bond] (Katrusiak, Kałuski, Pietrzak & Skolik, 1986) corroborates the above argument and shows the significance of the intramolecular N···N forces on the conformation of ring *C*. The inclination angle between the phenyl substituent and the N(1)—C(2)=C(3) group in (I) is only slightly more open than in (II); the relevant torsion angles N(1)—C(2)—C(18)—C(19) and C(3)=C(2)—C(18)—C(23) in (II) are −43.2 (8) and −44.6 (9)° respectively (compare the corresponding torsion angles in Fig. 2).

As can be seen in Fig. 3, crystals of (I) and (II) are essentially isostructural. This can also be observed by comparing the unit-cell dimensions: parameters *a* are identical, *b* is only slightly longer in (I) than in (II), but *c* is 1.2 Å longer in (II) than in (I), which corresponds to the orientation of the methyl substituent in structure (II) (Fig. 3*b*) [the unit-cell dimensions of (II) are $a = 7.569$ (3), $b = 9.381$ (1), $c = 13.684$ (4) Å, $\beta = 105.81$ (2)° (Małuszyńska, Boczoń & Kałuski, 1986)]. The comparison of structures (I) and (II) gives a volume of 31.2 Å^3 for the methyl substituent in (II). This volume is much larger than the volume of 21.5 Å^3 given by Kitajgorodski (1976), which was calculated from the molecular-fragment volumes (23.5 Å^3 per methyl substituent *minus* 2.0 Å^3 per H atom in an aromatic ring). It is also reflected in the density of crystals of (II) ($D_x = 1.147$ g cm^{-3}) which are less dense by over 2.5% than the crystals of (I). It appears that the poor stability of the crystals of (II) (Małuszyńska, Boczoń & Kałuski, 1986) is connected with the less-dense packing of the molecules in that structure. No intermolecular contacts shorter than the sum of the van der Waals radii are observed for the structures of (I) and (II).

We are grateful to Dr Wł. Boczoń for suggesting this study and providing the sample of the title compound.

References

ALLEN, F. H., KENNARD, O., WATSON, D. G., BRAMMER, L., ORPEN, A. G. & TAYLOR, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. 1–19.

ALLMANN, R. (1977). In *Monoatomic Rings, Chains and Macromolecules of Main Group Elements*, edited by A. RHEINGOLD, p. 30. Amsterdam: Elsevier.

BOCZOŃ, WŁ., KAŁUSKI, Z. & MAŁUSZYŃSKA, H. (1987). *Bull. Acad. Pol. Sci. Ser. Sci. Chim.* **35**, 541–550.

DOUCERAIN, P. H., CHIARONI, A. & RICHE, C. (1976). *Acta Cryst.* B**32**, 3213–3215.

DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*. New York: Plenum Press.

KATRUSIAK, A., FIGAS, E., KAŁUSKI, Z. & LESIEWICZ, D. (1989). *Acta Cryst.* C**45**, 1758–1760.

KATRUSIAK, A., KAŁUSKI, Z., PIETRZAK, P. & SKOLIK, J. (1986). *J. Cryst. Spectrosc. Res.* **16**, 191–206.

KENNARD, O., WATSON, D. G., ALLEN, F. H., ISAACS, N. W., MOTHERWELL, W. D. S., PETERSON, R. C. & TOWN, W. G. (1972). Editors. *Molecular Structures and Dimensions*, Vol. 41. Utrecht: Oosthoek.

KITAJGORODSKI, A. I. (1976). *Kryształy Molekularne*, p. 28. Warszaw: PWN.

KLYNE, W., SCOPES, P. N., THOMAS, R. N., SKOLIK, J., GAWROŃSKI, J. & WIEWIÓROWSKI, M. (1974). *J. Chem. Soc. Perkin Trans.* 1, pp. 2565–2570.

MAŁUSZYŃSKA, H., BOCZOŃ, WŁ. & KAŁUSKI, Z. (1986). *J. Cryst. Spectrosc. Res.* **16**, 687–694.

MOTHERWELL, W. D. S. (1976). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.

