

## A Novel Aromatic Iodination Method, with Sodium Periodate Used as the Only Iodinating Reagent<sup>†</sup>

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**Abstract:** Benzene, halobenzenes and some deactivated arenes readily reacted in *anhydrous* NaIO<sub>4</sub>/AcOH/Ac<sub>2</sub>O/concd. H<sub>2</sub>SO<sub>4</sub> mixtures to afford, after quenching with excess aqueous Na<sub>2</sub>SO<sub>3</sub> solution (*a reducing agent*), purified iodinated products in 27–88% yields. This novel method of aromatic iodination is simple, fairly effective and environmentally safe.

**Keywords:** Arenes, iodoarenes, aromatic iodination, sodium periodate, periodyl organic intermediates.

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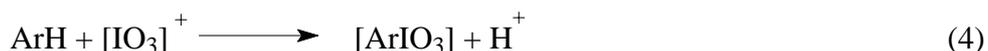
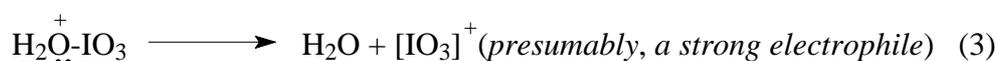
### Introduction

Only inorganic iodine(VII) derivatives are known and up to now not a single organoiodine(VII) compound has been synthesized and investigated [1,2]. The few reported attempts to synthesize *periodylarenes*, ArIO<sub>3</sub>, ended in failure. Willgerodt [3] oxidized iodylbenzene, PhIO<sub>2</sub>, with a hot 30% solution of perchloric acid, expecting to obtain periodylbenzene (“Superjodobenzol” or “Phenyljodtrioxyd”), PhIO<sub>3</sub>, but he obtained instead some white explosive crystals, probably an aromatic iodonium salt, Ph<sub>2</sub>I<sup>+</sup>ClO<sub>4</sub><sup>-</sup>. Lewitt and Iglesias [4] attempted to prepare PhIO<sub>3</sub> by adding benzene dropwise to a chilled solution of H<sub>5</sub>IO<sub>6</sub> in concd. H<sub>2</sub>SO<sub>4</sub>, but reported obtaining only a 48%

yield of periodobenzene, C<sub>6</sub>I<sub>6</sub>; they observed, however, that the initially colorless H<sub>5</sub>IO<sub>6</sub>/concd. H<sub>2</sub>SO<sub>4</sub> solution, after adding the benzene, turned first green, then red, and finally light yellow, as the yellow-tan C<sub>6</sub>I<sub>6</sub> gradually precipitated out. They remarked that the first formed *green intermediate* (presumably PhIO<sub>3</sub>) and the next red one should be further studied, and invited any investigators interested in this unusual reaction to pursue this avenue of research. Mattern [5] improved the above protocol for preparing either C<sub>6</sub>I<sub>6</sub> (45%) or 1,2,4,5-C<sub>6</sub>H<sub>2</sub>I<sub>4</sub> (60%) from benzene, but he made no attempt to study the green and red intermediates observed by Levitt and Iglesias [4]. Similarly, nobody has succeeded in preparing and investigating any single *organobromine(VII)* compound, while in contrast, the stable and unusually resistant to reduction *perchloryl aromatics*, ArClO<sub>3</sub>, have been known since 1958 [6].

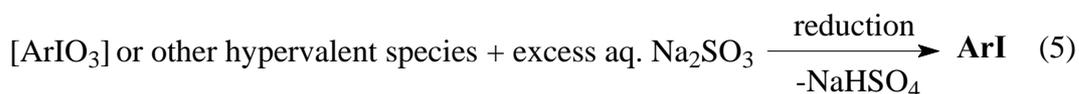
## Results and Discussion

As a continuation of our systematic studies on effective aromatic iodination reactions, which are related in detail in our two latest reviews [7,8], we recently decided to use sodium periodate NaIO<sub>4</sub>, *alone*, as an iodinating reagent. The reactions were carried out in *anhydrous* acetic acid/acetic anhydride solvent mixtures containing NaIO<sub>4</sub> and a chosen arene (Table 1), and then strongly acidified with *varied amounts* (see Table 1) of concd. (95%) sulfuric acid. We expected that the following subsequent reactions would probably proceed in the acidified reaction mixtures, viz.:



where: [IO<sub>3</sub>]<sup>+</sup> represents hypothetical transient periodyl cations and [ArIO<sub>3</sub>], the non isolable (*vide infra*), hypothetical periodyl intermediates. We must admit that in spite of our numerous attempts, we could not isolate from the final reaction mixtures any such ArIO<sub>3</sub> intermediates. In fact, after the addition of excess concd. hydrochloric acid to the cooled final reaction mixtures, we sometimes isolated the well-known [1-3,7] (dichloroiodo)arenes, ArICl<sub>2</sub>, in moderate yields, e.g. methyl 3-(dichloroiodo)benzoate, m.p. 108-109 °C (dec.), lit. [12] m.p. 104-105 °C (dec.), was isolated in 35% crude yield. These results suggest that the desirable aromatic *iodine(VII)* compounds must be obtained by a different route [9].

