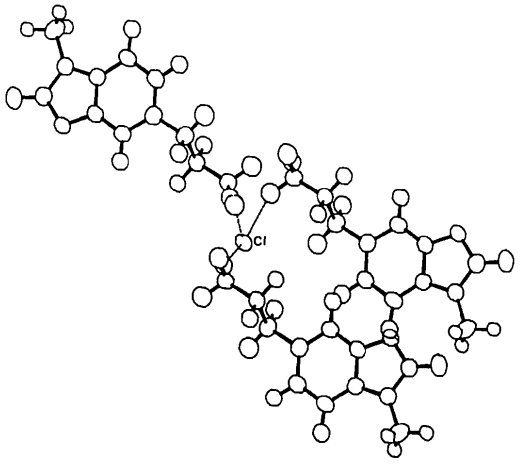

Fig. 2. Enchaînement moléculaire matérialisant les liaisons H autour de l'atome de chlore.

L'analogie avec la dopamine (Bergin & Carlström, 1968) est assez marquée. Cependant, on admet actuellement que l'interaction des agonistes dopaminergiques avec les récepteurs fait intervenir deux sites de liaison primaire correspondant au groupement aminé et à un hydroxyle en position *méta* de la chaîne latérale; la molécule ne possèderait donc pas toutes les caractéristiques structurales requises ce qui expliquerait sa faible affinité pour ces récepteurs. Par contre, la parenté avec la noradrénaline (Rouot, 1977) est évidente et le produit possède les caractéristiques structurales et conformationnelles des agonistes adrénergiques. En effet, la présence d'un hydroxyle sur le noyau benzénique ne constitue pas, dans cette série, un élément déterminant pour l'interaction avec les récepteurs. Ces conclusions sont en parfait accord avec l'activité cardiostimulante manifestée par cette nouvelle molécule.

Tableau 3. *Distances caractéristiques* (Å) *entre sites actifs*

	Présent travail	Dopamine	Noradrénaline
Azote N(14)–centre du noyau benzénique	5,129 (3)	5,14	5,1–5,2
Azote N(14)–plan du noyau benzénique	1,353 (2)	1,61	1,2–1,4

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The Structure of Methyl 2-Chloro-8-oxo-6*H*,8*H*-[1]benzopyrano[4′,3′:4,5]imidazo-[2,1-*b*][1,3]thiazine-10-carboxylate

BY DICK VAN DER HELM* AND DOUGLAS R. POWELL

Department of Chemistry, University of Oklahoma, Norman, OK 73019, *USA*

AND K. DARRELL BERLIN, LYLE W. SPRUCE, N. SHYAMASUNDAR AND A. S. RADHAKRISHNA

Department of Chemistry, Oklahoma State University, Stillwater, OK 74074, *USA*

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Abstract. $C_{15}H_9ClN_2O_4S$, $M_r = 348{\cdot}76$, orthorhombic, *Pbca*, $a = 7{\cdot}1732\ (6)$, $b = 13{\cdot}872\ (1)$, $c = 28{\cdot}627\ (2)$ Å, $V = 2848{\cdot}6\ (4)$ Å^3, $Z = 8$, $D_x = 1{\cdot}627$ g cm^{-3}, Cu $K\bar{\alpha}$, $\lambda = 1{\cdot}5418$ Å, $\mu = 38{\cdot}0$ cm^{-1}, $F(000) = 1424$, $T = 298$ K, $R = 0{\cdot}049$ for 2913 reflections. The molecule consists of a chlorophenyl, a pyran,

* To whom all correspondence should be addressed.

