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Structure of Monoamine Oxidase Inhibitors: 1-[(4-Naphtho[1,2-*b*]thienyl)methyl]-1*H*,3*H*$^+$-imidazolium Methanesulfonate

BY CHRISTINE VAN DER BREMPT, ANITA SOREE, GUY EVRARD AND FRANÇOIS DURANT

Laboratoire de Chimie Moléculaire Structurale, Facultés Universitaires Notre-Dame de la Paix, Rue de Bruxelles 61, *B*-5000 *Namur, Belgium*

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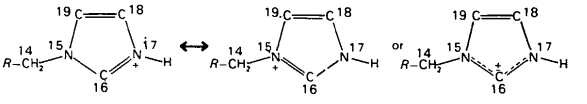
Abstract. $C_{16}H_{13}N_2S^+.CH_3O_3S^-$, $M_r = 360{\cdot}5$, monoclinic, $P2_1/n$, $a = 17{\cdot}631\ (2)$, $b = 10{\cdot}176\ (2)$, $c = 9{\cdot}604\ (2)$ Å, $\beta = 103{\cdot}58\ (2)°$, $V = 1674{\cdot}5$ Å^3, $Z = 4$, $D_x = 1{\cdot}43$ g cm^{-3}, $\lambda(\text{Mo } K\bar{\alpha}) = 0{\cdot}71069$ Å, $\mu = 0{\cdot}285$ cm^{-1}, $F(000) = 752$, $T = 293$ K, final $R = 0{\cdot}041$ for 2310 observed reflections. The pyridinic nitrogen of the imidazole ring is protonated by a methanesulfonic acid molecule, forming a strong (2·76 Å) and approximately linear [169·3 (2)°] intermolecular N—H···O bond. All the atoms of the naphtho[1,2-*b*]thienyl moiety are coplanar, as are those of the imidazole ring.

Introduction. X-ray diffraction analysis of the title compound was undertaken as part of a general comparative investigation on structural and electronic properties of various type A monoamine oxidase (MAO-A) inhibitors, in order to establish the 'structure–activity' relationships characteristic of this antidepressant family. The drug here studied behaves like a reversible, competitive and selective inhibitor of MAO-A (Storni, Blattner, Maitre & Waldmeier, 1980). The structure and geometry of the imidazole ring, whose important function in biological systems is well known, is here particularly discussed.

Experimental. The crystal was obtained by slow evaporation of a chloroform/diisopropyl ether solution. Colourless prismatic crystal 0·24 × 0·50 × 0·14 mm for all X-ray measurements, density not measured. Four-circle Enraf–Nonius diffractometer (CAD-4 system, graphite monochromator). Lattice parameters from least-squares refinement of 21 medium-angle reflections. ω–θ scan method, $4° \le 2\theta \le 56°$, $(\sin\theta/\lambda)_{max} = 0{\cdot}66$ Å^{-1}, $-21 \le h \le 21$, $0 \le k \le 12$, $0 \le l \le 11$. No absorption corrections. 4040 measured reflections, 2310 observed [$I \ge 2{\cdot}5\sigma(I)$], no significant variation in intensity of standard reflection. Direct methods (*SHELX*76: Sheldrick, 1976); 18 of the 19 heavy atoms of the MAOI compound and one methanesulfonic acid solvent molecule given by the most probable set of phases; the missing C(8) atom located on a difference Fourier map. Full-matrix least-squares refinement on F using *SHELX*76. All H atoms located on a difference Fourier map. Anisotropic temperature factors for the C, N, O and S atoms; isotropic ones for H atoms (corresponding to those of the carrier atoms). Final $R = 0{\cdot}041$, $wR = 0{\cdot}033$; $w = 1/[\sigma^2(F)]$, $(\Delta/\sigma)_{max} = 3{\cdot}095$ [x parameter of C(13)]. $S = 0{\cdot}74$, $-0{\cdot}35 \le \Delta\rho \le 0{\cdot}35$ e Å^{-3} in final difference map. Scattering factors from *SHELX*76. Structural analysis by *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976).

Discussion. The atomic parameters are shown in Table 1.* The bond distances and angles are given in Fig. 1, and the packing diagram is presented in Fig. 2. All the atoms of the naphtho[1,2-*b*]thienyl moiety are coplanar. As expected, the imidazole ring is planar too, and the N(15) and N(17) atoms are trigonal (Fig. 2). The torsion of this ring with regard to the naphtho[1,2-*b*]thienyl plane is important: the dihedral angle between their respective mean planes is 71·2°. The pyridinic N(17) atom of imidazole is protonated by a methanesulfonic acid solvent molecule, giving rise to an electronic delocalization between N(15) and N(17) *via* C(16), as already pointed out (Sundberg & Martin, 1974) and suggested by the following resonance scheme:



(I) (II) (III)

The intermolecular hydrogen bond thus formed between the imidazolium N(17) atom and the methanesulfonate O(21) is approximately linear [$N(17)_{x,y,z}$—$H(17)$—$O(22)_{x,y,z+1/2}$: 169·3 (2)°], and in the range attributed to strong N—H···O interactions (Hamilton & Ibers, 1968); N(17)—H(17)···O(22): 2·755 (3)–1·784 (2) Å. As already observed for other protonated

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and mean-plane data have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42525 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Final coordinates* ($\times 10^4$) *and* B_{eq} *values with e.s.d.'s in parentheses*

$B_{eq} = \frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j$.