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

SHELDRICK, G. M. (1986). *SHELXS*86. Program for crystal structure determination. Univ. of Göttingen, Germany.

SZYMCZAK, A. (1983). MSc thesis, Adam Mickiewicz Univ., Poznań, Poland.

Acta Cryst. (1993). C**49**, 500–504

Structure of 1-{4-[2-(Diethylamino)ethoxy]phenyl}-2-(4-methoxyphenyl)-1-phenylethan-1-ol, the Non-Steroidal Antiestrogen MER25

BY M. B. HOSSAIN, J. SYMERSKY, S. C. NEELY AND D. VAN DER HELM

Department of Chemistry and Biochemistry, University of Oklahoma, Norman, Oklahoma 73019, *USA*

AND R. A. MAGARIAN

Department of Medicinal Chemistry, College of Pharmacy, University of Oklahoma Health Science Center, Oklahoma City, Oklahoma 73190, *USA*

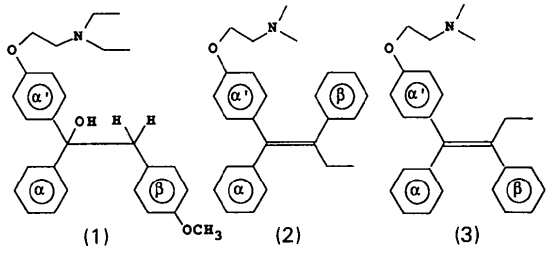
(*Received* 24 *December* 1991; *accepted* 21 *July* 1992)

Abstract. $C_{27}H_{33}NO_3$, $M_r = 419.6$, monoclinic, $P2_1/a$, $a = 22.833$ (6), $b = 9.370$ (3), $c = 11.434$ (4) Å, $\beta = 110.71$ (8)°, $V = 2288.2$ Å^3, $Z = 4$, $D_x = 1.22$ g cm^{-3}, λ(Cu $K\alpha$) = 1.54178 Å, $\mu = 5.8$ cm^{-1}, $F(000) = 904$, $T = 138$ K, $R = 0.049$ for 3265 observed reflections. The molecule of MER25 assumes an extended con-

0108-2701/93/030500-05$06.00

formation with rings α' and β in an antiperiplanar (*trans*) conformation giving the solid-state conformer a closer resemblance to the estrogenic (*E*) isomer of tamoxifen than the antiestrogenic (*Z*) isomer. The geometrical features of the triarylethan-1-ol moiety are comparable to related structures but the orientations of the phenyl rings are different. The O—C—C—N segment in the (diethylamino)ethoxy side chain has the uncommon *trans* conformation instead of the more commonly observed *gauche* conformation seen in tamoxifen and many of its derivative structures. The amino N atom forms a hydrogen bond with the hydroxyl group of a neighboring molecule to form an infinite chain along the *b* axis.

Introduction. MER25, also known as ethamoxytriphetol (1), the first non-steroidal antiestrogen, was found to inhibit estrogen in all species of animal tested (Lerner, Holthaus & Thompson, 1958). It also has shown the ability to prevent implantation of blastocysts in rats (Segal & Nelson, 1958) which led to the investigation for the potential clinical application of antiestrogens as contraceptives. Although MER25 was later withdrawn as a drug because of its low potency and toxic side effects (Lerner, 1981), its bioactivity studies led to the discovery of various other non-steroidal antiestrogens such as clomiphene (Herbst, Griffiths & Kistner, 1964) and the most widely known tamoxifen (2) (Precigoux, Courseille, Geoffre & Hospital, 1979) and its metabolites.



