1.30 (t, $J$ = 7 Hz, 3 H), 1.38 and 1.47* (s, 3 H), 3.04* and 3.69 (m, 1 H), 4.06-4.54 (m, 4 H), 5.17-5.43 (m, 2 H), 5.53-5.79 (m, 1 H); $^{13}$C NMR ppm 175.6*, 168.3* (C=O of the minor isomer were not detected), 131.4*-130.7, 120.9*-120.3, 69.5-69.3*, 62.2-62.0*, 54.0-53.8, 51.8*-47.4, 18.7*, 14.2*-14.8, 14.6. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.21; H, 7.16.

**Ethyl 4-isopropenyl-3-methyl-2-oxotetrahydrofuran-3-carboxylate (18)**: IR (neat) 1780, 1740, 1645 cm$^{-1}$; $^1$H NMR; $Z$ isomer $\delta$ 1.25 (t, $J$ = 7 Hz, 3 H), 1.61 (s, 3 H), 1.83 (s large, 3 H), 3.01 (dd, $J$ = 7.9, 11 Hz, 1 H), 4.0-4.6 (m, 4 H), 4.78 (s, 1 H), 5.00 (s, 1 H); $^{13}$C NMR ppm 14.1, 20.6, 23.1, 53.2, 61.9, 139.0, 168.4, 175.7; $E$ isomer (data from the two isomer mixture) 1.31 (t, $J$ = 7 Hz, 3 H), 1.63 (s, 3 H), 1.69 (s br, 3 H), 3.65 (t, $J$ = 7.8 Hz, 1 H), 4.0-4.6 (m, 4 H), 4.76 (s, br, 1 H), 5.03 (s br, 1 H); $^{13}$C NMR ppm 175.6, 170.7, 139.4, 114.5, 68.6, 62.3, 53.0, 50.0, 22.1, 20.06, 14.1. $Z$:$E$ = 58:42 (from $^1$H NMR). Anal. Calcd for $C_{11}H_{16}O_4$ (mixture): C, 62.24; H, 7.69. Found: C, 62.23; H, 7.67.

**Ethyl 4-(2-acetoxy-2-propenyl)-3-methyl-2-oxotetrahydrofuran-3-carboxylate (19)**: IR (neat) 1780, 1740 cm$^{-1}$; $^1$H NMR; $Z$ isomer $\delta$ 1.29 (t, $J$ = 7 Hz, 3 H), 1.54 (s, 3 H), 1.63 (s, 3 H), 1.70 (s, 3 H), 1.96 (s, 3 H), 2.55 (dd, $J$ = 8.2, 10.7 Hz, 1 H), 4.0-4.60 (m, 4 H); $^{13}$C NMR ppm 176.0, 169.4, 169.0, 80.2, 66.3, 61.8, 58.1, 51.9, 24.9, 14.0, 22.0, 21.9, 13.9; $E$ isomer (data from the two isomer mixture) 1.30 (t, $J$ = 7 Hz, 3 H), 1.51 (s, 3 H), 1.56 (s, 3 H), 2.00 (s, 3 H), 2.02 (s, 3 H), 3.29 (dd $J$ = 10.7, 8 Hz, 1 H), 4-4.6 (m, 4 H); $^{13}$C NMR ppm 175.7, 170.8, 169.4, 80.0, 66.5, 62.3, 53.6, 53.1, 24.9, 24.1, 22.3, 15.3, 14.0. $Z$:$E$ = 65:35 (from $^1$H NMR). Anal. Calcd for $C_{13}H_{20}O_6$ (mixture): C, 57.34; H, 7.40. Found: C, 57.29; H, 7.41.

**3,7-Dioxa-1-methyl-4-phenylbicyclo[3.3.0]octane-2,8-dione (20).** Oxidation of 1 g of diester 8 leads after column chromatography to 70 mg of recovered 8, 110 mg of acetate 21, and 700 mg of a mixture of 20 and 21, whose ratio determined by $^1$H NMR (based on benzylic proton signals) is 75:25, respectively. Yields were calculated from this result. Rechromatography of the mixture gave a sample of compound 20 for which only $^1$H NMR and MS data were obtained. $^1$H NMR: $\delta$ 1.45 (s, 3 H), 3.18 (td, $J$ = 6, 3 Hz, 1 H), 4.36-4.68 (AB part of a ABX multiplet, $J_{AB}$ = 10 Hz, 2 H), 5.3 (d, $J$ = 6 Hz, 1 H), 7.2-7.6 (m, 5 H). MS: $m/e$ (rel intensity 233 (7), 232 (42), 131 (11), 129 (27), 128 (20), 126 (11), 115 (22), 110 (26), 107 (30), 106 (20), 105 (60), 99 (100), 98 (34), 91 (46), 83 (13), 82 (17), 79 (15), 78 (20), 77 (62), 69 (63), 64 (10), 55 (13), 54 (19), 53 (16), 52 (10), 51 (34), 50 (4), 44 (25), 41 (35), 39 (50), 29 (19), 27 (27).

**Ethyl 4-($\alpha$-acetoxybenzyl)-3-methyl-2-oxotetrahydrofuran-3-carboxylate (21)**: IR (neat) 1774, 1740, 1717, 765, 706 cm$^{-1}$; the product is a mixture of four stereoisomers whose ratio could not be determined from the complex $^1$H NMR spectra. Major stereoisomer (data from the mixture): $^1$H NMR $\delta$ 1.00 (s, 3 H), 1.35 (t, $J$ = 7.1 Hz, 3 H), 2.03 (s, 3 H), 2.98 (q, $J$ = 9 Hz, 1 H), 4.20-4.60 (m, 4 H), 5.84 (d, $J$ = 9 Hz, 1 H), 7.27-7.41 (m, 5 H), (the spectra of the other isomers differ mainly by the chemical shift of the methyl groups and of the cyclic C$H$ whose signals appear at 3.6-4.1 ppm); $^{13}$C NMR ppm 175.3, 169.4, 168.7, 137.4, 129.2, 128.7, 127.2, 73.8, 68.5, 68.4, 52.2, 48.1, 32.4, 20.9, 19.7, 14.1. Anal. Calcd for $C_{17}H_{20}O_6$ (mixture): C, 63.75; H, 6.25. Found: C, 63.74; H, 6.19.

**Ethyl 4-(acetoxymethylene)-3-methyl-2-oxotetrahydrofuran-3-carboxylate (22)**: IR (neat) 3000, 1780, 1740, 1690 cm$^{-1}$; $^1$H NMR $\delta$ 1.27 (t, $J$ = 7 Hz, 3 H), 1.62 (s, 3 H), 2.19 (s, 3 H), 4.21 (q, $J$ = 7 Hz, 2 H), 4.92-5.01 (AB part of an ABX multiplet; $J_{AB}$ = 13 Hz, 2 H), 7.29 (t, $J$ = 2 Hz, 1 H); $^{13}$C NMR ppm 174.6, 168.5, 166.6, 130.9, 120.9, 67.1, 62.6, 51.1, 24.5, 19.9, 13.9. Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.49; H, 5.85.

**Acknowledgment.** We are especially indebted to Professor J. K. Crandall (Bloomington University) for help with the preparation of the manuscript.

# Monosubstitution versus Disubstitution in the $S_{RN}1$ Reaction of Dihalobenzenes with Sulfanions. The Role of the Monosubstitution Product and of Its Anion Radical

C. Amatore,*[†] R. Beugelmans,[‡] M. Bois-Choussy,[‡] C. Combellas,[§] and A. Thiebault*[§]

*Ecole Normale Supérieure, Laboratoire de Chimie, UA CNRS No. 1110, 24, rue Lhomond, 75231 Paris Cedex 05, France, Institut de Chimie des Substances Naturelles, CNRS, 91 190 Gif sur Yvette, France, and Laboratoire de Chimie et Electrochimie des Matériaux Moléculaires, UA CNRS No. 429, Ecole Supérieure de Physique et Chimie Industrielles, 10 rue Vauquelin, 75231 Paris Cedex 05, France*

*Received December 8, 1988*

The competition between mono- and disubstitution of dihalobenzenes by a series of aromatic sulfanions, via the $S_{RN}1$ reaction, is shown to involve two radical chains. The first one, recognized in the earliest works, involves one branching point at the level of the monosubstituted product anion radical. Reoxidation of the latter via electron transfer to the parent dihalide affords the monosubstituted product. Conversely, the route to the disubstituted product is opened when cleavage of the carbon-halogen bond in the monosubstituted product anion radical occurs before the electron transfer takes place; the disubstitution product is then obtained in its reduced (anion radical) form. Reoxidation of the latter, to afford the neutral disubstituted product, may involve competitively the parent dihalide or the neutral monosubstituted product, depending on the electron affinity of the arylthio moiety. In the first case the electron transfer propagates the first chain; in the second a new chain leading to the disubstitution is activated. The role of the two imbricated chains, under photochemical conditions, and thus that of the monosubstitution product is discussed quantitatively on the basis of the pertinent rate constants determined by cyclic voltammetry.

