Acta Cryst. (1973). B29, 369

The crystal and molecular structure of 1-benzyl-4-(2,6-dioxo-3-phenyl-3-piperidyl)piperidine, $C_{23}H_{26}N_2O_2$ (benzitimide).

By M. H. J. Koch, *Université de Louvain, Laboratoire de Chimie Physique et de Cristallographie, Schapenstraat* 39, 3000 *Leuven, Belgium* and O. Dideberg, *Université de Liège, Laboratoire de Cristallographie, Institut de Physique*, 4000 *Liège, Belgium*

(*Received* 9 *October* 1972; *accepted* 24 *October* 1972)

Crystals of benzitimide, $C_{23}H_{26}N_2O_2$, are monoclinic, space group $C2$ with $a=17{\cdot}661$, $b=6{\cdot}728$, $c=18{\cdot}452$ Å, $\beta=113{\cdot}36°$ and $Z=4$. The structure was solved by direct methods and refined by block-diagonal least-squares calculations to an R value of 0·05.

The title compound is an anticholinergic drug usually called benzitimide. It has been shown that the activity is due only to the (+) isomer for which Spek, Peerdeman, Van Wijngaarden & Soudijn (1971) determined the absolute configuration (*S*) from the structure of the hydrobromide.

Intensity data were collected on a Hilger and Watts computer-controlled diffractometer. Crystallographic and experimental data are listed in Table 1. The atomic factors used are those given in *International Tables for X-ray Crystallography* (1962). The E values were computed using a scale and temperature factor calculated by Wilson's method (1942) and renormalized on the parity groups.

Table 1. *Crystallographic and experimental data*

$C_{23}H_{26}N_2O_2$	M.W. 362·5
Monoclinic C_2	$a=17{\cdot}661$ (2) Å
	$b=6{\cdot}728$ (1)
	$c=18{\cdot}452$ (2)
	$\beta=113{\cdot}36°$
$Z=4$,	$F(000)=776$

Crystal dimensions: 0·3 × 0·3 × 0·3 mm
Source Cu $K\bar{\alpha}$; Ni filter; $\lambda=1{\cdot}5418$ Å; ω–2θ step scan; $\Delta 2\theta=\pm 0{\cdot}7°$, steps of 0·01°; $\theta_{max}=70°$
Confidence level: 2·0
Total number of independent reflexions: 1988
Total observed: 1806

The structure was solved by direct methods using the program *MULTAN* written by Germain, Main & Woolfson (1971). The fourteenth E map, according to the figures of merit which are known to be very unreliable for this type of space group, showed the entire molecule.

The structure was refined by block-diagonal anisotropic least-squares calculations (scheme 3 × 3, 6 × 6) using the programs written by Ahmed, Hall, Pippy & Huber (1966) to an R value $= \dfrac{\sum||F_o|-|F_c||}{\sum|F_o|}$ of 0·05.

The y coordinate of C(1) was kept fixed during the whole refinement process. Final coordinates and thermal parameters are given in Table 2. A table of observed and calculated structure factors has been deposited with the National Lending Library, England, as Supplementary Publication No. SUP. 30030.*

