

The Crystal and Molecular Structure of 7-Chloro-3,3-diethyl-2-oxo-9-phenylpyrazolo[5,1-*b*]quinazolinium Betaine (with Ethanol of Crystallization)

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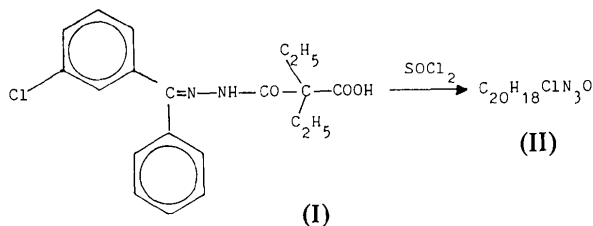
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7-Chloro-3,3-diethyl-2-oxo-9-phenylpyrazolo[5,1-*b*]quinazolinium betaine (with ethanol) $C_{20}H_{18}ClN_3 \cdot O \cdot C_2H_5OH$, is monoclinic, $P2_1/n$, with $a = 14.722(3)$, $b = 10.603(2)$, $c = 13.771(3)$ Å, $\beta = 103.08(5)^\circ$, $D_m = 1.27$, $D_x = 1.260$ g cm $^{-3}$ for $Z = 4$. The crystal structure, solved by direct methods, was refined by full-matrix least squares to an R value of 0.052 for 2203 'observed' reflexions measured by a single-crystal diffractometer. The molecular structure shows a mesoionic character.

Introduction

The action of benzodiazepine and benzodiazocine derivatives as psychopharmacological agents affecting the central nervous system is well known (Sternbach *et al.*, 1962; Sternbach, Randall & Gustafson, 1964; Stempel, Reeder & Sternbach, 1965; Sternbach, 1971). To study the effects of larger heterocyclic rings on the pharmacological activity, attempts were made to obtain benzotriazinone derivatives (in the Manetti & Roberts Laboratories, Firenze). The reaction between 2-amino-5-chlorobenzophenylhydrazine and ethyl diethylmalonate, and successive hydrolysis gave compound I. This acid, by the action of thionyl chloride, yielded, instead of the expected 9-chloro-3,3-diethyl-7-phenyl-1*H*-1,5,6-benzotriazinone-2,4-(3*H*,5*H*)-dione, a compound (II) with composition $C_{20}H_{18}ClN_3O$, $M_r = 351$ (Orzalesi, Selleri, Vittory, Grandolini & Innocenti, 1977).



Since chemical attempts to determine a suitable structural formula for this compound failed, a crystal structure analysis was performed. Crystals of (II), crystallized from ethanol as yellow prisms with m.p. 225–226°C, were kindly provided by Dr G. Orzalesi of Manetti & Roberts Laboratories.

Experimental

The crystals are monoclinic. The unit-cell dimensions were determined by a least-squares analysis of 25

reflexions measured on the single-crystal diffractometer (Philips PW 1100). The crystal data at room temperature are: $a = 14.722(3)$, $b = 10.603(2)$, $c = 13.771(3)$ Å, $\beta = 103.08(5)^\circ$, space group $P2_1/n$, $D_m = 1.27$ g cm $^{-3}$ (by flotation). This density, assuming $Z = 4$, made us suspect the presence of solvent molecules in the crystals, which was confirmed by an elemental chemical analysis and eventually by the crystal structure determination.

Three-dimensional intensity data were collected with graphite-monochromatized Mo $K\alpha$ radiation. Of 2987 independent data available within $\theta \leq 30^\circ$ and collected with the θ - 2θ scan, 2203 data with $I \geq 3\sigma(I)$ were considered observable and used in subsequent calculations.

