Electron-transfer Process with Pyridinium, Quinolinium, and Pyrazinium Salts; an Electron Spin Resonance Study

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Electron-transfer processes between nucleophilic neutral and charged free-radicals [hydroxy(diphenyl)methyl and naphthalene radical anion] and pyridinium, quinolinium, and pyrazinium salts have been investigated by e.s.r. The factors affecting the persistence of the heterocyclic radicals under photolytic conditions are discussed. Mechanistic implications concerning the reactions of nucleophilic free radicals with protonated heteroaromatic bases are emphasized.

A NEWLY emerging area of chemistry involves reactions of nucleophilic species (ionic and radical) with electron-deficient aromatic substrates. Two aspects are particularly interesting. (a) Several reactions which in effect are nucleophilic substitutions are now believed to occur by a mechanism involving electron-transfer steps and intermediate free radicals and radical anions.[1] The key step of this mechanism, symbolized S_{RN}, involves an electron transfer [equations (i) and (ii)]. (b) Despite the general-

$$\text{electron donor} + \text{ArX} \longrightarrow [\text{ArX}]^{\cdot -} \quad \text{(i)}$$

$$\text{electron donor} + [\text{ArHX}]^+ \longrightarrow [\text{ArHX}]^{\cdot} \quad \text{(ii)}$$

ization, still accepted, that the only factor directing the course of the reactions of alkyl radicals is the relative stability of the intermediates,[2] strong polar effects have been observed in the reactions of nucleophilic alkyl radicals and strongly electron-deficient aromatic substrates, especially protonated heteroaromatic bases. Exceptional selectivities and great synthetic interest are connected with these polar effects,[3,4] which have been explained by a mechanistic picture involving a transition

$$\text{R}^{\cdot} + \quad \longleftrightarrow \quad \text{R}^+ + \quad (\text{iii})$$
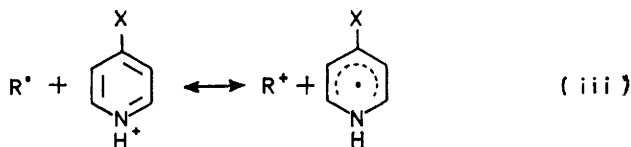
state similar to a charge-transfer complex[5] [equation (iii)]. The degree of charge development in the transition state depends on the donor character of the radical and the acceptor character of the aromatic ring, a complete electron transfer being the limiting case.

We now report spectroscopic evidence, in addition to chemical evidence, concerning this limiting case of complete electron transfer by a strongly nucleophilic

free radical with pyridinium, quinolinium, and pyrazinium salts.

RESULTS AND DISCUSSION

Salts of heteroaromatic bases are particularly suitable for the electron-transfer process of equation (ii). The high electron deficiency of protonated heteroaromatic bases is emphasized by the exceptional value (4) estimated for the Hammett σ constant[6] of the *para*-position in protonated pyridine, the corresponding value[7] for unprotonated pyridine being 0.93. It has been shown[8] that dihydropyridyl radicals are easily obtained by the reaction of classical ionic nucleophilic species (OH⁻, RO⁻, or amines) with N-methylpyridinium salts [equation (iv)]. Protonated pyridines cannot be used with these

$$+ \text{Y}^- \longrightarrow + \text{Y}^{\cdot} \quad (\text{iv})$$
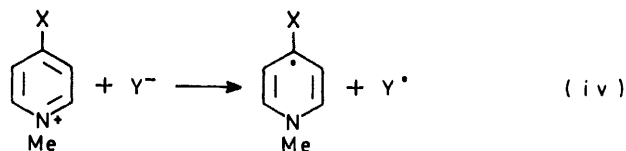
nucleophiles because the primary effect involves deprotonation of the base. This incompatibility does not occur with nucleophilic radicals, which can be used for electron transfer with protonated heteroaromatic bases.