	x	y	z	B_{eq}(Å^2)
S(1)	3941 (1)	−152 (1)	2669 (1)	5·60 (1)
C(2)	4393 (2)	−1396 (4)	3774 (4)	5·76 (1)
C(3)	5151 (2)	−1526 (3)	3783 (3)	4·77 (1)
C(4)	6156 (2)	−428 (3)	2585 (3)	3·68 (1)
C(5)	6272 (2)	556 (3)	1704 (3)	4·20 (1)
C(6)	5803 (2)	2484 (4)	158 (4)	4·97 (1)
C(7)	5222 (2)	3314 (4)	−468 (4)	5·91 (1)
C(8)	4465 (2)	3145 (4)	−250 (4)	5·67 (1)
C(9)	4306 (2)	2152 (3)	585 (4)	4·80 (1)
C(10)	4906 (2)	1286 (3)	1279 (3)	3·79 (1)
C(11)	5666 (2)	1442 (3)	1046 (3)	4·09 (1)
C(12)	5405 (2)	−581 (3)	2888 (3)	3·66 (1)
C(13)	4808 (2)	251 (3)	2210 (3)	3·94 (1)
C(14)	6814 (2)	−1346 (3)	3215 (3)	4·40 (1)
N(15)	7232 (1)	−922 (3)	4671 (3)	4·04 (1)
C(16)	7359 (2)	−1634 (3)	5842 (4)	4·40 (1)
N(17)	7785 (1)	−942 (3)	6916 (3)	4·61 (1)
C(18)	7918 (2)	269 (4)	6412 (4)	5·86 (1)
C(19)	7570 (2)	288 (4)	5002 (4)	6·08 (1)
S(20)	8509 (1)	−290 (1)	593 (1)	4·56 (1)
O(21)	8175 (1)	126 (3)	1758 (2)	7·77 (1)
O(22)	8109 (1)	−1420 (2)	−181 (2)	5·47 (1)
O(23)	8589 (1)	780 (2)	−365 (2)	6·32 (1)
C(24)	9461 (2)	−802 (4)	1377 (4)	6·00 (1)

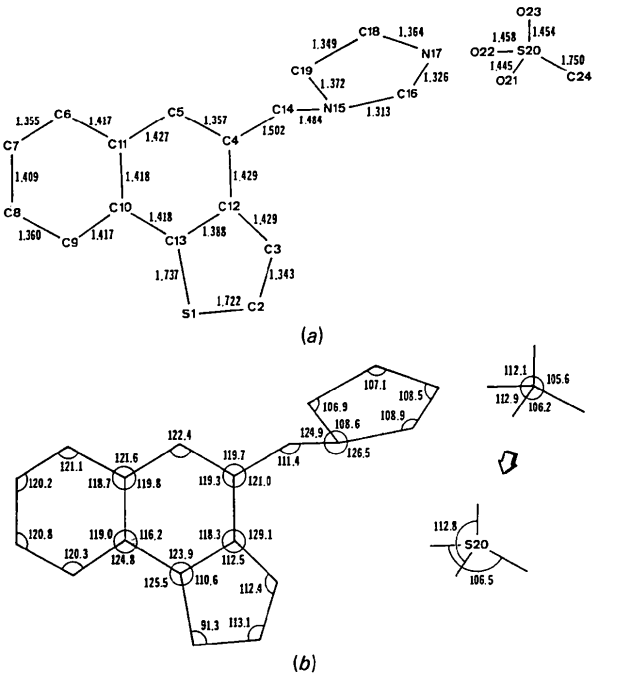

Fig. 1. (*a*) Atom numbering and bond lengths (Å) and (*b*) angles (°); e.s.d.'s are less than 0·005 Å and 0·4°.

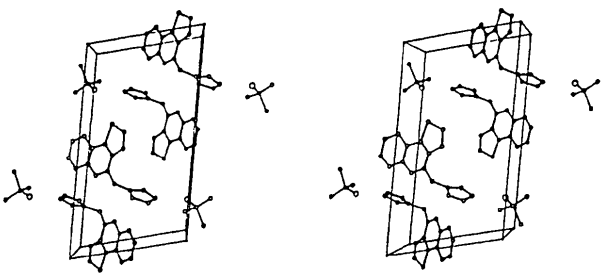

Fig. 2. Stereoview of the molecular conformation and crystal packing.

imidazole molecules (Veidis, Palenik, Schaffrin & Trotter, 1969; Blessing & McGandy, 1972; Freeman, Huq, Rosalky & Taylor, 1975), the angle N–C–N [108·9 (3)°] is equal to the two C–N–C angles [108·6 (3) and 108·5 (3)°] (Fig. 1), while in the neutral imidazole, the three angles are different [Martínez-Carrera (1966) (X-ray data); Craven, McMullan, Bell & Freeman (1977) (neutron data)]. The N–C–C angles are similar too: N(15)–C(19)–C(18) = 106·9 (3)° and N(17)–C(18)–C(19) = 107·1 (3)°. It is interesting to emphasize that the N(15)–C(16) bond length [1·313 (4) Å] is slightly shorter than that of N(17)–C(16) [1·326 (4) Å], in contrast with the values pointed out in the references cited herein. Indeed for the neutral molecule, the C(16)–N(17) bond length is shorter than N(15)–C(16) by 0·02 Å. In the imidazolium sulfate (Freeman *et al.*, 1975), this difference is less pronounced (0·01 Å) but still observed. The weak shortening of the bond N(15)–C(16) with regard to C(16)–N(17) observed in the title compound could be explained by the fact that the alkyl group C(14)H_2–*R* exerts a stabilizing effect on the partially positively charged N(15), favouring the resonance form (II). This effect is non-existent in the imidazole or imidazolium moieties, where the equivalent N(15) atom is linked to an H atom. The other structural features of the imidazole group here studied, are comparable to those reported by the above-mentioned authors.

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