

Electroreductive Dehalogenation of Chlorinated Aromatic Ethers. Unexpected Electrogenerated Base Catalyzed Reactions

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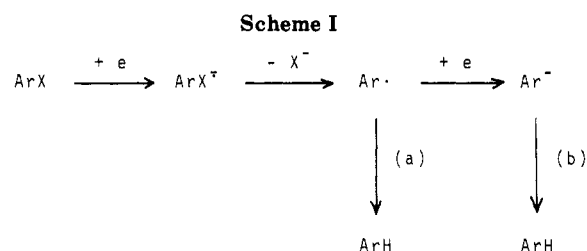
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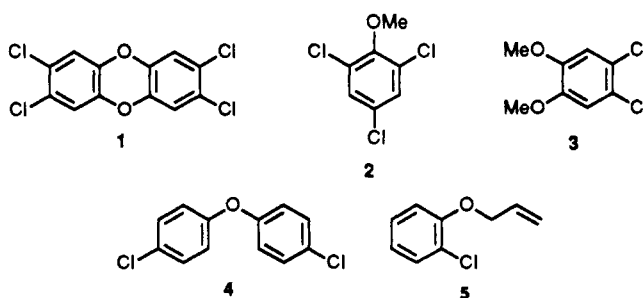
The electroreductive dehalogenation of several mono- and polychlorinated aromatic ethers that serve as models of dioxins has been studied. The dechlorination was achieved by a simple constant-current electrolysis using a lead cathode in dimethylformamide. It was shown that 2,4,6-trichloroanisole undergoes successive dechlorination and the chlorine in the 2-position is selectively eliminated. Competitive reactions and cyclic voltammetric measurements suggested the increasing reactivity order of mono- < di- < trichloride for the reductive dechlorination. Use of allyl 2-chlorophenyl ether as a probe for radical cyclization indicated that free radical intermediates are of little importance. Thus, incipient radicals are immediately reduced to anionic intermediates. The electrolyses in the presence of deuterium oxide revealed proton sources for the present dechlorination. In these attempts, novel phenomena due to electrogenerated base (EGB) were found: di- and trichlorides underwent an unexpected overincorporation of deuterium in their dechlorinated products; a selective formation of *Z*-enol ethers from the allylic ethers was encountered. The mechanistic features of the present electroreductive dechlorination are discussed.

Electrochemical reductions of aromatic halides (ArX) are useful for the dehalogenation to their parent hydrocarbons (ArH).¹ The accepted reduction sequence is illustrated in Scheme I, where ArH can be formed from two distinct intermediates of radicals² and/or anions.³ Recent interest in the electroreductive reaction of aromatic halides has focused on the chemistry of electron transfer as typically shown in the S_{RN}1 reactions.⁴ The electroreductive dehalogenation of simple bromo- or iodobenzenes has been established to proceed via the anionic path (b in Scheme I).^{3,5} In contrast, the electroreduction of aromatic chlorides has not been thoroughly studied because of their lower reactivity. The electroreductive dehalogenation of polychlorinated benzenes and biphenyls has been studied voltammetrically using a mercury electrode in dimethylformamide (DMF).^{6,7} For a special case, Kariv-Miller et al. have developed a method to dehalogenate less reactive fluorobenzenes electrochemically by using dimethylpyrrolidinium salts on a mercury cathode.⁸

It is known that dioxin, a serious environmental pollutant,⁹ is a complex mixture of polychlorinated aromatic ethers, the most toxic being 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (1). The detoxification of dioxin has been attempted by UV or γ irradiation,¹⁰ oxidation with ozone or



other strong oxidants,¹¹ and electrolysis.¹² The last one by electrolysis is based on the electrochemical oxidation of dioxin in ethanol. A toxicological study on dioxin revealed that the toxicity of 1 can be dramatically reduced by eliminating only one or two chlorine atoms.¹³ For this purpose, special reductants are to be used, as reported in the dechlorination of chlorobenzenes, such as sodium naphthalenide,¹⁴ a complex reducing agent of NiCl₂-NaH-t-BuOH,¹⁵ formates for Pd(0)-catalyzed hydrogenation,¹⁶ and sodium borohydride for photoreduction.¹⁷ We deemed that a more simple electroreductive method would be applicable to the dechlorination of chlorobenzenes.



(1) (a) Casanova, J.; Ebersson, L. In *The Chemistry of Carbon-Halogen Bond*; Patai, S., Ed.; John Wiley: New York, 1973; Part II, Chapter 15. (b) Becker, J. Y. In *The Chemistry of Halides, Pseudo-Halides and Azides*; Patai, S.; Rappoport, Z., Eds.; John Wiley: New York, 1983; Part I, Chapter 6. (c) Hawley, M. D. In *Encyclopedia of Electrochemistry of the Elements*; Bard, A. J., Lund, H. Eds.; Marcel Dekker: New York, 1980; Vol. XIV, Chapter 3. (d) Feoktistov, L. G. In *Organic Electrochemistry*; Baizer, M. M., Lund, H., Eds.; Marcel Dekker: New York, 1983; Chapter 7.

(2) (a) Grimshaw, J.; Trocha-Grimshaw, J. *J. Chem. Soc., Perkin Trans. 2* 1975, 215. (b) M'Halla, F.; Pinson, J.; Savéant, J. M. *J. Electroanal. Chem.* 1978, 89, 347.

(3) (a) Cockrell, J. R.; Murray, R. W. *J. Electrochem. Soc.* 1972, 119, 849. (b) De la Torre, R. A.; Sease, J. W. *J. Am. Chem. Soc.* 1979, 101, 1687.

(4) (a) Rossi, R. A.; de Rossi, R. H. In *Aromatic Substitution by the S_{RN}1 Mechanism*; American Chemical Society: Washington, DC, 1983. (b) See, for recent examples: Lexa, D.; Savéant, J. M.; Su, K.-B.; Wang, D.-L. *J. Am. Chem. Soc.* 1988, 110, 7617. Meijs, G. F.; Bunnett, J. F. *J. Org. Chem.* 1989, 54, 1123 and references cited therein.

