POLYHALOGENOHETEROCYCLIC COMPOUNDS—3²¹

RADICAL-ANIONS FROM HALOPYRIDINES

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Abstract—Electrochemical reduction of pentafluoropyridine and other polyhalopyridines gives bipyridyl derivatives etc. and it is inferred from the structures of the products that, in the intermediate radical-anion, charge- and spin-density is concentrated at the 1- and 4-positions. This is further supported by measurement of $Ep_{1/2}$ values. Trapping experiments with hydroquinone and carbon dioxide are described.

In earlier parts of this series we have been investigating the interesting orientation problems that fully halogenated compounds provide for nucleophilic aromatic substitution² and these problems are analogous to the well known orientation problems of electrophilic aromatic substitution. In principle, reactions of radical anions derived from fully halogenated aromatic compounds provide a way to explore the electron distributions in these species, as inferred from structures of their reaction products. Therefore, this publication is concerned with attempts to generate radical anions from highly halogenated pyridines, by electrochemical methods.

We have employed a conventional H-cell with a stirred mercury cathode and dimethylformamide containing tetraethylammonium tetrafluoroborate was chosen in order to maintain a high reduction potential for the solvent-electrolyte system.³ Using this system we have found that polyhalogenated pyridines may be reduced at the cathode and that, in each case, subsequent reaction occurs specifically at the 4position. Pentafluoropyridine (1) gave perfluoro-4,4'bipyridyl (4) while, in the presence of hydroquinone as a proton donor, 2,3,5,6-tetrafluoropyridine (6) was obtained. The most likely mechanism is that outlined in Scheme 1, involving coupling of the radical anion (3), followed by loss of halide ion, and this process is analogous to one described for the coupling of 4fluorobenzonitrile.⁴ Hydroquinone efficiently intercepts the radical anion (3) and no bipyridyl derivative (4) is obtained. In principle, a mechanism involving nucleophilic attack by the radical anion (3) or the



Scheme 1. (i) Hg cathode, D.M.F., Et₄NBF₄, -1.8 V (S.C.E.); (ii) hydroquinone.

carbanion (8) on the polyhalopyridines (1 or 2) could be invoked but it is established that nucleophilic attack on 2 occurs specifically at the 2-position i.e. by displacement of fluorine in preference to chlorine.⁵ Similarly, it is unlikely that 4 is produced via coupling of the radical 7 since 6 is obtained from pentafluoropyridine only in the presence of hydroquinone, whereas the radical 7 would be expected to abstract an H atom from solvent, electrolyte etc.

We have also reduced pentachloropyridine (9) at a lead cathode and a different situation obtains, to that observed for the fluorinated pyridines. Only a small amount of bipyridyl derivative was detectable and tetrachloropyridine (13) was obtained, without the addition of a proton donor. The different course of the reactions of fluorinated and chlorinated systems seems to stem from inhibition of the coupling of 10, due to the bulky ortho-chlorine atoms. Consistent with the process now involving 11, reduction of pentachloropyridine at a mercury cathode, gave bis(tetrachloropyridyl)mercury (14), in addition to 13.

Carbon dioxide is used extensively as a trap for carbonions and radical anions and we have attempted corresponding trapping experiments for the reductions of 1 and 9 at mercury. Only in the case of 9, however, were identifiable products obtained. Reduction of 9 gave 13 and also, after acidification, a mixture of carboxylic acids was obtained. These could not be identified directly but, on pyrolysis at 150°, a further quantity of 13 was obtained, together with a single heptachlorobipyridyl derivative and the m.p. and the ¹H chemical shift for this compound are in close agreement with the values reported for 15.6 Clearly the presence of carbon dioxide has completely altered the course of reaction from production of the mercurial (14), which was not obtained in this case, to a bipyridyl derivative (17) as a major product. It seems most likely that the radical anion (10) is trapped by carbon dioxide and a possible route for the formation of 17 is shown in Scheme 3. It is not possible to conduct an exactly analogous reduction of 16 since this material is highly insoluble. However, it is probable that formation of 16 and its immediate reduction at the electrode occurs.

