Electrostatic and Electrophilic Catalysis in the Reductive Cleavage of Alkyl Aryl Ethers. The Influence of Ion Pairing on the Regioselectivity

Francisco Casado,† Luisa Pisano,‡ Maria Farriol,† Iluminada Gallardo,† Jordi Marquet,*,† and Giovanni Melloni*,‡

Departament de Química, Universitat Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain, Dipartimento de Chimica, Università di Sassari, Via Vienna 2, I-07100, Sassari, Italy

Received July 1, 1999

Electrophilic and electrostatic catalysis have been identified as distinct contributions that affect the reactivity of radical anions in the reductive cleavage of alkyl aryl ethers. Two modes of mesolytic scission of these radical anions are possible: homolytic (dealkylation, a thermodynamically favored but kinetically forbidden process) and heterolytic (dealkoxylation). From our studies (alkali metal reductions, electrochemical studies, use of substrates with a preformed positive charge in certain positions of their structure) it can be concluded that the heterolytic scission is very much dependent on the electrophilic assistance by the counterion and it is only observed in contact ionic pairs with unsaturated cations (electrophilic catalysis). On the other hand, the homolytic scission is observed in solvent-separated ionic pairs, and it is especially efficient when the pair has a controlled topology with a tetralkylammonium cation (saturated cation) near the oxygen atom. The effect of the cation has, in this case, electrostatic origin (electrostatic catalysis), probably lowering the barrier of the intramolecular $\pi^*-\sigma^*$ electron transfer process and thus reducing the kinetic control of the reaction in such a way that the thermodynamically more favorable process is produced.

The electron distribution in reactive intermediates largely determines the outcome of a chemical or photochemical reaction. In the case of charged intermediates, however, the electron distribution is heavily influenced, among other factors, by the interaction with the counterion. As to the effect of the counterion on the outcome of a chemical process (“metal ion catalysis”, “electrophilic catalysis”, etc.),[1] it has been traditionally attributed[2] to Lewis acid complexation, ignoring the important associated electrostatic effect. Only recently has this electrostatic effect been recognized as responsible for the lowest energy conformation of the radical anion/cation pair in alkyl aryl ethers,[3] the acceleration of the electrocyclic reactions by metal cation complexation,[4] the strong association of cations to aryl rings even in aqueous solution,[5] and the acceleration of the catalytic acylation step by acetylcholinesterase.[6]

Unimolecular fragmentation of radical ions to yield radicals and ions (mesolytic cleavages) constitutes the elementary step of many electron-transfer-initiated processes.[7] The rates of these reactions are usually significantly faster than those observed for the homolytic cleavage of the same bonds in neutral substrates.[8,9]

Alkali metals are known to induce cleavage of the C−O bonds of aryl alkyl ethers under aprotic conditions in various solvents.[10] Cleavage of the alkyl−oxygen bond with formation of phenols (dealkylation) is most often observed; cleavage of the phenyl−oxygen bond (dealkoxylation) is achieved only in particular cases,[11] especially in the presence of potassium and in solvents of low[12] or very low[13] polarity. The first reaction step leads to radical anions, $ROAr^{\cdot-}$, known since 1968 from ESR studies.[14] Dianions were also discussed in the past as intermedi-

---

* To whom correspondence should be addressed. For J.M.: phone, 34-3-5811029; fax, 34-3-5811265; e-mail, iqor3@cc.uab.es.

† Universitat Autònoma de Barcelona.

‡ Università di Sassari.

[1] Loupy, A.; Tchoubar, B. *Salt Effects in Organic and Organometallic Chemistry*; VCH: New York, 1992.

[2] (a) Pregel, M. J.; Buncel, E. *J. Org. Chem.* **1991**, *56*, 5583. (b) Dunn, E. J.; Moir, R. Y.; Buncel, E.; Purdon, J. G.; Bannard, R. A. B. *Can. J. Chem.* **1990**, *68*, 1837. (c) Breslow, R.; Guo, T. *J. Am. Chem. Soc.* **1988**, *110*, 5613. (d) Casaschi, A.; Desimoni, G.; Faita, G.; Invernizzi, A. G.; Lanati, S.; Righetti, P. P. *J. Am. Chem. Soc.* **1993**, *115*, 8002.

[3] Lazana, M. C. R. L. R.; Franco, M. L. T. M. B.; Herold, B. J. *J. Am. Chem. Soc.* **1989**, *111*, 8640.

[4] (a) Jiao, H.; Schleyer, P. v. R *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1760. (b) Jiao, H.; Schleyer, P. v. R. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 1559. (c) Jiao, H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1995**, *117*, 11529.

[5] (a) Dougherty, D. A. *Science* **1996**, *271*, 163. (b) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303.

[6] Wlodek, S. T.; Antosiewicz, J.; Briggs, J. M. *J. Am. Chem. Soc.* **1997**, *119*, 8159.

[7] (a) Saveánt, J.-M. *Tetrahedron*, **1994**, *50*, 10117. (b) Maslak, P. *Top. Curr. Chem.* **1993**, *168*, 1. (c) Savéant, J.-M. *Acc. Chem. Res.* **1993**, *26*, 455.

[8] Chanon, M.; Rajzmann, M.; Chanon, F. *Tetrahedron* **1990**, *46*, 6193.

[9] (a) Maslak, P.; Narvaez, J. N.; Vallombroso, T. M., Jr. *J. Am. Chem. Soc.* **1995**, *117*, 12373. (b) Maslak, P.; Vallombroso, T. M.; Chapman, W. H., Jr.; Narvaez, J. N. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 73. (c) Maslak, P.; Narvaez, J. N. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 283.

[10] (a) Azzena, U.; Denurra, T.; Fenude, E.; Melloni, G.; Rassu, G. *Synthesis*, **1989**, 28. (b) Thornton, T. A.; Woolsley. N. F.; Bartak, D. E. *J. Am. Chem. Soc.* **1986**, *108*, 6497. (c) Koppang, M. D.; Woolsley N. F.; Bartak, D. E. *J. Am. Chem. Soc.* **1984**, *106*, 2799. (d) Patel, K. M.; Baltisberger, R. J.; Stenberg, V. I.; Woolsley, N. F. *J. Org. Chem.* **1982**, *47*, 4250. (f) Bhatt, M. V.; Kulkarni, S. A. *Synthesis* **1983**, 249.

[11] Maercker, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 972 and references therein.

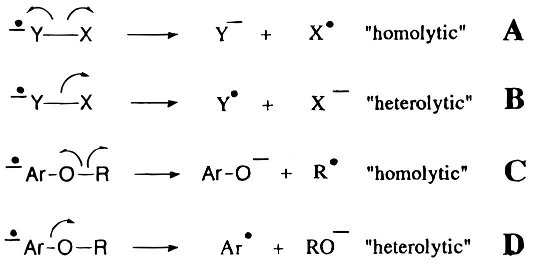
[12] Azzena, U.; Denurra, T.; Melloni, G.; Piroddi, A. M. *J. Org. Chem.* **1990**, *55*, 5386.

[13] (a) Azzena, U.; Denurra, T.; Melloni, G.; Fenude, E.; Rassu, G. *J. Org. Chem.* **1992**, *57*, 1444. (b) Azzena, U.; Denurra, T.; Melloni, G.; Fenude, E. *Gazz. Chim. Ital.* **1996**, *126*, 141.

[14] Bowers K. W. In *Radical Ions*; Kaiser, E. T., Kevan, L., Eds.; Wiley: New York, 1968, p 232.

10.1021/jo991059v CCC: $19.00

Scheme 1



ates,[15] although more recent literature[10−13] showed that, in most cases, this is an unnecessary hypothesis.

