° as compared with 76.3 (2), 74.9 (1) and 66.3 (2)° in (2), (3) and (4), respectively. The mean planes of the aminopropyl chain (N1,C6,C13,C14) and pyridyl rings in (1) and (4) are also inclined at right angles [89.2 (2) and 87.0 (2)°, respectively] compared with 34.2 (2) and 37.8 (2)° in (2) and (3), respectively. The aminopropyl chain lies almost in the phenyl ring plane [at 12.1 (2)°] in (1) as opposed to almost at right angles in (2) and (3) [80.2 (2) and 80.1 (1)°, respectively] and at 62.5 (2)° in (4). It is interesting to note that the longest fully extended chain in both (1) and (4) is comprised of atoms N1,C5,C6,C13,C14,C16 with C7 and C15 *cis* with respect to each other and 1.20–1.31 Å out of the least-squares planes of these atoms. On the other hand, in (2) and (3), N1,C6,C7,C13,C14,C16 constitute the longest chain with C5 and C15 *cis* to each other.

Experimental

Colourless prismatic crystals of the title compound (Sigma Inc.) were obtained from its solution in ethanol by slow evaporation at room temperature.

Crystal data

$C_{16}H_{21}N_2^+.C_4H_3O_4^-$
$M_r = 356.42$
Orthorhombic
Pbca
$a = 20.275\,(6)$ Å
$b = 17.006\,(4)$ Å
$c = 11.038\,(4)$ Å
$V = 3805\,(2)$ Å^3
$Z = 8$
$D_x = 1.244$ Mg m^{-3}

Mo *Kα* radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 9.0$–$20.0°$
$\mu = 0.087$ mm^{-1}
$T = 150$ K
Prism
0.60 × 0.43 × 0.35 mm
Colourless

Data collection

AFC-6*S* diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical (ψ scans of 3 reflections; North, Phillips & Mathews, 1968)
$T_{\min} = 0.703$, $T_{\max} = 0.996$
3768 measured reflections
3335 independent reflections
1349 observed reflections [$I > 3.00\sigma(I)$]

$\theta_{\max} = 25.0°$
$h = 0 \rightarrow 24$
$k = 0 \rightarrow 20$
$l = -13 \rightarrow 0$
3 standard reflections monitored every 200 reflections
frequency: 100 min
intensity decay: 0.6%

Refinement

Refinement on *F*
$R = 0.069$
$wR = 0.069$
$S = 2.640$
1349 reflections
235 parameters
H atoms geometrically idealized
Weighting scheme based on measured e.s.d.'s

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.34$ e Å^{-3}
$\Delta\rho_{\min} = -0.30$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

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

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

	x	y	z	U_{eq}
O1	0.9159 (2)	0.1819 (3)	0.5608 (4)	0.038 (2)
O2	0.9784 (2)	0.2402 (3)	0.6989 (4)	0.038 (1)
O3	1.0906 (2)	0.2895 (3)	0.7167 (4)	0.040 (2)
O4	1.1784 (2)	0.2935 (3)	0.6017 (5)	0.061 (2)
N1	0.8183 (2)	0.2085 (3)	0.7241 (4)	0.024 (1)
N2	0.7546 (3)	0.0790 (3)	1.0835 (5)	0.038 (2)
C1	0.6919 (4)	0.0751 (4)	1.1185 (7)	0.042 (2)
C2	0.6451 (4)	0.0263 (5)	1.0679 (8)	0.050 (3)
C3	0.6645 (4)	−0.0230 (5)	0.9761 (8)	0.051 (3)
C4	0.7294 (3)	−0.0224 (5)	0.9384 (7)	0.039 (2)
C5	0.7733 (3)	0.0296 (4)	0.9919 (6)	0.025 (2)
C6	0.8439 (3)	0.0367 (4)	0.9501 (6)	0.028 (2)
C7	0.8916 (3)	0.0158 (4)	1.0510 (6)	0.026 (2)
C8	0.8873 (4)	−0.0569 (5)	1.1040 (8)	0.056 (3)
C9	0.9297 (4)	−0.0798 (5)	1.1949 (9)	0.073 (3)
C10	0.9751 (4)	−0.0284 (5)	1.2394 (8)	0.051 (3)
C11	0.9804 (4)	0.0424 (5)	1.1883 (8)	0.059 (3)
C12	0.9372 (4)	0.0654 (4)	1.0939 (8)	0.054 (3)
C13	0.8560 (3)	0.1183 (4)	0.8946 (6)	0.027 (2)
C14	0.8032 (3)	0.1375 (4)	0.8011 (6)	0.025 (2)
C15	0.8303 (3)	0.2807 (4)	0.7959 (6)	0.036 (2)
C16	0.7637 (3)	0.2210 (4)	0.6350 (6)	0.032 (2)
C17	0.9687 (3)	0.2118 (4)	0.5930 (6)	0.028 (2)
C18	1.0238 (4)	0.2120 (5)	0.5035 (7)	0.041 (2)
C19	1.0849 (3)	0.2390 (5)	0.5116 (6)	0.037 (2)
C20	1.1201 (3)	0.2760 (4)	0.6153 (7)	0.033 (2)