(5) (a) Swartz, J. E.; Stenzel, T. T. *J. Am. Chem. Soc.* 1984, 106, 2520. (b) Amatore, C.; Otsuran, M. A.; Pinson, J.; Savéant, J. M.; Thiebault, A. *J. Am. Chem. Soc.* 1984, 106, 6318.

(6) Farwell, S. O.; Beland, F. A.; Geer, R. D. *J. Electroanal. Chem.* 1975, 61, 303, 315.

(7) Rusling, J. F.; Arena, J. V. *J. Electroanal. Chem.* 1985, 186, 225.

(8) (a) Kariv-Miller, E.; Vajtner, Z. *J. Org. Chem.* 1985, 50, 1394. (b) Swartz, J. E.; Mahachi, T. J.; Kariv-Miller, E. *J. Am. Chem. Soc.* 1988, 110, 3622.

(9) Rals, R. L. *Chem. Eng. News* 1983, June 6, 37.

(10) (a) Crosby, D. G.; Wong, A. S.; Plimmer, J. R.; Woolson, E. A. *Science* 1971, 173, 748. (b) Fanelli, R.; Chiabrando, C.; Salmona, M.; Garattini, S.; Galdera, P. G. *Experientia* 1978, 34, 1126.

(11) (a) Cavalloni, L.; Zecca, L. *Med. Term. Climatol.* 1977, 34, 73. (b) Ayres, D. C. *Nature* 1981, 290, 323. (c) Botre, C.; Memoli, A.; Alhauque, F. *Environ. Sci. Technol.* 1979, 13, 228.

(12) Harrison, J. M.; Inch, T. D.; Wilkinson, R. G. *Chem. Ind. (London)* 1982, 373.

(13) McConnell, E. E.; Moore, J. A.; Haseman, J. K.; Harris, M. W. *Toxic. Appl. Pharmacol.* 1978, 44, 335.

(14) Smith, J. G.; Ho, I. *J. Org. Chem.* 1973, 38, 3601.

(15) Coubère, P. *Angew. Chem., Int. Ed. Engl.* 1983, 22, 599.

(16) (a) Ciron, J. D.; Lyons, J. E.; Sommer, L. H. *J. Org. Chem.* 1969, 34, 638. (b) Pandey, P. N.; Purkayyasha, M. L. *Synthesis* 1982, 876. (c) Ram, S.; Ehrenkauf, R. E. *Synthesis* 1988, 91. (d) Anwer, M. K.; Sherman, D. B.; Roney, J. G.; Spatoro, A. F. *J. Org. Chem.* 1989, 54, 1284.

(17) Epling, G. A.; Florio, E. M. *J. Chem. Soc., Perkin Trans. 1* 1988, 703.

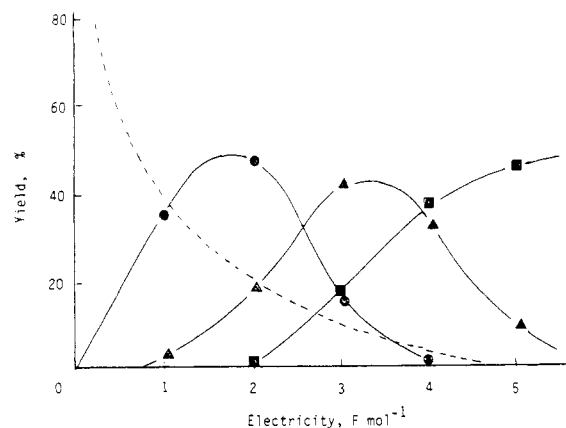


Figure 1. Successive change of dechlorination products in electrolysis of 2,4,6-trichloroanisole (2). Solid lines denote the change of 6 (●), 7 (▲), and 8 (■), and the broken line unreacted 2. For experimental, see footnote a in Table I.

The present study is on the scope and mechanism of simple electroreductive dechlorination of 2–4 as model compounds of highly toxic dioxin. Olefinic chloride 5 was utilized as a probe for intramolecular radical cyclization.^{18–21} During these attempts we have found unexpected base-catalyzed reactions by electrogenerated base (EGB),²² viz., the hydrogen exchange of polychlorides and the olefin isomerization of 5 to afford *Z*-enol ethers.

Results and Discussion

Preparative Electrolysis. A method of constant-current electrolysis was adopted generally as a simple and practical procedure. Preliminary cathodic electrolyses of 2,4,6-trichloroanisole (2) were carried out by using several electrodes, solvents, and electrolytes. When a lead plate was used as the cathode, completely dechlorinated anisole was formed in 41% yield after passage of electricity of 4.0 F/mol in DMF containing tetrabutylammonium perchlorate (TBAP). Use of other metallic electrodes such as Hg, Cu, and Al, or a carbon electrode, resulted in lower yields (20–32%) under the same conditions. The electroreductions with either a platinum electrode or acetonitrile as a solvent were quite ineffective. Appropriate electrolytes for the dechlorination were tetrabutylammonium salts like TBAP, whereas lithium salts were unsatisfactory because of the deposition of metal. Thus, a combination of Pb cathode and TBAP in DMF was chosen as a suitable electrolytic system and applied in the following electroreductions.

