Table 3. *Hydrogen bonds (the translation indicates intra- or intermolecular contacts)*

Compound	Bond			Translation
(I)	N(16)–H···N(4)	2·940 (3)Å	154°	—
(II)	N(16*A*)–H···N(4*A*)	3·013 (5)	142	—
(II)	N(16*B*)–H···N(4*B*)	2·923 (5)	99	—
(I)	N(12)–H···N(3)	2·989 (3)	166	$-x, -y, 1-z$
(I)	N(12)–H···O(15)	2·997 (4)	154	$0{\cdot}5-x, y-0{\cdot}5, 1{\cdot}5-z$
(I)	N(16)–H···O(14)	2·974 (4)	154	$x, y, 1+z$
(II)	N(12*A*)–H···N(3*A*)	2·991 (4)	173	$-x, 1-y, 1-z$
(II)	N(12*A*)–H···O(14*B*)	2·887 (4)	145	$x, y, 1+z$

attributed here to packing effects. The increasing deformation of the C(6)–C(11)–S(13) angle, 121·6 (2)° for (I) and 122·6 (3) and 124·0 (3)° for (II), is a logical consequence of this effect, to keep the planarity of the system, while the C(6)–C(11) and C(11)–S(13) bond lengths are not significantly different in all three molecules. The geometry around C(6) is influenced by the same effect.

Table 3 lists the most relevant hydrogen-bond contacts (< 3·05 Å): it is possible to distinguish a different pattern, which we correlate with the more pronounced lipophilic character of compound (II), determined by liquid chromatography.

We thank Professor Giovanni Orzalesi, Istituto di Chimica Farmaceutica, Florence University, for supplying samples of the two compounds.

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Molecular Structure Analysis of Monoamine Oxidase Inhibitors. VII. *cis* and *trans* Isomers of 3-[4-(5-Methoxymethyl-4-methyl-2-oxo-1,3-oxazolidin-3-yl)-phenoxymethyl]benzonitrile, $C_{20}H_{20}N_2O_4$

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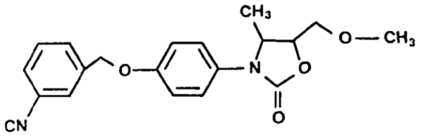
(*Received* 10 *March* 1983; *accepted* 18 *November* 1983)

Abstract. $M_r = 352{\cdot}4$, $P2_1/c$, $Z = 4$, $F(000) = 744$, Cu $K\bar{\alpha}$, $\lambda = 1{\cdot}54178$ Å, $T = 293$ K. *cis*(‘*Z*’) isomer: $a = 13{\cdot}491$ (2), $b = 14{\cdot}597$ (3), $c = 9{\cdot}187$ (3) Å, $\beta = 99{\cdot}85$ (2)°, $V = 1782{\cdot}5$ Å^3, $D_x = 1{\cdot}31$ Mg m^{-3}, $\mu = 0{\cdot}670$ mm^{-1}, $R = 0{\cdot}05$, 2010 significant reflections. *trans*(‘*E*’) isomer: $a = 16{\cdot}961$ (2), $b = 14{\cdot}656$ (2), $c = 7{\cdot}525$ (1) Å, $\beta = 97{\cdot}40$ (1)°, $V = 1855{\cdot}0$ Å^3, $D_x = 1{\cdot}26$ Mg m^{-3}, $\mu = 0{\cdot}644$ mm^{-1}, $R = 0{\cdot}03$, 1137 significant reflections. Compared to the demethyl analogue previously studied, the oxazolidinone group of both *cis* and *trans* isomers is more distorted and markedly inclined with regard to the adjacent phenyl. Nevertheless the three O atoms of the 5-methoxymethyl-oxazolidin-2-one moieties remain close by.

Introduction. This work is part of a more general study on the conformational properties of a new series of monoamine oxidase inhibitors (MAOI's) belonging to an oxazolidinone family. Indeed, some of these have been reported as potent antidepressant drugs; their reversibility and their selectivity towards A and B forms of the enzyme depend on the nature of the substituents (Dostert, Strolin-Benedetti & Jalfre, 1982). The two stereoisomers here described have the 4-methyl and 5-methoxymethyl substituents in either *cis* (‘*Z*’) or *trans* (‘*E*’) positions.