## Introduction

The photostimulated $S_{RN}1$ reactions of dihalobenzenes ($IC_6H_4X$, X = $o$, $m$, $p$-Br, Cl) with various nucleophiles are known to give monosubstitution or disubstitution products according to the nature of X and the nucleophile.[1,2] $m$-Chloroiodobenzene (**1,m**) is reported to afford only the monosubstitution product when treated with diethyl

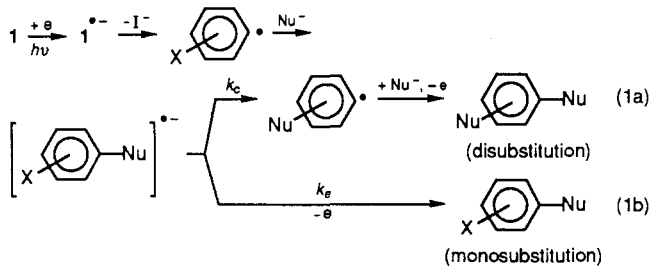
[†] Ecole Normale Supérieure.
[‡] Institut de Chimie des Substances Naturelles.
[§] Laboratoire de Chimie et Electrochimie des Matériaux Moléculaires.

(1) (a) Wolfe, J. F.; Carver, D. R. *Org. Prep. Proced. Int.* **1978**, *10*, 225. (b) Rossi, R. A.; Rossi, R. H. In *Aromatic Nucleophilic Substitution by the $S_{RN}1$ Mechanism*; American Chemical Society: Washington, DC, 1983; ACS Monograph 78.

(2) (a) Bunnett, J. F.; Creary, X. *J. Org. Chem.* **1974**, *39*, 3611; (b) 3612. (c) Bunnett, J. F.; Traber, R. P. *J. Org. Chem.* **1978**, *43*, 1867. (d) Bunnett, J. F.; Shafer, S. J. *J. Org. Chem.* **1978**, *43*, 1873; (e) 1877. (f) Bard, R. R.; Bunnett, J. F.; Traber, R. P. *J. Org. Chem.* **1979**, *44*, 4918.

0022-3263/89/1954-5688$01.50/0 

**Scheme I**

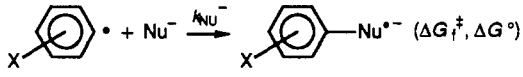



phosphite ion as the nucleophile, whereas the disubstituted product is obtained with only traces of the monosubstituted one, when thiophenoxide ion is used. This dichotomy was rationalized[3] by considering the fate of the monosubstituted product anion radical in Scheme I. When the latter is sufficiently frangible, the carbon–halogen bond is cleaved (route 1a) to afford a $\sigma$-aromatic radical that undergoes a nucleophilic attack to yield eventually the disubstitution product. Conversely when the stabilizing effect of the nucleophile moiety is larger, the monosubstituted product anion radical may live enough to be oxidized via a homogeneous electron transfer to the initial dihalide, thus affording the monosubstitution product (route 1b).[3b] In Scheme I the yield of mono- vs disubstitution is controlled by the competition occuring at the branching point in eq 1a,b. Thus at any time one obtains[4]

$$d[XPhNu]/d[NuPhNu] = (k_e/k_c)[IPhX] \qquad (2)$$

where $k_e$ and $k_c$ are the respective rate constants for the electron transfer (eq 1b) and cleavage (eq 1a) reactions.

Within such a framework the role of the nature of the halide X is easily understood. Indeed the rate constant $k_c$ should increase in the series Cl, Br, I, whereas the rate constant $k_e$ should remain close to the diffusion limit ($Nu^-$: $PhS^-$ or $(EtO)_2PO^-$). Thus a change of halogen in the series Cl, Br, I results a priori in an increase of the disubstitution. The role of the nucleophile is related to its ability to stabilize the odd electron in the monosubstituted anion radical. For example, the diethyl phosphite moiety having a larger stabilizing ability than a thiophenoxy one results in larger monosubstitution yields.[1b] Note that, within a related series of nucleophiles, stability is in principle also related to the ease of formation of the monosubstitution product anion radical by nucleophilic attack on the $\sigma$-aryl radical. Indeed for a related series of nucleophiles, i.e.,



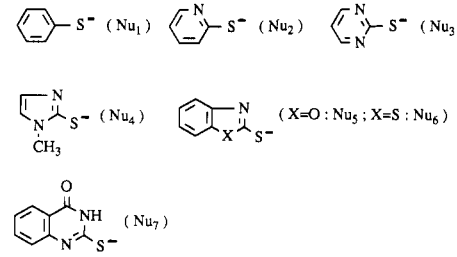

for a nearly constant energy of the carbon–nucleophile bond, the free energy of formation of the anion radical in the above reaction is obtained from thermochemical considerations as[5]

$$\Delta G^\circ = -BDE_{C\text{-}Nu} - FE^\circ_{ArNu/ArNu^{\bullet -}} + FE^\circ_{Nu^\bullet/Nu^-}$$

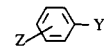
where $BDE_{C\text{-}Nu}$ is the carbon–nucleophile bond energy. Thus the less negative $E^\circ_{ArNu/ArNu^{\bullet -}}$, the easier the reaction.[6] On the other hand, based on the correlation between $\Delta G_f^{\ddagger}$ and $\Delta G^\circ$ in a related series, the smaller $\Delta G^\circ$, the smaller $\Delta G_f^{\ddagger}$ i.e., the larger the rate constant.[9]

The crudeness of such an analysis makes difficult the comparison of two different nucleophiles such as, e.g., $PhS^-$ and $(EtO)_2PO^-$, mainly because of the difficulty in estimating the value of $E^\circ_{Nu^\bullet/Nu^-}$.[8] However, within a series of related sulfanions, $RS^-$, in which the electron affinity of the R aromatic moiety can be tuned, one may expect to be able to test the above points. Indeed, it was recently reported[10] that drastic differences were observed for the

Nucleophiles:




Substrates and Products:



| Y | Cl | Cl | Cl | Cl | $Nu_1$ | $Nu_2$ | $Nu_3$ | $Nu_2$ | $Nu_2$ |
|---|---|---|---|---|---|---|---|---|---|
| Z, (o, m, p) | I | $Nu_1$ | $Nu_2$ | $Nu_3$ | $Nu_1$ | $Nu_2$ | $Nu_3$ | H | $\sigma^{\bullet or -}$ |
| N°, (o, m, p) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | $9^{\bullet or -}$ |

**Figure 1.** Nomenclature of different nucleophiles, substrates, and products considered in this study.

**Table I. Photostimulated $S_{RN}1$ Reactions of Halobenzenes with Sulfanions as Nucleophiles, in Refluxing Liquid Ammonia (−33 °C)[a]**

| substr (concn, mM) | nucleophile[b] | product (yield, %) ClPhNu | product (yield, %) NuPhNu |
|---|---|---|---|
| **1o** (50) | $Nu_1$ | **2o** (0) | **5o** (89) |
| **1m** (20) | $Nu_1$ | **2m** (0) | **5m** (91)[c] |
| **1p** (50) | $Nu_1$ | **2p** (0) | **5p** (77) |
| **1o** (50) | $Nu_2$ | **3o** (70) | **6o** (10) |
| **1m** (20) | $Nu_2$ | **3m** (83) | **6m** (12)[c] |
| **1p** (50) | $Nu_2$ | **3p** (87) | **6p** (12) |
| **1m** (20) | $Nu_3$ | **4m** (100) | **7m** (0)[c] |
| **1p** (50) | $Nu_3$ | **4p** (100) | **7p** (0) |
| **3m** (20) | $Nu_2$ | **3m** (35) | **6m** (65) |
| | | **3m** (5)[d] | **6m** (95)[d] |

[a] Reaction time 1 h except where otherwise mentioned. [b] In a threefold excess vis-à-vis the substrate. [c] From ref 10. [d] Reaction time 2 h.

(3) (a) See, e.g., ref 1b, pp 205–212. (b) Importantly the latter was assumed, and shown convincingly on the examples investigated, to be unreactive under the experimental conditions.