Remarkably, till recently, the role assigned to the metal in metal-promoted processes was merely that of acting as the electron source; no attention was given to its role in the rate-determining cleavage step. In particular, counterion-free radical anions have been usually invoked as key intermediates in the alkali metal-promoted reductive cleavage of ethers,[8,11] alkyl halides,[16] and sulfides.[17] Some years ago, Herold and co-workers[3] suggested that the position of the counterion (together with the relative orientation of the alkyl ether bond with respect to the benzene ring plane) was a main factor governing the regioselectivity of the radical anion fragmentation in alkyl aryl ethers. In particular, they proposed that dealkylation occurred when the countercation was close to the oxygen atom, but that dealkoxylation was the main process when the countercation moved to a position over the aromatic ring. On the other hand, Savéant and co-workers have recently demonstrated the effect of solvation and ion pairing on the rates of cleavage of radical anions of aryl halides.[18]

The "bond activation" achieved by electron transfer has thermodynamic origin; however, in aryl derivatives such as alkyl aryl ethers, the bond fragmentation requires that the excess of the electron density is transferred from the π^* system of the aryl ring to the area between the two atoms of the scissile bond. Such an electron density redistribution is responsible for the barrier observed in these processes. Considering the electron apportionment to the fragments, two modes of mesolytic scission are possible: the homolytic mode, where the charge density is largely localized on the same set of atoms before and after the scission (Scheme 1A), and the heterolytic mode, where the spin density is similarly "regioconserved" (Scheme 1B). Both cleavages show distinct properties, and in this context Guthrie and Maslak proposed the "spin regioconservation principle" from studies on benzyl aryl ethers.[19] These authors showed the existence of an intrinsic kinetic barrier for cleavage processes that do not regioconservate the spin density (homolytic cleavage mode, Scheme 1A). In Scheme 1 the two thermodynamically allowed fragmentation processes for alkyl aryl ether radical anions are described. The alkyl−O bond cleavage corresponds to a "homolytic" cleavage (Scheme 1C) that does not regioconservate the spin density and should therefore show an intrinsic kinetic barrier. On the other hand, the less favorable (from a thermodynamic point of view) aryl−O bond cleavage corresponds to a "heterolytic" cleavage (Scheme 1D), and therefore no extra kinetic barrier should exist in this case. This situation is reflected in the behavior of alkyl nitrophenyl ether radical anions, which are inert toward any fragmentation.[20]

Recently, some of us predicted that the alteration of the "normal" electron distribution of a charged intermediate through electrostatic interactions ("topologically controlled Coulombic interactions", TCCI)[20a,b] could lead to previously unknown processes. Following this idea, the previously unknown reductive cleavage of alkyl nitrophenyl ethers[20] and the change of regioselectivity in the reductive fragmentation of other ethers have been achieved.[21] On the basis of theoretical calculations,[20b] we have proposed that a positive noncoordinating charge (aminium radical cation or ammonium cation) placed in the neighborhood of the alkyl−oxygen bond reduces the intrinsic barrier for the intramolecular electron transfer $\pi^*-\sigma^*$ by stabilizing the σ^* state through electrostatic interactions. It seems that electrostatic effects allows the restriction imposed by the "spin regioconservation effect" to be overcome so that "homolytic" mesolytic cleavages become competitive under conditions where only the "heterolytic" cleavages are normally observed.

On the other hand, it has been also recently demonstrated that in some particular "heterolytic" mesolytic cleavage of ethers, lithium plays a key role in promoting the cleavage by acting as an internal Lewis acid in assisting the departure of the leaving group.[22]

We present here studies that indicate that the properties of the countercation (as a Lewis acid or just electrostatic) and the type and topology of ion pairs have a decisive influence on the evolution of radical anions, and we wish to introduce electrostatic catalysis as a distinct concept from the more commonly considered electrophilic catalysis when dealing with the effects of cations on chemical reactions. Indeed, our results indicate that "homolytic" mesolytic cleavages are mainly dependent on electrostatic catalysis, whereas "heterolytic" mesolytic cleavages show a strong dependence on electrophilic catalysis (Lewis acids). This study has been carried out with a single type of substrate, alkyl 2,6-diphenylphenyl ethers (Scheme 2). These substrates have a convenient reduction potential that allows both chemical (alkali metals) and electrochemical (cyclic voltametry and preparative electrolysis) studies to be carried out and compared. In addition, the presence of the phenyl rings in the 2 and 6 positions places the O−Me bond out of the plane of the central phenyl ring, thus eliminating the possible ambiguity derived from the existence of several conformers, which could be an additional factor contrib-

---

(15) (a) Testaferri, L.; Tiecco, M.; Tingoli, M.; Chianelli, D.; Montanucci, M. *Tetrahedron* **1982**, *38*, 3687. (b) Itoh, M.; Yoshida, S.; Ando, T.; Miyaura, N. *Chem. Lett.* **1976**, 271. (c) Eisch, J. J. *J. Org. Chem.* **1963**, *28*, 707. (d) Birch, A. J. *J. Chem. Soc.* **1947**, 102. (e) Birch, A. J. *J. Chem. Soc.* **1944**, 430.

(16) Garst, J. F. *Acc. Chem. Res.* **1971**, *4*, 400.

(17) (a) Screttas, C. G.; Screttas, M. M. *J. Org. Chem.* **1978**, *43*, 1064. (b) Cohen, T.; Bupathy, M. *Acc. Chem. Res.* **1989**, *22*, 152. (c) Severin, M. G.; Farnia, G.; Vianello, E.; Arevalo, M. C. *J. Electroanal. Chem.* **1988**, *251*, 369. (d) Severin, M. G.; Arevalo, M. C.; Farnia, G.; Vianello, E. *J. Phys. Chem.* **1987**, *91*, 466. (e) Arevalo, M. C.; Farnia, G.; Severin, M. G.; Vianello, E. *J. Electroanal. Chem.* **1987**, *220*, 201. (f) Griggio, L.; Severin, M. G. *J. Electroanal. Chem.* **1987**, *223*, 185.

(18) Andrieux, C. P.; Robert, M.; Savéant, J.-M. *J. Am. Chem. Soc.* **1995**, *117*, 9340.

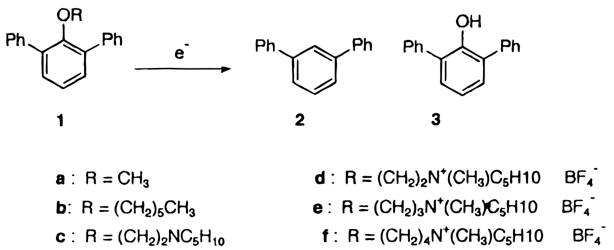
(19) (a) Maslak, P.; Guthrie, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 2628. (b) Maslak, P.; Guthrie, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 2637.

(20) (a) Cayón, E.; Marquet, J.; Lluch, J. M.; Martin, X. *J. Am. Chem. Soc.* **1991**, *113*, 8970. (b) Marquet, J.; Cayón, E.; Martín, X.; Casado, F.; Gallardo, I.; Moreno, M.; Lluch, J. M. *J. Org. Chem.* **1995**, 60, 3814. (c) Gonzalez-Blanco, R.; Bourdelande, J. L.; Marquet, J. *J. Org. Chem.* **1997**, *62*, 6910.

(21) Azzena, U.; Casado, F.; Fois, P.; Gallardo, I.; Pisano, L.; Marquet, J.; Melloni, G. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2563.

(22) Saá, J. M.; Ballester, P.; Deyá, P. M.; Capó, M.; Garcías, X. *J. Org. Chem.* **1996**, *61*, 1035.

Scheme 2



uting to the kinetic barriers in the intramolecular electron-transfer step.

Results

1. Studies on the Lithium-Promoted Reductive Cleavage of Alkyl 2,6-Diphenylphenyl Ethers (1). In Table 1 the reductive cleavage of 2,6-diphenylanisole (**1a**) with lithium in ethereal solvents and under different conditions is described. Formation of major amounts of *m*-terphenyl (**2**) (dealkoxylation) was observed in all the cases. The reaction was completely regioselective in THF (experiment 1), but a significant amount of 2,6-diphenylphenol (**3**) (dealkylation) was obtained when a more solvating solvent, such as DME (which favors the formation of solvent separated ionic pairs), was used (experiment 2). This trend was confirmed by carrying out the reaction in the presence of 12-crown-4 (experiment 3), which led to 43% of dealkylation still with complete conversion of the starting material. Related results have been reported for the reductive cleavage of several alkyl aryl ethers with alkali metals in polar aprotic solvents such as HMPA,[15a] where only dealkylation products were obtained.

