

# Radical-Chain, Electron-Transfer Dehalogenation Reactions<sup>1</sup>

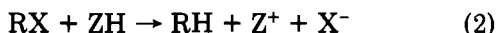
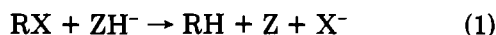
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My chief motivation in writing this Account is to tell about studies in my laboratory of the radical-induced dehalogenation of aryl halides by alkoxide ions. But also I want to point out that the reaction we have studied is of a broad category not well recognized, and to call attention to other processes within that category.

Most of the reactions in the category of interest conform to the abstract notation of eq 1. A few reactions appear to conform to eq 2. The category is



characterized by its mechanism, prominent features of which are abstraction of a hydrogen atom from ZH<sup>-</sup> or ZH, respectively, by radical R<sup>•</sup>, to form Z<sup>-</sup> or Z<sup>+</sup>, which are good electron donors, and ensuing transfer of an electron to RX, forming RX<sup>-</sup>, which fragments to regenerate R<sup>•</sup>.

## Radical-Induced Dehalogenation of Aryl Halides by Alkoxide Ions

A less abstract version of eq 1, appropriate to this case, appears in eq 3. One or both R groups may be hydrogen. There must be at least one  $\alpha$ -hydrogen.



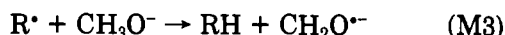
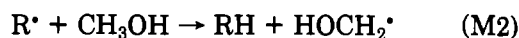
The radical-induced deiodination of aryl iodides by methoxide ion was first recognized by Carl Wamser,<sup>2</sup> an Sc.B. research student at Brown University, who was following up on an earlier, perceptive observation by postdoc Alan Happer,<sup>3</sup> of New Zealand. At the time, in 1965, I had no inkling that Happer's clue would lead

not only to discovery of a new type of reaction but also to insights into which antibonding orbitals are utilized in some variants of that reaction.

Most of Wamser's experiments were conducted in methanol with *m*-chloriodobenzene as substrate. Salient observations were that the reaction responds to typical radical initiators such as azobis(isobutyronitrile) (AIBN) and peroxydisulfate ion; that it requires methoxide ion (failing in neutral methanol); that in CH<sub>3</sub>OD the hydrogen that replaces iodine is protium (from the methyl group) rather than deuterium from the hydroxyl group; that it is strongly retarded by nitrobenzene; and that when *m*-chloriodobenzene undergoes deiodination in the solvent 50% methanol/50% benzene, a significant amount of *m*-chlorobiphenyl is formed.<sup>4</sup> These observations indicated the intermediacy of an aryl radical, rather than an aryl anion,<sup>5,6</sup> and suggested the involvement of an electron-transfer step that was cut off by nitrobenzene, a notorious electron thief.<sup>7,8</sup> On the basis of these observations, Wamser and I<sup>2</sup> proposed the mechanism of Scheme I.

In this mechanism, the crucial step in which an aryl iodide molecule becomes irrevocably involved is M5, in which it is forced to receive an electron from formaldehyde radical anion. The inhibitory effect of nitrobenzene is ascribed to its stealing electrons from formaldehyde radical anions before they can shove electrons onto aryl iodides. From the fact that strong base is essential, one judges that hydroxymethyl radical itself, generated in step M2 or M7, is not able to carry forward the chain by either electron transfer to aryl iodide or iodine abstraction<sup>9</sup> from it. Formaldehyde radical anion, formed from hydroxymethyl radical in acid-base equilibrium M4, is a much stronger electron donor.

### Scheme I



(1) A broad overview is in press for *Atti di Accademia Gioenia di Catania*.

(2) Bunnett, J. F.; Wamser, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 6712.

(3) On an earlier occasion, I took the opportunity to salute Happer's perspicacity.<sup>6</sup>

(4) The formation of *m*-chlorobiphenyl under similar conditions has more recently been confirmed by Jing-ji Cui in my laboratory.

(5) From current perspective, the idea that aryl anions might have been intermediates may seem naive. In 1966, it seemed a serious possibility, inasmuch as other dehalogenation reactions under study in my laboratory at that time did occur via aryl anions. See "Imposter Reactions" section.

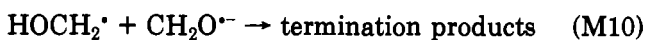
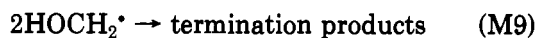
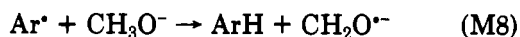
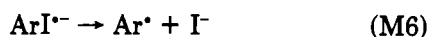
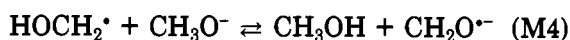
(6) Bunnett, J. F. *Acc. Chem. Res.* **1972**, *5*, 139.

(7) Russell, G. A.; Janzen, E. G.; Strom, E. T. *J. Am. Chem. Soc.* **1964**, *86*, 1807.

(8) Kerber, R. C.; Urry, G. W.; Kornblum, N. *J. Am. Chem. Soc.* **1964**, *86*, 3904.

(9) Bunnett, J. F.; Wamser, C. C. *J. Am. Chem. Soc.* **1966**, *88*, 5534.

Joseph F. Bunnett was born in Portland, OR, in 1921. His elementary education was at Wilkes School, which was small (80 pupils, eight grades, three teachers), located in a district near Portland that was half agricultural and half urban fringe. After Washington High School, he did undergraduate work at Reed College and graduate work at the University of Rochester (Ph.D., 1945). At the end of a year as research chemist for the Western Pine Association in Portland, he took a faculty post at Reed College. In 1952 he moved to the University of North Carolina, Chapel Hill. Further moves were to Brown University in 1958 and, finally (in 1966), to the one-year-old campus of the University of California, Santa Cruz, from which he formally retired last July. Important intellectual experiences were also years with hosts Christopher Ingold at University College, London (1949-1950), and Rolf Huisgen at the University of Munich (1960-1961), in both cases as a Fulbright grantee and at Munich also as a Guggenheim Fellow. His research has concerned mainly reaction mechanisms, particularly of reactions of aromatic compounds with nucleophilic reagents, with attention especially to two prominent substitution reactions (S<sub>N</sub>Ar and S<sub>N</sub>1). Outside of the lab, he has been a visiting professor at universities on all the world's continents plus New Zealand, was editor of *Accounts of Chemical Research* from the beginning of its organization in 1966 until 1986, and has served IUPAC as a member and chairman of the Commission on Physical Organic Chemistry and has an officer of the Division of Organic Chemistry, including a term as president. He has been a trustee of Reed College since 1970 and altogether may be said to be a Reed man. He has been elected a Fellow of the American Academy of Arts and Sciences and of the American Association for the Advancement of Science and an honorary member of the Società Chimica Italiana, the Pharmaceutical Society of Japan, the Sociedad Argentina de Investigaciones en Química Orgánica, and the Accademia Gioenia di Catania (Italy). He has been awarded the 1992 James Flack Norris Award in Physical Organic Chemistry, sponsored by the Northeastern Section of the American Chemical Society, administered by the American Chemical Society.



Some chemists prefer to represent the propagation cycle of a chain mechanism as in Figure 1, for the drawing of which we thank a referee.