(4) Reference 2e, p 1879 (eq 8).

(5) (a) Amatore, C.; Oturan, M. A.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1985**, *107*, 3451. (b) Amatore, C.; Combellas, C.; Pinson, J.; Oturan, M. A.; Robveille, S.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1985**, *107*, 4846.

(6) This assumes that (a) the rate constant of the nucleophilic attack of the $\sigma$-aryl radical is activation controlled; (b) the variations of energy of the carbon–nucleophile bond are negligible[7] vis-à-vis those of $E^\circ_{ArNu/ArNu^{\bullet -}}$, when $Nu^-$ is changed within a related series; (c) same as (b) for $E^\circ_{Nu^\bullet/Nu^-}$.[8]

(7) In a related series of nucleophiles, e.g., aromatic sulfanions $RS^-$, as the one considered in this study (vide infra) condition (b) in footnote 6 is likely to be fulfilled. However condition c (footnote 6) validity is more critical to appreciate.[8]

(8) Determination of $E^\circ_{RS^\bullet/RS^-}$ is made difficult because of the fast dimerization of $RS^\bullet$ radicals formed upon oxidation of the related sulfanion. See, e.g.: Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1982**, *104*, 817.

(9) (a) Andrieux, C. P.; Savéant, J. M.; Zann, D. *Nouv. J. Chim.* **1984**, *8*, 107. (b) Savéant, J. M. *Proceedings of the R. A. Welch Foundation Conferences on Chemical Research, XXX.* Advances in Electrochemistry, Houston, TX, 1986, pp 289–336. (c) See also: ref 5. (d) Andrieux, C. P.; Savéant, J. M.; *Investigations of Rates and Mechanisms of Reactions*; Bernasconi, C. F., Ed.; Vol. 6, 4/E, Part 2, Wiley: New York, 1986; Chapter VII, pp 305–390.

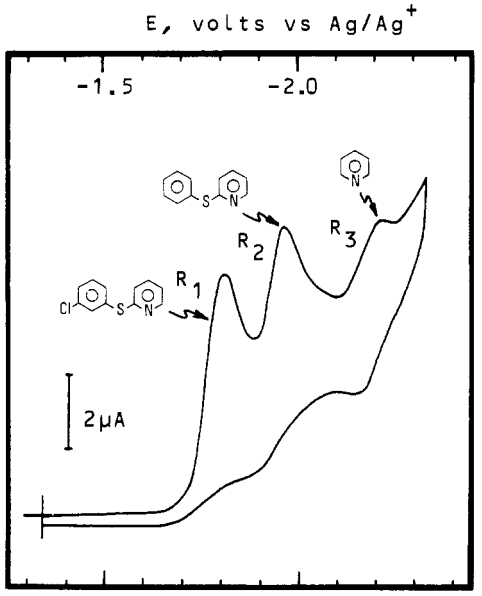



**Figure 2.** Cyclic voltammetry of 2-[(3-chlorophenyl)thio]pyridine (**3m**) in liquid ammonia at −38 °C, $v$ = 0.2 V $s^{-1}$. Gold disk (diameter = 0.5 mm) electrode. Potentials refer to $Ag/Ag^+$ 0.01 M.

photostimulated reaction of chloroiodoaromatics with a series of sulfanions (see Figure 1 and Table I). Thus $Nu_3$ reacted like diethyl phosphite to afford quantitatively the monosubstituted product, whereas a mixture (83/12) of mono- and disubstituted products was obtained with $Nu_2$ and, as reported previously, $Nu_1$ quantitatively gave the disubstitution product. These results appear to be controlled only by the nature of the nucleophile and to be nearly independent of the positions (o, m, p) of the second leaving group (see Table I).

## Results

**I. Reactivity of Sulfanions in $S_{RN}1$ Reactions.** The results of photochemical $S_{RN}1$ reactions involving chloroiodobenzenes with different sulfanions are presented in Table I. In agreement with normal expectations the various sulfanions considered behave as powerful nucleophiles under these conditions. Yet it is noticeable that although thiophenoxide ion leads to disubstitution, the 2-mercaptopyridine and pyrimidine anions give mainly monosubstitution.

In order to investigate the origin of the difference in reactivity of $RS^-$ anions as a function of R, we decided to compare their reactivity vis-à-vis a common σ-aromatic radical, 4-quinolyl. The corresponding data, presented in Table II, were obtained via competitive experiments with diethyl phosphite ion, monitored by rapid scan cyclic voltammetry according to a method previously reported.[11] It is seen from the data in Table II that all the sulfanions investigated react with the 4-quinolyl radical with rate constants close to the diffusion limit ($3 \times 10^{10}$ $M^{-1}$ $s^{-1}$ in liquid $NH_3$ at −40 °C) without really noticeable differences. Such results suggest that the differences in Table I do not arise from differences in the intrinsic reactivity of the sulfanions vis-à-vis σ-aryl radicals.[12] Therefore, in the following we will focus on one homogeneous series of nucleophiles, viz., $Nu_1$, $Nu_2$, and $Nu_3$.

**Table II. Absolute Rate Constants of the Reaction of 4-Quinolyl Radical with Different Sulfanion Nucleophiles As Determined by Electrochemistry in Liquid Ammonia at −38 °C[a]**

| $RS^-$ | $k_{RS^-}/k_{(OEt)_2PO^-}$ | $k_{RS^-}$, $M^{-1}$ $s^{-1}$ | $\Delta E°$, V[b] |
|---|---|---|---|
| $Nu_1$ | 2 | $3.2 \times 10^9$ | 0.26 |
| $Nu_2$ | 2 | $3.2 \times 10^9$ | 0.34 |
| $Nu_3$ | 1.25 | $2 \times 10^9$ | 0.31 |
| $Nu_4$ | 3.2 | $5 \times 10^9$ | 0.25 |
| $Nu_5$ | | $3 \times 10^8$ | $0.45_5$ |
| $Nu_6$ | | $1.2 \times 10^9$ | 0.46 |
| $Nu_7$ | 0.85 | $1.5 \times 10^9$ | 0.24 |

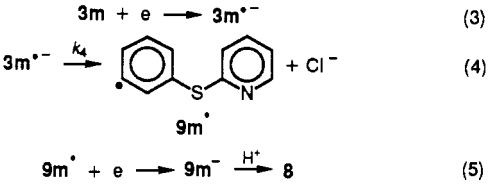
[a] Based upon competition experiments with diethyl phosphite ion, with $k_{(OEt_2)PO^-} = 1.6 \times 10^9$ $M^{-1}$ $s^{-1}$. [b] $\Delta E° = E°_{ArSR} - E°_{ArH}$.

**Table III. Thermodynamic[a] and Kinetic Parameters of the Reduction of Some Substituted Chlorobenzenes, in Liquid Ammonia at −38 °C**

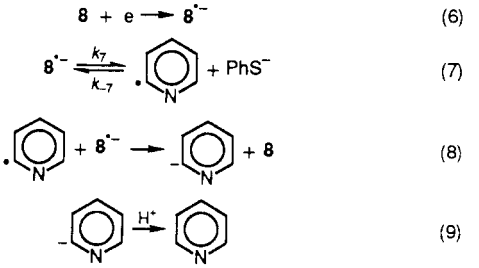
| ClPhSR | $E_p^{R1}$,[c] V | $E°_{ClPhSR}$ | $k$,[b] $s^{-1}$ | $E°_{RSPhSR}$ | $E°_{PhSR}$ |
|---|---|---|---|---|---|
| **2m** | $-1.90$[d] | | $3 \times 10^8 < k < 3 \times 10^9$ | −2.08 | −2.20 |
| **3o** | −1.80 | −1.92 | $7.5 \times 10^6$ | −1.83 | −1.97 |
| **3m** | $-1.80_5$ | −1.91 | $1.5 \times 10^6$ | −1.88 | −1.97 |
| **3p** | −1.83 | −1.93 | $7.5 \times 10^6$ | −1.93 | −1.97 |
| **4m** | $-1.63_5$ | *e* | $<10^2$ | *e* | −1.66[e] |

[a] Potentials in volts vs $Ag/Ag^+$ 0.01 M, in liquid $NH_3$. [b] Rate constant of the anion radical cleavage: $ArCl^{\bullet -} \rightarrow Ar^\bullet + Cl^-$. [c] Peak potential at 0.2 V $s^{-1}$ or [d] at 0.115 V $s^{-1}$. [e] Not determined.

