SHORT PAPER

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Liquid-phase and biphasic chlorination of some iodoarenes to form (dichloroiodo)arenes with sodium peroxodisulfate as the oxidant[†]

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Liquid-phase and biphasic (CCl_4/concd hydrochloric acid) chlorination of some iodoarenes to form the corresponding (dichloroiodo)arenes, prepared in 60–100% crude yields, are reported; dichlorine is produced as follows: $Na_2S_2O_8$ + 2 HCl (conc. aq.) → Cl_2 + 2 $NaHSO_4$.

(Dichloroiodo)arenes, $ArICl_2$, play an important role in organic synthesis. Some more stable examples, *e.g.* (dichloroiodo)benzene, are widely used as potent and selective chlorinating and/or oxidizing agents.[1] They have a practical advantage over elemental chlorine (dichlorine) due to their easy and safe handling. For example, it was possible to monochlorinate 4-aminoacetophenone with PhICl2 on a 24.8 kg scale, in 87% yield.[2] Moreover, $ArICl_2$ may be readily converted to other important organic hypervalent iodine reagents, viz. iodosylarenes, iodylarenes, (diacyloxyiodo)arenes, (difluoroiodo)arenes,[1] and diaryliodonium salts.[3]

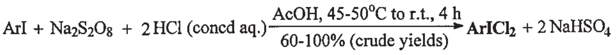
$ArICl_2$, yellow crystalline compounds, are light- and heat-sensitive and often unstable to storage. They do not usually give satisfactory microanalyses and their melting points (with decomposition) are rather *uncertain*, depending upon the purity of the crude products prepared, the time after their preparation, and the rate of heating; see footnote "a" in Table 1.

In 1885 Willgerodt[4] synthesized the first stable organic iodine(III) compound, (dichloroiodo)benzene: PhI + ICl_3 → $PhICl_2$ + ICl. $ArICl_2$ can also be made as follows:[3] Ar_2Hg + ICl_3 → $ArICl_2$ + ArHgCl; this reaction is of preparative significance in the case of the vinyl-type organomercurials. In 1886 Willgerodt[5] developed the most common method up to now for preparing $ArICl_2$, by passing a stream of Cl_2 through solutions of ArI in chloroform, at 0 °C. The yields are generally excellent when this method is applicable; $ArICl_2$ is not formed from ArI bearing oxidizable groups: *e.g.* OH, NH_2, ethylenic double bonds, *etc*. Anhydrous conditions previously demanded[6] are not necessary.[7] Recently, repeated preparations of $PhICl_2$ on a 20 kg scale (in 94% crude yield) were conducted[2] by direct chlorination of PhI, at –3 to +4°C, in CH_2Cl_2 as solvent.

A two-phase (CCl_4/concd hydrochloric acid) chlorination of several ArI to form the corresponding $ArICl_2$ (prepared in 50–98% crude yields) was recently reported.[8] Dichlorine was produced in the aqueous phase as follows: $KClO_3$ (solid) + 6HCl (conc. aq.) → ↑3 Cl_2 + KCl + 3 H_2O. In the present work (*vide infra*) we produced the dichlorine in the aqueous phase as follows: $Na_2S_2O_8$ + 2 HCl (conc. aq.) → ↑Cl_2 + 2$NaHSO_4$. However, a short preheating period (at 45 – 50°C) was necessary to start the oxidative reaction. In comparison with the classic Willgerodt method,[2,5–7] the biphasic chlorinating methods avoid the inconvenient use of gaseous Cl_2. Hence they are relatively safe – since escape of Cl_2 to the atmosphere is considerably limited.

The inconvenient use of gaseous Cl_2 to afford $ArICl_2$ from ArI may also be avoided as follows: (i) by the action of hydrochloric acid on either iodosylarenes or (diacyloxyiodo)arenes previously otherwise obtained from ArI;[1] (ii) by using liquid SO_2Cl_2 added to a solution of ArI either in wet diethyl ether[9] or (much better) in 98% acetic acid;[10] (iii) by the action of a liquid mixture: cobalt(III) acetate – KCl – 67% aq. CF_3COOH on PhI;[11] (iv) by the use of hydrochloric acid oxidized *in situ* with sodium perborate in either acetonitrile or carbon tetrachloride (*a* biphasic procedure) containing a dissolved ArI;[12] (v) by the use of hydrochloric acid oxidized *in situ* with chromium(VI) oxide in acetic acid containing a dissolved ArI.[13] However, some of these liquid-phase chlorination procedures demand the use of toxic oxidants.[11,13] Hence the wastes left after the reactions are unavoidably contaminated with Co(II) or Cr(III) salts, respectively.

