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AROMATIC IODINATION WITH ALUMINUM AND COPPER(II) CHLORIDES AND IODINE

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Aryl iodides have been synthesized by a simple reaction of aromatic compounds with iodine and an equimolecular mixture of aluminum and copper(II) chlorides. The reaction is widely capable of application, especially to liquid aromatic substrates, with fair to excellent yields.

Although halogenation of aromatic compounds with elementaly halogens is well-known reaction, bromination and chlorination easily proceed with or sometimes without Lewis acid catalysts, but iodination usually more difficult to take place. Except for active substrates, oxidizing reagents such as nitric acid, iodic acid, sulfur trioxide and hydrogen peroxide must normally be present to oxidize the iodine molecule to a better electrophile.[1] Aryl iodides are also prepared by the decomposition of diazonium salts or arylthallium bistrifluoroacetate[2] with potassium iodide. These procedures suffer some deficiencies. The most of serious of these are substrate limitations due to reaction conditions and the loss of iodine from the reaction as hydrogen iodide or metallic iodide.

Metal halides-catalyzed aromatic iodination with molecular iodine has also been reported. Uemura *et al.* reported an equimolar mixture of antimony(V) chloride and iodine to be a convenient reagent for aromatic iodination.[3] Baird and Surridge reported the aromatic iodination with molecular iodine in the presence of copper salts.[4] In this case, the more reactive substrates such as anisole and xylenes could be iodinated with molecular iodine, but more potent iodine donors (*e.g.*, Iron(II) or aluminum(III) iodides) were required for the less reactive substrates such as benzene and halobenzenes.

In the course of our studies on the Friedel-Crafts reactions in the presence of some oxidizing agents, it was found that the iodination of aromatic compounds by molecular iodine in combination with copper(II) chloride was much improved by the addition of aluminum chloride. When only copper salts were used as the catalyst, it was reported that the reaction conditions such as 80-150 °C and 3-50 h were required to accomplish the iodination reaction, but in the present case aromatic substrates could be iodinated with molecular iodine at about 40 °C and within 2 h.

The reaction of benzene and iodine with aluminum and copper(II) chlorides was studied to determine the ability of each salt to participate in the synthesis of aryl iodide. Iodine (3.8 g, 15 mmol) was dissolved in benzene (50 ml), to this

solution was added a mixture of anhydrous aluminum chloride (4.0 g, 30 mmol) and copper(II) chloride (4.0 g, 30 mmol; dried at 120 °C/ 3 mmHg for more than 3 h; 1 mmHg ≈ 133.322 Pa). The mixture was stirred at 40 °C for 2 h. The mixture was then poured into ice-water. The organic layer was washed with 10% aqueous sodium hydrogen sulfite, and worked up as usual. All products were characterized by comparisons of NMR and IR spectra and GLPC retention times with those of authentic samples. Table 1 presents the results of these experiments. The iodination product was iodobenzene alone, no diiodo compound was detected. When the amount of aluminum chloride was diminished to 0.5 and 0.1 equivalents, the yields of iodobenzene were decreased proportionally, and no iodobenzene was obtained without aluminum chloride. The same is observed about the copper salt. The highest yield of iodobenzene was obtained when the molar ratio of iodine, aluminum and copper(II) chlorides was 1:2:2. In this case, the iodine added was almost completely consumed, and two moles of aryl iodide were formed from one mole of iodine. Thus, the reaction appeared to occur in accord with the following stoichiometry:

$$2\,ArH + I_2 + 2\,CuCl_2 \xrightarrow{AlCl_3} 2\,ArI + 2\,HCl + Cu_2Cl_2$$

Although the actual attacking species is not yet clear, aluminum chloride acts as a Lewis acid to catalyzed the aromatic iodination, and copper(II) chloride oxidizes the iodide to iodine or iodine monochloride, a potent iodination reagent,[5] which iodinates a second mole of aromatics under the influence of aluminum chloride. Thus the complete utilization of iodine is achieved.

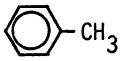
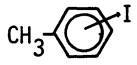
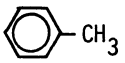
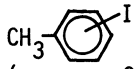
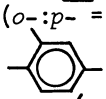
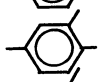
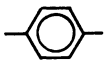
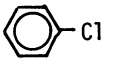
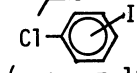
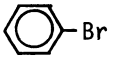
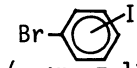
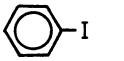
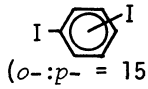
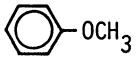
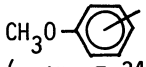
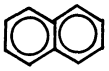
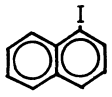
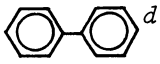
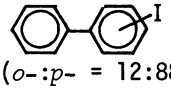
Table 1. Synthesis of Iodobenzene[a]

Run	Benzene [ml]	$AlCl_3$ [mmol]	$CuCl_2$ [mmol]	I_2 [mmol]	Iodobenzene Yield [%][b]
1	70	30	30	15	85.6
2	50	30	15	15	47.6
3	50	30	3	15	8.3
4	100	30	0	15	0.5
5	50	15	30	15	37.4
6	50	3	30	15	trace
7	100	0	30	15	—

a At 40 °C, for 2 h. *b* Determined by GLPC (PEG-20M 2 m column using indan as an internal standard).