The factors affecting the nucleophilic character of the alkyl radicals were discussed recently.[9] Because the substitution of a methyl radical by a phenyl or alkoxy-group strongly increases its nucleophilic character (Table 1), the radical $Ph_2\dot{C}$-OH must be considered strongly nucleophilic. This hydroxy(diphenyl)methyl radical was conveniently produced photochemically by the well known process of hydrogen abstraction by the T ($n\pi^*$) state of benzophenone, and we report a study of its behaviour with pyridinium, quinolinium, and pyrazinium salts.

[1] J. K. Kim and J. F. Bunnet, *J. Amer. Chem. Soc.*, 1970, **92**, 7463, 7464; R. A. Rossi and J. F. Bunnet, *ibid.*, 1974, **96**, 112; *J. Org. Chem.*, 1972, **37**, 3570; 1973, **38**, 1407, 3020; J. F. Bunnet and B. F. Gloor, *ibid.*, 1974, **39**, 382; J. F. Wolpe, J. C. Greene, and T. Hudlicky, *ibid.*, 1972, **37**, 3199; P. Pietra, M. Bartolozzi, and F. Del Cima, *Chem. Comm.*, 1971, 1232; J. A. Zoltewicz, T. M. Oestreich, and A. A. Sole, *J. Amer. Chem. Soc.*, 1975, **97**, 5889.

[2] R. L. Huang, S. H. Goh, and S. H. Ong, 'The Chemistry of Free Radicals,' Arnold, London, 1974, p. 103.

[4] F. Minisci, *Synthesis*, 1973, 1.

[4] F. Minisci and O. Porta, *Adv. Heterocyclic Chem.*, 1974, **16**, 123.

[5] A. Clerici, F. Minisci, and O. Porta, *J.C.S. Perkin II*, 1974, 1699; *Tetrahedron*, 1974, **30**, 4201.

[6] H. H. Jaffé, *J. Amer. Chem. Soc.*, 1955, **77**, 4445.

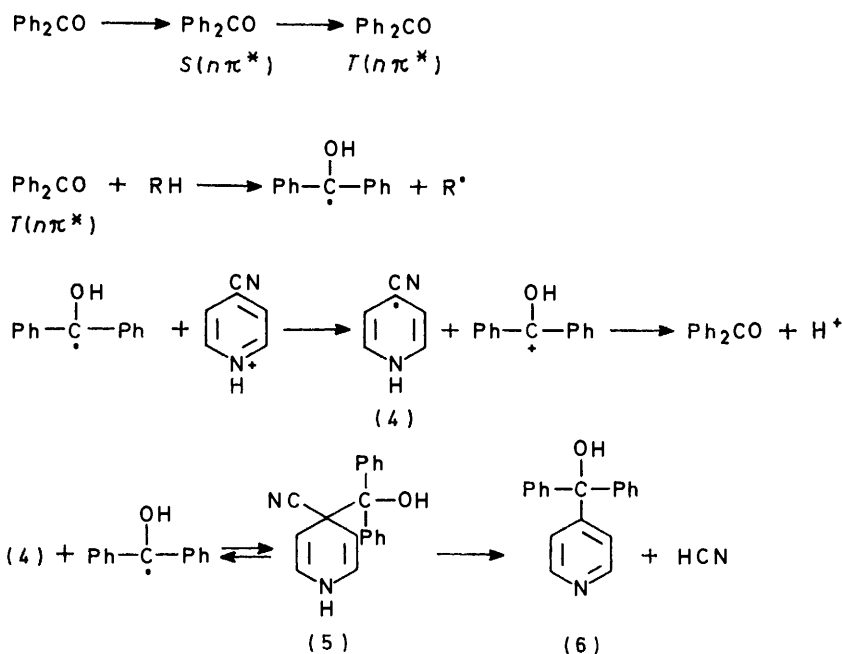[7] H. H. Jaffé, *J. Chem. Phys.*, 1952, **20**, 1954.

[8] L. Grossi, F. Minisci, and G. F. Pedulli, preceding paper.

[9] F. Minisci, *Topics Current Chem.*, 1976, **62**, 1.

