

Some Novel Concepts in Aromatic Reactivity

Joseph F. Bunnett

Thimann Laboratories, University of California
Santa Cruz, CA 95064

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Abstract: Suggestions¹ that radical-chain reactions of aryl halides with alkoxide ions, nucleophiles and alkenes occur via attack of these reagents on the aryl halide radical anion, rather than on the radical that results from fragmentation of the radical anion, are examined in detail. Several conceivable mechanisms for the suggested direct displacement of halide ion from the radical anion by a nucleophile are examined; all are unacceptable because of violation of quantum-mechanical principles or incompatibility with experimental observations. Steps involving attachment of a hydrogen atom or an alkene molecule to C-1 of an aryl halide radical anion, to form a cyclohexadienide ion intermediate, lack experimental precedent.

In recent years several types of reactions of aryl halides have been proposed to occur via mechanisms that involve electron transfer to the aryl halide, fragmentation of the resulting radical anion to an aryl radical, and ensuing reaction of the radical. In a 1991 paper,¹ Denney and Denney proposed instead that several such reactions involve direct involvement of the aryl halide radical anion in the "ensuing" reaction, without the aryl radical being an intermediate.

The Denneys' mechanistic proposals are novel, largely unprecedented, devoid of compelling experimental support, some might think absurd. But whether they are absurd is beside the point; many scientific concepts that struck some as ridiculous when first proposed subsequently became cornerstones of scientific theory. Witness van't Hoff's proposal of the tetrahedral carbon atom,² which was ridiculed by Kolbe in a notorious article.³ The only valid ground for rejection of an hypothesis is incompatibility with experimental ev-

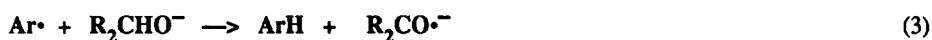
idence or with sound scientific theory.⁴ Accordingly, I recommend that persons interested in this area of chemistry study the Denneys' paper carefully, indeed, very carefully, as I shall later emphasize.

I. RADICAL-INDUCED DEHALOGENATION OF ARYL HALIDES BY ALKOXIDE IONS.^{5,6}

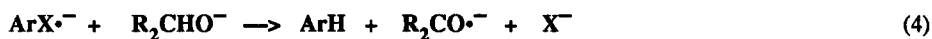
Overall reaction:^a



*Steps proposed by others:*⁶

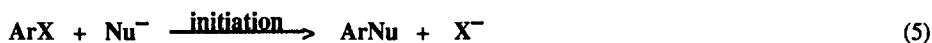


*Alternatively proposed by the Denneys:*⁷



II. RADICAL-CHAIN, ELECTRON TRANSFER NUCLEOPHILIC SUBSTITUTION.⁸⁻¹⁰

Overall reaction:^b



Steps proposed by others: ($S_{\text{RN}}1$):

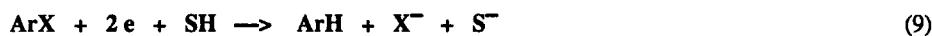


Alternatively proposed by the Denneys ($S_{\text{RN}}2$):



III. CATHODIC DEHALOGENATION OF ARYL HALIDES.¹¹

Overall reaction:^c



Steps proposed by others:^d



Alternatively proposed by the Denneys:



a M \cdot represents an initiator radical; Ar an aryl group.

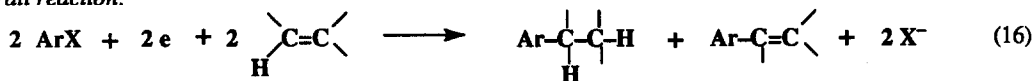
b Initiation by supplying electrons, or photons.

c SH represents a solvent molecule, a hydron donor.

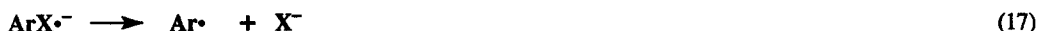
d Somewhat simplified.

