

1-[1-(3-Cyano-3,3-diphenylpropyl)-4-piperidinyl]-1,3-dihydro-3-(1-oxopropyl)-2H-benzimidazol-2-one (Bezitramide) Chloroform

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(Received 6 May 1977; accepted 21 May 1977)

Abstract. $C_{31}O_2N_4H_{32} \cdot CHCl_3$, monoclinic, $P2_1/n$, $a = 15.768$ (5), $b = 18.643$ (5), $c = 10.548$ (5) Å, $\beta = 98.25$ (5)°, $D_m = 1.33$, $D_c = 1.34$ g cm⁻³, $Z = 4$. Disordered chloroform molecules and bezitramide molecules are held together by van der Waals forces and very weak hydrogen bonds.

Introduction. This structure was solved as part of a study on the structure–activity relationship of narcotic analgesics. The title compound, commercially known as Burgodin®, is a hundred times more potent than morphine, with long-lasting activity. Colourless prismatic crystals were obtained from a chloroform/diethyl ether solution. The space group was determined from photographs. Cell dimensions and intensities were measured on a Nonius CAD-4 diffractometer with the experimental conditions given in Table 1.

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). The most probable *E* map contained the whole analgesic molecule, except for one atom which was located by Fourier series with the *SDP* program system (Okaya & Frenz, 1975). At this stage, full-matrix least-squares refinement with an overall temperature factor led to an *R* of 0.36.

A difference map revealed ten peaks corresponding to the Cl atoms of the chloroform molecule. Isotropic refinement including the population factors of the Cl atoms converged to an *R* of 0.17.

Table 1. *Experimental conditions*

Source: Cu $K\alpha$, $\lambda = 1.54178$ Å
 Scan: $\omega-2\theta$
 Graphite monochromator
 Confidence level: 2.5σ , with $\sigma^2(I) = S + B + (0.035)^2$ (*S* being the scan and *B* the background count)
 $\Delta\theta = 0.6 + 0.3 \text{ tg } \theta$
 $2.0 \leq \theta < 70.0^\circ$
 Aperture: $2.5 + 0.5 \text{ tg } \theta$
 Total number of independent reflexions: 6148; number observed: 3446

Table 2. *Final positional ($\times 10^4$) parameters with standard deviations in parentheses*

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	13386 (4)	4263 (0)	-5215 (5)
C(2)	12746 (1)	4137 (3)	-4262 (1)
C(3)	12150 (1)	4775 (7)	-4258 (0)
O(4)	12249 (6)	5340 (6)	-4799 (4)
N(5)	11420 (4)	4704 (1)	-3597 (3)
C(6)	10785 (2)	5211 (1)	-3601 (7)
C(7)	10699 (3)	5897 (5)	-4167 (5)
C(8)	9954 (0)	6277 (2)	-4025 (7)
C(9)	9327 (9)	5992 (1)	-3346 (2)
C(10)	9413 (9)	5286 (0)	-2777 (5)
C(11)	10161 (2)	4924 (1)	-2921 (5)
N(12)	10442 (1)	4240 (3)	-2528 (4)
C(13)	11206 (1)	4100 (5)	-2914 (5)
O(14)	11626 (0)	3540 (4)	-2722 (2)
C(15)	10027 (5)	3713 (3)	-1783 (4)
C(16)	9875 (1)	4024 (2)	-482 (1)
C(17)	9415 (1)	3473 (2)	239 (1)
N(18)	8607 (1)	3264 (3)	-527 (6)
C(19)	8785 (6)	2915 (3)	-1709 (2)
C(20)	9202 (6)	3443 (4)	-2533 (3)
C(21)	8092 (3)	2786 (4)	193 (4)
C(22)	7625 (6)	3190 (2)	1165 (1)
C(23)	7087 (1)	3859 (5)	587 (5)
C(24)	7649 (1)	4448 (7)	511 (3)
N(25)	8077 (1)	4946 (7)	516 (5)
C(26)	6419 (4)	4094 (5)	1446 (5)
C(27)	6015 (1)	4755 (7)	1188 (1)
C(28)	5388 (3)	4995 (10)	1888 (9)
C(29)	5186 (11)	4569 (16)	2909 (15)
C(30)	5578 (13)	3910 (6)	3174 (1)
C(31)	6220 (4)	3678 (4)	2437 (2)
C(32)	6599 (4)	3702 (4)	-777 (3)
C(33)	6836 (1)	4012 (3)	-1869 (1)
C(34)	6393 (2)	3847 (4)	-3060 (2)
C(35)	5699 (3)	3353 (4)	-3198 (9)
C(36)	5465 (5)	3034 (1)	-2120 (2)
C(37)	5904 (7)	3199 (2)	-880 (1)
Cl(38)	3444 (2)	3757 (1)	1192 (2)
Cl(39)	2126 (1)	2573 (1)	187 (2)
C(40)	2726 (14)	3312 (2)	-19 (12)
Cl(41)	2049 (3)	3334 (2)	1198 (3)
Cl(42)	3182 (1)	2578 (1)	-678 (3)
Cl(43)	2880 (2)	3758 (0)	1456 (9)
Cl(46)	1926 (1)	2942 (1)	696 (2)
Cl(47)	3766 (1)	3317 (3)	-230 (1)
Cl(48)	2636 (1)	2331 (1)	-236 (1)
Cl(49)	3754 (1)	3583 (1)	779 (1)
Cl(50)	3502 (1)	2970 (1)	-929 (4)

