Formation of Dihydrobenzofurans by Radical Cyclization

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Summary A survey of methods for the generation of aryl radicals from *o*-alkenyloxyarene diazonium salts demonstrates that dihydrobenzofuran derivatives can be efficiently formed by treatment of (**1**) or (**2**) with $\mathrm{Bu}^{n}_{3}\mathrm{SnH}$–$\mathrm{Et_2O}$ or with NaI–$\mathrm{Me_2CO}$; methods utilising the iodo-compound (**3**; X = I) are less effective.

Aryl radicals containing suitable *o*-alkenyl and similar substituents undergo rapid regiospecific *exo*-ring closure.[1] Previous studies of these reactions involved treatment of appropriate arenediazonium salts with titanous ion, or of aryl iodides with $\mathrm{Bu}^{n}_{3}\mathrm{SnH}$. We now survey convenient alternative procedures of possible synthetic utility.

The yields of dihydrobenzofuran derivatives obtained when suitable arenediazonium salts (**1**) or (**2**) were treated with various reagents are summarised in Table 1. The results show that $\mathrm{Bu}^{n}_{3}\mathrm{SnH}$ is a relatively efficient reagent for achieving reductive cyclization of (**1**) or (**2**). Although the reaction undoubtedly involves the intermediacy of aryl radicals, *e.g.* (**6**), the mechanism of their formation has not yet been clarified. However, a chain propagation step involving electron transfer appears reasonable,[2] and a possible reaction scheme is shown in equations (1)—(4).

$$(\mathbf{1}) + \mathrm{Bu_3Sn}\cdot \longrightarrow (\mathbf{6}) + \mathrm{N_2} + \mathrm{Bu_3Sn^+} \tag{1}$$

$$(\mathbf{6}) \longrightarrow (\mathbf{8}) \tag{2}$$

$$\mathrm{Bu_3SnH} + (\mathbf{8}) \longrightarrow \mathrm{Bu_3Sn}\cdot + (\mathbf{4};\ \mathrm{X} = \mathrm{H}) \tag{3}$$

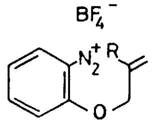
$$\mathrm{Bu_3Sn^+} + \mathrm{BF_4^-} \longrightarrow \mathrm{Bu_3SnF} + \mathrm{BF_3} \tag{4}$$

In accord with this scheme the reaction mixture was found to contain $\mathrm{Bu_3SnF}$ and $\mathrm{BF_3}$.

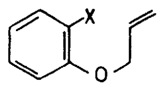
Table 1. Products from *o*-alkenyloxybenzene diazonium borofluorides.

Substrate	Reagent	Solvent[a]	Temp./°C	Time	Product	Yield/%
(**1**)	$\mathrm{Bu}^{n}_{3}\mathrm{SnH}$	$\mathrm{Et_2O}$	35	2 h	(**4**; X=H)	75[b]
(**1**)	$\mathrm{Bu}^{n}_{3}\mathrm{SnH}$	THF	67	15 min	(**4**; X=H)	76[b]
(**2**)	$\mathrm{Bu}^{n}_{3}\mathrm{SnH}$	$\mathrm{Et_2O}$	35	15 h	(**5**; X=H)	71
(**1**)	$\mathrm{Ph_3SnH}$	$\mathrm{Et_2O}$	35	15 h	(**4**; X=H) (**3**; X=H)	32[b] 5[b]
(**1**)	0·1M NaOMe	MeOH	65	15 min	(**4**; X=H)	47[b]
(**1**)	NaI	$\mathrm{Me_2CO}$	20	10 min	(**4**; X=I)	86
(**2**)	NaI	$\mathrm{Me_2CO}$	20	10 min	(**5**; X=I)	89
(**1**)	$\mathrm{CuBr_2}$	DMSO	20	15 h	(**4**; X=Br)	82
(**2**)	$\mathrm{CuBr_2}$	DMSO	20	15 h	(**5**; X=Br)	89
(**2**)	$\mathrm{CuCl_2}$	DMSO	20	15 h	(**5**; X=Cl)	63
(**2**)	CuCN	DMSO–pyridine	20	10 min	(**5**; X=CN)	40
(**2**)	$\mathrm{NaSBu^n}$[c]	DMSO	20	10 min	(**5**; X=$\mathrm{SBu^n}$)	63
(**2**)	NaSPh	DMSO	20	1 h	(**5**; X=SPh)	60

[a] THF = tetrahydrofuran, DMSO = dimethylsulphoxide. [b] Yield determined by g.l.c. [c] Copper powder was added to the reaction mixture before addition of the diazonium salt.



(1) R = H
(2) R = Me



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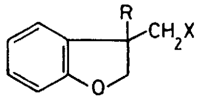
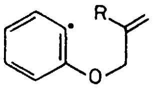
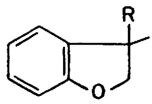


(4) R = H
(5) R = Me



(6) R = H
(7) R = Me



(8) R = H
(9) R = Me

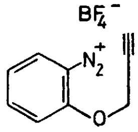
The formation of some uncyclized product (**3**; X = H) from treatment of (**1**) with $\mathrm{Ph_3SnH}$ involves direct hydrogen-atom transfer to (**6**). It is consistent with the fact that $\mathrm{Ph_3SnH}$ is a more effective hydrogen atom donor than $\mathrm{Bu^n_3SnH}$.[3]

Table 2. Products from *o*-iodoallyloxybenzene (**3**; X=I).

