Flavosemiquinone Model Systems. Part 3.[1] Molecular and Crystal Structure of the Cation Radical Salt 1,4,6,7-Tetramethylquinoxalinium Triiodide

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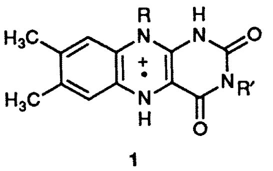
1,4,6,7-Tetramethylquinoxalinium cation radical **2** represents the essential part of the isoalloxazine π system in N(1), N(5)-diprotonated cationic flavosemiquinones **1**. The low-temperature X-ray crystal structure analysis of the stable radical salt of **2** with the sterically innocuous triiodide counterion has allowed us to examine intermolecular interactions between the aromatic cation radicals in the solid. Crystals of **2** I_3 are orthorhombic, space group *Pnma*, in a cell of dimensions $a = 1150.7(1)$, $b = 694.0(1)$, $c = 2032.5(3)$ pm; $R = 0.0323$ for 2385 observed reflections. Although the planar cations form centrosymmetric pairs within the crystal lattice, their arrangement is only controlled by packing effects and not by any significant π–π interactions.

Vitamin B_2 (riboflavin) and the flavin coenzymes FMN (flavin mononucleotide) and FAD (flavin adenine dinucleotide) contain the tricyclic isoalloxazine ring system which is responsible for unique enzymatic and chemical properties.[2–5] Besides the ability for $^3O_2$ activation, the capacity of flavins to undergo two- and one-electron processes is most remarkable, the latter giving rise to physiologically persistent 'flavosemiquinone' radical states.[2–7] EPR/ENDOR studies[1,6,7] have shown that it is the central 1,4-diazine ring system which is mainly responsible for the stability of the cationic,[2] *i.e.* N(1), N(5)-diprotonated flavosemiquinones **1**, the experimental and calculated spin distributions suggest a symmetry-perturbed 6,7-dimethylquinoxaline π system as essential spin-bearing moiety of the flavosemiquinone cation radicals.[1,6,7]

We have shown in recent years that even simple 1,4-dialkyl-1,4-diazine cation radicals derived from pyrazine[8] and quinoxaline[9–11] are indeed sufficiently stable to be conveniently isolated and studied structurally. Although the rather bulky counterion tetraphenylborate was used for the purpose of crystallization, no strong cation–anion associations were found in the corresponding solid state structures.[8,10] However, the BPh_4 anions can prevent the radical cations from possible[12,13] π–π homodimerization or homostacking through 'non-covalent bonding interactions'[14] so that a crystal structure with a sterically less demanding anion was desirable. We have now managed to obtain such a species, namely 1,4,6,7-tetramethylquinoxalinium triiodide **2** I_3 which, to a good approximation, respresents the spin-bearing π system of cationic flavosemiquinones (**1**).[15]



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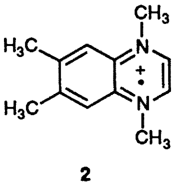

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Both flavins[16] and quinoxalines can undergo π–π interactions, the latter with DNA in cytostatic antibiotics.[17] We report here the molecular and crystal structure from a low-temperature X-ray diffraction study.

Experimental

Materials.—Sodium iodide was purchased from Aldrich and used without further purification. Acetonitrile had to be dried with P_4O_{10} to prevent uncontrolled redox processes prior to reduction of the dicationic precursor.[11]

1,4,6,7-*Tetramethylquinoxalinium Triiodide* (**2** I_3).—A sample (4.22 g, 11.7 mmol) of 1,4,6,7-tetramethylquinoxalinium bis(tetrafluoroborate)[11] was dissolved in 150 cm^3 acetonitrile and treated dropwise with a solution of 3.51 g (23.4 mmol) sodium iodide in 60 cm^3 MeCN. After reduction of the volume to 50 cm^3 and cooling to −28 °C, the cation radical salt was extracted from the dark precipitate with 500 cm^3 dichloromethane. Removal of the solvent, dissolution in 100 cm^3 acetonitrile, filtration and cooling of the filtrate at −28 °C gave 1.20 g (18%) of brownish plates suitable for X-ray crystallography (Found: C, 25.1; H, 2.9; N, 4.95. $C_{12}H_{16}I_3N_2$ requires C, 25.33; H, 2.83; N, 4.92%). A brownish crystal of **2** I_3 immersed in nujol was used for the crystal structure analysis.

