

One-Pot Procedures for Preparing (Dichloroiodo)arenes from Arenes and Diiodine, with Chromium(VI) Oxide as the Oxidant[†]

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Abstract: Ten representative (dichloroiodo)arenes, ArICl₂, were prepared from the corresponding arenes and diiodine in variable *anhydrous* mixtures, ArH/I₂/CrO₃/AcOH/Ac₂O/conc. H₂SO₄, followed by the addition of conc. hydrochloric acid, used as the source of chlorine; ArICl₂ are useful in organic synthesis as mild and selective chlorinating and/or oxidizing agents.

Keywords: (dichloroiodo)arenes, arenes, diiodine, chromium(VI) oxide as oxidant

Introduction

(Dichloroiodo)arenes, ArICl₂, have found growing importance in organic synthesis as mild and selective chlorinating and/or oxidizing agents. They offer practical advantages over gaseous Cl₂ due to their easy and safe handling. They may also be converted into other important hypervalent iodine reagents, e.g. ArIF₂, ArIO, ArIO₂, ArI(OAc)₂, etc. [1]

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/decomposition points are uncertain, depending upon the purity of their freshly prepared batches, the time elapsed since their preparation, and the rate of heating during their melting point estimations [1].

In 1886 Willgerodt [2] developed the most common method up to now for preparing ArICl_2 , by passing the stream of Cl_2 through cooled solutions of ArI in CHCl_3 . Recently, Japanese chemists [3] repeatedly produced PhICl_2 from PhI (in 94% crude yield) on a 20 kg scale using this classic method. Next, they selectively monochlorinated 4-aminoacetophenone with *crude* PhICl_2 on a 24.8 kg scale, in 87% yield.

To avoid the hazardous and inconvenient use of gaseous Cl_2 to prepare ArICl_2 from ArI , a considerable number of various either *two-phase* ($\text{CCl}_4/\text{conc. aq. HCl}$) or monophasic *liquid-phase* methods were reported; the full account of all those methods is given in our latest review [4]. The dichlorine was generated there *in situ* from conc. hydrochloric acid, used either as a separate phase or as cosolvent, under the action of various oxidants: $2\text{HCl} + [\text{O}] \rightarrow \text{Cl}_2 + \text{H}_2\text{O}$; mostly, such procedures are easy and relatively safe. However, all former methods [1-4] required the use of **iodoarenes**, ArI , as the starting substrates which are then chlorinated at their iodine atoms to afford ArICl_2 . Recently, we presented [5] a novel, one-pot (two-stage) method for preparing eleven ArICl_2 from corresponding **arenes** (ArH) and diiodine used as the starting substrates. ArH were first oxidatively substituted in appropriate *anhydrous* I_2/NaIO_4 or $\text{NaIO}_3/\text{AcOH}/\text{Ac}_2\text{O}/\text{conc. H}_2\text{SO}_4$ mixtures with some *iodine(III)* transient species, I^{3+} , to form *in situ* the organoiodine(III) intermediates, ArISO_4 , viz. $\text{ArH} + \text{I}^{3+} + \text{H}_2\text{SO}_4 \rightarrow \text{ArISO}_4 + 3\text{H}^+$. Next, excess conc. (36%) hydrochloric acid was added to the resulting reaction mixtures, containing the soluble ArISO_4 intermediates, to precipitate out the corresponding ArICl_2 , isolated in 46-88% crude yields, viz. ArISO_4 (*not isolated*) + $2\text{HCl} \rightarrow \downarrow\text{ArICl}_2 + \text{H}_2\text{SO}_4$. Our *environmentally benign* method avoided the use of costly iodoarenes, the hazardous application of gaseous Cl_2 and chlorinated solvents and, in our opinion, would be particularly suitable for *large-scale preparations* of ArICl_2 from the respective arenes; cf. Ref. [3]. But there are also some **inherent limitations** in the applicability of this method. Of course, only those isomeric $\text{RC}_6\text{H}_4\text{ICl}_2$ may predominantly be obtained from the monosubstituted benzenes RC_6H_5 , which are formed in agreement with common orientation rules in the electrophilic substitutions of the used substrates RC_6H_5 by said strongly electrophilic I^{3+} transient species, generated *in situ* in the *anhydrous* iodinating reaction mixtures. We have emphasized [5] that further studies are necessary to establish more precisely the limits of the scope of this novel "model" studies are presented below, but with using chromium(VI) oxide, CrO_3 , as the oxidant. Hence, it is necessary to recall the results reported in our two former papers [6, 7], where CrO_3 was also applied as the effective oxidant.

