Helical Distortion of *N*-Phenacyl-1,10-Phenanthrolinium Bromide

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Single crystal X-ray analysis of 1-[2-phenyl-2-oxoethyl]-1,10-phenanthrolinium bromide was undertaken to establish whether helical distortion, inferred from solution ^{1}H NMR spectra, persists in the solid state. The compound crystallizes in the orthorhombic space group $Pna2_1$ with a =19.7497(2), b = 6.5729(1), c = 25.9402(3) Å and Z = 8 (two independent formula units in the asymmetric unit). An intramolecular hydrogen bond between the pyridine N atom and one of the methylene H atoms occurs in each cation, resulting in helical distortion of the phenanthrolinium moiety, so that the N-C-C-N$^+$ torsion angles range between 3 and 7°.

Keywords: 1-[2-Phenyl-2-oxoethyl]-1,10-phenanthrolinium bromide, helical distortion, X-ray analysis

1,10-Phenanthroline is one of the most versatile compounds employed in several fields of chemistry and biochemistry. The rigid aromatic structure enables it to chelate with various metal cations, enhancing the triplet-state especially of lanthanides, or to act as intercalation or groove binding agent for DNA or RNA, resulting in successful genetic markers [1-5].

More recently, it was discovered that this versatile framework may be used in the synthesis of helical molecules such as 1,10-phenanthroline *N,N'*-dioxide [6] and pyrrolo[1,2-a][1,10]phenanthroline derivatives, which were synthesized *via* 1,3-dipolar cycloaddition reactions [7-11]. *N*-substituted 1,10-phenanthrolinium salts, which have been found to possess antifungal, high antimicrobial and carcinostatic activity [1,2,12], have recently been investigated for helical distortion [13]. A better understanding of the geometry of these molecules and of the necessary conditions for the existence of helicity may result in development of enhanced biological properties and many other potential applications.

Herein, we describe the stereostructure of 1-phenacyl-1,10-phenanthrolinium bromide, as deduced by ^{1}H-NMR spectroscopy and confirmed by X-ray analysis.

Experimental part

Melting points were determined on a Boëtius hot plate and are uncorrected. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C.

1-[2-Phenyl-2-oxoethyl]-1,10-phenanthrolinium bromide (**3**). 1.8 g (10 mmol) 1,10-phenanthroline and 2.2 g (11 mmol) 2'-bromoacetophenone in 30 mL acetone were refluxed for 8 h. The precipitate was filtered by suction and washed with acetone. Yield 82 %, m.p. 236-238 °C (from ethanol). Calcd. for $C_{20}H_{15}BrN_2O$: C 63.28, H 3.99, Br 21.06, N 7.39; Found C 63.41, H 4.23, Br 21.44, N 7.66.

^{1}H-NMR (DMSO-d_6; δ ppm; *J* Hz): 7.33 (bs, 2H, CH_2); 7.72 (tt, 2H, 7.7, 7.1; 1.4; H-3', H-5'); 7.84 (tt, 2H, 7.4, 1.4, H-4'); 7.88 (dd, 1H, 8.2, 4.3, H-8); 8.19 (dd, 2H, 7.7, 1.4, H-2', H-6'); 8.42 (dd, 1H, 4.3, 1.8, H-9); 8.48 (d, 1H, 8.8, H-5); 8.49 (d, 1H, 8.8, H-6); 8.63 (dd, 1H, 8.2, 5.9, H-3); 8.76 (dd, 1H, 8.2; 1.8; H-7); 9.62 (dd, 1H, 8.2, 1.4, H-4); 9.73 (dd, 1H, 5.9, 1.4, H-2).

^{13}C-NMR (DMSO-d_6; δ ppm): 69.6 (CH_2); 124.8 (C-3); 125.5 (C-8); 127.0 (C-6); 128.1 (C-3', C-5'); 129.3 (C-2', C-6'); 131.4; 132.0; 136.2; 138.4 (C-4a, C-6a, C-10a, C-10b); 134,2 (C-4'); 134.3 (C-1'); 138.0 (C-7); 148.1 (C-4); 148.6 (C-9); 152.0 (C-2); 190.7 (CO).