A common structural feature in these compounds is the presence of three aryl rings with a central ethylenic bridge. Structure–activity relationship studies of tamoxifen and its analogues have shown the importance of certain key structural features (Jordan, 1984). In general, those compounds derived from (*Z*)-tamoxifen (2) show antiestrogenic activity along with some estrogenicity, whereas (*E*)-tamoxifen (3) and its derivatives are purely estrogenic. In a recent study it has been shown that the positioning of the aminoethoxy side chain of the α' ring of tamoxifen, with respect to the three aryl rings, might be critical for antiestrogenic activity (Murphy, Parker, McCague & Jordan, 1991). X-ray structure investigations of tamoxifen and many of its derivatives have been carried out (Precigoux *et al.*, 1979; Kuroda, Cutbush, Neidle & Leung, 1985; Hunter, Payne, Rahman, Richardson & Zea Ponce, 1983; Precigoux, Hospital, Leroy, Delbarre & Roques, 1982) and all the structures have shown a consistent propeller conformation for their three aryl rings. It is quite surprising that no attempt was made to determine the structure of the original antiestrogen, MER25. As part of our continuing effort to study the conformational features of non-steroidal antiestrogens, the X-ray structure determination of MER25 was performed. We report the crystal and molecular structure of the compound.

Experimental. MER25 was crystallized by allowing hexane to diffuse into a saturated ethanol solution at around 273 K. A block-shaped crystal of size 0.25 × 0.30 × 0.45 mm was used for all X-ray measurements on an Enraf–Nonius CAD-4 diffractometer equipped with a liquid nitrogen low-temperature device and Cu $K\alpha$ radiation. Lattice parameters were determined from setting of 48 reflections with $30 < 2\theta < 50°$, 4700 unique reflections were measured using ω–2θ scans for $2\theta < 150°$, $-28 < h < 28$, $0 < k < 11$, $0 < l < 14$ [scan width $(0.80 + 0.20\tan\theta)°$, extended 25% on each side for background measurement, horizontal aperture $(2.40 + 0.86\tan\theta)$ mm, vertical aperture 4 mm]. Three standard reflections (555, 11,1,3 and $\bar{4}$,10,5), measured every 7200 s of X-ray exposure, showed maximum variation of 4.0%. Lorentz and polarization corrections were applied, but no absorption correction. 3265 reflections were observed on the basis $I > 3\sigma(I)$. The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1986), and refined by full-matrix least squares using *SHELX*76 (Sheldrick, 1976); $\sum w(F_o - F_c)^2$ was minimized, where $w = 1.804/\sigma^2(F_o)$. All H atoms were located from difference Fourier maps and refined with isotropic temperature factors. Final $R = 0.049$, $wR = 0.062$ for 3265 observed reflections; $(\Delta/\sigma)_{max} = 0.01$, $S = 2.0$ for 596 variables; highest/lowest peaks in the final difference map ± 0.3 e Å^{-3}. Atomic scattering factors were provided in *SHELX*76.

Discussion. The final positional and thermal parameters of the non-H atoms are listed in Table 1.* A perspective drawing of a single molecule of MER25 is shown in Fig. 1 along with the atom labelling. Bond distances and bond angles are listed in Table 2. The bond distances involving atom C(1) show the expected lengthening resulting from steric crowding.

* 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 55607 (31 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: GR0209]

