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Radical Reactions of Arenediazonium Ions: An Easy Entry into the Chemistry of the Aryl Radical

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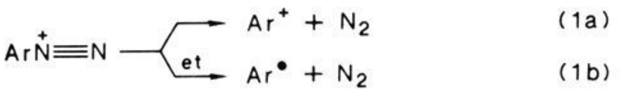
I. Introduction

The reactions of arenediazonium ions, ArN_2^+, have aroused mechanistic curiosity since the beginning of their extensive use in preparative chemistry. The present review will cover those processes where the diazo group is lost, that is, the *dediazoniation* reactions. These may take place, as we now understand them, either by a heterolytic (eq 1a) or by a homolytic (eq 1b) mechanism or also via an aryne intermediate (Scheme 1), as formed by stepwise (A or C) or concerted (B) pathways. This second possibility will not be considered here, and the interested reader is referred to previous reviews where the formation of arynes from diazonium salts is treated.[1,2] In addition, this review *will not* deal with those reactions where the diazo group is maintained (e.g., diazo coupling).



$$Ar\overset{+}{N}{\equiv}N \longrightarrow Ar^+ + N_2 \qquad (1a)$$

$$Ar\overset{+}{N}{\equiv}N \xrightarrow{et} Ar^\bullet + N_2 \qquad (1b)$$

Carlo Galli was born in Rome, Italy, in 1949. He obtained his Laurea degree from the University of Rome in 1972, with thesis work on ring-closure reactions, carried out under the supervision of G. Illuminati and L. Mandolini. After holding a position as researcher of the Italian CNR, he became Associate Professor in the Department of Chemistry of the University of Rome. He received a CNR–NATO fellowship (1979) and then a Fullbright Fellowship (1983) to support postdoctoral work with J. F. Bunnett at UC—Santa Cruz in the field of $S_{RN}1$ reactions. In 1985 he was awarded the Ciamician Medal of the Società Chimica Italiana. His research interests cover ring-closure reactivity and conformational aspects of cyclic molecules, and also electron-transfer processes.

The homolytic dediazoniation pathway (1b) requires an electron transfer (et) from a reducing agent. [Abbreviations such as et for electron transfer and lt for ligand transfer are commonly used in this review. In addition, outer-sphere (or nonbonded) et implies that charge only is transferred between two species whose coordination spheres are not directly involved in the process. Vice versa, an inner-sphere (or bonded) et implies that an electron is donated by means of a bridging group transferred from one coordination sphere to the other.] The heterolytic counterpart (eq 1a) is of the S_N1 kind, as in solvolytic reactions. Although the formation of Ar^+ would appear to be less likely in view of the high energy of this species,[3,4] the energetics of the two processes (1a and 1b) are not very different, in general, because the driving force is for a good share provided in both cases by the formation of a molecule of dinitrogen. As a consequence, depending also on the reaction conditions required for the ensuing reactive step(s), there often hides the possibility of competition or coexistence of the two mechanisms. In fact, the distinction between (1a) and (1b) was not always perceived clearly by the first investigators in the field. Therefore, although this review concentrates on homolytic dediazoniations, comments will be made

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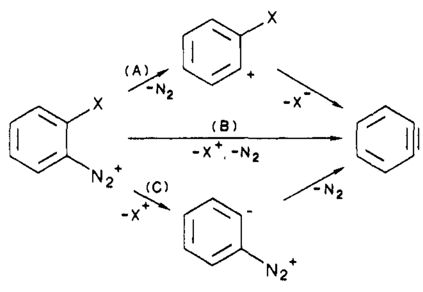

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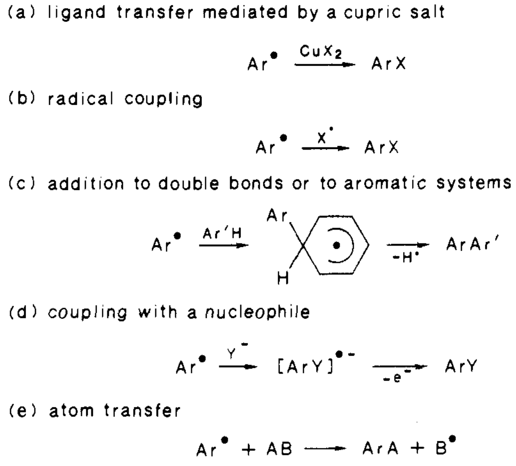


upon interference by the heterolytic mechanism, particularly in some ambiguous cases.

The homolytic mechanism is of great synthetic value in that a wider variety of pathways occur through it than in the heterolytic case, where solvolytic product(s) only is attainable. This wide variety is due both to the numerous reducing agents that have been used to generate the intermediate $Ar^\bullet$ and to the multiplicity of synthetic steps that are opened to the aryl radical.[1] The latter steps are schematically summarized as Scheme 2. Some of the steps in Scheme 2 may take place by a radical *chain* mechanism.

The literature of the homolytic dediazoniations, and in particular of the Sandmeyer reaction as the oldest and most studied among them, has been exhaustively covered by many authors. The papers or reviews that, in the opinion of this author, have provided in the course of time the most relevant and stimulating mechanistic contributions are those of Waters,[5] Kornblum,[6] Kochi,[7] Rüchardt,[8] Bunnett,[9] and Zollinger.[10] Many more exist, of course, and careful surveys of this literature, as well as refinements of the related mechanistic aspects, are published, apart from the previous papers, in the books of Saunders,[11] Waters,[12] Williams,[13] and Zollinger,[14] in the chapter of Hegarty,[2] updated again by Zollinger in a recent chapter of the Patai series.[15] Hence, it is certainly not literature coverage that is lacking in this field. Rather, it can become difficult to detect analogies and to extrapolate general trends among such an amount of experimental findings.

The present review is therefore systematic as to the aim, but it also seeks to be interpretative. It will summarize unambiguous homolytic reactions of arenediazonium ions, including cases of the recent literature not previously reviewed. It will focus the attention on the properties of the reducing agent needed for the electron-transfer step (1b). It will describe the wide spectrum of reactive steps accessible to $Ar^\bullet$. It will finally attempt to detect common mechanistic features among reactions that, although by different precursors, give origin to the aryl radical. The goal is to provide a general and hopefully unified view of the reactivity of this fundamental intermediate.

Some of the points that will be stressed in this endeavor are not new to the experts in the field. Nevertheless, this approach may be of interest to a less specialized reader who learns about homolytic dediazoniations in that fragmentary way in which the matter is still traditionally described, and not only in textbooks. The traditional description in fact tends to partition these reactions, placing excessive emphasis on specific experimental details that make, for example, the Gomberg reaction appear different from the Gattermann. It would be instead more profitable to lay down initially an assessment of the general behavior of the homolytic reactions as for a *class* of processes. This is possible in view of existing mechanistic similarities, such as the common requirement of an electron transfer (more or less manifest) to form the intermediate aryl radical.

Hopefully, a rationalization of the general features of the homolytic processes of arenediazonium ions will help to derive connections with other reactions, analogously leading to the $Ar^\bullet$ intermediate, and will help to provide a wider understanding of the radical phenomena.

II. Evolution of the Mechanistic View of the Diazonium Group Replacement

It may be interesting to make a quick digression upon the sequence of logic steps that have led to the present formulation of the mechanism of the dediazoniation of arenediazonium ions as partitioned in (1a) and (1b).

In 1864 Peter Griess[16] noticed the ready replacement of the diazonium group by iodide, to give ArI. Strangely enough, the replacement of $-N_2^+$ by bromide or chloride was more difficult and required stronger conditions so as to lead mainly to phenol in water solution.[17] The formation of ArBr or ArCl competed appreciably only when run in the presence of overwhelming amounts of the halide salts[18-20] and/or in a solvent less nucleophilic than water.[21,22]

In 1884 Traugott Sandmeyer[23] discovered that use of copper(I) chloride or bromide allowed chloro- or bromo-dediazoniations to proceed in a much easier and synthetically useful way. A few years later Ludwig Gattermann[24] found that the formation of chlorobenzene from benzenediazonium chloride could be carried out with freshly prepared copper powder as well. Some authors subsequently claimed that also copper(II) salts,[25,26] or even other metal salts such as $ZnCl_2$,[27-29] were effective as catalysts in these processes. The nature of these metal-catalyzed reactions was not completely understood. A further differentiation in the behavior of the halides came up when Balz and Schiemann discovered[30] that thermal decomposition of an arenediazonium tetrafluoroborate in the absence of solvent afforded a fairly good yield of aryl fluoride.

In addition to the halodediazoniations, other dediazoniation reactions had also appeared in the meantime, widening the scope and the synthetic utility of the arenediazonium chemistry. Sandmeyer himself had already observed (i) the successful preparation of arenenitriles by the use of cuprous cyanide,[23,31] and (ii) an aromatic nitration taking place under cuprous catalysis.[32] Pschorr[33] had developed an intramolecular arylation occurring both with and without copper catalysis. Mai[34] had described the reduction of an arenediazonium salt to ArH by means of hypophosphorous acid, as a more reliable method[1,14] with respect to the older one reported by Griess[35] and employing ethanol. Finally, a further way of decomposition of arenediazonium ions had been described (1924) in a heterogeneous arene/alkali mixture, through the intermediacy of aryl diazotates 1 (eq 2). The ensuing intermolecular arylation

$$ArN_2^+ + OH^- \xrightarrow{OH^-} \underset{1}{ArN{=}NO^-} \xrightarrow{Ar'H} ArAr' \quad (2)$$

afforded unsymmetrical biaryls. The reaction, known as the Gomberg–Bachmann reaction,[36] was suggested to be of homolytic character.[37] The intermediacy of the aryl cation (route 1a), on the contrary, was initially suggested to apply for the somewhat related Meerwein reaction,[38] where addition of the aryl group to a double bond occurs.

While this wealth of synthetic findings was being gathered, how far had the mechanistic description of dediazoniation reactions proceeded? If we go back to the Sandmeyer reaction, the formation of a precipitate on addition of cuprous halide to the solution of diazonium salt had been observed since the very first experiments.[39] This was ascribed to the formation of a complex featuring a covalent bond between Cu and nitrogen, and that species was considered to be an essential intermediate in all the Sandmeyer-like reactions induced by copper salts.[40,41]

The formation of aryl radicals in the dediazoniation reactions was clearly proposed for the first time by Grieve and Hey[37] in 1934. In contrast, Hodgson[29,42] put forward an "anionoid" mechanism for the Sandmeyer reaction. According to this view, the function of the copper salt was to render more active the halogen atom toward an attack to the aromatic carbon. As a consequence, the replacement of $-N_2^+$ by halide ion did not require a cuprous salt specifically. Rather, any metal halide (CuX_2, FeX_3, CoX_2, ZnX_2) able to *enhance* the reactivity of the octet of the halide ion could be used.

The true mechanistic breakthrough came then with Waters.[5] On the basis of concepts already advanced in a review with Hey,[3] which is a landmark paper for radical chemistry,[43] he explained that the Sandmeyer's cuprous salt functioned as a reducing agent to give an aryl radical (as in eq 1b) (eq 3). The $Ar^\bullet$ was suggested

$$ArN_2^+ + Cu(I) \rightarrow Ar^\bullet + N_2 + Cu(II) \quad (3)$$

to react subsequently with a halide ion to give the "Sandmeyer product" aryl halide or with another $Ar^\bullet$ to give a biaryl. In the presence of a suitable hydrogen atom donor, the aryl radical could also be reduced to ArH.[3] On the grounds of electrochemical evidence, Waters linked the uniqueness of the cuprous salt to its correct potential for bringing about the reductive step.[5,12] *Weaker* reductants such as Cd(II), Mn(II), Ni(II), Co(II), and Zn(II) were simply not able to give the electron-transfer step: The formation of some aryl halide and of phenol when they were employed had to be traced to the operation of the heterolytic mechanism (as in eq 1a). Waters also suggested that a single-electron-transfer[5] (probably the first time the SET term[44] was used) mechanism could operate with the fairly good reductant iodide ion as well. The other halide ions, on the contrary, that are poorer reductants and therefore unable to transfer the electron, would require the assistance of an accompanying cuprous cation in order to react.

The rationalization of Waters went further. The Gattermann reaction was indicated[5] as almost equivalent to the Sandmeyer, in that the electron transfer occurring at the surface of metallic copper presented the same characteristics of that occurring from cuprous ion. In the Pschorr reaction he remarked[5] the analogy to the preliminary reductive step by Cu(I), followed by the intramolecular attack of the intermediate $Ar^\bullet$ moiety. He pointed also out that the nonionic decomposition of aryldiazo hydroxides (Gomberg reaction; eq 2) could be viewed as if caused by the supply of an electron from the hydroxy nucleophile to the diazonium salt. Finally he suggested[5] that, besides the iodide ion, other nucleophiles such as nitrite, thiolate, xanthate, and sulfur dioxide, having a redox potential close to that of Cu(I), could replace the diazo group in the absence of a cuprous cation by giving the direct transfer of an electron to ArN_2^+.

A flaw in Waters' rationalization resides in the description of the second step of the Sandmeyer reaction, which he simply indicated as eq 4. Recent studies[45,46]

$$Ar^\bullet + (:\underset{\cdot\cdot}{\overset{\cdot\cdot}{Cl}}:)^- \longrightarrow Ar:\underset{\cdot\cdot}{\overset{\cdot\cdot}{Cl}}: + e^- \quad (4)$$

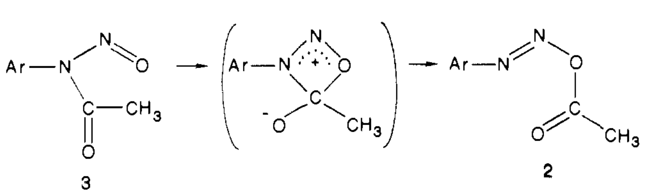
on the reaction of nucleophiles with aryl radical disregard such possibility, in that it would lead to the formation of the highly unstable $[ArX]^{\bullet-}$, which quickly fragments back to $Ar^\bullet$ and X^-. More than 10 years had to elapse before Kochi[7] gave the final touch to the mechanistic description of the second step of the Sandmeyer reaction, on the basis of a ligand transfer (lt) mediated by a *cupric* salt, which fulfills in this way the role of an inner-sphere oxidant (eq 5). The Waters plus Kochi formulation, with the *twofold* role of copper, is the generally accepted one.[2,13,15]

$$Ar^\bullet + CuX_2 \rightarrow ArX + CuX \quad (5)$$

The acceptance of the innovative intuition of Waters[5] from the chemical community was neither immediate nor smooth. Supporters of the heterolytic mechanism, as if it had necessarily excluded the homolytic one, made a point in stressing cases of dediazoniation not requiring a reducing agent, or apparently requiring a metal catalyst in the higher valence state.[42] Particularly confused was the perception of the twofold role that copper has to fulfill. According to the present view, in fact, it behaves as a reductant of ArN_2^+ in step 3, in the form of a Cu(I) salt or as Cu(0), while it is a ligand donor to $Ar^\bullet$ in step 5, as a Cu(II) salt. In contrast, either cuprous- or cupric-catalyzed Sandmeyer reactions were each time indicated as equally effective, or more suited to the experimental conditions, revealing a clear regression[47] with respect to the logic of Waters' explanation.

Another contradictory way of looking at the dediazoniation processes was that of Cowdrey and Davies.[39] In a kinetic study on a chloro-dediazoniation of

SCHEME 3



the Sandmeyer-kind, they correctly identified[48] $CuCl_2^-$ as the reactive species. [It is common to write Cu(I) to imply the presence of a cuprous species in solution, even though the Cu^+ ion is not stable but forms complexes such as CuX_2^-.] However, they maintained that the cuprous salt was required *not* for its being a reductant, but "...for its ability to form complexes so that both the reagents ArN_2^+ and Cl^- are activated and brought together more often".[39] Even a *transient* Cu(III) state was invoked by the same authors,[39] as leading to an intermediate where "...there would be little difficulty in the occurrence of an internal nucleophilic displacement by halogen". In conclusion, their 1952 paper can be viewed as a step backward in the evolution of the mechanistic description, although they have realized that a great number of dediazoniation reactions (including the Meerwein reaction[38]) possess common mechanistic features.[39] Strangely enough, the book of Zollinger,[14] 10 years later, appears a little less advanced from this point of view, since mechanistic connections among the wealth of dediazoniation examples there reported are rarely attempted. Besides, Zollinger was inclined to support the intermediacy of *cryptoradicals*[49,50] in the Gomberg reaction (or in the Meerwein one), which had previously been described as an intermolecular arylation via a free aryl radical. According to Hey,[51] in fact, the radical could originate from the decomposition of diazoacetate **2**, formed from ArN_2^+ and $CH_3CO_2^-$, with some analogy to eq 2[13] (eq 6).

$$\underset{\mathbf{2}}{\mathrm{ArN{=}NOCOCH_3}} \rightarrow \mathrm{Ar^{\bullet}} + \mathrm{N_2} + {}^{\bullet}\mathrm{OCOCH_3} \qquad (6)$$

Zollinger instead derived his belief from the Huisgen's study upon the equilibration of *N*-nitrosoacetylarylamine **3** with diazoacetate **2**, where a "rolling off" mechanism via a four-center 1,3-rearrangement is suggested[52] (Scheme 3). From an ensuing reaction, bound to involve a homolytic decomposition of **2**, Huisgen and co-workers obtained results not in agreement with the appearance of the Hey's *free* radicals. In fact, they were not able to identify any Kolbe-like coupling product that would derive from the decarboxylation of $CH_3CO_2^{\bullet}$, i.e. ethane, or to detect evolution of carbon dioxide.[53] From this point Zollinger extrapolated that the Gomberg arylation, although unquestionably a homolytic process, did not involve free radicals but only cryptoradicals.

