

Phenomenon of Radical Anion Fragmentation in the Course of Aromatic S_{RN}1 Reactions

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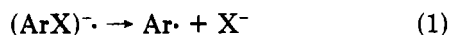
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Since the discovery of aromatic nucleophilic substitution by the S_{RN}1 mechanism by Kim and Bunnett,¹ the mechanism has been found to have wide scope with regard to both the substrates and the nucleophiles that participate.²⁻⁴

In general terms the S_{RN}1 mechanism is a chain reaction, and as such comprises initiation, propagation, and termination steps.

In the usual initiation step, an electron is added to an appropriate substrate by one of several procedures, especially by photostimulation,⁵ by adding solvated electrons,^{1,6} or by electrochemical methods.⁷ The radical anion thereby formed fragments into an aryl radical and the anion of the leaving group (eq 1). Next

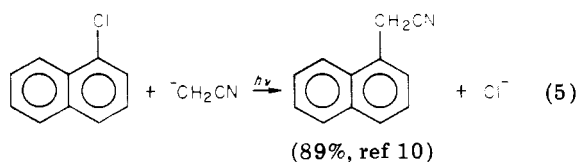


the aryl radical couples with the nucleophile, forming a new radical anion (eq 2), which finally transfers its "extra" electron to the substrate (eq 3). The nature of the termination step is very much dependent on the type of initiation, and is not very well-known yet.

Summation of these three steps gives eq 4, which amounts to an aromatic nucleophilic substitution that proceeds via radical and radical anion intermediates.

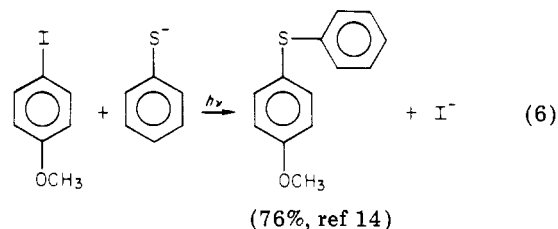


This mechanism is quite general insofar as the substrate and nucleophile are concerned and does not require activation of the aryl ring in order to occur. Benzene and benzene derivatives⁶ and polycyclic²⁻⁴ and heterocyclic⁸ aromatic hydrocarbons bearing halogens and trimethylammonio or other leaving groups have been observed to react with several carbanion nucleophiles of general structure R⁻CH-Z, where Z is CN,⁹⁻¹¹ COR',²⁻⁴ CO₂R',¹² or CONR'R'',¹³ and where R is an alkyl group or hydrogen. A representative example is given in eq 5.

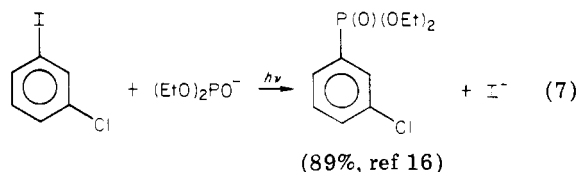


Roberto A. Rossi was born in Jesús María, Córdoba, Argentina, in 1943. He did both undergraduate and graduate studies in the Universidad Nacional de Córdoba and was awarded the degree Doctor en Bioquímica. He did postdoctoral work with Joseph F. Bunnett at the University of California, Santa Cruz, in 1970-1972. He is now Professor of Organic Chemistry at Córdoba and is a member of the Argentine Consejo Nacional de Investigaciones Científicas y Técnicas.

Ions derived from sulfur or selenium, such as benzenethiolate¹⁴ or phenylselenide¹⁵ ions, give good yields of substitution product, as, for instance, in photostimulated reaction with aryl iodides (eq 6).



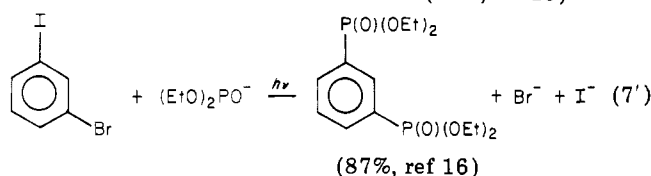
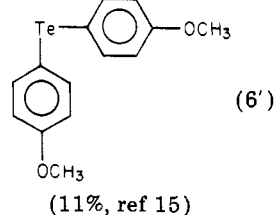
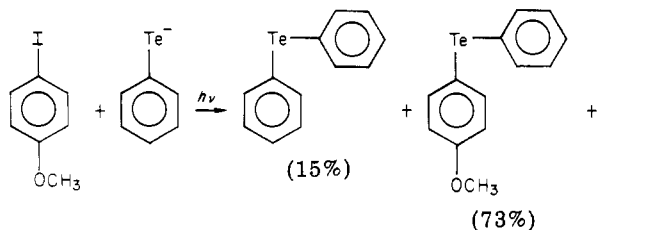
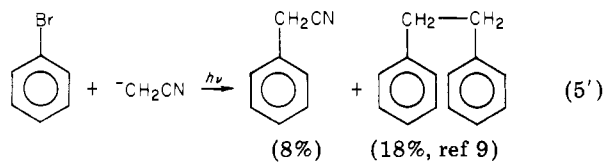
Phosphorus-derived nucleophiles, such as diethyl phosphite¹⁶ and diphenylphosphide ions,¹⁷ are superb nucleophiles, which react not only under photostimulation but also sometimes in the dark (eq 7).



However, not all observations have been that simple and straightforward. For instance, compare eq 5', 6', 7' with eq 5, 6 and 7.

