0·045 Å longer as a consequence of the rehybridization. These comparisons show that because of the electronic delocalization the N—O bond is short in the molecule discussed here. In fact, it is the shortest ever reported for 1,2-oxazines (Allen *et al.*, 1979) (Cambridge Structural Database, version 3.40).

Because of the 4,5 double bond, the six-membered heterocycle adopts a half-chair conformation. The endocyclic torsion angles −70·9 (8), 49·0 (8), −11·1 (8), −4·8 (8), −14·6 (8) and 50·1 (8)° indicate a large puckering [70·9 (8)°] at the N—O bond. The O atom is displaced by 0·64 (1) Å from the mean plane through the five other atoms. Large puckering has already been reported in chair conformations of perhydro-1,2-oxazines where the torsions around N—O are in the range 65–75° (Holzapfel, Kruger & Van Dijk, 1987).

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Structure of (±)-Aminoglutethimide

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Abstract. (±)-3-(4-Aminophenyl)-3-ethyl-2,6-piperidinedione, $C_{13}H_{16}N_2O_2$, $M_r = 232·3$, monoclinic, $P2_1/n$, $a = 16·895$ (2), $b = 8·519$ (1), $c = 8·762$ (1) Å, $\beta = 95·71$ (1)°, $V = 1254·9$ (2) Å^3, $Z = 4$, $D_x = 1·23$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0·785$ cm^{-1}, $F(000) = 496$, $T = 294$ K, $R = 0·064$ for all 3676 reflections. The molecule is L shaped with the *p*-aminophenyl and the piperidinedione groups forming the vertical arm and the base, respectively. The polar imide half of the piperidinedione group is in front of the L for the active + enantiomer and at the back for the less-active − enantiomer. The structure is very similar to that of phenobarbital. Intermolecular interactions include one strong and one weak hydrogen bond and an apparent interaction between one of the amino H atoms with the π cloud of the phenyl ring.

Introduction. Aminoglutethimide (AG) is a non-steroidal aromatase inhibitor that has been used clinically for the treatment of breast cancer in post-menopausal women (Santen, Worgul, Samojlik, Boucher, Lipton & Harvey, 1982; Shaw, Nicholls & Smith, 1988). Structure–activity studies of AG and other non-steroidal aromatase inhibitors are complicated by the large variation in the structures of active compounds (Banting *et al.*, 1988). AG (Elipten CIBA) was initially introduced as an anticonvulsant but later withdrawn because of adrenal toxicity (Camacho, Brough, Cash & Wilroy, 1966). It is

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structurally more related to other anticonvulsants, such as phenobarbital, than to other aromatase inhibitors. The + enantiomer of AG has been shown to be more active than the − enantiomer (Finch, Dziemian, Cohen & Steinetz, 1975), suggesting that the relative distances and orientations of the functional groups in the + enantiomer correspond to the required arrangement for binding to the active site of the enzyme.