SCHEME 4

$$\mathrm{ArN_2^+ + AcO^- \rightleftharpoons ArN{=}NOCOCH_3 \xrightarrow{AcO^-} ArN{=}N{-}O^- + (CH_3CO)_2O}$$

$$\text{or } \mathrm{ArN_2^+ + OH^- \rightleftharpoons \underset{\text{diazo hydroxide}}{ArN{=}NOH} \underset{}{\overset{OH^-}{\rightleftharpoons}} \underset{\text{diazotate}}{ArN{=}N{-}O^-}}$$

$$\text{common paths} \begin{cases} \mathrm{ArN{=}NO^- \overset{ArN_2^+}{\rightleftharpoons} \underset{\text{diazo anhydride}}{ArN{=}NON{=}NAr}} \\ \mathrm{ArN{=}NON{=}NAr \rightarrow Ar^{\bullet} + N_2 + {}^{\bullet}ON{=}NAr} \end{cases}$$

SCHEME 5

$$\mathrm{ArN{=}NO^- + ArN_2^+ \rightarrow ArN{=}NO^{\bullet} + ArN_2^{\bullet} \rightarrow Ar^{\bullet} + N_2}$$

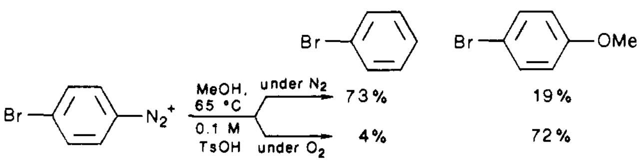
SCHEME 6

$$\mathrm{ArN_2^+ + {}^{\bullet}CH_2O^- \rightarrow Ar^{\bullet} + N_2 + CH_2O}$$

$$\mathrm{Ar^{\bullet} + CH_3OH \rightarrow ArH + {}^{\bullet}CH_2OH}$$

$$\mathrm{{}^{\bullet}CH_2OH + CH_3O^- \rightleftharpoons {}^{\bullet}CH_2O^- + CH_3OH}$$

SCHEME 7



Before this historical digression is closed, some other important contributions deserve mention. Kornblum has provided in 1950 the first detailed description of the mechanism of the reduction of an arenediazonium salt to ArH with hypophosphorous acid.[6] He has shown that a radical-chain process actually takes place (vide infra: hydrodediazoniation). The work of Rüchardt and his group[8] has widened still more the horizon of the homolytic dediazoniations, discovering, in line with the Waters' view, additional agents able to cause the preliminary electron transfer. Rüchardt has also provided a sound description[54] of the mechanism of the Gomberg reaction with AcO^- (and with OH^-) (Scheme 4), where *no* free carboxylate radical is invoked (vide infra), making clear the boundaries of the connection with the rearrangement of *N*-nitrosoacylarylamines reported in Scheme 3. The possibility of a direct et (Scheme 5) is made less likely,[8] although is not completely rejected, by kinetic evidence[55,56] and by the occasional isolation of the diazo anhydrides.[57] Bunnett was involved in several occasions with mechanistic aspects of arenediazonium chemistry.[58,59] Probably his most important contribution was to delineate the salient features of the hydro-dediazoniation in alkaline methanol,[9,60] pointing out the more likely species, i.e. $^{\bullet}CH_2O^-$, which is responsible for the electron-transfer step (Scheme 6). Along with DeTar,[61] he has also shown[9,60] how the simple variation of the reaction atmosphere from N_2 to O_2 (Scheme 7) is sufficient to divert the thermal dediazoniation in acidic methanol from the homolytic to the heterolytic route, respectively. In fact, the effect of O_2 on the homolytic pathway would be that of trapping the $Ar^{\bullet}$ intermediate in the initiation, so to prevent its entrance into the propagation chain of Scheme 6.

A last comment is devoted to a rather recent procedure that has been used to induce a Sandmeyer-like reaction.[62] Strictly speaking, this is not a dediazoniation, but a direct deamination of an arylamine into aryl halide by means of alkyl nitrite and copper(II) halide (eq 7). The effectiveness of copper(II) halides

$$\mathrm{2ArNH_2 + 2RONO + CuX_2 \xrightarrow{CH_3CN} 2ArX + 2ROH + CuO + H_2O + 2N_2} \qquad (7)$$

in producing a high yield of ArX, coupled with an experimentally observed ineffectiveness of copper(I) halides, puzzled the authors. In the attempt to find some mechanistic explanation of the peculiar role of copper(II) in this reaction, vague mention was even made of the old Hodgson proposal of cupric catalysis.[29,42] Later, the authors suggested[63] that the copper(II) salt may promote as a Lewis acid the nitrosation of the amine to diazonium ion and, subsequently, a copper(I) salt, to be formed in small amounts from nonspecified side reaction(s), is the true catalyst for the substitutive dediazoniation.

It is my opinion that a more satisfactory explanation could be that, from the reaction of the arylamine with the alkyl nitrite (eq 8), a diazo hydroxide is initially

$$ArNH_2 + RONO \rightarrow ArN_2^+OH^- \text{ (or } RO^-\text{)} + ROH \text{ (or } H_2O\text{)} \quad (8)$$

formed. It easily leads to the aryl radical according to the Rüchardt mechanism via the diazotate (Scheme 4). Nuclear halogenation of Ar•, by ligand transfer from the copper(II) halide (as in eq 5), would eventually afford the product ArX. Therefore, there is no need to seek initial formation of a Cu(I) salt by any side reaction, to justify the occurrence of the homolytic route. In fact, when the same reaction is run in the absence of CuX_2, reduction to ArH occurs[62] (eq 9), as confirmed by Ca-

$$ArNH_2 + RONO \rightarrow ArN_2^+RO^- \rightarrow Ar^\bullet \xrightarrow{RH} ArH \quad (9)$$

dogan,[65] indicating that the diazotate route suggested here already accounts for extensive formation of Ar•. In conclusion, what the authors[62-64] have described would not appear to be a novel procedure, but simply another entry into a well-documented mechanistic scheme.[54]

III. Homolytic Dediazoniation Reactions: A General Description

The acceptance of electron-transfer mechanisms and the inquiry for the intermediacy of radical species in numerous reactions are currently in vogue in organic chemistry. In particular, for the reactions of diazonium salts it is admitted that they are susceptible of ready reduction by agents capable of supplying a single electron. It is possible that the emphasis this review places on the homolytic Waters' mechanism and on the importance of the electron-transfer step is in part the consequence of the current trends, as it also transpires in the recent Zollinger reviews.[10,15] It will therefore be interesting to see whether in the future some of the present conclusions will be still accepted.

A. How the Homolytic Dediazoniation Takes Place

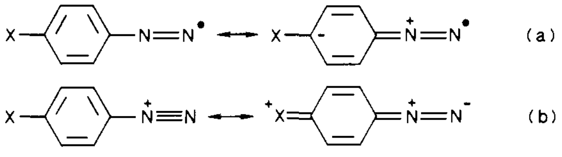
The general description of the class of homolytic dediazoniations we will attempt here is mainly grounded upon the views of Waters[5] and Kochi.[7] The description is divided into two sections, according to the two leading reaction events. This first section examines the conditions under which the homolytic step 1b can be made to occur. Then, in section B all the reaction pathways that are opened to the aryl radical so produced are examined.

TABLE I. Half-Wave Reduction Potentials of Arenediazonium Ions in Sulfolane[a]

substituent	$E_{1/2}$ (vs SCE), V	substituent	$E_{1/2}$ (vs SCE), V
p-NO_2	+0.450	p-SO_3^-	+0.297
p-CN	+0.433	none	+0.295
p-Cl	+0.350	p-CH_3	+0.250
p-Br	+0.383	p-OCH_3	+0.140
p-I	+0.383	p-$N(CH_3)_2$	-0.095
p-CO_2^-	+0.328		

[a] From ref 66.

SCHEME 8



1. Reduction at the Electrode

The most straightforward way of promoting step 1b is at the surface of an electrode. When a diazonium salt acquires an electron, it forms a diazenyl radical **4**, a rather labile species, that in turn gives up dinitrogen to form an aryl radical (eq 10 and 11). Electrochemical

$$ArN^+{\equiv}N \overset{e^-}{\rightleftharpoons} \underset{\mathbf{4}}{ArN{=}N^\bullet} \quad (10)$$

$$ArN{=}N^\bullet \rightarrow Ar^\bullet + N_2 \quad (11)$$

studies provide us with the basic information that diazonium salts are easily reducible species. The polarographic half-wave reduction potential ($E_{1/2}$) of benzenediazonium tetrafluoroborate in sulfolane is in fact +0.295 V (vs SCE, saturated calomel electrode), according to Elofson and Gadallah.[66] The $E_{1/2}$ increases to +0.450 V with a p-nitro substituent and decreases to +0.140 V with a p-methoxy group (Table I).[66,67] A good linear relationship with a slope of 0.22 has been found by these authors, between the $E_{1/2}$ values and the σ^+ substituent constants. The obtained correlation indicates that electron-withdrawing substituents increase the ease of reduction of the substrate, possibly stabilizing the diazenyl radical (Scheme 8a), while electron-releasing substituents stabilize the starting diazonium salt, decreasing in this way its tendency to acquire an electron (b). This point is confirmed by theoretical studies.[69] Hence, the trend of the substituents effect supports the expectation that the positive charge of the substrate vanishes in the step of interest, as required by eq 10.

The rate of decay of the diazenyl radical into Ar• and N_2 in eq 11 is not known exactly. There is indeed conflicting evidence for the very intermediacy of **4** from an ESR study.[70] However, a recent experiment by means of laser flash photolysis of Suehiro,[71] who was able to trap the diazenyl radical as PhN=NPh, gives a lowest limit of 5×10^5 s^{-1} for the rate of fragmentation in eq 11. Another group[72] had previously estimated a rate constant of 10^7–10^8 s^{-1} by CIDNP technique for loss of N_2 from an $ArN_2^\bullet$ moiety, deriving from the homolysis of an unsymmetrical azo compound (eq 12). A

$$ArN{=}NR \rightarrow ArN{=}N^\bullet + R^\bullet \quad (12)$$

recent paper on a laser-induced fragmentation of an unsymmetrical azoalkane[73] supports the stepwise mechanism of dissociation through a diazenyl radical (eq 13). The alkyl radical and N_2 are formed with a

$$\mathrm{RN{=}NR'} \rightarrow \mathrm{RN{=}N^\bullet} + \mathrm{R'^\bullet} \rightarrow \mathrm{R^\bullet} + \mathrm{N_2} + \mathrm{R'^\bullet} \qquad (13)$$

rate of $5 \times 10^7\ s^{-1}$, which is larger than that reported by Suehiro,[71] as expected for an aliphatic diazenyl radical on the basis of the well-known higher fragmentation tendency of primary aliphatic diazonium salts vs aromatic diazonium salts.[74] Indeed, the fragmentation step (11) cannot be much faster than $10^5\ s^{-1}$, since the Elofson and Gadallah study[66] substantiates the reversibility of the one-electron reduction (10).

An overlooked point remains whether or not the loss of dinitrogen from 4 may be reversible, as the preceding reductive step (10) is.

$$\mathrm{ArN{=}N^\bullet} \underset{?}{\rightleftharpoons} \mathrm{Ar^\bullet} + \mathrm{N_2} \qquad (11)$$

For the aryl cation, convincing evidence for a recombination step has been reached[75] (eq 14). Calculations at the STO-3G level support the dissociation–recombination mechanism for this nitrogen scrambling.[4b]

$$\mathrm{Ar^{15}N^{+}{\equiv}N} \rightleftharpoons [\mathrm{Ar^{+\,15}N{\equiv}N}] \rightleftharpoons \mathrm{ArN^{+}{\equiv}N^{15}} \qquad (14)$$

2. Radiolytic Approach

Another way of supplying an electron to a diazonium salt is by radiolytic technique. Solvated electrons produced in water solution by γ-radiation from a ^{60}Co source (eq 15) have been used by Packer et al.[76,77] to

$$\mathrm{H_2O} \xrightarrow{\gamma} \mathrm{e_{aq}^-} + \mathrm{HO^\bullet} + \mathrm{H^\bullet} + \mathrm{H_2} + \mathrm{H_2O_2} \qquad (15)$$

induce a free-radical chain reaction between arenediazonium ions and a variety of reducing agents (RH_2) (eq 16). The aryl radical produced by a solvated

$$\mathrm{e_{aq}^-} + \mathrm{ArN_2^+} \rightarrow \mathrm{ArN_2^\bullet} \rightarrow \mathrm{Ar^\bullet} + \mathrm{N_2} \qquad (16)$$

electron in the primary radiolytic step abstracts hydrogen from the reducing agent, forming a new radical ($^\bullet RH$), which then reduces diazonium ion in a chain-propagation process (eq 17 and 18). The overall re-

$$\mathrm{Ar^\bullet} + \mathrm{RH_2} \rightarrow \mathrm{ArH} + \mathrm{^\bullet RH} \qquad (17)$$

$$\mathrm{^\bullet RH} + \mathrm{ArN_2^+} \rightarrow \mathrm{Ar^\bullet} + \mathrm{N_2} + \mathrm{R} + \mathrm{H^+} \qquad (18)$$

action results in a hydrodediazoniation (eq 19). These

$$\mathrm{ArN_2^+} + \mathrm{RH_2} \rightarrow \mathrm{ArH} + \mathrm{N_2} + \mathrm{R} + \mathrm{H^+} \qquad (19)$$

authors used alcohols, aldehydes, or formate ion as reducing agents. They indicate[77] that the reaction between $^\bullet RH$ and ArN_2^+ is a true electron transfer and *does not* involve prior addition of the radical to the diazonium nitrogen with subsequent dissociation.[78] Reaction 20, suggested by Bargon and Seifert,[70] has

$$\mathrm{ArN_2^+} + \mathrm{^\bullet RH} \rightarrow [\mathrm{ArN{=}NRH}]^{\bullet +} \rightarrow \mathrm{Ar^\bullet} + \mathrm{N_2} + \mathrm{RH^+} \qquad (20)$$

been successively criticized by Rüchardt et al.[79] and by Packer et al.[80] This point is of considerable importance, in that it gives support to the numerous cases where alcohols, ethers, or acetals have been invoked as electron donors to diazonium salts.[8,10,15] It confirms that once the aryl radical has been generated by some reducing act in an initiation step, these solvents are able to sustain a radical-chain mechanism of reduction.

The group of Packer[77] was able to measure quantitatively the rate of electron transfer between the $^\bullet RH$ derived from benzyl alcohol and para-substituted diazonium salts. Correlation with σ^+ constants gave a good linear relationship with a ρ value of 0.55. As indicated by the positive sign of ρ, this finding upholds a reductive process via electron transfer, consistent with Elofson and Gadallah's polarographic reduction of diazonium salts.[66] We find therefore a gratifying uniformity of behavior between two different experimental techniques.

Another pulse radiolysis study once more confirms the true intermediacy of the diazenyl radical 4 (in eq 10 or 16), since evidence is given for its dimerization to produce a tetraaza diene ($ArN{=}NN{=}NAr$).[81]

3. Photoinduced Electron Transfer

A third method of formation of $Ar^\bullet$ from diazonium salts is by photochemical decomposition. Ando indicates[82] that the primary process is a homolytic scission of the C–N bond of the diazonium salt, as induced by the counterion. This follows from the excitation of a charge-transfer (CT) complex between the electron donor (X^-) and the arenediazonium ion, leading to an electron transfer (eq 21). In alcoholic solution, the

$$\mathrm{ArN_2^+X^-} \xrightarrow{h\nu} \mathrm{Ar^\bullet} + \mathrm{N_2} + \mathrm{X^\bullet} \qquad (21)$$

homolysis is essentially followed by hydrogen abstraction, and therefore an overall hydrodediazoniation results (eq 22).

$$\mathrm{Ar^\bullet} + \mathrm{CH_3CH_2OH} \rightarrow \mathrm{ArH} + \mathrm{CH_3\dot{C}HOH} \qquad (22)$$

Becker and his group[83] have carried out a kinetic study of a photoinduced et to arenediazonium ions in methanol. The rate of the et from pyrene, which produces the pyrene radical cation and diazenyl radical (eq 23), was measured for some para-substituted diazonium

$$\mathrm{pyrene} + \mathrm{ArN_2^+} \xrightarrow{h\nu} \mathrm{pyr^{\bullet +}} + \mathrm{ArN_2^\bullet} \qquad (23)$$

salts and gives $\rho = 0.38$ employing σ^+ constants. Radical-chain decomposition of arenediazonium ions, photosensitized by derivatives of anthraquinone and benzophenone, has also been described.[84]

In addition to the photolytic hydro-dediazoniation, Ando reports[82] that when X^- (in eq 21) is Cl^- or BF_4^-, the possibility of a light-induced homolytic Schiemann reaction does exist, leading to aryl halide (eq 24 and 25).

$$\mathrm{ArN_2^+Cl^-} \xrightarrow{h\nu} [\mathrm{Ar^\bullet} + \mathrm{N_2} + \mathrm{Cl^\bullet}] \xrightarrow[-\mathrm{N_2}]{} \mathrm{ArCl} \qquad (24)$$

$$\mathrm{ArN_2^+BF_4^-} \xrightarrow{h\nu} \mathrm{ArF} + \mathrm{N_2} + \mathrm{BF_3} \qquad (25)$$

Interestingly, a secondary process of lower probability, giving a significant contribution in water solution[82] or at λ <313 nm,[85] is a heterolytic one (eq 26), which re-

$$\mathrm{ArN_2^+Cl^-} \xrightarrow{h\nu} \mathrm{Ar^+} + \mathrm{N_2} + \mathrm{Cl^-} \qquad (26)$$

minds us of the possible competition of mechanism leading to solvolytic products, instead of reduction products, even under photodecomposition conditions[86] (eq 27). The heterolytic pathway may be drastically

$$\mathrm{Ar^+} + \mathrm{SOH}\ (\mathrm{or}\ \mathrm{X^-}) \rightarrow \mathrm{ArOS} + \mathrm{H^+}\ (\mathrm{or}\ \mathrm{ArX}) \qquad (27)$$

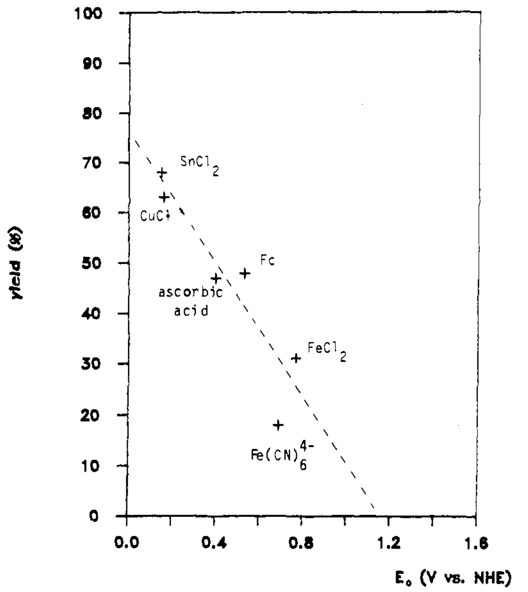


Figure 1. Dependence of the stimulant efficiency on the redox potential $E°$ (V).

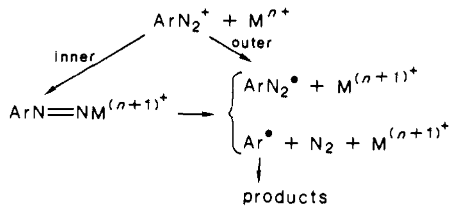
minimized, according to Ambroz and Kemp,[87] by employing counterions that are better reductants than Cl^-, so as to boost the photoinduced et. This raises a general consideration. When the counterion of a diazonium salt is not a suitable electron donor to give a *spontaneous* transfer of an electron according to the Waters' view,[5] there still exists a possibility that, under occasional *photostimulation*,[88] even by daylight,[22a] an et from the X^- can occur in an initiation step. Then, a free-radical chain process takes place, provided that it is sustained by a proper hydrogen donor solvent, as we have seen in eq 17 and 18 (vide infra). This increases the possibility of observing a homolytic mechanism, leading either to reduction or to substitution products.

4. Reduction by Metal Cations

Let us examine now what is perhaps the most familiar method of dediazoniation, that is, the one induced by metal cations. A cuprous salt is the most commonly used, and the reason is that, as correctly anticipated by Waters 50 years ago,[5] it has the right redox potential (i.e., 0.16 V) for release of an electron to the arenediazonium ion. Other cations however share the same requisite, and, consistently, they too are found effective for the dediazoniation, as indicated in the more recent literature.[15,89] Therefore, we see papers concerning et to diazonium salts by salts of the following: by Sn(II),[89,90] Cr(II),[91] Ti(III),[91-93] V(II),[91] Fe(II),[89,94-96] and $Fe(CN)_6^{4-}$;[68,96-99] by ferrocene (Fc)[89,100] or ascorbic acid;[89] by hemoglobin.[101] The relative reducing ability of the donors appears to grossly reflect their redox potential: The better the reductant, the more efficient was in fact a chloro-dediazoniation process (Figure 1).[89] A threshold value qualitatively appears, beyond which the et no longer occurs efficiently.

