

Hard Acid and Soft Nucleophile Systems 10.¹⁾ The Mechanistic Study for Debromination of *para*-Bromoanisole with Aluminum Chloride and Ethanethiol

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Halogens of *o*- or *p*-halophenols and their derivatives were reductively removed with the aluminum chloride and ethanethiol system. Analyses of the dehalogenation products from *p*-bromoanisole under various conditions suggested that this dehalogenation involved one-electron oxidation by aluminum chloride at the initial stage. The ESR measurement supported the generation of a radical cation from *o*- and *p*-bromoanisoles with aluminum chloride. This radical cation is then stabilized by forming a three-electron bonded species with ethanethiol. Prototropy followed by release of ethanesulfonyl bromide completes the dehalogenation.

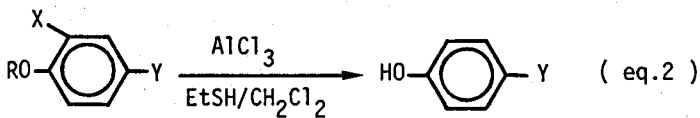
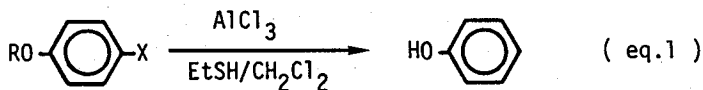
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In the course of our investigation on the bond cleavage reaction with a combination system consisting of a hard acid and a soft nucleophile,²⁾ we have found that treatment of *o*- or *p*-halophenols with the aluminum chloride and ethanethiol system provided a dehalogenated product in high yield. The generalization and limitation of this reductive dehalogenation were already investigated.³⁾ We describe here the mechanism of the reductive cleavage of carbon-bromine bond in *p*-bromoanisole with the combination system of aluminum chloride and ethanethiol.

In the previous report,^{3b)} we observed the following facts in the dehalogenation of halophenols with aluminum chloride and ethanethiol (Eqs. 1 and 2); bromo- or iodobenzene derivatives with a oxygen function at *ortho*- or *para*- position were easily dehalogenated, whereas *meta*- derivatives were not dehalogenated, the reaction rate decreased in the order of $\text{OH} \approx \text{OMe} > \text{OAr} > \text{OAc}$, and an electron-withdrawing group (Y) which was attached on the aromatic ring retarded the reaction rate. These observation evoked cationic species (**A** or **B** in Scheme 1 for *para*-halophenol derivatives) as an intermediate in this dehalogenation.

Three possible mechanisms shown in Scheme I can be taken into consideration for the dehalogenation of *p*-bromophenol derivatives. In the first two mechanisms, aluminum chloride acts as a Lewis acid to afford an intermediate species **A**, from which the bromine atom is expelled as a bromonium ion in *Ei* sense (pathway a), or

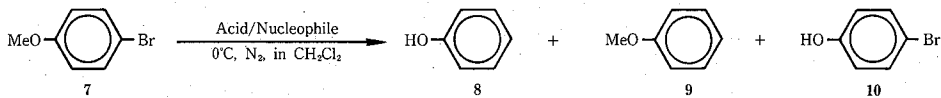
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X = I, Br ; Y = Me, CH₂CO₂Et, CO₂Me