In 1997 we developed [6] a simple oxidative method for the iodination of various arenes in variable *anhydrous* $\text{ArH}/\text{I}_2/\text{CrO}_3/\text{AcOH}/\text{Ac}_2\text{O}/\text{conc. H}_2\text{SO}_4$ systems. For benzene, halobenzenes, and *activated* arenes, the highest iodination yields were obtained with the following ratio of the reagents: $6\text{ArH} : 3\text{I}_2 : 2\text{CrO}_3$, which favoured the generation of some *iodine(I)* transient species, I^+ , acting there as the iodinating agents. In contrast, for *deactivated* aromatics, the following ratio of the reagents:

$2\text{ArH} : \text{I}_2 : 2\text{CrO}_3$ was applied, which was favourable for generating in the iodinating mixtures some more electrophilic *iodine(III)* transient species, I^{3+} , which reacted with said aromatics to form the soluble organoiodine(III) intermediates, ArISO_4 (*not isolated*); after pouring the resulting reaction mixtures into aqueous Na_2SO_3 solutions, the iodoarenes, ArI , were obtained as follows: $\text{ArISO}_4 + \text{Na}_2\text{SO}_3 + \text{H}_2\text{O} \rightarrow \text{ArI} + 2\text{NaHSO}_4$. For more details see either our former paper [6], or our latest review [4], pp 1334-1337.

In 1999 we reported [7] a simple method for the conversion of several ArI into corresponding ArICl_2 . We used excess concd hydrochloric acid oxidised *in situ* with CrO_3 prior dissolved in acetic acid containing also a dissolved (or suspended) ArI . These *liquid-phase* reactions proceeded according to the following stoichiometry: $3\text{ArI} + 2\text{CrO}_3 + 12\text{HCl} \rightarrow \downarrow 3\text{ArICl}_2 + 2\text{CrCl}_3 + 6\text{H}_2\text{O}$. For more details see either our former paper [7], or our latest review [4], p 1348.

Results and Discussion

We now report that by a proper *compilation* of our three former methods [5-7] it was possible to synthesise, in good or excellent crude yields, ten ArICl_2 from corresponding ArH and diiodine, but with using CrO_3 as the effective oxidant. To this end we have worked out three different preparative procedures explained below and detailed in the Experimental:

Two-stage Procedure 1 is applicable for *deactivated* arenes, e.g. benzoic acid and its methyl and ethyl esters, which are resistant to the action of CrO_3 in acidic media. The *whole* calculated portion of CrO_3 was added at the beginning to generate in the reaction mixtures some strongly electrophilic I^{3+} transient species, which reacted with said ArH to form the soluble ArISO_4 intermediates. Next, they were readily metathesised into insoluble ArICl_2 , by adding excess concd hydrochloric acid to the resulting reaction mixtures, coloured deep-green due to the presence of Cr(III) salts. After pouring into ice water, the yellow ArICl_2 were isolated by filtration, washed with water and CCl_4 , and air-dried *in the dark*.

Three-stage Procedure 2 is applicable for benzene and halobenzenes, which also are fairly resistant towards the action of CrO_3 in acidic media. However, higher iodination yields were obtained [6], when these arenes were iodinated *in situ* with some I^+ transient species to form corresponding ArI intermediates (*not isolated in this work*; cf. Ref. [6]). A *second portion* of CrO_3 had to be added to the resulting reaction mixtures, next followed by excess conc. hydrochloric acid in order to transform the ArI intermediates into ArICl_2 ; cf. Ref. [7] for the explanation and details.

Three-stage Procedure 3 is applicable for such *activated* arenes as toluene, 1,3-xylene, anisole, and phenetole, which are more or less readily oxidizable [7]. As above, they were at first iodinated with some I^+ transient species to form the corresponding ArI intermediates (*not isolated*); next, these intermediates were oxidatively chlorinated *in situ*, in a manner similar to that described for those in Procedure 2; see Experimental for some preparative differences, also explained in Ref. [7], p 65.

Thus, in this paper we present a useful *modification* of our former method [5]. It extends the applicability of the method not only by the use of another oxidant, i.e. CrO_3 , but also by the development of the one-pot (three-stage) Procedures 2 and 3. Because CrO_3 is a *stronger* oxidant in acidic media than the NaIO_4 or NaIO_3 previously used [4, 5], consequently in the two three-stage Procedures 2 and 3, the total amount of CrO_3 was *divided into two appropriate parts*. Its first portion was added at the beginning of the iodination reactions to form *in situ* the ArI intermediates (*not isolated*). Next, the second portion of CrO_3 was added, followed by excess conc. hydrochloric acid, which oxidatively chlorinated the ArI intermediates to form the final products, i.e. ArICl_2 , in the highest yields possible (Table 1).

Experimental

General

The starting arenes, ArH , were commercially available products or obtained by reported methods; they were freshly purified prior to use. The reactions were carried out under a fume hood. The *toxic* residues containing chromium salts were disposed of according to the local safety measures.

The melting points with decomposition (see Table 1) are uncorrected and were measured as follows: after an approximate mp had been taken in an open capillary tube, a new sample was introduced about $10\text{ }^\circ\text{C}$ below this point, and the temperature was raised at a rate of $10\text{ }^\circ\text{C min}^{-1}$. Mps found by us (Table 1) were fairly close to those reported in our former papers [5-9]. Iodometric titrations [2] of the freshly prepared ArICl_2 showed that they were of 91-97% purity.

