Acta Cryst. (1985). C**41**, 247–249

Molecular Structure Analysis of Monoamine Oxidase Inhibitors. XIII. (4*R**)-3-{4-[(3-Chlorophenyl)methoxy]phenyl}-5-(methylaminomethyl)-1,3-oxazolidin-2-one Methanesulphonic Acid, $C_{18}H_{19}ClN_2O_3.CH_3SO_3H$

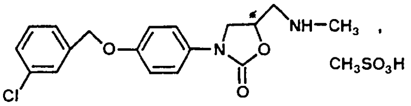
By François Durant, Bernadette Norberg, Françoise Bufkens and Guy Evrard

Laboratoire de Chimie Moléculaire Structurale, Facultés Universitaires de Namur, 61 rue de Bruxelles, B-5000 Namur, Belgium

(*Received 22 November 1983; accepted 1 June 1984*)

Abstract. $M_r = 442{\cdot}6$, $P2_12_12_1$, $a = 7{\cdot}396\,(1)$, $b = 45{\cdot}969\,(3)$, $c = 5{\cdot}822\,(1)$ Å, $V = 1979{\cdot}2$ Å^3, $Z = 4$, $D_x = 1{\cdot}49$ Mg m^{-3}, Cu $K\bar{\alpha}$, $\lambda = 1{\cdot}54178$ Å, $\mu = 2{\cdot}910$ mm^{-1}, $F(000) = 928$, $T = 293$ K, $R = 0{\cdot}05$ for 1937 significant reflections. The oxazolidinone moiety is hardly distorted. Quasi-coplanarity between the three rings is observed as in the 5-methoxymethyl analogue previously reported, but the nitrogen atom of the 5-methylaminomethyl moiety is here more distant from the two oxygen atoms of the oxazolidinone group; this nitrogen atom is bonded to solvent molecules by two H bridges which lie along an intermolecular chain parallel to **a**.

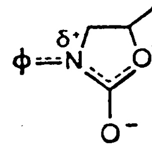
Introduction. This study is part of an investigation on structural properties of monoamine oxidase inhibitors (MAOI's) belonging to the oxazolidinone family whose activity/selectivity towards the A or B forms of the enzyme and reversibility depend on the nature of the substituents (Dostert, Strolin-Benedetti & Jalfre, 1982). The title compound was studied to examine the influence on the conformation of a $-CH_2-NH-CH_3$ moiety instead of the $-CH_2-O-CH_3$ side chain in the analogue previously reported (Durant, Lefevre, Evrard & Michel, 1982). Its absolute configuration was determined by the chemical method (Delalande Research Centre).



Experimental. Crystal $0{\cdot}05 \times 0{\cdot}21 \times 0{\cdot}30$ mm from methanol/*n*-butanol solution at room temperature. Enraf–Nonius CAD-4 diffractometer. Lattice parameters from least-squares refinement of 23 medium-angle reflections. Lorentz and polarization corrections, no absorption. No intensity variation of standard reflection. $4 \leq 2\theta \leq 148°$. 2390 independent reflections measured ($0 \leq h \leq 9$, $0 \leq k \leq 57$, $0 \leq l \leq 7$), 1937 observed, $I > 2{\cdot}5\sigma$ [$\sigma^2 = S + B + (0{\cdot}03S)^2$, S is scan and B background counts]. Direct methods (*MULTAN*80: Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); 25 non-H atoms found in best-FOM E map; missing C(5), N(6), O(15), C(23) located on difference Fourier map. Full-matrix least-squares refinement on F (*SHELX*76: Sheldrick, 1976). 15 H atoms located on difference Fourier map; the 8 missing H atoms calculated. Anisotropic temperature factors for non-H atoms and isotropic for H atoms (corresponding to those of carrier atoms). Final $R = 0{\cdot}05$ ($w = 1{\cdot}0$); $S = 1{\cdot}85$. $(\Delta/\sigma)_{\max} = 0{\cdot}493$ [for y of C(30)]; max. and min. heights in final difference Fourier synthesis 0·38 and −0·46 e Å^{-3}. Scattering factors from *SHELX*76.*

Discussion. The final atomic coordinates are given in Table 1. Fig. 1 shows the bond lengths and angles.