Crystal Data.—$C_{12}H_{16}I_3N_2$, $M = 569.0$. Orthorhombic, $a = 1150.7(1)$, $b = 694.0(1)$, $c = 2032.5(3)$ pm, $V = 1623.1(4)$ pm^3 10^{-6}. The setting angles of 33 reflections with $25° < 2\theta < 35°$ were measured and used to determine the cell constants, λ(Mo-Kα) = 0.710 69 Å. Space group *Pnma*,[18] $Z = 4$, $D_x = 2.328$ g cm^{-3}. Brownish crystals with dimensions 0.6 × 0.4 × 0.2 mm, μ(Mo-Kα) = 57.02 cm^{-1}, $F(000) = 1044$.

Data Collection.—Syntex $P2_1$ diffractometer, 173 K. Intensities of reflections with indices *h* 0–16, *k* 0–10, *l* 0–29 and their Friedels with $3° < 2\theta < 62°$ were measured (Wyckoff scan, scan speed from 2.00° to 29.30° min^{-1}) with graphite monochromatized Mo-Kα radiation. 5816 reflections (Friedel pairs) were measured of which 2772 were unique, and the 2385 with $F > 4.0\ \sigma(F)$ were labelled observed and used in the structure analysis (merging $R = 0.029$ after absorption correction). The intensities of two standard reflections were measured every 98 reflections, all data were corrected for Lorentz, polarization and absorption (semi-empirical, Ψ-scan, max./min. transmission factors 0.64/0.49), no extinction correction.

Structure Analysis and Refinement.—The structure was solved by 'direct methods' using the program SHELXTL-PLUS[19] on a VAX station 3200. Full matrix least-squares refinement was used with all non-hydrogen atoms anisotropic, hydrogen atoms were included with fixed isotropic *U* (riding model, 103 refined parameters). At convergence, $R = 0.0323$, $R_w = 0.035$, goodness-of-fit 1.03 (largest difference peak 1.1 e Å^{-3}, largest difference hole −1.3 e Å^{-3}). The weighting scheme used was of the form $w = 1/[\sigma^2(F) + 0.0019F^2]$. Scattering factors are from ref. 20.

Table 1 Bond lengths/pm for **2** I_3, with estimated standard deviations in parentheses

I(1)-I(2)	295.6(1)	I(1)-I(3)	289.6(1)
N(1)-C(11)	146.4(6)	N(1)-C(1)	137.0(7)
N(1)-C(4)	138.9(6)	C(1)-C(2)	136.4(7)
C(2)-N(2)	135.7(7)	N(2)-C(21)	148.4(7)
N(2)-C(3)	139.1(6)	C(3)-C(4)	140.5(7)
C(3)-C(8)	138.3(7)	C(4)-C(5)	141.2(7)
C(5)-C(6)	139.9(7)	C(6)-C(61)	150.1(8)
C(6)-C(7)	138.9(7)	C(7)-C(71)	152.8(8)
C(7)-C(8)	140.3(8)		

Table 2 Bond angles/° for **2** I_3, with estimated standard deviations in parentheses

I(2)-I(1)-I(3)	174.9(1)	C(11)-N(1)-C(1)	118.3(4)
C(11)-N(1)-C(4)	123.3(4)	C(1)-N(1)-C(4)	118.4(4)
N(1)-C(1)-C(2)	121.0(4)	C(1)-C(2)-N(2)	121.7(5)
C(2)-N(2)-C(21)	119.8(4)	C(2)-N(2)-C(3)	119.6(4)
C(21)-N(2)-C(3)	120.6(4)	N(2)-C(3)-C(4)	118.6(4)
N(2)-C(3)-C(8)	121.6(4)	C(4)-C(3)-C(8)	119.8(4)
N(1)-C(4)-C(3)	120.8(4)	N(1)-C(4)-C(5)	120.4(4)
C(3)-C(4)-C(5)	118.8(4)	C(4)-C(5)-C(6)	121.1(5)
C(5)-C(6)-C(61)	120.1(5)	C(5)-C(6)-C(7)	119.1(5)
C(61)-C(6)-C(7)	120.8(5)	C(6)-C(7)-C(71)	121.3(5)
C(6)-C(7)-C(8)	120.2(5)	C(71)-C(7)-C(8)	118.5(5)
C(3)-C(8)-C(7)	121.0(5)		