Table 1. *Atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

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

	x	y	z	U_{eq}
O(1)	0.83332 (8)	0.8585 (2)	0.5133 (1)	0.0361 (6)
O(2)	0.90308 (8)	1.3425 (2)	0.1760 (2)	0.0449 (7)
O(3)	0.91588 (8)	0.2447 (2)	0.7380 (2)	0.0455 (6)
N(1)	0.86594 (9)	−0.1166 (2)	0.7745 (2)	0.0333 (7)
C(1)	0.8687 (1)	0.7671 (2)	0.4629 (2)	0.0300 (7)
C(2)	0.9305 (1)	0.8407 (2)	0.4707 (2)	0.0319 (8)
C(3)	0.92307 (9)	0.9732 (2)	0.3909 (2)	0.0296 (7)
C(4)	0.9299 (1)	0.9664 (2)	0.2754 (2)	0.0359 (9)
C(5)	0.9236 (1)	1.0865 (2)	0.2009 (2)	0.0375 (9)
C(6)	0.9104 (1)	1.2167 (2)	0.2420 (2)	0.0332 (8)
C(7)	0.9039 (1)	1.2268 (2)	0.3580 (2)	0.0356 (8)
C(8)	0.9106 (1)	1.1059 (2)	0.4311 (2)	0.0337 (8)
C(9)	0.8288 (1)	0.7458 (2)	0.3246 (2)	0.0307 (7)
C(10)	0.7846 (1)	0.8476 (3)	0.2642 (2)	0.0374 (8)
C(11)	0.7494 (1)	0.8335 (3)	0.1372 (2)	0.050 (1)
C(12)	0.7586 (1)	0.7189 (4)	0.0709 (2)	0.054 (1)
C(13)	0.8039 (1)	0.6188 (3)	0.1308 (2)	0.049 (1)
C(14)	0.8386 (1)	0.6322 (3)	0.2566 (2)	0.0385 (9)
C(15)	0.8817 (1)	0.6234 (2)	0.5335 (2)	0.0303 (7)
C(16)	0.8317 (1)	0.5391 (2)	0.5333 (2)	0.0338 (8)
C(17)	0.8402 (1)	0.4115 (2)	0.5985 (2)	0.0343 (8)
C(18)	0.9008 (1)	0.3671 (2)	0.6683 (2)	0.0346 (8)
C(19)	0.9514 (1)	0.4484 (2)	0.6689 (2)	0.0366 (8)
C(20)	0.9421 (1)	0.5753 (2)	0.6019 (2)	0.0341 (8)
C(21)	0.8675 (1)	0.1430 (2)	0.7265 (2)	0.0368 (9)
C(22)	0.9014 (1)	0.0168 (2)	0.8060 (2)	0.0370 (9)
C(23)	0.8072 (1)	−0.1079 (3)	0.7982 (2)	0.042 (1)
C(24)	0.7664 (1)	−0.2385 (4)	0.7533 (3)	0.057 (1)
C(25)	0.9055 (1)	−0.2389 (3)	0.8372 (2)	0.0378 (9)
C(26)	0.9277 (1)	−0.2415 (3)	0.9799 (2)	0.045 (1)
C(27)	0.9144 (1)	1.3385 (3)	0.0615 (3)	0.050 (1)

The two C—C(phenyl) bonds, C(1)—C(9) = 1.533 (2) and C(1)—C(15) = 1.544 (3) Å, are significantly longer than the C(2)—C(3) bond of 1.515 (3) Å. Equivalent distances in two related structures are 1.540, 1.543 and 1.518 Å in 1-(4-methoxyphenyl)-2-phenyl-1-[2-(tetrahydropyran-2-yloxy)phenyl]-1-butanol (Kuroda *et al.*, 1985) and 1.540, 1.549 and 1.514 Å in tetraphenylethane (Destro, Pilati & Simonetta, 1980). Bond lengths C(6)—O(2) of 1.378 (3) and C(18)—O(3) of 1.369 (3) Å show the effect of shortening resulting from the influence of the aromatic rings. The geometry of the diethylamino moiety, with N—C distances of 1.462, 1.464 and 1.478 Å and angles at N of 110.7, 111.8 and 113.4°, is comparable to that of the dimethylamino group observed in several tamoxifen derivatives. All three phenyl rings are perfectly planar; the r.m.s. deviations of individual atoms from the respective ring plane are 0.006 (ring α), 0.004 (ring β) and 0.007 Å (ring α'). The methoxy group on ring β lies close to the plane of the phenyl ring; the deviation of C(27) is 0.09 Å.

The MER25 molecule assumes an extended conformation with rings α' and β in an antiperiplanar (*trans*) rather than the expected synclinal (*gauche*) conformation. This latter conformation would have given the MER25 molecule a conformation close to that of the (*Z*) isomer (2) of tamoxifen, the potent estrogen antagonist which also exhibits some estrogenic activity. Instead, the solid-state conformer of MER25 resembles the (*E*) isomer of tamoxifen (3)

Table 2. *Bond distances* (Å) *and bond angles* (°)