* Copies of this table may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

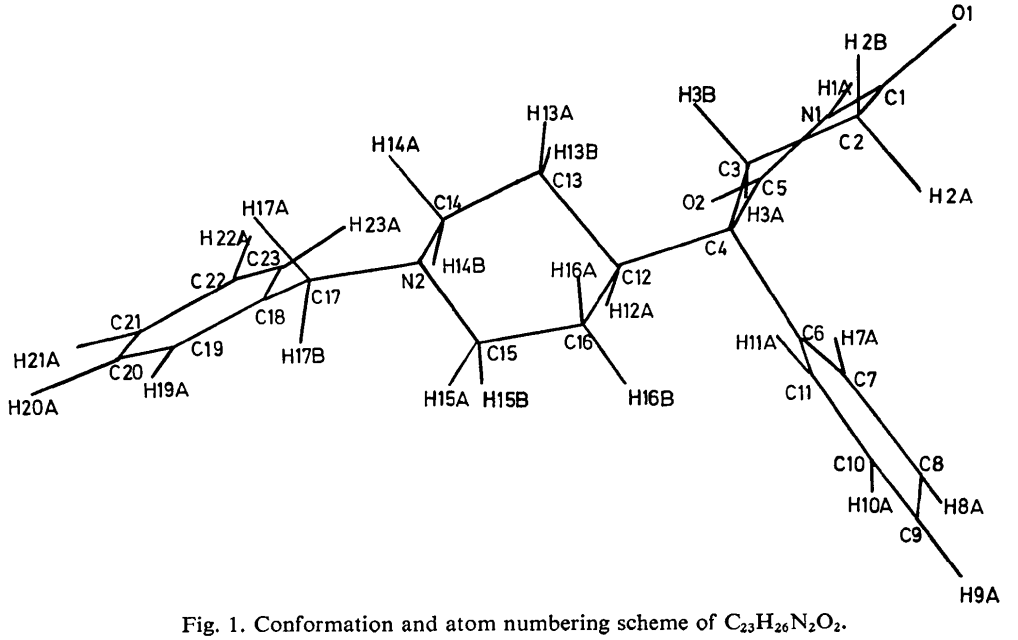

Fig. 1. Conformation and atom numbering scheme of $C_{23}H_{26}N_2O_2$.

Table 2. *Final coordinates and thermal parameters and their standard deviations* ($\times 10^4$)

$B = \exp(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl) \times 10^{-4}$

	x	y	z	B_{11}	B_{22}	B_{33}	B_{23}	B_{13}	B_{12}
C(1)	−1966 (2)	−795 (0)	−9226 (2)	34 (1)	193 (6)	33 (1)	18 (4)	23 (1)	−3 (4)
C(2)	−1525 (2)	952 (5)	−8744 (2)	38 (1)	182 (6)	37 (1)	−6 (5)	21 (2)	20 (4)
C(3)	−873 (2)	367 (5)	−7942 (2)	37 (1)	185 (6)	34 (1)	−21 (4)	28 (2)	16 (4)
C(4)	−295 (1)	−1282 (4)	−7989 (2)	30 (1)	160 (6)	30 (1)	−13 (4)	24 (1)	−1 (4)
C(5)	−818 (2)	−3024 (4)	−8443 (2)	33 (1)	165 (6)	33 (1)	−11 (4)	21 (1)	1 (4)
C(6)	228 (1)	−647 (5)	−8455 (1)	31 (1)	208 (6)	26 (1)	−2 (4)	23 (1)	3 (4)
C(7)	426 (2)	1329 (5)	−8507 (2)	55 (1)	215 (8)	51 (1)	−7 (6)	60 (2)	−23 (6)
C(8)	933 (2)	1855 (7)	−8894 (2)	66 (2)	326 (10)	59 (2)	8 (7)	76 (3)	−51 (7)
C(9)	1255 (2)	436 (7)	−9220 (2)	48 (1)	425 (13)	41 (1)	11 (7)	48 (2)	−25 (8)
C(10)	1069 (2)	−1521 (7)	−9168 (2)	50 (1)	398 (12)	37 (1)	−12 (7)	48 (2)	36 (7)
C(11)	562 (2)	−2070 (5)	−8789 (2)	41 (1)	251 (7)	32 (1)	−9 (5)	31 (2)	19 (5)
C(12)	301 (2)	−2011 (5)	−7151 (2)	32 (1)	232 (7)	28 (1)	8 (4)	21 (1)	−13 (4)
C(13)	−138 (2)	−2990 (6)	−6674 (2)	41 (1)	319 (10)	33 (1)	20 (5)	25(2)	−52 (6)
C(14)	503 (2)	−3697 (6)	−5874 (2)	53 (1)	317 (10)	37 (1)	43 (6)	28 (2)	−35 (7)
C(15)	1435 (2)	−1123 (7)	−5849 (2)	39 (1)	412 (13)	32 (1)	−3 (6)	19 (2)	−67 (7)
C(16)	856 (2)	−359 (6)	−6654 (2)	44 (1)	299 (9)	31 (1)	6 (5)	23 (2)	−74 (5)
C(17)	1489 (2)	−2512 (8)	−4618 (2)	60 (2)	410 (13)	39 (1)	46 (7)	21 (2)	30 (9)
C(18)	1753 (2)	−757 (7)	−4061 (2)	49 (1)	392 (11)	34 (1)	13 (6)	38 (2)	−27 (7)
C(19)	2451 (2)	−957 (9)	−3362 (2)	50 (1)	542 (18)	52 (2)	61 (10)	33 (2)	35 (10)
C(20)	2681 (3)	549 (11)	−2814 (2)	60 (2)	653 (23)	43 (1)	74 (11)	15 (3)	−118 (12)
C(21)	2233 (3)	2205 (9)	−2934 (2)	89 (2)	551 (18)	44 (1)	−39 (9)	64 (3)	−176 (12)
C(22)	1576 (3)	2482 (9)	−3618 (3)	91 (3)	379 (14)	4 (2)	47 (10)	96 (4)	38 (11)
C(23)	1319 (2)	941 (8)	−4185 (2)	50 (1)	471 (16)	42 (1)	63 (8)	26 (2)	−3 (8)
O(1)	−2635 (1)	−684 (4)	−9785 (1)	37 (1)	235 (5)	44 (1)	38 (4)	−2 (1)	−3 (4)
O(2)	−599 (1)	−4743 (4)	−8335 (1)	43 (1)	169 (4)	49 (1)	−15 (4)	14 (1)	19 (3)
N(1)	−1581 (1)	−2602 (4)	−9038 (1)	34 (1)	173 (5)	34 (1)	−12 (3)	14 (1)	−14 (3)
N(2)	971 (2)	−1993 (5)	−5427 (1)	44 (1)	348 (9)	31 (1)	22 (5)	22 (1)	−40 (5)

