Aromatic Bromination and Iodination with Mixtures of Antimony(V) Chloride and Halogens

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Equimolar mixtures of $SbCl_5$ and Br_2 or I_2 were found to be elegant reagents for the halogenation of certain aromatic substrates. In carbon tetrachloride, halogenobenzenes afforded the corresponding bromo- and iodo-derivatives with high *para*-selectivities (more than 95%) in good yields. The bromination of aromatic compounds with deactivating groups, such as ethyl benzoate and nitrobenzene, was simply achieved in 1,2-dichloroethane. Based on competitive halogenation data, the attack of BrCl or ICl (both formed *in situ*) on aromatics has been suggested.

Though aromatic halogenation with elementary halogens has been thoroughly investigated from the synthetic and mechanistic points of view, little is known about the halogenation by means of mixed halogens. The synthetic usage of ICl¹⁾ for aromatic iodination and that of IBr²⁾ or BrCl (*in situ*)³⁾ for bromination are discussed in the literature, but the given examples are limited to reactive substrates, such as phenols and aromatic amines. Recently, a new aromatic iodination using copper(II) chloride–iodide donor (*e.g.*, I_2, AlI_3, or $FeI_2\cdot4H_2O$) mixtures has been reported by Baird and Surridge,⁴⁾ though the formation of ICl as a potent iodinating agent as not definitely stated. In a previous paper,⁵⁾ we reported the mixed halogenation of olefins with ICl or BrCl formed *in situ* by the interaction of antimony(V) chloride and halogens. When this system was applied to aromatic substrates in carbon tetrachloride or 1,2-dichloroethane, aryl bromides and iodides were obtained in good yields even from less-reactive aromatics. The present paper will describe some characteristics of this reaction.

Results and Discussion

The treatment of aromatic compounds with equimolar mixtures of $SbCl_5$ and halogens (Br_2 or I_2) in chlorinated solvents afforded the corresponding aryl bromides and iodides with ease. Aromatic compounds bearing an activating group were readily brominated at 25 °C and iodinated at the refluxing temperature, both in carbon tetrachloride, with high yields. In the cases of less-reactive aromatic compounds (*e.g.*, ethyl benzoate and nitrobenzene), the use of a more polar solvent such as 1,2-dichloroethane was revealed to be preferable. In the bromination of acetophenone, three equivalents of $SbCl_5$ (to Br_2) were used, since the formation of a complex with ketone was expected, as in the case of $AlCl_3$ catalyst.⁶⁾ All the results are summarized in Table 1.

In these halogenations, more than one (nearly two) moles of aryl halides were generally formed from one mole of the halogenating agent; thus, the reaction appeared to occur in accord with the stoichiometry

$$2ArH + SbCl_5 + X_2 \longrightarrow 2ArX + SbCl_3 + 2HCl \quad (1)$$
$$(X{=}Br \text{ or } I)$$

shown by Eq. (1). Here, the net oxidation of X^- with $SbCl_5$ is involved, and the complete utilization of halogens is achieved. The $SbCl_5$–LiX mixture was also revealed to be effective as a halogenating agent, but the yields of halogenated compounds were somewhat unsatisfactory [see Runs 16, 17, and 26 in Table 1 and Eq. (2)].

$$ArH + SbCl_5 + LiX \longrightarrow$$
$$ArX + SbCl_3 + LiCl + HCl \quad (2)$$

As can be seen in Table 1, two marked characteristics noteworthy from the synthetic point of view are found in our halogenation. First, this method may serve as a simple procedure for the bromination of aromatic compounds bearing an electron-withdrawing group. For example, nitrobenzene afforded *m*-bromonitrobenzene in a 63% yield by treating with an equimolar mixture of $SbCl_5$ and Br_2 in 1,2-dichloroethane at 84 °C for 3 hr; ethyl benzoate was similarly brominated (yield, 74%) or iodinated (48%) on refluxing for 3—5 hr in the same solvent. The halogenations of these compounds are usually carried out under drastic conditions; that is, high temperatures and/or stronger electrophilic catalysts are necessary [*e.g.*, for benzoic acid, its ester, and nitrobenzene, the Fe-catalysed bromination (above 140 °C)⁷⁾ and the Ag(I) salt-catalysed bromination⁸⁾ or iodination⁹⁾ (in concentrated HNO_3 or H_2SO_4)]. Further, in the bromination of acetophenone, our method made the preformation of the ketone-Lewis acid complex before bromine addition unnecessary (see Experimental section and compare with the procedure in Reference 6; in CCl_4, yield 86%). Though our iodinating system was found to be more efficient than the $CuCl_2$–iodide system⁴⁾ (*e.g.*, for benzene, 76 °C, 0.5 hr, in CCl_4 *vs.* 80 °C, 5 hr, neat), its reactivity did not appear to be high enough. For example, attempts to prepare *m*-iodonitrobenzene and *o*-, *p*-diiodobenzenes were unsuccessful (86 °C, in dichloroethane), and the unreacted aromatics were recovered.