Structure determination

The structure was solved by the multiresolution method: 248 reflexions with $E \geq 2.10$ were used as input to the program *MULTAN* (Germain, Main & Woolfson, 1971). Eight phase sets were produced and an E map, calculated with the set having the highest figure of merit (combined $FOM = 2.95$), revealed 16 of the 24 non-hydrogen atoms of the molecule. This model was completed and roughly refined by successive Fourier syntheses, which also revealed the atomic positions of one C_2H_5OH solvent molecule in the asymmetric unit. After isotropic full-matrix least-squares refinement, followed by anisotropic refinement, a difference synthesis revealed the H atom locations. Two more cycles of anisotropic refinement including positional parameters for H atoms, which were assigned isotropic thermal parameters equivalent to those of the atoms to which they are bonded, resulted in a final conventional R value of 0.052.

A final difference synthesis revealed no abnormal features. Atomic coordinates and thermal parameters

Table 1. Fractional atomic coordinates and thermal parameters of non-hydrogen atoms with standard deviations in parentheses

Anisotropic temperature factors are in the form: $T = \exp\{- (h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23}) \times 10^{-4}\}$.

	<i>x</i>	<i>y</i>	<i>z</i>	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	0.7378 (1)	1.0148 (1)	0.0020 (1)	86 (1)	91 (1)	95 (1)	-4 (1)	65 (1)	6 (1)
O(1)	0.3179 (2)	0.8812 (2)	0.4417 (2)	65 (2)	96 (3)	87 (2)	-6 (2)	51 (2)	-11 (2)
O(2)	0.7236 (3)	0.9820 (4)	0.4031 (3)	145 (4)	159 (5)	84 (3)	70 (3)	34 (3)	10 (3)
N(1)	0.4077 (2)	0.9784 (3)	0.3484 (2)	52 (2)	67 (3)	71 (2)	0 (2)	36 (2)	-7 (2)
N(2)	0.4666 (2)	0.9305 (3)	0.3000 (2)	41 (2)	52 (3)	58 (2)	-2 (2)	24 (2)	-5 (2)
N(3)	0.5247 (2)	0.7354 (3)	0.2454 (2)	48 (2)	49 (3)	64 (2)	-3 (2)	28 (2)	-9 (2)
C(1)	0.6750 (3)	0.9343 (4)	0.0753 (3)	49 (2)	78 (4)	59 (3)	-5 (2)	29 (2)	2 (3)
C(2)	0.6218 (3)	1.0016 (3)	0.1255 (3)	49 (2)	56 (3)	59 (3)	0 (2)	26 (2)	3 (3)
C(3)	0.5709 (2)	0.9366 (3)	0.1857 (3)	39 (2)	51 (3)	49 (3)	-1 (2)	15 (2)	-6 (2)
C(4)	0.5756 (2)	0.8043 (3)	0.1901 (3)	40 (2)	57 (4)	54 (3)	-3 (2)	21 (2)	-5 (2)
C(5)	0.6320 (3)	0.7390 (4)	0.1375 (3)	56 (3)	58 (4)	64 (3)	3 (3)	29 (2)	-5 (3)
C(6)	0.6815 (3)	0.8020 (4)	0.0801 (3)	56 (3)	67 (4)	70 (3)	4 (2)	31 (3)	-7 (3)
C(7)	0.5145 (2)	1.0016 (3)	0.2412 (3)	37 (2)	47 (3)	50 (2)	-2 (2)	15 (2)	-2 (2)
C(8)	0.4732 (3)	0.7983 (3)	0.2916 (3)	42 (2)	44 (3)	52 (3)	-7 (2)	14 (2)	0 (2)
C(9)	0.3737 (3)	0.8757 (3)	0.3871 (3)	48 (2)	71 (4)	61 (3)	-2 (3)	24 (2)	-6 (3)
C(10)	0.4094 (3)	0.7508 (3)	0.3538 (3)	43 (2)	61 (3)	55 (3)	-6 (2)	21 (2)	0 (3)
C(11)	0.3271 (3)	0.6746 (4)	0.2894 (3)	45 (2)	89 (4)	63 (3)	-17 (3)	17 (2)	-2 (3)
C(12)	0.2719 (4)	0.7432 (6)	0.1993 (4)	65 (3)	155 (7)	59 (3)	-15 (4)	9 (3)	4 (4)
C(13)	0.4607 (3)	0.6699 (4)	0.4429 (3)	52 (3)	96 (5)	58 (3)	-8 (3)	14 (2)	8 (3)
C(14)	0.5452 (4)	0.7317 (6)	0.5080 (4)	63 (3)	155 (7)	69 (4)	-17 (4)	11 (3)	-1 (4)
C(15)	0.5060 (2)	1.1417 (3)	0.2408 (3)	37 (2)	53 (3)	50 (2)	2 (2)	20 (2)	0 (2)
C(16)	0.5815 (3)	1.2142 (4)	0.2861 (3)	52 (3)	66 (4)	77 (3)	-3 (3)	6 (3)	-3 (3)
C(17)	0.5745 (4)	1.3454 (4)	0.2806 (4)	61 (3)	61 (4)	93 (4)	-16 (3)	12 (3)	-9 (3)
C(18)	0.4943 (3)	1.4017 (4)	0.2283 (4)	63 (3)	56 (4)	88 (4)	4 (3)	32 (3)	5 (3)
C(19)	0.4200 (4)	1.3293 (4)	0.1842 (4)	52 (3)	88 (5)	101 (4)	19 (3)	17 (3)	25 (4)
C(20)	0.4249 (3)	1.1984 (4)	0.1894 (4)	46 (3)	60 (4)	89 (4)	1 (3)	11 (3)	4 (3)
C(21)	0.7767 (5)	0.8709 (5)	0.4196 (5)	82 (4)	121 (6)	119 (6)	11 (4)	26 (4)	-21 (4)
C(22)	0.8708 (5)	0.8858 (7)	0.4823 (6)	89 (5)	174 (9)	115 (5)	-16 (5)	30 (4)	16 (6)

