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HOMOLYTIC REDUCTIVE DEHALOGENATION OF ARYL HALIDES BY SODIUM BOROHYDRIDE

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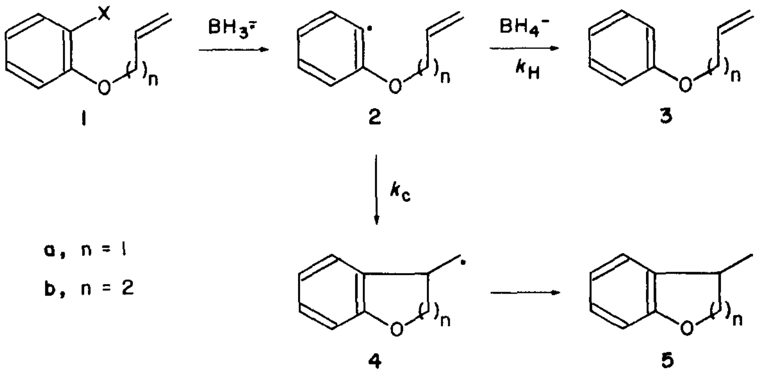
Abstract : Aryl iodides and some bromides, but not chlorides or fluorides, undergo efficient dehalogenation by UV photostimulated reduction with sodium borohydride and a free radical initiator in dimethylformamide.

Recent work in these laboratories has led to the development of an efficient dehalogenation procedure for a variety of organic halides involving UV photostimulated reduction with lithium aluminium hydride in the presence of di-tert-butyl peroxide.[1,2] In the reaction of aryl halides, the intermediacy of aryl radicals was demonstrated by the diagnostic ring-closure of the o-allyloxyphenyl radical (2a - 4a)[1,3,4].



In order to extend the scope of the reaction, and possibly to improve its selectivity, we decided to investigate the behaviour of other complex metal hydrides towards aryl halides under free radical conditions. We now describe the use of sodium borohydride for the reductive dehalogenation of aryl halides.

Early reports have described $NaBH_4$ as either being inert towards organic halides[5,6] or as being effective only in the reductive dehalogenation of secondary and tertiary alkyl halides capable of forming carbocation intermediates[7]. However, in polar aprotic solvents, $NaBH_4$ has been shown to reduce a variety of alkyl halides[8]. Interestingly, it has also been claimed that iodo- and bromo- as well as chloro-arenes can be photoreduced in quantitative yield by $NaBH_4$ in aqueous acetonitrile solution via a radical chain mechanism[9]. In the present study, preliminary experiments (runs 2,7,8) demonstrated that $NaBH_4$ in DMF solution was effective in reducing aryl iodides and bromides when subjected to UV irradiation in the presence of di-tert-butyl peroxide (DTBP) at 70-80°. Reduction was also observed at ambient temperature although at a slower rate (run 3). If the initiator (DTBP) was absent or photostimulation was not used yields were much reduced (runs 4 and 5), while when neither initiator nor photostimulation were employed, reduction became very slow indeed (runs 1 and 6). Temperatures in excess of 100° were undesirable due to the decomposition of the DMF solvent and the gradual discolouration of the reaction mixture.

The present dehalogenation procedure utilises radiation from a medium pressure Hg lamp, and contrasts with the photoreductions of Barltrop et al.[9] involving shorter wavelength (λ=254nm) radiation to which Pyrex glassware is essentially opaque. In a typical reaction, a well stirred mixture of the aryl halide(2 mmol), di-t-butyl peroxide (2 mmol) and 10 ml of a clear solution of 1M sodium borohydride in dimethylformamide was irradiated in a Pyrex flask at close range with a 250W medium pressure mercury lamp while the temperature was maintained at 70-80°. After 2-3 h, GLC usually indicated that all starting material had been consumed. The mixture was then acidified and the product isolated by extraction with ether. Product analysis was achieved by GLC using appropriate reference compounds and by NMR spectroscopy.

The results (see Table) show that the reductive dehalogenation process is most efficient for aryl iodides, but a reactive bromide, 1-bromonaphthalene, is also readily reduced. Other aryl bromides appear to undergo incomplete reaction under the usual conditions. Aryl chlorides are slow to react while fluorides are almost inert. These marked differences in the reducibility of the various halogens contrasts with the facile dehalogenation of iodo-, bromo-, chloro- and fluoro-arenes by $LiAlH_4$ under free radical conditions[2]. The much greater selectivity of $NaBH_4$ allows iodo functionality to be efficiently removed in the presence of chloro or fluoro substituents. The use of $NaBH_4$ as a deiodinating agent was further explored on a number of iodoarenes bearing a range of diverse substituents [COOMe, CN, CF_3, OMe, $N(Me)_2$]. In each case, the reduction was achieved selectively and in good yield. In particular, the reagent has an advantage over $LiAlH_4$ in that it does not reduce ester and nitrile functions.