The results of these preparative experiments, taken together with measurements of half-peak potentials (see later) allow us to draw firm conclusions about the



Scheme 2. (i) Pb cathode, D.M.F., Et_4NBF_4 , -1.5 V (S.C.E.); (ii) Hg cathode, -1.4 V (S.C.E.); (iii) solvent/electrolyte; (iv) 150°, vacuum



Scheme 3.

overall structure of the radical anions generated in these systems. The substitution patterns clearly indicate that the radical anions may be reasonably represented by the structures **18a**, **18b** and this conclusion has been supported by calculations at the INDO level on pentafluoropyridine.⁷ Preparative electrochemical reductions of pentafluorobenzene⁸ and various polychlorobenzenes⁹ have been carried out and, in the latter case, a correlation between electron-density calculations in the radical-anions and observed products was also possible.¹⁰



We have carried out some electroanalytical chemistry by measuring half-peak potentials at various scan rates. Such measurements could, in principle, reflect the relative stabilities of corresponding radical anions but this can only be quantitative for rigorously reversible electron transfer. We have examined a number of highly fluorinated pyridines with other substituents at the 2, 3, or 4positions (Table 1) but, in most cases, the processes were irreversible even when studied at high sweeprates in cyclic voltammetry. The exception was perfluoro-4,4'-bipyridyl (4), which showed reversible reduction at sweep-rates as low as 1 mv/sec. Because the values recorded in Table 1 involve almost entirely irreversible reductions, we are unable to make any sound quantitative deductions. However, the positional effect of substituents is very meaningful e.g. there is a significant difference between the $Ep_{1,2}$ values for the compounds with chlorine at the 4-, 3and 2-positions. Electron transfer could be accompanied by fission of a carbon -halogen bond but the results shown in Table 1 obviously do not reflect. solely, the strength of the weakest carbon halogen bond in the system, otherwise we might expect similar values for chlorine at all three positions. The results are, however, consistent with the effects that we might anticipate for radical anions of structure 18, where a substituent at the 4-position would have most effect. For the series of 4-X tetrafluoropyridine derivatives $(X = F \rightarrow I)$ is is not possible to determine whether the differences in $Ep_{1,2}$ values is attributable to changes in anion stabilisation or changes in carbon-halogen bond strength but, for the other substituents, strong stabilisation of the radical anion seems quite clear. The large difference in the values for perfluoro-4,4'and -3,3'-bipyridyl emphasizes this point. We have observed closely similar values for perfluoro-ethyl and -isopropyl groups at the 4-position and it is interesting that we have also shown that these groups have a similar activating influence on a fluorinated aromatic ring, towards nucleophilic aromatic substitution.¹¹

EXPERIMENTAL

Glc analysis was performed using a Griffin and George D6 instrument with a gas-density balance detector; preparative scale glc was performed on a Varian Autoprep instrument, IR spectra were recorded using Perkin Elmer Model 457 or 577 spectrophotometers; NMR spectra were recorded at 40° on a Varian A56/60D spectrometer, using $CFCl_3$ or TMS as internal refs; mass spectra were obtained on an A.E.I. MS9 instrument or a V.G. Micromass 12B, linked with a Pye 104 gas chromatograph.

Pentachloropyridine was obtained from I.C.I. Ltd. and pentafluoropyridine was prepared from it by a published route.¹² Other pyridine derivatives were prepared by published routes. Dimethylformamide (DMF) was purified by fractional vacuum distillation, first from anhydrous sodium carbonate and then from dry molecular sieve (type 4A). The purified DMF was stored over molecular sieve under an atmosphere of dry N₂. Tetracthylammonium tetrafluoroborate was prepared by reaction of tetracthylammonium bromide with sodium tetrafluoroborate and then recrystallisation of the precipitated salt from aqueous MeOH. It was dried by alternately heating to 150° under vacuum, crushing to a fine powder, and stored under dry nitrogen. Mercury was doubly distilled.

Electrolysis. The glass cell used for preparative work had a cathode compartment of 80 ml capacity, separated from the anode by a coarse glass frit. The anode was a simple platinum flag $(3 \text{ cm} \times 3 \text{ cm})$ in a soln of the base electrolyte. Unless otherwise stated the cathode was a mercury pool (10 cm^2) to which electrical contact was made through a platinum glass scal. All potentials were relative to a saturated calomel electrode, positioned close to the mercury surface. Stirring was performed by a magnetic follower. Nitrogen gas bubblers allowed deoxygenation of the cell.

The cathode potential was controlled by means of a custom-built potentiostat incorporating a DC 300W amplifier.