Experimental. The sample was provided by Ciba Geigy Corporation. Large rod-shaped crystals were obtained by slow evaporation of an aqueous methanol solution at 310 K. The crystal used for data collection was cleaved from a larger one and had approximate dimensions of 0·60 × 0·62 × 0·65 mm. Systematic absences ($h0l$, $h+l=2n$; $0k0$, $k=2n$) are consistent with space group $P2_1/n$. Nicolet $P3$ diffractometer, Mo $K\alpha$ radiation, Nb filter, $\theta/2\theta$ scan method. Unit-cell dimensions and orientation matrix were determined from 49 reflections with $22{\cdot}5 < 2\theta < 29{\cdot}9°$. There were 5250 reflections measured with $4 < 2\theta < 60°$, $-24 < h < 24$, $0 < k < 12$, $-1 < l < 13$. Intensities of six standard reflections ($\bar{1}5\bar{1}$, $\bar{1}\bar{1}1$, 101, 216, 534, $\bar{8}34$) were monitored after every 60th measurement but did not decline significantly. Orientation checks were not used. Lorentz and polarization corrections were applied but absorption correction was not considered necessary. Of the 3676 independent reflections ($R_{int}=0{\cdot}018$), 3013 had $F > 3\sigma(F)$ and were used in the refinement. $\sigma(F)$ was calculated according to Stout & Jensen (1968): $\sigma^2(F) = (k/4\mathrm{Lp}I)[\sigma^2(I) + (0{\cdot}007I)^2]$. The structure was determined by direct methods using *MULTAN* (Germain, Main & Woolfson, 1971) and refined by full-matrix least squares, minimizing $\sum w(F_o - F_c)^2$, where $w = 1/\sigma^2(F)$. Coordinates for all H atoms were determined from difference maps and refined with the non-H atoms after the anisotropic refinement had converged. The maximum value of the shift/e.s.d. during the last cycle of refinement was 0·10. Final R values are $R=0{\cdot}053$, $wR=0{\cdot}052$ for the data used in the refinement and $R_{all}=0{\cdot}064$ for all 3676 data; $S=3{\cdot}977$ with refinement of all 218 parameters. The final difference map had maximum and minimum densities of 0·28 and $-0{\cdot}25$ e Å^{-3}. Atomic scattering factors and dispersion corrections were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 71–147). Other programs used include Blessing's (1987) data reduction package, locally modified refinement and structure analysis programs based on programs in the Enraf–Nonius *SDP* package (Enraf–Nonius, 1979) and the plotting program *ORTEP*II (Johnson, 1976).

Discussion. Atomic coordinates for the D enantiomer and equivalent isotropic thermal parameters are listed in Table 1.* Fig. 1 shows the molecular conformation and the numbering scheme used. Selected bond lengths, bond angles and torsion angles are listed in Table 2.

Table 1. *Fractional atomic coordinates* ($\times 10^5$ *for non*-H *atoms*, $\times 10^4$ *for* H *atoms*) *and isotropic thermal parameters* ($\times 10^2$ *for non*-H *atoms*, $\times 10$ *for* H *atoms*) *for* (±)-*aminoglutethimide*

The equivalent isotropic thermal parameter for the non-H atoms is calculated as $B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}/B_{iso}(Å^2)
C(1)	15892 (7)	28318 (14)	40088 (14)	342 (3)
C(2)	12881 (8)	16178 (19)	48384 (17)	474 (4)
C(3)	17489 (9)	8122 (20)	59745 (17)	509 (4)
C(4)	25422 (7)	12007 (16)	63418 (15)	408 (3)
N(4)	30188 (10)	3930 (20)	74483 (18)	626 (5)
C(5)	28508 (7)	24057 (15)	55247 (16)	384 (3)
C(6)	23904 (7)	31867 (15)	43812 (16)	373 (3)
C(7)	10824 (7)	38143 (15)	28156 (14)	365 (3)
C(8)	15036 (9)	40746 (16)	13586 (16)	410 (3)
C(9)	16885 (8)	25377 (17)	6057 (18)	429 (4)
C(10)	9855 (7)	14724 (15)	3760 (15)	392 (3)
O(10)	9494 (6)	3712 (12)	−5131 (13)	524 (3)
N(11)	3593 (6)	17863 (14)	12120 (13)	411 (3)
C(12)	3221 (7)	29055 (16)	23480 (15)	395 (3)
O(12)	−2926 (5)	30664 (13)	29328 (12)	549 (3)
C(13)	8869 (9)	53947 (17)	35645 (18)	465 (4)
C(14)	3947 (15)	65467 (26)	25456 (30)	700 (6)
H(N11)	−88 (10)	1125 (18)	1018 (18)	55 (3)
H(N4*A*)	2750 (10)	−208 (23)	8014 (24)	68 (5)
H(N4*B*)	3478 (11)	759 (22)	7754 (24)	75 (5)
H(2)	737 (9)	1334 (17)	4642 (17)	52 (3)
H(3)	1513 (9)	−6 (20)	6484 (21)	63 (4)
H(5)	3416 (8)	2697 (15)	5706 (17)	48 (3)
H(6)	2631 (8)	3998 (16)	3819 (16)	45 (3)
H(8*A*)	1985 (8)	4736 (16)	1613 (16)	47 (3)
H(8*B*)	1145 (8)	4655 (15)	641 (16)	42 (3)
H(9*A*)	1866 (10)	2719 (18)	−342 (23)	62 (4)
H(9*B*)	2105 (8)	1944 (16)	1270 (17)	48 (3)
H(13*A*)	1409 (9)	5971 (17)	3917 (18)	55 (3)
H(13*B*)	606 (8)	5163 (17)	4496 (19)	50 (3)
H(14*A*)	296 (13)	7422 (28)	3084 (30)	97 (6)
H(14*B*)	731 (14)	7016 (27)	1632 (32)	109 (7)
H(14*C*)	−128 (14)	6004 (25)	2087 (28)	97 (6)

