Carbon–Oxygen Alkyl Ether Fragmentation in the Radical Anions of Phenyl and Nitrophenyl Methyl Ethers. An AM1 Study

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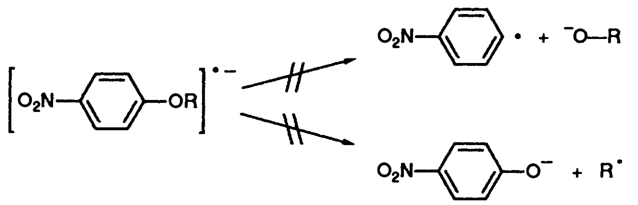
Alkyl ether fragmentations of radical anions of several phenyl and nitrophenyl methyl ethers have been theoretically studied by means of the AM1 semiempirical method. The cleavage occurs through a π^*–σ^* intramolecular electron transfer process, that is made possible by the lengthening of the C–O alkyl ether bond. The C–O scission is slowed down by the introduction of substituents that increase the σ^*–π^* energy gap.

Single electron transfer reactions (SET) have been the topic of recent widespread investigation[1] which has led to the development of novel reactions. In many cases the chemical activation achieved by single electron transfer is associated with enhancement of the reactivities of the individual radical ions with respect to the parent neutral molecules.[1a,2] Thus, strongly covalent C–C or C–heteroatom bonds in parent neutral molecules can be selectively labilized by SET processes.[3] In particular reactions that involve the breaking of formal three-electron bonds have attracted increased attention from organic chemists in recent years.[4] This bond breaking step is a critical component in such important processes as $S_{RN}1$ reactions[5] or the reductive cleavage of diaryl ethers and alkyl aryl ethers.[6] It is very surprising that in spite of the importance of these processes, almost no theoretical studies have been performed on them. A series of well established empirical rules, and the qualitative use of the 'reactive mixed valence approach' are the only available tools in predicting the organic reactivity in this particular field.[1a] The theoretical formulation[7] of reactive mixed valence isomers has been thorougly treated only for inorganic models.[8] Thus, and on qualitative bases, Symons,[9] Bunnett[10] and Rossi[11] have proposed that cleavage of C–X bonds in halogenoaromatic radical anions may be seen as the result of electron transfer from the π^* radical anion to the σ^* aryl-nucleofugal bond by an orbital crossing. This orbital crossing is made possible by lengthening, or out of plane wagging motion, of the C–X bond. In the first stage, a π^* radical anion, stable with respect to dissociation, would be formed. Then an intramolecular electron transfer would transform the π^* radical anion into a σ^* (fragmentative state) one. Efficient fragmentation in aryl and benzyl halides depends on a delicate balance. Thus, the same electron attracting groups that can make the initial electron transfer step easier, may keep the extra electron away from the σ bond that should be activated. When a cyano group replaces the nitro group either in *p*-nitroaryl or *p*-nitrobenzyl halides, the rate of dissociation of the radical anion measured by pulse radiolysis[12] increases by at least five orders of magnitude.

The reductive alkyl aryl ether cleavage has lately received important attention and the results up until 1986 have been reviewed by Maercker.[13] The first reaction step leads to radical anions $ROAr^{\bullet -}$, known since 1968 from EPR studies.[14] Dianions were also discussed in the past as intermediates[15] although more recent literature[13,16] shows that in most cases this is an unnecessary hypothesis. Intermediates of the $ROAr^{\bullet -}$ type share many common features with the previously mentioned aryl and benzyl halide radical anions important in $S_{RN}1$ reactions. Now an interesting problem of intramolecular selectivity of cleavage (Ar–O *vs.* R–O cleavage) appears after electron attachment. In those cases, and in addition to the previously indicated factors that can alter the fragmentation process, a new element must be taken into account, which is called the 'spin regioconservation principle'.[17] Guthrie and Maslak proposed such a concept based on fragmentation studies on aryl nitrobenzyl and benzyl nitroaryl ethers. Those authors state that the fission of alkyl aryl ether radical anions will only take place unproblematically if the spin density remains on the radical which is split off.

We have been involved lately in the study of the nitroaryl ethers nucleophilic photosubstitution,[18] and, in spite of a well demonstrated radical ion pair collapse mechanism,[19] no photocleavage of the ether linkages was observed in any case (Scheme 1). Similar results have been reported in the literature for photo-Smiles reactions[20] and for the photoreaction of 1-methoxy-4-nitronaphthalene with nucleophiles.[21] Those results can be qualitatively rationalized considering the effect of the $-NO_2$ group on the π^* state energy and on the spin density distribution in the radical anion, both effects acting in the same direction hindering the necessary intramolecular π^*–σ^* electron transfer and therefore preventing any fragmentation process.