4-*Cyano*-1-*methylpyridinium* *Iodide* (1) *and* 4-*Cyano-pyridinium* *Sulphate* (2).—Irradiation of the salt (1) in tetrahydrofuran (THF) containing small amounts of benzophenone gave rise to an intense and well resolved

(1)   (2)   (3)
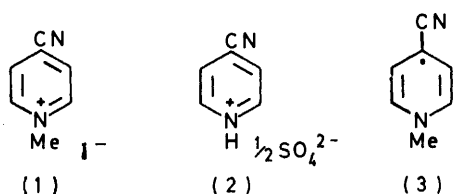
spectrum of the corresponding dihydropyridyl radical (3); in the absence of benzophenone only after prolonged irradiation was the same (weak) e.s.r. signal observed. The dihydropyridyl radical (3) may also be obtained by

presumably due to the 4-cyanodihydropyridyl radical (4); however the low intensity did not allow analysis of the spectrum. This result may appear surprising in view of the higher persistence of the radical (4) as compared with (3), particularly in alcoholic solution.[8] We think that chemical evidence can explain this discrepancy.

The main product of irradiation of the salt (2) in isopropyl alcohol in the presence of benzophenone is diphenyl-(4-pyridyl)methanol (6);[10] its formation is best explained by an electron transfer from the hydroxy-(diphenyl)methyl radical to the 4-cyanopyridinium ion (Scheme 1). The hydroxy(diphenyl)methyl radical, continuously generated by photolysis, acts as a scavenger of the dihydropyridyl radical (4) giving compound (5), which undergoes irreversible elimination of HCN.

Scheme 1

bringing into contact a solution in THF of the radical anion of naphthalene (produced by reduction with potassium) with the salt (1). The e.s.r. spectrum of the

In the case of the corresponding N-methylpyridinium salt (2) the equilibrium between the dihydropyridyl (3) and hydroxy(diphenyl)methyl radicals [equation (v)]

Table 1

Relative rates for homolytic substitution in position 2 of protonated 4-X-pyridines with methyl,[a] methoxy-methyl,[b] and benzyl [c] radicals

X	Me·	MeOCH₂·	PhCH₂·
CN	23.5	341	223.5
COMe	7	90.5	11.5
Cl	4.5		1
Me	1	1	

[a] F. Minisci, R. Mondelli, G. Gardini, and O. Porta, *Tetrahedron*, 1972, **28**, 2403. [b] Ref. 5. [c] A. Clerici, F. Minisci, and O. Porta, *Tetrahedron*, 1973, **29**, 2774.
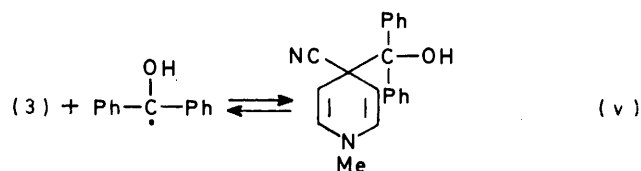
naphthalene radical anion disappears immediately to be replaced by a well resolved spectrum of the radical (3).

Irradiation of the salt (2) at −45 °C in 3 : 1 THF–MeOH containing benzophenone gives weak e.s.r. signals


cannot be shifted irreversibly in the same way owing to the impossibility of elimination of HCN. Thus the radical (4) has an intrinsic higher persistence than the radical (3), but when generated under photolytic conditions it is scavenged faster, making analysis of the e.s.r. spectrum difficult.