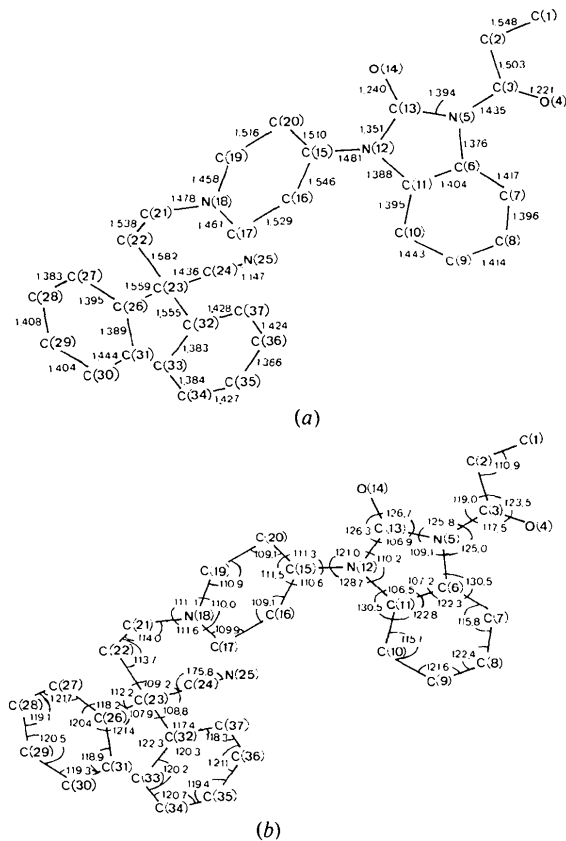


Fig. 1. (a) Bond distances (Å) and (b) bond angles (°). The maximum e.s.d.'s for the lengths are 0.015 Å and for the angles 0.9°.

The final positional (Table 2) and thermal parameters after anisotropic (Cl excepted) refinement converged to an R of 0.109.*

Discussion. The presence of ten distinct Cl atoms suggests disorder for CHCl_3 . In order to verify this point, we repeated the cell-dimension and intensity measurements at -120°C . However, refinement did not change the preceding results. It seems that the CHCl_3 molecules have no strong interactions with the bezitramide molecules.

The molecular packing is due to van der Waals interactions and very weak hydrogen bonds: O(14)-

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32716 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. Torsion angles (°)

C(1)–C(2)–C(3)–O(4)	–9.40
C(2)–C(3)–N(5)–C(13)	1.66
C(13)–N(12)–C(15)–C(20)	–114.46
C(11)–N(12)–C(15)–C(16)	–57.65
C(17)–N(18)–C(12)–C(22)	77.51
C(19)–N(18)–C(21)–C(22)	–160.27
N(18)–C(21)–C(22)–C(23)	50.82
C(21)–C(22)–C(23)–C(24)	–79.69
C(22)–C(23)–C(24)–N(25)	–110.84
C(22)–C(23)–C(26)–C(27)	167.91
C(22)–C(23)–C(32)–C(33)	–109.03

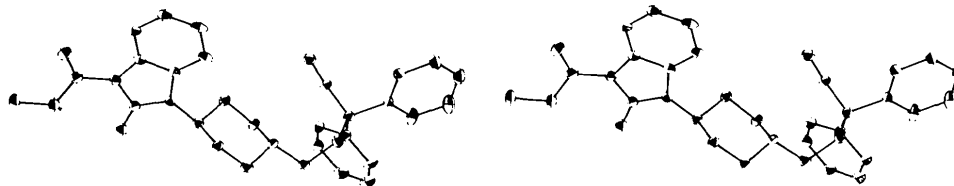


Fig. 2. Stereoscopic view (Johnson, 1965) of the molecule with 50% probability thermal ellipsoids.