C(1)—O(1)	1.432 (2)	C(13)—C(14)	1.381 (3)
C(1)—C(2)	1.545 (3)	C(14)—C(9)	1.382 (3)
C(1)—C(9)	1.533 (2)	C(15)—C(16)	1.387 (3)
C(1)—C(15)	1.544 (3)	C(16)—C(17)	1.387 (3)
C(2)—C(3)	1.515 (3)	C(17)—C(18)	1.395 (3)
C(3)—C(4)	1.385 (2)	C(18)—C(19)	1.381 (3)
C(4)—C(5)	1.388 (3)	C(19)—C(20)	1.389 (3)
C(5)—C(6)	1.378 (3)	C(20)—C(15)	1.399 (3)
C(6)—C(7)	1.390 (2)	C(18)—O(3)	1.369 (3)
C(7)—C(8)	1.383 (3)	C(21)—O(3)	1.429 (3)
C(6)—O(2)	1.378 (3)	C(21)—C(22)	1.525 (3)
C(8)—C(3)	1.389 (3)	C(22)—N(1)	1.464 (3)
C(9)—C(10)	1.383 (3)	C(23)—N(1)	1.462 (3)
C(10)—C(11)	1.395 (3)	C(25)—N(1)	1.478 (3)
C(11)—C(12)	1.373 (4)	C(23)—C(24)	1.513 (4)
C(12)—C(13)	1.384 (4)	C(25)—C(26)	1.528 (3)
		C(27)—O(2)	1.422 (2)

O(1)—C(1)—C(2)	110.1 (2)	C(12)—C(13)—C(14)	120.5 (2)
O(1)—C(1)—C(9)	106.2 (2)	C(9)—C(14)—C(13)	120.5 (2)
O(1)—C(1)—C(15)	110.0 (1)	C(1)—C(15)—C(16)	119.3 (2)
C(2)—C(1)—C(9)	108.4 (1)	C(1)—C(15)—C(20)	122.8 (2)
C(2)—C(1)—C(15)	110.9 (2)	C(16)—C(15)—C(20)	117.8 (2)
C(9)—C(1)—C(15)	111.1 (2)	C(15)—C(16)—C(17)	122.2 (2)
C(1)—C(2)—C(3)	115.2 (2)	C(16)—C(17)—C(18)	119.1 (2)
C(2)—C(3)—C(4)	120.7 (2)	C(17)—C(18)—C(19)	119.8 (2)
C(2)—C(3)—C(8)	121.8 (1)	C(17)—C(18)—O(3)	125.2 (2)
C(4)—C(3)—C(8)	117.5 (2)	C(19)—C(18)—O(3)	115.0 (2)
C(3)—C(4)—C(5)	121.7 (2)	C(18)—C(19)—C(20)	120.4 (2)
C(4)—C(5)—C(6)	119.7 (2)	C(15)—C(20)—C(19)	120.7 (2)
C(5)—C(6)—C(7)	119.7 (2)	O(3)—C(21)—C(22)	104.4 (2)
C(6)—C(7)—C(8)	119.6 (2)	C(21)—C(22)—N(1)	113.3 (2)
C(3)—C(8)—C(7)	121.7 (2)	C(6)—O(2)—C(27)	117.1 (2)
C(5)—C(6)—O(2)	124.7 (1)	C(18)—O(3)—C(21)	118.5 (2)
C(7)—C(6)—O(2)	115.5 (2)	C(22)—N(1)—C(23)	111.8 (2)
C(1)—C(9)—C(10)	119.2 (2)	C(22)—N(1)—C(25)	110.7 (2)
C(1)—C(9)—C(14)	121.7 (2)	C(23)—N(1)—C(25)	113.4 (2)
C(10)—C(9)—C(14)	119.0 (2)	N(1)—C(23)—C(24)	112.7 (2)
C(9)—C(10)—C(11)	120.3 (2)	N(1)—C(25)—C(26)	116.4 (2)
C(10)—C(11)—C(12)	120.3 (3)		
C(11)—C(12)—C(13)	119.3 (2)		

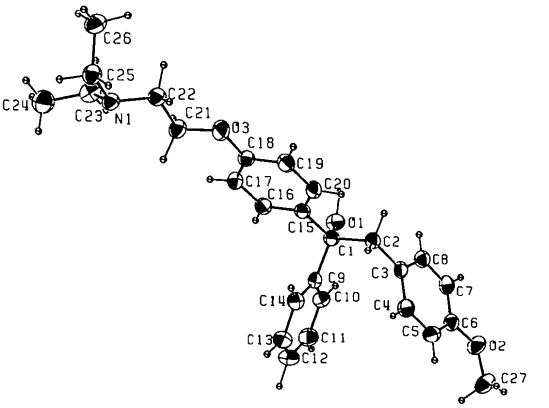


Fig. 1. A perspective *ORTEP* (Johnson, 1965) plot of a single molecule of MER25. Atom labelling is as in the text; thermal ellipsoids are drawn with 50% probability.