The ring containing the imide group is a nearly perfect half chair with C(7) and C(9) equally displaced (−0·129 and 0·127 Å, respectively) from the least-squares plane of the atoms C(7), C(9), C(10), C(12), N(11), O(10) and O(12) (r.m.s. deviation 0·079 Å) but much less than C(8), which is 0·650 Å below this plane. The imide group O(10)—C(10)—N(11)—C(12)—O(12) is somewhat asymmetric. Bond lengths and angles indicate a slightly greater contribution of the O^-—C=N^+ resonance form at C(10) than at C(12), but the whole group is nearly coplanar (r.m.s. deviation 0·024 Å). This ring geometry makes the exocyclic atom C(13) coplanar with C(7), C(8) and C(9). The phenyl ring is nearly eclipsed with the C(7)—C(12) bond. This orientation is most probably caused by the location of C(9) above the plane of the imide and the only potentially

* Lists of anisotropic thermal parameters, bond lengths and angles and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53455 (31 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å), *selected bond angles* (°) *and torsion angles* (°) *for* (±)-*aminoglutethimide*

C1—C2	1·389 (2)	C8—C9	1·513 (2)
C1—C6	1·394 (2)	C1—C7	1·533 (2)
C2—C3	1·383 (2)	C9—C10	1·492 (2)
C3—C4	1·387 (2)	C10—O10	1·217 (2)
C4—N4	1·381 (2)	C10—N11	1·372 (2)
C4—C5	1·383 (2)	N11—C12	1·384 (2)
C5—C6	1·377 (2)	C12—O12	1·211 (2)
C7—C8	1·538 (2)	C13—C14	1·518 (3)
C7—C12	1·521 (2)	C7—C13	1·548 (2)

C8—C7—C12	107·3 (1)	C2—C1—C7	123·7 (1)
C8—C7—C13	111·2 (1)	C6—C1—C7	120·3 (1)
C12—C7—C13	110·3 (1)	C7—C8—C9	111·7 (1)
C8—C9—C10	112·9 (1)	C9—C10—O10	122·9 (1)
C9—C10—N11	117·1 (1)	O10—C10—N11	120·0 (1)
C7—C12—N11	116·5 (1)	C7—C12—O12	124·4 (1)
C1—C7—C8	111·8 (1)	N11—C12—O12	119·0 (1)
C1—C7—C12	107·8 (1)	C7—C13—C14	116·1 (1)
C1—C7—C13	108·3 (1)	C10—N11—C12	127·6 (1)