R = H, alkyl, aryl, acyl

eq. 1 and 2

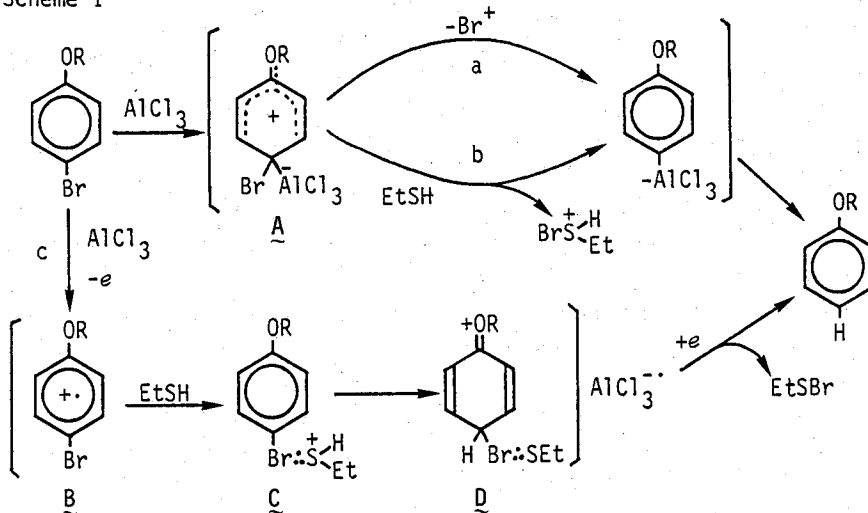
Table I. Debromination of *p*-Bromoanisole under the Various Conditions

run	acid (mol equiv.)		nucleophile	reaction time	Products, % yield			recovery of 7	ratio (8+9)/(8+10)
					8	9	10		
1	AlCl ₃	(0.4)	EtSH	1 h	20	50	3	19	3.0
2	AlCl ₃	(1.5)	Non	15 min	0	0	0	100	—
3	AlCl ₃	(1.5)	EtSH	15 min	45	36	6	0.3	1.6
4	AlCl ₃	(1.5)	EtSH ^{a)}	15 min	5	1	67	23	0.08
5	AlCl ₃	(1.5)	Et ₂ S	15 min	2	0.3	52	42	0.04
6	AlCl ₃	(1.5)	EtSH ^{b)}	15 min	12	17	44	19	0.52
7	SnCl ₄	(1.5)	EtSH	46 h	2	16	2	71	4.5
8	CF ₃ SO ₃ H	(1.5)	EtSH	4 h	41	30	0.9	18	1.7
9	CF ₃ SO ₃ H	(1.5)	Et ₂ S	4 h	—	0.7	2	95	0.35

a) The reaction was carried out in ethanethiol without dichloromethane

b) Galvinoxyl was used 0.2 molar equivalents for *p*-bromoanisole

Scheme I

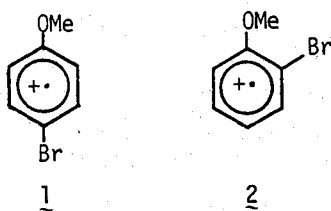


can be removed in S_N2 sense by the attack of a soft nucleophile, ethanethiol (pathway b). The last mechanism involves an initial generation of a radical cation **B** (pathway c). To distinguish these possibilities, *p*-bromoanisole was treated under a variety of conditions, the results of which were summarized in Table I.

Jacquesy and Jouannetaud⁴⁾ reported that isomerization of *o*- and *p*-bromophenols to *m*-bromophenol in superacids proceeds through the same type of intermediate as **A** followed by the loss of bromonium ion in $E1$ sense and recombination of the same ion at the *meta*-position. Pathway a is quite similar to this mechanism and was considered to be one of the most probable mechanisms because superacid can be used instead of aluminum chloride (run 8 in Table I). However, as indicated in run 2 in Table I, neither debromination nor transposition of the bromine atom to *meta*-position occurred without ethanethiol. This fact suggests the pathway a to be unlikely.

When the reaction was carried out in ethanethiol as a solvent, the rate of debromination was extremely retarded under the comparable conditions with dichloromethane as a cosolvent, while demethylation took place smoothly (compare run 4 with run 3 in Table I). This significant difference in product distribution by changing the solvent system can be attributed to the change of the mechanism involved in the demethylation and in the reductive debromination.