We believe that the reaction follows, at least in part, the mechanism adumbrated in the Scheme. Its essential radical character is indicated by the dramatic effect of the addition of initiator on the reaction rate (compare runs 1,2 & 4) and by the occurrence of the

Run	Halide	Conditions[a]	Product	% Yield[b]
1.	1-bromonaphthalene	80°/7h	naphthalene	6[c]
2.	"	DTBP/$h\nu$/80°/5h	"	95
3.	"	DTBP/$h\nu$/15°/9h	"	60[c]
4.	"	$h\nu$/80°/4h	"	40[c]
5.	"	DTBP/80°/4h	"	11[c]
6.	o-allyloxyiodobenzene	80°/2h	mixture[d]	10[c]
7.	"	DTBP/$h\nu$/80°/2h	mixture[e]	75
8.	"	DTBP/$h\nu$/80°/2h[f]	mixture[g]	88
9.	p-iodoanisole	DTBP/$h\nu$/70°/2h	anisole	89
10.	p-iodo-N,N-dimethylaniline	DTBP/$h\nu$/80°/3h	N,N-dimethylaniline	85
11.	p-iodobenzonitrile	DTBP/$h\nu$/70°/2h	benzonitrile	91
12.	p-iodobenzotrifluoride	DTBP/$h\nu$/70°/2h	benzotrifluoride	92
13.	p-iodomethyl benzoate	DTBP/$h\nu$/70°/3h	methyl benzoate[h]	90
14.	p-fluoroiodobenzene	DTBP/$h\nu$/70°/2h	fluorobenzene	82
15.	p-chloroiodobenzene	DTBP/$h\nu$/70°/2h	chlorobenzene	89
16.	p-bromo-N,N-dimethylaniline	DTBP/$h\nu$/80°/8h	N,N-dimethylaniline	44[c]
17.	4-bromobiphenyl	DTBP/$h\nu$/80°/6h	biphenyl	74[c]
18.	o-allyloxybromobenzene	DTBP/$h\nu$/80°/5h	mixture[i]	22[c]
19.	p-chlorotoluene	DTBP/$h\nu$/80°/5h	toluene	18[c]
20.	o-fluoroanisole	DTBP/$h\nu$/80°/8h	anisole	<1[c]
21.	o-3-butenyloxybromobenzene	DTBP/80°/2h	mixture[j]	50[c]

[a] The reactions were carried out as described in the text unless otherwise specified. The conditions indicate whether di-t-butyl peroxide (DTBP) and UV irradiation (h) were employed; and show the temperature and time for reaction. [b] As determined by GC analysis. [c] The remaining material was essentially the unreacted substrate halide. [d] Consisted of 3a ($\sim$5%) and 5a ($\sim$5%). [e] Consisted of 3a (44%) and 5a (31%). [f] [NaBH$_4$] = 0.5M. [g] Consisted of 3a (32%) and 5a (56%). [h] Also contained 4% of benzyl alcohol. [i] Consisted of 3a ($\sim$2%) and 5a ($\sim$20%). [j] see text.

diagnostic ring closure, 2a → 4a (runs 7 & 8). As expected (runs 7, 8) the ratio of the yield of allyloxybenzene (3a) to that of 3-methyl-2,3-dihydrobenzofuran (5a) increases with an increase in the concentration of NaBH$_4$. Surprisingly, this ratio is not the same for reactions of the bromide (1a, X=Br) as it is for the iodide (1a, X=I) under identical experimental conditions (runs 7, 18). The usual steady-state treatment indicates that $k_c/k_H.[BH_4^-]_m = 5a\%/3a\%$ where $[BH_4^-]_m$ is the mean concentration of sodium borohydride. When applied to the data for runs 7 and 18 it gives an apparent value for k_c/k_H of 10M at 80° for reduction of 1a(X=Br) and of 0.7M for reduction of 1a(X=I). Substitution of the value for

k_c (1.2×10^{10} s^{-1})[10] gives apparent values of k_H of 1.2×10^9 and 1.7×10^{10} $M^{-1}s^{-1}$ respectively. The discrepancy between the two values and the fact that the latter is unreasonably high suggests that there may be an alternative mechanistic pathway from **1a** to **3a**, which is more important for the iodide than it is for the bromide.

In an attempt to obtain a more meaningful value for k_H the bromide **1b(X=Br)** was treated with a large excess of a mixture of Bu_3SnH (0.05M) and $NaBH_4$ (0.45M) in DMF/benzene (85:15) to give **3b** and **5b** in relative yields of 14.5% and 85.5% respectively. Under these conditions both $[Bu_3SnH]$ and $[BH_4^-]$ are essentially constant during the reaction. The usual steady state treatment gives $R.k_c = k'_H[Bu_3SnH] + k_H[BH_4]$ where R is the ratio of yields **3b**%/**5b**%. Since R = 0.17 at 80°, and the values of k_c and k'_H, the rate constants for ring closure of **2b** and for hydrogen transfer from Bu_3SnH, are known[10,11] to be 8.11×10^8 s^{-1} and 7.94×10^8 $M^{-1}s^{-1}$ respectively the equation can be solved. The value obtained is $k_H = 2.1 \times 10^8$ $M^{-1}s^{-1}$ at 80°.

The nature of the alternative pathway from **1** to **3** has not yet been elucidated; possibly it involves carbanionic intermediates. The intimate nature of the reaction of $BH_3^{\bullet-}$ with aryl halides to afford aryl radicals also requires clarification. The simplest hypothesis consistent with the evidence involves intial electron transfer from $BH_3^{\bullet-}$ to ArX followed by dissociation of $ArX^{\bullet-}$ in the usual way. However, at this stage one cannot preclude direct halogen transfer.

Further studies designed to probe these and other unresolved mechanistic problems are in hand.

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11 The value of k_c for cyclisation of **2b** was determined by the tributylstannane method as previously described for cyclisation of **2a** (ref. 10).

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