The usual procedure involved filling the cell with base electrolyte soln (0.16 M tetracthylammonium tetrafluoroborate in DMF) and purging with dry N₂. A potential sweep was then performed by noting the current at intervals of 0.1 V, down to close to the limiting cathode potential. The organic substrate (2-8 g) was then added to the cathode compartment and the sweep repeated Analysis of the I, V curves obtained indicated potentials at which electrochemical reactions occurred and the background current was minimal. Suitable potentials were selected from these curves and electrolyses carried out under potentiostatic conditions. The current flowing was monitored at regular intervals and the charge passed thereby determined graphically. If necessary, the cell could be cooled during electrolysis by immersion in a water bath at room temp.

Some electrolyses were carried out on several occasions, varying the conditions and work-up method employed. Detailed experimental procedures are given for representative reactions.

Preparative-scale reductions

Pentafluoropyridine (1). Pentafluoropyridine 1 (2.65 g. 15.7 m.mol) was reduced at -1.80 V and 0.0135 F of charge passed, a quantity equiv to 0.86 e per molecule of 1. The mixture was distilled under reduced pressure and the early fractions were shown by glc (silicone gum rubber; 130°) to contain 1 (*ca* 0.41 g). The residue was added to dichloromethane, washed thoroughly, dried, and the solvent removed by distillation. The resultant tarry solid was heated under reduced pressure (0.05 mm, 50°) to yield an off-white sublimate (0.80 g), identified as 4 by comparison of its ¹⁹F NMR and IR spectra with those of an authentic sample;¹³ and an intractable residue (0.85 g). The current efficiency (C E) for production of 4 was calculated to be 49 "_o on the assumption that 2 electrons are required per molecule of 4 produced.

Pentafluoropyridine (1) with hydroquinone Pentafluoropyridine 1 (7.52 g. 44.5 m mol) was reduced at -2.40 V, with hydroquinone (2.66 g. 24 2 m.mol) dissolved in the cathode compartment and 0.0180 F consumed (0.40 e.molecule). The mixture was distilled under reduced pressure and the first fraction was shown by gle-mass spectrometry (silicone gum rubber; 100°) to contain 6 (ca 0.63 g: 46° a C.E. assuming

х F -1.80 сı -1.65 -1.90 -1.85 -1.79 -0.81 Bz -1.25 I -0.72 -1.94 н -1.96 -1.69 -1.59 CF 3 -1.38C₂F₅ -1.38 -1.16 C₁F7 4-C_FAN -1.18 -1.71 3-C.F.N -1.45 CEFS

Table 1. Half-peak potentials (Ep_{1,2}) in volts v S.C.E. measured at 20 mv./sec. sweep rate

2e/molecule required). This was separated by preparative scale glc and further identified by comparison of spectral data.¹⁴ The residue from the distillation was added to CH_2Cl_2 , washed, dried, and the solvent removed by distillation. Attempted sublimation of the residue under reduced pressure (0.05 mm, 50°) yielded none of 4.

4-Chlorotetrafluoropyridine (2). Compound 2 (2.21 g, 11.9 m.mol) was reduced at -1.60 V and 0.0064 F of charge passed (0.54 e/molecule). The catholyte was distilled under reduced pressure and the residue added to CH₂Cl₂, washed, dried, and the solvent removed by distillation. Sublimation of the resultant brown oil (0.79 g) under reduced pressure yielded 4 (0.34 g, 35% C.E. assuming 2 e/molecule of 4 required).

Pentachloropyridine (9). Compound 9 (5.49 g, 21.8 m,mol) was reduced at -1.40 V and 0.0107 F consumed. A purple colour was observed during the electrolysis. The DMF was removed from the catholyte by transference under vacuum into a cold trap. The residue was washed with water and the insoluble solid then washed with CH₂Cl₂ to leave a white solid (0.59 g), identified after recrystallisation from DMF as 14^{13} (17%) C.E. assuming 2e/molecule of 14), m.p. ca 250° with decomposition (Found: C, 18.7; N, 4.3; Cl, 45.2%; M⁺, 630. Calc. for C₁₀Cl₉HgN₂: C, 19.0; N, 4.4; Cl, 44.9%; M, 630).