The oxazolidinone moiety is distorted little and is coplanar with the adjacent phenyl ring, as shown in Table 2. This geometry leads to distances O(1)···C(10) and O(1)···H(10) smaller than the van der Waals contacts (3·05 and 2·55 Å, respectively). The N(8) atom is trigonal; its deviation from the mean plane C(2),C(7),C(9) is very small (Table 2) and the sum of valence angles is close to 360° (Fig. 1). The bond lengths in the oxazolidinone ring and the distance N(8)—C(9) are not significantly different from those observed in the 5-methoxymethyl analogue (Durant *et al.*, 1982) (Table 2); they agree well with the scheme of resonance already suggested for this type of oxazolidinone derivative.



---

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and selected torsion angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39526 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0108-2701/85/020247-03$01.50

Table 1. *Final coordinates* (×10⁴) *and* B_{eq} *values with e.s.d.'s in parentheses*

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

	x	y	z	$B_{\rm eq}$(Å^2)
O(1)	6835 (8)	1355 (1)	13155 (9)	4·62 (1)
C(2)	7547 (10)	1447 (1)	11412 (12)	3·14 (2)
O(3)	7485 (6)	1731 (1)	10880 (8)	3·93 (1)
C(4)	8401 (9)	1787 (1)	8705 (13)	3·25 (2)
C(5)	7069 (9)	1915 (1)	6990 (13)	3·28 (2)
N(6)	6791 (8)	2236 (1)	7241 (11)	3·41 (1)
C(7)	9068 (10)	1489 (1)	7937 (13)	3·73 (2)
N(8)	8503 (6)	1298 (1)	9815 (10)	2·81 (1)
C(9)	8726 (8)	992 (1)	9717 (12)	2·71 (1)
C(14)	9531 (9)	871 (1)	7744 (13)	3·20 (2)
C(13)	9825 (9)	576 (1)	7583 (12)	3·06 (1)
C(12)	9322 (10)	393 (1)	9346 (12)	3·25 (2)
C(11)	8494 (10)	508 (1)	11272 (13)	3·23 (2)
C(10)	8208 (9)	806 (1)	11454 (12)	3·21 (2)
O(15)	9697 (8)	104 (1)	9006 (9)	4·53 (1)
C(16)	9606 (10)	−89 (1)	10880 (13)	3·85 (2)
C(17)	10356 (9)	−379 (1)	10152 (13)	3·06 (1)
C(18)	11245 (10)	−410 (1)	8053 (13)	3·42 (2)
C(19)	11917 (9)	−681 (1)	7450 (13)	3·66 (2)
C(20)	11747 (10)	−919 (1)	8853 (13)	3·45 (2)
C(21)	10887 (9)	−884 (1)	10925 (13)	3·04 (1)
C(22)	10178 (9)	−616 (1)	11577 (12)	3·03 (2)
C(23)	6326 (13)	2339 (2)	9573 (15)	4·92 (2)
Cl(24)	10756 (3)	−1179 (1)	12801 (4)	4·49 (1)
S(1)	2294 (2)	2049 (1)	4919 (4)	3·44 (1)
C(30)	2541 (12)	1754 (2)	2994 (15)	4·62 (2)
O(31)	502 (6)	2171 (1)	4472 (13)	6·55 (2)
O(32)	2540 (6)	1933 (1)	7218 (10)	5·06 (1)
O(33)	3700 (6)	2260 (1)	4234 (10)	4·36 (1)

Table 2. *Comparison of values of main structural features in the title compound* (I) *and in the 5-methoxymethyl analogue* (II) (R*)

	(I)	(II)
Deviations (Å) from mean plane O(1), C(2), O(3), N(8)		
O(1)	0·003	0·001
C(2)	−0·007	−0·003
O(3)	0·002	0·001
N(8)	0·002	0·001
C(4)	0·036	0·171
C(7)	−0·068	−0·102
E.s.d.'s (Å)	0·005	0·002
Dihedral angle (°) between oxazolidinone mean plane and central phenyl ring	5·42	7·17
Contact distances (Å)		
O(1)···C(10)	2·895 (7)	2·930 (11)
O(1)···H(101)	2·407 (5)	2·260 (5)
O(3)···O(6)	—	2·865 (7)
O(3)···N(6)	3·184 (7)	—
Deviation (Å) of N(8) from the mean plane C(2), C(7), C(9)	0·065 (1)	0·029 (1)
Bond lengths (Å)		
O(1)—C(2)	1·218 (9)	1·185 (9)
C(2)—O(3)	1·343 (7)	1·349 (11)
O(3)—C(4)	1·459 (9)	1·464 (10)
C(4)—C(7)	1·523 (7)	1·538 (13)
C(7)—N(8)	1·463 (9)	1·466 (9)
N(8)—C(2)	1·354 (8)	1·393 (11)
N(8)—C(9)	1·417 (6)	1·439 (11)

