A Novel Aromatic Iodination Method, with Sodium Periodate Used as the Only Iodinating Reagent†

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Abstract: Benzene, halobenzenes and some deactivated arenes readily reacted in anhydrous NaIO₄/AcOH/Ac₂O/concd. H₂SO₄ mixtures to afford, after quenching with excess aqueous Na₂SO₃ 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.

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, ArIO₃, ended in failure. Willgerodt [3] oxidized iodylbenzene, PhIO₂, with a hot 30% solution of perchloric acid, expecting to obtain periodylbenzene ("Superjodobenzol" or "Phenyljodtrioxyd"), PhIO₃, but he obtained instead some white explosive crystals, probably an aromatic iodonium salt, Ph₂I⁺ClO₄⁻. Lewitt and Iglesias [4] attempted to prepare PhIO₃ by adding benzene dropwise to a chilled solution of H₂IO₆ in concd. H₂SO₄, but reported obtaining only a 48%
yield of periodobenzene, C₆I₆; they observed, however, that the initially colorless H₅IO₆/conc. H₂SO₄ solution, after adding the benzene, turned first green, then red, and finally light yellow, as the yellow-tan C₆I₆ gradually precipitated out. They remarked that the first formed green intermediate (presumably PhIO₃) 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 C₆I₆ (45%) or 1,2,4,5-C₆H₂I₄ (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, ArClO₃, 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 NaIO₄, alone, as an iodinating reagent. The reactions were carried out in anhydrous acetic acid/acetic anhydride solvent mixtures containing NaIO₄ 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.:

\[
\text{NaIO}_4 + \text{H}_2\text{SO}_4 \rightarrow \text{HIO}_4 + \text{NaHSO}_4
\]  

\[
\text{H}_2\text{O}-\text{IO}_3 + \text{H}_2\text{SO}_4 \rightarrow \text{H}_2\text{O} + [\text{IO}_3]^+ \quad (\text{presumably, a strong electrophile})
\]

\[
\text{ArH} + [\text{IO}_3]^+ \rightarrow [\text{ArIO}_3] + \text{H}^+
\]

where: [IO₃]⁺ represents hypothetical transient periodyl cations and [ArIO₃], 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 ArIO₃ 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, ArICl₂, 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 Na₂SO₃ (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 moniodinated 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 \( ^1\)H- and \( ^{13}\)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\(_2\)SO\(_4\) Added.

| Substrate | Product | Yield/% | \( \text{Concd H}_2\text{SO}_4^{a)} \) | Analysis/1% | Mp or Bp\(^{°}\)C/solvent \(^{b)}\) |
|-----------|---------|---------|-----------------|-------------|----------------|
| C\(_6\)H\(_6\) | 1,4-I\(_2\)C\(_6\)H\(_4\) | 52 | 2.13/40 | 76.95 (76.7) | 125-127/E (129) |
| PhI | 1,4-I\(_2\)C\(_6\)H\(_4\) | 69 | 4.26/80 | 76.95 (76.9) | 126-128/E (129) |
| PhBr | 4-BrC\(_6\)H\(_4\)I | 66 | 4.26/80 | 44.86 (44.8) | 89-91/E (91-92) |
| PhCl | 4-ClC\(_6\)H\(_4\)I | 27 | 5.33/100 | 53.22 (52.7) | 54-55/E (57) |
| PhCOOH | 3-IC\(_6\)H\(_4\)COOH | 82 | 6.39/120 | 51.17 (51.0) | 190-191/C (187-188) |
| PhCOOMe | 3-IC\(_6\)H\(_4\)COOMe | 82 | 6.39/120 | 48.43 (48.4) | 46-48/EW (54-55) |
| PhCOOEt | 3-IC\(_6\)H\(_4\)COOEt | 57 | 7.46/140 | 45.97 (45.9) | bp 180-181/69 (bp 150.5/15) |
| 4-MeC\(_6\)H\(_4\)COOH | 3-I-4-MeC\(_6\)H\(_4\)COOH | 88 | 6.39/120 | 48.43 (48.3) | 209-211/C (210-212) |
| 4-CIC\(_6\)H\(_4\)COOH | 3-I-4-CIC\(_6\)H\(_4\)COOH | 60 | 7.46/140 | 44.93 (44.5) | 214-216/EW (216-217) |
| 4-MeC\(_6\)H\(_4\)NO\(_2\) | 3-I-4-MeC\(_6\)H\(_4\)NO\(_2\) | 73 | 6.39/120 | 48.25 (47.8) | 52-53/E (61) |
| PhCONH\(_2\) | 3-IC\(_6\)H\(_4\)CONH\(_2\) | 61 | 12.78/240 | 51.37 (51.0) | 184-185/E (186.5) |
| PhCN | 3-IC\(_6\)H\(_4\)CONH\(_2\) | 59 | 13.85/260 | 51.37 (51.1) | 183-184/E (186.5) |
| PhCF\(_3\) | 3-IC\(_6\)H\(_4\)CF\(_3\) | 45 | 8.52/160 | 46.65 (46.2) | bp 70-72/40 (bp 182-183/760) |

\( a)\) The amount of concd H\(_2\)SO\(_4\) added dropwise to each of the cooled and stirred reaction mixtures.