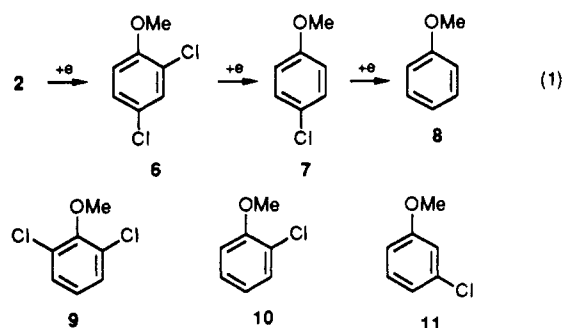
The cathodic reduction of 2 (see Experimental Section for details) afforded products of successive dechlorination. 2,4-Dichloroanisole (6), 4-chloroanisole (7), and anisole (8) were formed as the major products together with negligible

Table I. Preparative Electrolysis of Chlorinated Aromatic Ethers^a

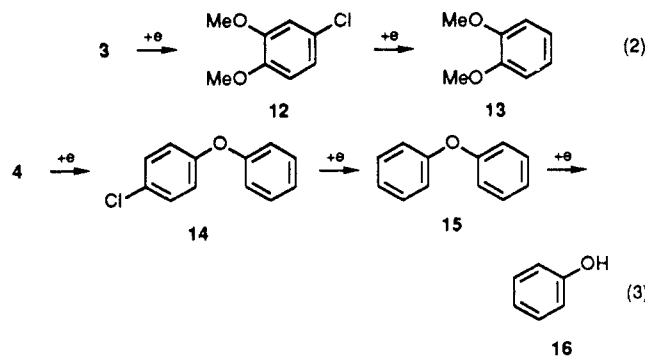
chloro compounds	F/mol ^b	unreacted, %	product (yield, %)
2,4,6-trichloroanisole (2)	4.0	3	6 (2), 7 (34), 8 (41), 9 (0), 10 (<1)
2,4-dichloroanisole (6)	4.0	7	7 (5), 8 (33), 10 (0)
2,6-dichloroanisole (9)	4.0	9	8 (39), 10 (7)
2-chloroanisole (10)	2.0	26	8 (54)
3-chloroanisole (11)	2.0	25	8 (50)
4-chloroanisole (7)	2.0	19	8 (57)
4,5-dichloro-1,2-dimethoxybenzene (3)	4.0	5	12 (6), 13 (38)
4-chloro-1,2-dimethoxybenzene (12)	2.0	45	13 (44)
4,4'-dichlorodiphenyl ether (4)	4.0	13	14 (5), 15 (35), 16 (7)

^a Performed under the standard conditions (0.1 A, Pb cathode, DMF, Bu₄NClO₄). See Experimental Section. ^b Amounts of electricity passed for near depletion of starting materials.

amounts of isomeric dichloride 9 and monochloride 10 (eq 1). The change of product compositions as exemplified



in Figure 1 shows the successive nature of the present dechlorination, that is, 6 or 8 may be obtained at the early or final stage, respectively. It is interesting to note that the chlorine atoms in the 2-position are eliminated selectively. The electrolyses of 4,5-dichloro-1,2-dimethoxybenzene (3) and 4,4'-dichlorodiphenyl ether (4) under the same conditions (Pb electrode and TBAP in DMF) gave the corresponding dechlorinated products 12–15 (eqs 2 and 3). In the case of 4, further reduction to phenol (16) was observed as reported in the reductive C–O bond cleavage of diphenyl ether.²³



In Table I are summarized products and yields from the electrolyses of 2–4 and related chlorides. Completely dechlorinated products, i.e., 8, 13, and 15, were obtained in moderate yields. Prolonged electrolyses yielded intractable substances, accompanying the reductive decomposition of

(18) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* 1980, 13, 317.

(19) (a) Beckwith, A. L. J.; Gara, W. B. *J. Am. Chem. Soc.* 1969, 91, 5689, 5691. (b) Beckwith, A. L. J.; Gara, W. B. *J. Chem. Soc., Perkin Trans. 2* 1975, 593, 795. (c) Beckwith, A. L. J.; Meijs, G. F. *J. Chem. Soc., Chem. Commun.* 1981, 136. (d) Beckwith, A. L. J. *Tetrahedron* 1981, 37, 3073. (e) Beckwith, A. L. J.; Goh, S. H. *J. Chem. Soc., Chem. Commun.* 1983, 905. (f) Abeywickrema, A. N.; Beckwith, A. L. J. *Tetrahedron Lett.* 1986, 27, 109. (g) Beckwith, A. L. J.; Meijs, G. F. *J. Org. Chem.* 1987, 52, 1922.

(20) Johnston, L. J.; Luszyk, J.; Wayner, D. D. M.; Abeywickrema, A. N.; Beckwith, A. L. J.; Sciano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.*, 1985, 107, 4594.

(21) Koppang, M. D.; Ross, G. A.; Woolsey, N. F.; Bartak, D. E. *J. Am. Chem. Soc.* 1986, 108, 1441.

(22) See, for reviews: (a) Baizer, M. M. *Tetrahedron*, 1984, 40, 935. (b) Shono, T. *Electroorganic Chemistry as a New Tool in Organic Synthesis*; Springer-Verlag: Berlin, 1984; Chapter 3. (c) Kashimura, S. *J. Synth. Org. Chem. Jpn.* 1985, 43, 549.

(23) (a) Koppang, M. D.; Woolsey, N. F.; Bartak, D. E. *J. Am. Chem. Soc.* 1985, 107, 4692. (b) Thornton, T. A.; Ross, G. A.; Patil, D.; Mukaida, K.; Warwick, J. O.; Woolsey, N. F.; Bartak, D. E. *J. Am. Chem. Soc.* 1989, 111, 2434. (c) Pacut, R. I.; Kariv-Miller, E. *J. Org. Chem.* 1986, 51, 3468.

Table II. Reduction Potentials in Cyclic Voltammetry of Chlorinated Aromatic Ethers^a

chloride	peak potential ^b
2,4,6-trichloroanisole (2)	-2.17, -2.47, -2.73
2,4-dichloroanisole (6)	-2.58, -2.91
2,6-dichloroanisole (9)	-2.55, -2.86
2-chloroanisole (10)	-2.89
3-chloroanisole (11)	-2.92
4-chloroanisole (7)	-2.77
allyl 2-chlorophenyl ether (5)	-2.83, -2.97
4,5-dichloro-1,2-dimethoxybenzene (3)	-2.74, -3.00
4-chloro-1,2-dimethoxybenzene (12)	-2.92
4,4'-dichlorodiphenyl ether (4)	-2.61, -2.71
4-chlorodiphenyl ether (14)	-2.72

^a Measured in 0.01 M chloride solution in DMF containing 0.1 M Bu₄NBF₄ at a scan rate of 0.1 V/s. ^b Peak potential (V) vs Ag/AgCl.