X-ray data were collected from a single crystal of compound **3** having dimensions 0.08 x 0.10 x 0.2 mm^3 on a Nonius Kappa CCD four-circle diffractometer. The crystal was mounted on a cryoloop with Paratone oil (Exxon, USA) and cooled in a constant stream of nitrogen vapour using a Cryostream cooler (Oxford Cryosystems, UK). Suitable combinations of ϕ- and ω-scans indicated by the program COLLECT [14] were employed for data-collection. Unit cell refinement and data-reduction were performed with DENZO-SMN [15]. Data were corrected for absorption using the program SADABS [16]. Successful structure solution in the space group $Pna2_1$ followed SHELXS-97 [17]. (Attempts to solve the structure in the alternative space group *Pnma* failed). Program SHELX-97 [18] was used for least-squares refinement on F^2, with all non-H atoms in the two independent formula units $(C_{20}H_{15}N_2O)^+Br^-$ refining anisotropically. All H atoms were located in difference electron density maps and were added in idealised positions in a riding model with U_{iso} values 1.2 times those of their parent atoms. The refined Flack parameter indicated correct assignment of the absolute structure.

Results and Discussion

N-Phenacyl-1,10-phenanthrolinium bromide (**3**) was obtained by refluxing 1,10-phenanthroline monohydrate (**1**) and 2-bromoacetophenone (**2**) in acetone. The structure of the cycloimmonium bromide **3** was assigned by elemental analysis and NMR spectroscopy. The most prominent feature of the ^{1}H-NMR spectrum of salt **3** recorded in DMSO-d_6 is the signal for the methylenic hydrogens, which appears as a broad singlet. This was attributed to non-planarity of the phenanthroline moiety.

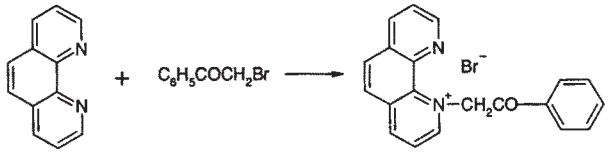

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Table 1
CRYSTAL DATA AND DETAILS OF REFINEMENT FOR **3**

CCDC deposition number	631485
Compound formula	$(C_{20}H_{15}N_2O)^+ Br^-$
Formula weight	379.25
Temperature (K)	113 ± 2
Crystal system	Orthorhombic
Space group	$Pna2_1$
Unit cell dimensions	a = 19.7497(2) Å
	b = 6.5729(1) Å
	c = 25.9402(3) Å
Volume	3367.37(7) Å^3
Z	8
Density (calculated)	1.496 g cm^{-3}
Radiation, wavelength	Mo-Kα, 0.71073 Å
Absorption coefficient	2.450 mm^{-1}
F(000)	1536
Theta range	0.21-26.37°
Index ranges	-24≤h≤24, -7≤k≤8, -32≤l≤31
Absorption correction	SADABS
Reflections collected	69883
Unique reflections	6792
Observed reflections, [I>2σ(I)]	5646
Data/restraints/parameters	6792/1/433
Goodness-of-fit on F^2	1.057
Final R indices [I>2σ(I)]	R_1 = 0.0314, wR_2 = 0.0520
R indices (all data)	R_1 = 0.0489, wR_2 = 0.0563
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0148P)^2+0.9641P]$
	where $P=(F_o^2+2F_c^2)/3$
Max. shift/e.s.d.	0.001
Flack parameter	0.022(6)
Largest diff. peak and hole	-0.427, 0.471 eÅ^{-3}

Table 1 lists crystal data and details of refinement for compound **3**. Figure 1 shows the asymmetric unit, composed of two crystallographically independent salt formula units. Their overall conformations are described by the torsion angles listed in table 2. Inversion of one cation yields a conformer with a close fit to the second cation, but there are significant differences in the listed chemically equivalent torsion angles.