IV. ARYLATION OF ALKENES.^{12,13}

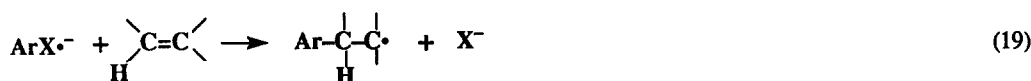
Overall reaction:



Steps proposed by others:



Alternatively proposed by the Denneys:



DISCUSSION

Lifetimes of Aryl halide Radical Anions. Central to the Denneys' hypotheses is their belief that aryl halide radical anions exist long enough to participate in postulated bimolecular steps 4, 8 and 19. It appears to stem from two sources: evidence that nitrophenyl halide radical anions are comparatively long-lived, and an impression that understanding of factors affecting the lifetimes of aryl halide radical anions is in disarray.

Most radical anions of halonitrobenzenes are comparatively long-lived. An extensive electrochemical investigation¹⁴ of $\text{ArX}^{\bullet-}$ fragmentation rates (at 23°C in DMF) revealed rate constants around 10^{-2} s^{-1} , implying half-lives of a minute or longer. For *o*-bromo- and *o*-iodonitrobenzenes, however, fragmentation was much faster; rate constants were, respectively, 20 and $>100 \text{ s}^{-1}$. Similar observations were made by other workers.¹⁵ In liquid ammonia at -40°C, fragmentation of the radical anions of halonitrobenzenes is very slow, but the dianions fragment.¹⁶ These observations, especially in ammonia at -40°C, are consistent with the Denney postulates for reaction type III, as represented in eqs. 13 and 14.

There are however many indications that the radical anions of phenyl and naphthyl halides, unsubstituted or bearing substituents such as methoxy or methyl, have extremely short lifetimes. Namiki¹⁷ examined optical and ESR spectra of γ -irradiated frozen ethanol solutions of the phenyl halides. He could not detect the radical anion of chloro-, bromo- or iodobenzene even at 4 K; the spectra indicated fragmentation to phenyl radical and halide ion. The radical anions of the chloro- and bromonaphthalenes and of fluorobenzene were observable under those conditions, but they fragmented on "warming" to 77 K. The most extensive determinations of fragmentation rates of aryl halide radical anions are due to Savéant and coworkers; their data^{10,18} show a wide spread, from rate constants (in dimethyl sulfoxide solution) around 10^{-2} s^{-1} for nitro-substituted phenyl halides up to about 10^{10} s^{-1} for *p*-cyanophenyl halides. Rate constants for unsubstituted phenyl ha-

lides are too high to be measured accurately even by sophisticated electrochemical techniques. The Savéant data^{10,19} show linear correlations of fragmentation $\log k$ with E° for $\text{ArX}/\text{ArX}^{\bullet-}$, for aryl bromides and chlorides. The rate constants of Savéant et. al. are broadly consistent with measurements by pulse radiolysis.^{20,21}

It is well recognized that cathodic cleavage of many aryl halides in solvents that are not good hydrogen atom donors is a two electron process, generating the aryl anion and halide ion. The Denneys aver that what cleaves is the aryl halide dianion (eq. 14), whereas Savéant et. al. interpret formation of the aryl anion in terms of steps 10 and 11. Important factors supporting the Savéant interpretation are that cathodic cleavage occurs at the potential of the $\text{ArX}/\text{ArX}^{\bullet-}$ couple, step 10 being extremely fast, and that the redox potential of the $\text{Ar}^\bullet/\text{Ar}^-$ couple is higher than of $\text{ArX}/\text{ArX}^{\bullet-}$. The work of Teherani and Bard¹⁶ shows that the potential required to effect reduction of $\text{ArX}^{\bullet-}$ to ArX^{2-} is some 0.8 v. more negative. Also, when reduction is performed in the presence of a redox catalyst that can carry electrons from the cathode to ArX molecules in the open solution, products of trapping of the phenyl radical are obtained.²²

That the Denneys consider understanding of factors affecting the lifetimes of aryl halide radical anions to be in disarray is suggested, for example, by statements concerning radical anions generated by pulse radiolysis. They said: "Dorfman²³ has commented on the difference between aromatic radical ions generated by pulse radiolysis and those produced by reduction with sodium in THF."¹ The suggestion of some incoherence in the data is not supported by Dorfman. He explained²³ that radical anions (e.g., of naphthalene) generated by reduction with Na in THF are ion-paired, except at very low concentrations, but "No such ion-pair complex exists in the alcohol solutions, and the aromatic radical anion may therefore be regarded as a free anion—not, of course, free of solvation, but free of any cation complexing." Although there is indeed a difference, it concerns factors well recognized by physical organic chemists, and if anything shows that the chemistry of radical anions is rather well understood. There are other statements from the literature in the Denneys' paper of similar character; although not exactly wrong, the statements don't quite convey what the cited authors said. Careful readers are therefore urged to read as well the papers cited by the Denneys.