Secondly, this halogenation may provide a convenient method for preparing *p*-dihalogenobenzenes with similar or dissimilar halogen atoms, since the *para*-selectivity of the reaction is quite high. In the bromination of chloro-, bromo-, and fluorobenzenes by a bromine molecule with a Fe- or $AlBr_3$-catalyst, the degree of *para*-substitution has been known to be in the 84—89% range,¹⁰⁾ except only for the Fe-catalysed reaction of fluorobenzene, in which a *para*-selectivity of 98% has been observed.¹¹⁾ The iodination of

TABLE 1. AROMATIC HALOGENATION BY ANTIMONY(V) CHLORIDE-HALOGEN DONOR COMBINATIONS
$SbCl_5$, 25 mmol; X_2 or LiX 25 mmol; solvent, 100 ml

Run	Substituent in ArH (mmol)	Halogen donor	Solvent	Temp. (°C)	Time (min)	Yield[a] (%)	Isomer distribution of ArX (%)[b]	
							o-	*p*-
	(a) Bromination							
1	CH_3O (100)	Br_2	CCl_4	25	5	86	12	88[c]
2	CH_3O (50)	Br_2	CCl_4	25	5	93	6	94[c]
3	CH_3 (100)	Br_2	CCl_4	25	5	92	38	62[c,d]
4	CH_3 (50)	Br_2	CCl_4	25	5	94	39	61[c]
5	H (50)	Br_2	CCl_4	25	5	88	—	—
6	F (50)	Br_2	CCl_4	76	10	90	1	99
7	Cl (100)	Br_2	CCl_4	76	30	96	8	92
8	Cl (50)	Br_2	CCl_4	76	30	84	4	96
9	Br (100)	Br_2	CCl_4	76	30	91	9	91
10	Br (50)	Br_2	CCl_4	76	30	86	5	95
11	Br (50)	Br_2	$ClCH_2CH_2Cl$	84	30	89	13	87
12	I (50)	Br_2	CCl_4	76	30	88	5	95
13	$COCH_3$	Br_2	CCl_4	35	30	86	only *meta*-	
14	$COOC_2H_5$ (100)	Br_2	$ClCH_2CH_2Cl$	84	180	74	only *meta*-	
15	NO_2 (100)	Br_2	$ClCH_2CH_2Cl$	84	180	63	only *meta*-	
16	CH_3 (100)	LiBr	CCl_4	76	5	75	41	59
17	H (100)	LiBr	CCl_4	76	5	61	—	—
	(b) Iodination							
18	CH_3O (50)	I_2	CCl_4	76	30	75	0	100[c]
19	CH_3 (50)	I_2	CCl_4	76	30	96	58	42[c]
20	H (50)	I_2	CCl_4	76	30	84	—	—
21	F (50)	I_2	CCl_4	76	30	74	2	98
22	Cl (100)	I_2	CCl_4	76	30	70	1	99
23	Br (100)	I_2	CCl_4	76	30	73	0	100
24	Br (50)	I_2	$ClCH_2CH_2Cl$	84	30	62	19	81
25	$COOC_2H_5$ (100)	I_2	$ClCH_2CH_2Cl$	84	300	48	only *meta*-	
26	H	LiI	CCl_4	76	60	22	—	—

a) Isolated yield (based on halogen donor, *cf.* Eqs. 1 and 2).
b) Determined by glc before isolation.
c) Determined also by NMR.
d) No *m*-isomer was formed (confirmed by NMR).
e) No *o*- and *p*-isomers were formed (confirmed by glc).

chloro- and bromo-benzenes with CuI_2–AlI_3 showed *o*/*p* ratios of 18/82 and 0/100 respectively, and the yields were rather low (*ca.* 30%).[4] In contrast to this, the halogenation of halogenobenzenes with $SbCl_5$–X_2 in carbon tetrachloride, where the molar ratio of a halogenobenzene and the halogenating agent was 2: 1, showed high selectivities in the *para*-attack (over 95% in bromination and over 98% in iodination). Moreover, the yields were generally good—nearly 85—90% in bromination and 70—75% in iodination. When excess amounts (more than 2 equivalents) of halobenzenes or anisole were used, a decrease in the *para*-selectivity was observed, while in the case of toluene no variation in selectivity was found. Thus, the preferred *para*-substitution might be the result of the coordination between the antimony salt and the hetero atom with lone pairs of electrons in aromatic substrates, which may depress an *ortho*-attack of the halogenating agent for steric reasons.