A similar situation was found when the ionic strength of the THF solution was increased by using lithium tetrafluoroborate in what seems to be a nonspecific salt effect (experiment 4). However, experiment 5 shows a very interesting specific salt effect by the tetraalkylammonium cation. Thus, the reaction carried out (experiment 5) in the presence of tetrabutylammonium tetrafluoroborate (same concentration as that of lithium tetrafluoroborate used in experiment 4) was significantly slower and, remarkably, afforded only the dealkoxylation product. It is well-known[23,24] that tetraalkylammonium cations in THF displace lithium cations from contact ionic pairs with large, delocalized anions, which is the case of the radical anion of 2,6-diphenylanisole. The result described in experiment 5, when compared with those of experiments 1−4, demonstrates on one side the dependence of the dealkoxylation reaction on the presence of the alkali cation and on the other side, the reluctance of the radical anion of 2,6-diphenylanisole to undergo dealkylation at the contact ionic pair stage.

To test the hypothesis that the aryl−O cleavage under our conditions happens at the radical anion level, we carried out our reactions in the presence of isotopically labeled hydrogen atom sources. The cleavage at the radical anion level leads to an aryl σ-radical that we would expect to be at least partially trapped by the isotopically labeled hydrogen atom source, despite its easy reduction by the alkali metal. On the other hand, cleavage at the dianion level would lead to an aryl σ-anion and no effect of the isotopically labeled hydrogen atom source would be expected in the outcome of the reaction. When experiment 1 of Table 1 was repeated in THF-d_8, 23% yield of deuterium-labeled *m*-terphenyl (**2**) was obtained (^{1}H NMR analysis). This result is at variance with what it is reported for the reduction of anisole with potassium in isooctane,[13a] where the hydrogen atoms come from the departing methoxyde group and no hydrogen atoms from the solvent are incorporated. To test this second possibility, the same reaction was repeated using 2,6-diphenylphenyl methyl-d_3 ether. In this case, a 10% yield of deuterium-labeled *m*-terphenyl was obtained (^{1}H NMR analysis). These results strongly support the hypothesis that the cleavage happens at the radical anion level.

In experiment 6, the corresponding reaction of *N*-methyl-*N*-[2-(2,6-diphenylphenoxy)ethyl]piperidinium tetrafluoroborate (**1d**) is described, where a very significant amount (41%) of dealkylation product is obtained. The obvious interpretation is that the short TCCI chain is not able to reproduce the geometry of the tight ionic pair but interferes with the lithium cation to afford the reaction of a solvent-separated-like ionic pair responsible for the dealkylation process.

Experiments 7−12 (Table 1), carried out under homogeneous conditions (catalytic amounts of naphthalene), show exactly the same trend of the reactions carried out under heterogeneous conditions, although with a lower regioselectivity, being possible in this case by using a short TCCI chain to achieve complete dealkylation (experiment 10). The smooth change in regioselectivity observed in these experiments (experiments 10−12) suggests that the same mechanism is operating in all the cases, since an alternative Grob type cleavage mechanism, which would lead to ethene and *N*-methylpiperidine from the radical anion of substrate **1d**, can be ruled out since this would only operate in a substrate with a two-methylene unit linkage. In addition, evidence for the formation of products of disproportionation of an alkyl radical was obtained by careful examination of the fraction soluble in water of the reaction mixture of experiment 10. ^{1}H NMR analysis of this fraction showed the presence of the *N*-ethyl-*N*-methylpiperidinium (**5**) and *N*-ethenyl-*N*-methylpiperidinium (**6**) cations in the ratio ca. 1:1 (Scheme 3).

2. Studies on the Electrochemically Promoted Reductive Cleavage of Alkyl 2,6-Diphenylphenyl Ethers. Cyclic voltammetry curves of substrates **1a** and **1d** (short TCCI alkyl chain) in DMF at two different sweep rates are shown in Figure 1. Substrate **1a** shows a reversible (one electron) reduction wave ($E° = -2.54$ V vs SCE) in both cases (Figure 1A,B); on the other hand, substrate **1d** shows an irreversible (two electrons) reduction wave at a slow sweep rate (0.1 V s^{-1}, Figure 1C) that changes to a slightly reversible wave (one electron) at a faster sweep rate (Figure 1D). In Figure 2 the variation of $i_p/cv^{1/2}$ (the current function) with respect to log v is shown for substrate **1d**, demonstrating the change from a reversible one-electron process at fast sweep rate to a two-electron irreversible process when slower sweep rates are used.

The reduction peak potential for the *N*-methyl-*N*-[2-(2,6-diphenylphenoxy)ethyl]piperidinium tetrafluoroborate (**1d**) was measured as a function of sweep rate and concentration in DMF to determine the molecular order

---

(23) Smid, J. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 112.
(24) Jensen, S.; Parker, V. D. *J. Am. Chem. Soc.* **1975**, *97*, 5211.

Table 1. Lithium-Promoted Reductive Cleavage of Alkyl 2,6-Diphenylphenyl Ethers (Scheme 2)

					products	
expt	subst	R	conditions[a]	conversion (%)	**2** (%)	**3** (%)
1	**1a**	CH_3	THF, 24 h	100	100	
2	**1a**	CH_3	DME, 24 h	100	81	19
3	**1a**	CH_3	THF, 24 h 12-crown-4	100	57	43
4	**1a**	CH_3	THF, 24 h $LiBF_4$ (25 equiv)	100	85	15
5	**1a**	CH_3	THF, 24 h TBATFB (25 equiv)	43	43	
6	**1d**	$(CH_2)_2N^+(CH_3)C_5H_{10}$	THF, 24 h	100	56	41
7[b]	**1a**	CH_3	THF, 24 h naphthalene (10%)	100	70	30
8	**1b**	$(CH_2)_5CH_3$	THF, 24 h naphthalene (10%)	100	95	5
9	**1c**	$(CH_2)_2NC_5H_{10}$	THF, 24 h naphthalene (10%)	100	72	28
10[b]	**1d**	$(CH_2)_2N^+(CH_3)C_5H_{10}$	THF, 24 h naphthalene (10%)	100		100
11[b]	**1e**	$(CH_2)_3N^+(CH_3)C_5H_{10}$	THF, 24 h naphthalene (10%)	100	20	80
12	**1f**	$(CH_2)_4N^+(CH_3)C_5H_{10}$	THF, 24 h naphthalene (10%)	100	95	5

[a] Li, 2.5 equiv, rt. [b] Previously reported in ref 20.

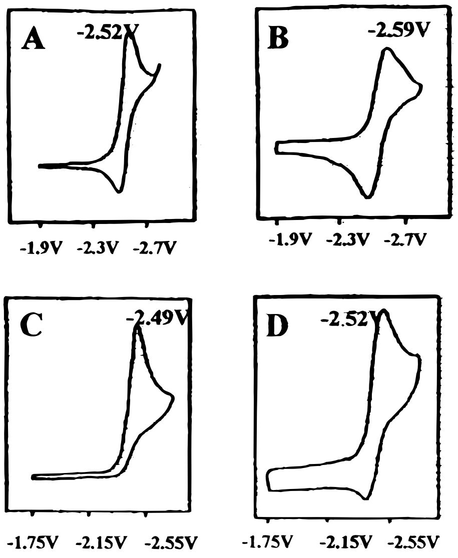
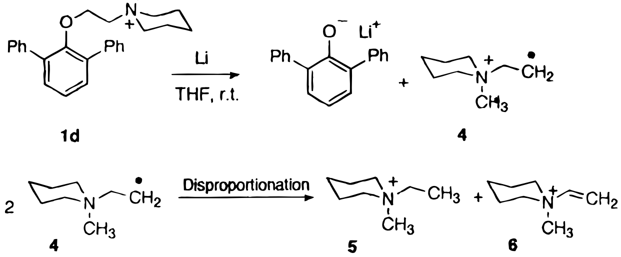


Figure 1. Cyclic voltammograms in DMF (0.1 M TBATFB, 13 °C): (A) 2,6-diphenylanisole (**1a**, 6.40 mM) at 0.1 V s^{-1} and (B) at 10 V s^{-1}; (C) *N*-[2-(2,6-diphenylphenoxy)ethyl]-*N*-methylpiperidinium tetrafluoroborate (**1d**, 2.99 mM) at 0.1 V s^{-1} and (D) at 10 V s^{-1}.