In the present work we used sodium peroxodisulfate (sodium persulfate), $Na_2S_2O_8$, a very potent,[14] inexpensive,[15] and often applied oxidant,[16] which oxidized *in situ* concentrated hydrochloric acid mixed with glacial acetic acid containing a dissolved iodoarene. However, it was necessary to warm up the stirred reaction mixture to 45–50°C, to initiate the following reaction (liquid-phase procedure 1):



$$ArI + Na_2S_2O_8 + 2\,HCl\ (\text{concd aq.}) \xrightarrow[\text{60-100\% (crude yields)}]{\text{AcOH, 45-50°C to r.t., 4 h}} \mathbf{ArICl_2} + 2\,NaHSO_4$$

Scheme 1

Thus, an appropriate iodoarene (Table 1) was previously dissolved or suspended in glacial acetic acid and an excess of $Na_2S_2O_8$ was added, followed with a large excess of concentrated hydrochloric acid. At first, it was necessary to warm the stirred reaction mixture to 45–50 °C. Next, the electric heating was turned off, and the stirring was continued for a further four hours. The final reaction mixture was poured into ice-water, the collected yellow precipitate was washed well with ice-cold water until the washings were neutral, next with CCl_4 to remove organic impurities and then air-dried with avoidance of light. The crude yields obtained varied from 60 to 100% (Table 1); the melting points (with decomposition) of the crude $ArICl_2$ were fairly close to those reported in the literature. [2,5–8,10–13,17,18] After air-drying, the crude $ArICl_2$ were immediately analysed iodometrically[5] to show a 89–95% purity. For the sake of comparison, iodobenzene, 4-iodoacetanilide, 2-iodobenzoic acid, and 1,4-fluoroiodobenzene were also chlorinated by the biphasic Procedure 2

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Chlorination of iodoarenes to the corresponding (dichloroiodo)arenes

Substrate	Product	Procedure	Crude yield, (%)
C_6H_5I	$C_6H_5ICl_2$[a]	1	100
		2	100
4–MeCONH–C_6H_4I	4–MeCONH–$C_6H_4ICl_2$	1[b]	60
		2[c,d]	90
4–MeO–C_6H_4I	4–MeO–$C_6H_4ICl_2$	2[d]	89
3–Me–C_6H_4I	3–Me–$C_6H_4ICl_2$	1	97
4–Me–C_6H_4I	4–Me–$C_6H_4ICl_2$	1	96
4–F–C_6H_4I	4–F–$C_6H_4ICl_2$	1	100
		2	100
4–Cl–C_6H_4I	4–Cl–$C_6H_4ICl_2$	1	86
4–Br–C_6H_4I	4–Br–$C_6H_4ICl_2$	1	74
1,4–$C_6H_4I_2$	4–I–$C_6H_4ICl_2$	1	100
2–I–4–NO_2–C_6H_3Me	2–ICl_2–4–NO_2–C_6H_3Me	1	77
2–I–C_6H_4COOH	2–ICl_2–C_6H_4COOH	1	93
		2	95
3–I–C_6H_4COOH	3–ICl_2–C_6H_4COOH	1	86
4–I–C_6H_4COOH	4–ICl_2–C_6H_4COOH	1	100
2–I–$C_6H_4NO_2$	2–ICl_2–$C_6H_4NO_2$	1	95
3–I–$C_6H_4NO_2$	3–ICl_2–$C_6H_4NO_2$	1	100
4–I–$C_6H_4NO_2$	4–ICl_2–$C_6H_4NO_2$	1	99

[a] M.p. (dec.) 112–115 °C; 91–94% purity. Due to the reasons explained in the text, the literature m.p.s (mostly with decomposition) reported for crude $ArICl_2$ are *uncertain*. *E.g.* for crude $PhICl_2$ the following m.p.s have been reported (°C): 113–117;[2] 115–116;[8] 117–119;[10] 121;[12] 111–112;[13] 120, 115–127, 110–136;[17] 120–121.[18] Keefer and Andrews[18] have observed that in the cases of the dichlorides of 4-iodonitrobenzene and of 4-iodobenzoic acid all the dichlorine apparently was expelled when melting occurred; the recorded m.p.s for these were the same as those of the initial iodo compounds.