Procedure 1

To a stirred and cooled mixture of glacial AcOH (10 mL) and Ac_2O (5 mL), CrO_3 (0.63 g, 6.3 mmol) was slowly added portionwise, followed by powdered I_2 (0.8 g, 6.3 mmol) while keeping the temperature below $30\text{ }^\circ\text{C}$. After one h, a *deactivated* arene (11.0 mmol) was added, followed by conc. (98%) H_2SO_4 (1.87 mL, 35 mmol) added dropwise with stirring, while the temperature was maintained below $25\text{ }^\circ\text{C}$; the stirring was continued for 12 h at rt, while the reaction mixtures changed colour from dark to deep-green. Conc. (36%) hydrochloric acid (15 mL, ca. 490 mmol) was slowly added with stirring and cooling; this stirring was continued for 2-3 h, at rt. After pouring into ice water (200 mL), the yellow precipitates were collected by filtration, washed well on the filter with cold water until the washings were colourless and neutral, then with a little CCl_4 , air-dried *in the dark*, and weighed. Their mps (with decomp.) were taken *without delay*, in the manner explained above.

Procedure 2

To a stirred and cooled solution of CrO_3 (0.66 g, 6.6 mmol) in a mixture of glacial AcOH (10 mL) and Ac_2O (5 mL), powdered I_2 (2.31g, 18.2 mmol) was added portionwise, and this was stirred for a

further one h. Benzene or a halobenzene (11.0 mmol) was added, followed by conc. (98%) H₂SO₄ (0.5 mL, 9.4 mmol) added dropwise while keeping the temperature below 25 °C. After one h, the second portion of CrO₃ (1.0 g, 10 mmol) was slowly added portionwise, next followed by conc. (36%) hydrochloric acid (15 mL, ca. 490 mmol), with cooling below 25 °C; the stirring was continued for an additional one h at rt. After pouring into ice water (200 mL), the yellow precipitates collected by filtration were next worked up as those in Procedure 1.

Procedure 3

To a stirred and cooled solution of CrO₃ (0.66 g, 6.6 mmol) in a mixture of glacial AcOH (10 mL) and Ac₂O (5 mL), powdered I₂ (2.31g, 18.2 mmol) was added portionwise. After the stirring for one h, at rt, an *activated* arene (11.0 mmol) was added, followed by conc. (98%) H₂SO₂ [0.26 mL, 4.9 mmol for toluene, or 1.33 mL, 25 mmol for 1,3-xylene, anisole, and phenetole] added dropwise with stirring and cooling below 25 °C; the stirring was continued for 60-90 min at rt, while the iodinating mixtures changed colour to deep-green. *Separately*, a cooled solution of CrO₃ (1.0 g, 10 mmol) in water (5 mL) was diluted with glacial AcOH (15 mL). Next, conc. (36%) hydrochloric acid (15 mL, ca. 490 mmol) was added dropwise with stirring and cooling below 25 °C. To this freshly prepared cold solution, the aforementioned deep-green iodinating mixtures were added *immediately*, with stirring and cooling; the stirring was continued for an additional one h at rt. After pouring into ice water (200 mL), the yellow precipitates collected by filtration were next worked up as those in Procedure 1.

Table 1. Preparative Details, Yields, and Melting Points (*with decomposition*) of Crude (Dichloroiodo)arenes Prepared from Arenes and Diiodine

Substrate	Product	Procedure	Yield [%]	Mp [°C]	Lit. Mp [°C]
PhH	PhICl ₂	2	94-95	110-112	111-112 [7]
PhF	4-FC ₆ H ₄ ICl ₂	2	75-77	104-105.5	106-107 [7]
PhCl	4-ClC ₆ H ₄ ICl ₂	2	84.5-85	110-111	110-112 [7]
PhMe	4-MeC ₆ H ₄ ICl ₂	3	80-81	97-98	97-98 [7]
PhOMe	4-MeOC ₆ H ₄ ICl ₂	3	63-65	75-78	72-73 [9]
PhOEt	4-EtOC ₆ H ₄ ICl ₂	3	97-97.5	88-92	not given [10]
1,3-Xylene	2,4-Me ₂ C ₆ H ₃ ICl ₂	3	75-76.5	95-98.5	91 [10]
PhCO ₂ H	3-HO ₂ CC ₆ H ₄ ICl ₂	1	75-76.5	185-187	183-185 [7]
PhCO ₂ Me	3-MeO ₂ CC ₆ H ₄ ICl ₂	1	41-42	108-110	108-110 [7]
PhCO ₂ Et	3-EtO ₂ CC ₆ H ₄ ICl ₂	1	69.5-70	99-100	98-100 [7]

References and Notes

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Sample availability: (Dichloroiodo)arenes are mostly unstable, even when stored in a cooler, therefore samples cannot be supplied on request.