Studies in Santa Cruz by Gaetano Tomaselli, of Catania, Sicily, have shown that dehalogenations can also be effected in liquid ammonia solvent, the sodium alkoxide (many are effective) being generated in situ. In such cases, AIBN was used as initiator, its homolysis being brought about by UV illumination. Further work, by Naser-ud-din of Peshawar, Pakistan, demonstrated that dimethyl sulfoxide (DMSO) is also a satisfactory solvent for these reactions.<sup>10</sup> Gaetano and Naser did many studies of relative reactivity, via competition experiments. Some of them are mentioned below.

**Overall Kinetics.** Considering the mechanism of Scheme I, and making the Bodenstein steady-state assumption,<sup>11</sup> one derives the kinetic expression of eq 4. It calls for a rate law first order in aryl iodide and half order in initiator (symbolized "In"). Experiment<sup>12</sup> indicated just those orders: 1.0 in aryl iodide (*m*-chloriodobenzene) and 0.5 in AIBN. The predicted order in methoxide ion depends on the relative rates of termination steps M9 thru M11. If M9 is so fast as to dwarf M10 and M11, the reaction should be first order in methoxide ion. Predominance of steps M10 and M11 leads to expectations of half and zero orders, respectively. The pseudo-first-order rate constant, at constant [ArI] and [AIBN], was found to be linear with potassium methoxide concentration, and the kinetic order was 0.86. Thus the agreement with expectation based on the mechanism of Scheme I is good.

$$\frac{-d[\text{ArI}]}{dt} = \frac{k_5 K_4 (k_1 f)^{1/2} [\text{ArI}] [\text{MeO}^-] [\text{In}]^{1/2}}{\{k_9 + k_{10} K_4 [\text{MeO}^-] + k_{11} K_4^2 [\text{MeO}^-]^2\}^{1/2}} \quad (4)$$

**Kinetics via Electrochemistry.** Using ingenious electrochemical methods, Savéant and co-workers<sup>13</sup> studied the reaction of present interest. Their results were in accord with the mechanism of Scheme I, except that initiation was by one-electron transfer to the aryl halide to form  $\text{ArX}^{\cdot-}$ . With strictly aliphatic alkoxides, high electron efficiencies were observed; for example, in the case of 2-chloroquinoline reacting with 2-propoxide, only 0.04 faraday/mol of substrate was required.<sup>14</sup> On the other hand, 1.09 faraday/mol was

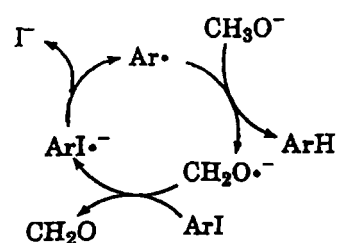


Figure 1. An alternative representation of the propagation cycle of Scheme I, showing steps M5, M6, and M8.

consumed in the induced reaction of 6-chloroquinoline with diphenylmethoxide ion; in this case, the radical anion resulting from hydrogen abstraction from the alkoxide (step M8) is benzophenone ketyl, which is stable in ammonia solution. Evidence was found that, in the cathodically induced reaction of 1-chloronaphthalene with diphenylmethoxide ion, some benzophenone dianion ( $[\text{Ph}_2\text{CO}]^{2-}$ ) was generated, and that it transferred electrons to 1-chloronaphthalene molecules. The studies of Savéant et al. allowed them to estimate rate constants for hydrogen capture step M8; they were in the range of  $10^7$ – $10^9$  L mol<sup>-1</sup> s<sup>-1</sup> at  $-40$  °C.

Other studies,<sup>15</sup> mainly utilizing cyclic voltammetry, have enabled evaluation of rate constants for the fragmentation of aryl halide radical anions. The constants depend on the identity of the halogen, the aromatic system, and substituents present, ranging from ca.  $10^{-2}$  s<sup>-1</sup> (for 4-chloronitrobenzene radical anion) to  $10^8$  s<sup>-1</sup> (for 2-chloronaphthalene radical anion) in solvent dimethylformamide (DMF) or DMSO, at 25 °C.

**Substituent Effects, with Aryl Iodides.** Relative reactivities, determined in competition experiments, of numerous ortho-, meta-, and para-substituted iodobenzenes afforded a good approximation to a linear plot of  $\log k_{\text{rel}}$  against  $\sigma$  constants.<sup>16</sup> The slope ( $\rho$ ) was +2.2. In organizing that plot, we used  $\sigma^\circ$  values of Exner<sup>17</sup> for meta and para substituents, and  $\sigma_o$  of Tribble and Traynham.<sup>18</sup> The latter are based on NMR chemical shifts of the hydroxyl proton in DMSO solutions of ortho-substituted phenols and seem legitimate and useful, although we recognize that there is not full agreement as to which  $\sigma_o$  values are best.

A curious feature of the Hammett plot is that most of the points for ortho-substituted iodobenzenes lay somewhat *above* the linear regression line established by the behavior of meta- and para-substituted iodobenzenes. That suggests, if not steric acceleration, at least the absence of steric hindrance.

The fact that the Hammett plot for meta- and para-substituted iodobenzenes closely approximated a straight line, with slope +2.2, seems unexceptional for a reaction that in its transition state has negative charge in a side chain. OK, but what is the side chain?

**Aromatic System Effects, with Aryl Iodides.** Further studies, also by competition methodology, were of the relative reactivities of a series of polynuclear aryl

(14) Reaction of 2-chloroquinoline with 2-propoxide was complicated by concurrent  $\text{S}_{\text{N}}\text{Ar}$  reaction to form 2-propoxyquinoline in 48% yield; the electron efficiency for hydrodehalogenation should therefore be expressed as 0.08 faraday/mol, which still demonstrates a chain mechanism.

(15) Summarized by Andrieux et al.: Andrieux, C. P.; Savéant, J. M.; Zann, D. *Nouv. J. Chim.* 1984, 8, 107.

(16) Tomaselli, G. A.; Chen, Q.-f.; Cui, J.-j.; Bunnett, J. F. *J. Chem. Soc., Perkin Trans. 2*, in press.

(17) Exner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; p 439.

(18) Tribble, M. T.; Traynham, J. G. *J. Am. Chem. Soc.* 1969, 91, 379.

(10) Desirable features of ammonia and DMSO as solvents for this reaction include their very low reactivity with aryl radicals. Cf.: Bunnett, J. F.; Scamehorn, R. G.; Traber, R. P. *J. Org. Chem.* 1976, 41, 3677.

(11) Bunnett, J. F. In *Investigation of Rates and Mechanisms of Reactions*, 4th ed.; Bernasconi, C. F., Ed.; John Wiley and Sons: New York, 1986; Part I, p 260.

(12) Tomaselli, G. A.; Bunnett, J. F. *J. Org. Chem.*, in press.

(13) Amatore, C.; Badoz-Lambling, J.; Bonnel-Huyghe, C.; Pinson, J.; Savéant, J.-M.; Thiébaud, A. *J. Am. Chem. Soc.* 1982, 104, 1979.

iodides ranging from iodobenzene to 9-iodoanthracene.<sup>19</sup> The maximum variation in reactivity, in AIBN-initiated reactions with MeONa in methanol, was about 8-fold. That there is so little change in rate with such a big change in the aromatic framework is remarkable. It tells a lot about the nature of the transition state.