Some of the above-mentioned reducing cations are experimentally less convenient than the cuprous cation, because they may be less or hardly stable in the low-valence reductant states and/or need to be prepared in situ. However, this is a problem that sometimes even cuprous salts present, due to spontaneous oxidation or to disproportionation.

SCHEME 9



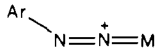
A still unanswered question is whether in the cation-induced dediazoniation a *direct* electron transfer truly occurs from the metal (eq 28) or rather an *adduct*

$$ArN_2^+ + M^{n+} \rightarrow ArN_2^\bullet + N^{(n+1)+} \quad (28)$$

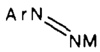
is initially formed (i.e., an arenediazenate),[102] with the arenediazonium ion acting as a sort of ligand of the metal (eq 29), and the electron is then transferred

$$ArN_2^+ + :M \rightarrow [ArN{=}NM]^+ \rightarrow [ArN_2{\cdot}M^{\bullet+}] \rightarrow Ar^\bullet + N_2 + {}^\bullet M^+ \quad (29)$$

within that bridge to finally form the aryl radical. The question can also be reasked as is whether an outer-sphere or an inner-sphere electron transfer is occurring.[103,104] The direct et appears at present to be favored,[68,89] particularly with good reductants, but it is fair to admit that the ingenuity of numerous chemists has been challenged in the past years trying to answer the question. Several techniques,[69] such as IR, NMR, or X-ray analysis, have been employed to evaluate the degree of triple-bond character of the NN group **5**,[105]



5



6

or the MNN angle, or the NN distance[15,106] in various possible diazonium–metal complexes **6**, searching for a covalent intermediate. However, there is at least one case of X-ray structural analysis *against* a covalent nature for a diazonium–metal interaction, in a complex precipitated from a concentrated solution of benzenediazonium salt and cuprous bromide.[107] We may remind that similar precipitates were instead considered to be covalent intermediates in the very first mechanistic descriptions of the Sandmeyer reaction.[39]

The choice in favor of an outer-sphere mechanism can be reached with certainty for electron-donor metals possessing the coordination sphere completely saturated. The case of the dediazoniation induced by $Fe(CN)_6^{4-}$, for example, is a clear manifestation of an outer-sphere pathway.[97] The same would appear to hold for ferrocene.[68]

In conclusion, it seems reasonable to summarize the picture of the metal cation induced dediazoniations, as reported in the Scheme 9 (where $n \geqslant 0$). The nature of the metal (and of its ligands) may be considered to be responsible for the choice of the pathway and for the timing of the fragmentation involved.

This picture is largely different from that invoked for the reactions of diazonium salts with Pd(0), in the form of organometallic compounds such as $Pd(PPh_3)_4$: An *arylpalladium* intermediate (ArPdX) is suggested to originate in these cases. Subsequent reaction, for instance with an olefin under typical Meerwein conditions, results in substrate reactivity and positional selectivity that differs with respect to the analogous case run under copper(I) catalysis, where the key intermediate is truly a free aryl radical.[102,108] Somewhat related considerations have been advanced for Cr(0) complexes, where both free-radical and organometallic intermediates, possessing different stereoelectronic requisites, appear to be present and responsible for the overall reactivity in the arylation of olefins.[109]

Coming back to the metals following Scheme 9, the influence of the redox potential of the reducing cation upon the selectivity of the dediazoniation reaction has been studied for Sn(II), Cu(I), and Fe(II) salts. Competition experiments between a para-substituted diazonium salt, and the unsubstituted benzenediazonium salt taken as reference, allowed determination of the relative reactivity (log k_{rel}) of the substrates from the amounts of the halo-dediazoniation products (Scheme 10). For each reducing metal cation (M^{n+}), a linear relationship has been obtained between σ^+ constants and the log k_{rel}.[110] Consistently, the log k_{rel} correlated linearly also with the $E_{1/2}$ of the diazonium salts. The ρ values obtained for the three reducing cations are 0.62, 0.67, and 1.0, respectively. This finding supports a rate-determining et in the halo-dediazoniation. In fact, a higher selectivity, accompanied by a lower reactivity, is obtained in the case of the worse reductant, i.e. the ferrous salt. A lower and comparable selectivity is obtained in the case of two cations (i.e., stannous and cuprous) that possess a higher and comparable reducing ability. If we also remember the previously reported ρ determinations,[77,83] it clearly follows that all the reducing techniques examined so far share the same kind of mechanism, involving the formation of the aryl radical intermediate via rate-limiting electron transfer. In addition, a gross trend emerges of an increase of selectivity, as the reducing ability of the reductant decreases.[13] A recent paper on the rate of the electron transfer from several reducing agents to $NO_2^\bullet$ (to produce NO_2^-) gives support to this point.[111] The rate constants, measured by flash photolysis, are 1.8×10^7 M^{-1} s^{-1} for ascorbate ion, 4.3×10^6 for $Fe(CN)_6^{4-}$, and 1.1×10^5 for I^-. The redox potentials of these compounds are 0.3 (at pH 6.5),[112] 0.69, and 1.3 V, respectively. Therefore, a general trend of a higher et rate vs a lower oxidation potential is confirmed to exist for some of the reducing agents that have been also used in the dediazoniation study.[89] These observations are admittedly rather qualitative, although they provide a rule of thumb to predict the behavior of a reductant. More quantitative studies have been published,[68,110] aimed at exploiting the Marcus treatment[113] to correlate rate constants for the et with the free energy change, in dediazoniation processes provoked by a few reductants. However, these attempts are in part frustrated by the unavailability of reliable values of the intrinsic barriers to the et for arenediazonium ions.

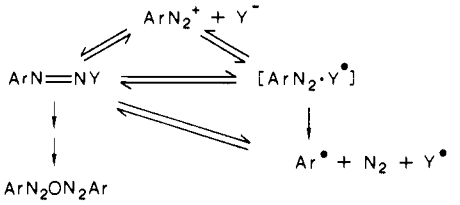
SCHEME 10

$$ArN_2^+ \xrightarrow{M^{n+}} Ar^\bullet + M^{(n+1)+} + N_2 \xrightarrow{CuX_2} ArX$$

$$PhN_2^+ \xrightarrow{M^{n+}} Ph^\bullet + M^{(n+1)+} + N_2 \xrightarrow{CuX_2} PhX$$

A paper by Doyle et al.[68] supports the outer-sphere nature of the et from $Fe(CN)_6^{4-}$ and also from decamethylferrocene to ArN_2^+. Direct measurements of the rate of et with substituted diazonium salts were made. The authors found a more satisfactory correlation with σ than with σ^+ constants, which seems rather uncommon.[114] A plot of their data vs σ^+ constants gives reasonable fit as well, with ρ values of 3.2 and 1.5, respectively, for the two reductants. The positive sign of these slopes is in line with the others found so far.[77,83,110] Only the ρ value for the $Fe(CN)_6^{4-}$ reductant appears too large, at least for being related to an et step.[13,115,116]

SCHEME 11[a]



[a] See Scheme 4.

TABLE II. Rate Data of Atom Abstraction by Aryl Radical (M^{-1} s^{-1})[a]

Hydrogen Abstraction	
sec-alkyl	$k_H = 3.3 \times 10^5$
tert-alkyl	$k_H = 1.6 \times 10^6$
methyl of CH_3OH	$k_H = 5 \times 10^5$
Halogen Abstraction	
I_2	$k_I = 1 \times 10^{10}$
i-PrI	$k_I = 1 \times 10^9$
ArI	$k_I = 9 \times 10^7$ [b]
CBr_4	$k_{Br} = 5 \times 10^9$
$CBrCl_3$	$k_{Br} = 2 \times 10^9$
CCl_4	$k_{Cl} = 3.5 \times 10^6$
Atom Addition	
PhH	$k = 1 \times 10^6$
$CH_2{=}CH_2$	$k = 8 \times 10^6$

[a] Generation of $Ph^\bullet$ occurred by thermal decomposition of PAT.[207] [b] Reckoned on averaging data from ref 201.

5. *Anion-Induced Dediazoniation*

The anion-induced dediazoniation is strictly related to the cation-induced one, as was foreseen by Waters,[5] in that it is also grounded on the redox potential of the electron-donor species (eq 30). A nucleophile, present

$$ArN_2^+ + Y^- \rightarrow ArN_2^\bullet + Y^\bullet \qquad (30)$$

as the counterion of the diazonium ion, or purposedly added in solution, may either give an outer-sphere et to ArN_2^+ or form a *covalent adduct*[13] with that cationic functionality, due to the favorable electrostatic interaction. The choice depends on the oxidation potential of the nucleophile and on the solvent features:[10] In solvents of low dielectric constant the formation of the adduct is in fact prevalent. The adduct may cleave subsequently, either photochemically[117] or even thermally,[118] in the latter case as due to the lability of the azo moiety (Scheme 11). In the formation and fragmentation of the covalent compound, an et of the inner-sphere kind *in essence* takes place. Alternatively, the ionic association leading to the covalent adduct may be reversible,[15] so that the outer-sphere et can in principle occur either as a primary event or following the preliminary formation of an unproductive covalent intermediate.[119] Finally, the nucleophile may also be the solvent itself, as will be reported in the last section.

The picture is made complex by the fact that certain nucleophiles are reported to give an outer-sphere et in some cases and an inner-sphere et in some others. Clearly, we are still far from a satisfactory knowledge of these phenomena. We can try to put together the existing evidence, to detect at least the common features that are behind.

Let us start by examining iodide ion as nucleophile. The standard redox potential ($E°$) of the iodide ion[103] is 1.3 V vs NHE (normal hydrogen electrode), and a direct release of the electron to an arenediazonium ion seems likely to take place.[89,120,121] Once the diazenyl radical has fragmented to give Ar•, coupling may occur with I•, with iodine, or with I_3^-, to produce aryl iodide[89,121-123] (Scheme 12). Evidence for the formation of $I_2^{\bullet-}$ has been reported.[121] This species can act as an alternative source of electrons to reduce the diazonium salt in a chain process. The direct reaction of I^- with Ar• that was suggested to take place[124] leads to the extremely unstable radical anion of the aryl iodide, which fragments back to Ar• and I^- with a rate constant higher than 10^{10} s^{-1}.[125] Evidence has been given[126] for lowering the rate of the fragmentation of $[ArI]^{\bullet-}$ in the presence of excess I^-, implying some reversibility for step 31. Nevertheless, it would appear unlikely that this step is the one responsible for the formation of ArI, particularly when one also considers the very high efficiency of the reaction of Ar• with iodine[82] (see Table II).

SCHEME 12

$$ArN_2^+ + I^- \longrightarrow Ar^\bullet + N_2 + I^\bullet$$

$$2I^\bullet \rightarrow I_2 \xrightarrow{I^-} I_3^-$$

$$Ar^\bullet + I^\bullet \rightarrow ArI$$

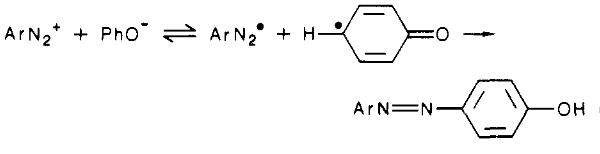
$$Ar^\bullet + I_2 \rightarrow ArI + I^\bullet$$

$$Ar^\bullet + I_3^- \rightarrow ArI + I_2^{\bullet-}$$

$$ArN_2^+ + I_2^{\bullet-} \rightarrow Ar^\bullet + N_2 + I_2$$

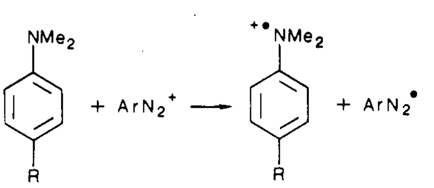
$$Ar^\bullet + I^- \rightleftharpoons [ArI]^{\bullet-} \qquad (31)$$

Nucleophiles that could likewise give the direct et to ArN_2^+, possibly followed by coupling of the radical fragments, are ArS^-,[127-130] xanthate ($ROCS_2^-$),[1] tertiary aliphatic amines,[8] $H_2PO_2^-$,[6] and perhaps nitrite ion,[92,131] or NAD(P)H models.[132] Evidence has been also reported that tertiary aromatic amines,[8] semiquinone,[133] and even aryl oxide ions may give the et step when the azo coupling reaction is inhibited,[134] although there is no general agreement upon a straightforward et for the latter nucleophile.[135] Incidentally, the azo coupling reaction itself has been described by Bubnov et al.[136] as an et process, on the basis of CIDPN evidence.



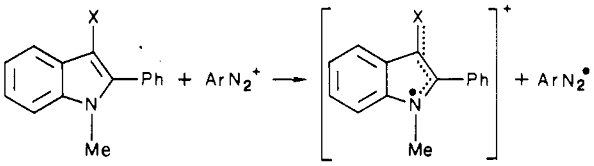
(32)

An analogous conclusion is advanced for the two following cases:[137]



(33)

$E_{1/2}$ = 0.46–0.24 V. vs Ag/AgClO$_4$



(34)

$E_{1/2}$ = 1.1–0.3 V. vs Ag/AgClO$_4$

Finally, the occurrence of et and the intervention of Ar• are demonstrated in the reaction of t-BuO$^-$ with a substituted diazonium salt in a Me$_2$SO/t-BuOH mixed solvent[138] (eq 35).

$$ArN_2^+ + t\text{-}BuO^- (CH_3SOCH_2^-) \rightarrow ArAr \qquad (35)$$

As far as radical anions are concerned, evidence for a direct et step from p-benzosemiquinone radical (QH•) to substituted diazonium salts was given[133] (eq 36). A correlation of the rate constants of the et vs σ^+ constants provided a ρ = 1.4. The ρ value decreased to 0.69 when with the tetrachloro 1,4-semiquinone radical anion ($Q^{\bullet-}$; $E_{1/2}$ = 0.35 V vs NHE[103]) and increased to 1.45 with the slightly worse reductant 7,7,8,8-tetracyanoquinodimethane radical anion ($E_{1/2}$ = 0.64 V vs NHE[103]).[139]

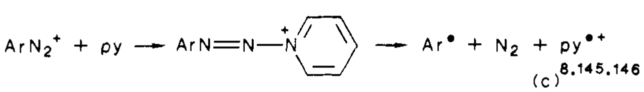
$$QH^\bullet + ArN_2^+ \rightarrow Q + H^+ + ArN_2^\bullet \qquad (36)$$
$$Q = \text{1,4-benzoquinone}$$

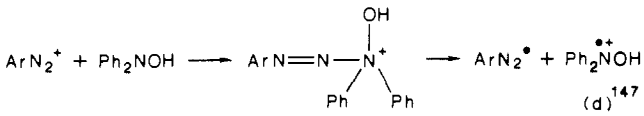
Chloride ($E°$ = 2.6 V)[103] and bromide ($E°$ = 2.0 V)[103] ions (and the fluoride ion, $E°$ = 3.6 V[103]) have redox potentials much higher than that of iodide ion. Therefore, they are not capable of a direct et to ArN_2^+[140] but must rely on a cuprous cation purposely added to fulfill that task (vide infra). Bromide ion represents probably a borderline situation, as far as the redox potential is concerned.[89,123] In fact, evidence of et without the need of a Cu(I) salt is reported in Me$_2$SO with diazonium salts bearing electron-withdrawing groups.[22] Astatide ion (At$^-$), on the other hand, is able to induce a direct homolytic dediazoniation.[15] Its redox potential is not known, but it is reasonable for it to be lower than that of iodide ion. In fact, in a dediazoniation with $^{211}At^-$ *and* $^{131}I^-$ in competition, more ArAt than ArI was obtained.[141]

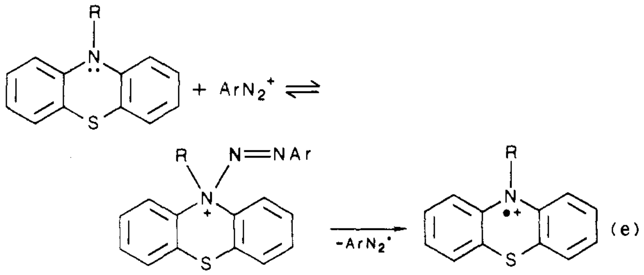
Hydroxide ion instead is to be considered as representative of the behavior of a second larger group of nucleophiles,[15] which includes other oxygen nucleophiles such as alkoxide and carboxylate (PhO$^-$ being a borderline case), pyridine, N,N-disubstituted hydroxylamine, perhaps NO_2^- (according to another point of view),[15,142] and finally some weak nucleophiles such as HMPT. Recent findings put ArS$^-$ in this group.[117,118] All these nucleophiles would not be able to release *directly* an electron to ArN_2^+. Rather, they are suggested to form a covalent compound with it, that in some cases can be isolated and that then or eventually cleaves (Scheme 11). The radical fragment originating from the nucleophile is in general not able to give coupling with Ar•, with the possible exception of $NO_2^\bullet$. A hydro-dediazoniation or an arylation of an unsaturated system is consequently the net result of most of these processes (vide infra):

$$\mathrm{ArN_2^+ + O{=}P(NMe_2)_3 \rightarrow ArN{=}NO\overset{+}{P}(NMe_2)_3 \rightarrow Ar^\bullet + N_2 + {}^\bullet O\overset{+}{P}(NMe_2)_3} \quad \text{(a)}^{143,144}$$

$$\mathrm{ArN_2^+ + NO_2^- \rightleftharpoons ArN{=}NNO_2 \rightarrow Ar^\bullet + N_2 + NO_2^\bullet} \quad \text{(b)}^{15}$$


(c)[8,145,146]


(d)[147]


(e)

The reaction of phenothiazine with diazonium salts (e) is described as belonging to this group.[148] The authors suggest a rapid formation of a covalent intermediate, which subsequently undergoes a rate-determining homolysis. Spectrophotometric determination of the rate of this process with substituted diazonium salts leads to a correlation with σ^+ constants and gives a $\rho = 1.86$. Analogously, the reaction of substituted arenediazonium ions with *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine ($E° = 0.25$ V vs NHE)[103] provided[149] a Hammett correlation with $\rho = 1.92$.

More complex are the reaction pathways followed with OH^- itself, i.e. the original Gomberg-Bachmann reaction[36] (see Scheme 4).

$$\mathrm{ArN_2^+ + HO^- \rightleftharpoons ArN{=}NOH \underset{H_2O}{\overset{OH^-}{\rightleftharpoons}} ArN{=}NO^-} \text{ (cis and trans aryldiazotate)}$$

$$\mathrm{ArN{=}NO^- + ArN_2^+ \rightleftharpoons ArN{=}NON{=}NAr} \text{ (diazo anhydride) } \mathrm{\rightarrow Ar^\bullet + N_2 + {}^\bullet ON{=}NAr}$$

or those followed with a carboxylate ion

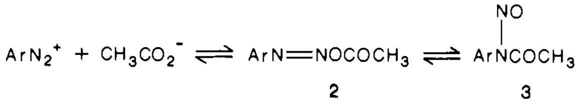
$$\mathrm{ArN_2^+ + RCO_2^- \rightleftharpoons \underset{\mathbf{2}}{ArN{=}NOCOR}}$$

$$\mathrm{ArN{=}NOCOR \xrightarrow{RCO_2^-} ArN{=}NO^- + (RCO)_2O}$$

$$\mathrm{ArN{=}NO^- \xrightarrow{ArN_2^+} ArN{=}NON{=}NAr} \text{ (and then as above)}$$

They were elucidated by Rüchardt,[8,54,55] who has corrected in this way both Hey's old formulation[51] (eq 6) and the cryptoradical suggestion.[49,50] The absence of decarboxylation, and of the formation of Kolbe-like coupling products deriving from the carboxylate, that were remarked by Huisgen,[53] finds indeed an explanation here, since *no* free carboxylate radical ($CH_3CO_2^\bullet$) is invoked. The *N*-nitrosoacetanilide (3) (Scheme 13) comes out to represent an entry into the chemistry of the homolytic dediazoniations.[54,150,151] A study of substituent effects has been carried out for the reaction of para-substituted arenediazonium ions with AcO^-Na^+.[152] The rate-determining step appears to be the decomposition of the diazoanhydride intermediate (Scheme 4), and the ρ value obtained is 1.9.

