

Oxidative monobromination of electron-rich arenes by conc. H₂SO₄ / alkali metal bromides

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The reaction of electron-rich arenes with alkali metal bromides such as sodium and potassium bromides in the presence of conc. H₂SO₄ to give *p*-bromoarenes is reported. The reaction is possible in the absence of any specialised oxidising agents and the yields are high.

Keywords: monobromination, arenes, sodium bromide, potassium bromide, conc. H₂SO₄

Halogenation of organic compounds and the chemistry of organic halides are of interest as major chemical fields due to the theoretical and practical value of halogenation reactions and their products. Their industrial application is wide.¹ Electrophilic substitution of aromatic hydrocarbons by bromine is a well-known organic reaction.² Classical nuclear bromination of aromatic compounds involves the use of bromine in the presence of a catalyst like FeCl₃, FeBr₃, iodine, thallium(III) acetate or light in a suitable solvent. These conditions often yield undesired co-products.³

Siddiq *et al.*⁴ have shown that a mixture of HgO/Br₂ in the presence of conc. H₂SO₄ in CCl₄ at reflux gives the monobrominated arenes. Prestwich *et al.*⁵ have explored the tetrabromination of *p*-toluic acid by dibromoisocyanuric acid dissolved in conc. H₂SO₄. Mattern⁶ has described the periodination of benzene with HIO₄/KI in conc. H₂SO₄ at 100°C after 10h. Minisci *et al.*⁷ have investigated the chlorination of alkyl benzenes with *N*-chlorodicyclohexylamine in 98% H₂SO₄. Recently, the reagents such as NBS in DMF,⁸ bromine adsorbed on Al₂O₃,⁹ bromine and thallium(III) acetate,¹⁰ quaternary ammonium polyhalides,^{11–17} KBr / NH₄VO₃ in a two-phase (H₂O/CHCl₃) system,¹⁸ HF/SbF₅ with sodium or potassium bromide,¹⁹ CuBr₂²⁰ and dodecyltrimethylammonium bromide (DTAB)/HNO₃,²¹ have been used for the selective monobromination of aromatic rings. Most of these reagents are complex with potential environmental problems due to the generation of hazardous waste and the polybromides obtained from quaternary ammonium bromides and Br₂ are generally found to be unstable under normal conditions. However, each example has its own specific set of conditions and hence, the reagents have their own advantages and limitations.

Recent work from this laboratory^{22–25} has described reduction of different functional groups by metals such as aluminium or zinc in the presence of ammonium salts under neutral conditions. As the metals are non-reactive in the absence of ammonium salts, the ammonium salts are expected to participate in these reactions. In order to explore the possibility of utilising the alkyl groups attached to the symmetric tetraalkylammonium halides (R₄NY, Y= Br, I) the reaction of R₄NY with arenes in presence of an acid was undertaken. Surprisingly, instead of alkyl group being transferred in a Friedel–Crafts manner *p*-haloarenes were obtained in high yields.²⁶

As the reaction developed by us involves the use of complex tetraalkylammonium bromides for the bromination of arenes, an attempt has been made in our laboratory to synthesise *p*-bromoarenes from simple alkali metal bromides in the presence of conc. H₂SO₄.

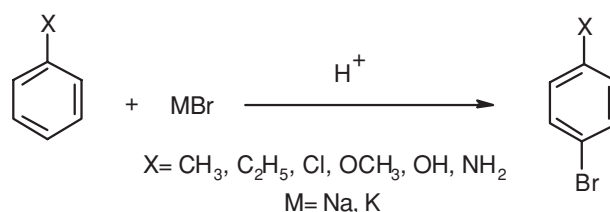
Initially, we carried out the reaction of aromatic hydrocarbons with sodium bromide in the presence of conc. H₂SO₄ and it

was found that bromination of arenes is also possible with this reagent. When, sodium bromide was replaced by potassium bromide the reaction still occurred. In this paper, we report a simple and extremely efficient method of *p*-bromination of substituted arenes by very simple reagents, sodium bromides and potassium bromides in the presence of conc. H₂SO₄ (Scheme 1).

In order to understand the mechanism of this reaction, a set of three Lewis acids and three Brønsted acids were chosen for the study (Table 1). The effect of the nature of these acids on the course of the reaction of chlorobenzene with sodium bromide has been studied in detail.

From Table 1, it is clear that, the reaction of chlorobenzene and sodium bromide is not possible in the absence of an acid (entry 6). It is also found from this table that, the reaction is facilitated by Brønsted acids only. Lewis acids on the other hand are found to be either non-reactive or to give a complex mixture of products (TLC). The presence of conc. H₂SO₄ was observed to have a profound effect upon the course of the reaction between sodium bromide and chlorobenzene. Two and three moles of acid were used to study the effect of the acid on the course of the reaction per mole of sodium bromide and it was found that two moles bring about the conversion and there was no significant change in the yield or the time of the reaction by increasing the amount of the acid used.