Let us ponder: which orbital in an aryl iodide receives the electron thrust upon it by formaldehyde radical anion? It must be an antibonding orbital. An obvious choice would be the  $\pi^*$  LUMO. Electron affinities (EAs) give an experimental report of the energy levels of the  $\pi^*$  LUMOs for the several parent hydrocarbons. The gas-phase EAs vary by 1.8 eV between the extremes of benzene and anthracene, with those for other systems studied (biphenyl, naphthalene, phenanthrene) intermediate between the extremes.<sup>20</sup> If we suppose that the transition state involves half-transfer of the electron from the  $\pi^*$  MO of formaldehyde radical anion into the aryl iodide's  $\pi^*$  LUMO, and assume that the iodine derivative  $\pi^*$  energy levels vary as do those for the parent hydrocarbons, we could expect a difference in activation enthalpy between iodobenzene and 9-iodoanthracene of 0.9 eV, or about 21 kcal/mol. If the two reactions had the same  $\Delta S^\ddagger$ , which seems probable, that would call for a difference in rate (at 70 °C, the temperature of the experiments) of about  $10^{12}$ -fold. Inasmuch as the observed rate difference between iodobenzene and 9-iodoanthracene was less than 1 power of 10, this transition state model is unsatisfactory.

Well then, how about a transition state with one-quarter transfer of the electron into the  $\pi^*$  LUMO? By the same sort of reasoning, one would anticipate a difference in rate of a million-fold, still orders of magnitude higher than the difference observed. Models of electron transfer into the  $\pi^*$  LUMO seem incompatible with experimental evidence.

An alternative possibility is transfer into the  $\sigma^*$  MO of the C-I bond. Theoretical calculations<sup>21,22</sup> indicate carbon-halogen  $\sigma^*$  MOs of aryl halides often to be comparable in energy to  $\pi^*$  LUMOs. Inasmuch as the C-I  $\sigma^*$  MO is orthogonal to the aromatic system's  $\pi$  MOs, negative charge in the  $\sigma^*$  MO cannot be delocalized by resonance. This model thus gives a reasonable account of why the effects of changing the aromatic system are so modest. The somewhat higher rates for iodine derivatives of larger aromatic systems can be attributed to aggregation of electronegativity and polarizability, which favor reaction by inductive and ion/induced dipole effects, respectively.

If electron transfer is indeed into the C-I  $\sigma^*$  MO, deiodination should occur just as readily with a substrate without a  $\pi$  system, that is, an alkyl iodide. To test this idea, we chose 2,2-dimethyl-1-iodopropane (neopentyl iodide), which is ill-suited to react with MeONa by either E2 elimination or S<sub>N</sub>2 substitution. In the event, neopentyl iodide underwent deiodination a little faster than iodobenzene. Deiodination was blocked by the presence of nitrobenzene; significantly,

no iodide release occurred in that experiment, showing indeed that neopentyl iodide is unreactive with MeONa by ionic mechanisms, under the conditions of our experiments.

We conclude that the model of transfer into the C-I  $\sigma^*$  MO is to be preferred.

Noteworthy is that, in rate comparisons between isomeric aryl iodides, the one with the more crowded iodine reacts faster. Thus 1-iodo- surpasses 2-iodo-naphthalene, and 2-iodo- excels 4-iodobiphenyl by factors of 2 or 3. Here again is a suggestion of steric acceleration.

Studies by others<sup>23-25</sup> indicate that, at room temperature, ArI<sup>-</sup> species either do not exist as discrete entities or are extremely short lived. Accordingly, one needs question whether ArI<sup>-</sup> shown as a product of step M5, Scheme I, is a legitimate intermediate. Perhaps steps M5 and M6 are merged, meaning that the C-I bond parts as it accepts an electron. If so, some steric acceleration by substituents crowding the iodine atom, as suggested by our experimental evidence, would reasonably occur.

Nevertheless, nearby substituents might retard reaction by blocking access of formaldehyde radical anion. The fact that they do not indicates that electron transfer occurs at a separation of reactants that exceeds the sum of the radii of carbon and of substituents such as methyl and phenyl. Other studies<sup>26</sup> have provided evidence that electron transfer can in favorable cases occur at separations of 10 Å or more.

The symmetries of the formaldehyde C-O  $\pi^*$  and the C-I  $\sigma^*$  MOs are, incidentally, good for them to interact. Both are antisymmetric about a nodal plane that intersects these bonds at right angles around the midpoint between the bound atoms.

**Halogen Identity Effects.** We have observed that in general, as long as the aromatic system is the same, reactivity diminishes in the order ArI > ArBr > ArCl. Reactivity ratios vary somewhat according to the alkoxide used. In ammonia solvent, with sodium methoxide, the PhI/PhBr ratio is about 200, and the *p*-bromoanisole/*p*-chloroanisole ratio about 120.<sup>27</sup> This trend, although it might seem to reflect the strengths of the several C-X bonds, can also be understood as a consequence of electron transfer into C-X  $\sigma^*$  MOs, inasmuch as their energy levels increase monotonically from iodine to chlorine.<sup>21</sup>

**Aromatic System Effects, with Aryl Bromides.** Reactivities of a series of polynuclear aryl bromides with MeONa in ammonia, initiated by photolysis of AIBN, were determined in a series of competitions with *m*-chlorobromobenzene.<sup>27</sup> In contrast to the analogous series of aryl iodides, reactivity within the aryl bromide set is considerably dependent on the nature of the aromatic system. For example, 9-bromoanthracene is 370 times as reactive as bromobenzene, and 9-bromo-

(23) Symons, M. C. R. *Pure Appl. Chem.* 1981, 53, 223.

(24) Parker, V. D. *Acta Chem. Scand.* 1981, B35, 595.

(25) Naff, W. T.; Compton, R. N.; Cooper, C. D. *J. Chem. Phys.* 1971, 54, 212. Arai, S.; Tagawa, S.; Imamura, M. *J. Phys. Chem.* 1974, 78, 519. Namiki, A. *J. Chem. Phys.* 1975, 62, 990.

(26) Namiki, A.; Noda, M.; Higashimura, T. *J. Phys. Chem.* 1975, 79, 2975. Miller, J. R.; Hartman, K. W.; Abrash, S. *J. Am. Chem. Soc.* 1982, 104, 4296. Mooney, W. F.; Whitten, D. G. *J. Am. Chem. Soc.* 1986, 108, 5712. Sisido, M.; Tanaka, R.; Inai, Y.; Imanishi, Y. *J. Am. Chem. Soc.* 1989, 111, 6790.

(27) Tomaselli, G. A. Research in Santa Cruz not yet prepared for publication.

(19) Bunnnett, J. F.; Tomaselli, G. A.; Chen, Q.-f.; Cui, J.-j. *New J. Chem.*, submitted for publication.

(20) Kebarle, P.; Chowdhury, S. *Chem. Rev.* 1987, 87, 523. Jordan, K. D.; Michejda, J. A.; Burrow, P. D. *J. Am. Chem. Soc.* 1976, 98, 7189.

(21) Fukui, K.; Morokuma, K.; Kato, H.; Yonezawa, T. *Bull. Chem. Soc. Jpn.* 1963, 36, 217.