Scheme 3



for the disappearance of the radical anion. At relatively slow scan rates (i.e., 0.1−2.0 V s^{-1}) the peak potential (E_{pc}) shifted in the positive direction with decreasing scan rate (v) so that $dE_{pc}/d(\log v) = -29$ mV. The peak potential was independent of concentration over a concentration range of 1.01−7.08 mM. These data are consistent with a first-order chemical reaction following electron transfer in a sequential ECE type mechanism.[25]

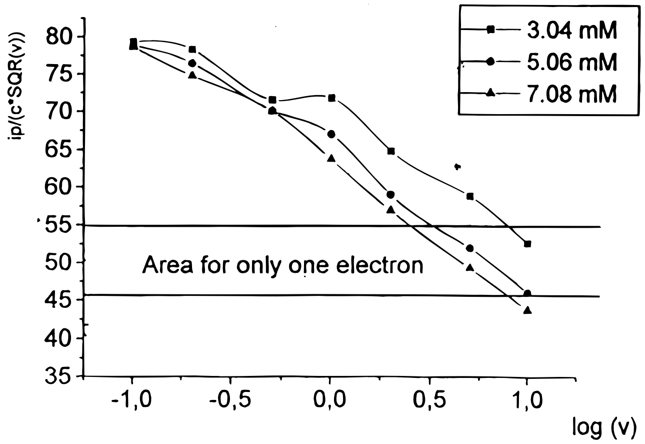


Figure 2. Variation of the current function with the sweep rate at different concentrations for *N*-[2-(2,6-diphenylphenoxy)ethyl]-*N*-methylpiperidinium tetrafluoroborate (**1d**).

In Figure 3, the corresponding cyclic voltammetries in THF are reported. In this solvent, substrate **1a** shows a less reversible behavior than in DMF (Figure 3A,B). However, in both cases a rather slow one-electron transfer was observed. In any case, it seems that the chemical process associated with the electron transfer corresponds to reduction of the solvent or of the supporting electrolyte rather than to any productive reaction (cleavage or reduction) from the substrate (see below, Table 3). With substrate **1d** (short TCCI chain), a significant dependence of the current function with the sweep rate was observed. Indeed, in a particular experiment in THF ([**1d**] = 3.01 mM), the value of $i_p/cv^{1/2}$ varied from 98.2 for $v = 0.1$ V s^{-1} (Figure 3C) to 58.9 for $v = 10$ V s^{-1} (Figure 3D), indicating the operation of a two-electron process when the sweep rate is slow enough that changes to a one-electron process at faster sweep rates. We assign the two-

---

(25) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods*; Wiley: New York, 1980; Chapter 11.

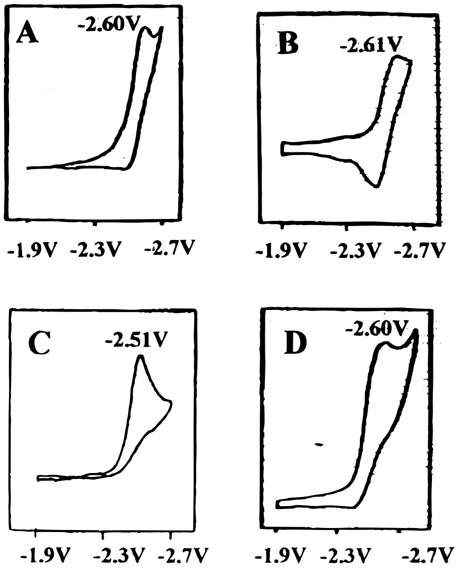


Figure 3. Cyclic voltammograms in THF (0.6 M TBATFB, 13 °C): (A) 2,6-diphenylanisole (**1a**, 2.10 mM) at 0.1 V s^{-1} and (B) at 10 V s^{-1}; (C) *N*-[2-(2,6-diphenylphenoxy)-ethyl]-*N*-methylpiperidinium tetrafluoroborate (**1d**, 5.03 mM) at 0.1 V s^{-1} and (D) at 10 V s^{-1}.

Table 2. Limiting Lifetimes for the Radical Anions of Substrates 1a and 1d at 13 °C, Measured by Cyclic Voltametry

entry	substrate	solvent	lifetime (τ) (ms)
1	**1a**	DMF	>200
2	**1a**	THF	50
3	**1d**	DMF	1
4	**1d**	THF	0.2

electron process to the cleavage of the radical anion of the substrate **1d** in an ECE type mechanism also in THF.

From the study of the variation of the cyclic voltammograms with the sweep rate, the radical anions limiting lifetimes indicated in Table 2 have been calculated. The introduction of the TCCI alkyl chain (substrate **1d**) significantly reduces the lifetime of the radical anion intermediate in all the cases.

In Table 3, the results of the preparative electrolysis at controlled potential (−2.6 V vs SCE) of substrates **1a** and **1d** in THF and DMF are reported (for comparison purposes, a charge consumption of 2.1 F was used in all except one of the cases of Table 3). The electrolysis of 2,6-diphenylanisole (**1a**) in THF (experiment 1) gives rise only to a trace of *m*-terphenyl (dealkoxylation). A trace amount of Birch reduction products could also be detected, but interestingly, no 2,6-diphenylphenol (dealkylation) was produced. This result (low Faradaic yield) confirms the reluctance of the radical anion of 2,6-diphenylanisole to undergo dealkylation at the contact ionic pair stage when a noncoordinating tetralkylammonium cation is the counterion. On the other hand, the corresponding electrolysis of **1a** in DMF afforded a 29% yield of 2,6-diphenylphenol (dealkylation), using the same applied potential and after the same current consumption. Traces of Birch reduction products could be detected also in this case by GC/MS analysis. Thus, the use of a solvent with better cation-solvating properties that would favor the presence of solvent-separated ionic pairs allows the intervention of the mechanistic pathway leading to dealkylation, but still with a low Faradaic yield. It is interesting to notice that in the absence of alkali metal no significant amount of dealkoxylation product was produced in any case.

No significant effect was observed when the electrolysis of **1a** was carried out (experiment 3) in THF in the presence of 2.8 equiv of lithium tetrafluoroborate, which is poorly soluble in THF. When the electrolysis in DMF was performed using lithium tetrafluoroborate as supporting electrolyte, the result was even worse than when a tetralkylammonium salt was used (experiment 4). In the first case, the result confirms that the lithium cation is not able to displace the tetrabutylammonium cation from the contact ionic pair with the aromatic radical anion in THF, and in the second the result probably means that, at the very low potential used, the lithium cation is partially reduced, consuming electricity in a nonproductive way. We have been unable to achieve electrochemically the conditions needed for the dealkoxylation process to be observed in a significant proportion. This confirms the crucial role played by the alkali cation, probably in a contact ionic pair, in these processes.

Experiments 5 and 6 in Table 3 correspond to reactions using *N*-methyl-*N*-[2-(2,6-diphenylphenoxy)ethyl]piperidinium tetrafluoroborate (**1d**) as starting material in THF and DMF, respectively. The reactions are now much more efficient, giving rise to 2,6-diphenylphenol (**3**) in very good yields (88% and 91%, respectively). No dealkoxylation product (*m*-terphenyl) could be detected. These results support the interpretation given for the corresponding reactions carried out under chemical conditions (experiments 6, 10, and 11 in Table 1). Thus, the short TCCI chain is not able to reproduce the geometry of the tight ion pair, but the internal ammonium cation competes efficiently with the external cations, precluding the formation of the contact ion pair with the external tetraakylammonium cation in the reaction carried out in THF. The high efficiency in the dealkylation process, observed in both reactions (experiments 5 and 6), can be explained by considering the intervention of “intramolecular solvent-separated-like ion pairs” of a very particular topology. Thus, in these intramolecular pairs, the positive charge must be located, as an average, much closer to the ether linkage than it is in an intermolecular solvent-separated ionic pair (experiment 2 and 4), and therefore the associated electrostatic effect on the ether bonds will be much more intense (see the Discussion). The necessity of two electrons (mechanism ECE) to drive the reaction to completion was strongly supported by the result of experiment 7 in Table 3. Thus, when only 1.1 F/mol was consumed, the yield of the reaction dropped to half.

