Crystal and Molecular Structure of 8a-Bromo-1,2,3,5,6,7,8,8a-octahydro-1,3-dioxoisoquinoline-4-carbonitrile

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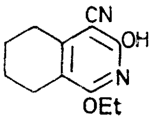
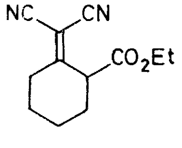
The crystal structure of the title compound has been determined by the heavy-atom method from 1 113 observed three-dimensional photographic data. Crystals are monoclinic with $a = 17.05$, $b = 7.11$, $c = 17.10$ Å (all ±0.02 Å), $\beta = 89.0$ (0.2)°, space group $C2/c$, with $Z = 8$. The structure was refined by block-diagonal least-squares to R 0.098. There is an intermolecular hydrogen bond of the N–H · · · O type. The cyclohexane portion of the molecule adopts a slightly distorted chair conformation.

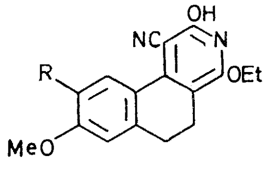
THE structure (1) has been assigned to an abnormal product obtained during the Knoevenagel condensation [1,2] [NH$_4$OAc–AcOH,benzene–EtOH (1 : 1) or benzene, as solvent] of ethyl 2-oxocyclohexanecarboxylate and malononitrile on the basis of spectral and degradation data. The same product is also obtained by keeping ethyl 2-dicyanomethylenecyclohexanecarboxylate (2) at room temperature for several days. A novel feature of this reaction is the retention of the ethoxy-group of the ester during cyclization of the intermediate (2). In view of this interesting feature, we wished to establish † the structure of (1) by *X*-ray crystallography. In order to obtain a suitable derivative containing a heavy atom and also incorporating the pyridine moiety of (1), we attempted to prepare (3b) from (3a) by bromination with dioxan dibromide.[3] To ensure that the substituted pyridine moiety would remain unaffected under these bromination conditions, a model experiment was carried out with compound (1). Unexpectedly, a crystalline bromo-compound was thus obtained from this reaction in diethyl ether.



(1)

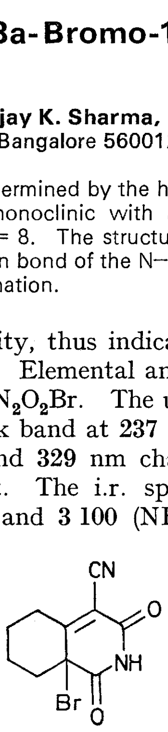


(2)

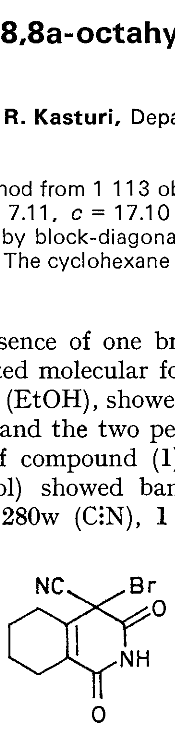


(3) a; R = H
b; R = Br

The mass spectrum of this compound exhibited a molecular-ion peak at 268 with an $M + 2$ peak of equal intensity, thus indicating the presence of one bromine atom. Elemental analysis indicated molecular formula $C_{10}H_9N_2O_2Br$. The u.v. spectrum (EtOH), showed only a weak band at 237 nm (ε 4 670) and the two peaks at 302 and 329 nm characteristic of compound (1) were absent. The i.r. spectrum (Nujol) showed bands at 3 200 and 3 100 (NH or OH), 2 280w (C⋮N), 1 720sh, 1 700 (C:O), and 1 620 cm^{-1} (C:C). The only conclusion that could be drawn from the n.m.r. spectrum ‡ (trichlorodeuteriomethane–deuteriodimethyl sulphoxide) was the absence of the ethoxy-group. On the basis of physical data, two structures, (4) and (5), were possible. In order to ascertain the structure, an *X*-ray crystal structure analysis was undertaken, and established the compound as (4).



(4)



(5)

EXPERIMENTAL

Bromination of (1) *with Dioxan Dibromide*.—A cooled solution of dioxan dibromide [3] (1.2 g) in dry ethyl ether (50 ml) was added to a cooled (ice–salt bath) ethereal solution of (1) (1 g) in dry ethyl ether (50 ml), with stirring, during 10 min. Stirring was continued for 8 h, during which the mixture was allowed to come to room temperature. It was then washed (water, 6 × 20 ml), and

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† The structure of this compound has since been confirmed, however, by degradation and synthetic studies, and results will be published elsewhere.

