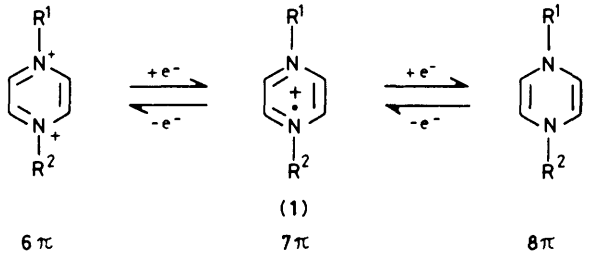
Flavosemiquinone Model Systems. Part 1. 4-Hydro-1-alkylpyrazinium Radical Cations

Wolfgang Kaim
Institut für Anorganische Chemie, Niederurseler Hang, D-6000 Frankfurt/Main 50, Federal Republic of Germany

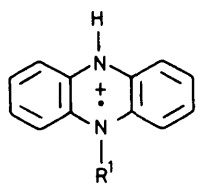
Reduction of 1-alkylpyrazinium iodides in acidic media produces 4-hydro-1-alkylpyrazinium radical cations. These persistent species were identified and characterized by high, resolution e.s.r., and assignments of coupling constants were made on the basis of deuteriation experiments and Hückel MO correlations. The spin distribution in these radicals and in related systems, especially in flavosemiquinone cations, is discussed.

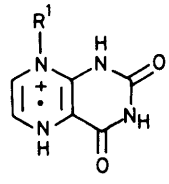
In the pyrazinium–1,4-dihydropyrazine redox system the paramagnetic 7π-electron oxidation state (**1**) displays exceptional stability.[1] Whereas the oxidized forms (6π) are stable only in highly electrophilic environments[2,3] and the reduced forms are electron-rich and possibly destabilized by cyclic 8π-electron interaction ('antiaromaticity'),[1,4,5] the radical cations with R^1, R^2 = H[6] and R^1, R^2 = alkyl[3,7–9] are persistent species (Scheme 1).[1]

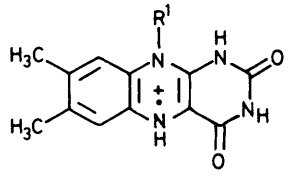
In the biochemical context of 1,4-diazinium radical chemistry,[1] the related radical cations of 10-hydro-5-alkylphenazines (**2**),[10] hydropteridines (**3**),[11] and in particular those of flavins, the flavosemiquinone cations (**4**), have been intensively studied.[12] Since these systems are unequally substituted at the 1,4-diazine nitrogen atoms ($R^1 \neq R^2$ = H), we have studied the unsymmetrically substituted mononuclear species (**1**) with R^1 = alkyl (Me, Et, Pr^n, Pr^i), R^2 = H, D, and also the corresponding ring-methylated derivatives (**5**)—(**8**) in order to assess the degree of asymmetry in the distribution of the unpaired electron.

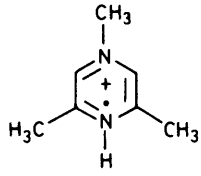


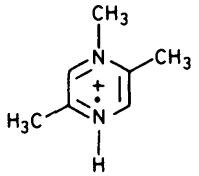
Scheme 1.

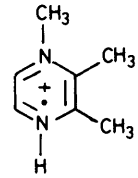

(2)

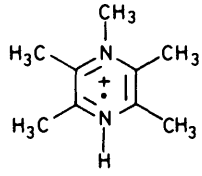

(3)


(4)


(5)


(6)

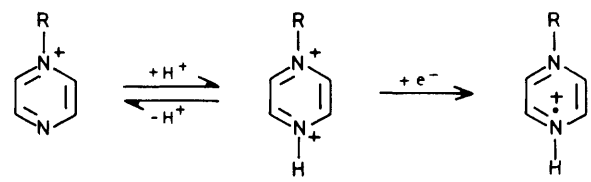

(7)


(8)