Results and Discussion

Upon recrystallization from acetonitrile and cooling to 245 K, the title compound **2** I_3 yielded single crystals suitable for X-ray diffraction at 173 K. Fig. 1 shows the labelling scheme for a cation–anion pair. Bond distances (Table 1) and angles (Table 2) are presented here; tables of thermal parameters and atomic coordinates have been deposited at the Cambridge Crystallographic Data Centre (CCDC).* Fig. 2 shows the crystal packing. The individual ions of **2** I_3 show no unusual structure. The triiodide anion is almost linear (Fig. 1), as in structures of the related 5,10-dialkylphenazinium cation radicals.[21] The cations **2** lie in crystallographic planes and show bond parameters (Tables 1 and 2) which are similar to those of 1,4-diethylquinoxalinium tetraphenylborate.[10] Although the difference is not significant in strict terms, the C(1)–C(2) bond seems to be a little longer in **2** [136.4(7) *vs.* 134.6(4) pm [10]] which may reflect the increased electron density[11] due to the electron-donating methyl substituents in positions 6 and 7.

The unit cell of **2** I_3 contains discrete radical cations and triiodide anions separated by normal van der Waals' contact distances. All non-hydrogen atoms occupy mirror planes at y = 0.25 and 0.75. The radical cations show no significant π–π overlap in the crystal (Fig. 2), they are equally spaced along the b axis and are surrounded by I_3 anions. The cations are arranged in such a way that the 6,7-dimethyl groups of the two cations are well separated and that one *N*-methyl group of each cation lies above or below the centre of the benzene ring of the other cation. Although this arrangement reflects a certain electron acceptor–donor interaction between the partially positively charged N–CH_3 groups and the dimethylarene moiety, it is clear that packing forces determine this arrangement.

Support for the dominance of packing effects comes from an inspection of intermolecular distances. The interplanar distance between the cations is $b/2$ = 347 pm and the shortest atom-to-atom distance is 347.9 pm between N(1) and C(5); these values are significantly larger than corresponding distances d < 330 pm in π–π interacting radical cation pairs.[12,13]

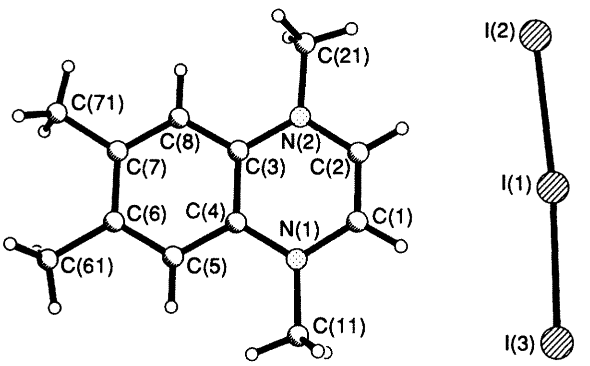

Fig. 1 Structure of a radical cation–anion pair in the crystal of **2** I_3 with the atom labelling scheme

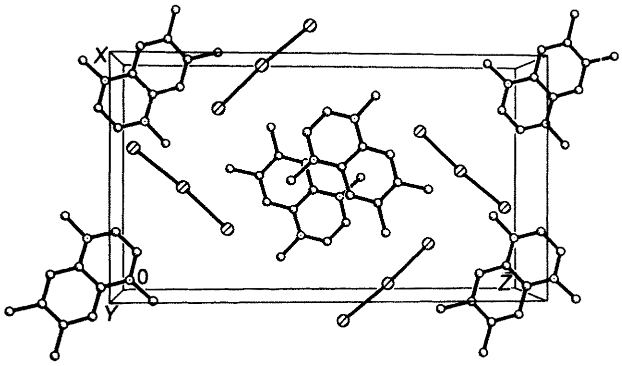

Fig. 2 Crystal packing of the cation radical salt **2** I_3

In summary these structural results confirm that simple 1,4-dialkyl-1,4-diazine radical cations are *intrinsically stable* paramagnetic species which, according to their electrochemical behaviour,[8–11] are neither electron donating nor accepting. We have shown that these radicals do not require π–π interactions for stabilization, even in benzannelated form and in the presence of non-interacting counterions. While this remarkable stability may disfavour applications with regard to intermolecular electron transfer and electrical conductivity, such robust radical cations may find uses, *e.g.* as cationic spin labels or as components of magnetic materials. The stability of flavosemiquinones under different biochemical conditions is thus not only due to the size of the tricyclic isoalloxazine system or to kinetic stabilization by proteins but it is also a characteristic of the particular 1,4-diazine functionality.

Acknowledgements

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* For details of the CCDC deposition scheme please see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, Issue 1.

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