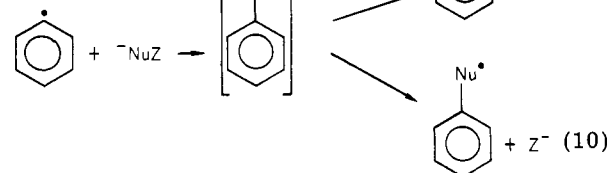
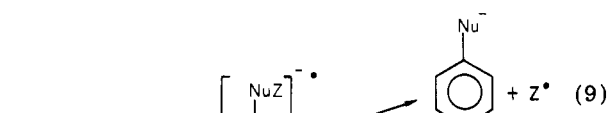
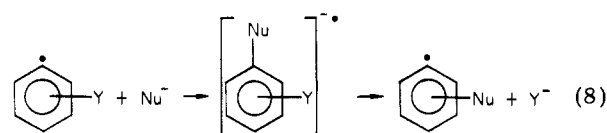
Besides the differences in products formed, there are in some cases important differences in rates of reactions. For instance, while 1-chloronaphthalene fully reacts with cyanomethyl anion in less than 15 min,¹⁰ only about 30% of bromobenzene reacts in 120 min.⁹ On the other hand, there is no major difference between the

- (1) Kim, J. K.; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7463, 7464.
- (2) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.
- (3) Wolfe, J. F.; Carver, D. R. *Org. Prep. Proced. Int.* **1978**, *10*, 224.
- (4) Beletskaya, I. P.; Drozd, V. N. *Usp. Khim.* **1979**, *48*, 793. *Russ. Chem. Rev. (Engl. Transl.)*, **1979**, *48*, 431.
- (5) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 1407.
- (6) Rossi, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 112.
- (7) Savéant, J. M. *Acc. Chem. Res.* **1980**, *13*, 323 and references cited therein.
- (8) Carver, D. R.; Komin, A. P.; Hubbard, J. S.; Wolfe, J. F. *J. Org. Chem.* **1981**, *46*, 204 and references cited therein.
- (9) Bunnett, J. F.; Gloor, B. F. *J. Org. Chem.* **1973**, *38*, 4156.
- (10) Rossi, R. A.; de Rossi, R. H.; López, A. F. *J. Org. Chem.* **1976**, *41*, 3371.
- (11) Rossi, R. A.; de Rossi, R. H.; Pierini, A. B. *J. Org. Chem.* **1979**, *44*, 2662.
- (12) Semmelback, M. F.; Bargar, T. *J. Am. Chem. Soc.* **1980**, *102*, 7765.
- (13) Rossi, R. A.; Alonso, R. A. *J. Org. Chem.* **1980**, *45*, 1239.
- (14) Bunnett, J. F.; Creary, X. *J. Org. Chem.* **1974**, *39*, 3173.
- (15) Pierini, A. B.; Rossi, R. A. *J. Org. Chem.* **1979**, *44*, 4667.
- (16) Bunnett, J. F.; Creary, X. *J. Org. Chem.* **1974**, *39*, 3612.
- (17) Swarts, J. E.; Bunnett, J. F. *J. Org. Chem.* **1979**, *44*, 340.



rates of formation of monosubstitution product in reaction 7 and disubstitution product in reaction 7'.

These results find explanation in the $S_{RN}1$ mechanism with some additional steps also included. Once the aryl radical couples with the nucleophile, the radical anion formed may suffer competitive reactions, namely, electron transfer (eq 3) or fragmentation (eq 8–10).



The relative importance of these two types of reaction determines the nature of the products formed.

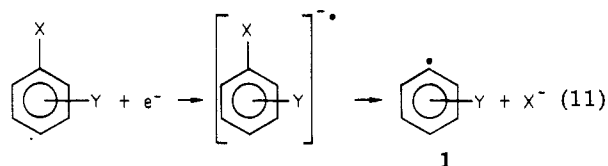
Fragmentation of the radical anion according to eq 8 was the explanation offered for the formation of disubstitution products in several reactions of dihalobenzenes with nucleophiles.^{15,18–22} When fragmentation occurs (as in eq 8–10) and produces aryl radicals that react with the nucleophile, the overall reactivity of the system does not decrease, as compared to those reactions in which the major pathway followed by the radical anion intermediate is electron transfer. But when

the fragmentation leads to an unreactive alkyl radical, the overall reactivity is low.

In all cases, the relative rates of fragmentation (eq 8–10) and electron transfer (eq 3) determine the reaction course. In this Account some of the factors that influence the rate of fragmentation are discussed.

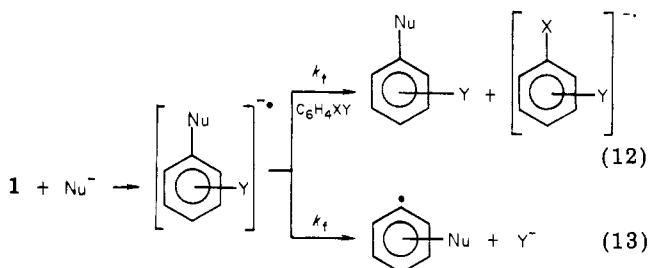
Fragmentation of the Radical Anion into Reactive Intermediates

Substrates with Two Leaving Groups. When a substrate bearing two nucleofugal groups, X and Y, accepts an electron, it forms a radical anion that fragments, giving a substituted aryl radical and a nucleofuge (eq 11). The halogen mobility decreases in the order



$\text{I} > \text{Br} > \text{Cl} > \text{F}$ when the aryl group is the same.

When the aryl radical (1) combines with a nucleophile, the radical anion formed has a potential leaving group and may suffer the two competing reactions mentioned, namely, electron transfer (eq 12) or bond fragmentation with the formation of a new aryl radical (eq 13).



The aryl radical formed in eq 13 reacts with the nucleophile in the sense of eq 2 and leads ultimately to the disubstitution product. Reaction 12 furnishes the monosubstitution product. Therefore the products obtained depend on the relative rates of fragmentation (k_f) and electron transfer ($k_t[\text{C}_6\text{H}_4\text{XY}]$).