Quaternization of the symmetrical phenanthroline molecule at one nitrogen centre leads to asymmetry in the bonds in the bay area of the derived cation (e.g. N1-C13 is significantly longer than N10-C11). These changes occur in the same sense for both independent cations (table 2). A further important effect of quaternization is the introduction of an abnormally short non-bonded distance, N10...C15, 2.675(4) Å, and its counterpart N25...C39, 2.676(4) Å, in the second cation. Evidence for resulting

Table 2
SELECTED MOLECULAR PARAMETERS FOR COMPOUND **3**
(DISTANCES IN Å, ANGLES IN DEGREES)

N1	-C2	1.338(4)			N34	-C33	1.338(4)		
N1	-C13	1.385(4)			N34	-C35	1.387(4)		
N1	-C15	1.471(4)			N34	-C39	1.486(4)		
N10	-C11	1.358(4)			N25	-C37	1.359(4)		
N10	-C9	1.317(4)			N25	-C26	1.321(4)		
C15	-C16	1.505(4)			C39	-C40	1.518(4)		
O17	-C16	1.230(4)			O41	-C40	1.212(4)		
C2	-N1	-C13	121.1(2)		C33	-N34	-C35	121.6(3)	
C2	-N1	-C15	116.0(2)		C33	-N34	-C39	115.6(2)	
C13	-N1	-C15	122.8(2)		C35	-N34	-C39	122.8(3)	
C9	-N10	-C11	119.0(3)		C26	-N25	-C37	119.0(3)	
N1	-C15	-C16	111.4(2)		N34	-C39	-C40	109.7(2)	
C15	-C16	-C18	118.7(3)		C39	-C40	-C42	118.1(3)	
N1	-C13	-C11	123.3(2)		N34	-C35	-C37	123.9(3)	
N10	-C11	-C13	120.3(2)		N25	-C37	-C35	120.3(3)	
N10	-C11	-C13	-N1	-7.3(5)	N34	-C35	-C37	-N25	2.9(5)
C13	-N1	-C15	-C16	77.2(4)	C35	-N34	-C39	-C40	-73.5(4)
N1	-C15	-C16	-C18	-165.8(3)	N34	-C39	-C40	-C42	164.2(3)
C15	-C16	-C18	-C23	30.0(4)	C39	-C40	-C42	-C47	-27.6(4)

steric strain is the significant difference in the exocyclic angles at the quaternized N atoms (e.g.∠ C13-N1-C15 is ~ 7° larger than ∠ C2-N1-C15). Similar effects occur at the exocyclic angles subtended at atoms C13 and C11, and at the equivalent atoms in the second cation (table 2).

The repulsive interaction is countered by the attractive intramolecular hydrogen bond C15-H...N10 (C39-H...N25 in the second cation), for which relevant hydrogen bonding data are listed in table 3. In each case, the second methylene H atom engages in a weak hydrogen bond to a bromide ion. Participation of one methylene H atom in an intramolecular bond thus proves that the -CH_2- protons are non-equivalent in the solid-state. If this situation were to prevail in solution, it would then account for the broad singlet observed in the ^{1}H - NMR spectrum. The 'locking-in' of one of the methylene H atoms above the plane of the fused ring system, reflected in figure 1, is further evidenced by a second abnormally short intramolecular contact, namely N10...C16 (2.680(4) Å) and its counterpart N25...C40 (2.653(4) Å) in the second cation. From the X-ray analysis, the net effect of these interactions in the bay regions of the cations is to helically distort the phenanthrolinium moiety, a result initially inferred from the ^{1}H - NMR data.