Table 2. Atomic coordinates of the hydrogen atoms

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)
H(O2)	0.708 (5)	0.004 (7)	0.455 (5)	9.56
H(20)	0.621 (3)	1.089 (4)	0.120 (3)	3.92
H(50)	0.633 (3)	0.647 (5)	0.142 (3)	4.31
H(60)	0.715 (3)	0.758 (5)	0.040 (4)	4.58
H(110)	0.356 (3)	0.592 (5)	0.269 (3)	4.62
H(111)	0.286 (3)	0.659 (4)	0.335 (4)	4.62
H(120)	0.598 (4)	0.732 (5)	0.471 (4)	6.44
H(121)	0.531 (4)	0.819 (6)	0.525 (4)	6.44
H(122)	0.567 (4)	0.684 (6)	0.567 (5)	6.44
H(130)	0.483 (3)	0.584 (5)	0.412 (3)	4.86
H(131)	0.413 (3)	0.649 (4)	0.488 (4)	4.86
H(140)	0.312 (4)	0.769 (5)	0.153 (4)	6.62
H(141)	0.246 (4)	0.821 (6)	0.221 (4)	6.62
H(142)	0.227 (4)	0.687 (6)	0.158 (4)	6.62
H(160)	0.643 (3)	1.172 (5)	0.322 (4)	5.05
H(170)	0.629 (4)	1.392 (5)	0.311 (4)	5.61
H(180)	0.492 (3)	1.490 (5)	0.226 (4)	5.09
H(190)	0.361 (4)	1.360 (5)	0.147 (4)	5.96
H(200)	0.372 (3)	1.146 (5)	0.161 (4)	5.00
H(210)	0.777 (4)	0.840 (6)	0.348 (5)	7.88
H(211)	0.741 (4)	0.819 (6)	0.454 (5)	7.88
H(220)	0.903 (5)	0.794 (7)	0.493 (5)	8.83
H(221)	0.908 (5)	0.928 (7)	0.455 (5)	8.83
H(222)	0.859 (5)	0.899 (6)	0.551 (5)	8.83