In order to obtain some information on the attacking species, the competitive halogenations of benzene and toluene were carried out under various conditions. Some data on the relative rate ratio (k_T/k_B) and on the isomer ratio (*o*/*p*) in the halotoluenes formed are shown in Table 2. The k_T/k_B and *o*/*p* ratios for iodination with $SbCl_5$–I_2 in CCl_4 were almost identical with

TABLE 2. COMPETITIVE HALOGENATION
benzene, 250 mmol; toluene, 50 mmol; halogenating agent 12.5 mmol; solvent, 100 ml

Run	Halogenating agent	Solvent	k_T/k_B	*o*/*p* ratio
	(a) Bromination[a]			
1	Br_2+SbCl_5	CCl_4	257	0.69
2	Br_2+SbCl_5	$ClCH_2CH_2Cl$	6.2	1.33
	(b) Iodination[b]			
3	I_2+SbCl_5	CCl_4	105	1.38
4	$ICl+SbCl_5$[c]	CCl_4	107	1.42
5	$ICl+SbCl_3$[c]	CCl_4	160	1.47
6	ICl	CCl_4	248	1.34

a) At 25 °C.
b) At 76 °C.
c) The amount of the catalyst ($SbCl_3$ or $SbCl_5$) was 12.5 mmol.

those for the $SbCl_5$-catalyzed iodination with ICl, while somewhat higher $k_{\rm T}/k_{\rm B}$ values were obtained in the $SbCl_3$-catalyzed one. All these $k_{\rm T}/k_{\rm B}$ values, however, are of the same order as the reported one (>140, in HOAc) for the $ZnCl_2$-catalyzed iodination with ICl,[12] and they differ greatly from that (2.0, in CH_3CN) for an electrochemical iodination involving the attack of I^+ species.[13] Besides, the obtained $k_{\rm T}/k_{\rm B}$ value for the ICl iodination (without catalyst) was considerably higher than those for the catalyzed reactions. Thus, it may be suggested that the formation of ICl *in situ* and the attack of polarized ICl (activated by $SbCl_5$) rather than I^+ are involved in our iodination in CCl_4. As to BrCl, though its formation *in situ* is highly probable, as has been shown previously in the bromochloriantion of olefins using the same halogenating system, a direct confirmation as in the case of ICl was difficult because of the inaccessibility of BrCl in the pure state. In the bromination with $SbCl_5$–Br_2 in CCl_4, however, the observed $k_{\rm T}/k_{\rm B}$ and *o*/*p* ratios were similar in magnitude to those (340 and 0.45, respectively) for the uncatalyzed bromination with Br_2 in aqueous HOAc, where the attack of molecular bromine is supposed.[14] On the other hand, when 1,2-dichloroethane was used as a solvent, quite a low $k_{\rm T}/k_{\rm B}$ value and a high *o*/*p* ratio were obtained. These values are comparable to those (3.6 and 2.33, respectively) for the $FeCl_3$-catalyzed bromination in CH_3NO_2, where Br^+ is considered to be the attacking species.[15] Thus, the existence of two different attacking species derived from BrCl is feasible, in view of the solvent used; *i.e.*, the attack of polarized BrCl (activated by $SbCl_5$) and Br^+ (probably as an ion-pair). The following facts should be noted here. In the bromination of anisole, the exclusive *para*-substitution has been previously reported in a synthetic procedure (Br_2 bromination in AcOH without catalyst);[16] we confirmed this by glc analysis. On the other hand, our bromination products were contaminated by the *o*-isomer. This can be explained by a higher reactivity of BrCl compared to that of the Br_2 species. In contrast to this, the iodination product was free from the *o*-isomer, as is anticipated from the mild reactivity of ICl.

Experimental

The NMR spectra were determined by means of a Varian A-60 spectrometer in $CDCl_3$, using TMS as the internal standard. Glc analysis was carried out on a Shimadzu 5APTF apparatus, using PEG 6000 (25%)-Chromosorb W (3m) and Apiezon L(30%)-Celite (1m) columns.

Materials. All the organic substrates, including the solvents, were used after distillation, while commercial $SbCl_5$, LiBr, LiI, Br_2, I_2, and ICl of the best grade were used without further purification.

Aromatic Halogenation with $SbCl_5$–Halogen Mixtures. Several examples are given below; they should be synthetically useful.