TBAP to tributylamine. GC-MS analyses of these reaction mixtures showed no formation of biphenyl-type products as often observed in the reduction of aryl chlorides.²⁴ In a practical sense, the present electroreductive system holds merit because of no formation of polychlorobiphenyls as a secondary pollutant. Since two electrons are necessary to reduce one C-Cl bond, the current efficiency for the electroreduction of trichloride **2** was calculated to be quite high, i.e., 97% at 4.0 F/mol. The current efficiencies for dichlorides **3** and **4** were moderate, i.e., 41% and 48%, respectively. It may be suggested that the detoxification of **1** by partial dechlorination is effective by the present electroreductive method.

It is reported that the electroreduction of 2,4,6-trichlorobiphenyl affords 4-chlorobiphenyl selectively.⁶ The product distribution from the electroreduction of **2** and **6** in Table I shows that the chlorine atom adjacent to the methoxy group is removed selectively. A competitive reduction showed that **2** is 7.5 times more reactive than 1,3,5-trichlorobenzene. This observation might be consistent with the assumption that the introduction of a methoxy group facilitates the elimination of neighboring chlorine atoms because of its steric congestion. However, the analogous reduction between **6** and **9** resulted in a rate ratio of only 1.5 and the relative rate ratio for **10**:**7**:**11** was 1.5:1.5:1. Accordingly, the observed site selectivity cannot be explained simply in terms of the steric effect of the methoxy group.

Cyclic Voltammetry. Reduction potentials for chlorinated aromatic ethers were measured by cyclic voltammetry (CV) in DMF solution. All waves obtained were irreversible and Table II lists the peak potentials vs Ag/AgCl. Trichloride **2** exhibited three peaks at -2.17, -2.47, and -2.73 V. A controlled-potential electrolysis of **2** was carried out, for example, at -2.2 V, i.e., its first cathodic peak. After passage of electricity of 2.5 F/mol, dichloride **6** was obtained selectively in 84% yield. In addition, the CV of a mixture of trichloride **2** and monochloride **7** gave a simple sum of each wave. Thus, three peaks of **2** are assigned as the reduction potentials of the successive dechlorinations. Since the three peaks were approximately of the same height, the substrate chloride was dechlorinated on the electrode surface successively without desorption.

In general, the number of peaks corresponds to the number of chlorine atoms involved. Monochloride **5** was the exceptional case and showed two peaks, one owing to

Table III. Deuterium Incorporation in Products from Electrolysis in the Presence of D₂O^a

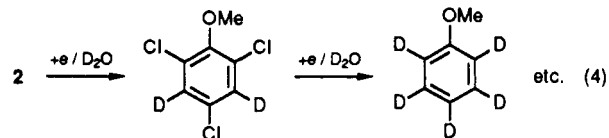
chloride	ArCl	F/mol	% yield of ArH	% deuterium ^b					
				d ₀	d ₁	d ₂	d ₃	d ₄	d ₅
	7	2.0	65	25	75	0	0	0	0
	5	2.0	69 ^c	24	76	0	0	0	0
	2	6.0	59	0	1	4	18	41	37
	6	4.0	69	0	7	30	44	19	0
	3	4.0	48 ^d	2	8	27	40	23	0

^a Electrolytic conditions: chloride, 2 mmol; D₂O, 20 mmol; electrolyte TBAP, 5 mmol in 25 mL of DMF. ^b Calculated from the relative intensities of molecular ions in the product. Errors lie within ±3%. ^c The product is allyl phenyl ether. ^d The product is veratrole.

the olefinic function.²⁵ The reduction potentials for dichlorides were in the range from -2.5 to -2.7 V, that for monochlorides being from -2.7 to -3.0 V. These E_p values seem to be comparable with the reported polarographic reduction potentials of -2.48 V vs SCE for 1,3-dichlorobenzene^{26a} and -2.62 V for chlorobenzene.^{26b} It is apparent from the order of reduction potentials that the ease of the electroreductive dechlorination increases in the order of mono- < di- < trichloride, which is consistent with the results of preparative electrolyses in Table I.

Electrolysis in the Presence of D₂O. A small amount of water has been suggested to act as a good proton donor in the electroreduction of aromatic iodides and bromides.²⁷ The electrolysis of **2-7** were conducted in the presence of D₂O and the products were analyzed by GC-MS (Table III). It was found that two kinds of incorporation of deuterium take place, depending on the type of chlorides. One type is for monochlorides. Electrolysis of **7** in the presence of 10 equiv of D₂O gave a mixture of anisole-*d*₀ and -*d*₁ in a ratio of 25:75 (see Table III). Similar results were obtained with 2-chlorophenyl ether **5**. NMR analyses of these products suggested that most of the deuterium was incorporated at the same position where chlorine was attached. Recovered **5** or **7** after the electrolysis showed no deuterium exchange. These observations support the anionic pathway b in Scheme I for these dechlorinations.

On the other hand, the electrolysis of trichloride **2** gave rise to a complex mixture of anisole-*d*_x with *x* ranging from 1 to 5 (see Table III). This unexpected incorporation of more than three deuteriums suggests that aromatic hydrogen atoms of **2** were also replaced during the electrolysis. In fact, recovered **2** at the initial stage of the electrolysis was shown to be converted to 2-*d*₂ in 60-80%. Therefore, this unusual overincorporation of deuterium appears to result from a facile deuterium exchange in the starting chloride (eq 4). Dichlorides **3** and **6** also under-



went an analogous overdeuteration, the extent of which was lowered owing to their reduced reactivity for the deuterium exchange.