(22) Nagai, S.; Gilbro, T. *J. Phys. Chem.* 1977, 81, 1793. Mishra, S. P.; Symons, M. C. R. *J. Chem. Soc., Perkin Trans. 2* 1981, 185.

phenanthrene is 30 times as reactive. These results suggest that  $\pi^*$  LUMOs are involved in electron acceptance in this series.

**Other Work in Support of the Mechanism of Scheme I.** Zoltewicz et al.<sup>28</sup> made a thorough study of the dehalogenation of 2-, 3-, and 4-iodopyridine and of 4-bromoisoquinoline by MeONa in MeOH at 165 °C, with some attention also to 3-bromo- and 4-chloroisoquinoline. Numerous observations were indicative of the mechanism of Scheme I: acceleration by AIBN, inhibition by nitrobenzene, and installation of protium in place of halogen when the reaction was conducted in CH<sub>3</sub>OD. They also saw the halogen mobility order I > Br > Cl.

Behar and Neta<sup>29</sup> reported that  $\gamma$  radiolysis of *o*-bromoacetophenone in aqueous 2-propanol at pH 12 gave acetophenone, and they suggested a chain mechanism like that of Scheme I.

Sawai and Shinozaki<sup>30</sup> examined the dechlorination of polychlorobiphenyls (PCBs) thru the action of  $\gamma$  radiation on alcoholic solutions. They found evidence of a chain reaction, with *G* values (yields of X<sup>-</sup> based on radiation received) up to 450 in alkaline 2-propanol, but no exalted *G* values in neutral 2-propanol or alkaline methanol. In one further study, by Nishiwaki et al.,<sup>31</sup> the quantum yield from photolysis of PCBs in alkaline alcoholic solutions was found to vary as the structure of the alcohol was changed, being highest in secondary alcohols, lower in methanol and primary alcohols, and lowest in benzyl alcohol. The same group<sup>32</sup> also showed that photolysis of four isomeric chlorobiphenyls in alkaline 2-propanol caused preferential removal of 2-chlorine if there was one. They invoked a mechanism much like that of Scheme I.

**Early Unrecognized Manifestations.** Now and then, years ago, people observed hydrodehalogenations that probably went by the mechanism of Scheme I. I now list some of those early observations. In some cases the means of initiation is unclear; dioxygen of the atmosphere sometimes acts as a radical-chain initiator.

Jackson and Gazzolo<sup>33</sup> (1899): Long refluxing of 1-iodo-2,4,6-trichlorobenzene with sodium ethoxide (doubtless in ethanol<sup>34</sup>) afforded 1,3,5-trichlorobenzene.

Montagne<sup>35</sup> (1908): Long refluxing of 2,4,6-tribromobenzophenone with KOH in "alcohol" (presumably ethanol) gave phenyl(4-bromophenyl)methanol.

De Crauw<sup>36</sup> (1931): 2-Iodo-1,4-dichlorobenzene, reacting with 2.9 M MeONa in methanol for 8 h at 180 °C, formed mainly 1,4-dichlorobenzene.

van de Lande<sup>37</sup> (1932): 1-Iodo-2,4-dichlorobenzene reacting with MeONa in methanol, for 3 h at 183 °C, formed 1,3-dichlorobenzene as well as phenols that doubtless resulted from S<sub>N</sub>Ar methoxydehalogenation and ensuing ether cleavage.

(28) Zoltewicz, J. A.; Oestreich, T. M.; Sale, A. A. *J. Am. Chem. Soc.* 1975, 97, 5889.

(29) Behar, D.; Neta, P. *J. Am. Chem. Soc.* 1981, 103, 2280.

(30) Sawai, T.; Shinozaki, Y. *Chem. Lett.* 1972, 865.

(31) Nishiwaki, T.; Ninomiya, A.; Yamanaka, S.; Anda, K. *Nippon Kagaku Kaishi* 1973, 2326.

(32) Nishiwaki, T.; Usui, M.; Anda, K.; Hida, M. *Bull. Chem. Soc. Jpn.* 1979, 52, 821.

(33) Jackson, C. L.; Gazzolo, P. S. *Am. Chem. J.* 1899, 22, 52.

(34) *Beilsteins Handbuch der Organischen Chemie*, 4th ed.; Prager, B., Jacobson, P., Eds.; Hauptwerk, Julius Springer: Berlin, 1922; Vol. 5, p 222.

(35) Montagne, P. *J. Recl. Trav. Chim. Pays-Bas* 1908, 27, 327.

(36) De Crauw, T. *Recl. Trav. Chim. Pays-Bas* 1931, 50, 780.

(37) van de Lande, L. M. F. *Recl. Trav. Chim. Pays-Bas* 1932, 51, 98.

Bansal et al.<sup>38</sup> (1972): Radiolysis of 5-halouracils in water/2-propanol at pH 7 gave high *G* values that diminished in the order ArBr > ArCl > ArF. A chain mechanism involving the 2-hydroxy-2-propyl radical was suggested but not detailed. This is perhaps a specific case of eq 2, with a mechanism similar to that of Scheme I, but with the 2-hydroxy-2-propyl radical acting as electron donor.

Pac et al.<sup>39</sup> (1972): Photoinduced reactions of halo-benzenes with *N,N*-dimethylaniline in methanol containing triethylamine gave (dimethylamino)biphenyls, attributed to cage recombination of phenyl radicals with dimethylaniline radical cations, and benzene. The yield of benzene decreased in the order PhI > PhBr > PhCl; this feature suggests possible operation of the mechanism of Scheme I.

Lubinkowski et al.<sup>40</sup> (1975) adduced evidence for a radical-chain mechanism for formation of benzene in reactions of diphenyliodonium salts with sodium alkoxides in the corresponding alcohols at 71 °C. Also formed was anisole, by an ionic mechanism. Radical-chain inhibitors, such as 1,1-diphenylethane, diminished the ratio of benzene to anisole. A mechanism resembling that of Scheme I warrants consideration.

Rigaudy et al.<sup>41</sup> (1982): 9-Bromoanthracene, on long refluxing with MeONa in pyridine, afforded 45% of anthracene plus a little 9-methoxyanthracene; a hydrogen isotope labeling experiment showed that the hydrogen that replaced bromine came from the methyl group of MeONa.

Olsen and Pruett<sup>42</sup> (1985): 2-Bromo-5-methyl-*cis*-stilbene in MeONa/MeOH, on UV irradiation, underwent debromination as well as cyclization to phenanthrene derivatives.

### Radical-Induced Dehalogenation of Alkyl Halides by Alkoxide Ions

Shortly after our first proposal of the mechanism of Scheme I, Sherman<sup>43</sup> found that  $\gamma$  radiolysis of alkaline methanol or 2-propanol solutions of methyl bromide or iodide gave exceptionally high *G* values for methane, indicative of a chain reaction. The mechanism he proposed is similar to that of Scheme I. He observed a higher *G* value for MeI than for MeBr, and higher *G* values in 2-propanol than in methanol.

A little earlier, Anbar and Neta<sup>44</sup> performed  $\gamma$  radiolysis of aqueous 2-propanol solutions of haloacetic acids and observed high *G* values indicative of a chain mechanism, e.g., for release of Br<sup>-</sup> from BrCH<sub>2</sub>COOH. Overall, their reactions conform to abstract eq 2.