4-*Acetyl*-1-*methylpyridinium* *Iodide* (7).—The presence

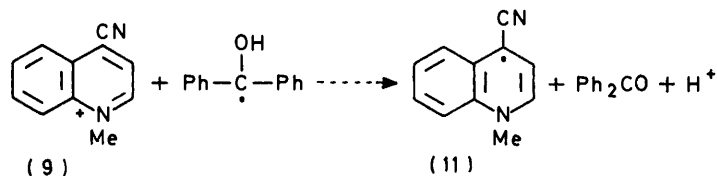[10] B. Vittinberga, F. Minisci, and S. Morrocchi, *J. Amer. Chem. Soc.*, 1975, **97**, 4397.

of benzophenone was found not necessary for the formation by irradiation in THF of the 4-acetyl-1-methyl radical (8). The mechanism of electron transfer is

(7)   (8)
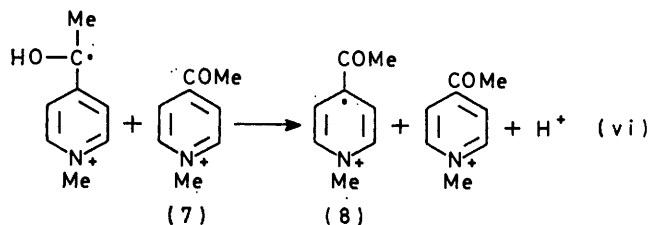
probably analogous to that of the corresponding cyanopyridinium salt, since the acetylpyridinium ion (7) can act as a source of 1-hydroxy-1-(methylpyridinio)ethyl radicals [equation (vi)]. A possible alternative mechanism is the direct formation of the dihydropyridyl radical
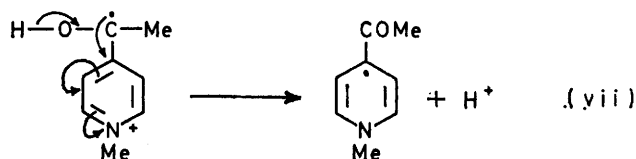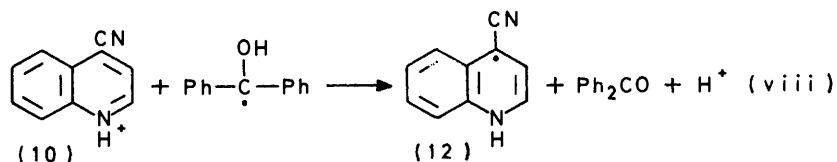

from the hydroxyethyl radical [equation (vii)]. The splitting constants of the 4-acetyl-1-methyldihydropyridyl radical are strongly dependent on the nature of

concern the assignments of the indicated splittings to protons 3, 6, and 8 which may be interchanged; this also applies to protons 5 and 7.

The 4-cyanodihydroquinolyl radical (12) was also readily obtained from the salt (10) by irradiation in THF–benzophenone. The measured hyperfine splittings are reported in Table 2.

The persistence of the dihydropyridyl radicals (3) and (4) was much less than of the corresponding dihydroquinolyl radicals (11) and (12) under all the conditions

TABLE 2

Hyperfine splitting constants (G) of the 4-cyano-1-methyl-dihydroquinolyl (11) and 4-cyanodihydroquinolyl (12) radicals

|	a_2	a_3	a_5	a_6	a_7	a_8	a_H^{CN}	a_N	a_R^{NR}
(11)	4.76	0.20	2.72	0.26	0.08	0.45	1.64	4.76	3.98
(12)	4.42	0.49	1.83	0.49	1.72	0.49	1.83	4.90	4.53

investigated. Thus (11) is quite persistent in alcoholic solvents, in which the corresponding dihydropyridyl radical (3) is immediately transformed into a cation radical,[8] and (12) is easily formed under conditions in which only a weak e.s.r. signal is observed from the dihydropyridyl radical (4). This difference is thought to be partially due to greater resonance stabilization in the quinoline series, but largely due to a steric factor

(9)   (11)

the solvent;[8] our values are however identical with those obtained in THF by using different reducing agents.