(I)

Experimental. Isomer '*Z*' crystallized from an *n*-butanol solution at room temperature. Colourless prismatic crystal 0·23 × 0·30 × 0·09 mm for all X-ray measurements. Enraf–Nonius CAD-4 diffractometer. Lattice parameters from least-squares refinement of 22 medium-angle reflections. No absorption correction. No intensity variation of standard reflection. $4 \leq 2\theta \leq 148°$. 3612 independent reflections measured ($-16 \leq h \leq 16$, $0 \leq k \leq 18$, $0 \leq l \leq 11$), 2010 observed [$I > 2{\cdot}5\sigma(I)$]. Direct methods (*MULTAN*80: Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); 24 of the 26 non-H atoms found in the best-FOM *E* map; the missing N(25), C(26) located on a difference Fourier map. Full-matrix least-squares refinement on *F* using *SHELX* (Sheldrick, 1976). 19 H atoms located on difference Fourier map; the last one, bonded to C(26), calculated. Anisotropic temperature factors for all non-H atoms and isotropic ones for H atoms (corresponding to those of the carrier atoms). Final $R = 0{\cdot}05$, $wR = 0{\cdot}06$, $w = 1/[\sigma^2(F) + 0{\cdot}001F^2]$, $(\Delta/\sigma)_{\max} = -0{\cdot}294$ [*x* of C(19)], $S = 0{\cdot}81$; max. and min. heights in final difference Fourier synthesis 0·25 and $-0{\cdot}24$ e Å^{-3}. Scattering factors from *SHELX*.

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

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

	x	*y*	*z*	B_{eq}(Å^2)
'*Z*' isomer				
O(1)	4936 (2)	3971 (2)	1556 (2)	7·29 (1)
C(2)	5314 (2)	3772 (2)	516 (3)	5·63 (1)
O(3)	4770 (1)	3723 (2)	−869 (2)	6·62 (1)
C(4)	5380 (2)	3292 (2)	−1849 (3)	5·81 (1)
C(5)	5119 (3)	3701 (3)	−3351 (3)	6·53 (1)
O(6)	4162 (2)	3374 (2)	−3984 (3)	8·52 (1)
C(7)	6467 (2)	3443 (2)	−1058 (3)	5·65 (1)
N(8)	6288 (2)	3555 (2)	464 (2)	5·24 (1)
C(9)	7095 (2)	3599 (2)	1684 (3)	4·86 (1)