The photostimulated reactions of *p*-chloriodobenzene, *p*-bromiodobenzene, and (*p*-iodophenyl)trimethylammonium ion with thiophenoxide ion in liquid ammonia afford mainly the disubstitution product, which shows that for these reactions $k_f \gg k_t[\text{C}_6\text{H}_4\text{XY}]$. On the other hand, *p*-fluoriodobenzene gives only the monosubstitution product, which means that $k_f \ll k_t[\text{C}_6\text{H}_4\text{XY}]$.¹⁸

The possibility that the monosubstituted product is formed but is consumed very fast was discarded because in competition experiments, *m*-chloriodobenzene was found to react 17 times faster than the monosubstitution product.¹⁸ Besides, in a short reaction time, when substantial amounts of substrate are still present, along with the disubstitution product, only traces of the monosubstitution product are formed.²⁰

With dihaloarenes bearing a chlorine atom as one of the leaving groups, the ratio of $k_f/k_t[\text{C}_6\text{H}_4\text{XY}]$ depends greatly on the nature of the nucleophile and its position in the molecule. *p*-Chloriodobenzene reacts with diethyl phosphite¹⁹ or thiophenoxide¹⁸ ions to give the disubstitution product. *m*-Chloriodobenzene gave the

(18) Bunnett, J. F.; Creary, X. *J. Org. Chem.* 1974, 39, 3611.

(19) Bunnett, J. F.; Traber, R. P. *J. Org. Chem.* 1978, 43, 1867.

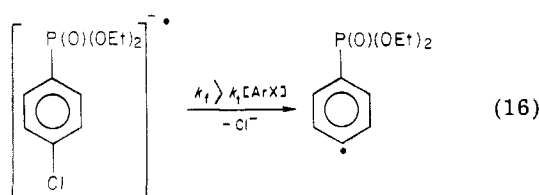
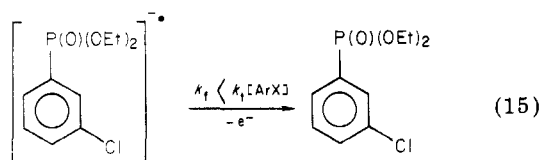
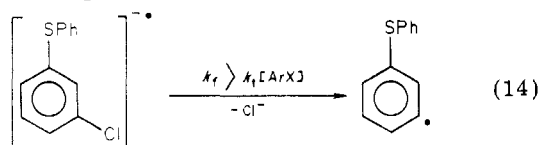
(20) Bunnett, J. F.; Shafer, S. J. *J. Org. Chem.* 1978, 43, 1873, 1877.

(21) Komin, H. P.; Wolfe, J. F. *J. Org. Chem.* 1977, 42, 2481.

(22) Alonso, R. A.; Rossi, R. A. *J. Org. Chem.* 1980, 45, 4760.

disubstitution product with thiophenoxide ion,¹⁸ but mainly the monosubstitution product with diethyl phosphite ion.¹⁹

Electron-transfer rates from aromatic radical anions to arene derivatives depend on the reduction potentials of donor and acceptor and become diffusion controlled when reaction occurs in the thermodynamically favored direction. In eq 14 and 15, the electron acceptor ArX



is the same; therefore the electron-transfer rate should be faster with the better electron donor (the phenylthio-substituted radical anion), unless the reaction is thermodynamically favored in both cases. Thus, k_t [ArX] for eq 14 is expected to be higher than or equal to k_t [ArX] for eq 15. It follows that the product ratio must be governed by the rate of fragmentation and not by changes in electron transfer rate constants.

The electron transfer rates of eq 15 and 16 are probably even more similar. Again the differences in products formed appear to be due to differences in the rates of fragmentation of the two compounds.

The rates of decomposition of haloarenes radical anions have been found to depend on (in addition to solvent and temperature) (1) the reduction potential of the parent haloarene—the more negative the potential, the faster is the decomposition; (2) the nature of the halogen—nucleofugality increases as the bond strength of C–X decreases; (3) the spin density at the carbon bonded to the halogen.

The reduction potential is a measure of the energy available for bond fragmentation. It has been suggested²³ that the reduction potential limit above which the haloarene radical anions can be considered stable ($t_{1/2} > 5$ s) is the following: Cl, $E^\circ > -1.6$ V; Br, $E^\circ > -1.2$ to -1.6 V; and I, $E^\circ > -1.1$ V (in DMF vs. SCE).²³ According to these rules, any radical anion whose reduction potential is more negative than these limits will have a lifetime of less than 5 s.

MO calculations,^{24,25} as well as ESR spectroscopy,²⁶ indicate that haloarenes can form π^* or σ^* radical anions, but dissociation takes place only when the odd electron is located in the σ^* orbital, which is a repulsive state.^{27,28} The probability of an electron being located

in one or the other of these MOs depends on their relative energies.

A σ^* radical anion often has the electron density localized at a particular σ bond. The likelihood that an electron located in an orbital can be intramolecularly transferred from a π^* into a particular σ^* MO depends on the energy gap between these two orbitals and on the spin density at the carbon atom to which the nucleofugal group is bonded,^{29,30} since the spin density is a measure of the probability of finding the electron on that carbon.