**II. Stabilities of Chlorophenyl Aryl Thioether Anion Radicals As Investigated by Cyclic Voltammetry.** Figure 2 presents the cyclic voltammetry of **3m**. Three reduction waves, $R_1$, $R_2$, and $R_3$, are observed. The two latter waves correspond respectively to the reductions of 2-(phenylthio)pyridine (**8**) and pyridine as indicated by comparison with authentic samples. Thus, the two-electron wave $R_1$ involves a chloride loss from the initial anion radical to afford the σ-aromatic radical, **9m**•, which is




further reduced to $\mathbf{9m}^-$ to afford **8** via protonation from the medium. The latter is then reduced via a two-electron process at wave $R_2$ to afford the thiophenoxide ion and a pyridine molecule through the sequence in eq 6–9.[13] The




pyridine is then further reduced at wave $R_3$.[5a] At shorter times, i.e., at faster scan rates, wave $R_2$ gradually becomes reversible, its peak height decaying from a two- to a one-electron consumption, which indicates that the carbon–

(10) Beugelmans, R.; Bois-Choussy, M. *Tetrahedron* **1986**, *42*, 1381.
(11) See ref. 5. Compare also: Galli, C.; Bunnett, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 7140.
(12) (a) However, see footnote 6a. The variations in $\Delta G_t^\ddagger$ may exist, although not apparent because of the diffusion control of the reaction. (b): For a discussion of this problem in the case of electron-transfer reactions, see: Schlesener, C. J.; Amatore, C.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 3567.
(13) Compare: (a) ref 1b, pp 212–218. (b) Bunnett, J. F.; Creary, X. *J. Org. Chem.* **1975**, *40*, 3740. (c) Reference 5b.

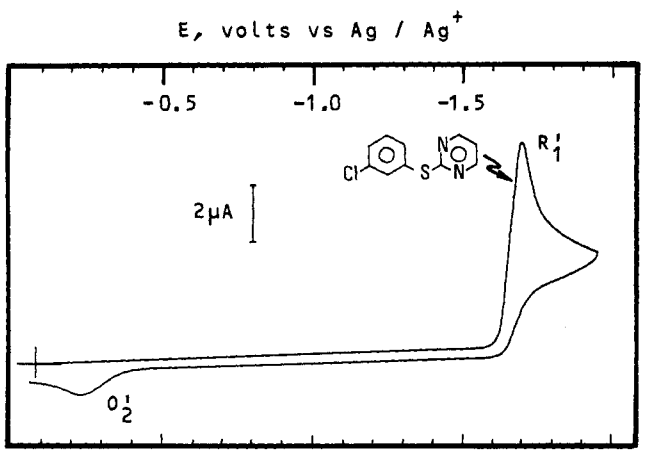
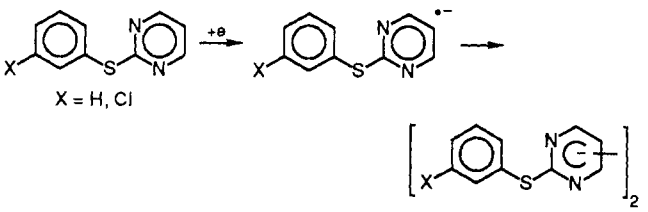



**Figure 3.** Cyclic voltammetry of 2-[(3-chlorophenyl)thio]pyrimidine (**4m**) in liquid ammonia at −38 °C, $v$ = 0.2 V $s^{-1}$. Gold disk (diameter = 0.5 mm) electrode. Potentials refer to $Ag/Ag^+$ 0.01 M.

sulfur bond cleavage in eq 7 is prevented. The rate constant $k_7$ = 25 $s^{-1}$ is determined from these variations.[9d] Since the rate constant $k_{-7}$ = $10^8$ $M^{-1}$ $s^{-1}$ of the reverse reaction has been determined previously,[5a] this allows the equilibrium constant $K_7$ = 2.5 × $10^{-7}$ M to be evaluated.

Similar results are obtained for the ortho and para chloro analogues of **3**, the only change being the exact location of the corresponding reduction wave $R_1$ (see Table III).

In strong contrast the pyrimidine derivative **4** gives rise to a one-electron irreversible reduction wave $R'_1$, in Figure 3. This wave is associated with an anodic wave, $O'_2$, observed during the reverse scan.[14a] Such a behavior indicates that the carbon–halogen bond cleavage does not occur at the level of the anion radical, but that the latter merely undergoes a dimerization. A similar behavior is




observed for the dechlorinated analogue, the rate constant of dimerization being estimated to be ca. $10^5$ $M^{-1}$ $s^{-1}$ from the variations of the reversibility of the reduction wave as a function of the scan rate.[9d] This allows one to estimate an upper limit of $10^2$ $s^{-1}$ for the loss of chloride ion in the anion radical, since the latter is necessarily smaller than the effective dimerization rate.[14b]

**III. Rate Constants of Chloride Loss from [(Chlorophenyl)thio]aryl Anion Radicals by Redox Catalysis.** The rate constant of chloride loss of the anion radicals of the pyridine derivatives **3** in eq 10 is too large to be determined by direct cyclic voltammetry. However redox

$$\mathbf{3}^{\bullet-} \xrightarrow{k_{10}} \mathbf{9}^{\bullet} + Cl^- \qquad (10)$$

catalysis, a well-documented process,[9,15,16] allows one to extend the domain of measurable rate constants well below $10^4$ $s^{-1}$.

In the absence of added aromatic halide the mediator (2,2′-bipyridine, bipy) wave exhibits a perfect reversible behavior featuring the Nernstian electron transfer in eq 11. Upon addition of increasing amounts of the organic

$$bipy + e \rightleftharpoons bipy^{\bullet-} \quad (E^\circ_{bipy} = -1.625 \text{ V vs } Ag/Ag^+) \qquad (11)$$

halide the reduction peak of 2,2′-bipyridine is enhanced and is accompanied by a concomittant decay of the associated reoxidation peak. This is due to the uphill electron transfer in eq 12, which is continuously displaced by the

$$bipy^{\bullet-} + \mathbf{3} \underset{k_{-12}}{\overset{k_{12}}{\rightleftharpoons}} bipy + \mathbf{3}^{\bullet-} \qquad (12)$$

chloride expulsion in eq 10.[16] For the different halides investigated here the electron transfer in eq 12 acts as a rapid preequilibrium since no concentration dependence with the mediator concentration (at a given excess of halide) is observed.[16] This enables one to evaluate the value of the rate constant ratio, $k_{10}(k_{12}/k_{-12})$, from the variations of the mediator current peak as a function of the scan rate and of the excess of halide. On the other hand, as previously established,[17] the following equation holds between the peak potential $E_p^{ArX}$, of the aromatic halide and the scan rate $v$. Incorporation of $(k_{10}k_{12}/k_{-12})$ as determined from redox catalysis experiments into eq 13 allows $k_{10}$ to be determined from the value of the peak

$$\ln k_{10} = (2F/RT)(E^\circ_{bipy} - E_p^{ArX}) + 2 \ln (k_{10}k_{12}/k_{-12}) - 1.56 \ln (Fv/RT) \qquad (13)$$

potential of the ArX wave at a given scan rate. Thus $k_{10}$ = 7.5 × $10^6$, 1.5 × $10^6$, and 7.5 × $10^6$ $s^{-1}$ are obtained respectively for the ortho, meta, and para pyridine chloro derivatives **3**. According to normal expectations the rate constants for the ortho and para derivatives are identical within the accuracy of their measurements whereas that of the meta chloride is ca. five times smaller. Yet the difference is considerably smaller than that observed (m/o = $10^{-2}$) for chlorobenzonitrile anion radicals[5a] under the same conditions.

Note that a similar procedure applied to the substrates **2**, with 2,3′-bipyridyl (bipy′) as the redox mediator, led to the conclusion that the overall process is governed by the rate of the electron exchange in the forward reaction 12b.

$$bipy'^{\bullet-} + \mathbf{2} \underset{k_{-12b}}{\overset{k_{12b}}{\rightleftharpoons}} bipy' + \mathbf{2}^{\bullet-} \qquad (12b)$$

This indicates that the chloride ion loss from $\mathbf{2}^{\bullet-}$ anion radicals (rate constant $k_{10b}$) is faster than the backward electron transfer in eq 12b. Thus $k_{10b} > k_{-12b}$(bipy′). By considering that the downhill electron transfer in eq 12b is diffusion limited, $k_{-12b} \sim 3 \times 10^{10}$ $M^{-1}$ $s^{-1}$,[18] one obtains

(14) (a) Note that the relative magnitude of waves $R'_1$ and $O'_2$ in Figure 2 does not represent directly the electron consumption at each wave, owing to the large peak potential separation. Thus an important fraction of the dimer (wave $O'_2$) is not oxidized because of its diffusion toward the bulk solution.[9d] (b) A first-order equivalent rate for dimerization can be estimated as $k^{ap} \simeq k_{dim.} C^\circ \simeq 10^5 \times 10^{-3} = 10^2$ $s^{-1}$, where $k_{dim.}$ is the rate constant of the dimerization and $C^\circ$ the concentration. Thus the nonobservation of any cleavage of the carbon–halide bond implies that $k_{cleavage} < k^{ap}$. For a more detailed analysis of such a competition, see: Amatore, C.; Savéant, J. M. *J. Electroanal. Chem.* **1981**, *125*, 23.