The aforesaid reaction mixtures were stirred at a temperature not exceeding 40 °C for 2 hours, then the temperature was *slowly* increased (over 30 min) to 60-70 °C, and the mixtures were finally stirred at this temperature for a further 40-50 min (at higher temperatures, the evolution of the iodine vapors and the appearance of some crystals were observed). During these reactions we did not observe any transient green or red colorations. After cooling, the final reaction mixtures were poured into ice-water containing a previously dissolved excess of Na<sub>2</sub>SO<sub>3</sub> (*a reducing agent*) to obtain the expected iodoarenes, ArI, viz.



Activated arenes, e.g. anisole, acetanilide, and *N,N*-dimethylaniline, were easily oxidized under the given reaction conditions to form some tarry products, while nitrobenzene was unaffected, and was recovered as such after completing the reactions shown in Eqs. 1-5. Benzene was deliberately diiodinated to afford pure 1,4-diiodobenzene in 52% yield. Benzonitrile, after completing all the reactions, gave only pure 3-iodobenzamide in 59% yield; cf. our former paper [10]. Halobenzenes and the nine deactivated arenes shown in Table 1 gave the purified monoiodinated products in 27-88% yields. Their purities and homogeneities were checked by TLC and the corresponding melting/boiling points were all close to those reported in the literature. The proposed chemical structures were also supported by elemental analyses (%I), and comparison of the <sup>1</sup>H- and <sup>13</sup>C-NMR solution spectra (not shown here) with the corresponding spectra of authentic specimens [11].

**Table 1.** Iodinated Pure Products Prepared and Volumes of Concd. H<sub>2</sub>SO<sub>4</sub> Added.

Substrate	Product	Yield/%	Concd H <sub>2</sub> SO <sub>4</sub> <sup>a)</sup> mL/mmol	Analysis/I%	Mp or Bp <sup>o</sup> C/solvent <sup>b)</sup>
				Calcd (Found)	(Lit [12] mp or bp <sup>o</sup> C)
C <sub>6</sub> H <sub>6</sub>	1,4-I <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	52	2.13/40	76.95 (76.7)	125-127/E (129)
PhI	1,4-I <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	69	4.26/80	76.95 (76.9)	126-128/E (129)
PhBr	4-BrC <sub>6</sub> H <sub>4</sub> I	66	4.26/80	44.86 (44.8)	89-91/E (91-92)
PhCl	4-ClC <sub>6</sub> H <sub>4</sub> I	27	5.33/100	53.22 (52.7)	54-55/E (57)
PhCOOH	3-IC <sub>6</sub> H <sub>4</sub> COOH	82	6.39/120	51.17 (51.0)	190-191/C (187-188)
PhCOOMe	3-IC <sub>6</sub> H <sub>4</sub> COOMe	82	6.39/120	48.43 (48.4)	46-48/EW (54-55)
PhCOOEt	3-IC <sub>6</sub> H <sub>4</sub> COOEt	57	7.46/140	45.97 (45.9)	bp 180-181/69 (bp 150.5/15)
4-MeC <sub>6</sub> H <sub>4</sub> COOH	3-I-4-MeC <sub>6</sub> H <sub>3</sub> COOH	88	6.39/120	48.43 (48.3)	209-211/C (210-212)
4-ClC <sub>6</sub> H <sub>4</sub> COOH	3-I-4-ClC <sub>6</sub> H <sub>3</sub> COOH	60	7.46/140	44.93 (44.5)	214-216/EW (216-217)
4-MeC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	3-I-4-MeC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	73	6.39/120	48.25 (47.8)	52-53/E (61)
PhCONH <sub>2</sub>	3-IC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	61	12.78/240	51.37 (51.0)	184-185/E (186.5)
PhCN	3-IC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	59	13.85/260	51.37 (51.1)	183-184/E (186.5)
PhCF <sub>3</sub>	3-IC <sub>6</sub> H <sub>4</sub> CF <sub>3</sub>	45	8.52/160	46.65 (46.2)	bp 70-72/40 (bp 182-183/760)

a) The amount of concd H<sub>2</sub>SO<sub>4</sub> added dropwise to each of the cooled and stirred reaction mixtures.

b) Solvents used for recrystallization: C: CHCl<sub>3</sub>; E: EtOH; EW: EtOH:H<sub>2</sub>O (1:1 v/v).