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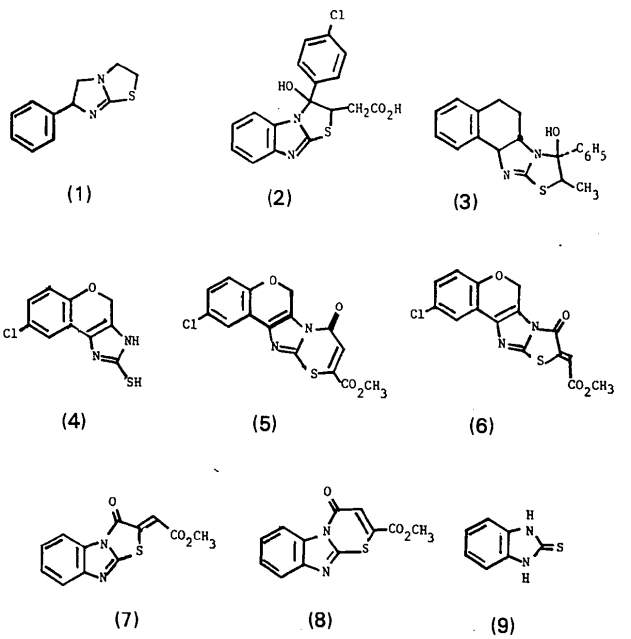
an imidazole and a thiazine ring which are fused together. The localized π-bonding network causes the molecule to be planar, including the attached groups. The C—S bonds in the thiazine ring are shorter (1·720, 1·726 Å) than previously reported values. The delocalization over the imidazole group is less than that found in similar ring systems, giving very unequal C—N bonds (1·302, 1·399 Å).

Introduction. Levamisole (2,3,5,6-tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride), (1), has shown powerful broad-spectrum anthelmintic properties (Thienpont, Vanparijs, Raemaekers, Vandenberk, Demoen, Allewijn, Marsboom, Niemegeers, Schellekens & Janssen, 1966; Englemann & Richardson, 1986) as well as a wide variety of other useful medicinal characteristics (Van Belle, 1972; Chan & Kellen, 1975; Chirigos, 1977, 1981; Symoens & Rosenthal, 1977; Hara, Kayama & Fukushima, 1981). Analogs of (1) have been a subject of considerable interest in recent years (Bell & Wei, 1976; Bhargave, Lee, Huang, Cunningham & Agrawal, 1977), such as (2) (Fenichel, Gregory & Alburn, 1976; Tagliabue, Allesandri, Polentarutti, Montovani, Falantano, Vecchi, Garattini & Spreafico, 1978) and (3) (Hara *et al.*, 1981), and have prompted research into newer methods to obtain highly substituted 2*H*-benzimidazole-2-thione systems. During the course of some work with thiazoloimidazole acetic acids (Radhakrishna & Berlin, 1978), we had the occasion to prepare 4,5-(8-chlorochroman)-[2,3-*d*]imidazole-2-thio (4). The formation of five- or six-membered rings in reactions of dimethyl 2-butynedioate (dimethyl acetylenedicarboxylate, DMAD) with unsaturated systems has resulted in ambiguities in the interpretation of the mechanism (Vogeli, von Philipsborn, Nagarajan & Nair (1978). We have discovered that the treatment of (4) with DMAD in methanol produced the title compound (5) in a yield of 92%. The question arose whether the structure was (5) or possibly (6). The ^{1}H NMR spectrum in F_3CCO_2H did reveal signals for the CH_3 (δ4·16), CH_2 (δ6·00), C=C—H (δ7·74) and for the aromatic protons, all of which support the structure (5). Nevertheless, structure (6) could not be eliminated from consideration since it possesses the same types of protons. During the course of our investigations, a paper was released which included the analogs (7) and (8) obtained from a similar reaction starting from (9) (Wade, 1979). It was shown that (7) rearranged into (8) by extended reaction times in boiling methanol. In our work, it was not possible to determine unequivocally the structure of (5) by simple spectroscopic examination. Thus, a single crystal of (5) was obtained and the structure determined by X-ray diffraction. To the best of our knowledge, no single-crystal structure of a member of the family illustrated by (5) has been published. Consequently the results included herein should serve as a useful basis for identification work by others in the field.



