Acta Cryst. (1982). **B38**, 3131–3132

4-[(4-Chlorophenyl)(5-fluoro-2-hydroxyphenyl)methyleneamino]butanamide: Progabide (SL 76.002)

BY CLAUDINE PASCARD

Institut de Chimie des Substances Naturelles, CNRS, 91190 *Gif-sur-Yvette, France*

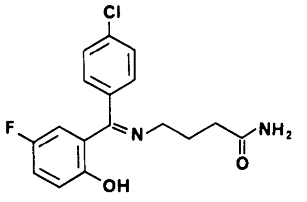
AND JEAN-PIERRE KAPLAN, BERNARD RAIZON AND BERNARD MOMPON

Laboratoire d'Etudes et de Recherches SYNTHELABO, 31 *avenue P.V. Couturier,* 92220 *Bagneux, France*

(*Received* 3 *March* 1982; *accepted* 21 *June* 1982)

Abstract. $C_{17}H_{16}ClFN_2O_2$, monoclinic, *Cc*, $a = 11{\cdot}018\,(3)$, $b = 15{\cdot}295\,(4)$, $c = 9{\cdot}736\,(2)$ Å, $\beta = 97{\cdot}63\,(2)°$, $Z = 4$, $D_c = 1{\cdot}37$ g cm^{-3}. The structure was refined to $R = 6{\cdot}4\%$ for 1107 observed reflections. The two halogenated rings are perpendicular to each other and an internal hydrogen bond between the phenolic group and the nitrogen of the imino group forms a six-membered ring.

Introduction. The title compound, Progabide (SL 76.002) (I) (Kaplan, Raizon, Desarmenien, Feltz, Headley, Worms, Lloyd & Bartholini, 1980), is the first apparently non-toxic, specific GABA receptor agonist available for clinical trials, (Morselli, Bossi, Henry, Zarifian & Bartholini, 1980). Therefore the determination of its molecular structure by X-ray analysis is of interest.



(I)

Suitable crystals (0·30 × 0·30 × 0·10 mm) were obtained by the slow evaporation of a solution of the product in dichloromethane.

Cell dimensions and intensities were measured on a Philips four-circle computer-controlled diffractometer with Mo *Kα* radiation. Of the 1441 independent reflections, 1107 had $I > 2\sigma(I)$. No corrections were made for absorption.

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). All heavy atoms were found in the first *E* map. Isotropic refinement with full-matrix least squares led to $R = 16\%$.

With anisotropic temperature factors for non-H atoms, and the introduction of all the H atoms which could be placed theoretically ($\angle$CCH = 109°, C–H = 1·000 Å), the *R* factor became 7·8%. At this stage a difference Fourier synthesis revealed the H atom bonded to the phenolic oxygen O(1). The two H atoms bonded to the terminal N did not appear and were introduced in the refinement at theoretical positions. The final *R* is 6·4%.*

Discussion. The final coordinates are given in Table 1, the bond lengths and angles in Tables 2 and 3, the torsion angles in Table 4. Fig. 1 is a view perpendicular to ring II, and represents the atom numbering used in the crystallographic calculations.

Although the e.s.d.'s appear rather large for the aromatic bond lengths, the distances between the halogens and the rings and the C–N distances in the amido and imino groups have normal values.

The conformational aspects of this molecule are of interest. A six-membered ring: –C(1)–C(8)–C(13)–O(1)–H(O1)–N(1) is formed by means of the hydrogen bond between O(1) and N(1). This ring is nearly coplanar with that of ring II. Rings I and II are perpendicular (α = 89·5°).

After C(14), which is in the ring II plane, the chain turns upward in such a way that the amido group is near ring I. The amido plane makes an angle of 123° with the chlorinated benzene ring. [The shortest distance between these two groups is N(2)···C(7): 3·94 (2) Å.]

The molecules are held together through hydrogen bonds and van der Waals interactions.

The amido group links the molecules through two hydrogen bonds, H(N2)*A*···O(2) and H(N2)*B*···O(1) along the *c* and *a* axes respectively (Fig. 2).