‡ A reliable n.m.r. spectrum could not be obtained because of the compound's insolubility in the first and instability in the second solvent.

[1] J. L. van der Baan and F. Bickelhaupt, *Chem. Comm.*, 1970, 326.

[2] T. R. Kasturi, V. K. Sharma, A. Srinivasan, and G. Subrahmanyam, *Tetrahedron*, 1973, **29**, 4103.

[3] D. C. Schlegel, C. D. Tipton, and K. L. Rinehart, jun., *J. Org. Chem.*, 1970, **35**, 849.

dried (Na_2SO_4). The yellow crystalline solid which separated, was washed with water, ether, and ethanol, and dried to give 8a-*bromo*-1,2,3,5,6,7,8,8a-*octahydro*-1,3-*dioxoisoquinoline*-4-*carbonitrile* (4) (0.2 g), m.p. 154—155 °C, M^+ 268 (^{79}Br) (Found: C, 44.6; H, 3.35; N, 10.85; Br, 28.4. $C_{10}H_9N_2O_2Br$ requires C, 44.6; H, 3.35; N, 10.4; Br, 29.7%).

Crystal Data.—$C_{10}H_9BrN_2O_2$, $M = 269$. Monoclinic, $a = 17.05 \pm 0.02$, $b = 7.11 \pm 0.02$, $c = 17.10 \pm 0.02$ Å, $\beta = 89.0$ (0.2)°, $U = 2\,072.5$ Å^3, $D_m = 1.735$ g cm^{-3} (by flotation), $D_c = 1.724$ g cm^{-3}, $Z = 8$. Space group Cc (C^4; No. 9) or $C2/c$ (C^6_{2h}; No. 15) from systematic absences, successful refinement with the latter. Cu-K_α radiation, $\lambda = 1.5418$ Å; μ(Cu-K_α) = 52.7 cm^{-1}. Unit-cell data were obtained from rotation and Weissenberg photographs taken with Cu-K_α radiation.

TABLE 1

Positional co-ordinates and anisotropic temperature factors * for non-hydrogen atoms (× 10^4), with standard deviations in parentheses

Atom	X/a	Y/b	Z/c	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	4 683(2)	5 741(4)	3 676(2)	42(1)	234(7)	37(1)	−5(2)	4(1)	−5(2)
C(1)	3 256(15)	4 262(40)	2 978(17)	40(10)	255(70)	39(11)	3(29)	0(8)	10(20)
C(2)	3 646(16)	2 872(42)	2 412(14)	49(11)	311(72)	19(9)	4(23)	−3(8)	−13(19)
C(3)	3 736(18)	0 986(39)	2 836(16)	58(12)	254(65)	25(9)	−1(22)	−1(8)	−9(18)
C(4)	4 212(17)	1 216(39)	3 556(16)	53(12)	240(62)	30(10)	25(21)	2(9)	−11(19)
C(5)	3 866(12)	2 598(28)	4 137(13)	30(7)	145(46)	24(8)	10(13)	−5(6)	6(13)
C(6)	3 655(14)	4 542(36)	3 791(15)	35(8)	212(57)	34(10)	16(17)	7(7)	−10(17)
C(7)	3 184(14)	5 716(32)	4 300(13)	40(9)	200(54)	20(8)	4(17)	4(6)	6(15)
C(8)	3 349(13)	3 569(31)	5 413(13)	36(8)	175(48)	20(7)	−1(15)	−3(6)	−9(14)
C(9)	3 708(13)	2 182(32)	4 894(13)	33(8)	186(49)	24(8)	3(15)	−1(6)	14(15)
C(10)	3 907(14)	0 435(34)	5 257(14)	37(9)	218(56)	26(8)	4(18)	−4(7)	−3(17)
N(1)	3 089(11)	5 183(27)	5 085(11)	36(7)	190(42)	22(7)	5(13)	1(5)	1(12)
N(2)	4 037(15)	−0 952(35)	5 552(17)	59(11)	258(61)	53(13)	6(20)	−11(10)	−1(21)
O(1)	2 915(11)	7 239(27)	4 052(11)	53(8)	257(44)	30(7)	23(15)	7(6)	11(13)
O(2)	3 238(13)	3 195(31)	6 118(11)	63(9)	322(54)	25(7)	−11(17)	1(7)	2(14)