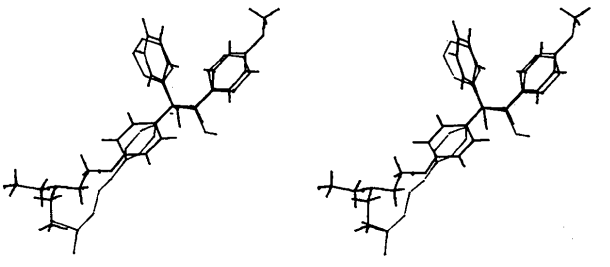
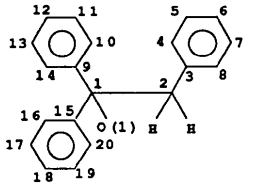


Fig. 2. Stereosuperposition of MER25 (with H atoms) and (*E*)-tamoxifen (without H atoms) (Kilbourn & Owston, 1970).

Table 3. *Conformational torsion angles* (°) *of triphenylethane in MER25 and two related compounds*



	Compound (*a*)	(*b*)	(*c*)
3—2—1—9	50.4	47.3	60.7
3—2—1—15	172.6	167.3	−176.2
3—2—1—O(1)	−65.4	−72.5	−62.4
O(1)—1—2—H	175	171	175
2—1—9—14	81.8	70.8	17.0
2—1—15—20	4.3	−17.0	101.0
1—2—3—8	82.9	66.7	67.5

Compounds: (*a*) present structure; (*b*) 1-(4-methoxyphenyl)-2-phenyl-1-[2-(tetrahydropyran-2-yloxy)phenyl]-1-butanol (Kuroda *et al.*, 1985); (*c*) (*E*)-4-hydroxy-2-methyltamoxifen (McCague *et al.*, 1988).

which is purely estrogenic (Harper & Walpole, 1967; Jordan, 1976; Terenius, 1971). Fig. 2 shows a stereoview of the superimposed molecules of MER25 and the (*E*) isomer of tamoxifen (Kilbourn & Owston, 1970). This structural determination of MER25 demonstrates the complexity of the undocine activity of the aminoethoxytriarylethylenes, since MER25 is an antiestrogen, and appears to exist in a conformation which should bestow only estrogenic activity upon the molecule.

The geometrical features of the triphenylethane moiety in MER25 compare very well with those in two related compounds, 1-(4-methoxyphenyl)-2-phenyl-1-[2-(tetrahydropyran-2-yloxy)phenyl]-1-butanol (MPTB) (Kuroda *et al.*, 1985) and (*E*)-4-hydroxy-2-methyltamoxifen (McCague, Leung, Jarman, Kuroda, Neidle & Webster, 1988), both of which possess the ethylenic single bond similar to that in MER25. Conformational parameters of the triarylethan-1-ol moiety of these compounds are shown in Table 3. It appears that the conformation related to the rotation about the C(1)—C(2) bond is quite similar in all three compounds. In this conformation the C(1) hydroxy group and one of the C(2) H atoms are in an antiperiplanar orientation. This preferred conformation is also seen in the solution conformation of (*E*)-4-hydroxy-2-methyltamoxifen (McCague *et al.*, 1988). However, the three phenyl rings are oriented quite differently in (*E*)-4-hydroxy-2-methyltamoxifen compared to those in MER25 and MPTB (Table 3).