C(10)	7057 (2)	4141 (2)	2905 (3)	5·79 (1)
C(11)	7868 (2)	4152 (2)	4087 (3)	5·78 (1)
C(12)	8696 (2)	3624 (2)	4040 (3)	5·10 (1)
C(13)	8743 (2)	3097 (2)	2814 (3)	6·26 (1)
C(14)	7946 (2)	3079 (2)	1646 (4)	6·16 (1)
O(15)	9509 (2)	3549 (2)	5147 (2)	6·45 (1)
C(16)	9550 (2)	4126 (2)	6399 (3)	5·78 (1)
C(17)	10492 (2)	3899 (2)	7469 (3)	5·20 (1)
C(18)	11372 (2)	3665 (2)	6982 (3)	6·16 (1)
C(19)	12234 (3)	3483 (3)	7973 (4)	6·97 (1)
C(20)	12240 (2)	3526 (3)	9479 (4)	6·64 (1)
C(21)	11362 (2)	3751 (2)	9970 (3)	5·66 (1)
C(22)	10484 (2)	3938 (2)	8969 (3)	5·40 (1)
C(23)	3794 (4)	3756 (4)	−5362 (4)	8·60 (1)
C(24)	11344 (3)	3814 (2)	11540 (4)	6·57 (1)
N(25)	11347 (3)	3879 (3)	12774 (3)	8·90 (1)
C(26)	6999 (3)	4276 (3)	−1539 (4)	7·33 (1)
'*E*' isomer				
O(1)	−98 (1)	3807 (1)	6891 (3)	5·90 (1)
C(2)	−166 (2)	3802 (2)	5273 (4)	4·70 (1)
O(3)	473 (1)	3861 (1)	4365 (3)	5·45 (1)
C(4)	202 (2)	3921 (2)	2449 (4)	4·89 (1)
C(5)	716 (2)	3363 (3)	1410 (5)	5·65 (1)
O(6)	1473 (1)	3772 (2)	1501 (3)	6·90 (1)
C(7)	−664 (2)	3626 (2)	2245 (4)	5·15 (1)
N(8)	−835 (1)	3720 (2)	4091 (3)	4·80 (1)
C(9)	−1612 (2)	3632 (2)	4604 (4)	4·62 (1)
C(10)	−1868 (2)	4198 (2)	5886 (4)	5·08 (1)
C(11)	−2628 (2)	4138 (2)	6306 (5)	5·51 (1)
C(12)	−3152 (2)	3530 (2)	5404 (4)	5·49 (1)
C(13)	−2908 (2)	2944 (3)	4152 (5)	6·00 (1)
C(14)	−2136 (2)	3000 (3)	3755 (5)	5·79 (1)
O(15)	−3913 (1)	3539 (2)	5873 (3)	7·25 (1)
C(16)	−4531 (2)	3151 (3)	4678 (6)	7·39 (1)
C(17)	−5312 (2)	3467 (2)	5226 (5)	6·01 (1)
C(18)	−6016 (3)	3211 (3)	4212 (6)	7·65 (1)
C(19)	−6740 (2)	3484 (3)	4662 (6)	8·36 (1)
C(20)	−6781 (2)	4019 (3)	6134 (6)	7·74 (1)
C(21)	−6083 (2)	4289 (3)	7149 (5)	7·17 (1)
C(22)	−5349 (2)	4017 (3)	6705 (5)	6·69 (1)
C(23)	1932 (3)	3386 (4)	269 (8)	10·20 (2)
C(24)	−6120 (3)	4873 (4)	8664 (6)	11·35 (2)
N(25)	−6157 (3)	5341 (5)	9854 (6)	18·31 (3)
C(26)	−1185 (3)	4199 (4)	924 (5)	7·93 (1)