(a) p-*Dibromobenzene.* To a homogeneous solution of $SbCl_5$ (7.5 g, 25 mmol) and Br_2 (4.0 g, 25 mmol) in CCl_4 (100 ml), bromobenzene (7.9 g, 50 mmol) was added, drop by drop, at 78 °C. Stirring was continued for 30 min. The reaction was accompanied by a considerable evolution of HCl gas, and the dark-red color of the solution disappeared. The reaction mixture was then cooled and treated with water. The inorganic precipitate thus formed was removed by filtration. The organic layer was separated from the aqueous one, and the solvent and unreacted bromobenzene were evaporated. A liquid fraction corresponding to isomeric dibromobenzenes (bp 102—103 °C/22 mmHg) was collected by distillation. The yield was 86% (10.2 g, 43.2 mmol). By a comparison of the retention times on glc with those of authentic samples, the *o*/*p* ratio was found to be 5/95. A single recrystallization from ethanol afforded the pure *p*-isomer; mp 88 °C (lit,[17] 87.3 °C).

(b) m-*Bromoacetophenone.* Acetophenone (6.0 g, 50 mmol) was added to a stirred mixture of $SbCl_5$ (22.5 g, 75 mmol) and Br_2 (4.0 g, 25 mmol) in CCl_4 (100 ml) at 35 °C. After 30 min, the reaction mixture was worked up as has been described above. Subsequent distillation afforded the product (8.6 g, 43.2 mmol) in an 86% yield; bp 92.5—93 °C/4 mmHg (lit,[6] 75—76 °C/0.5 mmHg). NMR: τ 1.98 (m, 4H), 7.49 (s, 3H).

(c) m-*Bromonitrobenzene.* A stirred mixture of $SbCl_5$ (7.5 g, 25 mmol), Br_2 (4.0 g, 25 mmol), and nitrobenzene (12.3 g, 100 mmol) in 1,2-dichloroethane (100 ml) was heated at 84 °C for 3 hr. After the usual work-up procedure, the product was obtained in a 63% yield (6.5 g, 31.6 mmol); bp 136—136.5 °C/22 mmHg (lit,[7b] 117—118 °C/9 mmHg). The absence of the *o*- and *p*-isomers was confirmed by glc analysis.

(d) Iodobenzene. To a mixture of $SbCl_5$ (7.5 g, 25 mmol) and I_2 (6.3 g, 25 mmol) in CCl_4 (100 ml), benzene (3.9 g, 50 mmol) was added in small portions at 76 °C. Stirring was then continued for 30 min, after which the reaction mixture was worked-up as before. Distillation afforded iodobenzene in an 84% yield (8.6 g, 42.1 mmol); bp 80—80.5 °C/22 mmHg (lit,[18] 69 °C/15 mmHg).

(e) p-*Bromoiodobenzene.* The procedure was the same as that described for benzene except that the aromatic substrate was used in excess. From bromobenzene (15.7 g, 100 mmol), the corresponding *p*-iodo derivative was obtained in a 73% yield (10.4 g, 36.8 mmol); bp 118.5—119 °C/14 mmHg; mp 92 °C (lit,[19] 92 °C). In addition, glc analysis revealed that no other isomers were formed in this reaction.

(f) Ethyl p-*Iodobenzoate.* When ethyl benzoate (15.0 g, 100 mmol) was treated similarly with a 1,2-dichloroethane solution (100 ml) containing $SbCl_5$ and I_2 at the refluxing temperature for 3 hr, the product (5.9 g, 24.1 mmol) was isolated in a 48% yield; bp 93—94 °C/1.5 mmHg (lit,[20] 153.5 °C/14 mmHg).

Competitive Halogenations of Benzene and Toluene. The competitive iodination was carried out as follows; a mixture of benzene (250 mmol) and toluene (50 mmol) was added, drop by drop, to a stirred CCl_4 solution (100 ml) containing $SbCl_5$ (12.5 mmol) and I_2 (12.5 mmol) at 76 °C; the resulting mixture was kept for 30 min at that temperature under stirring. On the other hand, an inverse addition was adopted in the competitive bromination because of its rapid reaction; *i.e.*, a CCl_4 solution (30 ml) of $SbCl_5$ and Br_2 was slowly stirred into a mixture of benzene (250 mmol) and toluene (50 mmol) in CCl_4 (70 ml) at 25 °C, after which the solution was allowed to stand for another 5 min. Both reaction mixtures were then worked up as usual. In both cases, the amounts of halobenzene and isomeric halotoluenes were determined by glc and the *o*/*p* ratio was determined by NMR spectra (the methyl protons of *o*- and *p*-iodotoluene were observed at τ 7.60 and 7.70 respectively, and those of *o*- and *p*-bromotoluene at τ 7.62 and 7.73 respectively).

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