Investigation of the fate of the alkyl chain after cleavage in these electrochemical experiments (experiments 5 and 6) was handicapped by the presence of a large excess of the tetraalkylammonium salt used as supporting electrolyte. Generally, the fraction of these reaction crudes soluble in water showed the presence of a complex mixture that was not studied further. In addition, ^1H NMR analysis of the mixture in experiment 6 showed the presence of a triplet at δ 1.0 that was attributed (comparison with an authentical sample) to the presence of *N*-ethyl-*N*-methylpiperidinium tetrafluoroborate (**5**) in the mixture. This is additional evidence for the occurrence of an ECE mechanism in these electrochemical reactions.

The results described in experiments 8 and 9 of Table 3, corresponding to the reactions of substrates **1e** (three

Table 3. Electrochemically Promoted Reductive Cleavage of Alkyl 2,6-Diphenylphenyl Ethers (Scheme 2)

				products	
expt	subst		conditions[a]	**2** (%)	**3** (%)
1	**1a**	CH_3	THF, TBATFB, 2.1 F	trace	
2	**1a**	CH_3	DMF, TBATFB, 2.1 F		29
3	**1a**	CH_3	THF, TBATFB LiTFB (*x* equiv), 2.1 F	trace	
4	**1a**	CH_3	DMF, LiTFB, 2.1 F		<5
5	**1d**	$(CH_2)_2N^+(CH_3)C_5H_{10}$	THF, TBATFB, 2.1 F		91
6	**1d**	$(CH_2)_2N^+(CH_3)C_5H_{10}$	DMF, TBATFB, 2.1 F		88
7	**1d**	$(CH_2)_2N^+(CH_3)C_5H_{10}$	DMF, TBATFB, 1.1 F		43
8	**1e**	$(CH_2)_3N^+(CH_3)C_5H_{10}$	DMF, TBATFB, 2.1 F		46[b]
9	**1f**	$(CH_2)_4N^+(CH_3)C_5H_{10}$	DMF, TBATFB, 2.1 F		59

[a] Controlled potential: −2.6 V relative to SCE at 13 °C. [b] Allyl 2,6-diphenylphenyl ether was also detected in this case.

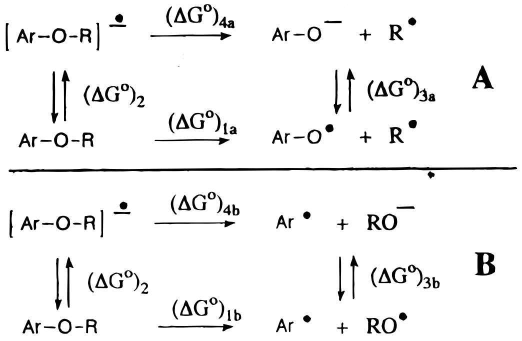


Figure 4. Thermodynamic cycles for calculation of free energy for C−O bond fragmentation in alkyl aryl ethers radical anions.

methylene units TCCI chain) and **1f** (four methylene units TCCI chain), respectively, indicate that the effect of the positive charge is smoothly reduced when its average distance to the ether bond increases. In the reaction carried out with substrate **1e**, another product, tentatively assigned to allyl 2,6-diphenylphenyl ether, was detected (it was not isolated from the mixture), in addition to 46% of phenol **3**. This constituted a significant difference from the other reactions reported in the Table 3. Considering the very low potential used in our reactions and the possibility that the allyl ether was produced by an elimination type reaction elicited by an electrogenerated base, we tested the stability of substrate **1e** in the presence of a very strong base such as potassium *tert*-butoxide in THF. Under these conditions **1e** gave rise to 13% of 2,6-diphenylphenol (**3**). In any case, the electrochemical reaction (experiment 8, Table 3) shows a significantly higher proportion of phenol, indicating that even though the elimination is in this particular case a competitive reaction, unimolecular cleavage must still be considered the main process from the radical anion.

Discussion

Before going into kinetic arguments, consideration of the thermodynamics for C−O bond fragmentation in the radical anions of our substrates provides a starting point to understand the regioselectivity preferences observed in our reactions. Figure 4 outlines the thermodynamic cycles that can be applied to calculate the standard free energy for C−O bond fragmentation, $(\Delta G°)_4$, from the radical anion, and Table 4 provides a tabular summary of the necessary equations and the calculated thermodynamic quantities.[26] Two modes of fragmentation are possible: (a) alkyl−O bond (homolytic fission) and (b) aryl−O bond (heterolytic fission). Three free energies are required for estimation of $(\Delta G°)_4$ (Table 4): the free energy for C−O bond homolysis in the neutral substrate, $(\Delta G°)_1$; the free energy for electrochemical reduction of the neutral substrate, $(\Delta G°)_2$; and the free energy for electrochemical reduction of one of the products of bond fission, $(\Delta G°)_3$. Table 4 provides a tabular summary of how each thermodynamic parameter was obtained or estimated. First, an estimate for the free energy of homolysis $(\Delta G°)_1$ was arrived at by taking the literature bond dissociation energies for anisole (Me−O,[27] 64 kcal/mol; Ph−O,[28] 98 kcal/mol) and using an entropy value which is typical[29] for C−O bond homolysis ($\Delta S \cong 17$ cal $mol^{-1}K^{-1}$; since both processes should show a similar entropy, the exact value is not very important for comparisons). These values lead to an estimate of $(\Delta G°)_{1a} \cong 59$ kcal/mol for the alkyl−O fission and $(\Delta G°)_{1b} \cong 93$ kcal/mol for the aryl−O fission. $(\Delta G°)_2$ was calculated from the experimentally measured $E°$ value (−2.54 V for the reduction of 2,6-diphenylanisole, relative to SCE, and −2.30 V, relative to NHE), and $(\Delta G°)_{3a}$ and $(\Delta G°)_{3b}$ were calculated from the reported standard potentials for the oxidation of 2,6-diphenylphenolate ($E° = 0.08$ V, relative to SCE; 0.32 relative to NHE)[30] and methoxide anion ($E° = 0.06$ V, relative to SCE; 0.30 relative to NHE),[31] respectively, both in acetonitrile. The values obtained for $(\Delta G°)_4$ indicate that demethylation of the radical anion of 2,6-diphenylanisole is a slightly downhill process [$(\Delta G°)_{4a} \cong -1$ kcal/mol], whereas the alternative demethoxylation process (in the absence of any assistance by the

Table 4. Thermodynamics of Carbon−Oxygen Bonds Fragmentation Estimated by Thermochemical Cycles[a]

parameter	value (kcal mol^{-1})	method of calculation
$(\Delta G°)_{1a}$	59	estimated as described in the text
$(\Delta G°)_{1b}$	93	estimated as described in the text
$(\Delta G°)_2$	53	$(\Delta G°)_2 = -F(E°)_2$, where $(E°)_2 = -2.30$ V
$(\Delta G°)_{3a}$	−7	$(\Delta G°)_{3a} = -F(E°)_a$, where $(E°)_a = 0.32$ V[4]
$(\Delta G°)_{3b}$	−7	$(\Delta G°)_{3b} = -F(E°)_b$, where $(E°)_a = 0.30$ V[14]
$(\Delta G°)_{4a}$	−1	$(\Delta G°)_{4a} = (\Delta G°)_{1a} + (\Delta G°)_{3a} - (\Delta G°)_2$
$(\Delta G°)_{4b}$	33	$(\Delta G°)_{4b} = (\Delta G°)_{1b} + (\Delta G°)_{3b} - (\Delta G°)_2$

[a] Refer to Figure 4 for definition of thermodynamic quantities. *F* is the Faraday constant (23.06 kcal mol^{-1} V^{-1}). In this particular table the potentials are reported relative to NHE.

---

[26] Wayner, D. D. M.; Parker, V. D. *Acc. Chem. Res.* **1993**, *26*, 287.

[27] Suryan, M. M.; Kafafi, S. A.; Stein, S. E. *J. Am. Chem. Soc.* **1989**, *111*, 1423.

[28] *Handbook of Chemistry and Physics*, 66th ed.; CRC Press: Boca Raton, 1985−1986; F-193.