## Conclusions

We present in this short paper a quite *novel* approach to aromatic iodination, which allows one to effectively obtain iodoarenes from benzene, halobenzenes and some moderately deactivated arenes. The protonated transient *meta*-periodic acid, O<sub>4</sub>I<sup>+</sup>H<sub>2</sub> (formed from the reagent grade NaIO<sub>4</sub>, which is sufficiently soluble in warm *anhydrous* and strongly acidic solutions, Eq. 1) was the sole iodinating agent present, capable of forming the stable C-I bond in the starting arenes. We failed however to isolate the expected aromatic *iodine(VII)* intermediates.

## Experimental

### General

All the reagents and solvents were commercial materials (Aldrich) and were used without further purification. The melting/boiling points of pure iodinated products (Table 1) are uncorrected. Elemental microanalyses (%I) were performed at the Institute of Organic Chemistry, the Polish Academy of Sciences in Warsaw.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra (not shown here) were recorded at the Medical University of Warsaw, at room temperature, with a Bruker Avance DMX 400 MHz spectrometer in  $\text{CDCl}_3$  solutions, and with TMS added as an internal standard.

### Optimized Preparations of Iodoarenes from Arenes

Powdered  $\text{NaIO}_4$  (3.51 g, 16.4 mmol; 2.5% excess) [for the iodination of halobenzenes: 3.42 g  $\text{NaIO}_4$  (16 mmol; 0% excess), and for the preparation of 1,4-diiodobenzene from benzene: 3.60 g  $\text{NaIO}_4$  (16.8 mmol; 5% excess)] was suspended with stirring in a mixture made up of glacial AcOH (15 mL) and  $\text{Ac}_2\text{O}$  (10 mL) cooled to 10 °C. A chosen *arene* (16 mmol, 0% excess) [for the iodination of *halobenzenes*: 16.8 mmol; 5% excess, and for the preparation of 1,4-diiodobenzene from *benzene*: 8 mmol; 0% excess] was added dropwise or portionwise. Still keeping the temperature at ca 10 °C, a given volume (see Table 1) of concd. (95%)  $\text{H}_2\text{SO}_4$  was slowly added dropwise. The resulting reaction mixture was stirred at temperatures not exceeding 40 °C for 2 hours, then the temperature of the reaction mixture was *slowly* increased (within 30 min) to 60-70 °C, and the mixture was stirred at this temperature for a further 40-50 min. After cooling to r.t., the final reaction mixture was poured into stirred ice-water (150 g) containing previously dissolved  $\text{Na}_2\text{SO}_3$  (4 g). The oily crude products were extracted with  $\text{CHCl}_3$  (3 x 20 mL), the combined extracts were dried over anhydrous  $\text{MgSO}_4$ , filtered, the solvent was distilled off, and the oily residues were fractionated under reduced pressure. The solid crude products were collected by filtration, washed well with cold water, air-dried in the dark, and recrystallized from appropriate organic solvents to afford the purified iodinated products (Table 1). The yields given for pure products were calculated from the total amounts of those reagents ( $\text{ArH}$  or  $\text{NaIO}_4$ ) which were used in the reactions in strictly stoichiometric quantities (0% excess).

## References and Notes

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9. In our opinion, the postulated transient  $[\text{IO}_3]^+$  and  $[\text{ArIO}_3]$  species, probably present momentarily in the reaction mixtures, would quickly decompose in the *anhydrous* AcOH/Ac<sub>2</sub>O/concd. H<sub>2</sub>SO<sub>4</sub> medium to form more stable *iodine(III)* intermediates, I(OSO<sub>3</sub>H)<sub>3</sub> and ArI(OSO<sub>3</sub>H)<sub>2</sub>, probably along with peracetic acid and/or peroxomonosulfuric acid. Such stable, though strongly hygroscopic, compounds as I<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>, I(OSO<sub>3</sub>H)<sub>3</sub>, ArISO<sub>4</sub>, and ArI(OSO<sub>3</sub>H)<sub>2</sub> are discussed and referred to the literature in the following review: Kasumov T. M.; Koz'min A. S.; Zefirov N. S. The Chemistry of Inorganic Sulfates and Sulfonates of Polyvalent Iodine (in Russian). *Usp. Khim.* **1997**, *66*, 936-952; *Russ. Chem. Rev.* **1997**, *66*, 843-857.
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*Sample Availability:* Contact the authors.

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