Experimental. *Synthesis of* (5). In a standard system consisting of a flask, condenser and stirrer (all under N_2) were placed 0·223 g (0·000935 mol) of (4), 0·255 g (0·0018 mol) of DMAD and 10 ml of anhydrous methanol. The solution was heated at reflux for 16 h and then cooled to room temperature. A solid was collected by filtration, which was washed with methanol and recrystallized (ethyl acetate); m.p. 513–514 K, yield 0·30 g (92%). The ^{1}H NMR data were collected on a Varian XL-100(15) spectrometer and the solution was at saturation. Analysis: Calc. for $C_{15}H_9ClN_2O_4S$: C, 51·65; H, 2·58; N, 8·03; S, 9·18; Cl, 10·19. Found: C, 52·03; H, 2·58, N, 7·86; S, 9·11; Cl, 10·27%. IR (KBr) 1751, 1715, 1626, 1600 cm^{-1}. ^{1}H NMR (F_3CCO_2H) δ4·16 (*s*, 3H, CH_3), 6·00 (*s*, 2H, CH_2), 7·00 [*d*, 1H, $J = 9$ Hz, ArH(4)], 7·32 [*dd*, 1H, $J = 9$ Hz, $J = 2$ Hz, ArH(3)], 7·48 [*d*, 1H, $J = 2$ Hz, ArH(1)], 7·74 (*s*, 1H, C=CH).

X-ray diffraction. Red plate-shaped crystals suitable for intensity measurements were grown by slowly cooling a heated solution of (5) in ethyl acetate. Intensity data on crystal (0·06 × 0·30 × 0·34 mm) collected on Enraf–Nonius CAD-4 diffractometer at 298 K. Ni-filtered Cu $K\alpha$ radiation. Unit-cell dimensions from 40 reflections with $60 \le 2\theta \le 70°$; 2913 unique reflections, $0 \le h \le 8$, $0 \le k \le 17$, $0 \le l \le 35$; $2\theta_{max} = 150°$; ω–2θ scan techniques; 2400 observed reflections, $I > 2\sigma(I)$, $\sigma(I)$ from counting statistics; no significant variation of three monitor reflections measured every 7200 s; Lorentz–polarization and absorption correction made on data (min. and max.

transmission factors are 0·33 and 0·80, respectively). Structure solved by direct methods using *SHELX*76 (Sheldrick, 1976), and refined on F by full-matrix least squares using all data and experimental weights $[1/\sigma^2(F)]$ using the same program. H atoms from difference Fourier map, refined isotropically. All other atoms anisotropic; final $R = 0{\cdot}049$, $wR = 0{\cdot}050$ for 2913 reflections; $(\Delta/\sigma)_{max} = 0{\cdot}03$; final difference map featureless $\Delta\rho = \pm 0{\cdot}25$ e Å^{-3}; $\sum w(\Delta F)^2$ showed no significant variation with either θ or F; atomic scattering factors as in *SHELX*76.*

Discussion. The final atomic coordinates are given in Table 1. The bond lengths and the atom-numbering scheme for methyl 2-chloro-8-oxo-6*H*,8*H*-[1]benzopyrano[4′,3′:4,5]imidazo[2,1-*b*][1,3]thiazine-10-carboxylate (5) are shown in Fig. 1, and the bond angles are given in Table 2. The molecule is made up of a chlorophenyl (*A*), a pyran (*B*), an imidazole (*C*), and a thiazine (*D*) ring. The thiazine ring also has a methyl ester side group, a carbonyl group, and a ring double bond.

The molecule as a whole is strikingly planar. The non-H atoms which exhibit the greatest deviation from the mean plane of the molecule are O(5) 0·194 (2), C(16) 0·150 (4) and C(4) 0·120 (2) Å. A calculation of the least-squares plane through each of the constituent rings shows that the pyran ring atoms have the greatest deviations. Atoms O(5) and C(6) deviate by −0·078 (2) and 0·073 (3) Å from the calculated *B* ring.