[29] Andersen, M. L.; Long, W.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1997**, *119*, 6590.

[30] Hapiot, P.; Pinson, J.; Yousfi, N. *New J. Chem.* **1992**, *16*, 877.

[31] Eberson L. *Acta Chem. Scand.* **1984**, *B38*, 439.

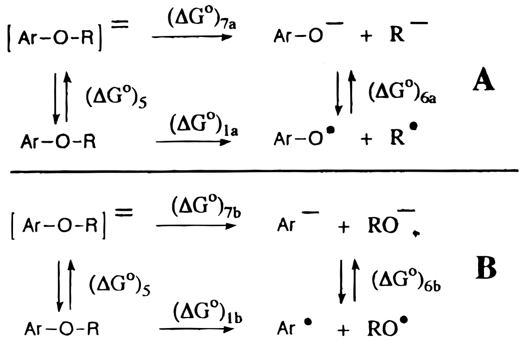


Figure 5. Thermodynamic cycles for calculation of free energy for C–O bond fragmentation in alkyl aryl ethers dianions.

metal) is strongly uphill [$(\Delta G°)_{4b} \cong +32$ kcal/mol), thus showing that the system, when no external influences are present, has a significant thermodynamic driving force in favor of demethylation.

Even though dianions[15] have not been considered lately as possible intermediates in these types of reactions, and our electrochemical results indicate that dealkylation must be produced from the radical anion, the hypothetical intervention of a dianion as intermediate in the dealkoxylation processes that we observe in the presence of alkali metals cannot be completely ruled out in the light of our preparative results (Table 1). Figure 5 outlines the thermodynamic cycles that can be applied to calculate the standard free energy for C–O bond fragmentation $(\Delta G°)_7$ from the dianion. The second reduction wave of 2,6-diphenylphenyl ethers is very close to the wall and no reliable measurements can be carried out on it. In any case, considering $(\Delta G°)_5$ is common to the two cycles (A and B) and that $(\Delta G°)_{6a} \cong (\Delta G°)_{6b}$, an important difference (>30 kcal mol^{-1}) in the thermodynamic driving force favoring demethylation would also exist in this case [$(\Delta G°)_{7a} \gg (\Delta G°)_{7b}$]. In the absence of external influences, the higher free energy of the dianion (reactivity), when compared to the radical anion, could justify a lower selectivity in the reaction but never the complete change of regioselectity observed when an alkali metal is the reducing agent. Therefore, it seems that there is no need to postulate a dianion as an intermediate and that the alkali metal must play a specific role on the radical anion other than simply acting as a reducing agent. To be more comfortable with this interpretation, the radical anion hypothesis was tested by carrying out experiments in the presence of isotopically labeled hydrogen atom sources. Deuterium incorporation into *m*-terphenyl in the reactions in the presence of alkali metals, carried out in THF-d_8 or using 2,6-diphenylphenyl methyl-d_3 ether as a substrate, strongly supports the operativity of the 2,6-diphenylphenyl radical as intermediate and therefore the occurrence of the cleavage at the radical anion level.

One extra possibility to consider is that the dealkoxylation took place in the dimeric form of radical anion[32] and that the counterion play their role in shifting the monomer–dimer equilibrium. The absence of concentration effects in the reactions described in Table 1 allows this possibility to be discarded. Therefore, an aniomesolytic cleavage of the radical anion is the best mechanistic hypothesis also for the dealkoxylation process.

As indicated, our preparative results show exclusive demethoxylation with lithium as reducing agent in THF (Table 1) or practically no reaction (trace of demethoxylation) under electrochemical conditions in the same solvent (experiment 1, Table 3). Cyclic voltametry experiments (Figure 1, Table 2) confirm the stability of the radical anion of 2,6-diphenylanisole toward fragmentation in THF, probably with a slow evolution through reduction of the solvent or of the supporting electrolyte. Interestingly enough, when the reaction with lithium was carried out by trying to mimic the conditions of the electrochemical experiments (the presence of tetrabutylammonium tetrafluoroborate, experiment 5, Table 1), the reaction slowed, but demethoxylation was still the exclusive fragmentation process. This result points out that the alkali cation are responsible for the success of the demethoxylation reaction and confirms the inertia of the radical anion to undergo demethylation, although this is the thermodynamically preferred process.

From the point of view of the initial spin delocalization, the vast majority of aniomesolytic reactions result in departure of a negatively charged fragment. It has been postulated[19] that the fragmentation process is controlled by factors other than product stability, and a mode of cleavage requiring a charge transfer across the scissile bond is kinetically preferred (the "spin regioconservation principle").

Dissociating π-radical anions can be divided into two different structural groups,[33-35] depending on whether the possibility of overlap between the π-network and the σ^* of the scissile bond exists (like in benzylic halides) or it is precluded (like in aryl halides). In the radical anions of aryl alkyl ethers, such as 2,6-diphenylanisole, the two different situations coexist, as they correspond to the two different C–O bonds. Thus, the cleavage of the aryl–O bond, orthogonal to the π-system bearing the unpaired electron, must involve, to occur, a discrete intramolecular $\pi^*-\sigma^*$ electron-transfer step (if the σ^* state is a local minimum)[36] or at least a large intramolecular $\pi^*-\sigma^*$ electron-transfer component (if the σ^* state is a fragmentative one). As to the alkyl–O bond, the possible direct overlap between the orbitals of interest should increase as the reaction progresses toward a resonance-stabilized anion or radical. The transition state for the cleavage of this type of bond may be described in terms of two different electronic configurations.[35,37] One of these configurations places significant negative charge on the departing fragment and has been compared with an elimination reaction. In our case, however, where the polarization of the bond is opposite to that of benzylic halides, this configuration can be neglected. The second configuration may be represented as a σ^* radical anion. The fragmentation is kinetically controlled by the ability of the system to delocalize the charge across the scissile bond. For radical anions where this tendency is reinforced by preexisting polarization of the scissile bond and by thermodynamic stability of the product to be formed, the reaction is facile. However, if such a charge shift leads to extensive "counterthermodynamic" charge accumula-

---

(32) Koppang, M. D.; Woolsley, N. F.; Bartak, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 4692.

(33) Dressler, R.; Allan, M.; Haselbach, E. *Chimia* **1985**, *39*, 385.

(34) Symons, M. C. R.; Bowman, W. R. *J. Chem. Soc., Perkin Trans. 2* **1988**, 584.

(35) Maslak, P.; Narvaez, J. N.; Kula, J.; Malinski, D. S. *J. Org. Chem.* **1990**, *55*, 4550.

(36) Pierini, A. B.; Duca Jr., J. S. *J. Chem. Soc., Perkin 2* **1995**, 1821.

(37) Guthrie, R. D.; Shi, B. *J. Am. Chem. Soc.* **1990**, *112*, 3136.

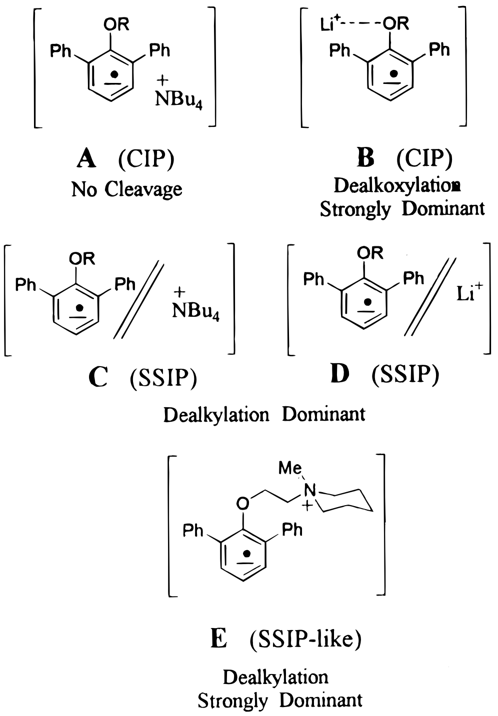


Figure 6. Ionic pairs involved in the reductive cleavage of alkyl 2,6-diphenylphenyl ethers.

tion on the leaving fragment, as in our case, an alternative mode of scission becomes dominant.[35] This mode is similar to the one described for aryl−O bonds and would involve a large component of $\pi^*-\sigma^*$ electron transfer followed by dissociation of the three-electron bond. Therefore, even though the two types of bonds involved in our study are very different, their mode of fragmentation must be similar, involving in both cases a $\pi^*-\sigma^*$ electron-transfer step or component in the transition state.