In view of mentioned evidence that the radical anions of the kinds of aryl halides (unsubstituted or lacking strong electron-attracting substituents) involved in most studies of reactions of types I, II and IV fragment rapidly (step 2, 6, or 17), the Denneys' mechanisms are very unlikely for the majority if not all such reactions that have been reported. Their hypothesized steps 4, 8 and 19 would have to be exceptionally fast, as Rossi and Palacios²⁴ have pointed out, in order for them to compete significantly with $\text{ArX}^{\bullet-}$ fragmentation. Energy factors (*vide infra*) would seriously retard nucleophilic substitution involving the Denneys' step 8.

Radical Characteristics. The key difference between the Denney hypotheses and mechanisms favored by others is the identity of the radical that interacts with the hydrogen donor reagent (I), or nucleophile (II) or alkene (IV). Step 4 contrasts with step 3, step 8 with step 7, step 19 with step 18. Others posit the radical to be an aryl radical; according to the Denneys it is an aryl halide radical anion. The two kinds of radical are quite different. An aryl radical, such as phenyl radical,²⁵ has its odd electron in a σ atomic orbital,

where the spin density is rather concentrated inasmuch as that σ orbital is orthogonal to the π orbitals of the aromatic system. For an aryl halide radical anion, accommodation of its odd electron in an antibonding π^* MO, which is diffuse, is generally energetically favored^{19,26,27} over accommodation in the C-X σ^* MO. ($\text{ArX}^{\bullet-}$ with odd electron in the C-X σ^* MO have however been observed at 77 K;^{27,28} such σ^* radical anions are fragile intermediates in the fragmentation of $\text{ArX}^{\bullet-}$, not robust enough to be the persistent $\text{ArX}^{\bullet-}$ the Denneys postulate.)

How Would a π^* $\text{ArX}^{\bullet-}$ Interact with a Nucleophile? I now consider what kind of transition state or intermediate might be involved if a bimolecular step such as the Denney step 8 could occur. Two general possibilities are a concerted displacement of X^- by Nu^- , and an attachment-detachment sequence via an intermediate. Specific possibilities for concerted displacement are sketched in Fig. 1. The first three of these can easily be discarded. The $\text{S}_{\text{N}}2$ -like transition state involves back-side attack on C-1, which is sterically

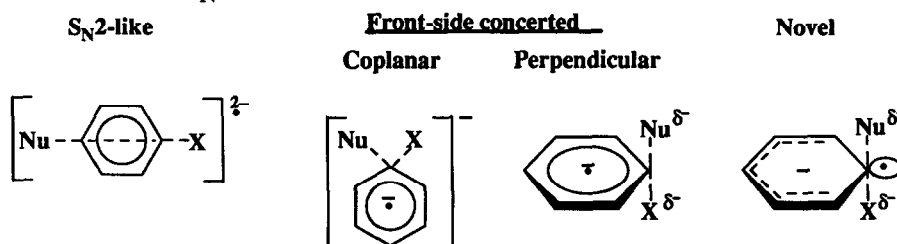


Figure 1. Conceivable $\text{S}_{\text{RN}}2$ displacement transition states.

blocked by C-4. Of the front-side concerted candidates, the coplanar is untenable because of the observed insensitivity of $\text{S}_{\text{RN}}1$ reactions to steric hindrance by *ortho* substituents,^{29,30} and the perpendicular because formation of half-bonds above and below the plane of the benzene ring would require utilization of the atomic p orbital of C-1, which cannot be “loaned” if aromatic character in the benzene π -system is to be preserved.³¹