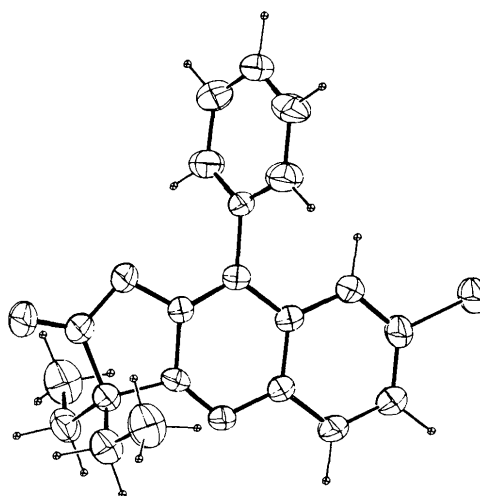


Fig. 1. An ORTEP view of the main molecule. Ellipsoids of the non-hydrogen atoms are at 50% probability level.

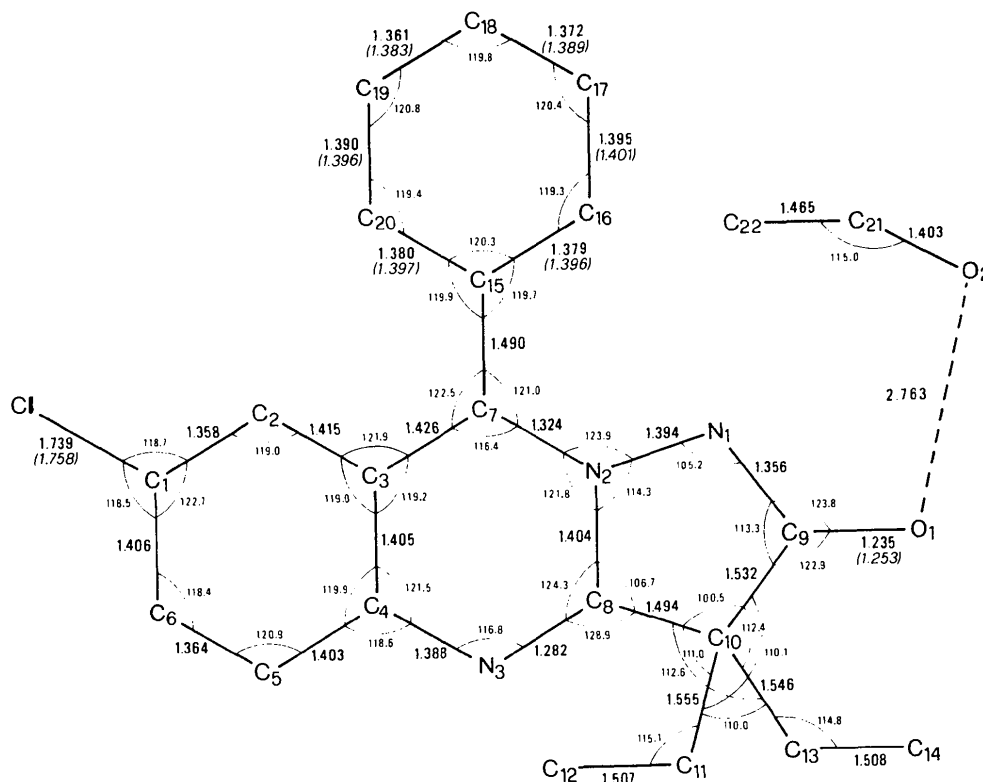


Fig. 2. Atom numbering, bond distances (Å) and bond angles (°) for non-hydrogen atoms. Values in parentheses are bond lengths after thermal motion correction. E.s.d.'s are in the range 0.004–0.008 Å for distances, and 0.1–0.3° for angles.

are listed in Tables 1 and 2.* An ORTEP drawing of the main molecule (Johnson, 1965) is shown in Fig. 1. Bond lengths and angles for non-hydrogen atoms are displayed in Fig. 2. The C–H distances are in the range 0.86–1.08 Å ($\sigma_{C-H} \leq 0.06$ Å), with a mean value of 0.98 Å.