Table 2 (*cont.*)

	x	y	z	B(Å^2)
H(1*A*)	−1868 (23)	−3580 (71)	−9385 (22)	4·6
H(2*A*)	−1218 (23)	1649 (73)	−9069 (22)	4·6
H(2*B*)	−1989 (23)	1797 (75)	−8262 (22)	4·6
H(3*A*)	−559 (23)	1508 (73)	−7714 (22)	4·6
H(3*B*)	−1203 (24)	−133 (76)	−7597 (22)	4·6
H(7*A*)	185 (23)	2435 (77)	−8261 (23)	4·6
H(8*A*)	1087 (25)	3405 (73)	−8933 (22)	4·6
H(9*A*)	1576 (23)	854 (72)	−9530 (21)	4·6
H(10*A*)	1301 (24)	−2564 (75)	−9393 (22)	4·6
H(11*A*)	388 (23)	−3602 (73)	−8785 (22)	4·6
H(12*A*)	687 (23)	−3060 (76)	−7241 (22)	4·6
H(13*A*)	−545 (25)	−2002 (73)	−6602 (23)	4·6
H(13*B*)	−413 (23)	−4155 (76)	−6902 (21)	4·6
H(14*A*)	197 (23)	−4335 (73)	−5520 (22)	4·6
H(14*B*)	939 (23)	−4626 (77)	−5937 (22)	4·6
H(15*A*)	1742 (23)	111 (77)	−5534 (21)	4·6
H(15*B*)	1848 (23)	−2092 (71)	−5907 (23)	4·6
H(16*A*)	493 (23)	752 (72)	−6552 (22)	4·6
H(16*B*)	1221 (24)	250 (75)	−6951 (22)	4·6
H(17*A*)	1135 (23)	−3398 (73)	−4375 (22)	4·6
H(17*B*)	2047 (23)	−3288 (74)	−4628 (22)	4·6
H(19*A*)	2781 (23)	−2205 (71)	−3303 (23)	4·6
H(20*A*)	3186 (23)	305 (75)	−2236 (22)	4·6
H(21*A*)	2438 (24)	3283 (73)	−2480 (22)	4·6
H(22*A*)	1198 (25)	3774 (73)	−3733 (22)	4·6
H(23*A*)	774 (24)	1063 (74)	−4722 (22)	4·6

Table 3. *Bond distances and angles*

C(1)–C(2)	1·493(4) Å	C(10)–C(11)	1·388 (5) Å
C(1)–O(1)	1·226 (4)	C(12)–C(13)	1·533 (4)
C(1)–N(1)	1·368 (3)	C(12)–C(16)	1·524 (5)
C(2)–C(3)	1·522 (4)	C(13)–C(14)	1·537 (5)
C(3)–C(4)	1·532 (4)	C(14)–N(2)	1·462 (5)
C(4)–C(5)	1·521 (4)	N(2)–C(15)	1·459 (5)
C(4)–C(6)	1·552 (4)	N(2)–C(17)	1·450 (6)
C(4)–C(12)	1·564 (4)	C(15)–C(16)	1·521 (4)
C(5)–N(1)	1·389 (4)	C(17)–C(18)	1·512 (6)
C(5)–O(2)	1·211 (4)	C(18)–C(19)	1·393 (5)
C(6)–C(7)	1·388 (5)	C(18)–C(23)	1·344 (7)
C(6)–C(11)	1·389 (4)	C(19)–C(20)	1·374 (8)
C(7)–C(8)	1·394 (6)	C(20)–C(21)	1·334 (8)
C(8)–C(9)	1·367 (6)	C(21)–C(22)	1·346 (8)
C(9)–C(10)	1·370 (7)	C(22)–C(23)	1·414 (7)
C(2)—H(2*A*)	1·06 (4) Å	C(13)–H(13*A*)	1·03 (5)
C(2)—H(2*B*)	1·04 (5)	C(13)–H(13*B*)	0·93 (5)
C(3)—H(3*A*)	0·94 (5)	C(14)–H(14*A*)	1·09 (4)
C(3)—H(3*B*)	1·07 (4)	C(14)–H(14*B*)	1·03 (5)
N(1)—H(1*A*)	0·92 (4)	C(15)–H(15*A*)	1·03 (5)
C(7)—H(7*A*)	1·05 (5)	C(15)–H(15*B*)	1·01 (5)
C(8)—H(8*A*)	1·09 (5)	C(16)–H(16*A*)	1·05 (5)
C(9)—H(9*A*)	0·99 (4)	C(16)–H(16*B*)	1·08 (4)
C(10)–H(10*A*)	0·98 (5)	C(17)–H(17*A*)	1·05 (5)
C(11)–H(11*A*)	1·08 (5)	C(17)–H(17*B*)	1·12 (5)
C(12)–H(12*A*)	1·04 (5)	C(19)–H(19*A*)	1·00 (4)
		C(20)–H(20*A*)	1·10 (4)
		C(21)–H(21*A*)	1·06 (5)
		C(22)–H(22*A*)	1·06 (4)
		C(23)–H(23*A*)	1·08 (4)