The “Novel” one at the right calls for explanation. One might think of it as being formed by attack of a nucleophile on a resonance structure of $\text{PhX}^{\bullet-}$ that has five of the six ring carbons in a cyclohexadienide anion arrangement and C-1 an uncharged radical center with the odd electron in a carbon p orbital. The Novel transition state has sp^2 hybridization at C-1; besides the half-bonds to Nu and X, C-1 has a half-occupied sp^2 σ -orbital. I am unsure how such a transition state would be formed, and know of no clear precedent for it. It is what one would expect for $\text{S}_{\text{N}}2$ displacement at the α -carbon of an alkyl radical. There is a report³² that β -haloalkyl radicals solvolyze rapidly in water; it mentions some unassigned processes that might conceivably involve α -haloalkyl radicals, but that is hardly a firm precedent.

The intermediate in an $\text{S}_{\text{N}}\text{Ar}$ -like $\text{S}_{\text{RN}}2$ reaction is shown at the right in Fig. 2, and beside it the usual $\text{S}_{\text{N}}\text{Ar}$ intermediate (from unsubstituted phenyl halides). An important difference is that the $\text{S}_{\text{N}}\text{Ar}$ -like $\text{S}_{\text{RN}}2$ intermediate would need to accommodate seven electrons in its π -system; it would be, so to speak, the radical anion of a cyclohexadienide ion, with charge -2. The presence of a second electron in the π -system is esti-

mated to raise its Gibbs free energy by about 18 kcal/mole.³³ That increase in ΔG^\ddagger would retard rate (at 25°C) about 1.4×10^{13} -fold. That alone makes the Denneys' hypothesis untenable.

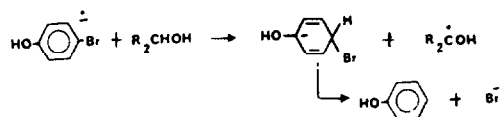
Both the "Novel" transition state and the $S_{\text{N}}\text{Ar}$ -like $S_{\text{RN}}2$ intermediate would be expected to be stabilized substantially by *o*- and *p*-nitro groups. Experimentally it has been observed, however, that nitrophenyl halides do not participate^{6,34} in the chain substitution reactions often designated $S_{\text{RN}}1$, whereas unsubstituted phenyl halides do.

Having found no transition state or intermediate for the postulated $S_{\text{RN}}2$ steps that is both acceptable in respect to quantum-mechanical theory and in accord with experimental facts,³⁵ I conclude that the $S_{\text{RN}}2$ mechanism is most unlikely for radical-chain, electron transfer nucleophilic substitutions (reaction type II).



Figure 2. The conventional $S_{\text{N}}\text{Ar}$ intermediate and an $S_{\text{N}}\text{Ar}$ -like $S_{\text{RN}}2$ intermediate

Reactions of Types I and IV. Inasmuch as $\text{ArX}^{\bullet-}$ species are radicals, although not σ -radicals, it is conceivable that they might abstract hydrogen atoms (type I) or attach to unsaturated C-atoms (type IV) to form intermediates of cyclohexadienide ion type. Thus, the following scheme from Denney and Denney:¹



Inasmuch as reaction steps such as Nos. 4 and 12, above, might not be especially fast, the probability of their being observed should be greater the longer-lived are $\text{ArX}^{\bullet-}$. Therefore, if a conscious search for compelling evidence of steps such as these were made, nitrophenyl halides would seem promising substrates. Insofar as radical-induced alkoxide dehalogenations (type I) are concerned, competing reactions ($S_{\text{N}}\text{Ar}$ alkoxydehalogenation, and reduction of the nitro group leading to azoxybenzenes, etc.³⁶) might however be troublesome. Certainly it would be interesting if one could find evidence that steps such as Nos. 4 and 19 can occur.

In summary, absolute rejection of the Denney hypotheses for all cases seems not possible. In particular, if it were demonstrated that aryl halide radical anions can react quickly with alkenes according to their postulated step 19, conclusions that aryl radicals are intermediates that have been drawn on the basis of intramolecular trapping by alkene structures³⁷ or intermolecular trapping by benzene⁶ would become dubious. Do some reactions involve steps such as shown in eq. 4 or 19?

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