C13—C7—C8—C9	−179·3 (1)	C1—C7—C12—N11	−84·3 (1)
C1—C7—C12—O12	93·3 (1)	C8—C7—C12—N11	36·3 (1)
C2—C1—C7—C8	−136·4 (1)	C2—C1—C7—C12	−18·6 (2)
C13—C7—C12—N11	157·6 (1)	C2—C1—C7—C13	100·7 (1)
C1—C7—C13—C14	179·2 (1)	C6—C1—C7—C12	165·0 (1)
C8—C7—C13—C14	55·9 (2)	C6—C1—C7—C13	−75·6 (1)
C12—C7—C13—C14	−63·1 (2)	C7—C8—C9—C10	50·3 (2)
C8—C9—C10—O10	162·0 (1)	C8—C9—C10—N11	−17·5 (2)
C9—C10—N11—C12	−5·7 (2)	O10—C10—N11—C12	174·8 (1)
C7—C12—N11—C10	−5·1 (2)	C1—C7—C8—C9	59·5 (1)
O12—C12—N11—C10	177·2 (1)	C12—C7—C8—C9	−58·6 (1)

close contact with the phenyl ring. The two conjugated systems, the *p*-aminophenyl group and the imide moiety are nearly perpendicular, with an angle between their least-squares planes of 88·8°. The geometry about the C(7)—C(13) bond is highly symmetric. C(1) is *trans* to C(14) and the endocyclic atoms C(8) and C(12) are *gauche* to C(14). The molecule appears L shaped with the aminophenyl moiety and the piperidinedione ring forming the vertical arm and the base, respectively. In the + enantiomer, the polar imide group forms the front of the base of the L while the backside is hydrophobic. Because the opposite is observed for the less-active − enantiomer, this orientation of the polar and hydrophobic groups may be important for binding to the binding enzyme.

AG is structurally very similar to phenobarbital. The only differences are in the addition of the *p*-amino group on the phenyl ring and the substitution of the asymmetric partially saturated piperidinedione group for the symmetric pyrimidinetrione in phenobarbital. Several crystal structures of phenobarbital have been reported (Kim & Rich, 1968; Williams, 1973, 1974). Detailed comparison of the structure of AG with that of the anhydrous uncomplexed form (Williams, 1974) shows that the molecular conformations are also very similar. The main differences are in the orientations of the phenyl rings relative to the rest of the molecules which differ by about 25° and in the displacement of the atoms C(9) and O(10) relative to the corresponding atoms in phenobarbital, owing to the chemical differences in that part of the molecule. Least-squares fitting of all corresponding atoms in both structures shows r.m.s. deviations of 0·258 Å with a maximum separation of 0·509 Å for C(5).

Fig. 2 shows the crystal packing of AG. The main intermolecular interactions consist of three hydrogen bonds: one symmetric pair of intermediate-strength bonds between N(11) and O(10) with the corresponding atoms of the inversion-center-related molecule, N(11)—H(N11)···O(10) $(-x,-y,-z)$: N···O 2·894 (1), N—H 0·94 (2), H···O 1·95 (2) Å, N—H···O 175 (1)°, and one weak bond N(4)—H(N4*B*)···O(12) $(\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z)$: N···O 3·131 (2), N—H 0·85 (2), H···O 2·30 (2) Å, N—H···O 165 (2)°. The weakness of the latter hydrogen bond is consistent with the observations of Voet (1972) and Gartland & Craven

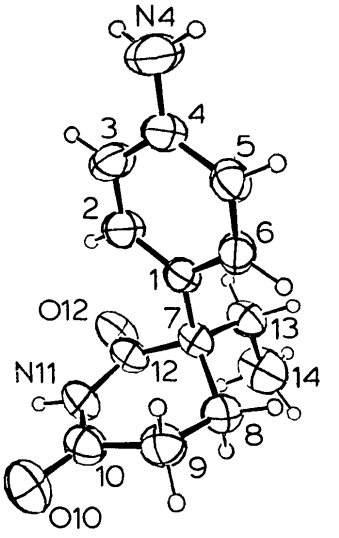

Fig. 1. Molecular structure of aminoglutethimide. The + enantiomer is shown. Thermal ellipsoids are shown at 50% probability levels.