\( b)\) Solvents used for recrystallization: C: CHCl\(_3\); E: EtOH; EW: EtOH:H\(_2\)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 \emph{meta}-periodic acid, OI\(^{+}\)H\(_2\) (formed from the reagent grade NaIO\(_4\), which is sufficiently soluble in warm \emph{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. $^1$H- and $^{13}$C-NMR spectra (not shown here) were recorded at the Medical University of Warsaw, at room temperature, with a Brucker Avance DMX 400 MHz spectrometer in CDCl$_3$ solutions, and with TMS added as an internal standard.

Optimized Preparations of Iodoarenes from Arenes

Powdered NaIO$_4$ (3.51 g, 16.4 mmol; 2.5% excess) [for the iodination of halobenzenes: 3.42 g NaIO$_4$ (16 mmol; 0% excess), and for the preparation of 1,4-diiodobenzene from benzene: 3.60 g NaIO$_4$ (16.8 mmol; 5% excess)] was suspended with stirring in a mixture made up of glacial AcOH (15 mL) and Ac$_2$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%) H$_2$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 Na$_2$SO$_3$ (4 g). The oily crude products were extracted with CHCl$_3$ (3 x 20 mL), the combined extracts were dried over anhydrous 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 (ArH or NaIO$_4$) which were used in the reactions in strictly stoichiometric quantities (0% excess).

References and Notes

1. (a) Varvoglis, A. The Organic Chemistry of Polycoordinated Iodine; VCH: Weinheim, 1992; (b) Varvoglis, A. Hypervalent Iodine in Organic Synthesis; Academic Press: San Diego, 1997.
2. Zhdankin, V.V.; Stang, P.J. Polycoordinate Iodine Compounds. In Chemistry of Hypervalent Compounds; Akiba, K., Ed.; Wiley-VCH: New York, 1999; Chapter 11, p. 349.
3. Willgerodt, C. Die organischen Verbindungen mit mehrwertigem Jod; Enke Verlag: Stuttgart, 1914; p. 6.
4. Levitt, L.S.; Iglesias, R. The Periodination Reaction: Fast One-Step Synthesis of C$_6$I$_6$ from C$_6$H$_6$. J. Org. Chem. 1982, 47, 4470.
5. Mattern, D.L. Periodination of Benzene with Periodate/Iodide. J. Org. Chem. 1983, 48, 4772-4773.
6. Inman, C.E.; Oesterling, R.E.; Tyczkowski, E.A. Reactions of perchloryl fluoride with organic compounds. I. Perchlorylation of aromatic compounds. J. Am. Chem. Soc. 1958, 80, 5286-5288.

7. Skulski, L. Organic iodine(I, III, V) chemistry: 10 years of development at the medical University of Warsaw, Poland (1990-2000). Molecules 2000, 5, 1331-1371. Avail. at URL: http://www.mdpi.org/molecules/papers/51201311.pdf.

8. Skulski, L. Novel easy preparations of some aromatic iodine(I, III, V) reagents, widely applied in modern organic synthesis. Molecules 2003, 8, 45-52. Avail. at URL: http://www.mdpi.org/molecules/papers/80100045.pdf.

9. In our opinion, the postulated transient [IO₃]⁺ and [ArIO₃] species, probably present momentarily in the reaction mixtures, would quickly decompose in the anhydrous AcOH/Ac₂O/concd. H₂SO₄ medium to form more stable iodine(III) intermediates, I(OSO₃H)₃ and ArI(OSO₃H)₂, probably along with peracetic acid and/or peroxomonosulfuric acid. Such stable, though strongly hygroscopic, compounds as I₂(SO₄)₃, I(OSO₃H)₃, ArISO₄, and ArI(OSO₃H)₂ 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.

10. Lulinski, P.; Skulski, L. The direct iodination of arenes with chromium(VI) oxide as the oxidant. Bull. Chem. Soc. Jpn. 1997, 70, 1665-1669, see p. 1667, the right column.

11. Lulinski, P. Studies on novel methods of the iodination of aromatic compounds (in Polish), Doctoral dissertation, Faculty of Pharmacy, Medical University of Warsaw, Poland, 2002.

12. Dictionary of Organic Compounds, 6th ed.; Chapman & Hall: London, 1996.

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