### Dehalogenation of Aryl Halides by Alkylamide Ions

Sometimes<sup>45,46</sup> dehalogenation of aryl halides occurs on reaction with reagents such as lithium diethylamide.

(38) Bansal, K. M.; Patterson, L. K.; Schuler, R. H. *J. Phys. Chem.* 1972, 76, 2386.

(39) Pac, C.; Tosa, T.; Sakurai, H. *Bull. Chem. Soc. Jpn.* 1972, 45, 1169.

(40) Lubinkowski, J. J.; Knapczyk, J. W.; Calderon, J. L.; Petit, L. R.; McEwen, W. E. *J. Org. Chem.* 1975, 40, 3010.

(41) Rigaudy, J.; Seuleiman, A. M.; Cuong, N. K. *Tetrahedron* 1982, 38, 3157.

(42) Olsen, R. J.; Pruett, S. R. *J. Org. Chem.* 1985, 50, 5457.

(43) Sherman, W. V. *J. Phys. Chem.* 1968, 72, 2287.

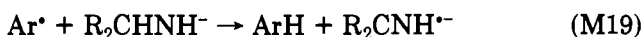
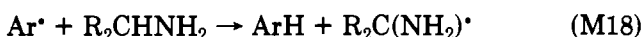
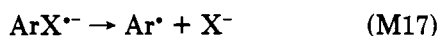
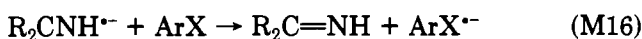
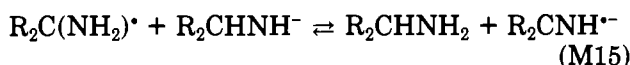
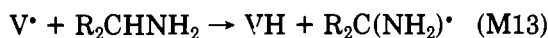
(44) Anbar, M.; Neta, P. *J. Chem. Soc. A* 1967, 837.

(45) Bunnett, J. F.; Brotherton, T. K. *J. Am. Chem. Soc.* 1956, 78, 6265 and papers cited therein.

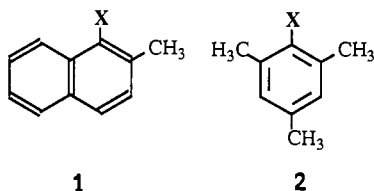
(46) Winiarski, J.; Bunnett, J. F. *J. Am. Chem. Soc.* 1985, 107, 5271.

Benzynes are often formed in such systems; it was suggested<sup>47</sup> that dehalogenation occurs via a benzyne intermediate. Another possibility occurred to Jerzy Winiarski (from Warsaw, Poland) and me; it is an adaptation of the mechanism of Scheme I and is sketched in Scheme II. (I am vague about termination steps; several are conceivable.)

### Scheme II



We found that lithium *cis*-2,6-dimethylpiperide, on reacting with aryl halides of types 1 and 2 in *cis*-2,6-dimethylpiperidine solution, effected considerable dehalogenation, without any straightforward aminodehalogenation, but minor amounts of telesubstitution (attaching dimethylpiperidino groups to methyl carbons).<sup>46</sup> Several further observations resembled those

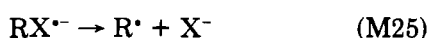
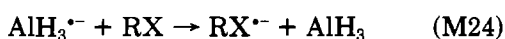
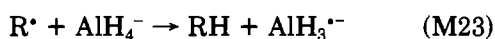


made with alkoxide dehalogenations: increases in dehalogenation yields when radical initiators were present, decreases in the presence of radical-chain inhibitors, and the halogen mobility order  $\text{I} > \text{Br} > \text{Cl}$ . These features are consistent with the mechanism of Scheme II, which we think may also obtain for dehalogenations with alkylamide ion reagents seen by other workers.

### Dehalogenation of Aryl Halides by Aluminoborohydrides

**By Lithium Aluminum Hydride and Related Reagents.** Readers no doubt sense that I approach this topic with bias. I confess that I would like to find evidence to support a radical-chain mechanism with a propagating cycle like that of Scheme III, the three steps of which resemble steps M8, M5, and M6 of Scheme I, with steps M24 and M25 possibly being merged. Accordingly, striving to be objective, I seek

### Scheme III



(47) Wittig, G.; Rentzea, C. N.; Rentzea, M. *Justus Liebig's Ann. Chem.* 1971, 744, 8.

evidence to disqualify this mechanism. There are a sufficient number of conflicting reports concerning this reaction, in both its preparative and mechanistic aspects, so that I should have a good chance of finding something contrary to my wishes. Well, what do you think of evidence that the reaction goes through organoaluminum intermediates?<sup>48,49</sup> Scheme III provides no place for such.

To be fair, I now offer a few items that favor the Scheme III mechanism and that resemble some of our observations on methoxide dehalogenations. Aryl and alkyl halides are both dehalogenated with considerable ease,<sup>50,51</sup> the mobility of halogens being in the order  $\text{I} > \text{Br} > \text{Cl} > \text{F}$ . Bridehead halides, such as 1-bromoadamantane, are dehalogenated in high yield without rearrangement.<sup>52</sup> "Cyclizable radical probes"<sup>53</sup> indicate the intermediacy of radicals.<sup>49,54,55</sup> Crowded iodine atoms on aromatic rings are replaced with special ease.<sup>50,56</sup> Indeed, in consideration of these facts, two groups of chemists have proposed the mechanism of Scheme III or a variant with the same essential characteristics.<sup>49,53,55,57</sup> How can I resist regarding that mechanism as the best representation of what happens?

But what about those organoaluminum intermediates? Beckwith and Goh<sup>49</sup> found evidence that the mechanism depends on reaction conditions. Reaction in tetrahydrofuran (THF) with strict exclusion of dioxygen was slow and gave indication of the intermediacy of organoaluminum compounds. (The indication is that, when dehalogenation is effected by  $\text{LiAlD}_4$  and ultimately quenched by protium oxide, little deuterium appears where halogen was, whereas when the final quench is with deuterium oxide, the degree of deuteration is high.)<sup>48,49</sup> When limited amounts of dioxygen were admitted to the system, reaction rate increased as did radical character of reaction intermediates. Even more effective in speeding reaction via radicals was to utilize a well-known initiation system: di-*tert*-butyl peroxide initiator and irradiation with UV light.

A dialkoxyaluminum dihydride,  $\text{Li}^+ - (\text{CH}_3\text{OCH}_2\text{CH}_2\text{O})_2\text{AlH}_2^-$ , also acts as a dehalogenation reagent.<sup>58</sup> Among halobenzenes, the reactivity order is  $\text{PhBr} > \text{PhCl} > \text{PhF}$ , PhF being "practically stable". Reaction rate is depressed by electron-releasing substituents.

**By Sodium Borohydride.** No doubt this reporter would also be pleased to see evidence that sodium borohydride dehalogenations occur by the mechanism of Scheme III, with "B" in place of "Al". Indeed, he found satisfaction in a report of Barltrop and Bradbury<sup>59</sup> that  $\text{NaBH}_4$ , in aqueous acetonitrile under 254-nm irradiation

(48) Adapa, S. R.; Sheikh, Y. M.; Hart, R. W.; Witiak, D. T. *J. Org. Chem.* 1980, 45, 3343.

(49) Beckwith, A. L. J.; Goh, S. H. *J. Chem. Soc., Chem. Commun.* 1983, 905.