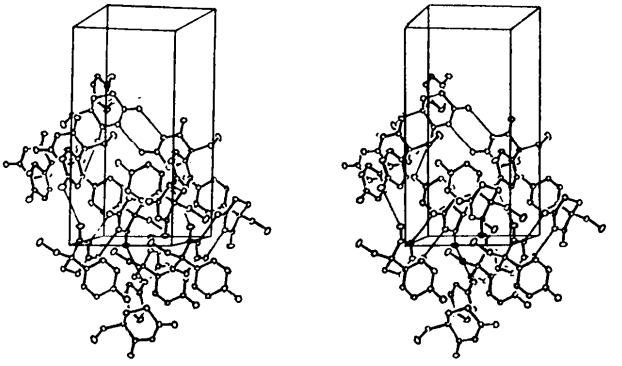

Fig. 2. Stereo packing diagram for (±)-aminoglutethimide, viewed approximately down the *c* axis. The *a* and *b* axes are vertical and horizontal, respectively.

(1974) for hydrogen bonds involving ureido groups. The latter investigators point out that the ureido groups are hydrogen-bond acids and that they therefore form long hydrogen bonds when used as acceptors. The second amino hydrogen H(N4*A*) does not form any hydrogen bonds. Cases where a potential hydrogen donor is not involved in any close contacts are very rare. H(N4*A*) appears to be directed towards the center of the phenyl ring of the molecule related by the transformation $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{3}{2}-z$. The closest atoms are C(5) and C(6): N(4)···C(5) 3·508 (2), H(N4*A*)···C(5) 2·66 (2); N(4)···C(6) 3·480 (2), H(N4*A*)···C(6) 2·69 (2) Å. If this interaction between the amino group and the π cloud of the phenyl ring is energetically favorable, it may also contribute to the weakening of the hydrogen bond involving H(N4*B*). The only other short intermolecular contact is the 3·240 (2) Å contact between C(5) and O(10) $(\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z)$.

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Structure of the Modified Nucleoside 2′,3′-Dideoxy-3′-fluorocytidine*

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Abstract. 1-(2,3-Dideoxy-3-fluoro-β-D-*erythro*-pentofuranosyl)cytosine, $C_9H_{12}FN_3O_3$, $M_r = 229{\cdot}21$, triclinic, $P\bar{1}$, $a = 6{\cdot}997\ (4)$, $b = 7{\cdot}396\ (4)$, $c = 10{\cdot}639\ (5)$ Å, $\alpha = 94{\cdot}48\ (4)$, $\beta = 107{\cdot}74\ (4)$, $\gamma = 104{\cdot}40\ (4)°$, $V = 500{\cdot}8\ (5)$ Å^3, $Z = 2$, $D_m = 1{\cdot}52$, $D_x = 1{\cdot}520$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}1198$ mm^{-1}, $F(000) = 240$, $T = 293$ K, final $R = 0{\cdot}033$ for 2321 unique observed $[F \geq 4\sigma(F)]$ reflections. The asymmetric unit contains two molecules *A* and *B*. For molecule *A*, the *N*-glycosidic torsion angle χ has a value of $-143{\cdot}5\ (3)°$, the sugar pucker is mixed $^2T_1/^2E$ with $P = 154\ (1)$ (C2′ *endo*) and $\psi_m = 40\ (1)°$, and the O5′*A*—C5′*A*—C4′*A*—C3′*A* torsion angle $\gamma = 63{\cdot}4\ (4)°$. For molecule *B*, $\chi = -153{\cdot}0\ (3)$, $\gamma = -71{\cdot}4\ (4)°$ and the sugar pucker is ^2E with $P = 164\ (1)$ (C2′ *endo*) and $\psi_m = 36\ (1)°$. The packing of the crystal is determined by a network of hydrogen bonds. Base pairing between *A* and *B* occurs, and in this way a pseudo-inversion centre is formed between the two bases. The conformational parameters are in accordance with the IUPAC–IUB Joint Commission on Biochemical Nomenclature [*Pure Appl. Chem.* (1983), **55**, 1273–1280] guidelines.

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