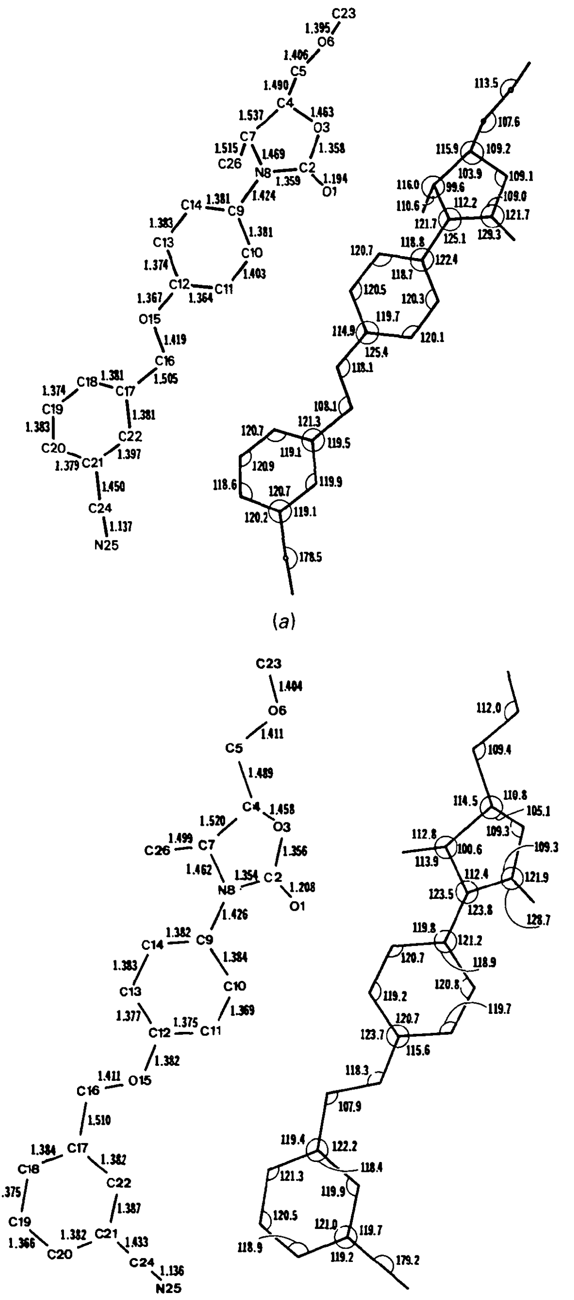


Fig. 1. Atom numbering, bond lengths (Å) and angles (°). (*a*) '*Z*' isomer; e.s.d.'s are smaller than 0·005 Å and 0·4°. (*b*) '*E*' isomer; e.s.d.'s are smaller than 0·008 Å and 0·6°.

Isomer '*E*' recrystallized from a methanol/2-propanol mixture at 278 K. Colourless needles. Crystal used 0·20 × 0·05 × 0·02 mm. Enraf–Nonius CAD-4 diffractometer. Lattice parameters from least-squares refinement of 25 medium-angle reflections. No absorption correction. No intensity variation of standard reflection. $4 \leq 2\theta \leq 130°$. 3093 independent reflections measured ($0 \leq h \leq 19$, $0 \leq k \leq 15$, $-8 \leq l \leq 8$), 1137 observed [$I > 2{\cdot}5\sigma(I)$]. Direct methods (*MULTAN*80; Main *et al.*, 1980); best-FOM *E* map showed all non-H atoms but one; the missing N(25) found on a Fourier map. Full-matrix least-squares refinement on *F* using *SHELX* (Sheldrick, 1976); 15 H atoms from a difference Fourier map, the other five calculated. Anisotropic temperature factors for all non-H atoms and isotropic ones for H atoms (constrained to those of the carrier atoms). Final $R = 0{\cdot}03$, $wR = 0{\cdot}03$, $w = 1/[\sigma^2(F) + 0{\cdot}001F^2]$, $(\Delta/\sigma)_{\max} = -0{\cdot}496$ [y of C(23)], $S = 0{\cdot}59$; max. and min. heights in final difference Fourier synthesis 0·12 and $-0{\cdot}16$ e Å^{-3}. Scattering factors from *SHELX*.

For both isomers *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) was used for structural analysis.

Discussion. Final atomic parameters are given in Table 1.* The atom numbering, bond lengths and bond angles are in Fig. 1, and stereoviews in Fig. 2.

Table 2. *Main torsion angles* (°) *with e.s.d.'s in parentheses, from coordinates corresponding to the configuration R for* C(4)

	'*Z*' isomer	'*E*' isomer
C(4)–C(5)–O(6)–C(23)	175·8 (3)	168·1 (3)
O(3)–C(4)–C(5)–O(6)	−72·3 (3)	69·5 (3)
C(5)–C(4)–C(7)–C(26)	24·9 (4)	99·2 (4)
O(1)–C(2)–O(3)–C(4)	−168·7 (3)	174·9 (2)
O(1)–C(2)–N(8)–C(9)	−5·7 (5)	−0·8 (5)
O(3)–C(2)–N(8)–C(9)	175·0 (3)	179·2 (3)
C(2)–N(8)–C(9)–C(10)	−22·1 (5)	−46·7 (4)
C(7)–N(8)–C(9)–C(14)	−34·8 (4)	−36·4 (4)
C(13)–C(12)–O(15)–C(16)	175·2 (3)	20·2 (5)
C(12)–O(15)–C(16)–C(17)	178·5 (3)	164·9 (3)
O(15)–C(16)–C(17)–C(18)	36·4 (4)	−177·2 (3)