Our results confirm that the mesolytic cleavage of the radical anion of 2,6-diphenylanisole is a kinetically controlled process, forbidden in the absence of external influences (experiment 1, Table 3), probably due to the unfavorable $\pi^*-\sigma^*$ electron-transfer energetics for the two alternatives (aryl−O or alkyl−O). The results reported in Tables 1 and 3 can be explained by considering different types of ionic pairs and the distinct electrophilic or electrostatic effect of the counterion in each case.

In Figure 6, the different ionic pairs likely involved in our reactions are described. The starting point would be contact ionic pair **A** (CIP, Figure 6), which would correspond to the case described in the experiment 1 of Table 3. It is well-known that tetraalkylammonium cations form contact ion pairs with delocalized anions in solvents of low polarity such as THF.[23,24] The electrochemical results suggest that this ionic pair is stable toward fragmentation, probably due to the electrostatic stabilization of the π^* state by the noncoordinating counterion in the tight ionic pair. However, when the counterion is a coordinating alkali cation, such as lithium, regioselective dealkoxylation is observed (experiment 1, Table 1). In this case a contact ion pair such as **B** (Figure 6) would be involved, where the lithium cation coordinated to the oxygen atom of the ether bond would be probably acting in two ways, first allowing the population of the σ^* state by electrostatic stabilization of this state (reducing the barrier for the $\pi^*-\sigma^*$ intramolecular electron transfer, vide infra)[20b] and afterward acting as a handle (Lewis acid) to which the leaving group RO^- adheres prior to detachment. Hence, we interpret the result of experiment 1 in Table 1 as a joint electrostatic plus electrophilic catalysis by the countercation in a contact ionic pair.

When solvents with stronger solvating properties are used, the demethylation process starts to take place. Indeed, the electrochemical reduction of 2,6-diphenylanisole in DMF leads in a poorly efficient process to 2,6-diphenylphenol (experiment 2, Table 3). In the same direction, when the chemical reductions are carried out in DME, in the presence of crown ethers, or in the presence of naphthalene (experiments 2, 3, 7, 8, and 9, Table 1), significant amounts of demethylation product are obtained. Maercker[10] had already noticed that solvent-separated ionic pairs favored the dealkylation process, and Testaferri et al.[14a] had reported major dealkylation in several reductive cleavages of alkyl aryl ethers carried out with sodium in a strongly cation-solvating solvent such as HMPA. From the results reported in Tables 1 and 3, it is evident that electrostatic interactions in the solvent-separated ionic pairs are responsible for the operation of the dealkylation pathway when it is operative. Thus, on the basis of theoretical calculations,[20b] we have proposed that a positive noncoordinating charge in the neighborhood of the ether bond reduces the barrier for the intramolecular electron transfer $\pi^*-\sigma^*$ by stabilizing the σ^* state through attractive electrostatic interactions. This is just the situation in the solvent-separated ionic pairs, where coordination with the ether oxygen bond is not possible. Both intramolecular $\pi^*-\sigma^*$ electron transfers should show electrostatic catalysis in the solvent-separated ionic pairs **C** and **D** (SSIP-**C**, SSIP-**D**, Figure 6), in equilibrium with the corresponding contact ionic pairs **A** and **B**, dealkylation probably being the favored reaction from the SSIP since electrostatic catalysis reduces the kinetic control and dealkylation is the thermodynamically preferred process.

Experiments 5 and 6 in Table 3 confirm the importance of the electrostatic interactions in the outcome of the fragmentation reaction. Cyclic voltammetry experiments show also a significant reduction in the lifetime of the radical anion of these substrates. In these cases, the SSIP must have a particular topology, with the positive charge concentrated in the neighborhood of the alkyl ether bond (SSIP-like-**E**, Figure 6). Therefore, the electrostatic interaction is now much more directional, the effect on the barrier of the $\pi^*-\sigma^*$ (alkyl bond) electron transfer being much larger than on the barrier of the $\pi^*-\sigma^*$(aryl bond) electron transfer, thus justifying the very efficient dealkylation process observed in these cases. A related situation is found in the chemical reduction (experiments 6 and 10, Table 1), the lower selectivity observed in experiment 6 probably being due to the fact that in this case a competition between two productive ionic pairs (CIP-**B** leading to dealkoxylation, and SSIP-**E** leading to dealkylation) can be envisaged. A parallel competition in the electrochemical experiments would involve a productive ionic pair, SSIP-**E**, and a nonproductive one, CIP-**A**, thus justifying the very high selectivity observed in these experiments (Table 3). The specific effect of the TCCI smoothly disappears upon increasing its length (experiments 10−12 in Table 1 and experiment 6, 8, and 9 in Table 3).

In conclusion, the first multiapproach (chemical, electrochemical, TCCI[20b]) to the reductive fragmentation of alkyl aryl ethers has provided insight into the mechanistic details that govern the regioselectivity of these reactions and has allowed the proposal of electrostatic and electrophilic catalysis as distinct contributions that affect the reactivity of the intermediate radical anions. Both fragmentations (alkyl−O and aryl−O) must involve an intramolecular $\pi^*-\sigma^*$ electron-transfer step, or at least a large component of $\pi^*-\sigma^*$ electron transfer in the transition state. The fragmentation of alkyl aryl ethers can thus be analyzed in terms of the factors that alter the $\pi^*-\sigma^*$ electron-transfer step for both processes and the evolution of the σ^* state. Thus, contact ion pairs (CIP) seem to evolve in a very different way, depending on the coordinating properties of the cation. CIP of noncoordinating cations (tetralkylammonium) are stable while CIP of cations with coordinating abilities (lithium) give rise to dealkoxylation in a process under kinetic control, catalyzed by the electrostatic and the electrophilic properties of the cation. On the other hand, the cases in which solvent-separated ionic pairs (SSIP) are involved give rise to dealkylation. Comparisons with experiments carried out with TCCI compounds, with well-defined electrostatic interactions in the ionic pair, have led to the identification of electrostatic interactions in the SSIP as the main responsible for the observed major dealkylation. This electrostatic catalysis would act by lowering the barrier of the intramolecular $\pi^*-\sigma^*$ electron transfer processes, reducing the kinetic control of the reaction (in its absence the alkyl−O bond cleavage is a forbidden process) in such a way that the thermodynamically more stable product is produced, overcoming the spin regioconservation principle.

It is interesting to notice that the regioselectivity of the mesolytic fragmentation can be completely reversed by playing with appropriately designed intermediate ionic pairs CIP-**B** and SSIP-**E** (Figure 6) and the associated kinetic or thermodynamic control for the reaction.

Experimental Section

General Considerations. ^{1}H NMR were recorded at 250 or 400 MHz and the ^{13}C NMR at 62.5 or 100 MHz for solutions in $CDCl_3$ and DMSO-d_6 with tetramethylsilane (TMS as an internal standard). Flash chromatography was performed on silica gel (ICN Silica 32−63, 60 Å). Elemental analyses were performed at the Microanalytical Laboratory of the Dipartimento di Chimica, Università di Sassari, or at the "Servei d'Analisi Química de la Universitat Autònoma de Barcelona".