Scheme 1

All this considered we decided to perform a theoretical study (based on AM1 semiempirical calculations[22]) on the alkyl ether fragmentation of differently substituted alkyl aryl ether radical anions, in order to establish the electronic influences of those substituents in the cleavage reaction. The hydroxy group in the *ortho* position with respect to the methoxy group was used as a model electron donor group, and the nitro group, in the *para* position with respect to the methoxy group, as a model electron attracting substituent. The placement of the substituents in the aryl ring was dictated by our intention of also studying the global effect of both substituents together. It is also well known that pH affects some of the radical anion fragmentation reactions.[23] The use of the nitro group as substituent in our theoretical calculations has also allowed us to evaluate the effect of radical anion protonation on the alkyl ether fragmentation of alkyl nitroaryl ether radical anions.

Method of Calculation

All molecular orbital calculations presented in this work have been carried out using the semiempirical AM1 quantum mech-

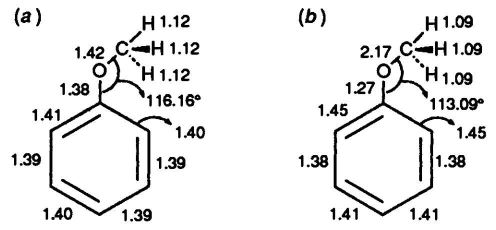


Fig. 1 Main geometrical parameters for neutral anisole (*a*) and its alkyl ether fragmentation transition state (*b*). Interatomic distances are given in Angstroms and bond angles in degrees.

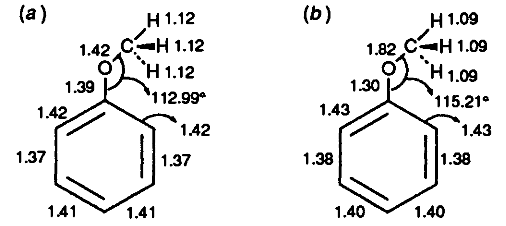


Fig. 2 Main geometrical parameters for the anisole radical anion (*a*) and its alkyl ether fragmentation transition state (*b*). Interatomic distances are given in Angstroms and bond angles in degrees.

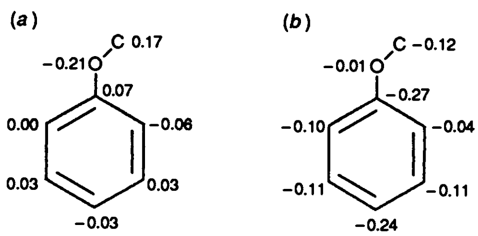


Fig. 3 Net charges for the neutral anisole (*a*) and net charge differences between the π^* radical anion and the neutral anisole (*b*). The charges correspond to each heavy atom plus its attached hydrogen atoms.

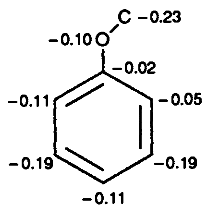


Fig. 4 Net charge differences between the σ^* radical anion and the neutral anisole. The charges correspond to each heavy atom plus its attached hydrogen atoms.

anical molecular model,[22] implemented in the AMPAC[24] package of computer programs. In dealing with open-shell systems the unrestricted Hartree–Fock (UHF) method[25] has been employed.

All geometries have been fully optimized by minimizing the energy with respect to all geometrical variables. The reactions have been followed by using the reaction coordinate method, taking the internuclear distance corresponding to the bond that is breaking as the reaction coordinate. Transition states found in this way have been refined using the McIver–Komornicki procedure,[26] which minimizes the gradient norm. The force constant matrix has been diagonalized to test the nature of each stationary point: no negative eigenvalue for a minimum energy structure and one negative eigenvalue for a transition state.

For the determination of excited states of the radicals, a configuration interaction (CI) within an AM1 formalism as implemented in the AMPAC package has been done. Thus, keeping $M_s = \frac{1}{2}$, all singly excited configurations arising from the highest occupied orbital to the three or four lowest virtual orbitals have been included in the variational space for the radical anions or the neutral species derived from the protonation of the 4-nitroveratrole radical anion. The CI calculations have been performed keeping invariant the geometries obtained for the corresponding radical ground states at the Hartree–Fock level.