The N—C—C—O system in the diethylaminoethoxy group has the uncommon *trans* rather than the more commonly occurring *gauche* conformation. The torsion angle O—C—C—N (τ) is −160.0° in the present structure, whereas it ranges between 60 and 100° in tamoxifen and seven of its known dervative structures. The exceptions are found in one of the two independent molecules in *cis*-tamoxifen [τ = −176° (Kilbourn & Owston, 1970)], nafoxidine [τ = −174° (Camerman, Chan & Camerman, 1980)] and (*Z*)-4-methylthiotamoxifen [τ = −178° (Blackburn, Goodman & Smith, 1988)]. These results indicate some degree of flexibility in the side-chain conformation. Kuroda *et al.* (1985) have shown by molecular-mechanics calculations that there is only 1 kcal mol^{-1} (4.2 kJ mol^{-1}) energy difference between the *gauche* and *trans* conformations. In the present structure, the extended conformation of the side chain is stabilized by an intermolecular hydrogen bond which links the amino N atom of each molecule with the hydroxyl group of a neighboring molecule.

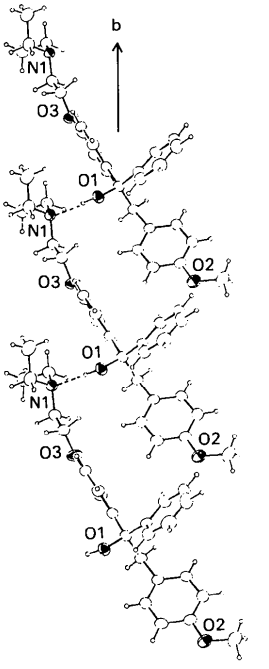


Fig. 3. Partial packing diagram showing the chain along the *b* axis. Hydrogen bonds are indicated by dashed lines.

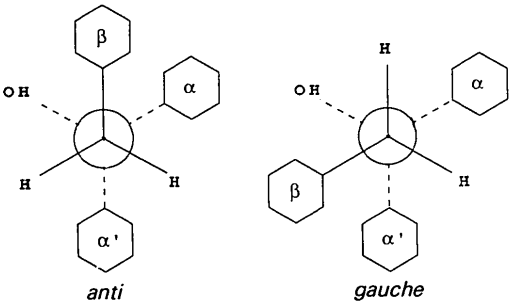


Fig. 4. Newman projections along C(1)–C(2) showing the *anti* (I) and *gauche* (II) conformations. Conformer (I) is close to that observed in the crystal structure of MER25; conformer (II) is closely related to the tamoxifen (*Z*) isomer.

In the crystal structure, the molecules form an infinite chain along the *b* crystallographic axis held together by O—H···N hydrogen bonds [O···N = 2.821, O—H = 1.02 (4), H···N = 1.83 (4) Å, O—H···N = 163 (3)°] (Fig. 3).

Since MER25 is a proven antiestrogen, and its solid-state conformer resembles the (*E*) isomer of tamoxifen, which is purely estrogenic, one must suspect that the MER25 conformation undergoes transformation from the *anti* [Fig. 4 (I)] to the *gauche* [Fig. 4 (II)] conformation *in vivo* when attaching to the estrogen receptor. Work is in progress to test this hypothesis through the preparation and testing of rigid conformers of MER25. Work is also in progress to investigate the various minimum-energy conformers of MER25 through extensive molecular-mechanics calculations. Preliminary results (Hossain, Magarian, Symersky & van der Helm, 1992) show that a low energy synclinal (*gauche*) conformer (II) of MER25 has energy which is only 1.2 kcal mol^{-1} higher than that of the *anti* conformation observed in the crystal structure. Details of these results will be published later.

The work was supported by NCI (NIH) Grants CA 17562 (DvdH) and CA 40458 (RAM).

References

BLACKBURN, G. M., GOODMAN, J. & SMITH, A. J. (1988). *Acta Cryst.* C**44**, 1629–1632.

CAMERMAN, N., CHAN, L. Y. Y. & CAMERMAN, A. (1980). *J. Med. Chem.* **23**, 941–945.

DESTRO, T., PILATI, T. & SIMONETTA, M. (1980). *Acta Cryst.* B**36**, 2497–2500.