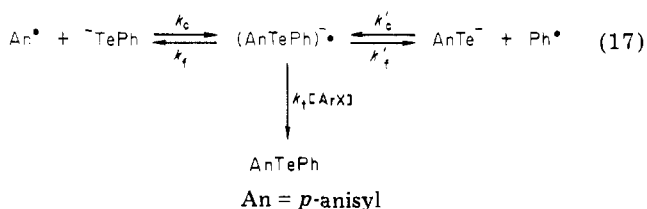
The energy of the σ^* orbital is not expected to be greatly affected by the nature of the aromatic moiety, whereas the π^* MO is very much dependent on the aromatic ring system. In a series of compounds with the same leaving group and for which the π^* MOs are lower than σ^* MOs in energy, the difference in energy between σ^* and π^* MOs should decrease as the reduction potential become more negative, and consequently the rate of fragmentation should increase.

On the basis of the considerations presented above, these results would indicate that the difference in energy between π^* and σ^* MOs is higher in diethyl arylphosphonate radical anions than in the phenyl aryl sulfide radical anions. This difference is probably due to differences in the π^* energy levels of the two systems, since the σ^* energy level of the C–Cl bond is not likely to be much affected by the presence of meta substituents.

The energy of the π^* MO is probably lower for the diethyl arylphosphonate derivatives, because the reduction potentials of diethyl arylphosphonates are more positive than those of aryl phenyl sulfides.³¹ Consequently they fragment slower and give mainly the monosubstituted product.

Nucleophiles with Low Carbon-Nucleophile Bond Energy. Remarkable differences were found in studies of nucleophiles of the general type PhM^- ($\text{M} = \text{S}, \text{Se}, \text{and Te}$) and also with nucleophiles of group 5A elements of type Ph_2M^- ($\text{M} = \text{P}, \text{As}, \text{and Sb}$).

While PhS^- and PhSe^- react with aryl halides giving straightforward substitution products, PhTe^- ion gives products in which aryl groups are scrambled. This difference in behavior was ascribed to the reversibility of coupling in the case of the latter nucleophile (eq 17).¹⁵



The radical anion formed from coupling of p -anisyl radical with PhTe^- suffers three competing reactions: reversion to starting reactants (k_f), fragmentation to form p -anisyltelluride ion and phenyl radical (k'_f), and

(27) Symons, M. C. R. *Pure Appl. Chem.*, 1981, 53, 223 and references cited therein.

(28) Canadell, E.; Karafiloglou, P.; Salem, L. *J. Am. Chem. Soc.* 1980, 102, 855.

(29) Grimshaw, J.; Trocha-Grimshaw, J. *J. Electroanal. Chem.* 1974, 56, 443. Nadjo, L.; Savéant, J. M. *Ibid.* 1971, 30, 41.

(30) Gores, G. J.; Koepf, C. E.; Bartak, D. E. *J. Org. Chem.* 1979, 44, 380.

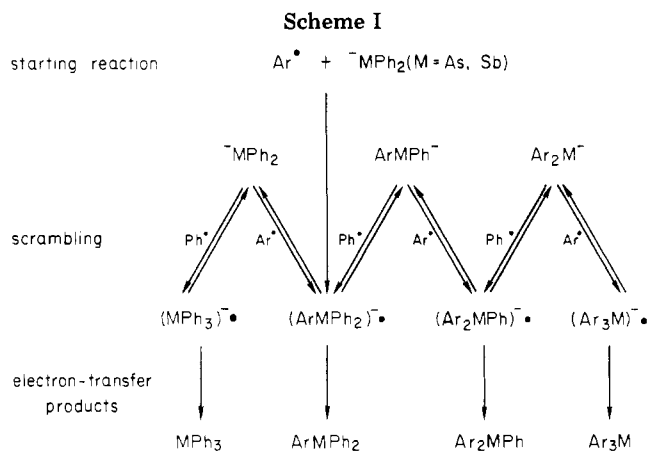
(31) Amatore, C.; Chaussard, J.; Pinson, J.; Savéant, J. M.; Thiebault, A. *J. Am. Chem. Soc.* 1979, 101, 6012.

(23) Alwair, K.; Grimshaw, J. *J. Chem. Soc., Perkin Trans. 2*, 1973, 1811.

(24) Beland, F. A.; Farwell, S. O.; Callis, P. R.; Geer, R. D. *J. Electroanal. Chem.* 1977, 78, 145.

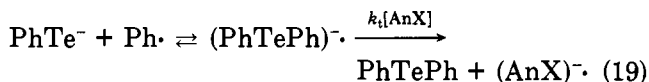
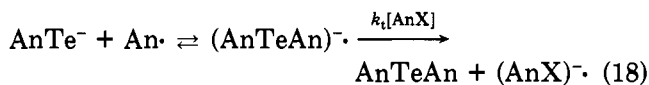
(25) Villar, H.; Castro, E. A.; Rossi, R. A. *Can. J. Chem.*, in press.

(26) Symons, M. C. R. *J. Chem. Soc., Chem. Commun.*, 1978, 313.



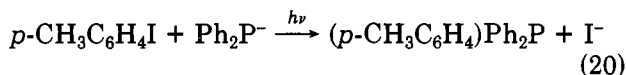
electron transfer to form *p*-anisyl phenyl telluride.

In eq 17 two new species are formed, namely, *p*-anisyltelluride ion and phenyl radical, and they can react with each other as in eq 17 (k'_c). Alternatively, they can diffuse apart and react with *p*-anisyl radical and phenyltelluride ion, respectively, giving the symmetrical tellurides (eq 18 and 19).¹⁵

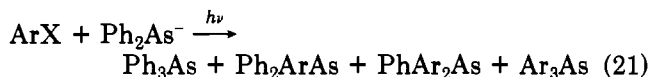


In this system $k_f \approx k'_f \approx k_t[AnX]$, leading to scrambling of aryl rings as depicted in eq 6'. If benzenethiolate or phenylselenide ion instead of phenyltelluride ion is the nucleophile, $k'_f \ll k_t[ArX]$, and only the straightforward substitution product is obtained.