Description of the structure

Intramolecular bond distances and angles are given in Table 3. As a reaction to steric crowding the C(4)–C(12) and C(4)–C(6) bonds are significantly longer than usual. One of the piperidine rings is considerably flattened due to the presence of the CO–NH–CO group. This is shown by the values of the torsional angles for this ring:

C(1)–C(2)–C(3)–C(4)	48·7°
C(2)–C(3)–C(4)–C(5)	−53·2
C(3)–C(4)–C(5)–N(1)	32·4
C(4)–C(5)–N(1)–C(1)	−6·8
C(5)–N(1)–C(1)–C(2)	0·2
N(1)–C(1)–C(2)–C(3)	−21·1

Table 3 (*cont.*)

O(1)—C(1)—C(2)	123·7 (2)°	C(14)—N(2)—C(15)	109·0 (3)°
N(1)—C(1)—C(2)	117·4 (2)	C(15)—N(2)—C(17)	112·8 (3)
N(1)—C(1)—O(1)	118·9 (2)	N(2)—C(15)–C(16)	110·7 (3)
C(1)—C(2)—C(3)	113·0 (2)	C(12)—C(16)–C(15)	111·4 (3)
C(2)—C(3)—C(4)	113·4 (2)	N(2)—C(17)–C(18)	114·2 (4)
C(3)—C(4)—C(5)	108·4 (2)	C(17)—C(18)–C(19)	118·4 (4)
C(3)—C(4)—C(6)	112·8 (2)	C(17)—C(18)–C(23)	123·2 (4)
C(3)—C(4)—C(12)	112·0 (2)	C(19)—C(18)–C(23)	118·3 (4)
C(5)—C(4)—C(6)	105·8 (2)	C(18)—C(19)–C(20)	120·3 (5)
C(5)—C(4)—C(12)	109·1 (2)	C(19)—C(20)–C(21)	120·7 (5)
C(6)—C(4)—C(12)	108·5 (2)	C(20)—C(21)–C(22)	120·3 (5)
N(1)—C(5)—O(2)	118·2 (3)	C(21)—C(22)–C(23)	119·8 (5)
C(4)—C(5)—O(2)	124·0 (3)	C(22)—C(23)–C(18)	120·3 (4)
C(4)—C(5)—N(1)	117·7 (2)	C(9)—C(10)–C(11)	120·8 (4)
C(5)—N(1)—C(1)	127·6 (2)	C(10)—C(11)–C(6)	120·8 (3)
C(4)—C(6)—C(7)	121·6 (3)	C(4)—C(12)–C(13)	114·0 (2)
C(4)—C(6)—C(11)	120·4 (2)	C(4)—C(12)–C(16)	112·7 (2)
C(7)—C(6)—C(11)	117·8 (3)	C(13)—C(12)–C(16)	108·5 (3)
C(6)—C(7)—C(8)	120·6 (3)	C(12)—C(13)–C(14)	109·8 (3)
C(7)—C(8)—C(9)	120·8 (4)	C(13)—C(14)–N(2)	109·6 (3)
C(8)—C(9)—C(10)	119·1 (4)	C(14)—N(2)—C(17)	112·1 (3)
C(1)—C(2)—H(2*A*)	106 (2)°	C(13)—C(14)–H(14*A*)	110 (2)°
C(1)—C(2)—H(2*B*)	104 (2)	C(13)—C(14)–H(14*B*)	112 (2)
C(3)—C(2)—H(2*A*)	108 (2)	N(2)—C(14)–H(14*A*)	106 (2)
C(3)—C(2)—H(2*B*)	111 (2)	N(2)—C(14)–H(14*B*)	105 (2)
H(2*A*)—C(2)—H(2*B*)	115 (3)	H(14*A*)–C(14)–H(14*B*)	114 (3)
C(2)—C(3)—H(3*A*)	108 (3)	N(2)—C(15)–H(15*A*)	108 (2)
C(2)—C(3)—H(3*B*)	106 (2)	N(2)—C(15)–H(15*B*)	112 (2)
C(4)—C(3)—H(3*A*)	109 (3)	C(16)—C(15)–H(15*A*)	106 (2)
