Hydrogen Transfer in NADH Models. An Intramolecular Photochemical Redox Reaction

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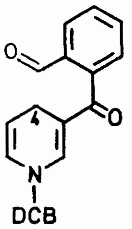
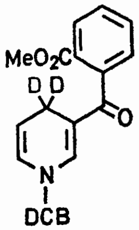
Summary Photolysis of *N*-(2,6-dichlorobenzyl-3-(*o*-formylbenzoyl)-1,4-dihydropyridine (**1**) gave the corresponding pyridinium alcohol; deuterium labelling showed the process to be intramolecular and to involve the transfer from C-4 of the dihydropyridine to the formyl carbon atom.

MODEL systems which emulate NADH dependent dehydrogenase reactions have relied on high electrophilicity in the 'substrate' to induce hydride ion transfer.[1] The catalysis of such processes has largely been ignored in model systems until recently[2] even though this is the basic function of the apoenzyme and fundamental to an understanding of the enzymic process. In order to examine the catalytic requirements of the process, an intramolecular hydrogen transfer system (**1**), m.p. 140—141°,† has been synthesised.

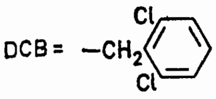
(**1**) was photolysed using a 125 W medium-pressure mercury lamp in benzene solution ($6\cdot6 \times 10^{-4}$M) in Pyrex during 6 h (Scheme). The reaction could also be carried out in acetonitrile, chloroform, and dimethylacetamide solutions The 378 nm absorption band present before photolysis disappeared. The product was distributed between 10% aqueous ammonium chloride and benzene and the aqueous solution reduced with buffered aqueous sodium dithionite, a process which was shown not to reduce the aldehyde function. Preparative layer chromatography gave the dihydropyridine alcohol (**3**), m.p. 114—118°.† By the use of filters the excitation was located in the region 350—400 nm, corresponding to the dihydronicotinamide chromophore [378 nm in (**1**)]. The intramolecular nature of the process was shown by the necessity of a dilute solution for the photolysis and by the lack of exchange when the photolysis was carried out in the presence of the 4-dideuteriated ester analogue (**2**).



(1)



(2)



Photolysis of the 4-monodeuteriated dihydropyridine (**1**) followed by reductive work-up gave a product shown by mass spectrometry to be essentially a monodeuteriated dihydropyridine alcohol (**3**). The spectra of authentic unlabelled, 4-monodeuteriated and α-monodeuteriated dihydro-compound (**3**) showed that despite the complexity

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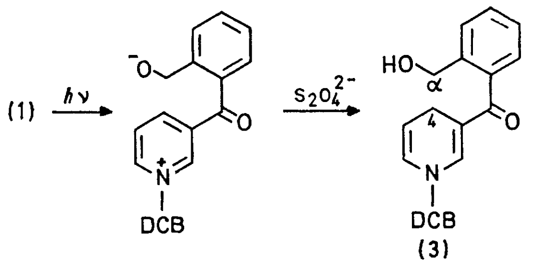
† All new compounds gave correct micro- or mass spectral analyses and the expected spectral data.



Scheme

of two chlorine atoms present in the molecule a clear distinction between the [4-^{2}H] and [α-^{2}H] species could be made on the basis of a series of ions at *m/e* 326, 328, 330 for the $^{2}H_0$ and [4-^{2}H] species and 327, 329, 331 for the [α-^{2}H] species, and ions at *m/e* 167, or 168 (dichlorobenzyl loss from 326/7). These ions therefore involve the loss of the hydrogen atoms from C-4 and the retention of those in the α-position. A comparison of these mass spectra with that of the photolysis showed that *ca.* 30% of the deuterium retained was located in the α-position (*m/e* 327, 329, 331) Since deuterium transferred to oxygen would have been lost in work-up, it follows that the remainder was still at the 4-position. This was confirmed by the presence of the 326, 328, and 330 ions.

The photochemical process thus involves the transfer of a hydrogen atom from C-4 of the dihydropyridine ring to the carbon atom of the carbonyl group. Although photochemical hydrogen shifts have been reported previously[3] the fate of the migrating hydrogen atoms have not been determined.

The award of a Salters Company Fellowship to J.D.S. is acknowledged.

(*Received, 22nd June* 1972; *Com.* 1082.)

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[1] For a recent survey, see U. Eisner and J. Kuthan, *Chem. Rev.*, 1972, **72**, 1, and references cited therein; J. J. Steffens and D. M Chipman, *J. Amer. Chem. Soc.*, 1971, **93**, 6694.

[2] D. J. Creighton and D. S. Sigman, *J. Amer. Chem. Soc.*, 1971, **93**, 6314; U. K. Pardit and F. R. Mas Crabbé, *Chem. Comm.*, 1971 552.

[3] J. A. Benson and E. Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 447; U. Eisner, J. R. Williams, B. W. Matthews, and H. Ziffer, *Tetrahedron*, 1970, **26**, 899.