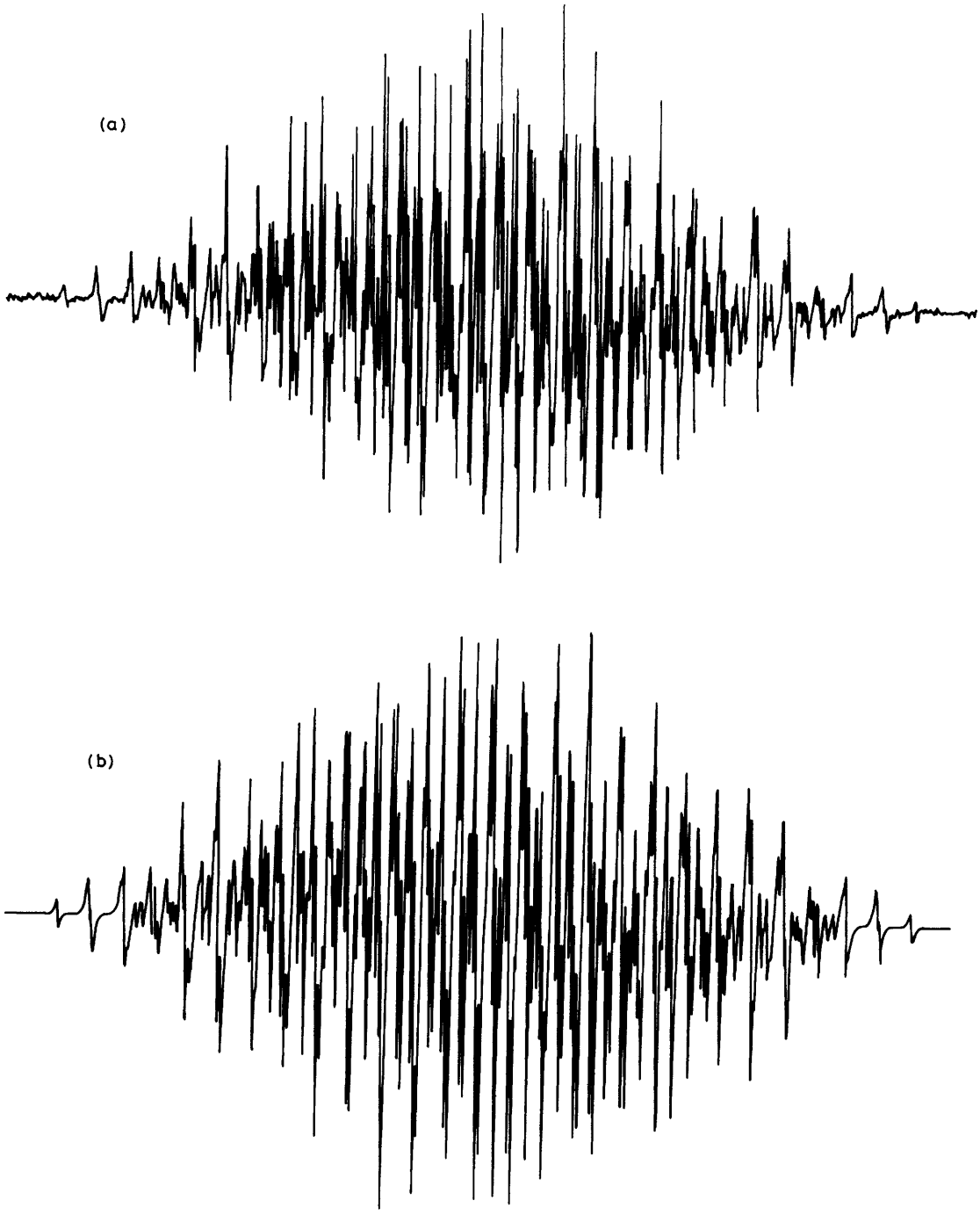
Results

4-Hydro-1-alkylpyrazinium radical cations are very easily formed as persistent species in aqueous or non-aqueous acidic media (Scheme 2). Dilute solutions of these radicals display well resolved e.s.r. spectra. The Figure shows one such spectrum together with its computer simulation. Except for the radical cations (**6**)—(**8**) which exhibit very complicated e.s.r. patterns, all other spectra could be analysed by the computer simulation technique; the e.s.r. parameters are summarized in Table 1. Assignments of the hyperfine splittings were made on the basis of deuteriation experiments NH→ND and using the established relations $a_H^{NH} \simeq 1.1 a_N^{NH}$ and $a_N^{NMe} \simeq 1.1 a_{Me}^{NMe}$.[13] Corresponding assignments were proposed for the 10-hydro-5-methylphenazinium radical cations (**2**) by Chew and Bolton.[10]

In order to assign the ring proton couplings, results from Hückel–McLachlan MO calculations have been applied. Calculations of cyclic six-centre π systems which are unequally perturbed in the positions 1 and 4 show[14] that a slightly higher Coulomb integral parameter h_N for the 4-position with respect to the 1-position causes an increase of the π spin population at positions 1, 3, and 5 and a decrease of π spin density at positions 2, 4, and 6.[14] When comparing the D_{2h} symmetric species (**1**; R^1 = R^2 = Me and R^1 = R^2 = H) with the radical (**1**; R^1 = Me, R^2 = H) in Table 1, the consistency of the assignments made becomes evident. The hyperfine splittings may also be translated into π spin populations ρ^π using McConnell-type equations $a = Q\rho^\pi$ with Q_H^{CH} = 2 930,[15] Q_H^{NH} 2 820, and Q_{Me}^{NMe} 2 620 μT (Table 2). 2,6-Dimethylpyrazine is quaternized in the unhindered 4-position[16] so that the paramagnetic species formed on reduction in acidic solution is the 4-hydro-1,3,5-trimethylpyrazinium radical cation (**5**).



