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OCCURENCE AND DRIVING FORCES FOR REDUCTIVE DEIODINATION OF HALOAROMATICS BY BULKY AMINES

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Reductive deiodination competes with nucleophilic aromatic substitution for some nitro-activated iodoaromatics and bulky amines, a radical route having been suggested.[1] We report here that such reductions neither are observed under aza-activation nor are the rule for nitro-activation itself. Thus, 2-iodo-, 2-bromo-, or 2-chloropyridine, as well as 2-iodopyrimidine, when heated in neat 2-methylpiperidine under N_2 gave, at all reaction times, only the respective products of normal aromatic substitution of the halogen, besides unreacted iodocompound, neither pyridine[2] nor pyrimidine[2] being detectable by v.p.c.. Moreover, 2-iodo-5-nitropyridine gave only a trace of the product of reductive deiodination, 3-nitropyridine,[2] when heated in 2-methylpiperidine, suggesting an inhibiting effect of the aza-group on reductive deiodinations induced by the nitro group.[1a]

To arrive at a plausible rationalization of the above chemistry, we have carried out two series of experiments. First, ordinary amine in the above experiments was replaced with labeled amine in order to ascertain the origin of the hydrogen incorporated into the reduced aromatics, and then the iodoaromatics were electrolytically reduced in order to learn about relative ease of reduction and lifetime of intermediates. Thus, nitrobenzene obtained from the reaction of 2-iodonitrobenzene with neat N-^{2}H-2-methylpiperidine showed no deuterium incorporation, suggesting that a nitrophenyl radical has abstracted C-H hydrogen atoms from the amine. In fact, either a conceivable carbanionic route to reductive deiodination via nucleophilic attack on the halogen,[3] or reduction by hydrogen iodide,[4] or, finally, a radical route[1] followed by reduction of the intermediate radical to a carbanion,[5] would have led to 2-^{2}H-nitrobenzene because the carbanion would have looked for the strongest available acid ($C_6H_{12}ND_2^+$, arising from competing aromatic substitution).

Then, we have found by cyclic voltammetry in dry DMF plus Et_4NClO_4, reference Ag/AgCl, that 2-iodopyridine and 2-iodopyrimidine are reduced, irreversibly at all potential sweep scan rates, to their radical anions at more negative potentials (-1.7 and -1.2 V, respectively) than either 2-iodonitrobenzene or picryl iodide

(−1.0 and −0.07 V, respectively, also always irreversibly). Therefore, aza-activated iodoaromatics are too poor reducing agents to abstract one electron from aliphatic amines, thus resisting reductive deiodination.

However, lack of reductive deiodination of 2-iodo-5-nitropyridine must have a different origin because this compound is reduced at a less cathodic potential (−0.77 V) than either 2- or 4-iodonitrobenzene. The point here is that the ortho-aza group imparts an appreciably greater stability to the iodoazanitroaromatic radical anion, as deduced by reversible reduction, than 4- and, particularly, 2-iodonitrobenzene radical anion.[6] Therefore, it is conceivable that decreased importance of reductive deiodination on going from 2-iodonitrobenzene to 4-iodonitrobenzene[7] and, finally, to 2-iodo-5-nitropyridine, with increasing lifetime of the intermediate radical anion results from back oxidation of the longer living intermediate, at a faster rate than it can lose iodide, probably by radical products of the short lived aminium radicals,[8] thus aromatic substitution gaining chances to predominate.

We conclude that in order to observe reductive dehalogenation of ground-state haloaromatics by amines not only must the red-ox potentials of the couple of reagents be favorable for electron transfer from the amine to the haloaromatic, but the instability requirements of the resulting haloaromatic radical anion may be quite stringent.[9] If these observation are general, these might also be conditions leading to aromatic nucleophilic substitution *via* the radical path[1] which, possibly, could also be realized for both these and other classes of heterocyclics by electroreduction in the presence of nucleophiles. To this end other good leaving-groups, such as tosyloxy, could prove useful. We acknowledge financial support from C.N.R., Roma, and thank the Laboratorio Guidotti, Pisa, for use of the apparatus for cyclic voltammetry.

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