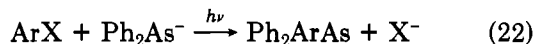
As for nucleophiles derived from group 5A elements, the first member of this series, diphenylphosphide ion, reacts with aryl radicals, giving cleanly unscrambled substitution products (eq 20).¹⁷



Diphenylarsenide ion gives mixed behavior: scrambling with some haloaromatic compounds, but the straightforward substitution product with 2-chloroquinoline or 4-chlorobenzophenone (eq 21 and 22).³²

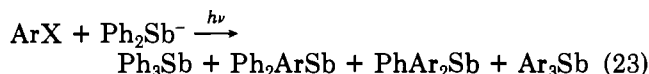


Ar = *p*-anisyl, *p*-tolyl; X = Cl, Br, I; ArX = 1-chloronaphthalene, 9-bromophenanthrene



ArX = 2-chloroquinoline, 4-chlorobenzophenone

On the other hand, diphenylstibide ion gives scrambling even with 4-chlorobenzophenone (eq 23).³³



ArX = *p*-bromoanisole, 4-chlorobenzophenone

(32) Rossi, R. A.; Alonso, R. A.; Palacios, S. M. *J. Org. Chem.* 1981, 46, 2498.

(33) Alonso, R. A.; Rossi, R. A. *J. Org. Chem.* 1982, 47, 77.

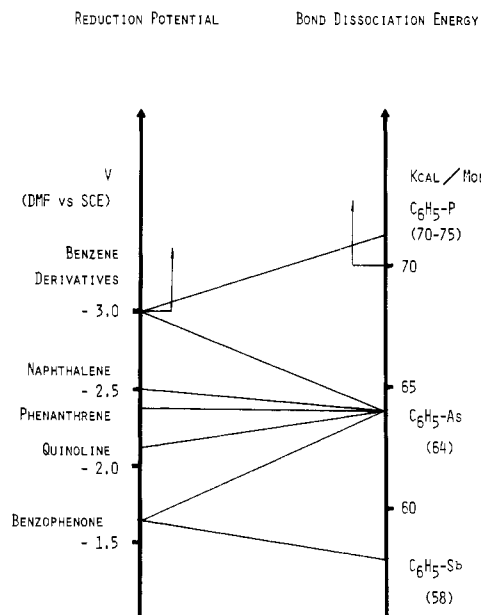


Figure 1. Reduction potential of arenes (left) and bond dissociation of Ph-M (M = P, As, Sb) (right) in relative scales.

The mixed products are thought to arise from the reversible coupling of the aryl radicals with the nucleophile and fragmentation of radical anion intermediates, as indicated in Scheme I.

The reduction potentials of aromatic compounds are related to their π^* MO energy levels: the more negative the reduction potential, the higher the π^* MO energy.³⁴ On the other hand, the bond dissociation energy (BDE) of a C-M bond decreases as we go down a group in the periodic table,³⁵ and parallels the σ^* MO energy level,³⁶ but it is probably not very much dependent on the nature of the aromatic moiety. Therefore in reactions of a particular aryl radical with PhM^- (M = S, Se, or Te) or Ph_2M^- (M = P, As, or Sb) nucleophiles, the difference in energy between the π^* and σ^* MOs decreases within group 5A or 6A as the molecular weight of the element increases, and the competition of bond fragmentation reactions becomes more important. Thus, for group 6A elements we find fragmentation of the radical anion intermediate only in the reactions of phenyltelluride ion. Among 5A elements, Ph_2P^- ion gives only the straightforward substitution product, Ph_2As^- ion gives such fragmentation with certain aryl radicals, but not with others, and Ph_2Sb^- ion evidences fragmentation of the intermediate with all the substrates studied.

In Figure 1 the relative energies involved in the reactions of Ph_2M^- (M = P, As, Sb) nucleophiles with aryl radicals are represented.³³ Figure 1 has been arranged with the Ph-P BDE higher than the reduction potential of anisole and toluene (which are known to be more negative than -3 V) because Ph_2P^- ion does not give aryl-scrambled products with iodotoluenes. The Ph-Sb BDE was placed lower than the reduction potential of benzophenone because the reaction of Ph_2Sb^- ion with 4-chlorobenzophenone gives scrambled products. In this relative scale the Ph-As BDE lies between the

(34) Streitwieser, A. "Molecular Orbital Theory for Organic Chemistry"; Wiley: New York, 1961.

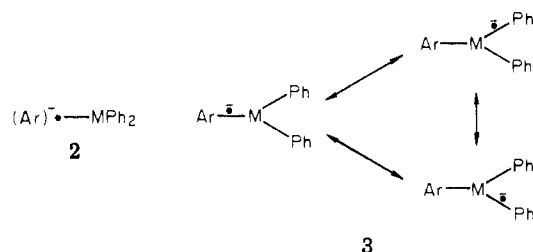
(35) Levason, W.; McAuliffe, C. A. *Acc. Chem. Res.* 1978, 11, 363.

(36) It has been suggested that as a σ bond becomes weaker, the energy level of the σ^* MO decreases. See: Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976; p 39.

reduction potential of phenanthrene (-2.4 V) and quinoline (-2.1 V).

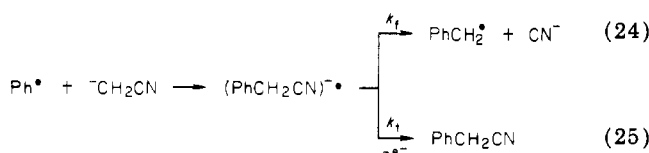
Figure 1 suggests that when an aromatic compound has a reduction potential higher (on this relative scale) than the BDE of the Ph-M bond that will be formed upon coupling of the aryl radical with the Ph_2M^- nucleophile scrambled products will be formed. Conversely, those aromatic systems that have lower reduction potentials will produce straightforward substitution products.