SCHEME 13



$$\mathrm{ArN_2^+ + CH_3CO_2^- \rightleftharpoons \underset{\mathbf{2}}{ArN{=}NOCOCH_3} \rightleftharpoons \underset{\mathbf{3}}{Ar\overset{NO}{N}COCH_3}}$$

Extensive work by Zollinger et al.[153] offers further support to the mechanism presented in Scheme 4. The obtainement of ^{15}N-CIDNP spectra employing OH^- as nucleophile strengthens the view of a homolytic nature of the process. Kinetic evidence is also given for the formation of the diazo anhydride.[56]

It is not difficult to realize that most of the above-examined reactions present common features with the thermolysis of azo compounds[8,13,60,154] (eq 37). It is also

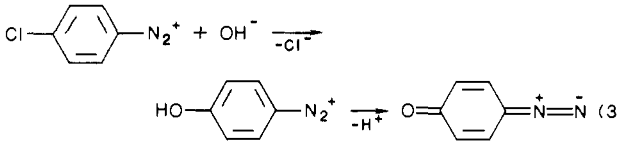
$$\mathrm{PhN{=}NCPh_3 \rightarrow Ph^\bullet + N_2 + {}^\bullet CPh_3} \qquad (37)$$

clear that there is always the risk, with strongly nucleophilic anions, of interference by the heterolytic mechanism, particularly when the nucleophiles are *not* good electron donors: typical is the case of fluoride ion. A fast reaction of the aryl cation with the nucleophile then intervenes, leading to "solvolytic" product(s).

$$\mathrm{ArN_2^+ \xrightarrow{slow} Ar^+ + N_2} \qquad (1a)$$

$$\mathrm{Ar^+ + Y^- \xrightarrow{fast} ArY} \qquad (27)$$

Incursion of a process of nucleophilic aromatic substitution is also documented.[155] This is due to the strong electron-withdrawing character of the $-N_2^+$ group that is capable of inducing, for example, nuclear substitution of a proper group by OH^- (eq 38).

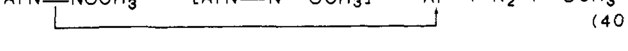

(38)

diazo tars

We discuss finally the reaction of ArN_2^+ with the methoxide ion, which presents peculiar features.[15] This mechanism of dediazoniation has been essentially elucidated by Bunnett and co-workers.[9,59,60] A very fast formation of a covalent intermediate, i.e. an arylazo ether (eq 39), takes place in alkaline methanol and is

$$\mathrm{ArN_2^+ + CH_3O^- \rightarrow ArN{=}NOCH_3} \quad \text{cis and trans} \qquad (39)$$

followed by a one- or two-step homolytic decomposition (eq 40), the cis arylazo ether being faster to fragment



$$\mathrm{ArN{=}NOCH_3 \rightarrow [ArN{=}N^\bullet\ {}^\bullet OCH_3] \rightarrow Ar^\bullet + N_2 + {}^\bullet OCH_3} \qquad (40)$$

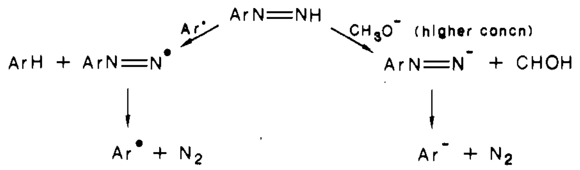
than the trans isomer.[59,156,157] In the case of the OH^- ion, an analogous homolytic decomposition of the covalent intermediate diazo hydroxide could not occur, because the latter is immediately converted into the

SCHEME 14

$$ArN{=}NOCH_3 + CH_3O^- \rightleftharpoons ArN{=}N^- + CH_2O + CH_3OH$$

$$ArN{=}NH \underset{CH_3OH}{\overset{CH_3O^-}{\rightleftharpoons}} ArN{=}N^- \xrightarrow[-N_2]{} Ar^- \xrightarrow{CH_3OH} ArH$$

SCHEME 15



diazotate (in Scheme 4). For the subsequent steps, Bunnett's data[9] support a chain propagation sequence (Scheme 6).

$$Ar^\bullet + CH_3OH \rightarrow ArH + {}^\bullet CH_2OH$$

$${}^\bullet CH_2OH + CH_3O^- \rightleftharpoons {}^\bullet CH_2O^- + CH_3OH$$

$$ArN_2^+ + {}^\bullet CH_2O^- \rightarrow ArN_2^\bullet + CH_2O$$

The overall hydro-dediazoniation comprises therefore a preliminary homolytic decomposition of a covalent adduct (eq 40), followed by direct et in the propagation chain.

Under *strongly alkaline* conditions, however, an independent heterolytic mechanism (Scheme 14) prevails.[59] Unambiguous proof of this dichotomy was reached with isotopic studies.[59,158] Incorporation of deuterium occurs in CH_3OD solution at higher concentrations of CH_3O^- (i.e., for intermediacy of aryl anion) but does not occur at lower concentrations of CH_3O^- (i.e., for intermediacy of aryl radical). It is in fact known that aryl radicals *do* react with hydrogen atom(s) of the methyl group of CH_3OH and *do not* react with hydrogen of the OH group, due to the different strength of these bonds.[159,160]

More recently Broxton had suggested[161] the possibility of a direct et from the alkoxide ion to the diazonium salt or to the arylazo ether (eq 41 and 42, respectively). As pointed out previously, straightforward et from an alkoxide ion is not considered to be very likely.[135] In a subsequent paper,[162] Broxton has modified his formulation, resurrecting the hypothesis that an aryl diimide is the common intermediate in the homolytic and in the heterolytic pathways. This hypothesis had been previously advanced,[163] but later rejected,[60] by Bunnett et al. for the thermolysis in acidic methanol (Scheme 15). The aryl diimide would result from a preliminary hydride transfer (eq 43). The Broxton homolytic pathway, however, is not a chain reaction, and it would be overwhelmed by the chain propagation sequence of Scheme 6.

$$CH_3O^- + ArN_2^+ \rightarrow ArN_2^\bullet + CH_3O^\bullet \qquad (41)$$

$$ArN{=}NOCH_3 \xrightarrow{CH_3O^-} [ArN{=}NOCH_3]^{\bullet -} \rightarrow Ar^\bullet + N_2 + CH_3O^- \qquad (42)$$

$$ArN_2^+ + CH_3O^- \rightarrow ArN{=}NH + CH_2O \qquad (43)$$

All the nucleophile-induced homolytic dediazoniations examined in this section lead to $Ar^\bullet$ and, as mentioned before, disclose the route to the formation

SCHEME 16

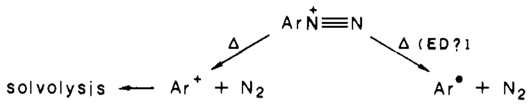


TABLE III. **Koppel and Paju's Solvent Parameter B[169]**

solvent	B	solvent	B	solvent	B
CH_2Cl_2	23	EtOH	235	DMF	291
AcOH	131	*i*-PrOH	236	DMSO	362
H_2O	156	acetone	224	HMPT	470
MeOH	218	CH_3CN	160	Py	475

either of a reduction product (ArH) or also of a substitution product (ArY). The latter product may arise from coupling of $Ar^\bullet$ with the $Y^\bullet$, formed in the preliminary outer- or inner-sphere et step (Scheme 11) or from other pathways (see section B).

6. Solvent-Induced Dediazoniation

In this last section we examine the thermal homolytic dediazoniation induced by the solvent. Actually, there exists a miscellanea of cases where weak interactions between an arenediazonium ion and the partner, i.e. the solvent, evolve into the formation of a covalent diazo intermediate (eq 44), which, under the influence of collisions, gives homolytic rupture of the bonds (see eq 37 and 45).[164] This provides the initiation of a radical chain process, which is then sustained by the solvent itself (eq 17 and 18). Of course, due to the lack of a manifest electron donor (ED), the possibility of competition by the heterolytic pathway is very strong in this case[75b] (Scheme 16). Typical is the well-known method of heterolytic hydroxy-dediazoniation in water, to obtain phenols. Nevertheless, Zollinger states that "... arenediazonium ions have a latent tendency to form aryl radicals and not aryl cations".[15] In addition, Bunnett and Yijima[9] have shown that the rate of homolysis in acidic methanol may be even 30 times higher than the rate of heterolysis. Indeed, the C_6H_5 moiety of a diazonium salt gains in aromaticity when an electron is added to it.[165,166] In any case, the experimental conditions must be carefully chosen to be sure to observe unambiguously either dediazoniation process.

Szele and Zollinger have found[167] that the thermal homolytic dediazoniation is favored by increasing the nucleophilicity of the solvent or by increasing the electrophilicity of the β-nitrogen atom of the diazonium salt, placing suitable substituents on the aromatic ring. This effect comes out because the solvent acts as an electron donor to the nitrogen atom[168] (eq 44), in agreement with the reaction scheme (Scheme 11) presented in the previous section. The higher the electron-donor capacity of the solvent, or the electrophilicity of ArN_2^+, as resulting from an electron-withdrawing substituent, the more the reaction will follow the homolytic decomposition pathway (eq 45). The two authors[167] were able to find a reasonable correlation of Koppel and Paju's[169] solvent parameter B (Table III), with characteristics of the solvent favoring either mechanism. For instance, solvents with a B parameter higher than 400 (e.g., HMPT or pyridine) are expected

$$ArN^+{\equiv}N + {:}ED \rightarrow ArN{=}N{-}ED^+ \qquad (44)$$

$$ArN{=}N{-}ED^+ \rightarrow Ar^\bullet + N_2 + {}^\bullet ED^+ \qquad (45)$$

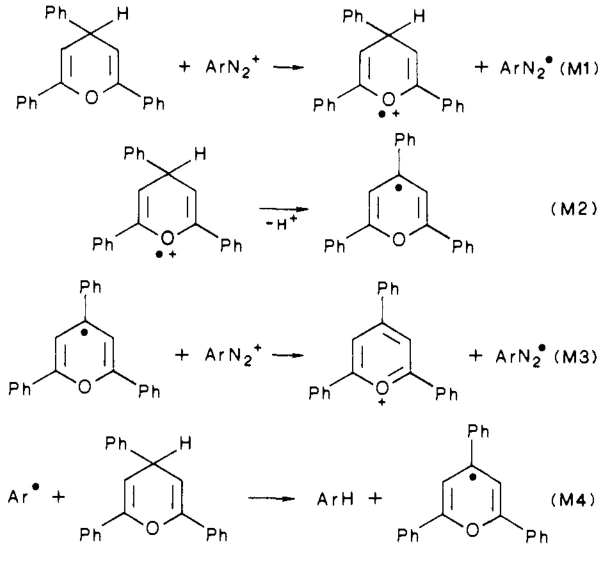
to give a homolytic dediazoniation (see previous section), while solvents with a *B* value lower than 150 are more prone to give the heterolytic dediazoniations (possibly among them the weakly nucleophilic fluorinated alcohols). The threshold value of 400 for the *B* parameter depends of course on the electrophilicity of the arenediazonium ion. In fact, a solvent with a *B* of only 190 is already sufficient to induce a homolytic dediazoniation with a *p*-nitro-substituted diazonium salt. We may indeed remember that a direct et occurred from the weak electron donor Br^- to $4\text{-}O_2NC_6H_4N_2^+$ in Me_2SO ($B = 362$), possibly as the result of a synergic effect between anion and solvent, but not in water ($B = 150$), or with a less strong electron-withdrawing substituent on the aromatic ring.[22] Incidentally, the homolytic thermal dediazoniation in EtOH causes in general a higher yield of hydro-dediazoniation product (and consequently a lower incidence of alkoxy-dediazoniation) with respect to MeOH.[92,170] This appears to be due to the slightly higher basicity of EtOH,[167] but also to the more easy formation of $CH_3\dot{C}HOH$,[76] which triggers a more efficient reduction chain. .

As far as the reaction environment is concerned, work on the thermolysis in *acidic* methanol by DeTar[61] and by Bunnett[9,60] has shown how strongly the dediazoniation can be affected by the nature of the reaction atmosphere. The heterolytic dediazoniation (1a) prevails in fact under O_2, while the homolytic one predominates under N_2 (see Scheme 7). Of course, electron-withdrawing substituents further encourage the radical mechanism. Formation of an inclusion complex between β-cyclodextrin and the arenediazonium ion protects the latter from contact with a normal O_2-containing reaction atmosphere, and the thermal dediazoniation proceeds exclusively via the homolytic pathway.[171]

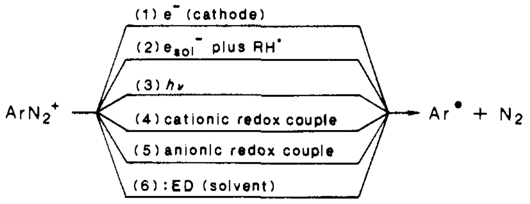
It is important to point out that the behavior of the *heterolytic* dediazoniation in studies of substituent effects is at variance with that of the homolytic counterpart.[15,172] In fact, when the aryl cation is the key intermediate, no meaningful correlation of the reactivity has been obtained with classical types of Hammett's substituent constant,[2] but instead bell-shaped profiles result. A decrease in solvolysis rate is observed with some –I and –R substituents, which is reasonable, but it can be observed as well with some electron-donor substituents.[173] It is by the use of dual or multiple parametric equations,[174] such as the Swain and Lupton equation,[175] that satisfactory quantitative correlations of substituent effects have been obtained in the heterolytic case as well.[172,176,177] There emerges a picture that is in line with the S_N1 mechanism, the field reaction constant *f* being *negative* in sign, as it is reasonable in a process where the positive charge becomes *more localized* on the aromatic moiety in the transition state,[178] while the resonance constant bears the opposite sign.[172]

Aside from other cases where alcohols, ethers, or acetals have been successfully employed in homolytic hydro-dediazoniations,[8] a last interesting example of electron donation to a diazonium salt is the one reported by Gragerov et al.[179] exploiting a 4*H*-pyran derivative (Scheme 17). The reaction is a hydro-dediazoniation and presents a chain character (M4 + M3). The driving force is the aromatization of the pyranyl radical to pyrylium salt (M3 in the propagation chain). The one-electron-exchange mechanism of steps M1 and M3 was proved on the basis of ESR evidence,[180] while literature data support it by giving an $E_{1/2} = -0.30$ V (vs SCE) for the redox couple 2,4,6-triphenylpyrylium ion/-pyranyl radical (in M3).[181]

SCHEME 17



SCHEME 18

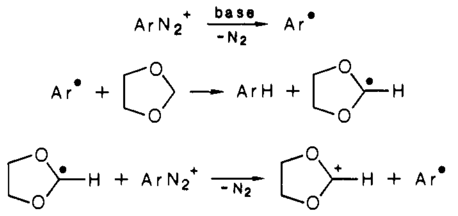


7. Summary

In conclusion, we have remarked in this section that the release of an electron to a diazonium salt (eq 1b) may be accomplished in several ways, invariably leading to the formation of an intermediate radical species. The range of applicability of the above methods, and the otherwise possible interference by the heterolytic mechanism (eq 1a), has been frequently pointed out here. The six "initiation" methods differ in the efficiency with which the actual et occurs, as also follows from the spread of ρ values recorded. The efficiency of the direct et appears to be grossly linked to the oxidation potential of the electron donor.

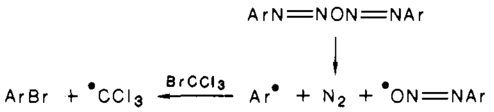
The initiation methods reported in Scheme 18 can be considered to provide equivalent entries into the chemistry of the aryl radical. Traditionally, instead, every reaction of diazonium salts has had its own specific technique of generation of the Ar• intermediate. Obviously, there are cases of initiation conditions that specifically determine the reaction products and consequently do not allow the alternative use of any other initiation technique. But from the viewpoint of a comprehensive mechanistic description of the radical phenomenon, the traditional lack of connection among the various methods of initiation is hopefully to be overcome. It is useful to test wider applications of a single technique and, henceforth, to confirm the *possibility*

SCHEME 19



of interchange among the various radical sources.

As a matter of fact, a few pertinent examples already exist in the literature. The Pschorr intramolecular arylation, which is traditionally induced by Cu(I) salts (case 4),[13,182] may be carried out in an equivalent way by means of iodide anion[183,184] or by employing pyridine[185] or also hypophosphite ion[6] (all cases 5); by photochemical decomposition (case 3);[186] or by electrochemical et (case 1).[187] As far as the synthesis of aryl halides is concerned (eq 46), they are accessible from diazonium salts not only by exploiting the Sandmeyer conditions, but also under Gomberg–Bachmann conditions, when a suitable source of halogen atom is added to intercept the Ar• intermediate[188,189] (case e in Scheme 2; see eq 48). In another example, a Gomberg-like intermolecular arylation originates upon electrochemical generation of Ar• from ArN_2^+ (case 1). The process occurs in an aprotic solvent containing an aromatic substrate[190] and is alternative to the route of the diazo anhydride cleavage (Scheme 4). The final example is the hydro-dediazoniation by 1,3-dioxolane in alkaline solution[8,95] (Scheme 19). There the function of the base is to catalyze in the initiation step the generation of the aryl radical according to the Gomberg's conditions (Scheme 4). This step is spurred by the addition of Cu(I) or Fe(II) salts, or also of KI, all of them being efficient electron donors. We will see later in this review how the independence of the spectrum of reactivity of Ar• from the method of generation is not only confined to the diazonium salts as substrates.



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B. Product Patterns of the Aryl Radical

The product of the dediazoniation reaction is determined by what Ar• reacts with. In the Introduction, a schematic description has been given (Scheme 2) of the possible reactive pathways. We will examine them in detail here and will try to draw a general picture of the reactivity of Ar•.