When **2** was treated with NaOD and excessive D₂O in DMF, a mixture of 2-*d*₁ and -*d*₂ was obtained. Since the reported pK_a for water is 34.7 in DMF,²⁸ and that for

(24) (a) For example, see: Colon, I.; Kelsey, D. R. *J. Org. Chem.* **1986**, *51*, 2627. (b) Torii, S.; Tanaka, H.; Morisaki, K. *Tetrahedron Lett.* **1985**, *26*, 1655. (c) Alam, N.; Amatore, C.; Combellas, C.; Tiébaud, A.; Verpeax, J. N. *Tetrahedron Lett.* **1987**, *28*, 6171.

(25) In fact, allyl phenyl ether exhibited a peak potential at -2.86 V. (26) (a) Stackelberg, M.; Stracke, W. Z. *Elektrochem.* **1949**, *53*, 118. (b) Zuman, P. *Substituent Effects in Organic Polarography*; Plenum press: New York, 1970; p 123.

(27) (a) Wawzonek, S.; Blaha, E. W.; Berkey, R.; Runner, M. E. *J. Electrochem. Soc.* **1955**, *102*, 235. (b) Webb, J. L.; Mann, C. K.; Walborsky, H. M. *J. Am. Chem. Soc.* **1970**, *92*, 2042.

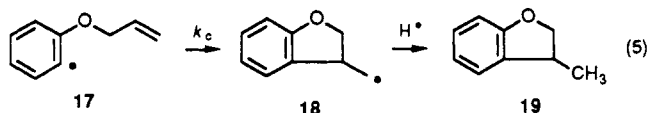
Table IV. Products from Cathodic Electrolysis of 5 under Several Conditions

run	conditions ^a	unreacted 5, %	product yield, %			
			19	20	21	22
1	lead	1	0	2	52	9
2	lead (H ₂ O, 10 equiv)	15	0	69	8	3
3	lead (MeCN)	14	0	81	1	0
4	platinum	0	1	1	40	21
5	copper	1	0	1	25	17
6	zinc	1	3	4	21	30
7	carbon	4	0	2	40	23
8	carbon (MeCN)	25	4	66	1	0
9	carbon (Et ₄ NOTs) ^b	11	1	62	6	0
10	lead (D ₂ O, 2 equiv) ^c	5	3	12	50	15

^a Electrolytic conditions, unless otherwise noted in parentheses: 5, 2 mmol; electrolyte TBAP, 5 mmol in 25 mL of DMF. Electrodes are listed and electricity passed is 2.0 F/mol. ^b Electrolyte, tetrabutylammonium *p*-toluenesulfonate. ^c Deuterium incorporations are summarized in Table V.

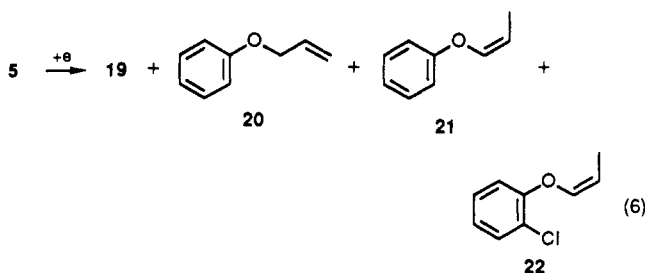
1,3,5-trichlorobenzene is 33.6,²⁹ the base strength of OD⁻ is enough to deprotonate the aromatic hydrogen of 2. It is interesting to note that OD⁻ as an EGB³⁰ can effect a base-catalyzed hydrogen exchange leading to the over-deuteration. An alternate route for OD⁻ ion is its formation from D₂O and Ar⁻ produced by the reduction of ArCl. The choice of the two pathways is not possible at present.

Electrolysis of Radical Probe 5. A method for the detection of radical intermediates is to apply the intramolecular cyclization of olefinic radicals.³¹ For example, 2-(allyloxy)phenyl radical (17) cyclizes to five-membered radical 18, affording furan derivative 19 (eq 5).¹⁹ The rate



constant (k_c) for the radical cyclization of 17 is reported to be $6.3 \times 10^9 \text{ s}^{-1}$ at 30 °C, the highest among known olefinic radicals.²⁰ In order to check any intervention of a radical intermediate in the present electroreduction, olefinic chloride 5 was chosen as a precursor of radical 17.

Electrolyses of 5 under several conditions gave product mixtures of 19–22 (eq 6) as listed in Table IV. The



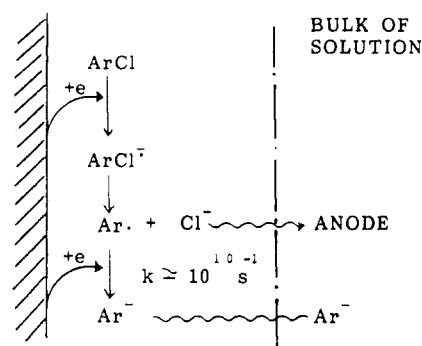
(28) (a) Barrette, W. C., Jr.; Johnson, H. W., Jr.; Sawyer, D. T. *Anal. Chem.* 1984, 56, 1890. (b) 31.4 in dimethyl sulfoxide: Olmstead, W. N.; Margolin, Z.; Bordwell, F. G. *J. Org. Chem.* 1980, 45, 3295.

(29) Streitwieser, A., Jr.; Juaristi, E.; Nebenzahl, L. L. In *Comprehensive Carbanion Chemistry*; Buncl, E., Durst, T., Eds.; Elsevier: New York, 1980; Part A, 323.

(30) OH⁻ ion as an EGB derived from direct reduction of water in DMF has been found to effect the alkylation of dialkyl phosphonates: Kimura, M.; Yamashita, T.; Sawaki, Y. *J. Chem. Soc., Chem. Commun.* In press.

