Tetrahedron Letters No. 38, pp 3323 - 3324, 1975. Pergamon Press. Printed in Great Britain.

REDOX REACTIONS OF PYRIDINIUM SALTS

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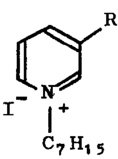
(Received in UK 4 August 1975; accepted for publication 14 August 1975)

Both the redox reactions of nicotinamide-dependent dehydrogenases with carbonyl compounds and alcohols and of analogous non-enzymic reactions are understood to proceed essentially via hydride transfer between the reactants.[1] Evidence for this has accrued chiefly from studies of isotope and substituent effects in the reactions of aromatic aldehydes and ketones.[2,3] The remaining major mechanistic problem in these reactions is the nature of any intermediate It would be valuable to study a general and versatile chemical model system that is capable of investigating the detailed interactions that take place between the reactants in pyridinium salt/dihydropyridine redox reactions. There has been no systematic study of these interactions in a single model system.

We selected 3-substituted-1-n-heptylpyridinium iodides (1a-c)and the lithium salts of substituted benzyl alcohols (3a-e) for study. In tetrahydrofuran solution at room temperature under an atmosphere of nitrogen, the pyridinium salts oxidise the alkoxides to aldehydes. Yields of aldehydes vary widely depending upon the substituents R^1 and R^2. For example 1a and 3a furnish only about 0.5% aldehyde[4] whereas 1c and 3e yield 60-65% aldehyde as shown by pmr. Only one other example of the non-enzymic oxidation of an alcohol by a pyridinium salt has been reported.[5]



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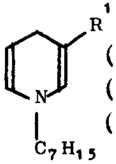

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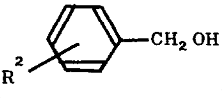
(a) R^1 =H
(b) R^1 =CON$(CH_2CH_2)_2O$
(c) R^1 =$SO_2N(CH_2CH_2)_2O$



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(a) R^2_2 =mCl
(b) R_2 =H
(c) R_2 =pMe
(d) R_2 =pOMe
(e) R =pNMe₂

A feature of our system is that it is possible to study the reaction beginning with either pyridinium salt or 1,4-dihydropyridine (2a-c). Accordingly, when 2c was treated with *p*-dimethylaminobenzaldehyde and lithium iodide under identical conditions to the pyridinium salt (1c) reactions, the product mixture again contained 60-65% aldehyde.

Further, by use of $1'-{}^{2}H_2$-3e or $4-{}^{2}H$-2c it was shown that deuterium is transferred between C-4 of the dihydropyridine 2c and the alcohol carbon of 3e. The distribution of deuterium observed showed that the reaction had attained equilibrium. Equilibrium constants were therefore calculated for each reaction studied and the plots of their logarithms versus the appropriate substituent constant (σ^*, σ for *m*-Cl) were linear with the following gradients: 1, 2a $\rho = 0$; 1, 2b $\rho = -0.8$; 1, 2c $\rho = -2.0$. These values show that the electron density at the aldehyde carbonyl group chiefly controls the position of equilibrium of reactions of 1b and 1c. However dihydropyridine 2a is so unstable that the substituents in the substrate have no effect on the position of equilibrium. It thus appears that alkoxides and pyridinium salts establish a redox equilibrium via hydrogen transfer. With this basis it is possible to investigate the detailed chemistry of intermediates in the reaction, if they are indeed formed.

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