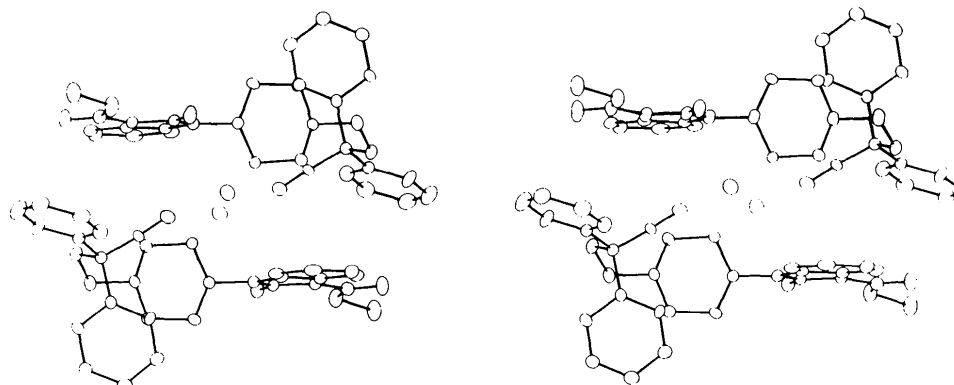


Fig. 3. Stereoscopic view (Johnson, 1965) of the molecular packing.

$[x, y, z]-C(40)[1+x, y, z]: 3.146 \text{ \AA}$ and $N(25)-[x, y, z]-C(40)[1-x, 1-y, \bar{z}]: 3.498 \text{ \AA}$.

The atomic numbering, bond distances and angles are given in Fig. 1, torsion angles in Table 3. Fig. 2 is a stereoview of the molecule and Fig. 3 shows the molecular packing.

We thank Dr P. A. J. Janssen (Janssen Pharmaceutica, B-2340 Beerse, Belgium) for providing the sample, and l'Institut pour l'Encouragement de la

Recherche Scientifique dans l'Industrie et l'Agriculture (IRSIA) for the award of a doctoral fellowship to CH.

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Acta Cryst. (1977). B33, 2951-2953

A Stable Benzocyclobutene: 1,4-Di(*tert*-butyl)-2,3-diphenyl-5,6-bis(1-phenyl-2,2-dicyanovinyl)benzocyclobutene-Acetone

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(Received 4 March 1977; accepted 10 May 1977)

Abstract. $C_{48}H_{38}N_4 \cdot C_3H_6O$, monoclinic, $P2_1/c$, $a = 12.772$ (2), $b = 15.970$ (3), $c = 22.230$ (3) \AA , $\beta = 109.35$ (1) $^\circ$, D_m (floatation) = 1.14, $D_x = 1.13$ g cm^{-3} , $Z = 4$. The structure of the title compound has been determined by X-ray diffraction. Although the structure of the skeletal eight-membered ring is in qualitative agreement with that deduced by MO calculations, it is highly strained by the bulky substituents.

Introduction. Deep-red crystals were recrystallized from acetone solution. Weissenberg photographs showed the systematic absences $h0l$, $l \neq 2n$, and $0k0$, $k \neq 2n$, indicating the space group $P2_1/c$. Intensities and accurate cell dimensions were measured on a Rigaku automated four-circle diffractometer using graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.7107 \text{ \AA}$). The intensities were corrected for Lorentz and polarization effects. Of the 5947 independent reflections ($2\theta \leq 45^\circ$), 2516 had intensities greater than $3\sigma(I)$. The structure was solved by the direct method (Karle & Karle, 1966).

The atomic parameters were refined by the least-squares method using a 9×9 block-diagonal matrix. During the isotropic refinement, thermal parameters of the acetone molecule became about three times as large as those of the other atoms. This could be attributed to the disorder and/or the low occupancy of acetone in the crystal. Therefore its parameters were fixed and the occupancy factor was assumed to be $\frac{2}{3}$. Although most of the H atoms were found by the difference synthesis, their positional parameters were fixed at values calculated geometrically. Their isotropic temperature

factors were also fixed at 5 \AA^2 . At the final stage of the refinement, anisotropic temperature factors were introduced for non-hydrogen atoms, except for those of acetone.

The weighting scheme was $w = 1/(\sigma + a|F_o|^2)$, where σ was from counting statistics and $a = 9 \times 10^{-6}$. The final R was 0.19 for all reflexions, and 0.10 for the non-zero reflexions.* Scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Final positional parameters and the bond lengths of the non-hydrogen atoms, with the crystallographic numbering system, are listed in Tables 1 and 2 respectively.*

Discussion. The present compound is the final product of the reaction of a substituted benzodicyclobutene (I) with tetracyanoethylene (TCNE) (Toda & Dan, 1976). At first a 1:1 adduct (II) is produced; this adduct is easily isomerized into the title compound (III) by heating.† Compounds with a benzocyclobutene skeleton are very unstable. The title compound may be the first derivative to be isolated in a stable form. The

* Lists of structure factors, anisotropic thermal parameters, and bond angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32721 (29 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

† On the basis of the resemblance to the reaction which had previously been reported by Huth, Straub & Müller (1973), Toda & Dan presumed that (III) would have the *anti* conformation with respect to the cyanovinyl groups and that (II) was its *syn* isomer.