Electrochemical Reactions. Part XVIII.[1] Reductive Cleavage of Aromatic Carbon–Halogen Bonds in the Presence of Deuterium Oxide

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Reductive dehalogenation of aromatic compounds at a mercury cathode in dimethylformamide containing 1% deuterium oxide with tetra-n-propylammonium perchlorate as supporting electrolyte may or may not result in deuterium incorporation, depending on the substrate. Compounds giving a radical anion intermediate which is detectable by cyclic voltammetry do not incorporate deuterium. The radical anion decomposes away from the electrode to a σ-radical which abstracts a hydrogen atom from the organic solvent. Compounds which give no detectable radical anion accept one electron in the initial step and fragment to a σ-radical at the electrode surface. This radical is reduced further to a carbanion which reacts with incorporation of deuterium into the product. Evidence for σ-radical intermediates in the latter cases comes from isolation of dimers or products of intramolecular radical cyclisation of appropriate substrates.

REDUCTION of aryl halides at a mercury cathode in dimethylformamide containing deuterium oxide and lithium perchlorate as supporting electrolyte proceeds with the replacement of halogen by deuterium. This is a method for the specific incorporation of deuterium which has been applied to the isomeric iodotoluenes and iodoanisoles [2] and also to alkyl halides.[3] On the other hand, many examples are known of the reduction of aryl halides in dimethylformamide with tetra-alkylammonium salts as supporting electrolyte where the reaction, illustrated in the Scheme for 4-chlorobenzophenone, involves formation of a radical anion, followed

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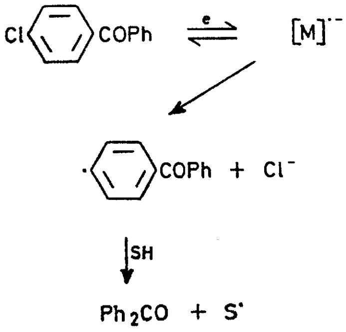
[1] Part XVII, J. Grimshaw and J. Trocha-Grimshaw, *J.C.S. Perkin I*, 1974, 1383.

[2] J. R. Cockrell and R. W. Murray, *J. Electrochem. Soc.*, 1972, **119**, 849.

[3] M. F. Semmelhack, R. J. DeFranco, and J. Stock, *Tetrahedron Letters*, 1972, 1371.

by its decomposition with loss of halide ion at a measurable rate to a σ-radical, which abstracts a hydrogen atom from the solvent. This path would result in no incorporation of deuterium from reduction in the presence of small amounts of deuterium oxide, because in the last step the σ-radical will prefer to abstract hydrogen from dimethylformamide rather than attack deuterium oxide. The overall reaction path is assumed to be insensitive to the small change in reaction medium due to addition of deuterium oxide. The path shown in the Scheme has been verified by using cyclic voltammetry to monitor the formation and decomposition of the intermediate radical anion. Halogenonitrobenzenes[4] and halogenobenzonitriles[5] have been studied by Hawley and others. For the compounds described in this paper the radical anion intermediate has been detected and a rate constant measured for its decomposition in the reduction of 4-chloro- and 4-bromobenzophenone,[6] 3-bromofluorene,[7] and 4-(4-chlorostyryl)pyridine.[8]



SCHEME

Reduction of halogeno-compounds in dimethylformamide containing deuterium oxide (1%)

Compound reduced	Reduction potential (−V)	Yield) (%)	M.p. (°C)	Dehalogenated product ^{2}H content (% ±3)
(1; $R^1 = R^2 = Cl$)	1·95	71	130 [b]	$^2H_0$, 18; $^2H_1$, 36; $^2H_2$ 28; $^2H_3$ 18
(1; $R^1 = R^2 = Br$)	1·90	65	154 [b]	$^2H_0$, 11; $^2H_1$, 36; $^2H_2$, 34; $^2H_3$, 14; $^2H_4$, 5
(2; R = Cl)	1·95	80	136 [c]	$^2H_1$, 0
(2; R = Br)	1·90	95	136 [c]	$^2H_0$, 30; $^2H_1$, 46; $^2H_2$, 24
1-Chloropyrene	1·60	70	150	$^2H_1$, 0
1-Bromopyrene	1·50	85	150	$^2H_1$, 23
4-Chlorobenzophenone	1·60	57	47	$^2H_1$, 0
4-Bromobenzophenone	1·45	53	47	$^2H_1$, 0
3-Bromofluorene	1·17	35	82	$^2H_1$, 0
4-(4-Chlorostyryl)pyridine	1·80	24	125	$^2H_1$, 0
4-Iodo-4′-methoxybenzanilide	1·50	75	157	$^2H_1$, 46
2-Bromo-4′-methoxybenzanilide	1·65	62	157	$^2H_1$, 58
2-Iodo-4′-methoxybenzanilide	1·20	62	157	$^2H_1$, 37
2-Iodo-4′-methoxy-*N*-methylbenzanilide	1·60	33	78	$^2H_1$, 57

[a] Replacement of halogen by ^1H or ^2H. [b] (1; R^1 = Cl or Br, R^2 = H; H_a, H_b, and H_c hydrogen or deuterium). [c] (1; $R^1 = R^2 =$ H).