The aqueous phase was extracted well with CH_2Cl_2 and all of the extracts combined, washed, dried, and the solvent removed by distillation Sublimation under reduced pressure (0.05 mm) at up to 140° yielded several fractions of white solid (total, 3.50 g), shown by glc-mass spectrometry (silicone gum rubber; 220°) and ¹H NMR to be mixtures of 13 (total *ca* 0.66 g; 57% C.E. assuming 2 e/molecule) and 9. Compound 13 was fully characterised in a later experiment. Sublimation of the residue under reduced pressure (200°, 0.05 mm) yielded a sticky orange solid (0.22 g), which could not be recrystallised. Its mass spectrum showed clusters around M⁺ 630 (14); 428 ($C_{10}N_2Cl_8$); 394 ($C_{10}N_2Cl_2H$); and unidentified higher masses.

Pentachloropyridine (9) at a lead cathode. A piece of lead plate $(3.3 \times 6.6 \text{ cm})$ was preconditioned by making it alternately the cathode and anode in an electrolysis of H_2SO_4 soln, washing and drying. It was used to reduce 9 (4g, 15.9 mmol) at -1.50 V. There was some difficulty in maintaining the current due to the formation of an insoluble film on the lead, which was periodically removed by briefly reversing the polarity. A purple colour was again observed and 0.0138 F of charge was passed (0.87 e/molecule). The solvent was removed from the catholyte by transference under vacuum into a cold trap and the residue washed well with water and dried in a desiccator (P_2O_5) to give a brown solid (3.11g), which was almost completely soluble in CH₂Cl₂. Sublimation under reduced pressure (0.05 mm, 80°) gave a white solid (2.29 g), shown by glc (silicone gum rubber, 220°) to be a mixture of 13 (ca 0.23 g, 15°_{0} C.E.) and 9. Sublimation at 175° under reduced pressure for several days yielded a yellow solid (0.26 g), identified after recrystallisation from CCl₄ as 16 (9% CE. assuming 2e/molecule) m.p. 218-220° (lit.16 221-222°) (Found. C, 27.6; N, 6.1; Cl, 65.2°, M⁺, 428. Calc. for C₁₀Cl₈N₂: C, 27.8; N, 6.5; Cl, 65.7; M, 428). An intractable brown residue remained (1.30 g).

Pentachloropyridine (9) with carbon dioxide. The base electrolyte soln was first saturated with CO2 by bubbling the gas through the cell contents, and this was continued throughout the electrolysis. Pentachloropyridine (2.11 g, 8.40 m.mol) was reduced at -1.30 V and 0.0094 F were consumed. No colour formed during the reaction. Volatile material was removed from the catholyte by transference under high vacuum into a cold trap, and the residue washed with water to give an insoluble solid A. The aqueous phase was acidified with HCl and a white solid B precipitated. The original volatile fraction was then distilled under reduced pressure and the residue from this distillation was added to CH2Cl2, washed, dried and the solvent removed by distillation to give a solid residue C. Heating A and C under reduced pressure (0.05 mm, 80°) gave white sublimates shown by glc to be mixtures of 9 and 13. At up to 180° no further sublimate was obtained. Solid B was slightly soluble in water, giving an acidic soln. It showed a strong IR absorption at 1690 cm⁻¹ (C=O) but its broad O-H absorption was only weak. Its mass spectrum showed large peaks at M⁺ 394 (C10N2Cl2H), and 215 (C5NCl4H), with a very large peak at 44 (CO_2), due to decarboxylation of the corresponding acids. Heating it to 150° under reduced pressure caused the evolution of a large amount of CO2, and fractional sublimation of the residue at 0.05 mm pressure gave:

(i) At 80°. a white solid, which was recrystallised from pet ether (60-80° fraction) and identified as 13, m.p. 90 91° (lit.^{1°} 90.5-91.5°. Compare with 2,4,5,6-tetrachloropyridine,

37.5–38° and 3,4.5,6-tetrachloropyridine, $21-22^{\circ}$). ¹H NMR showed a singlet at δ 7.86 ppm (lit. ¹⁵ 7.90 ppm) (Found: C, 28.0; H, 0.2; N, 6.5; Cl, 65.1°, ; M⁺, 215. Calc. for C₅HCl₄N: C, 27.7; H, 0.5; N, 6.5; Cl, 65.4°, ; M, 215).