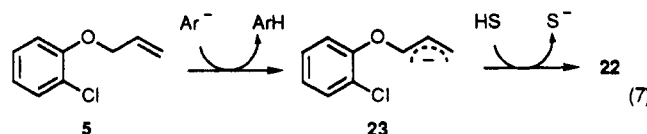
(31) (a) Giese, B. In *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: New York, 1986. (b) Relevant recent examples: Stork, G.; Reynolds, M. E. *J. Am. Chem. Soc.* 1988, 110, 6911. Trost, B. M.; Walchli, R. *J. Am. Chem. Soc.* 1987, 109, 3487.

(32) In the hope of formation of 19 as major product, we attempted the reductive radical cyclization of chloride 5 by the aid of cyano benzenes.⁵ But the attempt was unsuccessful owing to the facile reductive cleavage of the mediators.

Scheme II

electroreduction of 5 gave only trace or small amount of the expected cyclization product 19. Instead, considerable amounts of *Z*-enol ethers 21 and 22 were obtained as unexpected products as a result of double-bond migration. The isomerization to 22 was the major reaction at the initial stage (<1.0 F/mol) of the electrolysis. The isomerization of allyl ethers to *Z*-enol ethers³³ has been reported to be effected by a strong base such as *t*-BuOK.³⁴ Hence, the conversion of 5 to 22 is probably the isomerization induced by an efficient EGB. When 5 was electroreduced with other electrodes (runs 4–7), product distributions were essentially the same, i.e., 21 and 22 being the major products. Upon addition of water as a proton source, the isomerization was reduced and the formation of dechlorination product 20 became predominant (run 2). Similar results were obtained when acetonitrile or tetraethylammonium salt was used as weak proton sources²⁷ (runs 3, 8, and 9). These observations indicate that the isomerization to give 21 and 22 occurs preferentially in the absence of proton sources.

The anionic intermediate Ar⁻ in Scheme I may serve as an EGB to initiate the isomerization of 5 to 21 and 22. The isomerization may be written as in eq 7, HS being the



proton source. When HS is starting 5, a catalytic cycle is achieved to reproduce anion 23. The catalyzed isomerization of 5 to 22 is consistent with the deuterium incorporation in the recovered 5 and 22 from the reaction in the presence of 2 equiv of D₂O (see Table V). Since the D incorporation in 5 and 22 is only on the allyl group, the isomerization according to eq 7 is apparent.

The D incorporations in the dechlorinated products 20 and 21, as listed in Table V, were considerably high, but about one-fourth contained no deuterium. The fragment ion in the mass spectra of 20 and 21 suggested that the deuterium contents in the phenyl ring were 62% and 65%, respectively. This in turn means that about 35% of the protons in the dechlorinated phenyl ring comes from proton donors other than water. These results show that proton donors for Ar⁻ are contaminated water, allyl phenyl ethers, and solvents.

It has been shown that radical anions of aromatic halides, especially aromatic bromides, undergo rapid disso-

(33) This stereoselective formation of (*Z*)-olefin was originally explained by the effect of metal cations like K⁺.³⁴ However, the present results in the absence of metallic cations seem to support that the observed stereoselectivity can arise from the characteristic nature of allylic anions where the *Z* configuration is more stable than the *E*. See: Bank, S.; Schriesheim, A.; Rowe, C. A., Jr. *J. Am. Chem. Soc.* 1965, 87, 3244.

(34) Price, C. C.; Synder, W. H. *J. Am. Chem. Soc.* 1961, 83, 1773.

Table V. Deuterium Incorporation in the Cathodic Electrolysis of 5 in the Presence of D₂O^a

product	electricity, F/mol	yield, %	% D incorporation ^b					remark
			d ₀	d ₁	d ₂	d ₃	d ₄	
5	0.2	84	94	6	0	0	0	c
	2.0	5	35	45	20	0	0	c
22	0.2	7	67	33	0	0	0	c
	2.0	15	55	38	5	2	0	c
20	2.0	12	28	51	19	2	0	d
21	2.0	50	22	50	25	3	0	e

^a For conditions, see run 10 in Table IV. ^b Deuterium incorporations were determined from the relative intensities of molecular ions. ^c No incorporation of deuterium in the phenyl ring. ^d Deuterium incorporation in the phenyl ring: d₀:d₁:d₂ = 38:6:2. ^e In the phenyl ring, d₀:d₁:d₂ = 35:65:0.

ciation to aromatic radicals and halide ions.^{5,21} The inefficient or lack of formation of 19 (see Table IV) means that radical 17 is immediately reduced with a rate constant over 10¹⁰ s⁻¹. If the rate constant is lower than 10¹⁰ s⁻¹, a considerable amount of 19 should be, contrary to the observation, produced because the cyclization of 17 is very fast, i.e., k_c = 6 × 10⁹ s⁻¹.²⁰ Thus, no importance of free radical intermediates is established in the dechlorination of 5. In other words, the dechlorination occurs mostly on or near the electrode surface. The electroreduction sequence of aromatic chlorides is illustrated in Scheme II, where two electrons are supplied from the cathode to ArCl and Ar[•] species.

In conclusion, the present electroreductive dehalogenation of chlorinated aromatic ethers is shown to proceed via anionic intermediates (path b in Scheme I). Aromatic anions thus formed are protonated, during their diffusion toward the bulk of solution, by an appropriate proton source such as the solvent or electrolyte. When a suitable amount of water is present, the anion reacts with water to produce hydroxide ion, which can be an effective base to cause the unusual hydrogen exchange of polychlorides. In the absence of good proton donors, aromatic anions can effect a selective isomerization of allylic ethers to Z-enol ethers.

Experimental Section

Chemicals and Materials. Chloro-substituted ethers 2, 3, 5–11, and 12 were prepared from relevant chlorophenols and chloroveratroles by the reported methods.³⁵ Preparations of 4 and 14 were carried out according to the reported arylation procedure.³⁶ These known compounds showed expected spectroscopic properties in IR and NMR, and their purities were over 98% as determined by GLC analysis. ¹H NMR of 2,4,6-trichloroanisole (2): δ 3.79 (s, 3 H), 7.16 (s, 2 H). ¹H NMR of 3: δ 3.70 (s, 6 H), 6.70 (s, 2 H).