1. Hydrogen Atom Abstraction (Hydro-dediazoniation)

When a good hydrogen atom donor is present (in most cases the solvent itself), Ar• affords ArH (eq 47)

$$\mathrm{Ar}^\bullet + \mathrm{RH} \rightarrow \mathrm{ArH} + \mathrm{R}^\bullet \qquad (47)$$

by hydrogen atom abstraction, a process characterized by rate constants in the range of $10^5\ M^{-1}\ s^{-1}$ (see Table II). The principal outcome of many of the previously examined (section A) methods of one-electron donation is in fact a hydro-dediazoniation. However, the most specific and reliable procedure to accomplish that is the reduction by hypophosphorous acid,[170] which has been clearly shown to be a free-radical chain process[6] (Scheme 20). Cupric copper (or also other oxidizing agents) accelerates the process, because it oxidizes hypophosphite ion to the hypophosphite radical, which is the species responsible for the radical chain propagation.[6] Consistently, the process in Scheme 20 is inhibited by radical scavengers.[6] Finally, the reaction shows acceleration when initiated with cuprous copper[191] or with metallic copper,[6] both spurring the production of Ar• from the diazonium salt. Under these conditions and in nonpolar solvents, the addition of crown ethers apparently assists the reduction procedure.[191]

SCHEME 20

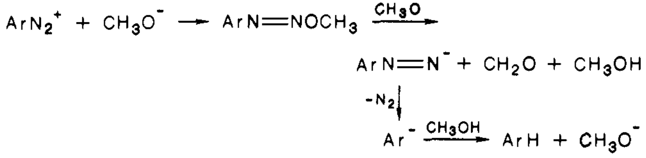
$$\mathrm{ArN_2^+ + H_2PO_2^- \rightarrow Ar^\bullet + N_2 + H_2PO_2^\bullet}$$

$$\mathrm{Ar^\bullet + H_3PO_2 \rightarrow ArH + H_2PO_2^\bullet}$$

$$\mathrm{H_2PO_2^\bullet + ArN_2^+ \rightarrow Ar^\bullet + N_2 + H_2PO_2^+}$$

$$\mathrm{H_2PO_2^+ \xrightarrow{H_2O} H_3PO_3 + H^+}$$

The reduction of an arenediazonium ion to arene does not occur by the heterolytic mechanism, with the exception of the reduction in *strongly* alkaline methanol,[59] which proceeds through the preliminary formation of the covalent adduct, common to the homolytic pathway (section A, Scheme 14),[9,59,60] and from a subsequent aryl anion intermediate.



Another reduction by an ionic pathway is the one by sodium borohydride (Scheme 21). In this case also a covalent intermediate is formed preliminarily.[8,192]

SCHEME 21

$$\mathrm{ArN_2^+ + BH_4^- \rightarrow ArN{=}N{-}H + BH_3}$$

$$\mathrm{ArN{=}NH \xrightarrow[-H^+]{} ArN{=}N^- \xrightarrow[-N_2]{} Ar^- \xrightarrow{SH} ArH}$$

2. Reaction with X⁻ (Halo-dediazoniation)

When a halogen-transfer agent like CuX_2 is present in solution,[7,193] the Sandmeyer nuclear halogenation takes place.

$$\mathrm{Ar^\bullet + XCuX \rightarrow ArX + CuX} \qquad (5)$$

The mechanism of this famous dediazoniation reaction requires deeper examination. The original Sandmeyer procedure prescribes the use of a copper(I) halide.[23] As we have noted before (section A, case 4), an et to the diazonium salt occurs preliminarily, producing the aryl radical and a copper(II) salt. The ligand-transfer agent Cu(II) is therefore generated in situ. When the aryl radical undergoes in step 5 the inner-sphere et to afford the Sandmeyer product, a copper(I) species is regenerated. The mutual interconversion of Cu(I) and Cu(II) allows an adequate supply of cupric halide to be achieved.[194] Consistently, even *catalytic* amounts of cuprous chloride have been employed for a chloro-dediazoniation.[7] The supply of a Cu(II) salt *only* is also possible, provided that it is at least in part reduced in

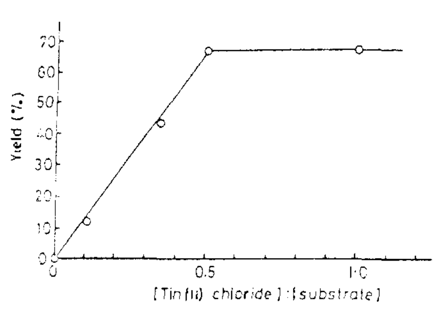


Figure 2. Yield (%) of chlorobenzene as a function of tin(II) chloride to substrate molar ratio. Reprinted with permission. Copyright 1981, The Royal Society of Chemistry.

situ to the Cu(I) species by side reactions.[195] However, this interconversion makes people sometimes to forget that *two* separate functions have to be fulfilled by the metal ion:[196] the reduction and the transfer of a ligand. As happens frequently, it is better to have two different species to carry on the two functions rather than have only one species spinning back and forth to fit two needs. The foremost appeal of copper is that, aside from being a good reductant for a diazonium salt in the cuprous form (but we have seen that this property is shared by other species too), it is in the cupric form an excellent ligand-transer agent. Ferric ion, for example, is by far less effective.[197] Titanium(IV) ion is also capable of transferring ligands to radicals.[198]

Use in the Sandmeyer reaction (i) of copper salts in *both* valence states or (ii) of a suitable reductant other than the cuprous salt in combination with a Cu(II) salt not only satisfies the mechanistic formalism but also improves the efficiency of the halo-dediazoniation.[89] In fact, although the conventional procedure[23] gives in general satisfactory yields of ArX, it is spoiled by numerous competing reactions.[62] Formation of biaryls or of azo compounds has more chance to compete with the halo-dediazoniation when the amount of Cu(II) is low, as is the case when the latter is generated in situ and is not present from the beginning of the reaction. The same holds for interference by the reduction to ArH (as in eq 47), particularly when the reaction is performed in ethanol or in aqueous acetone, that are good $H^\bullet$ sources. In turn, when it is the amount of the cuprous salt that is less than equimolar,[7] the heterolytic mechanism (1a) can begin to interfere. It is not surprising, therefore, that the Sandmeyer reaction gives cleaner results when performed with 1 equiv of a Cu(I) salt along with 1 equiv of a Cu(II) salt.[89] Furthermore, in this way it proceeds smoothly at 5–10 °C, while the conventional Sandmeyer procedure often requires heating at 60–100 °C, whereby incursion of the heterolytic mechanism becomes more likely. Although the need for this heating has never been commented in detail, it is probably required by an energy-consuming rearrangement of the solvation sphere of copper during the change of valence. Figure 2, where the yield of PhCl in a chloro-dediazoniation carried out at 5 °C in water is given, throws some light on this point. In these experiments the amount of the Cu(II) cation was always equivalent to that of the diazonium substrate, while the *molar ratio* of the reductant (in this case $SnCl_2$) was increased from 0.1 to 1.0 with respect to the substrate. The yield of PhCl increases accordingly, until a plateau is reached for a 0.5/1 reductant to substrate molar ratio. Stannous cation is a two-electron reductant, and the trend in Figure 2 clearly shows that it is required in stoichiometric amount. This indicates that the step of the reduction and the step of the ligand transfer are distinctly *separated* and also that the Cu(I) species originated from eq 5 has no time to compete with Sn(II) in the reduction step, at least at the temperature chosen, for reasons possibly linked to the time requirements of the rearrangement of the solvation sphere of copper previously referred to.

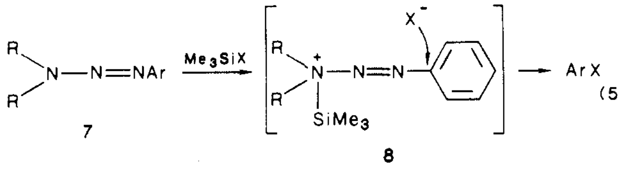
Coming back to the side reactions afflicting the Sandmeyer reaction in its conventional procedure, methods for minimizing them have been reported, either by stabilizing the diazonium salt through complexation with poly(ethylene glycols)[199] or with crown ethers[200] or rather by following alternative procedures. The most efficient of them is the scavenging of $Ar^\bullet$ with aryl halides,[146,168,201-203] or with alkyl halides,[21,92,204-206] to give atom-transfer processes (eq 48), whose reactivity

$$Ar^\bullet + CX_4 \rightarrow ArX + CX_3^\bullet \qquad (48)$$

has been determined by Lorand et al. (Table II).[207] The very fast reaction of $Ar^\bullet$ and I_2, with respect to the slower hydrogen abstraction, confirms the Ando finding[82] that, in the photolysis of *p*-nitrobenzendiazonium ion, the reduction to $PhNO_2$ is dramatically depressed in the presence of iodine, due to the fast reaction (49).

$$O_2NC_6H_4^\bullet + I_2 \rightarrow O_2NC_6H_4I + I^\bullet \qquad (49)$$

Another alternative procedure exploits 1-aryl-3,3-dialkyltriarenes **7**, formed by reaction of diazonium salt with a dialkylamine[208] (eq 50). The triazene may be



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attacked by a trimethylsilyl halide,[209] due to the marked affinity of the Me_3Si group toward nitrogen, to give intermediate **8**. There, nucleophilic attack by the halide counterion (I^- or Br^-) leads to the product ArX. The method is claimed to be valuable for the synthesis of radiopharmaceuticals, whenever radiohalides are employed in the initial preparation of the Olah's reagent (Me_3SiX).[209] Alternatively, treatment of a triazene with 70% HF in pyridine affords aryl fluorides.[210] These nucleophilic reactions on the triazenes present, however, heterolytic character. Finally, the deamination procedure described in paragraph II (eq 7),[62] which makes use of alkyl nitrite and copper(II) halide (X = Br, Cl), represents another efficient route to the synthesis of haloarenes.

As to the rate of transfer of a ligand from the Cu(II) ion, Jenkins and Kochi[211] have determined by radical clock experiments a rate of $4.3 \times 10^9\ M^{-1}\ s^{-1}$ for transfer of bromine from $CuBr_2$ to an alkyl radical and a corresponding rate of $1.1 \times 10^9\ M^{-1}\ s^{-1}$ in the case of chlorine. The rate of these ligand-transfer processes is slightly higher (with bromine) or much higher (with chlorine) than the corresponding rate of the atom-transfer processes (Table II). The Jenkins and Kochi quantitative determination gives a k_{Br}/k_{Cl} ratio of 3.9 for the relative rate of transfer of the two halogens from a cupric cation. It is interesting to find that, under Sandmeyer conditions, when Br^- and Cl^- were pitted together (eq 51) in competition experiments for a di-

$$ArN_2^+ + Br^- + Cl^- + Cu(II) \xrightarrow{\text{reductant}} ArBr + ArCl \qquad (51)$$

azonium salt in the presence of cupric nitrate,[197b] a k_{Br}/k_{Cl} ratio of ca. 3.0 could be reckoned, on the basis of the yields of the two aryl halides produced, as the relative efficiency of the ligand-transfer steps to the aryl radical. There appears to be good agreement between the quantitative data and the preparative results. This may be caused either by a fortuitous coincidence or, more likely, by the analogous selectivity of the two radicals (alkyl and aryl) in ligand-transfer processes.[206]

It may be useful to conclude this section by remembering that the heterolytic thermal decomposition of $ArN_2^+BF_4^-$ (or PF_6^-), as carried out on the dry salt or in a proper solvent,[212] is the current method of choice for the synthesis of aryl fluorides (Balz–Schiemann reaction[30]). Absence of a homolytic fluoro-dediazoniation,[1] apart from the light-induced one (section A, case 3),[82] is due both to the unfeasibility of an et to ArN_2^+ from F^-, an anion with a very high oxidation potential, and to the inefficiency of the transfer of the fluoro ligand to Ar• from any Cu(II) salt.[213] By analogy, heterolytic thermal decompositions could be extended to bromide and chloride ions as well, by way of $ArN_2^+BBr_4^-$ or $ArN_2^+BCl_4^-$ salts (eq 52), respectively.[214] But, the yields of these processes do not always seem to compare favorably with those obtainable under Sandmeyer conditions.

$$ArN_2^+BBr_4^- \xrightarrow[-N_2]{} Ar^+BBr_4^- \rightarrow ArBr + BBr_3 \qquad (52)$$

3. Other Sandmeyer-like Reactions

Besides the halides, other nucleophiles that happen to enter the coordination sphere of Cu(II) ion are amenable to transfer to Ar•. Cyanide ion is a well-known case[23,31] (eq 53). Nitrite ion is another exam-

$$Ar^\bullet + Cu(CN)_2 \rightarrow ArCN + CuCN \qquad (53)$$

ple,[32,215] since aromatic nitrations can be performed under copper catalysis. Due to its oxidation potential ($E° = 1.0$ V vs NHE),[103] nitrite ion is also a likely candidate for the fulfillment of the et to the diazonium salt.[65b,92,131,142,216] It is even indicated as capable of direct attack to the aryl radical,[131,217] giving a rather stable radical anion.[218] Consequently, there are at least three possible pathways by which the homolytic nitration can be accomplished:

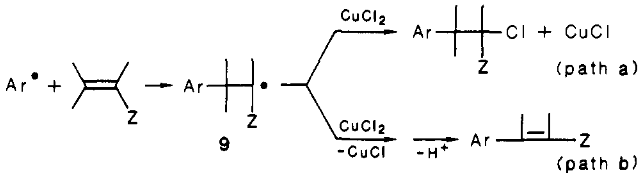
$$ArN_2^+ \xrightarrow[-N_2]{CuX} Ar^\bullet \xrightarrow{Cu(NO_2)_2} ArNO_2 \text{ (lt)}$$

$$ArN_2^+ + NO_2^- \xrightarrow[-N_2]{} Ar^\bullet + {}^\bullet NO_2 \rightarrow ArNO_2 \text{ (coupling)}$$

$$Ar^\bullet + NO_2^- \rightarrow [ArNO_2]^{\bullet -} \xrightarrow[-e^-]{} ArNO_2 \ (S_{RN}1)$$

As a ligand, NO_2^- is outdone by H_2O (vide infra) in the transfer from a Cu(II) cation.[89] Hence, satisfactory yields of nitration are best obtained in aprotic solvents. Transfer of SCN^- and of N_3^- also occurs from Cu(II) salts.[219]

SCHEME 22



Sulfate, bisulfate, perchlorate, and nitrate anions, other common counterions of Cu(II) salts, are not transferred to Ar•.[196] For this reason they are employed when the nucleophile *water* needs to be transferred. This hydroxy-dediazoniation (54) has been discovered

$$ArN_2^+HSO_4^- \xrightarrow[H_2O,\ \text{room temp}]{Cu_2O,\ Cu(NO_3)_2} ArOH \qquad (54)$$

by Cohen et al.[220] and provides a mild, alternative procedure to the heterolytic one that occurs in boiling water. The Cu(I) salt fulfills the reduction step into Ar•, while the Cu(II) salt performs the transfer of the ligand water. The analogous transfer of the ligand methanol, for a synthesis of aryl ethers, is less favored by about a factor of 10, with respect to water.[221] But the theoretically possible homolytic methoxy-dediazoniation is overwhelmed by the much higher rate of abstraction of hydrogen from the methyl of the solvent methanol[221] (eq 55). It is also worthwhile to point out that the

$$ArN_2^+HSO_4^- \xrightarrow[CH_3OH,\ \text{room temp}]{Cu_2O,\ Cu(NO_3)_2} ArH \text{ (and } \textit{not } ArOCH_3) \qquad (55)$$

halogens outdo water in the ligand transfer from Cu(II).[196,198] Therefore, they must be avoided as counterions of the diazonium salt in synthetic procedures of the Cohen type.[220] This last feature of the homolytic mechanism is at variance with the situation of the heterolytic mechanism, where the decomposition of the diazonium salt in boiling water solution always affords major amounts of phenol, even in the presence of considerable amounts of halide ions.[17-20]

4. Addition to Olefins

The Meerwein reaction[38] is strongly analogous to the Sandmeyer reaction. Olefins activated by an electron-withdrawing group (Z) are arylated by means of a diazonium salt with catalysis by a copper(II) halide. The reaction was first believed to be heterolytic.[38] Subsequently, the homolytic mechanism was preferred,[39] but the involvement of a cryptoradical was suggested,[49,50] until the identity of the reductant was clarified by Kochi. He showed[195,222] that some of the Cu(II) ion is reduced by the solvent acetone to a Cu(I) species (eq 56), which then provides the required electron-transfer

$$CuCl_2 + CH_3COCH_3 \rightarrow CuCl + ClCH_2COCH_3 + H^+ \qquad (56)$$

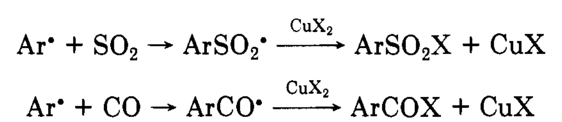
step.[223] The resulting aryl radical adds to the double bond giving the intermediate **9**, which on ligand transfer leads to what is a homologation product (pathway a) of a Sandmeyer reaction (Scheme 22). From **9**, a simple arylation pathway (b) may also result, involving an et back to CuX_2 and subsequent loss of H^+.[93] In both pathways the reducing species CuX is regenerated, and the original copper(II) halide can be supplied in less than stoichiometric amounts.[95] Meerwein reactions have also been performed by resorting to the deamination of arylamines with alkyl nitrite (see eq 7 and 9).[224,225] As it is found in the case of the olefins, sulfur dioxide and carbon monoxide are reported to react with Ar• to form adducts (Scheme 23) that are converted into products by ligand transfer.[196]

SCHEME 23

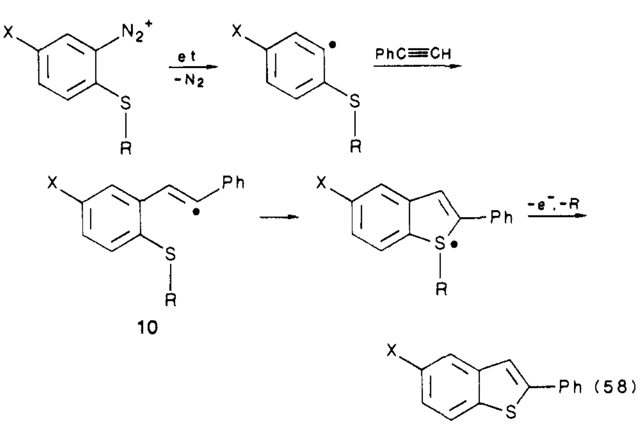
$$Ar^{\bullet} + SO_2 \rightarrow ArSO_2^{\bullet} \xrightarrow{CuX_2} ArSO_2X + CuX$$

$$Ar^{\bullet} + CO \rightarrow ArCO^{\bullet} \xrightarrow{CuX_2} ArCOX + CuX$$

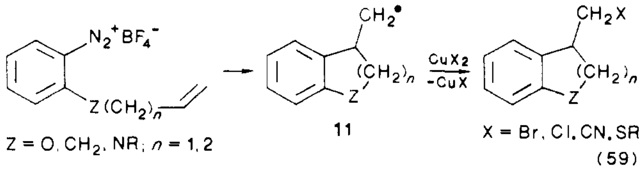
Use of a stronger reductant like Ti(III) promotes not only the reduction of the diazonium salt for the addition to the double bond[226] but also the reduction of the intermediate radical resulting from the addition step[227] (eq 57).