Thermal motion analysis

The vibrational motion of the molecule in the crystal was analysed in terms of the rigid-body model of Schomaker & Trueblood (1968). At first, all non-hydrogen atoms were included in the least-squares fitting of the atomic thermal ellipsoids to the T, L and S tensors. The r.m.s. ΔU^{ij} (corrected for the number of degrees of freedom) was found to be 0.0074 Å², significantly higher than the average value (0.0019 Å²) of $\sigma(U^{ij})$. This shows that the whole molecule does not behave as a rigid body, as was indeed expected from its geometry.

A considerable improvement was obtained by fitting the rigid-body model to two separate fragments of the molecule. Fragment I consisted of the phenyl group and C(7), and fragment II the three fused rings, and Cl(1) and O(1). The librational tensors for the two fragments are given in Table 3. The r.m.s. U^{ij} 's are now reduced to 0.0049 and 0.0034 Å² for fragments I and II respectively. The librational motion for fragment I is very anisotropic, the principal r.m.s. amplitudes of vibration being 9.36, 4.15 and 2.23°. The first unusually large libration occurs around an axis roughly parallel to the C(7)–C(15)–C(18) direction, which represents the axis of lowest moment of inertia of the phenyl ring and C(7). This high value of the principal r.m.s. amplitude may be indicative of some dynamic disorder affecting the phenyl group. For fragment II there is a librational movement of large amplitude (5.15°) about an axis nearly parallel to the direction determined by the mid-points of the C(7)–N(3) and C(2)–C(5) bonds, associated with a principal moment of inertia which is much smaller than the other two.

A librational-motion bond-length correction was calculated for the two molecular fragments following Schomaker & Trueblood (1968). For fragment II, corrections are in the range 0.002–0.007 Å, of the same order as the e.s.d.'s on the bond lengths, and were

* A table of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32227 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. *Rigid-body motion parameters*

The tensors are referred to a Cartesian coordinate system defined by **a**, **b**, **c***.

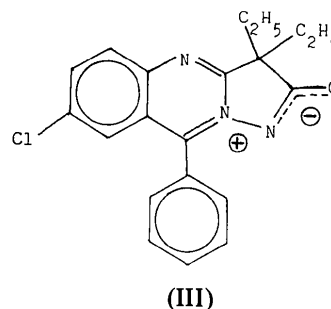
L ($\text{rad}^2 \times 10^{-4}$)	Eigenvalues, ($^\circ$) ²	Direction cosines		
Fragment I				
$\begin{bmatrix} 31 (12) & -6 (16) & -18 (10) \\ & 260 (41) & -40 (19) \\ & & 44 (13) \end{bmatrix}$	87.70 17.27 5.00	-0.0109 -0.6485 0.7611	0.9846 0.1258 0.1212	-0.1743 0.7507 0.6372
Fragment II				
$\begin{bmatrix} 55 (10) & 6 (2) & -33 (7) \\ & 26 (2) & -4 (2) \\ & & 36 (7) \end{bmatrix}$	26.55 8.43 3.66	0.7970 -0.0722 0.5996	0.1226 0.9915 -0.0436	-0.5914 0.1083 0.7991

thus ignored. For fragment I, the corrections are significantly greater than the relative e.s.d.'s on the bond lengths, and corrected values are therefore reported in parentheses in Fig. 2. Riding-motion corrections (Busing & Levy, 1964) were applied to the C(1)—Cl and C(9)—O(1) bonds. The corrected bond lengths are 1.758 and 1.253 Å respectively.

Discussion

From the X-ray determination, the title compound has the molecular skeleton shown in Fig. 2. Since no satisfactory covalent cyclic structure can be written which does not involve separation of charge, the compound

must be classed as 'mesoionic' with the following structural formula:

Table 4. *Equations of the least-squares planes*

Equations are in the form $lx + my + nz = p$, where x , y and z are monoclinic fractional atomic coordinates referred to the cell axes.