(50) Brown, H. C.; Krishnamurthy, S. *J. Org. Chem.* 1969, 34, 3918.

(51) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* 1982, 47, 276.

(52) Jefford, C. W.; Kirkpatrick, D.; Delay, F. *J. Am. Chem. Soc.* 1972, 94, 8905.

(53) Ashby, E. C. *Acc. Chem. Res.* 1988, 21, 414.

(54) Chung, S.-K.; Chung, F.-f. *Tetrahedron Lett.* 1979, 2473.

(55) Ashby, E. C.; Pham, T. N.; Amrollah-Madjdabadi, A. *J. Org. Chem.* 1991, 56, 1596.

(56) Karabatsos, G. J.; Shone, R. L. *J. Org. Chem.* 1968, 33, 619.

(57) The validity of conclusions based on finding cyclized products when cyclizable radical probes are employed has been questioned by Newcomb and Curran: Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* 1988, 21, 206. Ashby<sup>53</sup> has responded to the criticism.

(58) Kraus, M. *Collect. Czech. Chem. Commun.* 1972, 37, 3052.

(59) Barltrop, J. A.; Bradbury, D. *J. Am. Chem. Soc.* 1973, 95, 5085.

tion, efficiently dehalogenates iodo-, bromo-, and chlorobenzene, with quantum yields 7.5, 5.7, and 0.5, respectively. The former two bespeak chain mechanisms. A radical mechanism was indicated by the behavior of the system when acrylonitrile was added: dehalogenation was stopped, and products (including 3-phenylpropanenitrile) that represent trapping of phenyl radical were formed. Another cogent experiment involved addition of sodium metal to an ammonia/acetonitrile solution of PhI and NaBH<sub>4</sub>; benzene was formed in 675% yield (based on Na). The authors proposed a radical-chain mechanism like that of Scheme III.

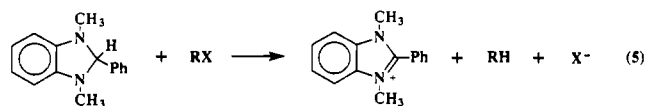
Shortly thereafter, Groves and Ma<sup>60</sup> suggested basically the same mechanism for the NaBH<sub>4</sub> dehalogenation of *gem*-dibromocyclopropanes in DMF solution. Among items of evidence indicative of a radical mechanism, they found that if the reaction mixture were prepared under air, but then covered by an inert atmosphere, vigorous reaction occurred after an induction period of less than 10 min. Furthermore, the reaction is inhibited by oxygen.

An extensive study<sup>61</sup> of the chemistry of the BH<sub>3</sub><sup>-</sup> radical anion revealed several features that are compatible with the foregoing proposals.

A further contribution was made by Japanese workers<sup>62</sup> who acknowledged the Barltrop-Bradbury mechanism but showed that there is more to the story. They carried out the dechlorination of 3- and 4-chlorobiphenyl by means of NaBH<sub>4</sub> in MeCN/H<sub>2</sub>O (10/1) with various combinations of protium and deuterium in the ingredients. The biphenyl formed had deuterium content that did not strictly represent introduction of hydrogen from the borohydride reagent. One noteworthy result was that dechlorination with NaB<sup>1</sup>H<sub>4</sub> in <sup>2</sup>H<sub>2</sub>O afforded biphenyl 39% monodeuterated from 3-chlorobiphenyl but only 8% deuterated from 4-chlorobiphenyl. How hydrogen from water became attached to carbon is not entirely clear. A possibility not mentioned by the authors is that the solutions became alkaline and that base-catalyzed hydrogen exchange via aryl anions occurred ortho to chlorine.<sup>6</sup> Formation of an aryl anion at the 2-position of 3-chlorobiphenyl is likely to be assisted by the proximity of the phenyl group, with its electronegativity and polarizability, whereas removing 3-H from 4-chlorobiphenyl would be less favored.

### Dehalogenation of $\alpha$ -Halo Ketones by 1,3-Dimethyl-2-phenylbenzimidazoline

This is a textbook-quality example of abstract eq 2. The overall reaction occurs according to eq 5. Indi-



cative of a radical-chain, electron-transfer mechanism are initiation by AIBN, inhibition by *p*-dinitrobenzene, and trapping of R<sup>•</sup> by an alkene.<sup>63</sup> A typical substrate

(60) Groves, J. T.; Ma, K. W. *J. Am. Chem. Soc.* 1974, 96, 6527.

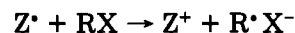
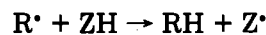
(61) Giles, J. R. M.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* 1982, 1699.

(62) Tsujimoto, K.; Tasaka, S.; Ohashi, M. *J. Chem. Soc., Chem. Commun.* 1975, 758.

(63) Tanner, D. D.; Chen, J. J. *J. Org. Chem.* 1989, 54, 3842. Tanner, D. D.; Chen, J. J.; Chen, L.; Luelo, C. *J. Am. Chem. Soc.* 1991, 113, 8074.

is  $\alpha$ -bromoacetophenone. The propagation cycle of Scheme IV, in which ZH is the heterocycle at the left, has been advocated.<sup>63</sup>

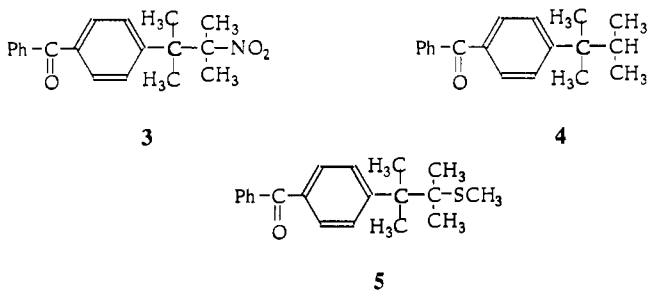
### Scheme IV



### Related Reactions That Do Not Fit the Title of This Account

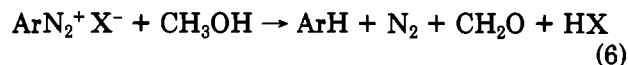
Halogens are nucleofugal groups, but they are not the only ones. Some others also suffer replacement by hydrogen in ways that suggest mechanisms analogous to that of Scheme I.

**Denitration of *tert*-Alkyl Nitro Compounds by Thiolate Ions.** Kornblum et al.<sup>64</sup> found that compound 3 and some other nitroparaffins of similar structure underwent almost exclusively hydrodenitration to form products such as 4 on treatment with sodium methanethiolate in DMF solution under gentle irradiation. [In contrast, the same reactant in hexamethylphosphoric triamide (HMPA) solution gave mainly methylthiodenitration products, such as 5.] Hydro-



denitration was strongly retarded by known radical and electron scavengers. For it, they suggested a mechanism very similar to that of Scheme I. As to why the change of solvent had such a marked effect on the product formed, they offered an interpretation that would not occur to chemists less knowledgeable about the systems investigated.

**Deidiazonation in Neutral or Acidic Alcohols.** Many diazonium salts suffer replacement of the diazonio group by hydrogen on being boiled in methanol or ethanol solution.<sup>65,66</sup> The reaction (for the case of methanol) is as represented in eq 6, which is a specific case of abstract eq 2. Although it has been recommended in some textbooks for "deamination" preparative purposes, yields in the absence of strongly electron attracting substituents are often poor. The difficulty is competing alkoxydeidiazonation, which forms alkyl aryl ethers.