(15) For application of redox catalysis to $S_{RN}1$ mechanisms and rate constant determination, see: (a) Amatore, C.; Oturan, M. A.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1984**, *106*, 6318. (b) References 5a and 5b. For the scope and limitation of the method, see: (c) ref 9d, p 378. For application to $S_{RN}1$ reactions with preparative scopes, see: (d) Swartz, J. E.; Stenzel, T. T. *J. Am. Chem. Soc.* **1984**, *106*, 2520. (e) Alam, N.; Amatore, C.; Combellas, C.; Pinson, J.; Savéant, J. M.; Thiébault, A.; Verpeaux, J.-N. *J. Org. Chem.* **1988**, *53*, 1496. (f) Alam, N.; Amatore, C.; Combellas, C.; Thiébault, A.; Verpeaux, J.-N. *Tetrahedron Lett.* **1987**, *28*, 6171.

(16) (a) Reference 15c. (b) Andrieux, C. P.; Blocman, C.; Dumas-Bouchiat, J. M.; Savéant, J. M., *J. Am. Chem. Soc.* **1979**, *101*, 3431. (c) Andrieux, C. P.; Blocman, C.; Dumas-Bouchiat, J. M.; M'Halla, F.; Savéant, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 3806. (d) Andrieux, C. P.; Blocman, C.; Dumas-Bouchiat, J. M.; M'Halla, F.; Savéant, J. M. *J. Electroanal. Chem.* **1980**, *113*, 19.

(17) Reference 5a, p 3455, footnote 16.

Table IV. Variations of the Yields in Mono- and Disubstituted Product as a Function of the Concentration, $C°$, of the Chloroiodobenzene[a]

| ArX | $C°$, mM | product yield, % monosubs | product yield, % disubs | $\kappa_0^{exp}$ [b] | $\kappa_0^{exp}/C°$, [c] $M^{-1}$ | $k_{14}/k_{15}$, [d] $M^{-1}$ |
|---|---|---|---|---|---|---|
| 1o | 50 | 70 | 18 | 13 | 260 | $4 \times 10^3$ |
| | 5 | 43 | 46 | 2.3 | 460 | |
| 1m | 50 | 90 | 3 | 300 | $6\ 10^3$ | $2 \times 10^4$ |
| | 20 | 83 | 12 | 25 | $1.25\ 10^3$ | |
| | 5 | 0 | 100 | <0.02 | <4 | |
| 1p | 50 | 70 | 10 | 27 | 540 | $4 \times 10^3$ |
| | 20 | 35 | 65 | 1.2 | 60 | |

[a] Conditions identical with those in Table I, reaction time 1 h, nucleophile $Nu_2$ in a threefold excess. [b] From eq 16. [c] According to the competition in eq 14 and 15, $\kappa_0^{exp}/C°$ should be invariant and equal to $k_{14}/k_{15}$, as given in the last column. [d] From electrochemical determinations (Table III).

$k_{10b} > (3 \times 10^{10}) \times (5 \times 10^{-3}) = 1.5 \times 10^8\ M^{-1}\ s^{-1}$, since the bipyridyl concentration was in the range of $5 \times 10^{-3}$ M. An estimate for $k_{10b}$ may also be obtained from CV peak potential values. Rearrangement of eq 13 yields

$$\ln k_{10b} = (2F/RT)(E_p^{ArX} - E°_{bipy'}) - 2 \ln (k_{12b}/k_{-12b}) + 1.56 + \ln (Fv/RT) \quad (13b)$$

Using $-1.905\ V < E_p^{ArX} < -1.900$ V, at 0.2 V $s^{-1}$, $E°_{bipy'} = -1.675$ V, and $k_{12b} = 90 \pm 10\ M^{-1}\ s^{-1}$, as determined by cyclic voltammetry, one obtains $k_{10b} = (5 \pm 2) \times 10^8\ M^{-1}\ s^{-1}$ for the rate constant of the chloride loss from $\mathbf{2m}^{\bullet -}$, a result in agreement with the above estimation.

## Discussion

I. **Monosubstitution vs Disubstitution as a Function of the Nucleophile Sulfanion.** The reactivities of the different sulfanion nucleophiles considered in this study are comparable, as evidenced by the rate constants in Table II. This is particularly true for the limited series of $RS^-$ where R = phenyl, 2-pyridyl, and 2-pyrimidyl (rows 1–3 in Table II). Nevertheless their $S_{RN}1$ reactions with, e.g., *m*-chloroiodobenzene are quite different as evidenced by Table I.

Following the original proposal by Bunnett and coworkers,[2] we thus ascribed this dramatic change of reactivity to the fate of the monosubstituted anion radical $RSPhCl^{\bullet -}$. Indeed, the dichotomy in eq 14 and 15 is

$$RSPhCl^{\bullet -} \xrightarrow{k_{14}[IPhCl]} RSPhCl \quad (14)$$

$$RSPhCl^{\bullet -} \xrightarrow{k_{15}} Cl^- + RSPh^{\bullet} \quad (15)$$

controlled by the parameter $\kappa_0 = (k_{14}/k_{15})[IPhCl]_0$ (compare eq 16). On the other hand, the electron transfer in eq 14 is exergonic by at least 0.6 V, which indicates that the rate constant $k_{14}$ is close to the diffusion limit. Thus for a concentration of ca. 0.02 M used in the photochemical experiments in Table I, the parameter $\kappa_0$ is evaluated, at time zero, as $(0.86 < \kappa_0 < 2)$, $4 \times 10^2$, and $(>6 \times 10^6)$ respectively for the sulfanions $RS^-$ when R = phenyl, 2-pyridyl, and 2-pyrimidyl. The theoretical yields (in percent) of monosubstituted products are then evaluated from eq 16 to be respectively $(28\% < y_{mono} < 45\%)$, 98.5%, and 100%.

$$y_{mono} = 100 - 100[\ln (1 + \kappa_0)]/\kappa_0 \quad (16)$$

With the exception of the pyrimidyl sulfanion, these yields are larger than those observed experimentally (rows 2, 5, and 7 in Table I). From the experimental yields in Table I eq 16 would predict that $\kappa_0^{exp} < 0.02$ and $23 < \kappa_0^{exp} < 27$ for the thiophenoxide and 2-thiopyridyl sulfanions, respectively, when considering a 1% uncertainty in the yield determination. Although some error may be introduced when comparing these values to the determined above ones [the temperature of the photochemical substitution ($NH_3$ reflux, i.e., ca. −33 °C) is above that (−38 °C) used for the electrochemical experiments], the two sets of data seem to be difficult to reconcile. Indeed, an increase of temperature should not affect drastically the diffusion rate limit constant $k_{14}$, vis-a-vis its effect on the carbon–halogen cleavage rate constant $k_{15}$. Thus one should admit that $k_{15}$ increases by a factor comprised between 45 and 100 for the thiophenoxide anion and ca. 15 for the 2-thiopyridyl anion when the temperature is increased from −38 °C (electrochemical determination) to ca. −33 °C (photochemical preparative experiments). Such variations are clearly too high.

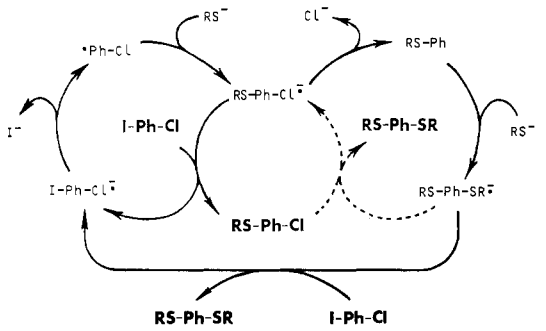
A second factor that militates against the simple dichotomy in eq 14 and 15 is the variation of the yields of mono- or disubstitution product as a function of the concentration, $C°$, of the starting dihalide, in Table IV. Indeed for each run $\kappa_0^{exp}$ may be determined from eq 16 and therefore $\kappa_0^{exp}/C°$. If the mono- vs disubstitution product distribution were only governed by the competition in eq 14 and 15, this ratio would be constant for a given dihalide/sulfanion couple, $\kappa_0^{exp}/C° = k_{14}/k_{15}$ being an intrinsic constant for each system (compare last column in Table IV).