In a typical experiment, 10 mmole of sodium bromide and 20 mmole of conc. H₂SO₄ were treated with 10 mmole of arene. The contents were heated at 60°C with constant stirring, until the initial dark orange colour substantially faded (– 2 h).



Scheme 1

Table 1 Reaction of sodium bromide with chlorobenzene in the presence of different acids at 60°C

Entry	Acid	Time h	Product	Yield %
1	AlCl ₃	2	a	–
2	ZnCl ₂	2	a	–
3	FeCl ₃	2	b	–
4	conc. H ₂ SO ₄	2	<i>p</i> -bromochlorobenzene	90
5	35% HCl	2	b	–
6	67% HNO ₃	2	b	–
7	No catalyst	24	a	–

^aThere was no reaction.

^bA complex mixture of products was obtained (TLC) which was not characterised.

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The reaction mixture was extracted with ether and the ethereal extract was washed with saturated sodium bicarbonate solution, water and the solvent was removed to get the crude product. Silica gel chromatography of the crude material using pentane as a solvent gave the *p*-bromoarene (90%).

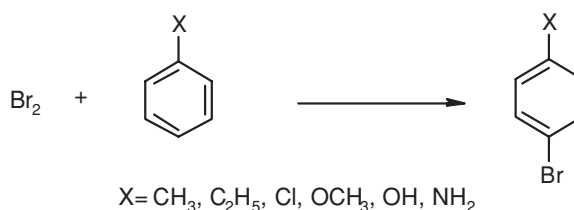
In order to standardise this reaction, the reaction of chlorobenzene and sodium bromide was carried out at different reaction temperatures (25°, 40°, 60°, 80°, 100°, 120°C) in the presence of acid and it was found that, the reaction went to completion within 2 h at 60°C to give *p*-bromochlorobenzene in 90% yield. It was also found that at lower temperatures ($\leq 60^\circ\text{C}$) the reaction was either incomplete or the product is a mixture of *o*- and *p*-bromochlorobenzenes; for example, at 25°C, the reaction went about 40% conversion and the *o/p* ratio of the product was 23:77 by GC analysis. There was no significant change in the yield or the time of the reaction by increasing the reaction temperature above 60°C. This observation is attributed to the fact that, at lower temperatures the kinetic control predominates and at higher temperatures thermodynamic control of the product formation predominates to give *p*-brominated arenes.²⁷

To explore the possibility of using sodium and potassium bromides for bromination of arenes, different substituted aromatic hydrocarbons were chosen and the reaction was carried out under similar reaction conditions. The reaction went to completion smoothly giving the expected products, *p*-bromoarenes in excellent yields (Table 2).

From Table 2, it can be seen that, except anisole, bromination can occur in electron rich arenes with alkali metal bromides to give monobromoarenes in excellent yields. A competitive hydrolysis in anisole is noticed giving a mixture of *p*-bromoanisole and *p*-bromophenol (entries 5 and 6).

It is known that hot conc. H_2SO_4 oxidises sodium bromide or potassium bromide to give a mixture of bromine and hydrobromic acid.²⁸ The present reaction is also expected to proceed by the reaction of the bromine molecule which may form by the decomposition of respective metal bromides in the presence of conc. H_2SO_4 as shown in the Scheme 2.

In conclusion, we have demonstrated for the first time the direct generation of valuable synthons of bromoarenes from the readily available, less hazardous and inexpensive alkali-metal bromides and an inexpensive mild oxidising agent conc. H_2SO_4 . The reaction may be considered as simple from practical point of view and has great potential for future applications. The obvious advantages of the proposed method



Scheme 2

over previous methods are – simplicity, convenience, the high purity of the product and the less hazardous conditions.

Experimental

All the standard *p*-bromoarenes were prepared by Sandmeyer reaction from respective anilines. A Nicolet 400D FT-IR spectrophotometer was used for IR spectral analysis and NMR spectra were recorded on a Jeol 90 FQ and Bruker AC 250 instruments and the chemical shift values (ppm) are reported relative to TMS in CDCl_3 as solvent. Boiling points are recorded using the open capillary method²⁹ and are corrected. Yields refer to the isolated yields of the products.