Plane	Atoms defining the plane	l	m	n	p
A	C(1), C(2), C(3), C(4), C(5), C(6)	9.056	0.723	8.618	7.440
B	C(7), N(2), C(8), N(3), C(4), C(3)	8.831	0.496	8.845	7.160
C	N(1), C(9), O(1), C(8), N(2)	8.821	0.428	8.858	7.097
D	C(15), C(16), C(17), C(18), C(19), C(20)	-8.049	0.227	12.931	-0.700
E	C(1), C(2), C(3), C(4), C(5), C(6) C(7), N(2), C(8), N(3), N(1), C(9), C(10)	8.895	0.539	8.784	7.202

Deviations of atoms ($\text{Å} \times 10^{-3}$) from the least-squares planes

	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	
A	-2	-3	8	-8	3	2	23				
B		-63	-12	2	3		13	-7			-43
C							7	2	2		-30
D							-95				
E	-33	-29	12	20	25	-5	33	-1	-7		-48
	C(15)	C(16)	C(17)	C(18)	C(19)	C(20)	N(1)	N(2)	N(3)	O(1)	Cl
A									-42		-7
B	4			-81			7	-5	8		
C							4	-5	19		-3
D	0	-5	10	-8	3	1					
E	29						12	6	16	-20	-75

The trend in bond lengths is consistent with this suggested formula. A C=N bond, 1.282 Å long, is localized between C(8) and N(3). The other C—N distances in the molecule show a hybrid character, resonating between single and double bonds. C(9)—O(1) is significantly longer than the expected exocyclic C—O distance in pentatomic rings. N(1)—N(2) is somewhat shorter than a N—N single bond.

The C—C bond length in the phenyl ring averages 1.380 Å (1.394 Å after thermal motion correction). A hydrogen bond is localized between the O atoms of the ethanol molecule and the betaine molecule: the O...O distance is 2.763 Å with the H atom well aligned between the two O atoms, the O—H...O angle being 158°.

All the intermolecular distances are normal. Least-squares planes through several atomic groups in the molecule were computed. The equations of the best planes with deviations from planarity are reported in Table 4. The three fused rings are slightly twisted, the extent of the torsional buckling being shown by the deviations from plane *E* in Table 4. The phenyl ring is planar (plane *D*), within the limits of experimental error, and makes an angle of 70.4° with the mean plane through the fused rings.

The authors are indebted to Dr Orzalesi for supplying the crystals for this investigation and to Dr Filippini and Dr Gramaccioli for the program for the rigid-body-motion analysis.

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The Crystal and Molecular Structure of an NH_4^+ –Tetranactin Complex

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$\text{C}_{44}\text{H}_{72}\text{O}_{12}\cdot\text{NH}_4\text{SCN}$, $M_r = 869.17$, crystallizes in the monoclinic system, space group $P2_1/n$ with $a = 15.889$ (8), $b = 20.695$ (10), $c = 15.371$ (8) Å, $\beta = 90.48$ (5)°, $Z = 4$, $D_x = 1.142$ g cm⁻³. The final *R* value was 0.080 for 5527 observed reflexions. The NH_4^+ cation is trapped in the tetranactin molecule and forms strong hydrogen bonds with the other O atoms.

Introduction

The nactins exhibit a very high selectivity for the NH_4^+ ion in ion transport through lipid bilayer membranes (Scholer & Simon, 1970; Eisenman, Krasne & Ciani, 1975). In the alkali-metal–nactin complexes, a distorted

cubic coordination is completed with the four tetrahedrally oriented carbonyl O atoms and the four tetrahedrally oriented ether O atoms (Dobler, Dunitz & Kilbourn, 1969; Iitaka, Sakamaki & Nawata, 1972) and a strong interaction was observed between the cation and the carbonyl groups (Kyogoku, Ueno, Akutsu & Nawata, 1975). This coordination geometry may well fit the NH_4^+ ion, which possesses a tetrahedral symmetry, but no strong interaction was observed between

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