Results and Discussion

As mentioned in the introduction the purpose of this paper is the study of the alkyl ether cleavage of radical anions of several phenyl and nitrophenyl methyl ethers. However, for the sake of comparison, we have analysed the alkyl ether scission in the neutral anisole. This process takes place through a transition state that imposes an enthalpy barrier of 50 kcal mol^{-1}.* The main geometrical parameters of both anisole and the transition state are depicted in Fig. 1. It is obvious that such a barrier is too high for the C–O cleavage to occur under thermal conditions.

The situation is very different for the alkyl ether cleavage in the anisole radical anion. The geometries of the minimum energy structure and of the transition state are displayed in Fig. 2. Significantly, the enthalpy barrier now appears to be 19.5 kcal mol^{-1}, a value notably lower than that corresponding to the neutral species. It is interesting to note that the alkyl ether bond orders (based on a Mulliken analysis) are 0.976 and 0.971 for the neutral species and the radical anion, respectively. Thus, in spite of the fact that the strength of the C–O bond seems to be the same for both cases, the breaking barriers are clearly different. In what follows we try to analyse this point.

When one electron is added to neutral anisole to form the corresponding radical anion, a π^* molecular spin orbital becomes occupied. This molecular orbital arises mostly from the linear combination of the p_z atomic orbitals centred at the ring carbon atoms. Thus, the C–O alkyl ether bond practically remains unaffected, as the value of the associated bond order shows. A Mulliken charge analysis confirms this statement. In Fig. 3 we have presented the net charges for the neutral anisole and the net charge differences between the radical anion and the neutral anisole. Note that for the sake of clarity the charges associated with each heavy atom plus the corresponding attached hydrogen atoms are shown. The additional electron is essentially localized in the ring.

Our results indicate that the electronic ground state for the anisole radical anion is a π^* state that does not favour the fragmentation. Then we have to assume an intramolecular electron transfer from the π^* ground state to an excited state to justify the experimentally observed C–O alkyl ether bond cleavage.[13] This will probably be a σ^* excited state that involves the occupation of a σ^* antibonding C–O alkyl ether molecular spin orbital. This σ^* molecular orbital appears in our calculations 8.18 eV above the π^* molecular orbital. A better indication of the energy difference between both electronic states is obtained by means of the CI calculation, which provides a value of 2.82 eV. It should be noted that the charge distribution corresponding to the σ^* state (Fig. 4) is clearly different from that associated with the π^* state (Fig. 3), the C–O alkyl ether bond order taking a value of 0.81 in the former case.

The intramolecular electron transfer can be understood in terms of a suitable diabatic (one that does not diagonalize the Born–Oppenheimer electronic Hamiltonian of the system) two bases set. It consists of two electronic wave functions that can be directly identified in a valence-bond structure sense with the π^* ground state and the σ^* excited state, respectively. Assuming a classical frame, the electron transfer must occur at the inter-

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* 1 cal = 4.184 J.

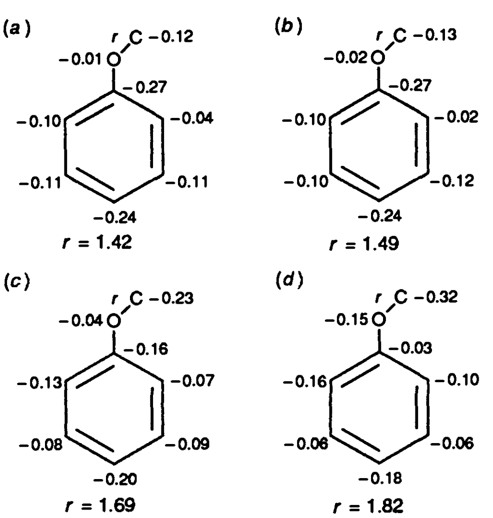
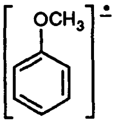
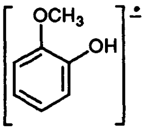
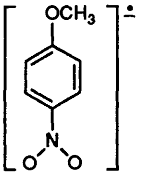
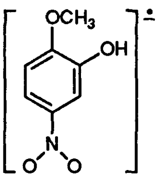
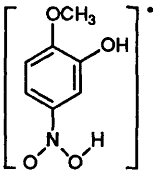


Fig. 5 Net charge differences of the anisole radical anion with respect to the neutral anisole at selected values of the C–O alkyl ether bond distance (in Angstroms). The charges correspond to each heavy atom plus its attached hydrogen atoms.