Inspection of Table IV shows that, with the exception of the second run, $\kappa_0^{exp}/C°$ decreases when $C°$ decreases, indicating that the yield in monosubstituted product decays faster than predicted by eq 16 when $C°$ decreases. Interestingly, for *m*-chloroiodobenzene the experimental values of $\kappa_0^{exp}/C°$ (rows 3–5) are always smaller than that $(2 \times 10^4\ M^{-1})$ obtained on the basis of the electrochemical determination of $k_{14}$ and $k_{15}$.

Such results indicate that considering only one branching point in eq 14 and 15 is not sufficient to explain the results in Tables I or IV. A tentative explanation could be that a second chain is photoinitiated, which converts the monosubstituted product formed in eq 14 while the initial dihalide reacts. The monosubstitution product from the reaction of *m*-chloroiodobenzene with 2-thiopyridine anion was reacted under conditions identical with those in Table I to investigate such a possibility. From the results reported in Table I (two last rows), it is seen that although such a chain may be triggered photochemically, its kinetics are too slow to account for the deviations in Table IV. Moreover, the kinetics of such a chain should be invariant or decrease with the concentrations of the starting halide and sulfanion nucleophile. Thus the interference of the second possible chain is expected to be less when $C°$ and $[RS^-]$ are decreased, in contradiction with the experimental observations in Table IV.

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

**Scheme II**




However, in the presence of the starting dihalide the above second chain may be stimulated via the electron transfer in eq 17, as featured in Scheme II. Indeed the

$$\text{RSPhSR}^{\bullet-} + \text{RSPhCl} \xrightarrow{k_{17}} \text{RSPhSR} + \text{RSPhCl}^{\bullet-} \quad (17)$$

$\sigma$-phenyl radical thus formed via eq 15 undergoes a nucleophilic attack in eq 18 to afford the disubstituted phenyl anion radical $\text{RSPhSR}^{\bullet-}$. The latter may be reoxidized

$$\text{RSPh}^{\bullet} + \text{RS}^{-} \rightarrow \text{RSPhSR}^{\bullet-} \quad (18)$$

via electron transfer to the starting dihalide in eq 19 or to the product of monosubstitution in eq 17.[20] The competition in eq 17 and 19, i.e., the probability that the

$$\text{RSPhSR}^{\bullet-} + \text{IPhCl} \xrightarrow{k_{19}} \text{RSPhSR} + \text{IPhCl}^{\bullet-} \quad (19)$$

second chain be initiated, depends on the relative concentrations of monosubstituted product and starting dihalide, as well as on the relative magnitude of the corresponding rate constants $k_{17}$ and $k_{19}$. When the disubstituted product is easily reducible vis-a-vis the two halides, as, e.g., in the case of the pyrimidyl sulfanion, one has $k_{19} \gg k_{17}$. Thus, with an exception for the latest percents of conversion of the dihalide, reaction 19 always overcomes reaction 17, and the second chain is never triggered. However when the electroaffinity of the R group of the nucleophile decreases, the anion radical $\text{RSPhSR}^{\bullet-}$ may become sufficiently reductant so that both $k_{17}$ and $k_{19}$ are close to the diffusion limit. Then the competition between eq 17 and 19 depends only on the relative concentrations of the substrate and monosubstitution product and is thus more and more in favor of eq 17 as the overall reaction proceeds. In a general case, when taking into account the two branching points (i.e., reactions 14 vs 15 and reactions 17 vs 19), the relative rates of production of the mono- and disubstituted products are obtained in eq 20. This

$$\frac{d(\text{RSPhCl})}{d(\text{RSPhSR})} = \frac{k_{14}}{k_{15}}(\text{IPhCl}) - \frac{1}{1 + (k_{19}/k_{17})[\text{IPhCl}]/[\text{RSPhCl}]} \quad (20)$$

equation involves two terms that pertain to each branching point (compare eq 2). Of interest is that the first term, which corresponds to eq 16, is concentration dependent, whereas the second term, which originates from the competition between eq 17 and 19, is concentration independent. Thus when the concentration of the starting dihalide is decreased, the role of the first term in eq 20, on the control of mono- vs disubstitution, tends to be lowered vis-a-vis that of the second term. In other words, at large concentrations, the ratio of mono- vs disubstitution product tends to be controlled by the competition between eq 14 and 15; conversely this ratio is more and more influenced by the building up of the second chain (Scheme II) at lower concentrations of the starting dihalide. Obviously when RSPhSR is easily reduced, the large magnitude of the ratio $k_{19}/k_{17}$ makes the second term always negligible. Thus this effect can be observed only for rather difficultly reducible RSPhSR products.

From Table III, which compares the reduction potentials of the monosubstitution, ClPhSR, and disubstitution product, RSPhSR (columns 2 and 5), it is seen that when R = 2-pyridyl, the two $E^{\circ}$ are relatively close (identical or within 30 mV) for the meta and para derivatives, which is in favor of a rather large rate constant $k_{17}$, although smaller than the diffusion limit.[19] Interestingly, for the ortho derivative, which gives a different behavior (rows 1–2 in Table IV), the disubstitution product is reduced ca. 100 mV before the monosubstitution product, which leads to the conclusion that $k_{17}$ is considerably smaller than that for the meta and para derivatives. Thus it appears reasonable that a different concentration effect is observed for the ortho derivative.

For the thiophenoxide derivatives, $E^{\circ}_{\text{RSPhSR}}$ is more negative than the peak potential of the product of monosubstitution by ca. 180 mV. Thus in this series $k_{17}$ is expected to be rather close to the diffusion limit, and therefore $k_{17}/k_{19}$ is close to unity. On the other hand for this series $k_{14}/k_{15}$ is estimated to be comprised between 10 and 100, i.e., smaller than that for the other series corresponding to R = 2-pyridyl or 2-pyrimidyl. Thus for the phenyl series the second term in eq 20 (reactions 17 vs 19) is expected to have a larger role than that for the other two series. This is in favor of an increased participation of the second chain when R = phenyl, in agreement with our experimental observations. Indeed no monosubstitution is observed for the ortho derivative with $PhS^-$ as a nucleophile (Table I), although a 9% to 45% yield should be obtained on the basis of the electrochemical determination of $k_{14}/k_{15}$ and eq 16.

Thus the effects predicted on the basis of eq 20 are in rather good agreement with our experimental observations: (i) $\kappa_0^{\text{exp}}/C^{\circ}$ smaller than its value, $k_{14}/k_{15}$, determined by electrochemistry; (ii) $\kappa_0^{\text{exp}}/C^{\circ}$ decaying with increasing $C^{\circ}$; (iii) deviation from the predictions based on eq 16, being the larger, the lower the electron affinity of the R group of the sulfanion $RS^-$. However, a precise determination of the interference between the two chains in Scheme II during the conversion of the starting halides appears extremely difficult in a general case.[21]

**II. Role of the Electron Affinity of the R Group of the Nucleophile Sulfanion $RS^-$.** As discussed above the electron affinity of the R group of the nucleophile $RS^-$ plays a considerable role on the competition between mono- or disubstitution of the parent dihalide. A second factor associated with this electron affinity concerns the

(19) For most outer-sphere electron transfer involving molecules with sizes comparable to those investigated in this study, diffusion control of the reaction is expected as soon as $|\Delta E^{\circ}| \geq 150$–300 mV. See, e.g.: (a) Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1981**, *103*, 6930. (b) Kojima, H.; Bard, A. J. *J. Am. Chem. Soc.* **1975**, *97*, 6317. See also: ref 12b.

(20) This is a situation similar to that observed in entrainment experiments in $S_{RN}1$ reactions (compare e.g.: (a) Scamehorn, R. C.; Bunnett, J. F. *J. Org. Chem.* **1977**, *42*, 1449. (b) Swartz, J. E.; Bunnett, J. F. *J. Org. Chem.* **1979**, *44*, 340) or in preparative electrolysis via redox catalysis (ref 15d–f).

