Competition Between Reductive Dehalogenation and Nucleophilic Aromatic Substitution of Nitro-activated Iodine by Amines

By FRANCESCO PIETRA,* MAURO BARTOLOZZI, and FRANCESCO DEL CIMA
(*Department of Chemistry, Università di Pisa,* 56100 *Pisa, Italy*)

Summary Reductive dehalogenation competes effectively with nucleophilic aromatic substitution in nitro-activated halogeno-compounds when the nucleophile is a bulky amine and the halogen is iodine, but not when it is chlorine or fluorine; a radical mechanism is suggested.

IN rare instances reductive dehalogenation occurs alongside nucleophilic aromatic substitution and the factors determining this are not understood.

We report here that such reductive dehalogenations are much more common than previously thought, and often occur in attempts to replace a nitro-activated iodine atom by a bulky amine. Thus, we have observed that by heating 1-iodo-2-nitrobenzene (*ca.* 5×10^{-2} M) in neat 2-methylpiperidine at 100°, nitrobenzene and *N*-(2-nitrophenyl)-2-methylpiperidine are obtained as the main products (v.p.c.). Nitrobenzene predominated over the substitution product for all reaction times, and after *ca.* 150 h the initial iodo-compound had almost completely disappeared. The corresponding reaction of 1-iodo-4-nitrobenzene was similar, although formation of both nitrobenzene and *N*-(4-nitrophenyl)-2-methylpiperidine is much slower, 150° and 250 h being required, and the yields were low.

Since the reactions of both iodo-compounds with piperidine are relatively rapid at 50° (the 2-nitro- reacts more quickly than the 4-nitro-compound) and since iodine is quantitatively replaced by the amino-nitrogen in both cases, the reductive deiodinations are suggested to have a steric origin. In accordance with this, another sterically hindered amine, di-isopropylamine, gives mainly nitrobenzene when heated with 1-iodo-2-nitrobenzene. Its reaction with 1-iodo-4-nitrobenzene is much too slow, even at 150°, to be followed.

The hindrance of the amine which is required for reductive deiodination appears to be greater as the iodine atom becomes more activated. Thus, both piperidine and 2-methylpiperidine quantitatively replace iodine from picryl iodide in benzene. However, a more hindered amine, *cis*-2,6-dimethylpiperidine,[1] gives more trinitrobenzene than *N*-picryl-*cis*-2,6-dimethylpiperidine in benzene at 60°.

It is important to note that among the halogens so far investigated reductive dehalogenation seems to be peculiar to iodine. In the case of fluorine only substitution by hindered amines occurs.[1] We have now observed that the same is true for chlorine. Heating of 1-chloro-2-nitrobenzene (*ca.* 5×10^{-2} M) in neat 2-methylpiperidine for 16 days at 100° gave no nitrobenzene, while 25% of the theoretical amount of *N*-(2-nitrophenyl)-2-methylpiperidine was obtained. In the corresponding case of 1-chloro-4-nitrobenzene again no nitrobenzene was formed, while 5% of the theoretical amount of *N*-(4-nitrophenyl)-2-methylpiperidine was obtained after 20 days at 150°

Thus, when a high activation barrier (due to primary steric effects) hinders nucleophilic aromatic substitution of a nitro-activated iodine, reductive deiodination becomes competitive.† It is also clear from the above data and from a comparison with previous work[2] that no especially high primary steric effects are involved in the case of iodine relative to the other halogens. Thus, for reactions with 2-methylpiperidine, formation of the substitution product is faster for 1-iodo- than for 1-chloro-2-nitrobenzene and the *ortho:para* ratios are greater than unity for reactions of both iodo- and chloro-compounds.

Any mechanistic suggestion must thus involve some property of iodine other than its size. We have considered the possibility that iodonitrobenzenes behave as electron acceptors from some electron donating species thus generating a radical anion from which iodide is readily lost to give a nitro-aryl free radical. This can abstract hydrogen to give the observed products of reductive dehalogenation.‡

Two pieces of evidence give some support to this mechanism. Thus, the reaction of 1-iodo-2-nitrobenzene with 2-methylpiperidine in the presence of *ca.* 5×10^{-2} M *m*-dinitrobenzene (which is a better electron acceptor than a mononitroaryl compound[3]) caused a reduction in the formation of nitrobenzene, Moreover, when 1-iodo-2-nitrobenzene was heated with excess of neat tri-n-butylamine for 10 days at 150°, 45% of the theoretical amount of nitrobenzene was formed. No nitrobenzene was observed in the corresponding reaction with 1-chloro-2-nitrobenzene. This suggests that the amino-nitrogen behaves as the electron donating species.

It is more difficult, without further research, to answer the question of whether the products of iodine substitution by the amino-nitrogen arise entirely *via* S_NAr.[4] In fact, added *m*-dinitrobenzene slightly (but measurably) depresses also the formation of *N*-(2-nitrophenyl)-2-methylpiperidine in the reaction of 1-iodo-2-nitrobenzene with 2-methylpiperidine. We acknowledge financial support from C. N. R., Roma.

(*Received, August* 10*th,* 1971; *Com.* 1388.

† That the products of reductive deiodination reported here do not arise from thermal decomposition of either the starting iodo-compounds or of the products of nucleophilic aromatic substitution was proved by heating the appropriate compounds in benzene for periods and at temperatures similar to those used in the runs with the amines.

‡ Formation of aryl radicals from 5- or 6-iodo-pseudocumenes *via* a similar path has recently been suggested. (J. K. Kim and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 7463, 7464). Moreover, it has been recently shown that the lifetime of radical anions from 4-nitrobenzyl halides (for decomposition into 4-nitrobenzyl radical and halide ion) sharply decreases with increasing halogen atomic number (M. Mohammad, J. Hajdu, and E. M. Kosower, *J. Amer. Chem. Soc.*, 1971, **93**, 1792). This suggests also that some reductive dehalogenation might be observed even for bromo-compounds and hindered amines.

[1] F. Pietra and F. Del Cima, *J. Org. Chem.*, 1968, **33**, 1411.
[2] F. Pietra, D. Vitali, F. Del Cima, and (in part) G. Cardinali, *J Chem. Soc.* (*B*), 1970, 1659, and references therein.
[3] N. Kornblum, R. E. Michel, and R. C. Kerber, *J. Amer. Chem. Soc.*, 1966, **88**, 5660.
[4] F. Pietra, *Quart. Rev.*, 1969, **23**, 504.

Printed by W Heffer & Sons Ltd Cambridge England