C(4)—C(3)—H(3*B*)	110 (3)	C(16)—C(15)–H(15*B*)	110 (2)
H(3*A*)—C(3)—H(3*B*)	111 (4)	H(15*A*)–C(15)–H(15*B*)	110 (4)
C(5)—N(1)—H(1*A*)	120 (3)	C(15)—C(16)–H(16*A*)	107 (2)
C(1)—N(1)—H(1*A*)	112 (3)	C(15)—C(16)–H(16*B*)	109 (2)
C(6)—C(7)—H(7*A*)	120 (2)	C(12)—C(16)–H(16*A*)	110 (2)
C(8)—C(7)—H(7*A*)	120 (2)	C(12)—C(16)–H(16*B*)	110(2)
C(7)—C(8)—H(8*A*)	120 (2)	H(16*A*)–C(16)–H(16*B*)	111 (3)
C(9)—C(8)—H(8*A*)	119 (2)	N(2)—C(17)–H(17*A*)	109 (2)
C(8)—C(9)—H(9*A*)	119 (3)	N(2)—C(17)–H(17*B*)	107 (2)
C(10)—C(9)—H(9*A*)	121 (3)	C(18)—C(17)–H(17*A*)	103 (2)
C(9)—C(10)–H(10*A*)	120 (3)	C(18)—C(17)–H(17*B*)	110 (2)
C(11)—C(10)–H(10*A*)	119 (3)	H(17*A*)–C(17)–H(17*B*)	114 (3)
C(10)—C(11)–H(11*A*)	120 (2)	C(18)—C(19)–H(19*A*)	116 (3)
C(6)—C(11)–H(11*A*)	119 (2)	C(20)—C(19)–H(19*A*)	123 (3)
C(4)—C(12)–H(12*A*)	106 (2)	C(19)—C(20)–H(20*A*)	120 (2)
C(13)—C(12)–H(12*A*)	108 (2)	C(21)—C(20)–H(20*A*)	119 (2)
C(16)—C(12)–H(12*A*)	107 (2)	C(20)—C(21)–H(21*A*)	116 (2)
C(12)—C(13)–H(13*A*)	110 (3)	C(22)—C(21)–H(21*A*)	123 (2)
C(12)—C(13)–H(13*B*)	113 (3)	C(21)—C(22)–H(22*A*)	122 (2)
C(14)—C(13)–H(13*A*)	111 (3)	C(23)—C(22)–H(22*A*)	117 (2)
C(14)—C(13)–H(13*B*)	103 (3)	C(22)—C(23)–H(23*A*)	122 (2)
H(13*A*)–C(13)–H(13*B*)	110 (4)	C(18)—C(23)–H(23*A*)	118 (2)

Each molecule is hydrogen bonded to two neighbours:

$$O(1)\cdots H\text{–}N(1) \quad [N(1): -\tfrac{1}{2}-x, \tfrac{1}{2}+y, -z-2]$$

and

$$N(1)\text{–}H\cdots O(1) \quad [O(1): -x-\tfrac{1}{2}, y-\tfrac{1}{2}, -z-2]\,.$$

We thank Dr P. A. J. Janssen (Janssen Pharmaceutica, Beerse, Belgium) for providing the crystals. M. K. thanks the Fonds National de la Recherche Scientifique for a grant.

References

AHMED, F. R., HALL, S. R., PIPPY, M. E. & HUBER, C. P. (1966). *World list of Crystallographic Computer Programs*, 2nd Ed. Appendix, p. 52. Utrecht: Oosthoek.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.

SPEK, A. L., PEERDEMAN, A. F., VAN WIJNGAARDEN, I. & SOUDIJN, W. (1971). *Nature, Lond.* **232**, 575–576.

WILSON, A. J. C. (1942). *Nature, Lond.* **150**, 152.