Such dehalogenations can also be effected with solutions of the preformed radical anions of nitrobenzene[9] or naphthalene[10] as reducing agent, and a reaction mechanism like that described above has been proposed. In the case of reactions with sodium naphthalenide a different reaction path is favoured by some workers. Here the σ-radical is thought to be reduced further to a carbanion which attacks the solvent.[10]

Previously[1] we have shown that reduction of the dichloropyrazole (2; R = Cl) at a mercury cathode in dimethylformamide containing 1% deuterium oxide and tetrapropylammonium perchlorate resulted in no incorporation of deuterium. This was taken as evidence that reduction proceeded by steps like those of the Scheme, although it was not possible with the apparatus available to demonstrate the reversible formation of a radical anion intermediate in anhydrous dimethylformamide. We have now studied the reduction of a number of halogeno-compounds under these conditions to see if deuterium can, in some circumstances, be incorporated into the product.[11]

EXPERIMENTAL

Dimethylformamide was kept over anhydrous copper sulphate and then distilled under nitrogen (b.p. 42° at 12 mmHg). Nitrogen was purified over BTS catalyst[12] and dried over a molecular sieve. All potentials were measured *vs.* s.c.e. The potentiostat used was constructed in this department.

Electrochemical Reduction.—The electrolyte was dimethylformamide containing deuterium oxide (1% v/v) and tetra-

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[4] T. Kitagawa, T. P. Layloff, and R. N. Adams, *Analyt. Chem.*, 1963, **35**, 1086; J. G. Lawless and M. D. Hawley, *J. Electroanalyt. Chem.*, 1969, **21**, 365; W. C. Danen, T. T. Kensler, J. G. Lawless, M. F. Marcus, and M. D. Hawley, *J. Phys. Chem.*, 1969, **73**, 4389; R. P. van Duyne and C. N. Reilley, *Analyt. Chem.*, 1972, **44**, 158.

[5] D. E. Bartak, D. J. Houser, B. C. Rudy, and M. D. Hawley, *J. Amer. Chem. Soc.*, 1972, **94**, 7526; K. J. Houser, D. E. Bartak, and M. D. Hawley, *ibid.*, 1973, **95**, 6033.

[6] L. Nadjo and J. M. Savéant, *J. Electroanalyt. Chem.*, 1971, **30**, 41.

[7] J. Grimshaw and J. Trocha-Grimshaw, *J. Electroanalyt. Chem.* 1974, **56**, 443.

[8] K. Alwair and J. Grimshaw, *J.C.S. Perkin II*, 1973, 1150.

[9] A. R. Metcalfe and W. A. Waters, *J. Chem. Soc.* (*B*), 1969, 918.

[10] J. G. Smith and I. Ho, *J. Org. Chem.*, 1973, **38**, 3601, and references cited therein; G. D. Sargent, *Tetrahedron Letters*, 1971, 3279.

[11] Preliminary report, J. Grimshaw and J. Trocha-Grimshaw, *Tetrahedron Letters*, 1974, 993.

[12] M. Schutze, *Angew. Chem.*, 1958, **70**, 697; Badische Anilin und Soda Fabrik AG, Technical Bulletin 'BTS Catalyst.'

propylammonium perchlorate (0·1M). An H-type reduction vessel was used, the two compartments being separated by two fritted glass discs. The anode was platinum and the cathode a stirred mercury pool (diam. 2·5 cm). The cell was washed with 5% deuterium oxide in dimethylformamide before use. The halogeno-compound (0·50 g) was dissolved in the electrolyte (10 ml) and reduced at a potential near the foot of the first polarographic wave until the current fell to a low value. The reaction mixture was then evaporated to a small volume under reduced pressure, water was added, and the precipitate was collected. This was chromatographed on alumina and crystallised to yield the pure dehalogenated product. Deuterium content was determined with an A.E.I.-MS902 mass spectrometer with an ionising beam energy of 12 eV so as to suppress any $M^+ - 1$ peak. The results are given in the Table.

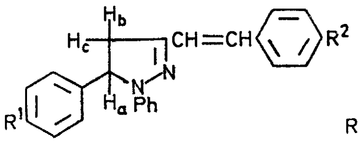
1-*Chloro and* 1-*bromopyrene*. The product was chromatographed in benzene on alumina. Crystallisation from ethanol afforded pyrene and the very insoluble 1,1′-bipyrenyl (10%), m.p. 325—328° (lit.,[13] 327—328°), M^+ 402.

3-*Bromofluorenone*, 4-*bromobenzophenone, and* 4-(4-*chlorostyryl)pyridine*. Amorphous dimeric material was also formed in these reductions and was separated by chromatography.

2-*Iodo*-4′-*methoxy*-N-*methylbenzanilide*. Products of intramolecular radical substitution were also isolated.[11] Only 4′-methoxy-*N*-methylbenzanilide showed deuterium incorporation.