The planarity of the molecule is due to the delocalized π-bonding network. The C—C bond lengths, which range from 1·345 (3) [C(9)—C(10)] to 1·480 (3) Å [C(6)—C(6a)], indicate that all of these bonds have some π-bonding character. The length of the S—C(10) bond of 1·720 (2) Å is much shorter than the 1·733 (Chu & Yang, 1976) and 1·746 Å (Wei & Einstein, 1978) distances reported for similar S—C(sp^2) bonds. Moreover, the S—C(11a) bond of 1·726 (2) Å is shorter than the previously reported values of 1·741 (Carpy, Gadret & Leger, 1979), 1·750 (Talberg, 1974) and 1·756 Å (Kálmán & Argay, 1978) for similar bonds.

The imidazole group shows somewhat less delocalization than is seen in related compounds. The C(11a)—N(7) and C(11a)—N(12) distances are 1·399 (2) and 1·302 (2) Å, respectively. The corresponding distances in benzimidazole (Dik-Edixhoven, Schenk & van der Meer, 1973) are 1·353 and 1·313 Å and in thiabendazole are 1·339 and 1·319 Å (Trus & Marsh, 1973).

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43968 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates for the non-*H *atoms in* (5) ($x \times 10^4$, $yz \times 10^5$)

The geometric mean of the diagonal terms of the vibration tensor is given as U_{eq}(Å$^2 \times 10^4$).

	x	y	z	U_{eq}
C(1)	3293 (3)	56371 (15)	−5715 (7)	365 (10)
C(2)	3687 (3)	54354 (15)	−10339 (7)	374 (10)
Cl	4469 (1)	63609 (4)	−13982 (2)	548 (3)
C(3)	3505 (3)	45167 (17)	−12125 (7)	427 (11)
C(4)	2946 (3)	37704 (16)	−9232 (7)	435 (12)
C(4a)	2554 (3)	39542 (14)	−4584 (7)	360 (10)
O(5)	2087 (3)	31784 (10)	−1864 (5)	472 (9)
C(6)	1367 (4)	32640 (15)	2759 (8)	432 (12)
C(6a)	1675 (3)	42433 (13)	4656 (6)	310 (9)
N(7)	1418 (2)	45946 (10)	9146 (5)	309 (8)
C(8)	808 (3)	40860 (14)	13103 (6)	353 (10)
O(8)	380 (2)	32413 (10)	12768 (5)	468 (9)
C(9)	739 (3)	46313 (16)	17411 (7)	423 (11)
C(10)	1174 (3)	55674 (15)	17961 (6)	385 (10)
S	1898 (1)	63435 (3)	13640 (2)	396 (3)
C(11a)	1907 (3)	55698 (13)	8920 (6)	316 (9)
N(12)	2416 (2)	58361 (11)	4749 (5)	336 (8)
C(12a)	2280 (3)	50055 (13)	2119 (6)	306 (9)
C(12b)	2711 (3)	48905 (13)	−2808 (6)	315 (9)
C(13)	1039 (4)	59920 (18)	22755 (7)	489 (13)
O(14)	520 (4)	55591 (15)	26108 (6)	722 (13)
O(15)	1534 (3)	69110 (12)	22757 (5)	575 (10)
C(16)	1509 (6)	74078 (28)	27241 (11)	767 (22)

Table 2. *Selected bond angles* (°) *in* (5)

E.s.d.'s range from 0·1 to 0·2°.