4-Cyano-1-methylquinolinium iodide (9) and 4-Cyano-quinolinium sulphate (10). The 4-cyano-1-methyldihydroquinolyl radical (11) is easily obtained from the salt (9) by irradiation in THF containing benzophenone. It was also obtained in THF by reduction with potassium and by treatment with zinc powder in ethanol. Owing

which prevents the quinolinyl radicals from dimerizing or reacting with the hydroxy(diphenyl)methyl radical. Chemical evidence shows the great steric influence that the H-5 of quinoline has on the reactivity of position 4. Thus quinoline[11] is selectively alkylated in positions 2 and 4 by primary and secondary alkyl radicals, position 4 being slightly more reactive than position 2, but with tertiary alkyl radicals only position 2 is attacked.[11] On

(10)   (12)

to the complexity of the e.s.r. spectrum, complete resolution was necessary for its interpretation; this was achieved at ca. 0 °C and the resulting hyperfine splitting constants are reported in Table 2. The assignments are based on McLachlan spin density calculations and are consistent with those expected. The only doubts

the other hand in pyridine position 4 is more reactive than position 2, even with tertiary alkyl radicals.[11] Further chemical evidence is offered by the photochemical behaviour in the presence of benzophenone of protonated 4-cyano- (10) and 2-cyano-quinoline (13); the former (10) gives rise to the very persistent radical (12) by the electron-transfer process of equation (viii), whereas (13) gives compound (14) in good yields; this

11 F. Minisci, R. Bernardi, F. Bertini, R. Galli, and M. Perhinunno, *Tetrahedron*, 1971, **27**, 3575.

product is formed according to Scheme 2.[12] [Radical (15) can also be obtained through sensitisation of (13).[12]] Thus the 2-cyanodihydroquinolinyl radical (15) is less persistent than the 4-cyanodihydroquinolyl radical (12) exclusively for steric reasons. The lack of dimerisation

anion (18) of naphthalene. An electron transfer takes place immediately between this radical and N-methyl-pyridinium salts according to equation (x). Intense and well resolved e.s.r. spectra were also obtained in this way, and were identical with the spectra already reported.
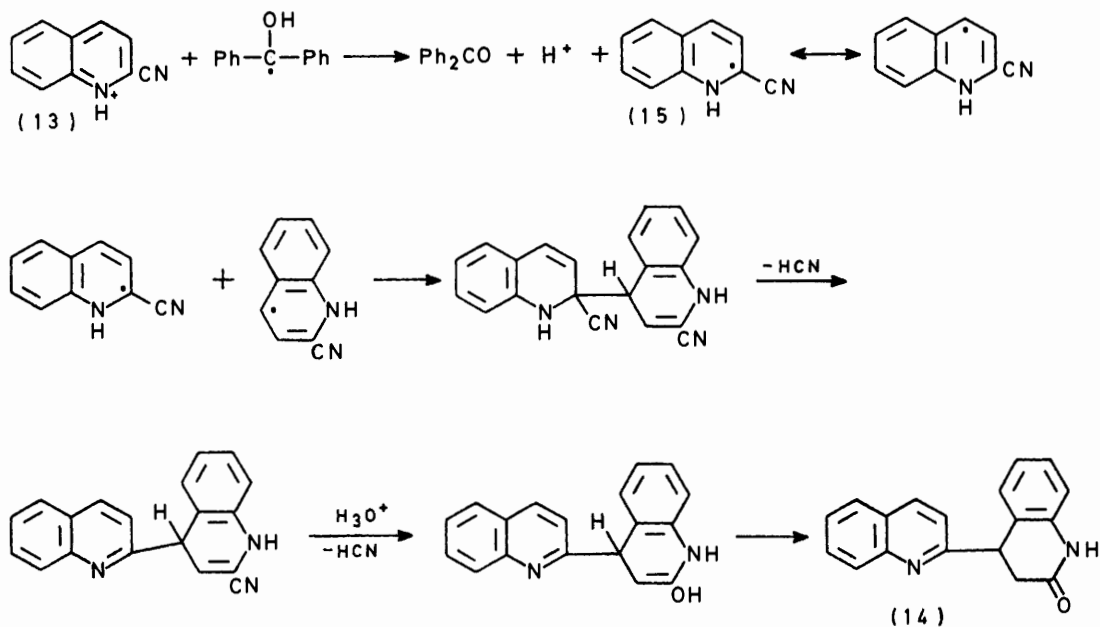
SCHEME 2

of (12) through the unhindered C-2 can be related to the fact that the spin density at C-4 is higher than at C-2. On the other hand the steric hindrance at position 4 of (12) is greater than at positions 2 and 4 of (15).