A case of addition of aryl radical to phenylacetylene is also of the Meerwein type: Either metallic copper, or Fe(II), or I⁻ is reported as a radical source.[228] The radical intermediate **10** is attacked intramolecularly by the sulfur atom of an ortho thioether group, to give eventually a benzothiophene derivative in very high yields (eq 58). Analogously, the synthesis of substituted indoles via Meerwein arylation of 2-nitrobenzenediazonium chloride with vinyl acetate, and subsequent reductive cyclization, has been reported.[229] Addition of an aryl radical to the double bond of the enol form of β-dicarbonyl compounds has also been described.[230]



Intramolecular examples of the Meerwein reactions have been reported as well.[231] Beckwith and Meijs[130] use cupric salts in Me_2SO (eq 59) and remark that the reaction is much cleaner than when employing cuprous salts. This again is consistent with a lower incidence of side reactions, when the ligand-transfer agent is present in large excess to trap the intermediate radical **11**. The reductant required for the preliminary et step could well be identified in tiny amounts of cuprous impurities present in the cupric salt, as the authors point out.[130] But this is not strictly necessary, since the reaction is carried out in Me_2SO, a solvent able to induce on its own a homolytic process with the diazonium salt (section A, case 6).[167] In fact, substitution of acetone (a worse solvent from this point of view; see Table III) for Me_2SO halved the yields, and the reaction mixture was contaminated with tars.[130]



In this investigation, the authors found[130] that the intramolecular addition of the aromatic radical to the double bond is very fast ($k \sim 10^9$ s^{-1}) and overcomes possible competition by bimolecular processes, leading to nuclear substitution products, such as ligand transfer from the cupric cation. Incidentally, the addition of Ar• to a double bond is rather fast also in intermolecular processes (Table II), and this is why the conventional Meerwein reaction (Scheme 22) does not suffer in general from competition of ligand-transfer steps to the original Ar• radical.

Another paper by Abeywickrema and Beckwith[118] concerns an intramolecular Meerwein reaction, where the competition by a bimolecular nuclear substitution is significant, at variance with the previous example. The radical source in this case is the benzenethiolate anion. The authors offer evidence for a very rapid bimolecular reaction between the diazonium cation and the anion ($k \geq 10^9$ M^{-1} s^{-1}), leading to the covalent intermediate diazo sulfide (eq 60 and 61). Thermal

$$ArN_2^+ + PhS^- \rightarrow ArN{\rightleftharpoons}NSPh \qquad (60)$$

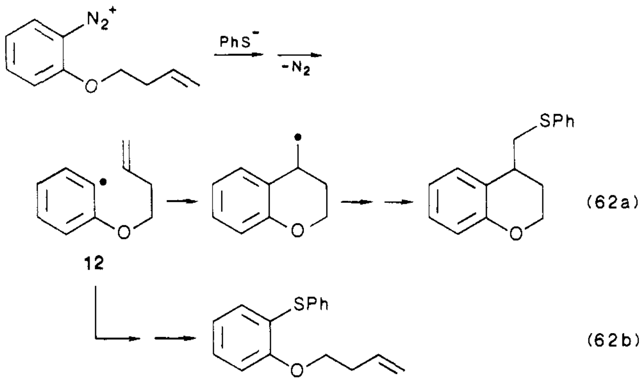
$$ArN{=}NSPh \rightarrow Ar^{\bullet} + N_2 + {}^{\bullet}SPh \qquad (61)$$

homolysis of the latter produces the aryl radical in the initiation step, in line with the general description already presented in Scheme 11. No direct et from the thiolate would occur. Intramolecular addition of the aryl radical to the double bond leads to ring closure and then to a substituted bicyclic product (eq 62a). However, as is known from studies on the $S_{RN}1$ reaction,[232,233] aryl radicals such as **12** react readily with the benzenethiolate ion. The rate constant that the authors[118] evaluate, i.e. (2–4) × 10^8 M^{-1} s^{-1}, compares well with previous determinations of Savéant et al. ($k \sim 10^7$–10^{10} M^{-1} s^{-1}).[234] As a result, a competitive route (eq 62b) can take place *before* ring closure, to afford a

$$PhS^- + Ar^{\bullet}\ (\text{i.e. } \mathbf{12}) \rightarrow [PhSAr]^{\bullet -}$$

$$[PhSAr]^{\bullet -} + ArN{=}NSPh\ (\text{or } ArN_2^+) \rightarrow PhSAr + Ar^{\bullet} + N_2 + PhS^- \qquad (62b)$$

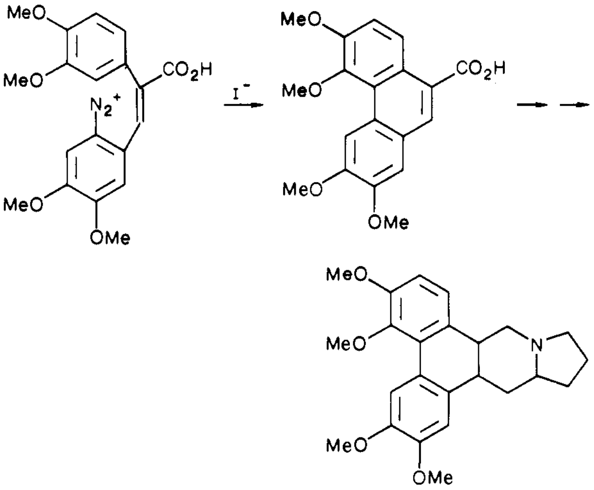
radical anion that starts a chain propagation by electron transfer to the diazo sulfide and leads to a diaryl sulfide. The dependence of the products ratio (in eq 62) on the relative concentrations of ArN_2^+ and of PhS^- confirms the delicate interplay of the competing pathways.



Recently, the use of iodide ion as the electron source in the same process (eq 62) has been described.[121]

5. Arylation of Aromatic Compounds

Now the reaction of $Ar^\bullet$ with another aromatic molecule is examined. This arylation reaction may occur in an intramolecular (Pschorr) or in an intermolecular way (Gomberg-Bachmann). The Pschorr reaction[33] is one of the oldest dediazoniation reactions.[13,182,235] It may be also viewed as an application of the chemistry of arenediazonium ions to the building of molecules with a rather elaborated skeleton:[1] An example reported by Giese's recent book[236] illustrates the point in the synthesis of the alkaloid tylocrebrine[237] (eq 63).



(63)

The preliminary reduction step, responsible for the production of the intermediate aryl radical, has been successfully accomplished by means of several agents: Cu(I) salts or Cu(0),[238] I^-,[183,184b] pyridine,[185] hypophosphorous acid,[170,235] photochemical decomposition,[186] or electrochemical et.[187] Also adopted was the homolytic cleavage of a diazotate in the Gomberg fashion.[239] The intermediate aryl radical, on intramolecular addition to the other aromatic ring, gives a further radical intermediate, which in turn loses an electron (to reduce more diazonium ion) and then a proton, to afford the final product (Scheme 24). Alternatively, a bystander radical can abstract directly the $H^\bullet$ to give the product.

The advantage of intramolecularity makes the heterolytic mechanism via aryl cation become competitive with the homolytic one in the case of the Pschorr reaction.[182,240] A beautiful example by Lewin and Cohen illustrates the point (Table IV).[241] Heterolytic decomposition of the diazonium salt of 2-aminobenzophenone in 0.1 M H_2SO_4 water solution at 45 °C gives the product from the intramolecular electrophilic arylation plus the solvolytic product. Addition of a cuprous salt diverts the reaction into the homolytic pathway, which at 25 °C gives almost exclusively the radical intramolecular arylation plus a tiny amount of hydro-de-diazoniation. Use of both Cu(I) and Cu(II) salts makes the ligand transfer of water prevail over the arylation within the homolytic mechanism. Finally, use of a cuprous salt only, but in dioxane (an excellent $H^\bullet$ source) instead of water solution, gives a quantitative reduction of the aryl radical.

However, apart from this well-tailored example, the intramolecular arylation is the prevailing course of reaction in most of the Pschorr processes. Even in those cases where the initial et is due to I^-, the intramolecular step largely outdoes the iodo-dediazoniation.[123,184a,242] An example is represented by eq 64, where intramolecular arylation and concurrent aromatization lead exclusively to the ring-closure product.[220]

SCHEME 24

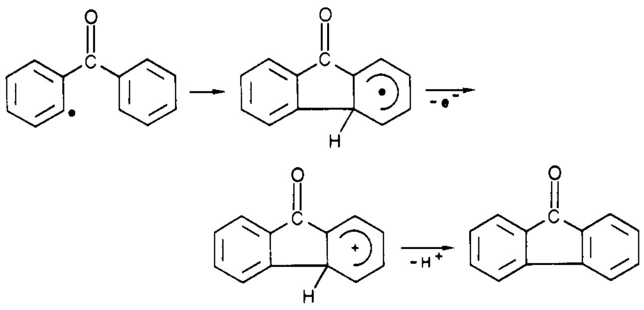
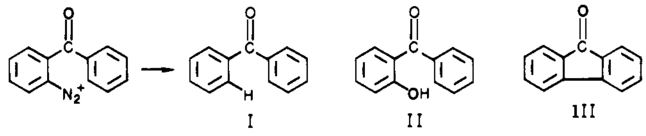
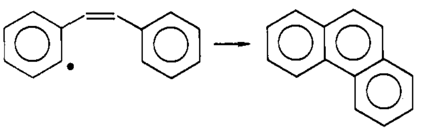


TABLE IV. Product yields for the Reaction[a]



conditions	yields, %		
	I	II	III
(a) 45 °C, H_2O, 0.1 M H_2SO_4		32	68
(b) 25 °C, H_2O, Cu_2O	3	4	93
(c) 25 °C, H_2O, Cu_2O, Cu(II)[b]	1	88	11
(d) 25 °C, dioxane, Cu_2O	100		

[a] From ref 241. [b] In excess.

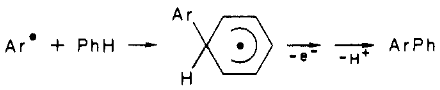


(64)

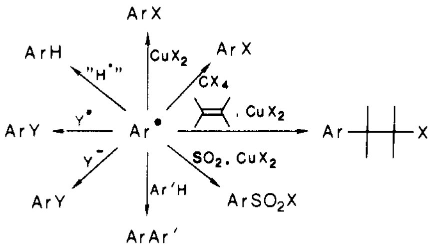
Gadallah et al. explain the advantage of the intramolecularity on the grounds of an internal CT formation between the two aromatic rings.[187] This intramolecular redox system would allow the Pschorr reaction to proceed well even in the absence of added reducing agent(s).

Without the advantage of intramolecularity, a Pschorr-like *intermolecular* arylation suffers from the competition of side processes. It is for this reason that the Gomberg–Bachmann alkaline reactions[36] (eq 2) had been developed.[3] We have commented already on the mechanism of the decomposition of the covalent intermediates formed by OH^- or by RCO_2^- with a diazonium salt (Scheme 4).[8,54,150] In both cases an aryl radical is formed, which arylates another aromatic compound present as the solvent (Scheme 25). The Gomberg arylation displays however a low positional and substrate selectivity that makes it less attractive than the Pschorr reaction from a synthetic viewpoint. Competition from reduction pathways is also significant. Alternative procedures have therefore been developed in the attempt, not always successful, to minimize these drawbacks. We have described before (Schemes 3 and 13)[54,150,243] the arylation by *N*-nitrosoacetanilide discovered by Bamberger.[244] The direct deamination of an aromatic amine with alkyl nitrite (eq 9) produces an aryl radical, giving an intermolecular arylation with the aromatic solvent.[245,246] The electro-

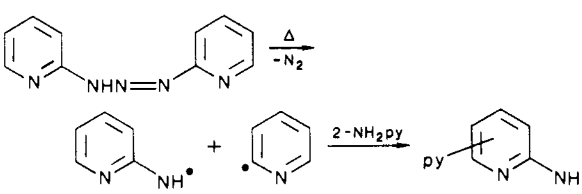
SCHEME 25



SCHEME 26



chemically provoked intermolecular arylation has been already mentioned.[190] Finally, the formation of triazenes with subsequent homolytic cleavage has been exploited as a source of aryl radicals.[236] A specific example[247] concerns the arylation of pyridine, resulting in a mixture of the possible isomers



(65)

A recent paper by Minisci et al.[248] shows that protonation of pyridine increases reactivity and positional selectivity toward attack of the aryl radical. In addition, it shows that the intermolecular arylation is significantly depressed, at variance with the intramolecular one, from scavenging the aryl radical with alkyl iodide.

6. Conclusions

The constancy of product patterns in all the above described reactions strongly supports the intermediacy of a free aryl radical, which shows independence of reactivity from the radical sources. The overall spectrum of reactivity of Ar• may be summarized as shown in Scheme 26.

The approach attempted here by the author tries to systematize the chemistry of the ArN_2^+ group as that of a true "functional group". Admittedly, the examples described so far represent unambiguous cases of homolytic behavior. There are instead other cases where the competition by the heterolytic pathway, or by alternative homolytic pathways, affect(s) badly the intelligibility of the results of a specific homolytic process. Examples of possible interferences have been pointed out by and large. The reactivity "profile" of the homolytic reaction emerges clearly only from the concurrent interplay of at least four prominent requisites: the affinity toward the electron of the diazonium substrate, the reducing efficiency of the electron donor, the characteristics of the reaction environment, and the rates of the reactive steps opened to the aryl radical. Whenever a good balance among these features is reached, the behavior of the homolytic reactions of arenediazonium ions lends itself to a rationalization and to a systematization comparable to those we expect from ionic reactions. More quantitative data would be desirable, however, to give further support to the mechanistic schemes here presented.

IV. Related Reactions

It is common practice of physical organic chemistry to group reactions according to their mechanism or to the intermediate they all share. This practice is useful for a deeper understanding of the reaction processes and for the possibility of prediction of the reactivity that may ensue.

There are several reactions that share a common feature with the homolytic dediazoniation: An aryl radical is the reaction intermediate. The sources of the aryl radical in these reactions are of various kinds. However, once Ar• has formed, there is good reason in principle to expect common patterns of product(s) formation with those described before in the case of the diazonium salts. Is this expectation supported by experimental evidence? Let us try to answer the question by examining typical cases available from the literature.

A. Intermediacy of the Aryl Radical

In sections A and B of paragraph III we mentioned a few other reactions leading to the aryl radical: for example, the equilibration of *N*-nitrosoacetylarylamines with diazoacetates (Scheme 3),[52,54,150] or the cleavage of triazenes, or the thermal fragmentation of azo compounds,[236] notably among the others phenylazotriphenylmethane (PAT, eq 37). Another family of compounds characterized by rather weak bonds are the diacyl peroxides. Thermal decomposition of them (eq 66) yields aryl radicals,[249] and a supply of a cuprous salt (or of a ferrous salt) significantly lowers their decomposition temperature.[196,250]

$$(PhCO_2)_2 \rightarrow 2PhCO_2^\bullet \rightarrow Ph^\bullet + CO_2 \qquad (66)$$

Aryl iodides, possessing a rather weak C–iodine bond, lend themselves to photohomolysis into aryl radicals[202,251-253] (eq 67). Slightly more difficult is the

$$ArI \xrightarrow{h\nu} Ar^\bullet + {}^\bullet I \qquad (67)$$

photolysis on aryl bromides or chlorides, but nevertheless some examples of it are reported.[202,251,254] Photoinduced cleavage of the carbon–thallium bond occurs rather easily in arylthallium bis(trifluoroacetates)[255] (eq 68). Aryl radicals are also produced in

$$ArTl(OCOCF_3)_2 \xrightarrow{h\nu} Ar^\bullet \qquad (68)$$

the vapor-phase pyrolysis of a number of benzene derivatives[202] or from iodine abstraction by way of the tributyltin radical[236] (eq 69) or of other suitable radicals.[201]

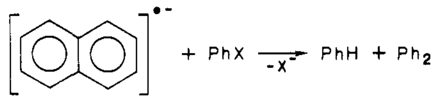
$$Bu_3Sn^\bullet + ArI \rightarrow Ar^\bullet + Bu_3SnI \qquad (69)$$

Electron-transfer methods have been applied as well to the formation of aryl radicals, for example, the photochemical generation of the sulfate radical anion in the presence of the benzoate anion[256] (eq 70). Well

$$SO_4^{\bullet -} + PhCO_2^- \rightarrow SO_4^{2-} + Ph^\bullet + CO_2 \qquad (70)$$

documented are the γ-radiolysis of nitroarenes,[202] the supply to aryl halides of solvated electrons produced by alkali metal in liquid ammonia,[257] the use of electrochemical reduction techniques[258] (eq 71), or the et (eq 72) from a radical anion.[259] Photochemically in-

$$\mathrm{ArX} \xrightarrow{e^-} [\mathrm{ArX}]^{\bullet -} \longrightarrow \mathrm{Ar}^\bullet + \mathrm{X}^- \tag{71}$$



(72)

duced et between dialkylanilines and aryl halides[251] (eq 73) or photoejection of electron from a nucleophile[260] (eq 74) represents other important sources of the aryl radical.

$$\mathrm{PhX} + \mathrm{PhNMe_2} \xrightarrow{h\nu} [\mathrm{PhXPhNMe_2}]^* \rightarrow [\mathrm{PhX}]^{\bullet -} + [\mathrm{PhNMe_2}]^{\bullet +} \tag{73}$$

$$\mathrm{ArX} + \mathrm{Y}^- \xrightarrow{h\nu} [\mathrm{ArX}]^{\bullet -} + \mathrm{Y}^\bullet \tag{74}$$

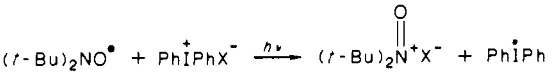
Many other examples are known in the literature, and the above compilation is not meant to be exhaustive. Rather, two examples will be commented on in detail: the reactions of diaryliodonium ions and the $S_{RN}1$ processes.

1. Reactions of Diaryliodonium Ions

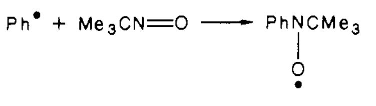
Diaryliodonium salts ($\mathrm{ArIAr^+X^-}$) have been the subject of considerable research interest for their ability to arylate a wide variety of substrates. They react quite readily with reducing agents. From an electrochemical study of Beringer and Messing,[261] these substrates come out to present an ease of reduction ($E_{1/2} = -0.2$ to -0.1 V vs Ag/AgCl in H_2O) a little lower than that of arenediazonium ions. From electroreduction at controlled potential, $\mathrm{Ar}^\bullet$ and ArI result from fragmentation of the diaryliodine **13** (eq 75) initially formed at the electrode. At a potential lower than −1.4 V, the reduction of ArI begins to contribute as well.

$$\mathrm{ArI^+Ar} \xrightarrow{e^-} \underset{\mathbf{13}}{\mathrm{Ar\dot{I}Ar}} \rightarrow \mathrm{Ar}^\bullet + \mathrm{ArI} \tag{75}$$

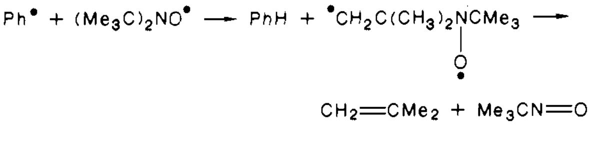
Under photosimulation, di-*tert*-butyl nitroxide donates electrons to a diphenyliodonium ion[201] (eq 76). The ESR spectrum of phenyl *tert*-butyl nitroxide is observed (eq 77) and supports the intermediacy of the phenyl radical. Evidence for the formation of the reduction product PhH is obtained as well (eq 78). With



$$(t\text{-Bu})_2\mathrm{NO}^\bullet + \mathrm{Ph\overset{+}{I}PhX^-} \xrightarrow{h\nu} (t\text{-Bu})_2\overset{\overset{\displaystyle O}{\|}}{\mathrm{N}}{}^+\mathrm{X}^- + \mathrm{Ph\dot{I}Ph} \tag{76}$$

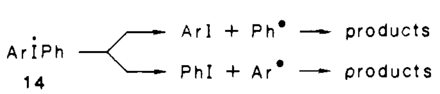


$$\mathrm{Ph}^\bullet + \mathrm{Me_3CN{=}O} \longrightarrow \mathrm{Ph}\underset{\underset{\displaystyle \dot{O}}{|}}{\mathrm{N}}\mathrm{CMe_3} \tag{77}$$



$$\mathrm{Ph}^\bullet + (\mathrm{Me_3C})_2\mathrm{NO}^\bullet \longrightarrow \mathrm{PhH} + {}^\bullet\mathrm{CH_2C(CH_3)_2}\underset{\underset{\displaystyle \dot{O}}{|}}{\mathrm{N}}\mathrm{CMe_3} \longrightarrow \mathrm{CH_2{=}CMe_2} + \mathrm{Me_3CN{=}O} \tag{78}$$

unsymmetrical iodonium salts ($\mathrm{ArI^+Ph}$), the fragmentation branching of the diaryliodine **14** produced by the nitroxide reduction reflects the relative stability of the two aromatic radicals (eq 79). This fragmentation



(79)

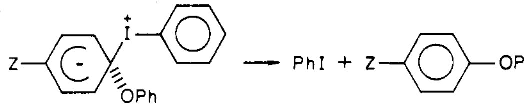
branching matches exactly the one obtained from the reaction of the same iodonium salt with phenoxide ion. Therefore, an et step from this anion is also strongly supported, leading to the same intermediate radical **14** (eq 80). As in the case of the diazonium salts, the

$$\mathrm{PhO^-} + \mathrm{ArI^+Ph} \rightarrow \mathrm{PhO}^\bullet + \mathrm{Ar\dot{I}Ph} \tag{80}$$

nature of this et step, either outer or inner sphere, is unsettled. The phenoxy radical then undergoes coupling with the two radicals $\mathrm{Ph}^\bullet$ and $\mathrm{Ar}^\bullet$ to produce the ethers PhOPh and ArOPh, respectively.