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

N1—C14	1.508 (8)	C13—C14	1.521 (8)
N1—C15	1.482 (8)	C17—C18	1.491 (9)
N1—C16	1.495 (7)	C18—C19	1.325 (9)
N2—C1	1.330 (9)	C19—C20	1.488 (10)
N2—C5	1.368 (8)	O1—C17	1.237 (7)
C5—C6	1.508 (9)	O2—C17	1.280 (8)
C6—C7	1.517 (9)	O3—C20	1.289 (8)
C6—C13	1.538 (9)	O4—C20	1.229 (7)
C14—N1—C15	113.3 (5)	C6—C7—C12	123.6 (7)
C14—N1—C16	109.6 (5)	C8—C7—C12	117.5 (7)
C15—N1—C16	110.8 (5)	C6—C13—C14	110.6 (5)
C1—N2—C5	116.7 (7)	N1—C14—C13	114.3 (5)
N2—C1—C2	124.7 (7)	O1—C17—O2	123.4 (7)
N2—C5—C4	121.9 (6)	O1—C17—C18	117.3 (6)
N2—C5—C6	116.1 (6)	O2—C17—C18	119.2 (6)
C4—C5—C6	122.0 (6)	C17—C18—C19	131.1 (7)
C5—C6—C7	111.2 (5)	C18—C19—C20	130.3 (7)
C5—C6—C13	110.2 (6)	O3—C20—O4	120.6 (7)
C7—C6—C13	113.7 (6)	O3—C20—C19	121.4 (6)
C6—C7—C8	118.9 (7)	O4—C20—C19	118.0 (7)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H···O1	0.95	1.79	2.714 (7)	165
O3—H···O2	0.95	1.47	2.433 (6)	180

The crystals did not diffract well. Even with a large crystal of the approximate dimensions 0.60 × 0.43 × 0.35 mm and collecting data at a temperature of 170 K, only 50% of the reflections were observed for $\theta = 20°$ (2100 measured reflections) which dropped further to 20% in the θ range of 20–25°, yielding only 1349 (40%) observed data.

The space group was uniquely determined to be *Pbca* (61) from the systematic absences: $0kl$, $k = 2n + 1$; $h0l$, $l = 2n + 1$; $hk0$: $h = 2n + 1$. H atoms, located from a ΔF map, were included at geometrically idealized positions with C—H, N—H and O—H = 0.95 Å.

Data collection and cell refinement: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Data reduction: *TEXSAN* (Molecular Structure Corporation, 1994). Structure solution: *DIRDIF* (Beurskens *et al.*, 1992). Structure refinement: *TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Preparation of material for publication: *TEXSAN*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, least-squares-planes data and complete geometry have been deposited with the IUCr (Reference: FG1077). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Attractive Edge–Face Arene–Arene Interactions in Combination with Close Packing of Alkoxy Chains for 1,4-Didecyloxybenzene

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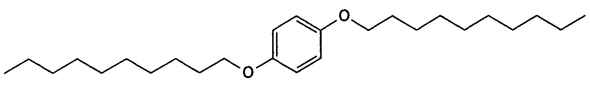
Abstract

The crystal structure of 1,4-didecyloxybenzene, $C_{26}H_{46}O_2$, displays a packing motif which is determined primarily by attractive edge–face arene–arene interactions and is cooperative with the close packing of the alkyl chains. The oblique topology of the benzene moieties is essentially similar to that found for the homologous 1,4-dimethoxy and 1,4-diethoxy derivatives.

Comment

For many applications of simple π-conjugated compounds in material science, besides appropriate molecular properties, intermolecular π-overlap is an additional prerequisite. It is well established that numerous simple planar π-systems tend to aggregate edge–face in the solid state (Hunter, 1994, and references therein). Nevertheless, the intermolecular organization required for favourable π-overlap between constituents, *i.e.* a face-face orientation, may be induced *via* selective substitution with either long alkyl or alkoxy chains. Recently, we have shown by comparing solid-state packing motifs of 1,2,4,5-tetramethoxybenzene (herringbone-like; von Deuten & Klar, 1979) and 1,2,4,5-tetradecyloxybenzene (board-like; Keegstra *et al.*, 1995) that the introduction of the decyloxy chains markedly affects intermolecular interactions and hence intermolecular organization. As expected (Jorgensen & Severance, 1990, and references therein), no edge–face interactions are discernible in the case of 1,2,4,5-tetramethoxybenzene.



(I)

To gain insight to what extent this observation is affected by the number, length and substitution pattern of alkoxy chains, we decided to determine the single-crystal X-ray structure of 1,4-didecyloxybenzene. Single-crystal X-ray structures have been reported for the homologous 1,4-dimethoxybenzene (Goodwin, Przybylska & Robertson, 1950) and 1,4-diethoxybenzene (Haisa & Kashino, 1977). Edge–face interactions play an important role in determining their solid-state packing motif. As can be seen from Fig. 2, 1,4-didecyloxybenzene also possesses a packing motif which is primarily determined by attractive edge–face arene–arene interactions. The acute angle between the least-squares planes through the symmetry-related phenyl rings is 69.1 (2)°. The distance between the cen-

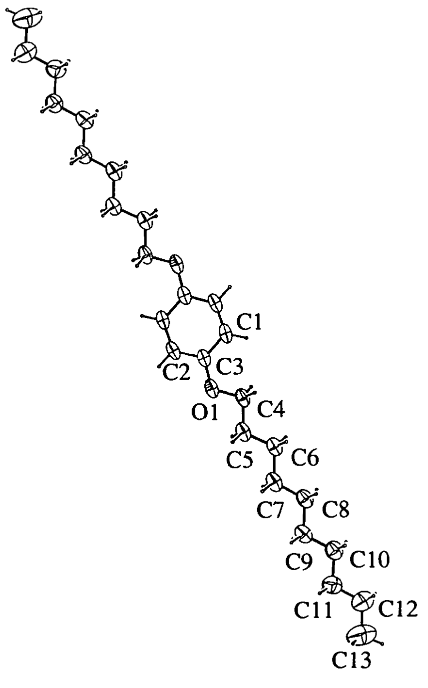


Fig. 1. Displacement ellipsoid plot (30% probability level) of 1,4-didecyloxybenzene.