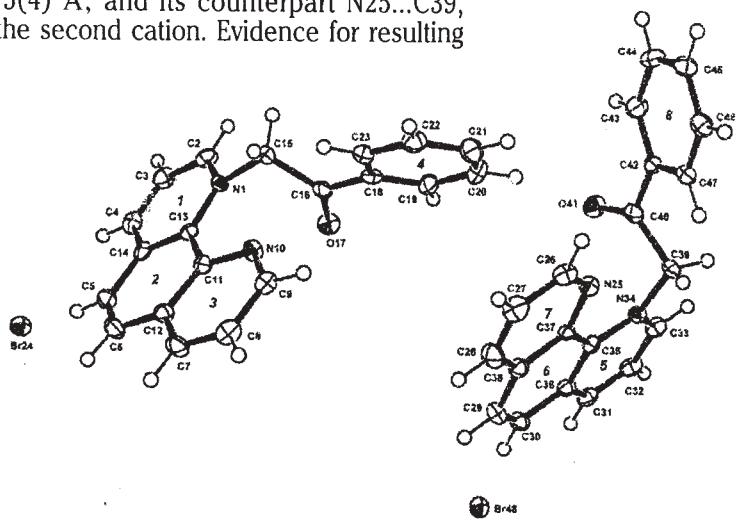

Fig. 1. ORTEP diagram of the asymmetric unit in compound **3**. Thermal ellipsoids are drawn at the 50% probability level

Table 3

SELECTED HYDROGEN BOND DATA FOR COMPOUND **3** (DISTANCES IN Å, ANGLES IN DEG.)

D-H···A	D-H	H···A	D···A	∠D-H···A
C15-H15A···N10	0.99	2.29	2.675(4)	102
C15-H15B···Br24^{i}	0.99	2.72	3.645(3)	156
C39-H39B···N25	0.99	2.31	2.676(4)	101
C39-H39A···Br48^{i}	0.99	2.72	3.664(3)	159

Symmetry operators: *(i): 1/2+x, 1/2-y, z*

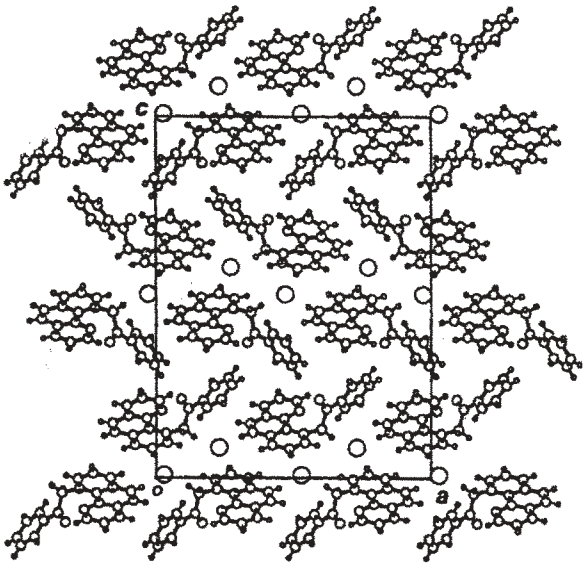

Fig. 2. Projection of the crystal structure of compound **3** down [010]. Large circles represent bromide ions.

One measure of the helical distortion is the torsion angle N-C-C-N^{+}, whose magnitudes are ~3° and 7° in the two cations (table 2). The angles of intersection between the labelled planes in the phenanthrolinium moieties in figure 1 are as follows: 1∧2 3.3(2)°, 2∧3 3.7(2)°, 1∧3 6.7(2)° for the first cation and 5∧6 1.9(2)°, 6∧7 1.5(2)°, 5∧7 3.2(2)° for the second. The phenyl rings 4 and 8 are significantly inclined to their respective tricyclic systems (e.g. 4∧1 59.9(2)°, 8∧5 50.1(2)°). The extent of helical distortion observed here is comparable to that found in the closely related compound 1-(4-chlorophenacyl)-1,10-phenanthrolinium bromide [13], where the N-C-C-N^{+} torsion angle has the value 7.4(5)° and the helical distortion arises from analogous intramolecular hydrogen bonding and steric congestion in the cation bay region. The analogous short contact N10...C15 in 1-(4-chlorophenacyl)-1,10-phenanthrolinium bromide was found to be 2.743(4) Å, but because of a larger C15-H...N10 angle (~120°), a second short contact of the type found in **3** (*viz.* N10...C16, involving the carbonyl C atom), does not occur in that species.