Determination of the substituent effect for the reduction of diaryliodonium salts with phenoxide ion[201] indicates that electron-withdrawing groups on the iodonium salt favor the process and yields a good Hammett plot with $\rho = 1.63$. The positive sign of ρ and its magnitude are in line with those obtained with diazonium salts in reductive steps from several electron donors (paragraph III, section A).

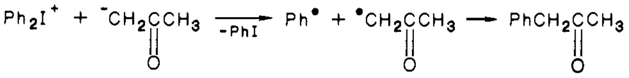
Interestingly, diaryliodonium salts containing strongly electron-withdrawing groups Z also react by the nucleophilic aromatic substitution mechanism with phenoxide ion (eq 81). A dramatic change in the ArOPh/PhOPh product ratio, resulting from nucleophilic attack at the two aromatic moieties, is found when Z = NO_2 or CN, with respect to the fragmentation branching ($\mathrm{Ar}^\bullet/\mathrm{Ph}^\bullet$) shown in the same cases by the nonnucleophilic nitroxide reductant (eq 79). Therefore, interference from an ionic mechanism may affect the course of radical reactions of diaryliodonium ions. However, in contrast to what is observed with diazonium ions, this interference appears to be limited to a few cases. In fact, the simple heterolytic decomposition (eq 82) postulated by Lukas et al.,[262] as driven by the good leaving group ArI, occurs only under very strong conditions ($T > 155$ °C), if any.



(81)

$$\mathrm{Ar_2I^+} \rightarrow \mathrm{Ar^+} + \mathrm{ArI} \tag{82}$$

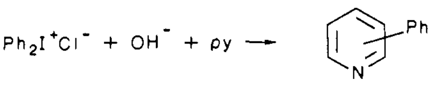
Enolates of ketones[257] or of β-diketones[263] and the anion of 2-nitropropane[264] are examples of other nucleophiles capable of transferring electrons to diaryliodonium salts (eq 83). Again, coupling of the phenyl



$$\mathrm{Ph_2I^+} + {}^-\mathrm{CH_2}\underset{\underset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{CH_3} \xrightarrow[-\mathrm{PhI}]{} \mathrm{Ph}^\bullet + {}^\bullet\mathrm{CH_2}\underset{\underset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{CH_3} \longrightarrow \mathrm{PhCH_2}\underset{\underset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{CH_3} \tag{83}$$

radical with the radical derived from the nucleophile is responsible for the product formation[257] in a radical-nonchain process.

The decomposition of $\mathrm{Ph_2I^+Cl^-}$ in sodium hydroxide solution in the presence of pyridine is a well-known source of phenyl radical. A mixture of the three α-, β-, and γ-phenylpyridines results from a free-radical arylation described for the first time by Gomberg and Bachmann[36] (eq 84). The first attempt of determination of the relative amounts of the three α, β, and γ isomeric products is reported by Hey et al.[265] as 2.5/1/1, respectively.

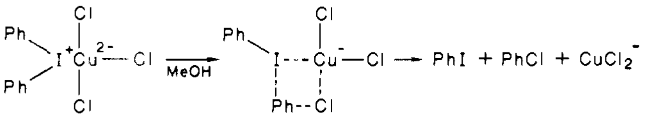


(84)

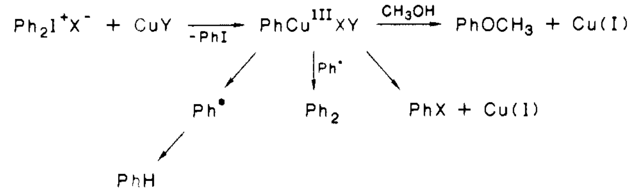
mixture of isomers

Strongly reducing metal salts, such as titanium(III) chloride or chromium(II) chloride, are also successfully

SCHEME 27



SCHEME 28



employed to give an et to the iodonium cation.[198] The fate of the resulting aryl radical is determined by the partner reagent and by the solvent. In water, the aryl radical reacts with the Ti(IV) species formed in situ, to afford ArCl in a ligand-transfer process. In methanol, on the contrary, the predominant pathway is hydrogen abstraction from the solvent, to afford ArH. The hydrogen abstraction pathway is in any case the prevailing one, instead, in the reduction via a Cr(II) salt, because the Cr(III) species is not a good ligand-transfer agent.

The picture is less clear when a cuprous salt, a less strong reductant, is employed. Contrasting evidence is reported in the literature. Beringer and Bodlander[198] found PhI and PhCl as the only products from the reduction of $Ph_2I^+Cl^-$ by cuprous ion in methanol (Scheme 27). The reaction did not yield any benzene or biphenyl, suggesting in the authors opinion the absence of free-radical intermediates. A decomposition in a four-center complex was instead proposed. Lockhart,[266] on the other hand, obtained PhI, $PhOCH_3$, and PhBr from the reduction of $Ph_2I^+Br^-$ by cuprous ion in methanol, while observing considerable amounts of PhH and Ph_2 when running the same reaction in CH_2Cl_2. He postulated the intermediacy of a phenylcopper(III) species, and spectroscopic evidence for it was sought, but not found (Scheme 28). He also explained that benzene and biphenyl would derive from the phenyl radical formed by homolytic cleavage of the phenylcopper bond.

It is likely that the discrepancies between the experimental work above arise from problems related to the lower ease of reduction of the *diaryliodonium* ions, with respect to the analogous case with *arenediazonium* ions. A noteworthy clue is represented by the finding[198] that the reaction of Ph_2I^+ with a cuprous salt is faster than with the more strongly reducing Ti(III) and Cr(II) salts, suggesting that a straightforward et is not simply taking place with cuprous cation. This is at variance with the finding that the reactivity of Ti(III) and Cr(II) salts with Ph_2I^+ reflects instead their relative reducing power, or also with the situation of the diazonium salts, where a general tendency of the reactivity to increase with the increasing power of the reducing agent is found.[89]

It is the opinion of this author that, without looking for decidedly alternative formulations of the reaction mechanism, as those indicated by Beringer and Lockhart in the Schemes 27 and 28, a satisfactory description of the process could be formulated as an et from a nucleophilic counterion "mediated" by the cuprous salt (Scheme 29). Combination of the fragments in a cage had already been postulated by Roberts et al.[267] Escape from the cage could account for the formation of ArH and Ar_2. A very recent paper by Stang[268] on displacement reactions of alkynylphenyliodonium salts disfavors both a simple et from cuprous copper and the intermediacy of a copper(III) species and seems to share a mechanistic formulation in terms of a metal-assisted nucleophilic addition, followed by loss of iodobenzene as a neutral leaving group.

SCHEME 29

$$Ar_2I^+ + X^- \xrightarrow{Cu^IX} \overline{Ar\dot{I}Ar + Cu^{II}X} \longrightarrow ArI + ArX + Cu^IX$$

We will encounter another case of et from a nucleophile, *mediated* by a metal cation, in the field of the $S_{RN}1$ reactions, where the ease of reduction of the substrate (ArX) is still lower.[269] It is likely that, within these complexes between nucleophile and metal cation, factors other than the simple redox capacity may become more important to control the reactivity.[270]

To further check the intermediacy of the aryl radical, even in the cuprous-induced reactions of diaryliodonium salts, an experiment has been attempted, making use of a competing mixture of Br^- and Cl^- in the presence of a cuprous salt and of a cupric salt[271] (eq 85). A

$$Ph_2I^+ + Br^- + Cl^- + Cu(II) \xrightarrow{Cu(I)} PhI + PhBr + PhCl \quad (85)$$

mixture of phenyl halides is obtained, from which a k_{Br}/k_{Cl} ratio of 3.2 is reckoned for the relative efficiency of transfer of bromide and chloride as ligands. A similar ratio (i.e., 2.9) is obtained when a stannous salt is employed as the reductant. If an organometallic intermediate (as in Scheme 28) had been involved, it would have been more than a coincidence to obtain the same k_{Br}/k_{Cl} ratio from two different metals. This appears to suggest instead that the *same* reactive intermediate, i.e. $Ar^•$, is formed from the reaction of Cu(I) and of Sn(II) with the diaryliodonium salt. Furthermore, the agreement of the two k_{Br}/k_{Cl} ratios with those (i.e., 3.0 + 0.1) obtained before (eq 51)[197b] in the reduction of arenediazonium ions with different reductants (such as Cu(I), Sn(II), Fe(II), or ferrocene), confirms again the $Ar^•$ as the common intermediate in all these cases.

2. *$S_{RN}1$ Reactions*

Nucleophilic substitutions at unactivated aromatic substrates can occur by the $S_{RN}1$ mechanism, involving radical intermediates, as indicated in the propagation chain sequence[45] of Scheme 30. The substrates most commonly used in these processes are the aryl halides, and rather strong electron-donor agents are required to generate the $[ArX]^{•-}$ in the initiation step. In fact, the reduction potential of the aryl halides is rather low ($E_{1/2}$ = −1.6 to −2.8 V vs SCE) and, in particular, much lower than those of the arenediazonium ions and of the diaryliodonium ions.

SCHEME 30

$$[ArX]^{•-} \rightarrow Ar^• + X^-$$

$$Ar^• + Y^- \rightarrow [ArY]^{•-}$$

$$[ArY]^{•-} + ArX \rightarrow ArY + [ArX]^{•-}$$

Injection of solvated electrons into the reaction medium, produced by dissolving metals in proper sol-

TABLE V. Cation-Stimulated $S_{RN}1$ Reactions[a]

substrate	nucleophile	salt, (%)[b]	solvent	time	product	yield, %
PhI	$^-CH_2COCMe_3$	$FeSO_4$ (15)	NH_3	20 min	$PhCH_2COCMe_3$ (**15**)	87
PhBr	$^-CH_2COCMe_3$	$FeSO_4$ (15)	NH_3	75 min	**15**	58
PhI	$(EtO)_2PO^-$	$FeSO_4$ (15)	NH_3	20 min	$PhPO(OEt)_2$ (**16**)	98
PhBr	$(EtO)_2PO^-$	$FeSO_4$ (15)	NH_3	75 min	**16**	0.3
PhI	$^-CH_2COCH_3$	$FeCl_2$ (17)	Me_2SO	10 min	$PhCH_2COCH_3$	60
PhI	$^-CH_2COCH_3$	$SnCl_2$ (35)	Me_2SO	10 min	$PhCH_2COCH_3$	5
PhI	$(EtO)_2PO^-$ and $^-CH_2COCMe_3$	$h\nu$ (eq 87)	NH_3	12 s	**16** + **15**	50[c]
PhI	$(EtO)_2PO^-$ and $^-CH_2COCMe_3$	$FeSO_4$ (15)	NH_3	12 s	**16** + **15**	93[c]
PhI	$(EtO)_2PO^-$ and $^-CH_2COCMe_3$	CuCl (15)	NH_3	5 min	**16** + **15**	13[c]

[a] From ref 269. Reactions were run at −33 °C in NH_3 or at 25 °C in Me_2SO. [b] Percentage of dry salt with respect to the substrate. [c] Overall yield.

vents,[257] has been frequently exploited as an initiation mode (see eq 71). Electrons supplied from a cathode represent an even better way to generate the radical anion of the aryl halide.[258] This technique has in fact allowed the direct measurement of the reactivity of some nucleophiles toward the aryl radical.

Many aromatic $S_{RN}1$ nucleophilic substitutions occur under photostimulation at "Pyrex filtered 350 nm",[45] and evidence for the intermediacy of the aryl radical has been provided.[272] The mechanistic details of this useful initiation procedure begin to be unveiled. Three ways of production of the aryl radical by photoinitiation are conceivable:[273] (i) homolytic cleavage of the carbon–halogen bond

$$ArX \xrightarrow{h\nu} Ar^\bullet + {}^\bullet X$$

(ii) photojection of an electron from the anion to the excited aryl halide

$$ArX \xrightarrow{h\nu} [ArX]^* \xrightarrow{Y^-} [ArX]^{\bullet -} + Y^\bullet$$

(iii) electron transfer within an excited charge-transfer complex formed between substrate and anion.

$$[ArX\cdots Y^-] \xrightarrow{h\nu} [ArX^{\bullet -} \ldots Y^\bullet]$$

Clearly, the nature of the halogen (X) and of the nucleophile (Y^-) may be relevant in making one of the photoinitiation modes predominate over the others. Elegant work by Fox et al.[274] indicates that in the case of ketone enolate ions as the nucleophiles ($RCOCH_2^-$) the photoinitiation occurs as in (iii) with both PhI and PhBr, triggering the radical-chain $S_{RN}1$ process. The ease of the et within the excited CT complex depends on the reduction potential of the aryl halide and on the region of absorption of the CT complex. In agreement with this point, the easily reducible 9-bromoanthracene does not require photostimulation, but spontaneously accepts an electron from the enolate. On the contrary, in the case of another typical nucleophile, i.e. diethyl phosphite ion, $(EtO)_2PO^-$, the importance of CT excitation is lower, and aryl iodide homolysis as in (i) is probably the photoinitiation mode at play.[274] In fact, the reaction of $(EtO)_2PO^-$ with PhBr is extremely sluggish, because at the wavelength commonly employed in photostimulated $S_{RN}1$ reactions (i.e., 350 nm) photohomolysis of the stronger C–Br bond is much more difficult.

TABLE VI. Reactivity under Photostimulation of Diethyl Phosphite Ion and Pinacolone Enolate Ion in NH_3 at −33 °C[a]

PhX	nucleophile	time, s	product yield, %
PhI	CH_2COCMe_3	15	**15** 83
PhBr	CH_2COCMe_3	15	**15** 38
PhI	$(EtO)_2PO$	60	**16** 46
PhBr	$(EtO)_2PO$	60	**16** 0.1
PhI	$(EtO)_2PO$ and CH_2COCMe_3	33	**16** + **15** 53:37[b]
PhBr	$(EtO)_2PO$ and CH_2COCMe_3	75	**16** + **15** 33:30[b]

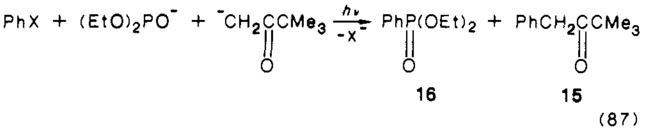
[a] From ref 232 and unpublished results. [b] Ratio of **16** to **15**.

The last discovered method of initiation of a $S_{RN}1$ process is by ferrous ion catalysis (Table V).[269] Equation 86 takes place without photostimulation, and

$$ArX + Y^- \xrightarrow{\text{Fe(II)}} Ar^\bullet \qquad (86)$$

even in the dark, with amounts of cation considerably lower than stoichiometric. The order of substrate reactivity is again ArI > ArBr > ArCl ≫ ArF, as in the photostimulated reactions. An exact knowledge of the mechanism of this initiation is not available, but probably the ferrous cation mediates the et from the nucleophile to the substrate, by analogy with the suggestion made for Cu(I) catalysis in the decomposition of diaryliodonium salts (Scheme 29). A reasonable clue that a simple et from the Fe(II) cation to ArX does not occur stems from the largely unfavorable energy balance for this step, as based on the redox potentials of the two species. But also from the finding that *stronger* reducing cations are by far *less* effective than ferrous cation (Table V). Whatever is the true nature of such catalysis, the procedure is made attractive from a synthetic viewpoint by the convenient handling and by the inexpensive experimental requirements. Complexes of Ni(0)[275] or of Ni(I)[276] seem on the other hand to be capable of direct et to ArX, with subsequent formation of $Ar^\bullet$ from the radical anion (ESR evidence)[275] and production of ArH. Comparison of efficiency among three initiation techniques (i.e., photostimulation, Ni(0) induction, electrons from dissolving metals) in an intramolecular $S_{RN}1$ reaction has been reported.[277]

Support for the mechanistic scheme of the $S_{RN}1$ reaction emerges from another fashinating feature of these chain processes: the entrainment. A reaction between one nucleophile and an aryl halide may be rather unreactive at initiation, but quite reactive in propagation. The addition of tiny amounts of another substrate (or nucleophile) that is more reactive in the initiation increases the generation of the reactive intermediate(s) and allows the less reactive substrate (or nucleophile) to start its own propagation.[278] Typical is the case of diethyl phosphite, whose reactivity with PhBr is much lower than that with PhI (Table VI),[279] at variance with what occurs with a ketone enolate ion, for reasons linked to the different mechanism of photostimulation of the two anions (cases i and iii, respectively, as examined before). The example of entrainment comes about in the photostimulated reaction of a mixture of diethyl phosphite and pinacolone enolate ions for PhBr and also for PhI (Table VI; eq 87).



$$\mathrm{PhX + (EtO)_2PO^- + {}^-CH_2\underset{\underset{O}{\|}}{C}CMe_3 \xrightarrow[-X^-]{h\nu} Ph\underset{\underset{O}{\|}}{P}(OEt)_2 + PhCH_2\underset{\underset{O}{\|}}{C}CMe_3} \qquad (87)$$

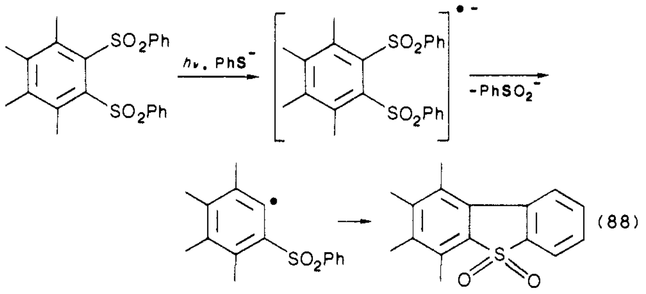
16 15

The efficient initiation step of the *enolate* ion provides easy access to the phenyl radical intermediate to the *phosphite* anion. The latter, on the other hand, is slightly more reactive than the enolate ion in the attack to $Ph^\bullet$, and, consequently, *more* diethyl phenylphosphonate (**16**) than benzyl *tert*-butyl ketone (**15**) is eventually produced from the propagation chain. The time required for more than 50% consumption of PhBr in reaction of the two combined nucleophiles, when compared to the meager extent of reaction of $(EtO)_2PO^-$ alone with PhBr, shows how strong is the importance of the initiation step for this nucleophile.[279]

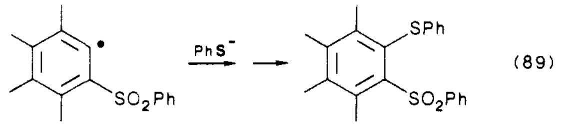
B. Interchange of Product Patterns

We have seen in paragraph III that the chemical patterns available to the aryl radical, whenever it is unambiguously formed in homolytic *dediazoniations*, result to be independent from the radical source employed in its generation. Let us try to widen the validity of this observation, by also including examples relative to other reactions, like the ones we have examined in the previous section, equally leading to the aryl radical.