A significant observation of DeTar and Kosuge<sup>67</sup> was that product selection, between ArH and ArOR, was strongly dependent on the atmosphere above the reacting mixture for some diazonium salts, in particular the *p*-bromo and *p*-methoxy derivatives. Reaction under O<sub>2</sub> gave mainly ethers, and reaction under N<sub>2</sub> gave

(64) Kornblum, N.; Carlson, S. C.; Smith, R. G. *J. Am. Chem. Soc.* 1979, 101, 647.

(65) Kornblum, N. *Org. React. (N.Y.)* 1944, 2, 262.

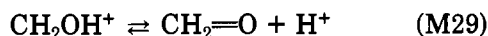
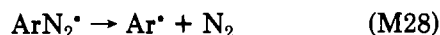
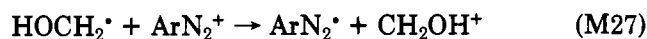
(66) Zollinger, H. *Azo and Diazo Chemistry*; Interscience Publishers: New York, 1961; p 141.

(67) DeTar, D. F.; Kosuge, T. *J. Am. Chem. Soc.* 1958, 80, 6072.

mainly bromobenzene or anisole. Product studies<sup>68</sup> by Trevor Broxton (from Australia) and Chang Hum Paik (from Korea) in my lab in Santa Cruz supported the conclusion of DeTar and Kosuge that ethers are formed by an ionic mechanism and hydrodediazonium products by a radical mechanism. Especially supporting the latter view are the facts that dediazonation of benzenediazonium fluoroborate under N<sub>2</sub> in CH<sub>3</sub>OD either neutral or acidified with D<sub>2</sub>SO<sub>4</sub> gave benzene virtually deuterium-free, and that *p*-bromobenzenediazonium fluoroborate behaved similarly. As we said,<sup>68</sup> aryl radicals are known to abstract hydrogen from the  $\alpha$ -carbon of methanol much faster than from the hydroxyl group.<sup>69</sup> A kinetic study of Chino Yijima (from Tokyo, Japan), also at Santa Cruz, showed that, for reaction in acidic methanol, changing the atmosphere from O<sub>2</sub> to N<sub>2</sub> had negligible effect on the rate of formation of *p*-bromoanisole but increased the rate of bromobenzene formation by 2 orders of magnitude.<sup>70</sup> The effect of O<sub>2</sub> is thus to inhibit a radical-chain process, as it often does.<sup>71</sup>

An attractive mechanism for dediazonation in neutral or acidic alcohols,<sup>70</sup> resembling one proposed by DeTar and Turetzky,<sup>72</sup> has the propagation cycle of Scheme V. (Strictly, step M29 is not a propagation

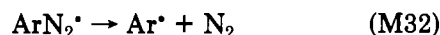
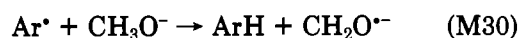
#### Scheme V



step, but it is an integral part of the reaction.) Two proposals have been offered as to the nature of the initiation step. One is that a covalent azo ether, Ar-N=NOCH<sub>3</sub>, is formed by coordination of diazonium ion with methanol and hydron loss;<sup>72</sup> that interpretation is, however, inconsistent with the fact that the rate of hydrodediazonation does not vary significantly as *p*-toluenesulfonic acid concentration is varied 100-fold.<sup>70</sup> We are inclined to think that initiation involves electron transfer directly from methanol to the diazonium ion, forming a diazenyl radical that enters the propagation cycle as step M28.

**Dediazonation in Alkaline Alcohols.** Dediazonation occurs faster and with better yields in alkaline methanol than in neutral or acidic solutions. Superficially, that might seem to be an obvious consequence, inasmuch as the propagation cycle of Scheme VI could operate. But the situation is a little com-

#### Scheme VI



(68) Broxton, T. J.; Bunnett, J. F.; Paik, C. H. *J. Org. Chem.* **1977**, *42*, 643.

(69) Norman, R. O. C. *Spec. Publ.—Chem. Soc.* **1970**, No. 24, 131–133. König, E.; Musso, H.; Zahorszky, U.-I. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 45; *Angew. Chem.* **1972**, *84*, 33.

(70) Bunnett, J. F.; Yijima, C. *J. Org. Chem.* **1977**, *42*, 639.

(71) Walling, C. *Free Radicals in Solution*; John Wiley & Sons: New York, 1957; p 169.

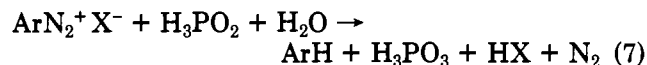
(72) DeTar, D. F.; Turetzky, M. N. *J. Am. Chem. Soc.* **1955**, *77*, 1745.

plicated, although in one respect it is simpler: no ethers of type ArOCH<sub>3</sub> are formed.<sup>73</sup> One remarkable feature is that in CH<sub>3</sub>OD solution the ArH formed is sometimes Ar<sup>1</sup>H and sometimes Ar<sup>2</sup>H; the former indicates an aryl radical and the latter an aryl anion intermediate. Hiroaki Takayama (from Tokyo, Japan) showed in my lab at Brown University that the aryl anion route is favored by ortho halogen substituents and by high methoxide ion concentrations,<sup>74</sup> but *p*-nitrobenzenediazonium ion goes entirely by the radical route.<sup>74,75</sup> Another feature not found in acidic solutions is that arylazo alkyl ethers, such as ArN=NOCH<sub>3</sub>, play major roles.<sup>73,76–80</sup> Furthermore, the azo ethers can exist as syn and anti stereoisomers.

Space does not suffice for a full discussion of these interesting systems. The reader is referred to the papers cited.

**Dediazonation by Means of Formaldehyde in Alkaline Aqueous Solution.** This method for “deamination” is simple, quick, and inexpensive and gives quite good yields.<sup>81</sup> Inasmuch as formaldehyde exists in water mainly as its covalent hydrate, CH<sub>2</sub>(OH)<sub>2</sub>,<sup>82</sup> and alcohols are about as acidic as water, alkaline aqueous formaldehyde must contain an appreciable concentration of the hydroxide–formaldehyde adduct, HOCH<sub>2</sub>O<sup>-</sup>, the structure of which suggests that it should readily yield a methylene hydrogen to an attacking aryl radical, forming ArH and HOCH=O<sup>-</sup>. The latter is the radical anion of formic acid and is probably a good electron donor. Two other probable modes of behavior are coordination with a diazonium ion to form an azoether, ArN=NOCH<sub>2</sub>OH (syn and/or anti), and acid–base equilibrium reaction with hydroxide ion to form a little <sup>-</sup>OCH=O<sup>-</sup>, which as a radical dianion should be an exceptionally strong electron donor. The system thus should have many of the same characteristics as dediazonation in alkaline alcohols. Additional features, however, should be the formation of a diazohydroxide, ArN=NOH (syn and/or anti), and their further reactions with hydroxide ion to form diazoates, ArN=NO<sup>-</sup>.<sup>83</sup>

**Dediazonation by Action of Hypophosphorous Acid.** This reaction, which occurs according to eq 7, is highly regarded as a preparative method.<sup>65</sup> It rep-



resents another concrete case of abstract eq 2. An investigation by Kornblum et al.<sup>84</sup> revealed several features indicative of a radical mechanism. They proposed the propagation cycle of Scheme VII, which has been generally accepted.<sup>85</sup> The [H<sub>2</sub>PO<sub>2</sub>]<sup>+</sup> generated in step

(73) Broxton, T. J.; Bunnett, J. F. *Nouv. J. Chim.* **1979**, *3*, 133.