---

* Lists of structure factors, anisotropic thermal parameters, hydrogen-atom coordinates, mean-plane equations and relevant inter- and intramolecular distances have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38026 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0567-7408/82/123131-02$01.00

Table 1. *Atomic coordinates* ($\times 10^4$) *and isotropic temperature factors* (Å^2) *of the heavy atoms with e.s.d.'s in parentheses*

$$B_{\text{eq}} = \tfrac{4}{3}\sum_i \sum_j \beta_{ij}\mathbf{a}_i\cdot\mathbf{a}_j.$$

	x	y	z	B_{eq}
Cl	4860	8020 (2)	3056	9·35
F	9194 (6)	4866 (4)	6328 (9)	6·73
O(1)	12662 (6)	6555 (4)	3778 (8)	4·63
O(2)	10150 (6)	10396 (4)	1215 (8)	3·98
N(1)	10944 (7)	7481 (5)	2465 (9)	3·80
N(2)	9801 (7)	10349 (5)	3439 (9)	4·26
C(1)	10167 (9)	7123 (6)	3154 (11)	3·46
C(2)	8843 (8)	7405 (6)	3061 (11)	3·33
C(3)	7952 (10)	7020 (6)	2063 (12)	4·70
C(4)	6767 (12)	7213 (8)	2055 (14)	5·58
C(5)	6436 (8)	7789 (8)	3022 (15)	5·27
C(6)	7270 (10)	8206 (7)	3999 (13)	5·35
C(7)	8497 (8)	7996 (6)	4017 (11)	4·26
C(8)	10514 (8)	6402 (5)	4130 (10)	2·89
C(9)	9667 (10)	5955 (7)	4787 (12)	4·03
C(10)	10040 (12)	5299 (7)	5702 (13)	5·21
C(11)	11324 (10)	5076 (7)	6060 (13)	4·77
C(12)	12150 (10)	5512 (6)	5415 (11)	4·37
C(13)	11795 (8)	6158 (6)	4437 (11)	3·44
C(14)	10654 (8)	8182 (6)	1442 (11)	4·08
C(15)	11651 (8)	8884 (6)	1604 (11)	4·16
C(16)	11516 (8)	9521 (6)	2788 (12)	4·31
C(17)	10399 (8)	10118 (6)	2416 (12)	3·38

Table 2. *Interatomic distances* (Å)

Cl–C(5)	1·776 (10)	C(4)–C(5)	1·373 (19)
F–C(10)	1·353 (15)	C(5)–C(6)	1·387 (18)
O(13)–C(13)	1·362 (12)	C(6)–C(7)	1·388 (15)
O(2)–C(17)	1·240 (14)	C(8)–C(9)	1·380 (15)
N(1)–C(1)	1·279 (14)	C(8)–C(13)	1·452 (14)
N(1)–C(14)	1·469 (14)	C(9)–C(10)	1·368 (17)
N(2)–C(17)	1·313 (14)	C(10)–C(11)	1·452 (18)
C(1)–C(2)	1·512 (14)	C(11)–C(12)	1·349 (17)
C(1)–C(8)	1·473 (14)	C(12)–C(13)	1·392 (15)
C(2)–C(3)	1·415 (16)	C(14)–C(15)	1·530 (14)
C(2)–C(7)	1·386 (15)	C(15)–C(16)	1·532 (16)
C(3)–C(4)	1·338 (18)	C(16)–C(17)	1·537 (14)
O(1)–HO(1)	1·02 (10)	N(1)–HO(1)	1·70 (10)

Table 3. *Bond angles* (°)