Figure 2 shows the crystal packing in the title compound viewed down the short *b*-axis. Layers of bromide ions straddling the (002) crystal planes are separated by cationic bilayers. In addition to the interactions listed in table 3, the crystal structure is stabilised by several intermolecular C-H...O and C-H...Br hydrogen bonds. Only two π-stacking interactions with ring centroid-centroid distance < 4 Å are evident in the crystal. These are Cg(1)...Cg(3)^{ii} (Cg(X) = centroid of ring X, (ii) = *x, -1+y, z*) with distance 3.744 Å, and Cg(5)...Cg(7)^{ii} with distance 3.722 Å.

Conclusions

For the title compound, helical distortion of the phenanthrolinium moiety, initially inferred from solution ^{1}H NMR data, has been found to occur also in the solid state. Single crystal X-ray analysis permitted determination of the origin of this effect, as well as its magnitude.

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References

1. SUMMERS, L.A., Adv. Heterocycl. Chem. **22**, 1978, p. 2
2. SAMMES, P.G., YAHIOGLU, G. Chem. Soc. Rev. **23**, 1994, p. 327
3. GABBAY, E.J., DE STEFANO, F., SANFORD, K., Biochem. Biophys. Res. Commun. **46**, 1972, p. 155
4. GABBAY, E.J., SCOFIELD, R.E., BAXTER, C.S., J. Am. Chem. Soc. **95**, 1973, p.7850
5. EBRIGHT, R.H., EBRIGHT, Y.W., PENDERGRAST, S.P, GUNASEKERA, A., Proc. Natl. Acad. Sci. USA, **87**, 1990, p. 2882
6. ROZEN, S., DAYAN, S., Angew. Chem. Int. Ed. **38**, 1999, p. 3471
7. DUMITRAŞCU, F., CAIRA, M.R., DRĂGHICI, C., CĂPROIU, M. T., BARBU, L., BĂDOIU, A., J. Chem. Crystallogr. **35**, 2005, p. 361
8. DUMITRAŞCU, F., CAIRA, M. R., DRĂGHICI, C., CĂPROIU, M. T., BĂDOIU, A. Molecules, **10**, 2005, p. 321
9. RAMONA, D., CONSTANTINESCU, M., ROTARU, A., VLAHOVICI, A., CRETESCU, I., DRUŢĂ, I., Rev. Chim.(Bucharest), **56**, 2005, p. 85
10. DUMITRAŞCU, F., DRĂGHICI, C., CAIRA, M.R., BĂDOIU, A., BARBU, L., CRISTEA, M., Arkivoc **(x)**, 2005, p. 165
11. DUMITRAŞCU, F., DRĂGHICI, C., CAIRA, M.R., BARBU, L., Rev. Chim. (Bucureşti), **56**, 2005, p. 521
12. DRUŢĂ, I., DANAC, R., UNGUREANU, M., GROSU, G., DROCHIOIU, G., Ann. Pharm. Fr., **60**, 2002, p. 348
13. DUMITRAŞCU, F., CAIRA, M.R., DRĂGHICI, C., CĂPROIU, M. T., BĂDOIU, A., J. Chem. Crystallogr., **34**, 2004, p. 577
14. COLLECT. Nonius 2000; Nonius B.V.: Delft, The Netherlands, 2001.
15. OTWINOWSKI, Z., MINOR, W. In Methods in Enzymology; CARTER, C.W., SWEET, R.M. Eds., Academic Press: New York, 1996, p.307
16. SHELDRICK, G.M. SADABS, Program for Empirical Absorption Correction of Area Detector Data; University of Göttingen, Germany., 1996
17. SHELDRICK, G.M. Acta Crystallogr., A **46**, 1990, p. 467
18. SHELDRICK, G.M. SHELXL-97, Program for the Refinement of Crystal Structures; University of Göttingen, Germany., 1997

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