HARPER, M. J. K. & WALPOLE, A. L. (1967). *J. Reprod. Fertil.* **13**, 101–119.

HERBST, A. L., GRIFFITHS, C. T. & KISTNER, R. W. (1964). *Cancer Chemother. Rep.* **43**, 39–41.

HOSSAIN, M. B., MAGARIAN, R. A., SYMERSKY, J. & VAN DER HELM, D. (1992). Unpublished work.

HUNTER, D. H., PAYNE, N. C., RAHMAN, A., RICHARDSON, J. F. & ZEA PONCE, Y. (1983). *Can. J. Chem.* **61**, 421–426.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

JORDAN, V. C. (1976). *Cancer Treat. Rep.* **30**, 1409–1419.

JORDAN, V. C. (1984). *Pharmacol. Rev.* **36**, 245–276.

KILBOURN, B. T. & OWSTON, P. G. (1970). *J. Chem. Soc. B*, pp. 1–5.

KURODA, R., CUTBUSH, S., NEIDLE, S. & LEUNG, O.-T. (1985). *J. Med. Chem.* **28**, 1497–1503.

LERNER, L. J. (1981). *The Non-Steroidal Antiestrogens*, edited by R. L. SUTHERLAND & V. C. JORDAN, pp. 1–16. Sydney: Academic Press.

LERNER, L. J., HOLTHAUS, F. J. & THOMPSON, C. R. (1958). *Endocrinology*, **63**, 295–318.

MCCAGUE, R., LEUNG, O.-T., JARMAN, M., KURODA, R., NEIDLE, S. & WEBSTER, G. (1988). *J. Chem. Soc. Perkins Trans.* 2, pp. 1201–1208.

MURPHY, C. S., PARKER, C. J., MCCAGUE, R. & JORDAN, V. C. (1991). *Mol. Pharmacol.* **39**, 421–428.

PRECIGOUX, C., COURSEILLE, S., GEOFFRE, S. & HOSPITAL, M. (1979). *Acta Cryst.* B**35**, 3070–3072.

PRECIGOUX, G., HOSPITAL, M., LEROY, F., DELBARRE, A. & ROQUES, B. P. (1982). *Acta Cryst.* B**38**, 312–315.

SEGAL, J. S. & NELSON, W. O. (1958). *Proc. Soc. Exp. Biol. Med.* **98**, 431–436.

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

SHELDRICK, G. M. (1986). *SHELXS*86. program for the solution of crystal structures. Univ. of Göttingen, Germany.

TERENIUS, L. (1971). *Acta Endocrinol. (Copenhagen)*, **66**, 431–438.

Acta Cryst. (1993). C**49**, 504–506

Structure of (−)-β-Hydrastine

BY RAJNIKANT AND K. N. GOSWAMI

Department of Physics, University of Jammu, Jammu Tawi-180 001, *India*

V. S. YADAVA AND V. M. PADMANABHAN

Solid State Physics Division, Modular Laboratories, Bhabha Atomic Research Centre, Trombay, Bombay-400 085, *India*

AND S. K. BANERJEE

Natural Products Chemistry Division, Regional Research Laboratory (CSIR), Jammu Tawi-180 001, *India*

(*Received* 10 *December* 1990; *accepted* 22 *June* 1992)

Abstract. 6,7-Dimethoxy-3-(5,6,7,8-tetrahydro-6-methyl-1,3-dioxolo[4,5-*g*]isoquinolin-5-yl)-1(3*H*)-isobenzofuranone, $C_{21}H_{21}NO_6$, $M_r = 383$, tetragonal, $P4_3$, $a = 7.542$ (2), $c = 33.266$ (2) Å, $V = 1892$ Å^3, $Z = 4$, D_m(flotation) = 1.334, $D_x = 1.344$ Mg m^{-3}, λ(Cu $K\alpha_1$) = 1.5405 Å, $\mu = 0.733$ mm^{-1}, $F(000) = 808$, $R = 0.061$ for 1579 observed reflections with $I > 2.5\sigma(I)$. The N-containing ring has a half-chair con-

0108-2701/93/030504-03$06.00