Purification of DMF commercially available from Wako Chemicals (guaranteed grade, water content < 0.2%) was carried out by being heated over calcium hydride at 80 °C for 6 h, followed by fractional distillation under reduced pressure. Electrolytes, such as TBAP (Bu₄NClO₄), from Tokyo Kasei were dissolved in dry DMF and the solution was stored over 4A molecular sieves.

Metallic plates, e.g., lead and platinum, purchased from Japan Lamp Industrial, were cut into 1 × 3 cm pieces and connected with a copper wire. The electrode surface was polished with emery paper before each electrolysis.

Apparatus and Instruments. For the preparative electrolysis, a cylindrical glass cell of ca. 40-mL volume (30-mm diameter and 80-mm depth) was equipped with a cathode electrode, a porous porcelain cup (13-mm diameter), and a rubber stopper, through which a gas inlet syringe and a thermometer, etc., were inserted. Inside the porcelain cup, a platinum anode was equipped. The

platinum anode and the cathode were separated by 1 cm and connected with a DC power supply (Takasago GPO 52-2) through a digital coulomb-amperehour meter (Hokuto Denko HF 201). A potentiostat (Hokuto Denko HA 301) was used for controlled potential electrolyses.

Cyclic voltammetric measurements were carried out with a Yanagimoto P 1100 polarographic analyzer, using a hanging mercury electrode as the working electrode. DMF solutions of 0.01 M substrate and 0.1 M electrolyte were measured at a scan rate of 100 mV s⁻¹ under nitrogen and the results are listed in Table II.

GLC analyses were performed with a Yanagimoto G 180 gas chromatograph equipped with columns (4 mm × 1 m) of PEG 20M, 10% on Chromosorb WAW and Silicon DC 550, 15% on Chromosorb WAW; a Shimadzu CR-3A integrator was used for the quantitative analysis. GC-MS analyses were carried out on a JEOL D 300 mass spectrometer and mass spectra were recorded at 20 eV. ¹H NMR spectra were recorded with a Hitachi R 24B (60 MHz) spectrometer using TMS as internal standard in CCl₄.

General Procedure of Preparative Electrolysis. A solution of 2 mmol of chloro aromatic ether in 25 mL of DMF containing 0.2 M TBAP was placed in the electrolysis chamber, and 5 mL of a DMF solution of 0.2 M TBAP was placed in the porcelain cup. The chloride solution was electrolyzed cathodically at a constant current of 0.1 A with magnetic stirring at ambient temperature (i.e., mostly at 25–30 °C). Aliquots of 0.1 mL of reaction mixture were syringed out from time to time in order to monitor the reaction; after the addition of an internal standard such as bibenzyl or biphenyl, the sample was diluted with ether and washed with water and analyzed by GLC. The electrolysis was continued until the starting material reached almost depletion.

The resulting electrolysis solution was poured into an aqueous sodium bicarbonate solution and extracted repeatedly with ether (100 mL). The combined organic layers were washed successively with water and brine, dried over sodium sulfate, and subjected to GLC and GC-MS analyses. Identification of products was based on the coincidence in GLC retention times and mass spectra with those of the authentic samples (Table I). After evaporation of the solvent, the residue was weighed and its IR and NMR spectra were recorded.

The electrolyses were done mostly under air since no significant difference was observed between the electroreduction under air and that under nitrogen.

Electrolysis in the Presence of D₂O. The procedure described above was employed for the electroreduction of chloride in the presence of 20 mmol of D₂O. The crude product was subjected to bulb-to-bulb distillation in order to obtain 200-MHz NMR spectra. The position of deuterium incorporation was inferred from a comparison with authentic 4-deuterioanisole and allyl 2-deuteriophenyl ether, which were prepared from the corresponding Grignard reagents and D₂O. The contents of deuterium were calculated from the relative intensities of the molecular ion peaks as determined by GC-MS and are shown in Table III.

Electrolysis of Radical Probe 5. Electrolyses of 5 were carried out similarly under the typical conditions using other metallic cathodes. The workup and analysis were as described before and results are listed in Table IV. The product of phenyl (Z)-propenyl ether (21) was isolated by column chromatography on silica gel (hexane-ethyl acetate (9:1 v/v) as eluant) in slightly impure form, which was contaminated with a small amount of 2-chlorophenyl (Z)-propenyl ether (22). Products were identified

(35) (a) Allen, C. F. H.; Gates, J. W., Jr. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 140. (b) Vyas, G. N.; Shah, N. M. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. III, p 836.

(36) Ungnade, H. E.; Orwoll, E. F. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 566.

by comparing their GC-MS and NMR spectra with those of authentic samples.

The authentic sample of 3-methyl-2,3-dihydrobenzofuran (19) was prepared according to the literature;^{19b} ¹H NMR δ 1.26 (d, $J = 7$ Hz, 3 H), 3.1-3.6 (m, H), 3.90 (t, $J = 8$ Hz, H), 4.50 (t, $J = 9$ Hz, H), 6.5-7.3 (m, 4 H). Authentic samples of phenyl (*Z*)-1-propenyl ether (21) and 2-chlorophenyl (*Z*)-1-propenyl ether (22)³⁷ were prepared according to the literature method.³⁴ ¹H

NMR of 21: δ 1.65 (q, $J = 5$ and ~ 1.5 Hz, 3 H), 4.4-4.9 (m, H), 6.0-6.3 (m, H), 6.5-7.3 (m, 5 H). ¹H NMR of 22: δ 1.73 (q, $J = 6$ and ~ 1.5 Hz, 3 H), 4.8-5.1 (m, H), 6.2-6.4 (m, H), 6.9-7.4 (m, 4 H).