C(1)—C(2)—Cl	119·3	N(7)—C(6a)—C(12a)	105·4
C(1)—C(2)—C(3)	121·5	N(7)—C(8)—O(8)	120·0
C(1)—C(12b)—C(4a)	119·8	N(7)—C(8)—C(9)	115·8
C(1)—C(12b)—C(12a)	124·2	N(7)—C(11a)—S	124·3
C(2)—C(1)—C(12b)	118·9	N(7)—C(11a)—N(12)	112·8
C(2)—C(3)—C(4)	119·8	C(8)—N(7)—C(11a)	127·0
Cl—C(2)—C(3)	119·2	C(8)—C(9)—C(10)	126·6
C(3)—C(4)—C(4a)	119·7	O(8)—C(8)—C(9)	124·2
C(4)—C(4a)—O(5)	116·8	C(9)—C(10)—S	126·2
C(4)—C(4a)—C(12b)	120·3	C(9)—C(10)—C(13)	118·2
C(4a)—O(5)—C(6)	123·4	C(10)—S—C(11a)	100·1
C(4a)—C(12b)—C(12a)	115·9	C(10)—C(13)—O(14)	124·1
O(5)—C(4a)—C(12b)	122·8	C(10)—C(13)—O(15)	111·2
O(5)—C(6)—C(6a)	111·3	S—C(10)—C(13)	115·6
C(6)—C(6a)—N(7)	130·0	S—C(11a)—N(12)	122·9
C(6)—C(6a)—C(12a)	124·6	C(11a)—N(12)—C(12a)	104·1
C(6a)—N(7)—C(8)	127·8	N(12)—C(12a)—C(12b)	127·3
C(6a)—N(7)—C(11a)	105·3	C(13)—O(15)—C(16)	116·9
C(6a)—C(12a)—N(12)	112·5	O(14)—C(13)—O(15)	124·7
C(6a)—C(12a)—C(12b)	120·2		

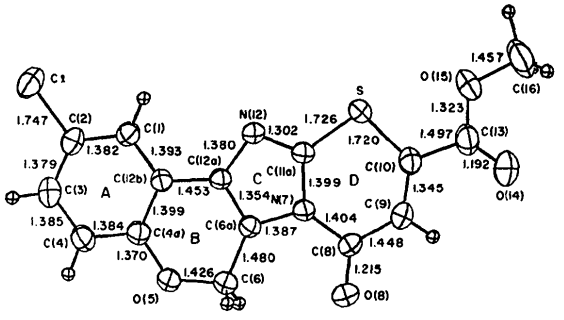


Fig. 1. Atom numbering and bond distances in (5). E.s.d.'s are in the range 0·002 to 0·004 Å.

Intermolecular contacts are all of the van der Waals type. Regions of contact which are less than the sum of the van der Waals radii are between N(12) and H(6*b*) ($\frac{1}{2}-x$, $\frac{1}{2}+y$, z) 2·67 (4) Å and O(14) and H(3) ($\frac{1}{2}-x$, $1-y$, $\frac{1}{2}+z$) 2·53 (4) Å.

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Structure of the Hydrate Form of a β-Thiotrifluoromethyl Ketone, a Potent Esterase Inhibitor

By M. M. Olmstead and W. K. Musker

Department of Chemistry, University of California, Davis, California 95616, *USA*

and B. D. Hammock

Departments of Entomology and Environmental Toxicology, University of California, Davis, California 95616, *USA*

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Abstract. 1,1,1-Trifluoro-5-phenyl-4-thiapentane-2,2-diol, $C_{10}H_{11}F_3O_2S$, $M_r = 252{\cdot}25$, $P2_1/c$, $a = 11{\cdot}476$ (4), $b = 10{\cdot}112$ (2), $c = 9{\cdot}794$ (3) Å, $\beta = 104{\cdot}42$ (2)°, $V = 1100{\cdot}7$ (5) Å^3, $Z = 4$, $D_x(130\ K) = 1{\cdot}52$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 3{\cdot}0$ cm^{-1}, $F(000) = 512$, $T = 130$ K, $R = 0{\cdot}039$, 1937 unique reflections. The molecular structure of the hydrated ketone has two equivalent hydroxyl groups bonded to the C atom of the ketone functionality. One of the hydroxyl H atoms is hydrogen bonded across a center of symmetry to another molecule. The other hydroxyl H atom exhibits an intramolecular H bond to the thioether S atom with H···S of 2·37 (5) Å.

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Introduction. Several laboratories have demonstrated that molecules containing the highly polarized trifluoromethylketone functionality can be potent inhibitors of carboxylesterases from a variety of species (Brodbeck, Schweikert, Gentinetta & Rottenberg, 1979; Gelb, Svaren & Abeles, 1985; Abdel-Aal &