Scheme 2.



Experimental (a) and computer-simulated (b) e.s.r. spectrum of the 4-hydro-1-methylpyrazinium radical cation at 297 K in water (1M-$HClO_4$). Linewidth for computer simulation 22 μT, 648 theoretical lines

Discussion

The 4-hydro-1-alkylpyrazinium radical cations are as persistent as their 1,4-dihydro and 1,4-dialkyl analogues.[3,6–9] The different nitrogen-substituents cause only a slight perturbation of the π spin distribution when compared for example to the situation in 1-alkylpyrazinium radicals.[17] Nevertheless, this slight dissymmetry can be detected by e.s.r., and as the β- and γ-*N*-alkyl couplings suggest, this may be attributed to σ–π-hyperconjugative delocalization of spin out of the heterocyclic π system into the *N*-alkyl group.

The substantial decrease of $a_{H(\beta)}$ in the series of the methyl-, ethyl-, or n-propyl- and isopropyl-substituted radical cations reflects the tendency for in-plane movement of the small H(β) atoms *versus* the bulkyl alkyl groups. Following the convention of McKinney and Geske,[18] *R* values of 0.63 and 0.32 may be calculated for the ethyl and isopropyl substituents, respectively [equation (i)]. θ Is the torsion angle between the C–H σ bond and the axis of the π-orbital at the substitution centre.

$$R = \frac{a_H^{CH_2X}}{a_H^{CH_3}} = \frac{\langle \cos^2\theta \rangle}{0.5} \qquad \text{(i)}$$

Table 1. E.s.r. coupling constants a_X(μT) of 4-hydro-1-alkylpyrazinium radical cations and related species[a]

Radical	R^1	R^2	a_N^{NR}	a_H^R	a_N^{NH}	a_H^{NH}	$a_{H_{2,6}}$	$a_{H_{3,5}}$	Solvent	Ref.
(1)	Me	Me	840	800			285	285	H_2O	7
(1)	H	H			745	805	316	316	H_2O	6
(1)	Me	H	891	855	714	773	290	318	H_2O	
(1)	Me	H	891	851	705	756	292	310	DMF	
(1)	Me	D	890	850	710	121[b]	292	315	DMF	
(1)	Et	H	*c*	536 (β) 23 (γ)	*c*	771	292	315	H_2O	
(1)	Pr^n	H	890	540 (β) 270 (β)	712	775	290	312	H_2O	
(1)	Pr^i	H	890	15 (γ)	713	773	287	318	H_2O	
(5)	Me	H	890	860	615	645	300	280[d]	H_2O	
(2)	Me		693	635	600	645			H_2O	10
(3)	Me		586	586	739	816	586[e]	127[e]	CF_3COOH	11
(4)	Me		471	494	740	811			$C_6H_5CH_3$- CF_3COOH	12

[a] The *g* values of the pyrazinium radical cations are 2.0034 ± 0.0001. [b] a_D^{ND}, I_D = 1. [c] Could not be determined individually, $a_N^{NR} + a_N^{NH}$ = 1 600 μT. [d] Methyl coupling constant. [e] Numbering refers to the pyrazinium system (**1**).

Table 2. π Spin populations ρ^π of pyrazinium radical cations (**1**)

Radical (**1**)					
R^1	R^2	ρ_1^π	ρ_4^π	$\rho_{2,6}^\pi$	$\rho_{3,5}^\pi$
H	H	0.284	0.284	0.108	0.108
Me	H	0.326	0.274	0.099	0.108
Me	Me	0.306	0.306	0.097	0.097

The overall effect of unsymmetrical spin distribution is fairly small for all the pyrazinium radicals investigated. A similar effect was reported for the 10-hydro-5-methylphenazinium radical cation (**2**; R = Me);[10] there, the NH and NMe hyperfine splittings are reduced to *ca.* 80% of what they are in (**1**) by the delocalization of spin into the carbocyclic rings.