* In the form: $T = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

Three-dimensional intensity data were collected by use of Cu-K_α radiation for the layers $h0$—$6l$ and $hk0$—2, with rotation along the b and c axes respectively. All intensities were estimated visually and corrected for Lorentz, polarization, and spot-shape factors.[4] An approximate correction for absorption [5] was made assuming a cylindrical crystal (μt 1.00). Of 1 596 reflections within the regions surveyed 1 113 were measured. By use of 78 common reflections, data for both axes were correlated by the method of Rollett and Sparks.[6]

Structure Determination and Refinement.—A three-dimensional Patterson map enabled location of the bromine atom, and a Fourier map, phased on this revealed the remaining non-hydrogen atom positions. Positional parameters, individual isotropic temperature parameters, and individual layer scale factors were then refined.[7] The quantity minimized was $\Sigma\, w(|F_o| - |F_c|)^2$, where w is the weight of an observation. The distribution of $\Sigma|\Delta F|^2$ *vs.* $\langle|F_o|\rangle$ suggested a weighting scheme [8] of the form $w = (10.0 + |F_o| + 0.02|F_o|^2)^{-1}$. A three-dimensional difference electron-density map computed at this stage showed peaks ranging from 0.3 to 0.7 eÅ^{-3}, in positions where hydrogen atoms were expected to occur. Three cycles of refinement with anisotropic temperature factors for all non-hydrogen atoms and refining the overall scale-factor, gave R 0.098 for all observed 1 113 reflections. Hydrogen atoms were included in calculated positions (assuming C–H 1.0 and N–H 0.9 Å). The shifts in the parameters after the last cycle were $< 0.1\sigma$. In all structure-factor calculations, atomic scattering factors for non-hydrogen atoms were taken from ref. 9, and for hydrogen from ref. 10, those for bromine being corrected for anomalous dispersion effects according to ref. 11.

Final positional and thermal parameters are recorded in Tables 1 and 2. Observed and calculated structure-factors are listed in Supplementary Publication No. SUP 21410 (3 pp., 1 microfiche).†

TABLE 2

Positional co-ordinates (× 10^3) of hydrogen atoms with their isotropic temperature factors

	X/a	Y/b	Z/c	B/Å^2
H(C11)	321	553	272	4.51
H(C12)	269	392	302	4.51
H(C21)	417	336	225	4.15
H(C22)	330	270	194	4.15
H(C31)	399	004	248	4.51
H(C32)	320	048	299	4.51
H(C41)	476	161	341	3.93
H(C42)	428	−005	382	3.93
H(N)	283	595	542	2.91

DISCUSSION AND DESCRIPTION OF THE STRUCTURE

The analysis showed the structure to be compound (4). Estimated standard deviations in bond lengths are 0.024 (C–Br) and 0.034 Å for those involving carbon, nitrogen, and oxygen atoms, and for bond angles *ca.* 2.0° (Table 3). The C–Br distance (1.950 Å) is in good

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† For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin II*, 1974, Index issue.

[4] D. C. Phillips, *Acta Cryst.*, 1954, **7**, 746.

[5] J. H. Palm, *Acta Cryst.*, 1964, **17**, 1326.

[6] J. S. Rollett and R. A. Sparks, *Acta Cryst.*, 1960, **13**, 273.

[7] R. Shiono, 1970, refinement program, personal communication.

[8] D. E. Pilling, D. W. J. Cruickshank, A. Bujosa, F. M. Lovell, and M. R. Truter, 'Computing Methods and the Phase Problem in *X*-ray analysis,' ed. R. Pepinsky and J. M. Robertson, Pergamon, Oxford, 1961.

[9] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

[10] R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

[11] 'International Tables for *X*-Ray Crystallography,' 1968, vol. III, 214.

agreement with the usual value for a C(sp^3)–Br bond.[12] The C(7)–N(1) and C(8)–N(1) bond lengths (1.402 and 1.355 Å) are not significantly different from the reported mean (1.374 Å),[13,14] which suggests that they possess partial double-bond character. The C(7)–O(1) and C(8)–O(2) bond distances (1.253 and 1.246 Å) are in agreement with the value (1.252 Å) observed for carboxylate ions.[15] The observed bond lengths of C(7)–O(1), C(7)–N(1), N(1)–C(8), and C(8)–O(2) suggest π-electron delocalization. The least-squares plane through atoms O(1), C(7), N(1), C(8), and O(2) shows that it is strictly planar. Values (1.431 and 1.132 Å) for C(9)–C(10) and C(10)–N(2) are in good agreement with the means[16-23] (1.446 and 1.132 Å) for the corresponding bonds in the C–CN fragment. The value (126.3°) for angle C(7)–N(1)–C(8) is close to the mean (125.0 ± 0.2°), reported for systems with an annular hydrogen atom at nitrogen. (The internal angle at nitrogen atom has mean 115.7 ± 0.2° when there is no such substitution.[12]) The angles at C(2), C(3), and C(6) within the cyclohexane portion are close to the normal tetrahedral value but those at C(1) and C(4) are slightly larger.