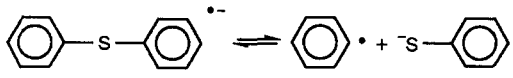
(21) Integration of the rate law in eq 20 needs the knowledge of the relationship between [IPhCl] and [RSPhSR] or [RSPhCl] concentrations at each time. This relationship can be obtained only under a differential formulation. Thus the overall calculation, although feasible in principle via numerical procedures, is critically dependent on the overall propagation of the two chains, i.e., on the exact experimental conditions (compare ref 19a for a single chain).

stability of the monosubstituted anion radical $ClPhSR^{\bullet-}$, vis-à-vis the chloride loss in eq 21. Indeed, from Table

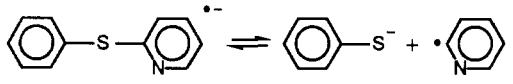
$$ClPhSR^{\bullet-} \rightarrow Cl^- + RSPh^{\bullet}, \text{ etc.} \quad (21)$$

III it is seen that the corresponding rate constant increases by a factor larger than $3 \times 10^6$ when R is varied from 2-pyrimidyl to phenyl. This variation is to be paralleled with that of the standard reduction potential of PhSR in Table III. Indeed as observed and rationalized previously,[9a,b] the more negative $E°_{PhSR}$, i.e., the higher the energy of the $\pi^*$ orbital, the larger the rate constant for the halide loss. Moreover, the variations observed in this study for the rate constant in eq 21 with $E°_{PhSR}$ are comparable to that expected from the previously reported correlation in ref 9a.

The role of the electron affinity of the R group of the $RS^-$ sulfanion is also evidenced by considering the relative stabilities of the $PhSR^{\bullet-}$ anion radical. Indeed when R = phenyl, the anion radical undergoes a rapid but reversible cleavage in eq 22, with a forward rate constant of $10^4$ $s^{-1}$


(22)

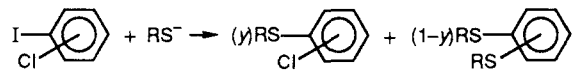
and an equilibrium constant of ca. $3 \times 10^{-5}$ M. When R = 2-pyridyl, a similar trend is observed, yet in agreement with the larger electron affinity of the pyridyl group, the forward rate constant in eq 23 is only 25 $s^{-1}$ and the


(23)

equilibrium constant, ca. $2.5 \times 10^{-7}$ M. However, when R is 2-pyrimidyl, the anion radical undergoes no cleavage reaction, but rather dimerizes with a rate constant of $10^5$ $M^{-1}$ $s^{-1}$. Interestingly, the variation of the cleavage rate constant in eq 22 and 23, as a function of the standard reduction potential $E°_{PhSR}$ of the diaryl thioether (Table III) roughly parallels those observed for the variations of the rate constant for the chloride loss in eq 21.

## Summary and Conclusion

The $S_{RN}1$ reaction of chloroiodobenzenes with various aryl sulfanion nucleophiles was shown to lead to mono- or disubstitution product as a function of the nucleophile. The general trend observed for the mono- vs disubstitution agrees roughly with the predictions based on former studies: the larger the electron affinity of the R moiety of the nucleophile $RS^-$, the larger the yield of the monosubstituted product. In previous works, this yield, $y$ in eq 24, was suggested to be essentially controlled by the com-


(24)

petition in eq 14 and 15 between the reoxidation of the monosubstitution product anion radical and the cleavage of the carbon–chloride bond in the same intermediate. Thus the larger the electron affinity of the R group, the lesser the rate of the chloride loss and the larger the yield of monosubstitution.

Although in rough agreement with our data the above simple consideration is not sufficient to rationalize our results quantitatively. Indeed the electrochemical determination, via redox catalysis, of the pertinent rate constants shows that the experimental yields of monosubstitution are lower than those predicted on the basis of the dichotomy in eq 14 and 15. These deviations can be qualitatively interpreted by considering the development of a second chain, which converts the monosubstitution product formed via the photochemically initiated chain into the disubstitution product. This second chain is initiated by the electron transfer in eq 25, from the disub-

$$RSPhSR^{\bullet-} + RSPhCl \rightarrow RSPhSR + RSPhCl^{\bullet-} \rightarrow \text{etc.} \quad (25)$$

stituted product anion radical to the monosubstituted product, which amounts to introducing a feedback loop in the first chain.[22] However, the efficiency of reaction 25, which is opposed to the downhill electron transfer to the starting dihalide, is controlled by the reductive power of the anion radical $RSPhSR^{\bullet-}$. Thus again, the larger the electron affinity of the R group, the larger the yield of the monosubstitution.[23]

## Experimental Section

**General Procedures.** Melting points are uncorrected and were measured on a Reichert melting point apparatus. Low resolution mass spectra (MS $m/z$) were obtained on an AEI MS 50 spectrometer; $^1H$ NMR spectra ($CDCl_3$) were recorded on a Varian T60 spectrometer; chemical shifts from tetramethylsilane are given in $\delta$. Purification of products was achieved by thin layer chromatography.

Instrumentation and procedure for cyclic voltammetry in liquid ammonia were the same as previously described.[5] The working electrode was a gold disc of 0.5-mm diameter. The reference electrode was an $Ag/Ag^+$ (0.01 M) electrode. KBr (0.1 M) was used as supporting electrolyte. The amount of ammonia contained in the cell was 80 mL in all experiments.

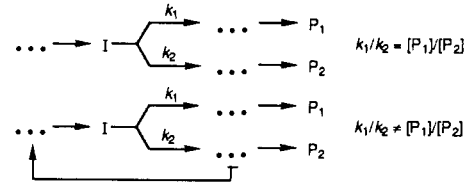
Kinetic data from direct or indirect (redox catalysis) electrochemistry were treated along standard procedures[9d] to afford the rate constants reported in the text or in the tables.

**Starting Materials.** The substrates **1o,m,p** iodochlorobenzene, or 2-chloroquinoline, and all of the thiols ($Nu_1$, $Nu_2$, $Nu_3$) used as nucleophiles are commercially available and were purified before use when necessary. The other nucleophiles were obtained as previously described.[10]

**General Procedure for Photostimulated $S_{RN}1$ Experiments.** Ammonia (50 mL) was condensed into a 100-mL two-necked Pyrex flask fitted with a dry ice condenser. A threefold excess of nucleophile $RS^-$ was generated from the corresponding thiol and equimolecular amount of freshly sublimed $t$-$C_4H_9OK$. The substrate was then added and the flask was illuminated by a 450-W Hanovia high pressure mercury lamp. The reaction was quenched after 1 h by addition of $NH_4Cl$, the solvent was evaporated, and after addition of water (50 mL) the product was extracted by methylene chloride ($3 \times 20$ mL). The organic phase, washed with water, dried over $Na_2SO_4$, and evaporated gave the crude $S_{RN}1$ product. Yields are calculated for the substrate by weighing isolated pure $S_{RN}1$ product.

**Products of Photostimulated Reactions.** Reactions of **1o,m,p** with thiophenol ($Nu_1$) were initially reported by J. F. Bunnett[2a]; reactions of **1m** with thiopyridine ($Nu_2$) or thiopyrimidine ($Nu_3$) have been reported in a previous report.[10] These experiments have been repeated under the above standard con-

(22) This stresses the point that when relative rate constants are to be deduced from the corresponding product yields ratio, one must make sure that no feedback occurs between the reaction sequences occuring after the considered branching point and those intervening before the branching point, i.e.:




(23) However the role of the R moiety on the distribution between mono- and disubstitution tends to be minor when the $\pi^*$MO energy is lower for the parent dihalide. For example, when 5-chloro-7-iodo-8-hydroxyquinoline is reacted under photochemical conditions with the same series of sulfanions, monosubstitution is mainly observed.[10]

ditions for the sake of comparison and the corresponding $S_{RN}1$ products **2o,p**, **3m**, **4m**, and **6m** have spectroscopic data consistent with their structure.

The reaction of **1o** with $Nu_2$ was not precedented and gave **3o** + **6o**, unknown in the literature.

**2-[(2-Chlorophenyl)thio]pyridine (3o)**: mp 40 °C; $^1$H NMR δ 6.2–7.0 (m, 2 H), 7.0–7.5 (m, 5 H), 8.20 (dd, 1 H); MS 223, 221 ($M^+$), 222, 220, 186, 185. Anal. Calcd for $C_{11}H_8ClNS$: C, 59.63; H, 3.61; N, 6.32. Found: C, 59.50; H, 3.82; N, 6.15.