*Pyrazinium Salts* (16).—Irradiation of benzophenone

The results obtained in this work emphasize two general aspects of electron-transfer processes. (i) A similar type of reactivity is exhibited by classical ionic nucleophiles and nucleophilic radicals; the electron donor in equation (ii) can be a charged (*e.g.* OH⁻) or uncharged (*e.g.* R_3N)
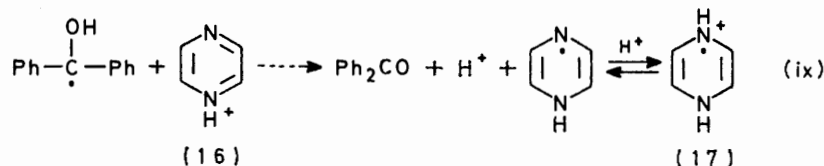
in THF–methanol in the presence of pyrazinium salts immediately gives the corresponding radical (17) by electron transfer from the hydroxy(diphenyl)methyl radical [equation (ix)]; an intense and well resolved e.s.r. spectrum is observed. The splitting constants agree well with those of the same radical produced in a different way.[13] The radical (17) is also formed by irradiation of protonated pyrazine in THF or THF–methanol in the absence of benzophenone, but the e.s.r. signal appears more slowly under the same conditions. A different mechanism is responsible in this case; the radical (17) is formed by hydrogen abstraction from alcohol–THF by the excited state of the pyrazine (Scheme 3).

Another strongly nucleophilic free radical is the radical

ionic nucleophile, or a charged (*e.g.* naphthalene radical anion) or uncharged [*e.g.* hydroxy(diphenyl)methyl] free radical. In all cases the essential step is the same, an electron transfer from the nucleophile to the electron-deficient substrate. (ii) Electron transfer between
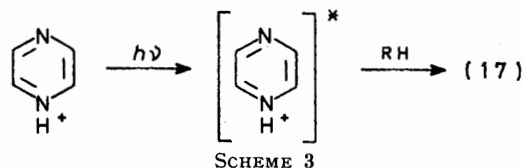

SCHEME 3

hydroxy(diphenyl)methyl radical and pyridinium, quin-olinium, and pyrazinium salts is the limiting case of a general mechanism [equation (iii)] involving the reactions

[12] T. Caronna, S. Morrocchi, and B. Vittimberga, unpublished results.

[13] S. L. Barton and G. K. Fraenkel, *J. Chem. Phys.*, 1964, **41**, 1455.

of a large variety of nucleophilic free radicals and proton-
ated heteroaromatic bases.   Our results strongly support
a mechanism characterized by a large degree of charge
separation in the transition state, indicated by the
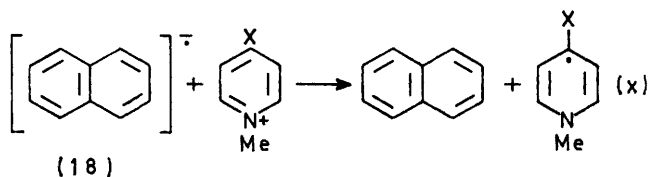
exceptional substrate and positional selectivities, and
resulting in the great synthetic potential of these
reactions.[3,4,9]

[14] F. H. Hamer, *J. Chem. Soc.*, 1939, 1008.
[15] A. D. McLachlan, *Mol. Phys.*, 1960, **3**, 233.
[16] S. L. Barton and G. K. Fraenkel, *J. Chem. Phys.*, 1963, **39**,
1793.

[17] P. H. Riefer and G. K. Fraenkel, *J. Chem. Phys.*, 1963, **39**,
609.