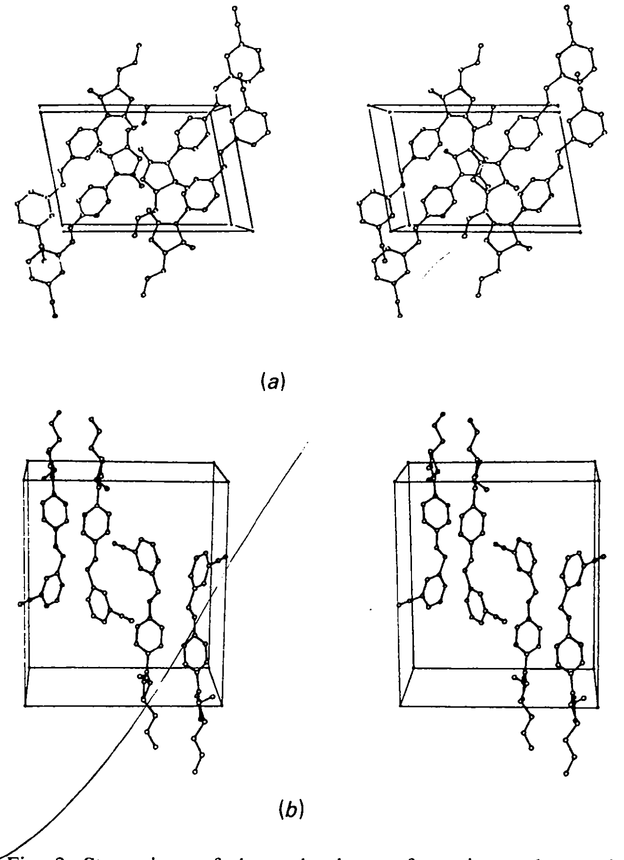


Fig. 2. Stereoviews of the molecular conformation and crystal packing. (*a*) '*Z*' isomer. (*b*) '*E*' isomer.

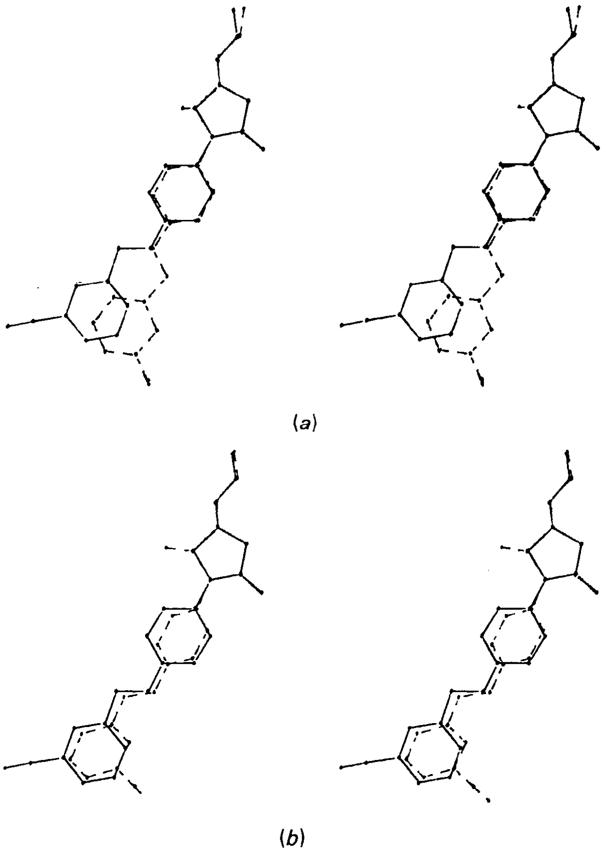


Fig. 3. Stereoscopic views of pairs of molecules after a least-squares fitting of the N(8)–C(2)–O(3) moieties using the program *OSIRIS* (Michel, 1978). The molecules have the asymmetric atom C(7) in the *R* configuration. (*a*) '*Z*' isomer (dotted lines) and demethyl analogue. (*b*) '*E*' isomer (dotted lines) and demethyl analogue.