DISCUSSION

Reduction of the pyrazoline derivatives resulted in the incorporation of three and, in the case of the bromo-derivative, possibly up to four atoms of deuterium per molecule. The products have previously been shown to possess structures (1; R^1 = Cl or Br, R^2 = H).[1]



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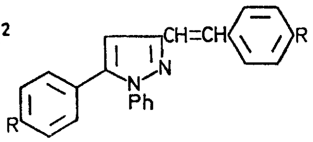

(2)

Their n.m.r. spectra indicated replacement by deuterium of H_a, H_b, and H_c attached to the pyrazoline ring. This replacement must be a reaction of the corresponding radical anions since the pyrazolines remained undeuteriated after a long period in dimethylformamide containing deuterium oxide. 1,5-Diphenyl-3-styryl-Δ^2-pyrazoline gives a radical anion which is stable in dimethylformamide on the time scale of cyclic voltammetry.[1] Because of this complicating factor the first two results in the Table are ignored in the subsequent discussion.

There is evidence for σ-radical intermediates being formed during reduction of all the compounds mentioned in the Table. Reduction of 2-iodo-4′-methoxy-*N*-methylbenzanilide and the corresponding bromo-compound gave other products which can only be rationalised in terms of the cyclisation of a radical intermediate.[11] We therefore infer that radical intermediates are involved in the reduction of the 2- and 4-halogenobenzanilides examined. 5-(2-Chlorophenyl)-1,3-diphenylpyrazole gives a good yield of the product of intramolecular cyclisation of a radical intermediate,[14] so again this is taken as evidence for radical intermediates in the reduction of the pyrazole derivatives (2; R = Cl or Br). Bipyrenyl is formed during reduction of 1-chloro- and 1-bromo-pyrene in both anhydrous and moist dimethylformamide, which points to radical intermediates being involved. Radical anion intermediates have been characterised for the other compounds listed in the Table.

At the outset of this investigation we wished to use deuterium incorporation into the product as a test for the presence of a strongly basic carbanion intermediate in the halogen replacement reactions. The difference in composition between the double layer at the mercury surface and the bulk solution may influence the outcome of this test. Tetra-alkylammonium ions are strongly adsorbed at a mercury solution interface and this interfacial layer is depleted in water relative to the bulk of the solution. It has been suggested that this depletion can explain the good yields of adiponitrile which result from reduction of acrylonitrile in the presence of quaternary ammonium salts as opposed to the result from reduction in the presence of alkali metal ions when propiononitrile is the major product.[15] In these reactions an anionic intermediate, $^-CH_2{\cdot}CH_2{\cdot}CN$, is thought to add to acrylonitrile in the water-depleted layer but to be protonated in the presence of solvated alkali metal ions. Application of this argument to the dehalogenation process suggests that reaction *via* a carbanion species can result in no deuterium incorporation because the intermediate will abstract a proton from another source, *e.g.* the quaternary ammonium ion, in a type of Hofmann reaction, in this layer which is depleted of deuterium oxide faster than it can diffuse into the bulk of the solution. However, a simple reasoning based on carbon–halogen bond strengths (Cl > Br > I) combined with the knowledge that the radical anions of 3-bromofluorenone, 4-chloro- and 4-bromo-benzophenone, and 4-(4-chlorostyryl)pyridine fragment at relatively low and measurable rates shows that it is the compounds expected to fragment *rapidly* which incorporate deuterium. Thus the reactions most likely to take place in this deuterium-oxide-depleted layer in fact incorporate deuterium into the product. Other workers have noted that reduction of aryl halides in acetonitrile and deuterium oxide gives a greater introduction of deuterium with lithium than with tetraethylammonium perchlorate as electrolyte.[2] This suggests that the nature of the mercury solution interfacial layer may influence the extent of deuterium incorporation but not to the total exclusion of this reaction under our conditions.

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[13] E. Clar and O. Kühn, *Annalen*, 1956, **601**, 181.

[14] W. J. Begley, J. Grimshaw, and J. Trocha-Grimshaw, *J.C.S. Perkin I*, 1974, 2633.

[15] I. Gillet, *Bull. Soc. chim. France*, 1968, 2919; F. Beck, *Ber. Bunsengesellschaft Phys. Chem.*, 1968, **72**, 380.

Reduction potential does not itself determine whether deuterium is incorporated or not over the range studied. There are examples of both types of reaction at −1·2 and at −1·8 V.

The results of deuterium incorporation can all be accommodated by a slight modification of the Scheme illustrated for reduction of 4-chlorobenzophenone. If the initially formed radical anion is sufficiently stable it can diffuse outside the electrode layer before fragmenting. The reaction then takes the course illustrated and deuterium is not incorporated into the product. In other cases the radical anion may have a very short life or the steps of electron addition and carbon–halogen bond fragmentation may be combined so that the radical anion is no longer a discrete intermediate though one electron only is transferred in this first step. The σ-radical will now be generated close to the electrode surface where it can undergo further reduction to a carbanion, and this reacts with a proton or a deuteron.

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