C(1)–N(1)–C(14)	124·5 (9)	C(9)–C(8)–C(13)	118·4 (9)
N(1)–C(1)–C(2)	123·7 (9)	C(8)–C(9)–C(10)	120·1 (1·1)
N(1)–C(1)–C(8)	121·6 (9)	F–C(10)–C(9)	119·1 (1·1)
C(2)–C(1)–C(8)	114·7 (9)	F–C(10)–C(11)	118·9 (1·1)
C(1)–C(2)–C(3)	119·9 (9)	C(9)–C(10)–C(11)	121·9 (1·1)
C(1)–C(2)–C(7)	119·6 (9)	C(10)–C(11)–C(12)	117·9 (1·1)
C(3)–C(2)–C(7)	120·3 (1·0)	C(11)–C(12)–C(13)	121·6 (1·1)
C(2)–C(3)–C(4)	120·0 (1·1)	O(1)–C(13)–C(8)	120·8 (9)
C(3)–C(4)–C(5)	119·1 (1·2)	O(1)–C(13)–C(12)	119·2 (9)
Cl–C(5)–C(4)	119·3 (1·0)	C(8)–C(13)–C(12)	120·0 (9)
Cl–C(5)–C(6)	117·1 (1·0)	N(1)–C(14)–C(15)	110·7 (8)
C(4)–C(5)–C(6)	123·6 (1·2)	C(14)–C(15)–C(16)	112·6 (9)
C(5)–C(6)–C(7)	117·3 (1·1)	C(15)–C(16)–C(17)	110·8 (9)
C(2)–C(7)–C(6)	119·8 (1·0)	O(2)–C(17)–N(2)	123·5 (1·0)
C(1)–C(8)–C(9)	122·4 (9)	O(2)–C(17)–C(16)	119·8 (9)
C(1)–C(8)–C(13)	119·1 (9)	N(2)–C(17)–C(16)	116·6 (9)
C(13)–O(1)–HO(1)	109·5 (1·5)	O(1)···HO(1)–N(1)	140·2 (1·5)

Table 4. *Relevant torsion angles* (°) *according to Klyne & Prelog* (1980) *convention*

C(9)–C(8)–C(1)–N(1)	−174·0 (1·2)
C(3)–C(2)–C(1)–N(1)	89·5 (1·1)
C(2)–C(1)–N(1)–C(14)	−3·2 (1·3)
C(8)–C(1)–N(1)–C(14)	177·9 (1·2)
C(1)–N(1)–C(14)–C(15)	137·5 (0·9)
N(1)–C(14)–C(15)–C(16)	−80·1 (1·0)
C(14)–C(15)–C(16)–C(17)	−70·0 (1·0)
C(15)–C(16)–C(17)–N(2)	145·8 (1·0)

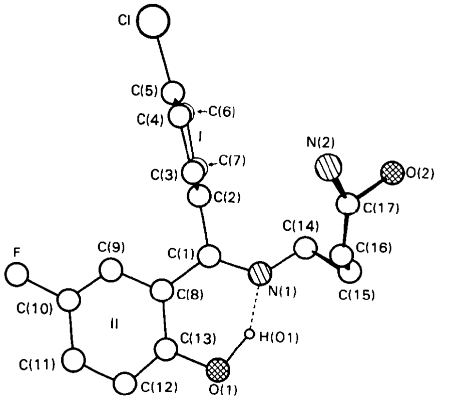


Fig. 1. Perspective view of the molecule (*PLUTO*; Motherwell, 1976).

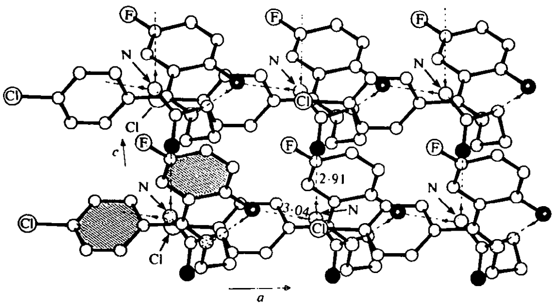


Fig. 2. Packing projected on the ($x0z$) plane. Filled circles: oxygen O(2). Filled circles with white centre: oxygen O(1). Dotted lines: hydrogen bonds. Distances are in Å.

References

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* **A27**, 368–376.

Kaplan, J. P., Raizon, B. M., Desarmenien, M., Feltz, P., Headley, P. M., Worms, P., Lloyd, K. G. & Bartholini, G. (1980). *J. Med. Chem.* **23**, 702–704.

Klyne, W. & Prelog, V. (1960). *Experientia*, **16**, 521–523.

Morselli, P. L., Bossi, L., Henry, J. F., Zarifian, E. & Bartholini, G. (1980). *Brain Res. Bull.* **5**, Suppl. 2, 411–414.

Motherwell, W. D. S. (1976). *PLUTO. A Program for Plotting Molecular and Crystal Structures.* Univ. Chemical Laboratory, Cambridge, England.