(74) Bunnett, J. F.; Takayama, H. *J. Am. Chem. Soc.* **1968**, *90*, 5173.

(75) Also, when benzene was present as cosolvent (50%) in a system such as affords Ar<sup>1</sup>H in CH<sub>3</sub>OD, 31% of a biaryl, ArPh, was formed. That is a further indication of an aryl radical intermediate. Bunnett, J. F.; Takayama, H. *J. Org. Chem.* **1968**, *33*, 1924.

(76) Boyle, W. J., Jr.; Broxton, T. J.; Bunnett, J. F. *J. Chem. Soc., Chem. Commun.* **1971**, 1469.

(77) Ritchie, C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1972**, *94*, 1589.

(78) Broxton, T. J.; Roper, D. L. *J. Org. Chem.* **1976**, *41*, 2157.

(79) Broxton, T. J.; McLeish, M. J. *J. Org. Chem.* **1982**, *47*, 3673.

(80) Broxton, T. J.; McLeish, M. J. *J. Org. Chem.* **1983**, *48*, 191.

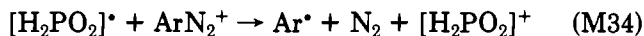
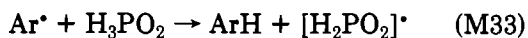
(81) Brewster, R. Q.; Poje, J. A. *J. Am. Chem. Soc.* **1939**, *61*, 2418.

(82) Bell, R. P. *Adv. Phys. Org. Chem.* **1966**, *4*, 1.

(83) Reference 66, p 47.

(84) Kornblum, N.; Cooper, G. D.; Taylor, J. E. *J. Am. Chem. Soc.* **1950**, *72*, 3013.

## Scheme VII



M34 was indicated to react with water to form  $\text{H}_3\text{PO}_3$  and  $\text{H}^+$ . An electron spin resonance spectroscopic study of such systems by Beckwith<sup>86</sup> revealed characteristics of  $[\text{H}_2\text{PO}_2]^{\bullet}$  radicals and their reactions with diazonium ions.

## Imposter Reactions

There are a few reactions that masquerade as members of the select group that is the focus of this Account, but really are not. Sometimes you have to look twice to tell the difference. We have already encountered some alkoxide-effected dediazoniations that appear to go through carbanion intermediates. Others involve nucleophilic displacement *on* halogen, effective positive halogen capture and generating aryl anion intermediates.

Some of the positive halogen capture reactions are effected by carbanions. Rae Victor, who started Ph.D. research with me at Brown University and completed it at Santa Cruz, investigated such as case.<sup>87</sup> She started by looking into the debromination of 1,2,4-tribromobenzene through the action of potassium *tert*-butoxide (*t*-BuOK) in 50% *t*-BuOH/50% DMSO at 53 °C; *p*-dibromobenzene was formed in 70% yield.<sup>88</sup> She found evidence that the reaction involves nucleophilic displacement by dimethyl anion ( $\text{CH}_3\text{SOCH}_2^-$ ) on the 2-bromine, the nucleofuge being 2,5-dibromophenyl anion. Two principal lines of support for this conclusion were that the halogen removed was typically ortho to another halogen (ortho halogens strongly stabilize aryl anions<sup>89</sup>) and that it was necessary for the cosolvent (with *t*-BuOH) to be of structure readily converted to

(85) Cf.: Levit, A. F.; Kiprianova, L. A.; Gragerov, I. P. *Zh. Org. Khim.* 1975, 11, 2351; *J. Org. Chem. USSR (Engl. Transl.)* 1975, 11, 2395.

(86) Beckwith, A. L. *J. Aust. J. Chem.* 1972, 25, 1887.

(87) Bunnett, J. F.; Victor, R. R. *J. Am. Chem. Soc.* 1968, 90, 810.

(88) Moyer, C. E., Jr. Dissertation, Brown University, 1964; *Diss. Abstr.* 1965, 25, 4412.

(89) This topic was mentioned briefly in an earlier Account.<sup>6</sup>

a carbanion by *t*-BuOK. Cosolvents that supported debromination included *N*-methylpyrrolidone and *N,N*-dimethylacetamide, but reaction failed when the cosolvent was HMPA or diphenyl sulfoxide.

Dehalogenations of this type, especially in 2-butanone/methanol and DMSO/methanol solvents, have been investigated extensively by Bolton and co-workers.<sup>90</sup> Their kinetic and other studies support the type of mechanism that Rae and I suggested.

Diethyl phosphite ions,  $(\text{EtO})_2\text{PO}^-$ , react with *o*-haloiodobenzenes in the dark to generate *o*-halophenyl anions, which then capture hydrons from the ammonia solvent to form halobenzenes and, in the cases where the ortho halogen is bromine or iodine, detach halide ion to form benzyne.<sup>91</sup> When illuminated, the same reactants undergo  $\text{S}_{\text{RN}}1$  reactions via *o*-halophenyl radical intermediates to form (*o*-halophenyl)phosphonic esters or *o*-phenylenebis(phosphonic esters).

A perceptive review of a variety of reactions of this general sort, which they call *X-phylic* reactions, has been provided by Zefirov and Makhon'kov.<sup>92</sup>

## Concluding Remarks

Because editors of *Accounts* don't like manuscripts to be too long, I'd better close now. Surely some work that ought to have been mentioned escaped attention in this Account, and for that I apologize. Perhaps some of my judgments will provoke challenges. If so, I hope that the challengers will perform well-designed experiments to correct my errors, and thus to advance knowledge.

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(90) Bolton, R.; Sandall, J. P. B. *J. Chem. Soc., Perkin Trans. 2* 1977, 278. Bolton, R.; Moore, C.; Sandall, J. P. B. *J. Chem. Soc., Perkin Trans. 2* 1982, 1593.

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(92) Zefirov, N. S.; Makhon'kov, D. I. *Chem. Rev.* 1982, 82, 615.

## The Principle of Nonperfect Synchronization: More Than a Qualitative Concept?<sup>1</sup>

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In trying to understand chemical reactivity, the physical organic chemist has traditionally relied on models or concepts that are qualitative and intuitive.

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Perhaps the best-known physical organic concept is the Hammond postulate<sup>3</sup> along with its various extensions

(1) This Account is based, in part, on a talk I presented during a symposium honoring Professor Joseph Bunnett on the occasion of his retirement from active service at the University of California at Santa Cruz. The talk was entitled "From Bunnett's Variable Transition State Theory to the Principle of Non-Perfect Synchronization". Except for the introduction, which summarizes the basic features of the principle of nonperfect synchronization (PNS), most of the material is new. Specifically, there is very little overlap with an earlier Account that was entitled "Intrinsic Barriers of Reactions and the Principle of Nonperfect Synchronization".<sup>2</sup>