Table 1 C–O bond distances (Å) in the transition state, enthalpy barriers (in kcal mol^{-1}) and the σ^*–π^* CI energy differences (in kcal mol^{-1}) at the ground state minimum energy structures

Substrate	r	$\Delta H^{\ddagger}$	$\Delta E(\sigma^*-\pi^*)$
	1.82	19.48	2.60
	1.83	18.39	2.60
	1.89	30.61	3.68
	1.90	29.47	3.54
	2.14	46.22	6.41

section region of the diabatic potential energy surfaces corresponding to both diabatic states. This intersection region is reached by a suitable fluctuation in the nuclear coordinates of the π^* state, essentially the lengthening of the C–O alkyl ether bond. After the electron transfer this C–O bond dissociates directly. The reaction barrier arises from the energy required to deform the radical anion up to the minimum energy value of the intersection region.

Further insight on the details of the process can be obtained by analysing the evolution of the electronic distribution along the reaction path. In Fig. 5. the net charge differences between the anisole radical anion and the neutral anisole at selected values of the C–O alkyl ether bond distance, which is the parameter that defines the reaction coordinate, are shown. These charges correspond to the adiabatic ground state for each value of the C–O reaction coordinate. When the C–O bond distance evolves towards the value corresponding to the transition state, an intense migration of electronic charge from the ring to the C–O alkyl ether bond is observed. This indicates that on going from the minimum energy structure to the transition state, the π^* and σ^* diabatic electronic states energetically approach each other, the adiabatic ground state becoming more and more a mixture of them.

So far we have focused only on the anisole radical anion cleavage. Now we will discuss the effect of the introduction of substituents in the aromatic ring. To this aim we have studied the C–O alkyl ether cleavage in the radical anions formed by addition of one electron to the following neutral species: veratrole (2-methoxyanisole), 4-nitroanisole and 4-nitroveratrole. In addition we have considered the fragmentation of the neutral species derived from the protonation of the 4-nitroveratrole radical anion. Table 1 shows the C–O bond distances in the transition state, the enthalpy barriers and the CI energy differences between the σ^* and the π^* electronic states at the ground state minimum energy structure, for each system. The values corresponding to the anisole radical anion have also been included.

Inspection of the enthalpy barriers in Table 1 clearly discloses that the substitution of anisole in the *para* position by a strong electron-withdrawing group such as NO_2 prevents the C–O alkyl ether fragmentation, giving in this way a long-lived radical anion in good agreement with experimental results[19c] and the 'spin regioconservation principle'.[17] This is a consequence of the increase in the energy gap between the π^* and σ^* electronic states when the $-NO_2$ group is introduced. Then more energy is required in order to reach the intersection region. It is evident that an electron-acceptor group like the nitro group does not favour electron accumulation far from itself and in the vicinity of the C–O alkyl ether bond, so stabilizing the π^* state more than the σ^* state. Incidentally, we can mention that the atoms of the $-NO_2$ group contribute to the π^* molecular spin orbital through their p_z atomic orbitals.

Conversely, the introduction in the *ortho* position of an electron-releasing substituent such as –OH tends to reduce the energy gap, but the effect is very small. Therefore, the enthalpy barriers are practically unchanged, although the C–O alkyl ether breaking is predicted to be somewhat easier in veratrole and 4-nitroveratrole than in anisole and 4-nitroanisole, respectively.

On the other hand, protonation of the $-NO_2$ group causes a dramatic effect. In this case the π^* molecular spin orbital is more concentrated in the nitro group than in the ring. The huge gap between both electronic states explains why the enthalpy barrier is so enormous. Our results suggest that the alkyl ether cleavage in nitrophenyl ether radical anions, when possible, will be very dependent on the pH. In addition they agree with the experimental data about the decomposition of nitrobenzyl halide anion radicals by means of the C–X bond scission. This fragmentation occurs in neutral and alkaline solutions. In the acid region, however, the nitro group in the radical is protonated and the decomposition is considerably slowed down.[23]

To summarize, in this paper we have shown that the alkyl ether cleavage of radical anions of phenyl and nitrophenyl methyl ethers can be explained *via* a π^*–σ^* intramolecular electron transfer process. This is made possible by the lengthening of the C–O alkyl ether bond. The introduction in the ring of an electron-attracting group, like the nitro group, increases the energy gap between the σ^* and the π^* electronic states, thus preventing the C–O alkyl ether bond fragmentation.

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