In terms of MO energy considerations, the results reported suggest that the predominant radical anion resulting from the coupling of an aryl radical and a nucleophile is of a π^* nature if the reduction potential of the parent aromatic compound is lower than the BDE of the Ph-M bond on the relative scale of Figure 1. In this case the transfer of the odd electron to a σ^* MO is energetically unfavorable, and consequently slow, and fragmentation of the radical anion intermediate is not observed. On the other hand, when the BDE of the Ph-M bond is lower than the reduction potential of the parent arene, the radical anion intermediate may be π^* (2) or σ^* (3), but the difference in energy between them is small and fragmentation occurs, leading to scrambling of aryl rings.



Fragmentation of the Radical Anion into Unreactive Intermediates

Cyanomethyl Anion. As mentioned before, the photostimulated reaction of bromobenzene with cyanomethyl anion gives mainly phenylacetonitrile and 1,2-diphenylethane (eq 5').⁹ These products come respectively from electron transfer and from fragmentation of the radical anion intermediate, as sketched in eq 24 and 25.



The benzyl radical formed in eq 24 dimerizes, giving the observed 1,2-diphenylethane.⁹ Similar behavior is observed when a 2-halothiophene is the substrate; i.e., the 2-thienylacetonitrile radical anion gives fragmentation and electron-transfer-derived products.³⁷

On the other hand, the radical anion intermediate formed when the substrate is a halogen derivative of pyridine, biphenyl, or naphthalene gives only products of electron-transfer reaction, with no indication of fragmentation.¹⁰

In this system, the odd electron of the radical anion intermediate formed from the coupling of an aryl radical with cyanomethyl anion can reside in the π^* MO

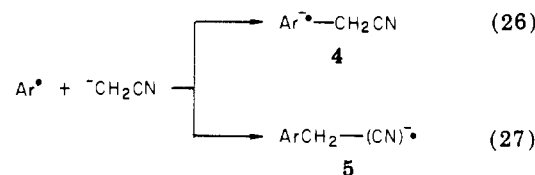
(37) Goldfarb, I. L.; Ikubov, A. P.; Belenki, L. I. *Khim. Geterotsikl. Soedin.* 1979, 1044.

Table I
Rate of Decomposition of Radical Anions Derived from 4-Nitrobenzyl Compounds³⁹

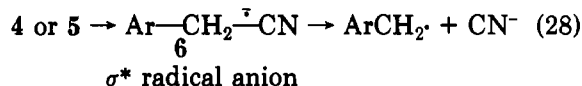
$p\text{-O}_2\text{NC}_6\text{H}_4\text{CH}_2\text{X}$, X =	$\log k$, s^{-1}	bond strength, ^a kcal/mol
Br	2	55
Cl	1-1.3	69
F	-2	90 ^b
CN	-1	
SCN	0.8-0.9	

^a Bond strength of PhCH_2X taken from "Handbook of Chemistry and Physics", 61st ed., CRC Press: Boca Raton, FL, 1981, F-243. ^b Value estimated.

of the aromatic moiety (eq 26) or in the π^* MO of the cyano moiety (eq 27).



However, intramolecular electron transfer from 4 or 5 to the σ^* MO of the C-CN bond gives radical anion 6, which leads to fragmentation (eq 28).



Intramolecular electron transfer is well known in systems having two π^* MOs,³⁸ and transfer from a π^* to a σ^* MO is known to occur.³⁹⁻⁴²

The rates of decomposition of several 4-nitrobenzyl compounds have been found roughly to parallel the C-X bond energy (Table I).³⁹ It was suggested that the odd electron in the π^* MO is gradually transferred into the σ^* MO of the C-X bond and that the σ^* radical anion then decomposes.⁴⁰ This passage of an electron from a π^* MO to a σ^* MO will certainly require more energy and occurs at slower rate the higher the difference in energy between these MOs.

Recently the rates of fragmentation of the radical anions of *o*-, *m*-, and *p*-nitrobenzyl halides⁴¹ and *o*-, *m*-, and *p*-cyanobenzyl halides,⁴² which are believed to be a measure of the rate of intramolecular electron transfer from a π^* MO to a σ^* MO, have been determined. It was found that these rates of decomposition depend not only on the halogen but also on the positions of substituents on the ring. Fragmentation rates decrease in the order $\text{I} > \text{Br} > \text{Cl}$ and *ortho* > *para* > *meta*.

The lower rates for the meta isomers are attributed to the low spin density at the meta carbon atoms. Although in the *p*- and *o*-nitrohalobenzene radical anions the highest spin density is found in the nitro group, a certain amount can be expected at the *ortho* and *para* positions, and it is channelled through the $-\text{CH}_2-$ to the halogen.⁴¹

On the basis of the results indicated above, the fast rates of decomposition of phenylacetonitrile and 2-

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(39) Mohammad, M.; Hajdu, J.; Kosower, E. M. *J. Am. Chem. Soc.* 1971, 93, 1792.

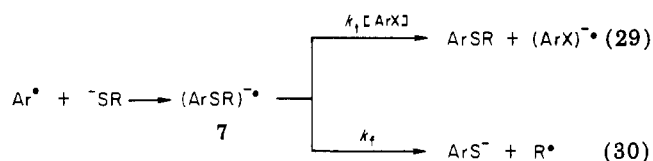
(40) Pearson, R. G. "Symmetry Rules for Chemical Reactions"; Wiley: New York, 1976; p 440.

(41) Neta, P.; Behar, D. *J. Am. Chem. Soc.* 1980, 102, 4798.