The deuterium incorporation from the reaction in the presence of D₂O was monitored by GC-MS analyses of products. The D contents were determined from molecular ions of the products, i.e., by subtracting the natural abundance from observed values of $M + 1$, $M + 2$, and $M + 3$. The D contents in the phenyl ring are easily calculated from the fragment ions of the phenoxy group.

(37) Yamamoto, K.; Higashimura, T. *J. Polym. Sci.* 1974, 12, 613.

Direct Lithiation of Alkoxyphenols: Metalation vs Demethylation. An Experimental and Theoretical (MNDO) Study

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The direct lithiation of simple alkoxyphenols has been studied both from a theoretical and an experimental viewpoint. Efficient lithiations were achieved by using a 2:1 tBuLi-tBuOLi mixture (LICLIOR) in THF at room temperature. In most cases alkoxy groups are responsible for the regioselectivity observed, although for the case of 2-methoxyphenol both the OMe and OLi groups actually act as ortho-directing groups during lithiation. Demethylation has been shown to be a common side reaction of lithiation of phenolic or nonphenolic alkoxy aromatics. MNDO calculations provide good support for all the experimental observations. Thus, lithiation and demethylation are shown to be competing pathways, the former being kinetically favored whereas the latter leads to the thermodynamically more stable compounds. Calculations also show that the so-called geminal demethylations are more favored processes than the alternative vicinal demethylations. Moreover, MNDO allows the measurement of the extent of agostic activation of the ortho hydrogens with respect to the OMe and OLi groups involved in lithiation. Finally, MNDO nicely predicts the important role of reaction temperature in successful direct lithiation of simple alkoxyphenols.

The direct ring metalation of phenolic compounds¹ and closely related substances² has gained recent attention as a potentially useful methodology for the direct introduction of functional groups and alkyl side chains into monphenolic compounds and related systems. However, apart from the lithiation of phenol¹ itself and naphthols,³ only a handful of other cases have been reported in the literature.⁴ Therefore, it seemed worthwhile to study the direct metalation of relevant phenols in more detail, so as to determine the real scope and limitations of this potentially powerful synthetic method.

Our plan was to avoid the rigidly controlled conditions required for achieving direct metalation of simple hydroxy aromatics^{1,3,4} since, mainly as a result of the difficulty in stirring a highly viscous mass, a number of problems arise when these reactions are scaled-up. Thus, on the one hand, large amounts of starting materials are usually recovered unchanged,^{4d,e} and, on the other, important side reactions show up as a consequence of high local concentration of reactants and/or the uncontrolled increase of temperature.

Being aware of these experimental difficulties we focused our attention on using complex bases such as tBuLi-tBuOK and related systems, usually referred to as LIC-KOR reagents.⁵ Actually we were driven to employ the easy-to-prepare tBuLi-tBuOLi (LICLIOR) mixture instead of the more commonly used tBuLi-tBuOK. The ultimate reason behind this choice was the fact, noticed both by Posner and ourselves during the tBuLi-THP promoted lithiation of hydroxy aromatics,^{1,3,4} that the solvent used (tetrahydropyran, THP) was being partially cleaved to the corresponding alkoxide (6,6-dimethylheptan-1-ol lithium salt) by the action of tBuLi.

Though the role played by the alkoxide in this reaction has yet to be properly defined, we speculated that its action might significantly determine two very distinct though intimately related questions, namely, the structure of the lithiated reagents and products and, last but not least, the solubility of these compounds in the reaction medium. In very recent disclosures MacGarrity et al.^{6,7} have provided convincing evidence not only in regard with the actual constitution of the mixed complexes co-occurring in RLi-ROLi mixtures, but also on the expected reactivity,

(1) Posner, G. H.; Canella, K. A. *J. Am. Chem. Soc.* 1985, 107, 2571.

(2) (a) Figuly, G. D.; Loop, C. K.; Martin, J. C. *J. Am. Chem. Soc.* 1989, 111, 654. (b) Block, E.; Eswarakrishnan, V.; Gernon, M.; Ofori-Okai, G.; Saha, C.; Tang, K.; Zubieta, J. *Ibid.* 1989, 111, 658. (c) Smith, K.; Lindsay, C. M.; Pritchard, G. J. *Ibid.* 1989, 111, 665.

(3) Coll, G.; Morey, J.; Costa, A.; Saá, J. M. *J. Org. Chem.* 1988, 53, 5345.

(4) (a) Saá, J. M.; Llobera, A.; García-Raso, A.; Costa, A.; Deyá, P. M. *J. Org. Chem.* 1988, 53, 4263. (b) Costa, A.; Saá, J. M. *Tetrahedron Lett.* 1987, 28, 5551. (c) Saá, J. M.; Llobera, A. *Tetrahedron Lett.* 1987, 28, 5045. (d) Santucci, L.; Gilman, H. *J. Am. Chem. Soc.* 1958, 80, 4537. (e) See: Gilman, H.; Morton, J. W., Jr. *Organic Reactions*; Wiley: New York, 1954; Vol. 8 and references therein.

(5) (a) Lochmann, L.; Pospisil, J.; Lim, D. *Tetrahedron Lett.* 1966, 257.

(b) Schlosser, M. *J. Organomet. Chem.* 1967, 8, 9. (c) Lochmann, L.; Trékoval, J. *Ibid.* 1987, 326, 1. (d) Schlosser, M.; Strunk, S. *Tetrahedron Lett.* 1984, 25, 741. (e) For a closely related system, see: Screttas, C. G.; Steele, B. R. *J. Org. Chem.* 1989, 54, 1013 and references therein.

(6) McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* 1985, 107, 1805.

(7) McGarrity, J. F.; Ogle, C. A.; Brich, Z.; Loosli, H. R. *J. Am. Chem. Soc.* 1985, 107, 1810. See also: Al-Aseer, M. A.; Allison, B. D.; Smith, S. G. *J. Org. Chem.* 1985, 50, 2715. Baryshnikov, Yu. N.; Kaloshina, N. N.; Vernovskaya, G. I. *J. Gen. Chem. USSR* 1977, 47, 2535.