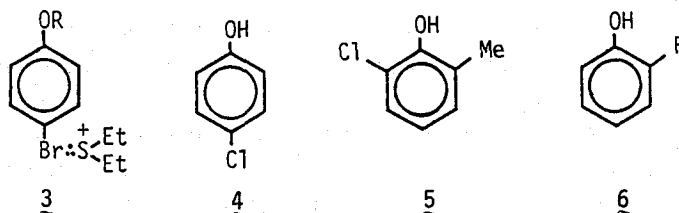
Aluminum chloride has been known to be an effective one-electron oxidant which can oxidize the compounds possessing a first ionization potential of ~ 8 eV.⁵⁾ As the first ionization potential of *p*-bromoanisole has been reported to be 8.49 eV determined by photoelectron spectroscopy,⁶⁾ the possibility for the formation of radical cation from *p*-bromoanisole with aluminum chloride was examined by ESR spectroscopy. A solution of *p*-bromoanisole and aluminum chloride in dichloromethane afforded a green-colored solution, where the presence of the radical cation **1** was proved by ESR spectrum ($g=2.0031$).⁷⁾ Aluminum chloride also effects the formation of the radical cation **2** from *o*-bromoanisole, which was supported by the ESR spectrum ($g=2.0040$). However, *m*-bromoanisole proved not to afford the corresponding radical cation under the same conditions. The results of ESR studies are consistent with the radical cation process c shown in Scheme I. Dichloromethane has been claimed to be the most satisfactory solvent for the one-electron oxidation with aluminum chloride.⁸⁾ Thus, it may be concluded that aluminum chloride can act both as a Lewis acid and a one-electron oxidant in dichloromethane. On the other hand, it merely functions as a Lewis acid in ethanethiol. This explains the different course in the reaction of *p*-bromoanisole with and without dichloromethane (runs 3 and 4 in Table I). When a radical scavenger (galvinoxyl) was added in the reaction mixture,



Formulas 1 and 2

the rate of the debromination was extremely retarded, while the rate of the demethylation was not changed (compare run 6 with run 3 in Table I). This result also supports the radical cation process for the debromination of *p*-bromoanisole.

Addition of ethanethiol to the initially generated radical cation **B** may afford another radical species **C** stabilized by the three-electron bond between bromine and sulfur.⁹⁾ Prototropy from **C** gives **D** which is further transformed to the final dehalogenated product by one-electron transfer from an anionic species of aluminum chloride with concomitant formation of ethanesulfonyl bromide. This process can explain the fact that use of diethylsulfide hardly afforded the debrominated products under the conditions where ethanethiol gave them (compare runs 3 and 8 with 5 and 9 in Table I, respectively). Even though the initially generated radical cation **B** can be stabilized by forming three-electron bonded species **3** in the presence of diethylsulfide, absence of the proton in **3** may prevent further transformations. Chlorophenols **4** and **5** and *o*-fluorophenol (**6**) were not reactive under the standard reaction conditions.³⁾ This is because they possess a higher ionization potential than that of bromo- or iodo-derivatives,^{10,11)} or the subsequently formed three-electron bond between sulfur and chlorine or fluorine in the intermediate is less stable than that between sulfur and bromine or iodine.⁹⁾



Formulas 3~6

The most puzzling observation in Table I was that a superacid promoted the dehalogenation (run 8). When *p*-bromoanisole was treated with triflic acid in dichloromethane, it gave the ESR spectrum which was coincident with that obtained by the action of aluminum chloride. Thus, it can be concluded that a radical cation process operates even when a superacid is used. We suspect that some reactions which have been considered to be an acid-catalyzed process might involve a radical species as exemplified in our case.

EXPERIMENTAL SECTION

General Procedure for Dehalogenation. A mixture of *p*-bromoanisole (1 mmol), ethanethiol (0.4 mL), methanol-free dichloromethane (2 mL), and acid was stirred in nitrogen under the conditions described in Table I. The reaction mixture was poured into water and extracted with dichloromethane. The organic layer was washed with brine, dried (Na₂SO₄), filtered, and evaporated to afford a residue which was analyzed by GLC (a Shimadzu Model GC-4CM instrument). GLC analyses were performed with a 20% SF-96 (3 m × 3 mm) column. Column tem-

perature and internal standards are as follows, respectively. For phenol and anisole; at 100°C, n-decane. For *para*-bromophenol and *para*-bromoanisole; at 150°C, n-tridecane.

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