Synthesis of Starting Materials and Reaction Products. *m*-Terphenyl (**2**) and 2,6-diphenylphenol (**3**) were purchased from Aldrich. 2,6-Diphenylanisole (**1a**) was prepared according to a literature method.[38] 2,6-Diphenylphenyl hexyl ether (**1b**) and *N*-(−2-(2,6-diphenylphenoxy)ethyl)-*N*-methylpiperidinium tetrafluoroborate (**1d**) were prepared as previously described.[21]

***N*-[2-(2,6-Diphenylphenoxy)ethyl]piperidine** (**1c**) was prepared by the reaction of the sodium salt of **3** (prepared by treatment of **3** with excess NaH in THF) with N-(2-chloroethyl)piperidine (purchased from Aldrich) in THF under reflux for 15 h and purified by bulb-to-bulb distillation at 1 Torr (bath temperature, 210 °C): ^{1}H NMR ($CDCl_3$) δ 1.21−1.42 (m, 6H), 1.90−2.02 (m, 4H), 2.11 (t, $J = 6.0$ Hz, 2H), 3.32 (t, $J = 6.0$ Hz, 2H), 7.19−7.27 (m, 1H), 7.29−7.37 (m, 4H), 7.38−7.46 (m, 4H), 7.58−7.65 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 24.16, 25.72, 54.26, 58.37, 70.18, 124.19, 125.05, 128.01, 129.51, 130.22, 136.10, 138.67, 154.02. Anal. Calcd for $C_{25}H_{27}NO$: C, 83.99; H, 7.61; N, 3.92. Found: C, 83.72; H, 7.50; N, 3.85. The *N*-methylpiperidinium tetrafluoroborates **1e** and **1f** were prepared by the method described in ref 20b, through the corresponding amines, as white solids, and purified by recrystallization from Me_2CO/Et_2O.

***N*-[2-(2,6-diphenylphenoxy)propyl]piperidine** was purified by bulb-to-bulb distillation at 1 Torr (bath temperature, 230 °C): ^{1}H NMR ($CDCl_3$) δ 1.21−1.43 (m, 8H), 1.83 (br t, $J =$ 7.8 Hz, 2H), 2.03 (br s, 4H), 3.16 (t, $J = 6.3$ Hz, 2H), 7.15 (dd, $J = 7.2$ Hz, $J = 6.6$ Hz, 1H), 7.23−7.40 (m, 8H), 7.52, 7.59 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 24.33, 25.79, 27.10, 54.18, 55.82, 71.69, 124.07, 126.95, 127.96, 129.45, 130.11, 136.02, 138.70, 153.87. Anal. Calcd for $C_{26}H_{29}NO$: C, 84.06; H, 7.87; N, 3.77. Found: C, 83.90; H, 7.92; N, 3.65.

***N*-[-3-(2,6-Diphenylphenoxy)propyl]-*N*-methylpiperidinium tetrafluoroborate** (**1e**): mp 179−182 °C; IR (KBr) 3048, 2939, 1106, 1068, 1044, 761, 705 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.36−1.80 (m, 8H), 2.77 (s, 3H), 2.77−2.84 (m, 2H), 2.95−3.05 (m, 2H), 3.11−3.50 (m, 4H), 7.20−7.60 (m, 13H); ^{13}C NMR (DMSO-d_6) δ 19.3, 20.6, 22.0, 46.9, 60.1, 60.3, 69.8, 124.9, 127.6, 128.5, 129.3, 130.4, 135.4, 138.2, 153.1. Anal. Calcd for $C_{27}H_{32}NOBF_4$: C, 68.51; H, 6.81; N, 2.96. Found: C, 68.09; H, 7.03; N, 2.88.

***N*-[2-(2,6-Diphenylphenoxy)butyl]piperidine** was purified by bulb-to-bulb distillation at 1 Torr (bath temperature, 230 °C): ^{1}H NMR ($CDCl_3$) δ 1.08−1.19 (m, 4H), 1.32−1.45 (m, 2H), 1.45−1.59 (m, 4H) 1.88−2.02 (m, 2H), 2.19 (s, 4H) 3.12−3.22 (m, 2H), 7.17−7.22 (m, 1H), 7.28−7.36 (m, 4H), 7.36−7.46 (m, 4H), 7.59−7.66 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 23.14, 24.43, 25.89, 27.90, 54.27, 58.78, 72.92, 123.99, 126.92, 127.92, 129.34, 129.44, 130.11, 136.02, 138.75, 154.02. Anal. Calcd for $C_{27}H_{31}NO$: C, 84.11; H, 8.10, N, 3.63. Found: C, 83.95; H, 7.90; N, 3.58.

N-[-4-(2,6-Diphenylphenoxy)butyl]-*N*-methylpiperidinium tetrafluoroborate (**1f**): mp 230−231.5 °C; IR (KBr) 3045, 2948, 1063, 760, 740 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.98−1.28 (m, 4H), 1.37−1.82 (m, 6H), 2.80 (s, 3H), 2.92−3.15 (m, 6H), 3.21 (t, $J = 5$ Hz, 2H), 7.23−7.61 (m, 13H); ^{13}C NMR (DMSO-d_6) δ 18.1, 19.3, 20.8, 26.2, 47.1, 60.1, 62.1, 72.2, 124.7, 127.4, 128.4, 129.4, 130.4, 135.7, 138.5, 153.5.

General Procedure for the Lithium-Promoted Reductive Cleavage of Compounds (1a−f) Described in Table 1. Li metal [50 mg atom, 1.15 g of a 30% dispersion in mineral oil (Aldrich),[39] 2.5 equiv] was placed under Ar in a two-necked flask equipped with reflux condenser and magnetic stirrer, washed with anhydrous THF (3 × 10 cm^3), and suspended in anhydrous THF (30 cm^3). To this suspension, cooled to 25 °C if necessary, the appropriate substrate (**1a**−**f**) (20 mmol) was added at once without solvent, and the mixture was stirred at 25 °C for 24 h. The mixture was cooled to 0 °C and quenched by slow dropwise addition of H_2O (10 cm^3) (**Caution! Strongly exothermic!**). After 1 h of stirring at room temperature the mixture was neutralized with aqueous HCl, cooled, and extracted with Et_2O (3 × 30 cm^3); the organic layer was then separated and dried ($CaCl_2$) and the solvent evaporated. The ratio between the reaction products (Table 1) was determined on the crude reaction mixture by ^{1}H NMR; this ratio was confirmed, and the yields were determined by separation of the reaction products on flash chromatography, with mixtures of hexane and EtOAc as eluent. In the case of the *N*-methylpiperidinium tetrafluoroborates (**1d**−**f**), the aqueous layer after the Et_2O extraction was evaporated to dryness to afford an untractable sticky residue; any attempt to purify this mixture failed.

Electrochemical Measurements. The electrochemical cell and measurement procedures for CV have been described previously.[40] All potentials are reported vs an aqueous saturated calomel electrode (except when indicated, i.e., Table 4); glassy carbon was used as working electrode. The limiting

---

[38] Luttringhaus, A.; Saaf, G. v. *Liebigs Ann. Chem.* **1939**, *542*, 241.

[39] Lithium metal tends to accumulate in the upper layer of commercially available dispersions; drawing a sample without homogenizing the dispersion with a spatula can lead to stoichiometric errors.

[40] Andrieux, C. P.; Larumbe, D.; Gallardo, I. *Electroanal. Chem.* **1991**, *304*, 241.

lifetimes for the radical anions were calculated using $k = RT/Fv$ as described in ref 25. Electrolysis reactions were carried out by using a P.A.R. 273 A potentiostat.

General Procedure for the Electrochemically Promoted Reductive Cleavage of Compounds 1a,d−f Described in Table 3. A solution of starting material **1a,d−f,** (0.64 mmol) in 150 mL of THF or DMF (0.1 M Et_4NBF_4 as supporting electrolite except in experiment 4 where $LiNBF_4$ was used) was electrolyzed using −2.6 V as the applied potential with glassy carbon as electrode and under inert (N_2) atmosphere. After 2.1 F were consumed, the reaction was quenched by addition of 30 mL of 1 M HCl. The reaction crude was extracted between ether/water and the organic layer washed several times with water. The organic layer was dried and evaporated. Analysis of the residue by GC and ^1H NMR indicated the presence of traces of *m*-terphenyl (**2**) in experiments 1 and 3, and 2,6-diphenylphenol (**3**) as a single product in experiments 2, 4−9. The presence of a large excess of supporting electrolyte in the aqueous layer precluded any detailed study on the fate of the alkyl chain after the cleavage when compounds (**1d**−**f**) were used as starting material.

Acknowledgment. Financial support from DGES (MEC of Spain) through project PB96-1145, from MURST (40% and 60% Funds), and from “Generalitat de Catalunya” through the project 1997SGR00414 and a grant for F.C. is gratefully acknowledged.

JO991059V