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

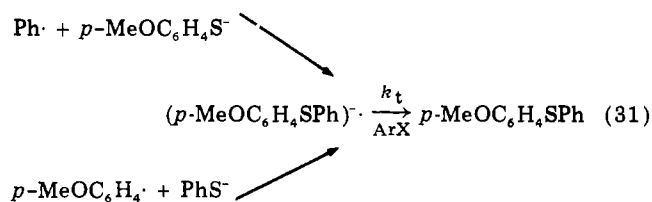
thienylacetonitrile radical anions can be attributed to an easy transfer of the odd electron from relatively high energy π^* MOs to the σ^* MO of the C-CN bond in the radical anion intermediate. When the aryl moiety has a lower energy π^* MO, as in the case of 1-naphthyl radical, the radical anion intermediate has the odd electron in this MO, and intramolecular electron transfer to the σ^* MO of the C-CN bond is slow and cannot compete with the intermolecular electron-transfer reaction, which forms the straightforward substitution product.

Alkanethiolate Ions. Photostimulated reactions of haloarenes with alkanethiolate ions yield as substitution products aryl alkyl sulfides and/or arenethiolate ions. Depending on the identities of the reactants, sometimes the product is virtually all Ar-S-R, sometimes virtually all Ar-S⁻, and sometimes a mixture of both. These results (eq 29, 30) were explained along the lines previously discussed.⁴³



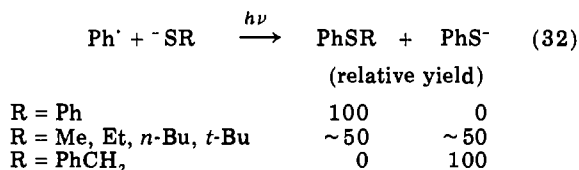
The outcome of competition between these two pathways depends on the natures of the aryl moiety Ar and the alkyl moiety R in the radical anion intermediate 7.⁴⁴

The reaction of benzenethiolate ion with an aryl iodide gives the straightforward substitution product, as was demonstrated by using the two reacting pairs shown in eq 31. If the radical anion had fragmented,



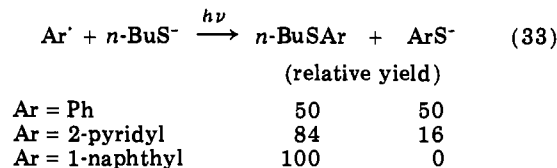
the symmetrical sulfides would have been formed; thus $k_f < k_t[\text{ArX}]$.⁴³

On the other hand, the photostimulated reactions of iodobenzene with methane,⁴⁴ ethane,⁴³ *n*-butane-1,⁴⁴ and 1,1-dimethylethanethiolate⁴⁴ ions afforded almost equal amounts of substitution and fragmentation derived products; thus $k_f \approx k_t[\text{ArX}]$. With phenylmethanethiolate ion, only the fragmentation product was found, meaning that $k_f > k_t[\text{ArX}]$ (eq 32).⁴⁴

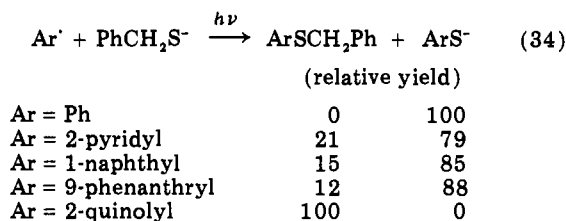


Equation 32 shows the changes observed in the product composition as the alkyl moiety of the thiolate ion is varied. However, differences in the product composition were also observed when the aryl moiety

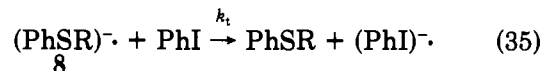
was changed. For instance, with 1-butanethiolate ion, iodobenzene gives roughly equal amounts of both reactions ($k_f \approx k_t[\text{ArX}]$)⁴⁴ but there is an increase in the electron-transfer component with 2-chloropyridine⁴⁴ and an even greater increase with 1-chloronaphthalene⁴⁵ (eq 33).



Similar behavior was found with the phenylmethanethiolate ion as the nucleophile. With phenyl radical only the fragmentation products were formed; 2-pyridyl, 1-naphthyl, and 9-phenanthryl radicals gave both types of product, and only electron-transfer-derived product was obtained with 2-chloroquinoline (eq 34).⁴⁴



It is unlikely that the differences found in the ratios of products coming from the competing reaction pathways (eq 29, 30) among the different aryl halide-thiolate ion reacting pairs are due to changes in the rate of the electron-transfer reaction shown in eq 35.



The reduction potentials of the parent compounds of radical anions 8 are -2.549 V (R = Ph),⁴⁶ -2.751 V (R = Me),⁴⁶ -2.734 V (R = Et),⁴⁶ -2.638 V (R = *t*-Bu)⁴⁶ and -2.569 V (R = benzyl).⁴⁶ These are in all cases more than 1 V more negative than the reduction potential of iodobenzene (-1.21 V).⁴⁷ Therefore reaction 35 probably occurs at encounter-controlled rate in all cases. However, there are great differences in product distribution along the series, for diphenyl sulfide radical anion gives *only* the electron-transfer reaction, benzyl phenyl sulfide radical anion gives *only* bond fragmentation-derived products, and all the others gave mixtures indicating about the same participation for both reaction pathways.

We conclude that the differences observed are due to changes in bond fragmentation rates of the radical anions 8 and not to differences in rates of electron transfer to the substrate.

The bond fragmentation rates depend on the structure of the radical anion involved, and in particular on the energies of the π^* and σ^* MOs. When bond fragmentation is important, it can be inferred that the difference between π^* and σ^* MOs is small.