The dihedral angles along the N(8) side chain show that the molecule is stretched and flattened favouring the crystal packing. The O(15) atom seems to have an sp^2 character like that already observed in the 5-methoxymethyl analogue; this is shown by the shortened C(12)—O(15) bond length, the C(12)—O(15)—C(16) valence angle (~120°) and the C(11)—C(12)—O(15)—C(16) torsion angle (~180°).

The nitrogen atom of the methylaminomethyl moiety is bonded to solvent molecules by two H bridges to form an intermolecular chain parallel to the a axis: N($6^{\rm i}$)···H(331)—O($33^{\rm i}$) 1·779 (6), N($6^{\rm i}$)—H(61)···O($33^{\rm ii}$) 1·959 (5) Å [(i) x, y, z, (ii) $-\frac{1}{2}+x$, $\frac{1}{2}-y$, $1-z$]. N(6) is a little more distant from O(3) than is O(6) in the methoxymethyl analogue (Table 2). As illustrated in Fig. 2, O(6) is located above the oxazolidinone ring whereas N(6) is outside it on account of the intermolecular H bonds.

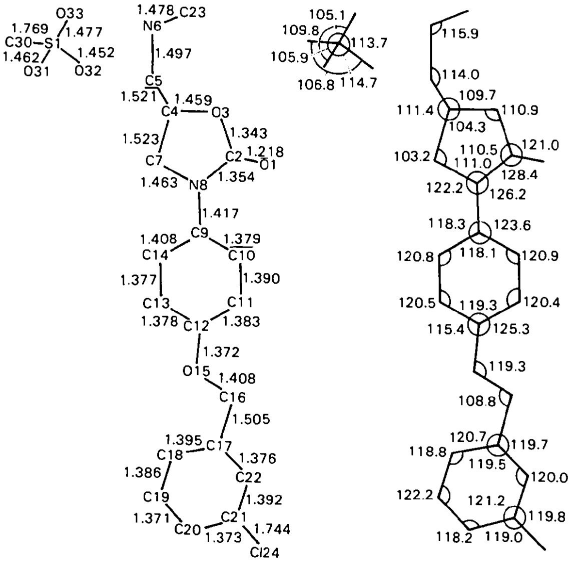


Fig. 1. Atom numbering, bond lengths (Å) and angles (°); e.s.d.'s are less than 0·011 Å and 0·6°.

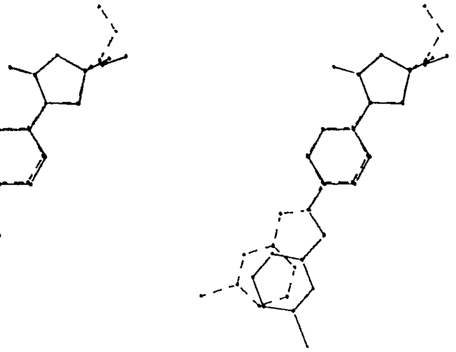


Fig. 2. Stereoscopic view after a least-squares fitting of the N(8)—C(2)—O(3) moieties of the title compound (dotted lines) and the methoxymethyl analogue, using the *OSIRIS* program (Michel, 1978).

The authors are grateful to Drs Dostert and Langlois from Delalande Research Centre (Rueil-Malmaison, France) for providing the title compounds and helpful discussions.

References

DOSTERT, P., STROLIN-BENEDETTI, M. & JALFRE, M. (1982). *Monoamine Oxidase, Basic and Clinical Frontiers,* edited by K. KAMIJU, E. USDIN & T. NAGATSU. *Excerpta Med. Int. Congr. Ser.* No. 564, pp. 197–208.

DURANT, F., LEFEVRE, F., EVRARD, G. & MICHEL, A. (1982). *Bull. Soc. Chim. Belg.* **91**, 831.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain-la-Neuve, Belgium.