TABLE 3

Bond lengths, bond angles, and torsion angles

(*a*) Selected torsion angles (deg.)

C(6)–C(1)–C(2)–C(3)	54.1(3.0)
C(2)–C(1)–C(6)–Br	66.7(2.6)
C(2)–C(1)–C(6)–C(5)	−45.8(2.9)
C(2)–C(1)–C(6)–C(7)	−173.5(2.2)
C(1)–C(2)–C(3)–C(4)	−58.4(2.9)
C(2)–C(3)–C(4)–C(5)	59.1(2.9)
C(3)–C(4)–C(5)–C(6)	−51.5(2.9)
C(3)–C(4)–C(5)–C(9)	125.4(2.6)
C(4)–C(5)–C(6)–Br	−76.1(2.0)
C(9)–C(5)–C(6)–Br	106.9(2.1)
C(4)–C(5)–C(6)–C(1)	42.3(2.7)
C(9)–C(5)–C(6)–C(1)	−134.7(2.3)
C(4)–C(5)–C(6)–C(7)	168.0(2.0)
C(9)–C(5)–C(6)–C(7)	−9.0(3.2)
Br–C(6)–C(7)–N(1)	−101.1(2.1)
C(1)–C(6)–C(7)–N(1)	136.6(2.2)
C(5)–C(6)–C(7)–N(1)	11.9(3.1)
Br–C(6)–C(7)–O(1)	74.1(2.5)
C(1)–C(6)–C(7)–O(1)	−48.2(3.1)
C(5)–C(6)–C(7)–O(1)	−172.9(2.1)
N(1)–C(8)–C(9)–C(5)	8.4(3.2)
N(1)–C(8)–C(9)–C(10)	−174.4(2.0)

(*b*) Bond lengths (Å)

Br–C(6)	1.96	C(6)–C(7)	1.44
C(1)–C(2)	1.53	C(7)–N(1)	1.40
C(2)–C(3)	1.53	C(7)–O(1)	1.25
C(3)–C(4)	1.50	C(8)–C(9)	1.45
C(4)–C(5)	1.51	C(8)–N(1)	1.36
C(5)–C(6)	1.55	C(8)–O(2)	1.25
C(5)–C(9)	1.36	C(9)–C(10)	1.43
C(6)–C(1)	1.44	C(10)–N(2)	1.13

(*c*) Bond angles (deg.)

C(2)–C(1)–C(6)	116.9	C(5)–C(6)–C(7)	114.6
C(1)–C(2)–C(3)	108.1	C(6)–C(7)–N(1)	118.5
C(2)–C(3)–C(4)	110.7	C(6)–C(7)–O(1)	119.9
C(3)–C(4)–C(5)	113.6	N(1)–C(7)–O(1)	121.4
C(4)–C(5)–C(6)	114.9	C(9)–C(8)–N(1)	117.3
C(4)–C(5)–C(9)	123.9	C(9)–C(8)–O(2)	120.1
C(6)–C(5)–C(9)	121.2	N(1)–C(8)–O(2)	122.4
Br–C(6)–C(1)	111.6	C(5)–C(9)–C(8)	120.8
Br–C(6)–C(5)	102.4	C(5)–C(9)–C(10)	124.1
Br–C(6)–C(7)	107.4	C(8)–C(9)–C(10)	115.1
C(1)–C(6)–C(5)	109.3	C(9)–C(10)–N(2)	177.6
C(1)–C(6)–C(7)	111.2	C(7)–N(1)–C(8)	126.3