**1,2-Bis(pyridin-2-ylthio)benzene (6o)**: mp 67–68 °C; $^1$H NMR δ 7.10 (m, 4 H), 7.3–7.8 (m, 6 H), 8.40 (dd, 2 H); MS 296 ($M^+$), 218, 186. Anal. Calcd for $C_{16}H_{12}N_2S_2$: C, 64.86; H, 4.05; N, 9.44. Found: C, 64.8; H, 3.91; N, 9.52.

The reaction between **1p** and $Nu_2$ or $Nu_3$, not precedented either, gave (**3p** + **6p**) or **4p**.

**2-[(4-Chlorophenyl)thio]pyridine (3p)**: oil; $^1$H NMR δ 7.0 (m, 2 H), 7.45 (m, 5 H), 8.50 (dd, 1 H); MS 223–221 ($M^+$), 222–220, 185 (lit.[24] no spectroscopic data).

**1,4-Bis(pyridin-2-ylthio)benzene (6p)**: mp 103–105 °C; $^1$H NMR δ 7.1 (m, 4 H), 7.6 (m, 6 H), 8.50 (dd, 2 H); MS 296 ($M^+$), 295, 186. Anal. Calcd for $C_{16}H_{12}N_2S_2$: C, 64.86; H, 4.05; N, 9.44. Found: C, 64.57; H, 4.08; N, 9.59.

**2-[(4-Chlorophenyl)thio]pyrimidine (4p)**: mp 73–74 °C; $^1$H NMR δ 6.90 (t, 1 H), 7.3–7.55 (m, 4 H), 8.40 (d, 2 H); MS 224–222 ($M^+$) (lit.[25] mp 73–74 °C; no spectroscopic data).

**[(3-Chlorophenyl)thio]benzene (2m)**: oil; $^1$H NMR δ 6.90 (s, 1 H), 6.9–7.4 (m, 8 H). MS 222–220 ($M^+$), 184 (lit.[26] no spectroscopic data).

**Registry No.** **1m**, 625-99-0; **1o**, 615-41-8; **1p**, 637-87-6; **3m**, 106920-23-4; **3o**, 122899-23-4; **3p**, 28856-69-1; **4m**, 73226-33-2; **4p**, 26547-31-9; **5m**, 122899-24-5; **5o**, 122899-25-6; **5p**, 122899-26-7; **6m**, 119993-76-9; **6o**, 60372-34-1; **6p**, 39544-83-7; $Nu_1$·K, 3111-52-2; $Nu_2$·K, 79236-86-5; $Nu_3$·K, 57590-85-9; $Nu_4$·K, 96592-02-8; $Nu_5$·K, 57590-84-8; $Nu_6$·K, 7778-70-3; $Nu_7$·K, 80882-73-1; 4-quinolyl radical, 115826-07-8.

(24) King, K. F.; Bauer, L. *J. Org. Chem.* **1971**, *36*, 1641.

(25) Brown, D. J.; Ford, P. W. *J. Chem. Soc. C* **1969**, 2720.

(26) Campbell, J. R. *J. Org. Chem.* **1964**, *29*, 1830.

# Preparation of Seven-Membered-Ring Cyclic Ethers and 3-Alkylidenetetrahydropyrans from the Cyclization of Oxonium Cations Derived from Unsubstituted and Silicon-Containing 4-Alken-1-ols[1]

Armando Castañeda,[2] David J. Kucera, and Larry E. Overman*

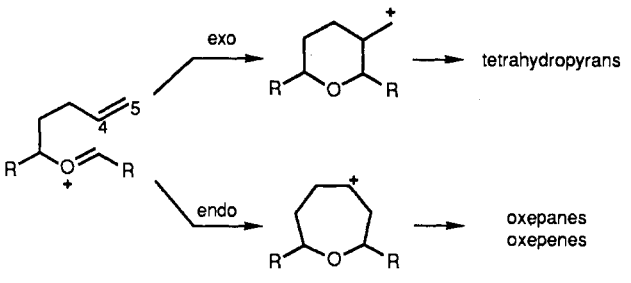
*Department of Chemistry, University of California, Irvine, California 92717*

*Received July 11, 1989*

Lewis acid promoted cyclization of mixed acetals derived from 4-alken-1-ols provides direct access to seven- or six-membered cyclic ethers. Ring size is determined primarily by the electronic bias of the alkene participant. Of particular significance are (a) the formation of 2,3,6,7-tetrahydrooxepins from the cyclization of acetals **10**, **12**, and **13** derived from 4-(trimethylsilyl)-4-penten-1-ol, (b) the completely stereoselective formation of the *cis*-2,7-disubstituted-2,3,6,7-tetrahydrooxepin **14** from **13**, and (c) the stereospecific cyclization of acetals derived from (*E*)- and (*Z*)-4-nonen-1-ol to afford the (*E*)- and (*Z*)-pentylidenetetrahydropyrans **21** and **23**, respectively. The divergent behavior of acetals **24** and **26** highlights the close balance that exists between simple cyclization and more complex rearrangement pathways.

The formation of cyclic ethers by C–C bond-forming cationic cyclization reactions has been known for nearly 40 years,[3] although this approach to oxacyclics is less common than strategies involving C–O bond formation. Prins–Kriewitz cyclization[4] of oxonium cation intermediates (α-alkoxycarbenium ions) derived from the condensation of homoallylic alcohols and carbonyl compounds is a standard method for forming hydropyran derivatives and has received renewed attention of late.[1,5] A notable example, due to Ohloff and co-workers,[6] is a key step in a commercial synthesis of muscone (eq 1). In marked contrast, there exist only a few reports[5i,7] of forming seven-membered ring ethers (oxacycloheptanes or oxepanes)[8] from the cyclization of oxonium cations derived from 4-alken-1-ols.

**Scheme I**




In this paper we report details of our studies of Lewis acid promoted cyclization reactions of mixed acetals de-

(1) A small part of this study was reported in preliminary form; see: Overman, L. E.; Castañeda, A.; Blumenkopf, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 1303.

(2) COSNET-SEP Mexico Graduate Fellow, 1982–1986.

(3) Williams, P. H.; Ecke, G. G.; Ballard, S. A. *J. Am. Chem. Soc.* **1950**, *72*, 5738.

(4) For brief reviews of Prins cyclization reactions that form carbocycles, see: (a) Thieme, J. In *Methoden der Organischen Chemie*, Houben-Weyl, Ed.; Thieme: Stuttgart, 1980; Vol. VI/1a, Part 2, pp 793–799. (b) Snider, B. S. In *Comprehensive Organic Synthesis*; Heathcock, C. H., Ed.; Pergamon: New York; Vol. 5, in press.

(5) Recent examples include: (a) Nishiyama, H.; Itoh, K. *J. Org. Chem.* **1982**, *47*, 2496. (b) Nishiyama, H.; Narimatsu, S.; Sakuta, K.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1982**, 459. (c) Kay, I. T.; Williams. E. G. *Tetrahedron Lett.* **1983**, *24*, 5915. (d) Bunnelle, W. H.; Seamon, D. W.; Mohler, D. L.; Ball, T. F.; Thompson, D. W. *Tetrahedron Lett.* **1984**, *25*, 2653. (e) Melany, M. L.; Lock, G. A.; Thompson, D. W. *J. Org. Chem.* **1985**, *50*, 3925. (f) Winstead, R. C.; Simpson, T. H.; Lock, G. A.; Schiavelli, M. D.; Thompson, D. W. *J. Org. Chem.* **1986**, *51*, 275. (g) Nussbaumer, C.; Fråter, G. *Helv. Chim. Acta* **1987**, *70*, 396. (h) Nussbaumer, C.; Fråter, G. *J. Org. Chem.* **1987**, *52*, 2096. (i) Lolkema, L. D. M.; Hiemstra, H.; Moolweer, H. H.; Speckamp, W. N. *Tetrahedron Lett.* **1988**, *29*, 6365. See also ref 1.

(6) Schulte-Elte, K. H.; Hauser, A.; Ohloff, G. *Helv. Chim. Acta* **1979**, *62*, 2673.

(7) (a) Kocienski, P.; Cockerill, G. C. *J. Chem. Soc., Chem. Commun.* **1983**, 705. (b) Coppi, L.; Ricci, A.; Taddei, M. *J. Org. Chem.* **1988**, *53*, 911.

(8) For a brief review of the synthesis and chemistry of seven-membered ring ethers, see: Boyd, D. R. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Lwowski, W., Eds.; Pergamon Press: Oxford, 1984; Vol. 7, Chapter 5.17.

0022-3263/89/1954-5695$01.50/0 