MICHEL, A. (1978). *OSIRIS.* A molecular graphics system. Facultés Universitaires, B-5000 Namur, Belgium.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

Acta Cryst. (1985). C**41**, 249–252

Stereochemical Studies of Oligomers. XIV.* Structures of 2,4-Pentanediyl Bis(*p*-chlorobenzoate) and of 1,3-Butanediyl Bis(*p*-chlorobenzoate) (PEDP and BUDP), $C_{19}H_{18}Cl_2O_4$ and $C_{18}H_{16}Cl_2O_4$

BY GABRIELE BOCELLI

Centro di Studio per la Strutturistica Diffrattometrica del CNR, Via M. D'Azeglio 85, 43100 *Parma, Italy*

AND M. F. GRENIER-LOUSTALOT

Institut Universitaire de Recherche Scientifique, Avenue Philippon, 64000 *Pau, France*

(*Received* 28 *May* 1984; *accepted* 20 *July* 1984)

Abstract. Ni-filtered Cu $K\alpha$ radiation, $\bar{\lambda} = 1{\cdot}5418$ Å, room temperature. PEDP: $M_r = 381{\cdot}3$, monoclinic, $P2_1/n$, $a = 15{\cdot}274\,(3)$, $b = 11{\cdot}099\,(2)$, $c = 11{\cdot}559\,(3)$ Å, $\beta = 106{\cdot}24\,(4)°$, $V = 1881{\cdot}4\,(8)$ Å^3, $Z = 4$, $D_x = 1{\cdot}35$ g cm^{-3}, $\mu = 33{\cdot}25$ cm^{-1}, $F(000) = 792$, $R = 0{\cdot}048$ for 2573 observed reflections. BUDP: $M_r = 367{\cdot}2$, monoclinic, $P2_1/n$, $a = 16{\cdot}935\,(3)$, $b = 6{\cdot}045\,(2)$, $c = 16{\cdot}887\,(3)$ Å, $\beta = 95{\cdot}01\,(3)°$, $V = 1722{\cdot}2\,(7)$ Å^3, $Z = 4$, $D_x = 1{\cdot}42$ g cm^{-3}, $\mu = 36{\cdot}13$ cm^{-1}, $F(000) = 760$, $R = 0{\cdot}054$ for 2049 observed reflections. The conformation of the propanediyl segment of the chain is *gauche–gauche* in the two compounds. The values of the remaining torsion angles cause in PEDP a rotation of one aromatic ring with respect to the other with a resulting *endo* conformation of the molecule. The two carboxylic groups are tilted by 8·3 (1), 13·1 (1)° and 3·6 (1), 6·7 (1)° with respect to their phenyl rings in the two compounds, respectively.

Introduction. The interest in conformational changes of this series of compounds has now focused on the presence of chlorine atoms on the aromatic rings or methyl groups on the aliphatic chain. In earlier papers we gave analyses of compounds similar to PEDP but without chlorines (Bocelli & Grenier-Loustalot, 1983*a*) or with chlorine atoms in *meta* positions (Bocelli & Grenier-Loustalot, 1983*b*), while Pérez & Brisse (1977, 1976) have reported two structures: one without methyl groups and chlorines and a second without methyls and with *p*-chlorines.

The two structures here reported constitute another step towards the final goal to have, for all compounds of this series, the crystal structures of all the possible derivatives with or without a methylated chain and with or without halogens.

Experimental. For both compounds: crystallographic system and cell parameters by least squares (30 reflections with θ range 13·1–69·5°, 26 with θ range 12·2–20·1° for PEDP and BUDP, respectively); Siemens AED single-crystal diffractometer equipped with a General Automation Jumbo 220 computer; intensities collected with modified version (Belletti, Ugozzoli, Cantoni & Pasquinelli, 1979) of the Lehmann & Larsen (1974) procedure; data corrected for Lorentz and polarization effects but not for absorption; one standard reflection monitored every 50 counts; atomic scattering factors of *SHELX* (Sheldrick, 1976).†

---

* Part XIII: Bocelli & Grenier-Loustalot (1984*b*).

† Lists of structure factors, anisotropic thermal parameters and H coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39655 (29 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0108-2701/85/020249-04$01.50