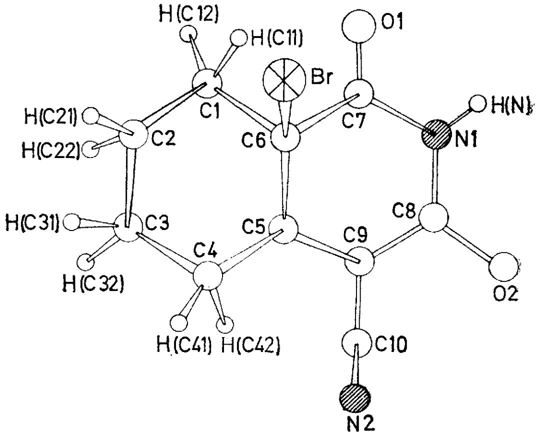

FIGURE 1 A diagram of the molecule

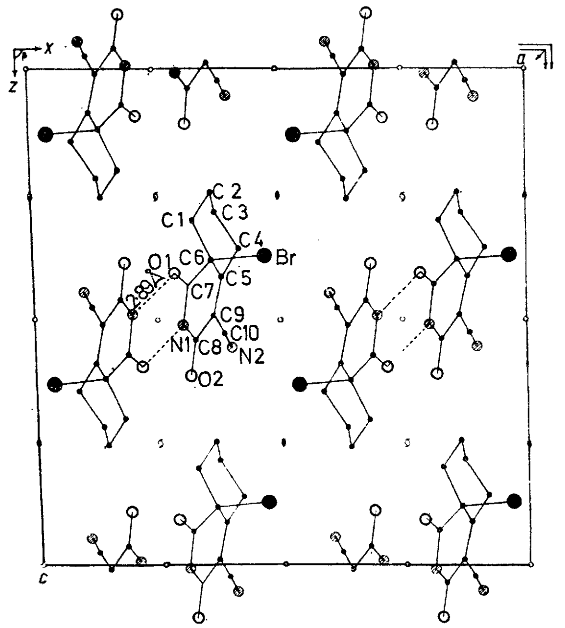

FIGURE 2 View of the structure projected down *b*; large closed circles Br, small closed circles C, open circles O, and hatched circles N atoms

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[12] *Chem. Soc. Special Publ.*, No. 14, 1958.

[13] C. Chartar Singh, *Acta Cryst.*, 1965, **19**, 861.

[14] G. R. Pettit, R. B. von Dreele, G. Bolliger, P. M. Traxler, and P. Brown, *Experientia*, 1973, **29**, 521.

[15] R. E. Marsh and J. Donohue, *Adv. Protein Chem.*, 1967, **22**, 235.

[16] D. A. Bekoe and K. N. Trueblood, *Z. Krist.*, 1960, **113**, 1.

[17] R. E. Long, R. A. Sparks, and K. N. Trueblood, *Acta Cryst.*, 1965, **18**, 932.

[18] I. Karle and A. V. Fratini, *Acta Cryst.*, 1970, **B26**, 596.

[19] B. Greenberg and B. Post, *Acta Cryst.*, 1968, **B24**, 918.

[20] J. L. Stalick and J. A. Ibers, *J. Amer. Chem. Soc.*, 1970, **92**, 5333.

[21] F. L. Hirshfeld, *Israel J. Chem.*, 1964, **2**, 87.

[22] D. A. Mathews, J. Swanson, M. H. Mueller, and G. D. Stucky, *J. Amer. Chem. Soc.*, 1971, **93**, 5945.

[23] J. Silverman, A. P. Krukonis, and N. F. Yannoni, *Cryst. Struct. Comm.*, 1974, **3**, 261.

Conformation of the Molecule.—From the least-squares plane through atoms C(5), C(6), C(2), and C(3) the deviations of atoms C(1) and C(4) are −0.59 and 0.62 Å, showing that the ring has a chair conformation. However a closer examination of the torsion angles (Table 3) within the ring suggest that the conformation does not correspond to an ideal chair. This may be ascribed to the presence of an sp^2 hybridized carbon atom, C(5), and the axially substituted bromine in the cyclohexane moiety. The partial double-bond character of the bonds involving atoms O(1), O(2), C(5), C(7)—(10), N(1), and N(2) suggests that they may be expected to lie in a plane. However this is not so, the torsion angle C(5)–C(9)–C(8)–N(1) being 8.4°. Least-squares plane calculations reveal that C(5), C(8)—(10), N(2), and O(2) define one plane and O(1), C(7), N(1), C(8), and O(2) another. The torsion angle N(1)–C(7)–C(6)–C(5) (11.9°) is such that the intermolecular distance between Br at C(6), in an axial position, and O(1), is increased.

Crystal Packing and Hydrogen Bonding.—The packing of the molecules in the unit cell is illustrated in Figure 2. The structure is stabilized by van der Waals interactions. The molecules are associated in centrosymmetric dimers through hydrogen bonds between N(1) of one molecule and the lone-pair of the oxygen O(1) in the next, with N(1) · · · O(1) 2.89 Å.

We thank the C.S.I.R. (India) for financial assistance (to T. N. G. and V. K. S.).

[5/189 *Received, 28th January,* 1975]