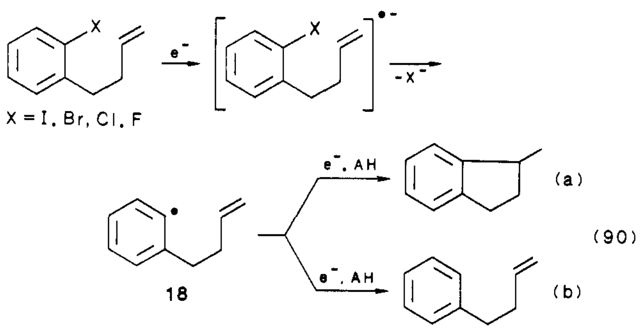
(1) An $S_{RN}1$ photostimulated reaction of PhS^- with an o-bis(phenylsulfonyl)arene triggers an efficient intramolecular arylation through the radical intermediate **17**.[280] This arylation (eq 88) is of the Pschorr type. Competition by bimolecular nucleophilic attack on the same radical (eq 89) is relatively unimportant and can be suppressed by initiating the reaction electrochemically.[281]



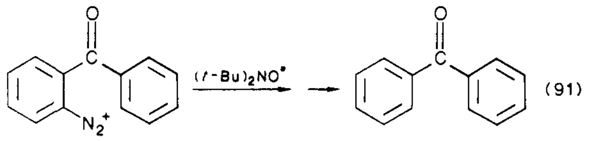
17



(2) Analogous to a Meerwein procedure (eq 62)[118] is an $S_{RN}1$ reaction induced by solvated electrons[282] (eq 90). The branching between intramolecular arylation of the olefin and reduction of the uncyclized radical **18** are affected by the nature of the halogen X. In fact, the extent of the two reactions depends on the gradient of the solvated electrons as they diffuse in solution and on the timing of fragmentation of the radical anion of the substrate. How much cyclization can occur depends on how rapidly substrate electronation and the ensuing fragmentation occur before the arrival of more electrons terminates all radical activity. Consistently, the ratio of (a) to (b) increases strongly on going from X = F to X = I.



(3) Donation of electrons to arenediazonium salts by di-*tert*-butyl nitroxide ($E_{1/2}$ = 0.6 V vs SCE) takes place[283] as in the case of diaryliodonium ions (eq 76).[201] Photostimulation is however not required by the more easily reducible diazonium salt. The aryl radical in this way generated affords various products (H abstraction or halogen abstraction) according to the reaction environment chosen. Interestingly, the diazonium salt derived from 2-aminobenzophenone leads exclusively to hydro-dediazoniation by way of hydrogen abstraction from the *t*-Bu group (eq 91). This result is exactly analogous to the one obtained by Lewin and Cohen[241] for the analogous *cuprous-induced* dediazoniation in the good hydrogen-donor dioxane solvent (Table IV).

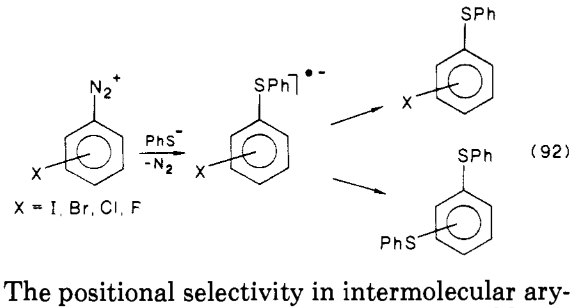


(4) The $S_{RN}1$-like reaction of ArS^- with a diazonium salt represents a mild and efficient approach to the synthesis of diaryl sulfides,[284] as reported before.[118] A radical-chain process takes place (Scheme 31). When the arenediazonium ion bears a halogen substituent, the possibility of mono- vs disubstitution arises at the level of the $[ArX]^{\bullet-}$ species (eq 92). It parallels the product patterns obtained in the analogous $S_{RN}1$ reactions carried out on various dihalobenzenes.[285,286]

SCHEME 31

$$ArN_2^+ + Ar'S^- \rightarrow ArN{=}NSAr' \rightarrow Ar^\bullet + N_2 + Ar'S^\bullet$$

$$Ar^\bullet + Ar'S^- \rightarrow [ArSAr']^{\bullet-} \xrightarrow[-e^-]{} ArSAr'$$



(5) The positional selectivity in intermolecular arylations of the Gomberg type has been thoroughly investigated. In particular, the study of the isomeric

distribution for the arylation of pyridine represents a sort of test reaction (see eq 84). It emerges that the α-, β-, and γ-arylpyridines are uniformly formed in the ratio of 55/30/15, irrespective of the radical sources employed.[287] These equivalent sources of the aryl radical are (a) decomposition of benzoyl peroxide,[288] (b) electrochemical reduction of ArN_2^+,[190] (c) decomposition of PAT,[287,289] (d) interconversion of *N*-nitrosoacetanilide,[289,290] (e) photoinduced cleavage of the carbon–thallium bond in arylthallium compounds,[291] (f) homolytic cleavage of triazenes,[247,292] and (g) decomposition of lead tetrabenzoate.[293] A common reaction mechanism, along with a common reactivity of the aryl radical intermediate, ensues from these examples.

(6) Another test reaction already encountered (eq 51 and 85)[197b] is the competition of two halides for $Ar^\bullet$, in the ligand-transfer step mediated by Cu(II) ion. When applied during the thermal decomposition of benzoyl peroxide, the competition gives a k_{Br}/k_{Cl} ratio of 4.7 (eq 93 and 94). This number, when allowance is made for the effect of the temperature upon the selectivity of the aryl radical in the ligand-transfer step,[294] is in more than reasonable agreement with the values obtained at lower temperature in the same competition process, when carried out in the case of other radical processes (eq 51 and 85).

$$(PhCO_2)_2 \xrightarrow{\Delta} 2Ph^\bullet + 2CO_2 \qquad (93)$$

$$Ph^\bullet + Br^- + Cl^- \xrightarrow{Cu(II)} PhBr + PhCl \qquad (94)$$

(7) The entrainment, a feature typical of free-radical chain processes such as the $S_{RN}1$ reaction, is shared also by the H_3PO_2-induced hydro-dediazoniation (Scheme 20).[6] The rate of reduction of *p*-tolyldiazonium ion is more than 300 times increased by addition of trace amounts of the more easily reducible pentabromobenzendiazonium (or *p*-nitrobenzendiazonium) ion. The effect on the reduction rate is due to the larger number of chains that are initiated by the better electron acceptor and *then* carried on by the more abundant *p*-tolyldiazonium salt.

(8) Iodobenzene can undergo $S_{RN}1$ substitution reactions with diethyl phosphite ion *even without* photostimulation, by exploiting the initiation provided by the thermal decomposition of phenylazotriphenylmethane (PAT)[273] (Scheme 32).

SCHEME 32

$$PAT \rightarrow Ph^\bullet + N_2 + Ph_3C^\bullet$$

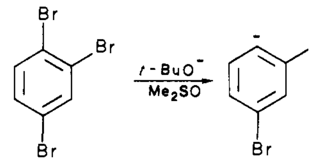
$$Ph^\bullet + (EtO)_2PO^- \rightarrow [PhP(O)(OEt)_2]^{\bullet-}$$

$$[PhP(O)(OEt)_2]^{\bullet-} + PhI \rightarrow PhP(O)(OEt)_2 + [PhI]^{\bullet-}$$

(9) A case where a rather delicate balance among reaction pathways exists is represented by the reduction of aryl halides to arenes, as brought about by metal hydrides such as $NaBH_4$ or $LiAlH_4$. The reaction (95)

$$ArX + BH_4^- \rightarrow Ar^- + HX + BH_3 \xrightarrow{SH} ArH \qquad (95)$$

is described to take place via nucleophilic attack of hydride ion on halogen, to give the aryl anion and finally the arene.[295] Similar dehalogenation reactions, as shown by Bunnett in a comprehensive study with other nucleophiles,[138,296] are made easier by the presence of electron-withdrawing groups that, by stabilizing the anionic intermediate, promote the abstraction of the positive halogen (eq 96).



(96)

The possible intervention of a radical pathway in eq 95, with the donation of an electron to ArX, has sometimes been invoked. Competition between electron transfer and S_N2 is indeed documented by Ashby[297] in reaction of the *alkyl* halides. He points out that the extent of et is a function of the hydride reagent, the solvent, the substrate, and the leaving group.

Interestingly, evidence of radical-chain mechanism is unmistakably given for the *photoreduction* of ArX by $NaBH_4$. The reactivity order among the halides is ArI > ArBr > ArCl ≫ ArF, and quantum yields in excess of unity are often measured. Homolysis of the carbon–halogen bond occurs in the initiation, and then a propagation chain leads to the reduced product[298] (Scheme 33). Inhibition of the process by small amounts of acrylonitrile, i.e. a good radical scavenger, demonstrates the intervention of the aryl radical. The authors[298] propose also that the reduction of ArX to ArH with $LiAlH_4$ in THF, that was observed by Brown and Krishnamurty[299] and that proceeded in the dark, was probably a radical process as induced by the presence of peroxides in the solvent. A paper by Beckwith and Goh[300] confirms indeed this point, showing that fragmentation of di-*tert*-butyl peroxide is able to promote a propagation chain in the reduction of ArX with $LiAlH_4$ (Scheme 34). The fact that, without photostimulation, the hydro-dediazoniation by BH_4^- proceeds essentially through the ionic pathway (Scheme 21)[192] would be simply due to the fast formation of the covalent adduct ArN=NH, that efficiently intercepts the ArN_2^+ and prevents any electron-transfer step from the BH_4^- that has an electron-donor capacity lower than $BH_3^{\bullet-}$. Nevertheless, CIDNP evidence of radical formation in reaction of $NaBH_4$ with a diazonium salt has been recorded,[301] indicating that under well-chosen conditions the radical pathway can give a contribution as well.

SCHEME 33

$$ArX \xrightarrow{h\nu\ (254\ nm)} [ArX]^* \rightarrow Ar^\bullet + X^\bullet$$

$$Ar^\bullet + BH_4^- \rightarrow ArH + BH_3^{\bullet-}$$

$$ArX + BH_3^{\bullet-} \rightarrow [ArX]^{\bullet-} + BH_3 \qquad \text{propagation}$$

$$[ArX]^{\bullet-} \rightarrow Ar^\bullet + X^-$$

SCHEME 34

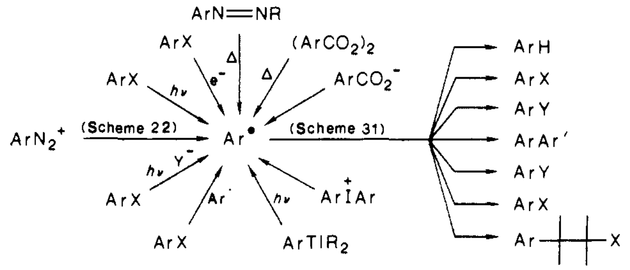
$$t\text{-BuOOBu-}t \rightarrow 2t\text{-Bu}^\bullet + O_2$$

$$t\text{-Bu}^\bullet + AlH_4^- \rightarrow AlH_3^{\bullet-} + t\text{-BuH}$$

$$AlH_3^{\bullet-} + ArX \xrightarrow[-X^-]{} Ar^\bullet \xrightarrow{AlH_4^-} ArH + AlH_3^{\bullet-}$$

(10) By means of laser flash photolysis technique,[252] iodobenzene or benzoyl peroxide have both been exploited as aryl radical precursors in a kinetic study. No

SCHEME 35



appreciable differences were detected in the absolute rate constants toward 17 substrates, between experiments making use of PhI or of $(PhCO_2)_2$ as the $Ph^•$ source. Therefore, these kinetic data must reflect the behavior of a common radical intermediate in both systems: This can only be the phenyl radical. The rate constants obtained in this investigation for the reactivity of phenyl radical are in excellent agreement with earlier ones reported by Lorand et al. (Table II),[207] which were determined by exploiting the thermal decomposition of PAT. Compelling evidence for independence of the reactivity of $Ph^•$ from all these methods of generation is therefore provided. Such a finding is particularly important in that, by photodecomposition,[252] one could have postulated the intermediacy of an "excited $Ph^•$", possibly endowed with a reactivity different from that of the "thermal $Ph^•$".[207] No such dichotomy seems to show up.

The present list of examples is certainly not exhaustive of all the cases of constancy of product patterns that have been reported in the literature among reactions of the aryl radical. Anyhow, they are enough to support the conclusion that the chemistry of the aryl radical is of very wide scope (Scheme 35). Clearly, the arenediazonium salts, with their high affinity toward electrons, represent the most easy entry into the chemistry of this fundamental intermediate.

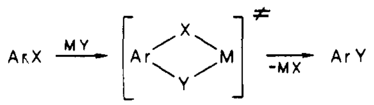
It is my hope that the general rationalization offered for the homolytic reactions of diazonium salts and for the related processes may be useful both from a mechanistic and from a synthetic viewpoint. It is also appropriate to remark that quantitative information on the reactivity in this field is scanty. This is particularly true for the et steps leading to the generation of the $Ar^•$ species, but also for the reactive steps available to it.

V. Unrelated Reactions

Homolytic reactions induced by the transfer of an electron and involving a free-radical species cannot obviously be considered the unique possibility of reaction mechanism. This is particularly true for substrates not endowed with a very high electron affinity, as the aryl halides are. In this case, the familiar S_NAr mechanism, boosted by the presence of strong electron-withdrawing substituents, or the benzyne mechanism, caused by the use of strong bases, represent two possible alternative pathways that are, however, outside the scope of this review. Instead, we will briefly examine cases of metal-assisted or metal complex assisted nucleophilic substitutions in nonactivated aromatic substrates. Once again, the list of examples does not pretend to be exhaustive but only tries to summarize the most recent achievements, wherefrom previous literature can be traced.

Copper salts are again prominent examples of catalytic agents in these reactions.[302,303] But nickel, palladium, rhodium, cadmium, cobalt, iron, or chromium salts have also been employed with success;[304-307] and even the use of platinum or gold salts is reported.[304] The reason why these reactions are indicated here as "unrelated" to those examined before is that the intermediacy of a free-radical species is in general not postulated or warranted.

The ways in which these reactions are believed to occur, and the chemistry that they make accessible, have been reviewed by Bunnett and Zahler,[58] by Bacon and Hill,[308] and more recently by Lindley.[302] Possibilities exist of (1) four-center transition state[309-311]



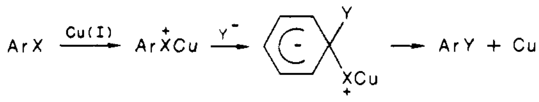
(2) bond insertion, also referred to as oxidative addition, with the formation of a bridged arylmetal intermediate, featuring the metal in a high-valence state, e.g. Cu(III),[307,312-315] sometimes also leading to reductive dehalogenation[316-319]

$$ArX + CuY \rightarrow ArCuX(Y) \rightarrow ArY + CuX$$

(3) electron transfer from the nucleophile to the aromatic substrate mediated by the metal[320,321]

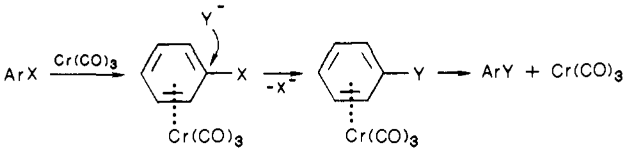
$$M^{n+}Y^- \rightarrow Y^• + M^{(n-1)+} \xrightarrow{ArX} [ArXY]^• \xrightarrow[-X^•]{} ArY$$

(4) atom abstraction in a coordination complex, displaying either ionic character[58,303] or radical character[276,322]



$$ArX + M^{n+} \longrightarrow \overline{Ar^• + M^{(n+1)+}X^-}$$

(5) activation of the aromatic substrate by π-coordination, followed by nucleophilic displacement (an "activated" S_NAr route),[323] for example[306]



(6) cross-coupling via organometallic species,[324-327] for example[328]

$$ArCdX + RX \rightarrow ArR + CdX_2$$

In some cases the proposed pathway presents ionic character. In some others, the intermediacy of an aryl radical is implied, but only within a cage.[304,329,330] Other clues that these nucleophilic substitution, or coupling, reactions present different features with respect to the "aryl radical chemistry", come from the fact that uncommon patterns of reactivity are observed[331] or that good yields of substitution product are obtained where the other conditions failed.[312] A typical example is the good reactivity of the oxygen nucleophiles or that scavengers of free electrons or of free radicals do not severely hamper the reactivity of the process.[304,332] In addition, there is often the necessity for reaction temperatures higher, or much higher, than room temperature.[58,302,308]

Intermediacy of four-center species,[198] or of copper(III) species,[266] which had been advanced by some authors in cases of the "aryl radical chemistry" previously examined, find a more likely justification in this kind of chemistry. Admittedly, it is sometimes difficult to discriminate between a free-radical process and a coupling process. Examples of a Ni(0)-induced $S_{RN}1$ reaction have been advanced, implying aryl radical and radical anion intermediacy.[275,277] But, on the other hand, a coupling reaction of ArX by use of a Ni(I) salt[315] or a Meerwein-like arylation of a double bond by use of a Ni(0) complex[333] or a Pd(0) complex,[334] without evidence for the intermediacy of $\mathrm{Ar}^{\bullet}$, have been reported as well.

The case of the Ullmann biaryl synthesis[335] is typical. Following the first mechanistic formulations in terms of a ionic mechanism or of a free-radical mechanism,[5] suggestions in terms of a coupling process,[317,336–338] or of a four-center process,[311] or for the intervention of a Cu(III) intermediate[339] were all advanced at time to describe this reaction. Undoubtedly, some confusion was due to the fact that even small changes in the reaction conditions may lead to a significant change in the mechanism. In any case, all the more recent evidence[302,340,341] points to the cuprous salt as the reactive species, either present as such or produced in situ by reduction of a cupric salt. In addition, studies of the effect of substitutents provide us with small and positive ρ values (0.5–1.1) that are at variance with typical ρ values of 3–7 for true uncatalyzed nucleophilic aromatic substitutions.[341,342]

In conclusion, although some firm points have been established in this field, further mechanistic studies are needed and will still encounter fertile grounds to investigation.

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