From these results, the iodination of various aromatic substrates was examined using iodine and an equimolar mixture of aluminum and copper(II) chlorides. The results are summarized in Table 2, together with the results obtained by Baird and Surridge using copper(II) chloride in combination with iodine or iodine donors.[4] As can be seen in the Table, the present iodination reaction proceeds well under more mild conditions in comparison with the method using copper(II) chloride alone as the catalyst. In the case of strongly activated substrates such as anisole

Table 2. Synthesis of Aryl Iodides[a]

Run	Substrate	Reaction Conditions Temp [°C]	Time [h]	Product	Yield[b] [%]	Yield [%][c] by I_2-$CuCl_2$
1		40	2		79 (97)	65 (AlI_3-$CuCl_2$)
2		40	2		(80)	81 (FeI_2-$CuCl_2$)
3		70	2	 (o-:p- = 35:65)	73 (100)	
4		40	2		(23)	13
5		40	2		(61)	63
6		40	2		65	34
7		40	2	 (o-:p- = 18:82)	79 (100)	29 (AlI_3-$CuCl_2$)
8		50	4	 (o-:p- = 13:87)	88	33 (FeI_2-$CuCl_2$)
9		50	4	 (o-:p- = 15:85)	100	
10		40	2	 (o-:p- = 34:66)	69 (88)	80
11	 *d*	40	2		33	44
12	 *d*	40	4	 (o-:p- = 12:88)	72	45

a Aromatic substrate 50 ml; I_2 15 mmol; $AlCl_3$ 30-33 mmol; $CuCl_2$ 30-33 mmol. *b* Isolated Yield, value given in parentheses was determined by GLPC (Silicone SE-30 1 m or Silicone OV-17 2 m column using nitrobenzene or indan as an internal standard). *ortho*:*para* ratio was obtained by GLPC or ^{1}H-NMR. *c* Lit. 4). *d* Substrate (30 mmol) in nitromethane (50 ml).

and xylenes, the present procedure has not much advantage over the latter method in the yields. On the other hand, the iodination of the less reactive substrates such as benzene, toluene, and especially halobenzenes readily proceeds with molecular iodine under mild conditions in almost quantitative yields. These data indicate that the addition of aluminum chloride is particularly effective for the less activated substrates. Nitrobenzene and benzonitrile, however, were not iodinated even under severe conditions and recovered without change. Those aromatic compounds, ethyl benzoate, acetophenone, benzotrifluoride and *o*-nitroanisole, also failed to undergo the iodination and gave complicated side-reaction products,

benzoic acid, unknown products, benzotrichloride, and *o*-nitrophenol respectively, after prolonged reaction time.

The *ortho*:*para* distributions of the iodination products of toluene and chlorobenzene are corresponding to those reported in the reactions by iodine-copper(II) chloride or aluminum iodide-copper(II) chloride combinations, 41:59 and 18:82 respectively.[4] Bromobenzene yielded bromoiodobenzene in which the *ortho*:*para* ratio is 13:87, this is in marked contrast to the exclusive production of *para* isomer by iron(II) iodide-copper(II) chloride combination.[4]

It is known that benzene is polymerized by aluminum chloride-copper(II) chloride to give polyphenyl.[6] The production of polyphenyl could be minimized to a trace by adding a mixture of aluminum and copper(II) chlorides into a mixture of iodine and benzene. In the case of anisole and chlorobenzene, no polyaryl was detected. No diiodo compound was also detected in the reaction products. When xylenes were used as substrates, a resinous material remained as the distillation residue, which appeared to be polyxylyl, and probably it caused the low yields.

In contrast with the liquid substrates, the solid substrates gave only insufficient results though the reaction conditions were not optimized. Naphthalene and biphenyl were iodinated using nitromethane as a solvent to give 1-iodonaphthalene and iodobiphenyls respectively, but polymers which assumed to be binaphthyl and *p*-sexiphenyl respectively[7] were by-produced.

References

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3) S. Uemura, A. Onoe, and M. Okano, *Bull. Chem. Soc. Jpn.*, 47, 147 (1974).
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5) For a review, see H. P. Braendlin and E. T. McBee, "Friedel-Crafts and Related Reactions," Vol. III, ed by G. A. Olah, Wiley, New York (1964), Chap. 46.
6) P. Kovacic and A. Kyriakis, *J. Am. Chem. Soc.*, 85, 454 (1963).
7) P. Kovacic and R. M. Lange, *J. Org. Chem.*, 29, 2416 (1964); P. Kovacic and F. W. Koch, *ibid.*, 30, 3176 (1965).

Added in Proof: After the manuscript was finished, it was shown by Ono *et al.* that a complex of aluminum and copper(II) chlorides, $Cu(AlCl_4)_2$, was the effective catalyst for the polymerization of benzene. This result provides a possibility that this complex formed *in situ* can also be the reactive catalyst in the present iodination reaction. N. Kitajima, Y. Hakone, and Y. Ono, *Chem. Lett.*, 1982, 871.

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