The comparison with the hyperfine splitting in cationic radicals of 5-hydro-8-alkylpteridines (**3**) and in flavosemiquinone cations (**4**) exhibits an entirely different situation. There is much more π spin population at the NH centre than in the NR part of the radicals.[11,12] The redistribution of π spin density is obviously caused by the additional asymmetry introduced through the neighbouring pyrimidinedione ring. Although this heterocyclic part of the molecule seems to accommodate only a negligible share of the total π spin density,[12,19] it nevertheless induces a substantial redistribution of unpaired π electron population which masks the relatively small perturbation effect of different nitrogen substituents.

Experimental

Pyrazines were purchased from Aldrich. 1-Alkylpyrazinium iodides were prepared from pyrazines and alkyl iodides by the method of Stoehr;[16,20] reaction times varied from a day to several weeks at room temperature.

For radical generation, the recrystallized (EtOH) and dried 1-alkylpyrazinium iodides were dissolved in 1M solutions of $HClO_4$ or CF_3COOD in H_2O or DMF. These solutions which often already contained trace amounts of the radical cation[1] were then transferred into a thin electrolysis cell for e.s.r. measurement. In order to produce the radical cations, very low potentials (*ca.* 0.2 V) were applied.

The e.s.r. spectra were recorded at room temperature with a Varian E-9 spectrometer in the *X* band and with a 100 kHz field modulation. The spectra were calibrated using the perylene radical anion in DME;[21] computer simulations were carried out with the program ESPLOT[22] at the Hochschulrechenzentrum, Frankfurt.

Acknowledgements

The research on electron-transfer reactivity was supported by the Deutsche Forschungsgemeinschaft (DFG).

References

1 W. Kaim, *Angew. Chem.*, 1983, **95**, 201; *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 171.
2 A. S. Chia and R. F. Trimble, *J. Phys. Chem.*, 1961, **65**, 863; P. J. Brignell, C. D. Johnson, A. R. Katritzky, N. Shakir, H. O. Tarhan, and G. Walker, *J. Chem. Soc. B*, 1967, 2396.
3 T. J. Curphey and K. S. Prasad, *J. Org. Chem.*, 1972, **37**, 2259.
4 W. Kaim, *J. Am. Chem. Soc.*, 1983, **105**, 707.
5 W. Kaim, *J. Mol. Struct. THEOCHEM.*, in the press.
6 B. L. Barton and G. K. Fraenkel, *J. Chem. Phys.*, 1964, **41**, 1455.
7 M. K. Ahn and C. S. Johnson, Jr., *J. Chem. Phys.*, 1969, **50**, 632.
8 A. Alberti and A. Hudson, *J. Organomet. Chem.*, 1983, **248**, 199.
9 W. Kaim, unpublished data.
10 V. S. F. Chew and J. R. Bolton, *J. Magn. Reson.*, 1980, **37**, 231.
11 A. Ehrenberg, P. Hemmerich, F. Müller, and W. Pfleiderer, *Eur. J. Biochem.*, 1970, **16**, 584.
12 M. Bock, W. Lubitz, H. Kurreck, H. Fenner, and R. Grauert, *J. Am. Chem. Soc.*, 1981, **103**, 5567; *cf.* also P. Hemmerich, V. Massey, H. Michel, and C. Schug, *Struct. Bonding (Berlin)*, 1982, **48**, 93; F. Müller, *Top. Curr. Chem.*, 1983, **108**, 71; D. E. Edmondson and G. Tollin, *ibid.*, p. 109.
13 K. Scheffler and H. B. Stegmann, 'Elektronen spinresonanz,' Springer-Verlag, Heidelberg, 1970, pp. 166 and 174.
14 W. Kaim, U. Lechner-Knoblauch, P. Hänel, and H. Bock, *J. Org. Chem.*, 1983, **48**, 4206.
15 *Cf.* T. Rakowsky and J. K. Dohrmann, *Ber. Bunsenges. Phys. Chem.*, 1979, **83**, 495.
16 C. T. Bahner and L. L. Norton, *J. Am. Chem. Soc.*, 1950, **72**, 2881.
17 H. Zeldes and R. Livingston, *Mol. Phys.*, 1974, **27**, 261.
18 T. M. McKinney and D. H. Geske, *J. Am. Chem. Soc.*, 1967, **89**, 2806.
19 W. Kaim, *J. Chem. Soc., Perkin Trans. 2*, in the press.
20 C. Stoehr, *J. prakt. Chem.*, 1894, **49**, 392; 1895, **51**, 449.
21 J. R. Bolton, *J. Phys. Chem.*, 1967, **71**, 3702.
22 W. Kaim and H. Bock, *J. Organomet. Chem.*, 1979, **164**, 281.

Received 22nd *September* 1983; *Paper* 3/1676