[b] Acetic anhydride (25 ml) was additionally added to the starting reaction mixture in order to slow down (as much as possible) the acid hydrolysis of the acetamido group – particularly within the short preheating period (at 45–50°C).

[c] This example shows that for iodoarenes substituted with *hydrolysable* groups, Procedure 2 is preferable.

[d] It may be deduced from ref. 12 that it is preferable to obtain $ArICl_2$ from iodoanisoles and highly activated ArI with using either the biphasic[8,12] or the classic Willgerodt[2,5–7] methods, where ArI and a *less active* molecular chlorine, Cl_2, are both dissolved and reacting in an inert solvent. On the other hand appropriate liquid-phase oxidative chlorination protocols seem to be more suitable for *deactivated* ArI – because such ArI are reacted upon with some more active, though short-living, chlorine species, formed there *in statu nascendi*.

(experimental); the crude yields [except of 4-(dichloroiodo)acetanilide] and purities of the $ArICl_2$ obtained were the same as those obtained with procedure 1. We failed to chlorinate with Procedure 1: 2-iodo-1,4-xylene, iodomesitylene, and 1,3,5-trichloro-2-iodobenzene.

In conclusion, we have presented two easy and inexpensive laboratory procedures for the effective preparation of crude $ArICl_2$ from some ArI listed in Table 1. In comparison with the classic Willgerodt method,[2,5–7] they avoid the inconvenient use of gaseous Cl_2. The strongly acidic wastes left after the chlorination reactions contained no strongly toxic contaminants; they were disposed of, without problem, after neutralization and dilution. Hence, the present chlorination procedures are relatively environmentally benign. Procedure 1 is particularly suitable for *deactivated* iodoarenes (including all isomeric iodonitrobenzenes and iodobenzoic acids which are chlorinated within four hours) and, possibly, for large-scale preparations of $PhICl_2$; see our former papers[8,13] as well as footnotes "c" and "d" in Table 1. Procedure 2 is particularly suitable for highly activated ArI, *e.g.* iodoanisoles, and for ArI substituted with hydrolysable groups, *e.g.* iodoacetanilides.

Experimental

The starting iodoarenes, ArI, were either commercial products or obtained in our laboratory from studies[19] on novel iodination methods. They were freshly purified prior to use. 4-Iodoacetanilide was obtained by the acylation of commercial 4-iodoaniline.[20] Sodium peroxodisulfate, $Na_2S_2O_8$, was a commercial product (Aldrich).[15] All the chlorination reactions were carried out under a fume hood.

Procedure 1: *Liquid-phase chlorination of ArI to the corresponding $ArICl_2$*: An appropriate iodoarene (25 mmol) was dissolved or suspended in glacial acetic acid (50 ml). Powdered $Na_2S_2O_8$ (8.9 g, 37 mmol; 48% excess) was added to the stirred solution, followed with conc. (36%) hydrochloric acid (20.4 ml, 24.4 g, 244 mmol). The well stirred mixture was warmed up to 45–50°C. Then the electric heating was turned off and the stirring was continued for 4 hours. The resulting mixture was poured, with stirring, into ice-water (100 g). The yellow precipitate was collected by filtration, washed well with ice-cold water until the washings were neutral and then with CCl_4. The crude products were air-dried *in the dark*. See Table 1 for more details.

Procedure 2: *Biphasic chlorination of some ArI to the corresponding $ArICl_2$* : An appropriate iodoarene (25 mmol) was dissolved or suspended in carbon tetrachloride (50 ml). This was added to a vigorously stirred mixture composed of: concd (36%) hydrochloric acid (20.4 ml, 24.4 g; 244 mmol) and powdered $Na_2S_2O_8$ (8.9 g, 37 mmol; 48% excess). The resulting mixture was warmed up, with stirring, to 45–50°C, then the electric heating was turned off, and the vigorous stirring was continued for 4 hours. The following workup was the same as that in Procedure 1. See Table 1 for more details.

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