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39473 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Bond lengths* (Å) *in the oxazolidinone moiety for the unsubstituted oxazolidinone* (*Turley,* 1972), *the demethyl analogue* (*Durant et al.,* 1982) *and the title compounds*

	Unsubstituted oxazolidinone	Demethyl analogue	Title compounds 'Z'	'E'
O(1)–C(2)	1·210 (8)	1·213 (10)	1·194 (4)	1·208 (4)
C(2)–O(3)	1·356 (10)	1·344 (9)	1·358 (3)	1·356 (4)
O(3)–C(4)	1·453 (8)	1·444 (13)	1·463 (4)	1·458 (4)
C(4)–C(7)	1·497 (10)	1·491 (13)	1·537 (4)	1·520 (5)
C(7)–N(8)	1·466 (7)	1·465 (10)	1·469 (4)	1·462 (4)
N(8)–C(2)	1·301 (8)	1·360 (10)	1·359 (4)	1·354 (4)
N(8)–C(9)	—	1·414 (8)	1·424 (3)	1·426 (4)

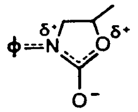
Table 4. *Comparison of the values of the main structural features in the demethyl analogue* (*Durant et al.,* 1982) *and the title compounds*

	Demethyl analogue	'Z' isomer	'E' isomer
Deviation (Å) of N(8) from mean plane C(2),C(7),C(9)	0·028	−0·083	0·048
Deviations (Å) from mean plane O(1),C(2),O(3),N(8)			
O(1)	−0·001	−0·001	−0·003
C(2)	0·003	0·004	0·007
O(3)	−0·001	−0·001	−0·002
N(8)	−0·001	−0·001	−0·002
C(4)	0·098	−0·263	0·136
C(7)	0·017	0·146	−0·158
E.s.d.'s (Å)	0·002	0·002	0·005
Dihedral angle (°) between oxazolidinone mean plane and adjacent phenyl	4·5	25·3	43·9
Contact distances (Å)			
O(1)···C(10)	2·942 (7)	2·929 (4)	3·054 (4)
O(1)···H(101)	2·235 (4)	2·381 (28)	2·706 (28)
C(14)···C(26)		3·459 (5)	3·334 (6)

The main structural features observed for the two title stereoisomers are compared below to those of the 4-demethyl analogue previously reported (Durant, Lefevre, Evrard & Lamotte, 1982).

In both isomers, the oxazolidinone moiety is more distorted as shown in Table 4 and Fig. 3. N(8) deviates slightly from the plane of the three adjacent C atoms C(2), C(7) and C(9): −0·083 and 0·048 Å for the *'Z'* and *'E'* derivatives respectively (Table 4).

The bond lengths within the oxazolidinone moiety are comparable to those of the demethyl analogue except for O(3)—C(4) and C(4)—C(7) which are greater (Table 3). The C(2)—N(8) distances are significantly different from that published for the unsubstituted oxazolidinone (Turley, 1972). These observations lead to the resonance scheme:



(II)

As expected, substitution on C(7) by a methyl group enhances steric hindrance which prevents coplanarity between the oxazolidinone and phenyl rings. The dihedral angles between the mean planes of these two rings (25·3 and 43·9°) result directly from van der Waals contacts between O(1) and C(10)–H(101) or C(14) and C(26) atoms (Table 4).

As the torsion angles C(12)–O(15)–C(16)–C(17) approach 180° [178·5 (3) and 164·9 (3)° respectively] (Table 2), the N(8) side chains are stretched as in the demethyl analogue. The shortened bond lengths C(12)–O(15) [1·367 (3) and 1·382 (4) Å] as well as the torsion angles C(13)–C(12)–O(15)–C(16) [175·2 (3) and 20·2 (5)°] seem to indicate a certain sp^2 character for the O(15) atoms, as previously reported (Durant *et al.,* 1982). The two O atoms O(3) and O(6) keep the same *gauche* conformation as in the demethyl compound so the proximity of the three O atoms of the 5-methoxymethyloxazolidin-2-one moieties is not influenced by the presence of a 4-methyl substituent.

The authors are indebted to the Delalande Research Centre (Rueil-Malmaison, France) for supplying the samples and to Drs Dostert and Langlois for helpful discussions.

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