General procedure for the bromination of arenes of *p*-bromochlorobenzene: Sodium bromide (1.03 g, 10 mmol) and conc. H_2SO_4 (1.96 g, 20 mmol) were treated with chlorobenzene (1.125 g, 10 mmol) and the contents were heated with constant stirring in an oil bath maintained at 60°C. The reaction was monitored by TLC (pet. ether 40–60°C) and comparison with an authentic sample. After completion of the reaction (2 h), the reaction mixture was quenched with water (10 ml) and the organic layer was extracted with ether (3×10 ml). The combined ethereal extract was washed with saturated sodium bicarbonate solution and water and then dried over anhydrous sodium sulfate and the solvent removed. The silica gel chromatography of the crude material using pentane gave *p*-bromochlorobenzene as a colourless solid in 90% yield (1.72 g). *p*-Bromochlorobenzene was characterised by direct comparison with an authentic sample on TLC (pet. ether 40–60°C) and by IR and ^1H NMR spectral analysis and by melting point (Table 3).

Different substituted arenes were treated with alkali metal bromides in the presence of conc. H_2SO_4 , and the respective *p*-bromoarenes were obtained. The yields based on 10 mmol of the starting arenes are presented in Table 2, and the physical and spectral data are given in Table 3.

Table 2 Reaction of different substituted arenes with alkali metal bromides in the presence of conc. H_2SO_4 at 60°C

Entry	Substrate	Metal bromide	Product	Yield %
1	Chlorobenzene	NaBr	<i>p</i> -bromochlorobenzene	90
2	Chlorobenzene	KBr	<i>p</i> -bromochlorobenzene	95
3	Toluene	NaBr	<i>p</i> -bromotoluene	89
4	Toluene	KBr	<i>p</i> -bromotoluene	92
5	Anisole	NaBr	(i) <i>p</i> -bromoanisole	68
			(ii) <i>p</i> -bromophenol	17
6	Anisole	KBr	(i) <i>p</i> -bromoanisole	71
			(ii) <i>p</i> -bromophenol	21
7	Phenol	NaBr	<i>p</i> -bromophenol	83
8	Phenol	KBr	<i>p</i> -bromophenol	87
9	Aniline	NaBr	<i>p</i> -bromoaniline	87
10	Aniline	KBr	<i>p</i> -bromoaniline	86
11	<i>o</i> -cresol	NaBr	4-bromo-2-methylphenol	80
12	<i>o</i> -cresol	KBr	4-bromo-2-methylphenol	76
13	Naphthalene	NaBr	1-bromonaphthalene	74
14	Naphthalene	KBr	1-bromonaphthalene	79
15	2-Naphthol	NaBr	1-bromo-2-naphthol	89
16	2-Naphthol	KBr	1-bromo-2-naphthol	86
17	Ethylbenzene	NaBr	<i>p</i> -bromoethylbenzene	81
18	Ethylbenzene	KBr	<i>p</i> -bromoethylbenzene	80

Table 3 Physical and spectroscopic data of *p*-bromoarenes

Entry	Product	m.p/b.p Observed	^o C Lit.	IR (C-Br) ν (cm ⁻¹) ³⁵	¹ H NMR (CDCl ₃) δ (ppm) ^c
1	<i>p</i> -bromochlorobenzene	66 ^a	64.6 ³⁰	1020	7.15(d, 2H), 7.4(d, 2H).
2	<i>p</i> -bromotoluene	184 ^b	183.6 ³¹	1025	2.3(s, 3H), 7.2(d, 2H), 7.4 (d, 2H).
3	<i>p</i> -bromoanisole	213 ^b	213 ¹²	1040	3.7 (s, 3H), 6.7(d, 2H), 7.3 (d, 2H).
4	<i>p</i> -bromophenol	64 ^a	63 ¹⁷	1055	6.6 (d, 2H), 6.85 (s, 1H, broad), 7.25 (d, 2H).
5	<i>p</i> -bromoaniline	66 ^a	66 ¹³	1070	3.5 (s, 2H), 6.5 (d, 2H), 7.2 (d, 2H)
6	4-bromo-2-methylphenol	63 ^a	64 ³²	1065	2.1 (s, 3H), 4.9 (s, 1H), 7 (m, 3H).
7	1-bromonaphthalene	284 ^b	283–285 ³³	985	7.35 (m, 7H)
8	1-bromo-2-naphthol	80 ^a	79–81 ³⁴	1080	5.8 (s, 1H, broad), 7.45 (m, 6H).
9	<i>p</i> -bromoethylbenzene	204 ^b	205 ¹³	1070	1.2 (t, <i>J</i> = 7 Hz, –CH ₃), 2.5 (q, <i>J</i> = 7 Hz, –CH ₂ –), 7.0 (d, 2H), 7.3 (d, 2H).

^aMelting point^bBoiling point at 760 torr.^cFor all the products the coupling constant for aromatic protons is *J* = 8 Hz; the AA 'XX' system appeared as two doublets at 90MHz

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