(45) Rossi, R. A.; de Rossi, R. H.; López, A. F. *J. Am. Chem. Soc.* **1976**, *98*, 1252.

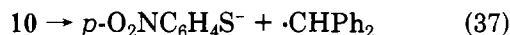
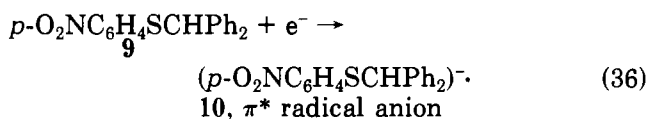
(46) The reduction potential is in DMF vs. Ag/AgCl, 0.15 M *n*-Bu₄NI as supporting electrolyte: Gerdill, R. *J. Chem. Soc. B* **1966**, 1071.

(47) The reduction potential is in DMF vs. Ag/AgBr, 0.02 M Et₄NBr as supporting electrolyte: Sease, J. W.; Bunton, F. G.; Nickol, S. L. *J. Am. Chem. Soc.* **1968**, *90*, 2595.

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(44) Rossi, R. A.; Palacios, S. M. *J. Org. Chem.* **1981**, *46*, 5300.

The electrochemical reduction of **9** in DMF leads to bond fragmentation (eq 36 and 37), with an activation



energy of 21 kcal/mol.⁴⁸ Since ESR studies indicate that in the radical anion **10** the odd electron is located in the π^* MO, the high activation energy for the decomposition probably indicates that electron transfer of the odd electron from the π^* MO of the *p*-nitrophenyl moiety to the σ^* MO of the S-CHPh₂ bond is energetically unfavorable.

The stability of the radical anion formed when phenylmethanethiolate ion reacts with aryl radicals depends on the aryl moiety. If phenyl is the radical, inasmuch as the reduction potential of benzene has the highest negative value of the series, only fragmentation is observed ($k_f > k_t[\text{ArX}]$). Then follow pyridine, naphthalene, and phenanthrene, with values between -2.7 and -2.4 V, in which both processes compete ($k_f \approx k_t[\text{ArX}]$). Finally with quinoline as substrate (-2.1 V), only the electron-transfer product is obtained ($k_f < k_t[\text{ArX}]$).

When the aromatic substrate is kept constant, as in eq 32, the competition between the two reaction pathways depends on the alkyl moiety of the thiolate ion, as expected since the bond strength of the S-R bond changes. Accordingly if R = phenyl ($D_{\text{PhS-Ph}} = 76$ kcal/mol),⁴⁹ only electron transfer is observed; if R = Me, Et, *n*-Bu or *t*-Bu ($D_{\text{PhS-R}} = 59\text{--}65$ kcal/mol),⁴⁹ both reactions are observed; and with R = PhCH₂ ($D_{\text{PhS-CH}_2\text{Ph}} = 51$ kcal/mol),⁴⁹ only bond fragmentation is observed.

These results indicate that in order for good yields of substitution products in the reaction of alkane-thiolate ions with aryl radicals to be obtained, it is required that the aryl ring have a low energy π^* MO. The energy of this orbital should be lower as the bond dissociation energy of the S-R bond decreases.

Concluding Remarks

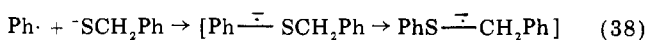
From the results presented in this Account, it is evident that in the S_{RN}1 mechanism of aromatic nucleophilic substitution, whether a straightforward substitution product is formed or not depends not only on the ability of aryl radicals to couple with the nucleophiles but also on the structure and frangibility of the radical anion intermediates.

When the aryl radical couples with a nucleophile, a radical anion intermediate is formed. A question arises

as to what is the reaction coordinate leading to this intermediate.

Qualitatively it can be visualized as follows. When the aryl radical and the nucleophile approach each other, σ and σ^* MOs start to be formed, and the gap between them increases as the reactants come closer. If the final energy level of the σ^* MO is higher than the lowest available π^* MO in the molecule, there will be a point in the reaction coordinate where both energies are equal, and by orbital crossing the electron transfers to the low energy π^* MO.⁵⁰ This simple analysis implies that under these circumstances the radical anion will be of π^* nature.

Similarly if there is a σ^* MO available that has lower energy than that of the bond being formed, the odd electron will transfer to this MO in the process of coupling. For example, in the coupling of phenyl radical with phenylmethanethiolate ion, there will be a point where the energy of the σ^* MO being formed reaches that of the σ^* MO of the PhCH₂-S bond and where the odd electron transfers to this MO (eq 38) with consequent fragmentation (eq 39).



The intermolecular electron transfer to iodobenzene does not compete with the bond fragmentation of **11**, although the electron-transfer rate is probably diffusion controlled.

Although this description is correct from an energetic point of view, we are aware that other factors might make the transfer of an electron during the coupling process between MOs of equal energy unfavorable, which leads in all cases to the σ^* radical anion in which the odd electron occupies the σ^* MO of the bond formed, with the transfer to another MO occurring in a separate step.⁵¹ Further research in this area is required to settle this point.

I wish to express my gratitude to my co-workers who carried out most of the experimental work described here. Dr. A. F. López collaborated in the studies with acetonitrile anion, Dr. A. B. Pierini discovered the scrambling reactions, and Dr. R. A. Alonso and Lic. S. M. Palacios found how to avoid them. I also like to thank my wife, Dr. Rita H. de Rossi, for her cooperation and for stimulating discussions. It is a special pleasure to acknowledge the invaluable contribution of Professor Joseph F. Bunnett, who not only introduced me into this fascinating area of chemistry but also has helped in other respects. Research in our laboratory has been supported by grants from the Consejo Nacional de Investigaciones Científicas y Técnicas and the Secretaría de Ciencia y Tecnología, Argentina.

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