(ii) At 140°, a white solid, identified after recrystallisation from CCl₄ as 15.⁶ m.p. 171.5 · 173° (lit. 171 172°). ¹H NMR showed a singlet at δ 7.08 ppm (lit. 7.10 ppm). (Found: C, 30.5: H. 0.2; N, 7.4; Cl, 62.8 $_{.6}^{\circ}$; M⁺, 394. Calc. for C₁₀HCl₇N₂: C, 30.2; H, 0.3; N, 7.1; Cl, 62.5 %; M, 394).

Voltammetry. Single-sweep voltammetry and cyclic voltammetry at sweep rates up to 100 mV/sec, was performed using a Beckmann Electroscan 30 instrument. The electrolysis cell was a microcell of ca 2.5 ml capacity. The anode and cathode were parallel cylindrical pt wires of 0.5 mm dia., scaled in glass to maintain a constant cell geometry, with a separation of 2.5 mm and exposed length of 20 mm. The reference was a S.C.E. with a salt bridge with its tip close to the cathode. The cathode potentials relative to this were checked using a Fluke 8000A Digital Multimeter. Solutions used were 0.35 M tetraethylammonium tetrafluoroborate in DMF, with the substrate at 4mM concentration. These were deoxygenated by purging with dry N_2 for 10 min prior to running the voltammograms in still solns. Voltammograms were recorded at sweep rates of 4, 10, 20, 40 and 100 mV/sec. and half-peak potentials $(Ep_{1,2})$ measured. Those obtained at 20 mV/sec. are shown in the Table. The $Ep_{1,2}$ values varied with sweep rate, except for 4 which was constant, but these fluctuations were not large enough to affect the order of ease of reduction. Values obtained under identical conditions were reproducible to ± 0.02 V. The reduction of 4 was found to be completely reversible under these conditions but none of the other derivatives showed any sign of reversibility Dr. A. Tyson of the Electricity Council Research Centre, Capenhurst, kindly allowed his cyclic voltammetry apparatus to be used to investigate these compounds, but even at a sweep rate of 10 V/sec. only 4 showed any reversibility.

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REFERENCES

- ¹Part 30. R. D. Chambers, W. K. R. Musgrave and D. E. Wood, J. Chem. Soc. Perkin I 1978 (1979).
- ²See R. D. Chambers, *Fluorine in Organic Chemistry*, Wiley-Interscience, New York (1973) for other refs.
- ³L. E. Eberson and N. L. Weinberg, Chem. Eng. News 49, 40 (1971)
- ⁴M. R. Asirvatham and M. D. Hawley, J. Am. Chem. Soc. 97, 5024 (1975).
- ⁵R. D. Chambers, J. S. Waterhouse, and D. L. H. Williams, J. Chem. Soc. Perkin 11 585 (1977).
- ⁶J. D. Cook, N. J. Foulger and B. J. Wakefield, *Ihid.* Perkin I 995 (1972).
- ⁷R. D. Chambers, D. T. Clark, C. R. Sargent and F. G. Drakesmith, *Tetrahedron Letters* 1917 (1979).
- ⁸B. H. Campbell, Anal. Chem. 44, 1659 (1972).
- ⁹S. O. Farwell, F. A. Beland and R. D. Geer, J. Electroanal. Chem. Interfacial Electrochem. **61**, 303 (1975).
- ¹⁰F. A. Beland, S. O. Farwell, P. R. Callis and R. D. Geer, *Ihid* **78**, 145 (1977).
- ¹¹R. D. Chambers, J. S. Waterhouse and D. L. H. Williams, *Tetrahedron Letters* 743 (1974).
- ¹²R. D. Chambers, J. Hutchinson and W. K. R. Musgrave, J. Chem. Soc. 3573 (1964).
- ¹³R. D. Chambers, J. Hutchinson and W. K. R. Musgrave, *Ibid.* 5040 (1965).
- ¹⁴R. D. Chambers, F. G. Drakesmith and W. K. R. Musgrave, *Ibid.* 5045 (1965).
- ¹⁵J. D. Cook and B. J. Wakefield, J. Organomet. Chem. 13, 15 (1968).
- ¹⁶W. H. Taplin, U.S. Patent 3,420,833 (1969); Chem. Abstr. 71, 3279 (1969).
- ¹⁷H. J. den Hertog, J. C. M. Schogt, J. de Bruyn and A. de Klerk, *Recl. Trac. Chun. Pays-Bas* 69, 673 (1950).