	Solvent	Temp./°C	Time	Products	Yield/%
Sodium naphthalenide	THF	20	10 min	(**4**; X=H) (**3**; X=H)	3 14
$[\mathrm{Cr^{II}en_2(ClO_4)_2}]$	$\mathrm{DMF{-}H_2O}$	20	10 min	(**4**; X=H) (**3**; X=H)	16 69
U.v. irradiation[a]	NaOMe in MeOH (2·2M)	30	12 h	(**4**; X=H)	45
U.v. irradiation[a]	$\mathrm{n{-}C_6H_{12}}$	30	12 h	(**4**; X=I)	65[b]

[a] Irradiated in a Rayonet apparatus fitted with seven 35 W low-pressure mercury lamps. [b] Starting material (20%) was recovered.

The Bunnett procedure[4] for generation of aryl radicals from diazonium salts gives only modest yields of cyclized products but is convenient for large scale work. It is useful, also, for reduction of substrates containing an alkynyl group. Thus, treatment of (**10**) with 0·1M NaOMe in MeOH affords (**11**) (31%), whereas the reaction with $\mathrm{Bu^n_3SnH}$ gives only the benzofuran (**12**) (50%) presumably *via* $\mathrm{BF_3}$-catalysed rearrangement of (**11**).



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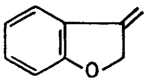

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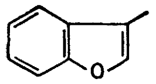

(12)

We also investigated reactions of (**1**) and/or (**2**) with a number of other reagents including hypophosphorous acid, Zn–EtOH, $\mathrm{NaBH_4}$, $\mathrm{Me_3SiH}$, sodium stannite, and $\mathrm{Cu_2O}$–dioxan. Most of them gave cyclic products in small yield but the mixtures were heavily contaminated with tars.

The diazonium salts (**1**) and (**2**) are also useful precursors for functionalised dihydrobenzofurans. The formation of halides or cyanides, *e.g.* (**4**; X = I, Br, Cl, CN) in moderate to good isolated yields accords with the view[5] that reagents such as NaI in $\mathrm{Me_2CO}$, $\mathrm{Cu^{II}}$ halides, or CuCN generate aryl radicals from diazonium salts. When (**1**) was treated with reagents believed to generate carbonium ions,[6] *viz.* hot dilute $\mathrm{H_2SO_4}$,† or hot $\mathrm{CF_3CH_2OH}$, no dihydrobenzofurans were detected.

The reactions affording (**5**; X = SBu or SPh) are of especial interest because their mechanisms appear to involve the chain propagation steps (5) and (6) [$\mathrm{Y}^\bullet \equiv$ (**9**)].

$$\mathrm{Y}\bullet + \mathrm{RS}^- \longrightarrow \mathrm{YSR}^{\bullet -} \tag{5}$$

$$\mathrm{YSR}^{\bullet -} + (\mathbf{2}) \longrightarrow \mathrm{YSR} + (\mathbf{7}) + \mathrm{N_2} \tag{6}$$

Similar radical anions, $\mathrm{ArSR}^{\bullet -}$, have been postulated as intermediates in reactions of aryl radicals with alkanemercaptides.[7]

Methods utilizing the aryl iodide (**3**; X = I) were less effective for the preparation of bicyclic systems. Treatment of (**3**; X = I) with electron-transfer agents gave mainly uncyclized reduction product; clearly a second reduction step, $\mathrm{Ar}\bullet \xrightarrow{e} \mathrm{Ar}^-$, competes effectively with cyclization. However, u.v. irradiation of (**3**; X = I) in alkaline MeOH or in $\mathrm{C_6H_{12}}$ gave moderate yields of (**4**; X = H) and (**4**; X = I) respectively. In the latter case careful control of the reaction is necessary for (**4**; X = I) is itself subject to photolysis.

In summary, $\mathrm{Bu^n_3SnH}$ in $\mathrm{Et_2O}$, or NaI in $\mathrm{Me_2CO}$, appear to be particularly efficient reagents for effecting radical cyclization of suitable diazonium salts.

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† Some *o*-allyloxyphenol was formed in this experiment.

[1] A. L. J. Beckwith and W. B. Gara, *J. Chem. Soc., Perkin Trans.* 2, 1975, 593, 795.

[2] E. V. Blackburn and D. D. Tanner, *J. Am. Chem. Soc.*, 1980, **102**, 692.

[3] D. J. Carlsson and K. U. Ingold, *J. Am. Chem. Soc.*, 1968, **90**, 7047.

[4] J. F. Bunnett and H. Takayama, *J. Am. Chem. Soc.*, 1968, **90**, 5173.

[5] D. H. Hey, G. H. Jones, and M. J. Perkins, *Chem. Commun.*, 1970, **1438**; S. H. Pines, R. M. Purick, R. A. Reamer, and G. Gal, *J. Org. Chem.*, 1978, **43**, 1337; A. F. Hegarty in 'The Chemistry of Diazonium and Diazo Groups,' ed. S. Patai, Wiley, New York, 1978, vol. 2, ch. 12, and references cited therein.

[6] H. Zollinger, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 141; H. B. Ambroz and T. J. Kemp, *Chem. Soc. Rev.*, 1979, **8**, 353.

[7] J. F. Bunnett and X. Creary, *J. Org. Chem.*, 1975, **40**, 3740.