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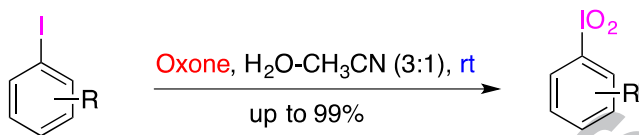
## Graphical Abstract

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R = H, 4-Me, 3-Me, 2-Me, 3,5-Me<sub>2</sub>, 3-MeO, 2-Cl, 3-Cl,  
4-Cl, 4-Br, 4-NO<sub>2</sub>, 2-I, 3-CF<sub>3</sub>, 3-CO<sub>2</sub>H, 4-CO<sub>2</sub>H, 2-IO<sub>2</sub>



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## Mild and Efficient Synthesis of Iodylarenes using Oxone as Oxidant

Natalia Soldatova<sup>a</sup>, Pavel Postnikov<sup>a</sup>, Anna A. Troyan<sup>a</sup>, Akira Yoshimura<sup>b</sup>, Mekhman S. Yusubov<sup>a, \*</sup> and Viktor V. Zhdankin<sup>a, b, \*</sup>

<sup>a</sup> The Tomsk Polytechnic University, 634050 Tomsk, Russia

<sup>b</sup> Department of Chemistry and Biochemistry, University of Minnesota Duluth, Duluth, Minnesota, 55812, USA

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### ABSTRACT

Mild and efficient method for the preparation of iodylarenes by oxidation of iodoarenes with Oxone in aqueous acetonitrile at room temperature is described. This new procedure allows the preparation of various iodylarenes with electron-donating or electron-withdrawing substituents in the aromatic ring including the previously unknown 1,2-diiodylbenzene.

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### 1. Introduction

Within the broader field of hypervalent iodine chemistry,<sup>1</sup> iodylarenes, ArIO<sub>2</sub>, have attracted a significant current interest as mild and highly selective reagents for the oxidation of alcohols to carbonyl compounds as well as for a variety of other synthetically useful oxidative transformations.<sup>2,3</sup> The most important representative of this class of compounds is 2-iodoxybenzoic acid, IBX (which exists in the cyclic benziodoxole tautomeric form);<sup>4</sup> however, a variety of other iodylarenes, including the parent iodylbenzene,<sup>2,3a</sup> have found important synthetic application. During the last several years the preparation and synthetic utilization of numerous new iodylarenes have been reported.<sup>5</sup>

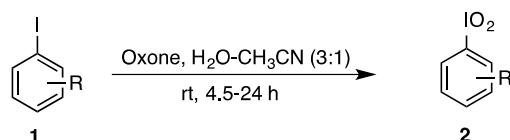
A typical procedure for the preparation of iodylarenes involves the oxidation of an iodoarene with a strong oxidizing reagent at high temperature.<sup>6</sup> Common experimental methods for the preparation of iodylbenzene (PhIO<sub>2</sub>) involve the generally unsafe and inefficient procedures such as the disproportionation of iodosylbenzene (PhIO) under steam-distillation,<sup>6a</sup> oxidation of iodobenzene with potassium peroxysulfate in concentrated sulfuric acid,<sup>6b</sup> oxidation of iodobenzene with sodium periodate in boiling water for 8–16 h,<sup>6c,d</sup> or oxidation with peracetic acid at 100 °C.<sup>6e</sup> A milder procedure involving a RuCl<sub>3</sub>-catalyzed direct one-pot conversion of ArI to ArIO<sub>2</sub> using peracetic acid as a stoichiometric oxidant at 40 °C has also been reported.<sup>6f</sup> This procedure, however, requires the use of a transition metal catalyst, which should be avoided, especially in the

pharmaceutical industry and research. A milder method for the preparation of PhIO<sub>2</sub> by oxidation of PhI with sodium hypochlorite in acetic acid for 24 h is also known.<sup>6g</sup>

We now report a transition-metal-free, mild, and convenient method for the preparation of iodylarenes by oxidation of various aryl iodides with Oxone in aqueous acetonitrile at room temperature. Oxone (2KHSO<sub>5</sub>·KHSO<sub>4</sub>·K<sub>2</sub>SO<sub>4</sub>) is an easy to handle, not toxic, cheap and stable commercial product, which makes it an especially attractive oxidizing reagent.<sup>7</sup>

### 2. Results and discussion

We have found that various iodoarenes smoothly react with Oxone in aqueous acetonitrile at room temperature to afford the corresponding iodylarenes as white, microcrystalline precipitates (Scheme 1). Reaction times (determined by the disappearance of starting iodoarenes in the reaction mixture using TLC) and the yields of isolated product are shown in Table 1.

































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**Scheme 1.** Preparation of iodylarenes **2** by oxidation of iodoarenes **1** with Oxone in aqueous acetonitrile.

\* Corresponding author. e-mail: yusubov@mail.ru

\* Corresponding author. Tel.: +1-218-726-6902; fax: +1-218-726-7394; e-mail: vzhdankin@d.umn.edu

**Table 1.** Iodylarenes produced via Scheme 1<sup>a</sup>

Entry	Iodoarene <b>1</b>	Iodylarene <b>2</b>	mp, °C	Reaction time, h	Yield %
1	 <b>1a</b>	 <b>2a</b>	230 (expl)	12	87
2	 <b>1b</b>	 <b>2b</b>	211 (expl)	4.5	59
3	 <b>1c</b>	 <b>2c</b>	220 (expl)	24	69
4	 <b>1d</b>	 <b>2d</b>	232 (expl)	12	89
5	 <b>1e</b>	 <b>2e</b>	217 (expl)	12	94
6	 <b>1f</b>	 <b>2f</b>	219 (expl)	18	60
7	 <b>1g</b>	 <b>2g</b>	209 (expl)	7	88
8	 <b>1h</b>	 <b>2h</b>	232 (expl)	12	68
9	 <b>1i</b>	 <b>2i</b>	248 (expl)	12	99
10	 <b>1j</b>	 <b>2j</b>	242 (expl)	24	82
11	 <b>1k</b>	 <b>2k</b>	209 (expl)	12 <sup>b</sup>	51
12	 <b>1l</b>	 <b>2l</b>	n/a <sup>c</sup>	8 <sup>d</sup>	98
13	 <b>1m</b>	 <b>2m</b>	214 (expl)	12	87
14	 <b>1n</b>	 <b>2n</b>	250 (expl)	4.5	91
15	 <b>1o</b>	 <b>2o</b>	240 (expl)	18	76

<sup>a</sup>The reaction was conducted by stirring iodoarene **1** (1 mmol), Oxone (2.46 g, 4 mmol) in 4 mL H<sub>2</sub>O-MeCN (3 : 1 by volume) for the indicated time until full disappearance of ArI. Products **2** were filtered after addition of water (20 mL), washed on filter with water (3x10 mL) and acetone or hexane (10 mL), and dried in

vacuum. See Supporting Information for further experimental details. **CAUTION: Iodylarenes are potentially explosive compounds and appropriate precautions should be taken while handling these products. A safety shield must be used and it is recommended to avoid using metal spatulas.**

<sup>b</sup>Concentrated H<sub>2</sub>SO<sub>4</sub> (0.495 g, 0.25 ml, 5 mmol) was added to the reaction mixture.

<sup>c</sup>A sample of product **2l** exploded at room temperature when it was placed in a capillary tube for melting point measurement.

<sup>d</sup>The reaction was conducted at 50 °C.

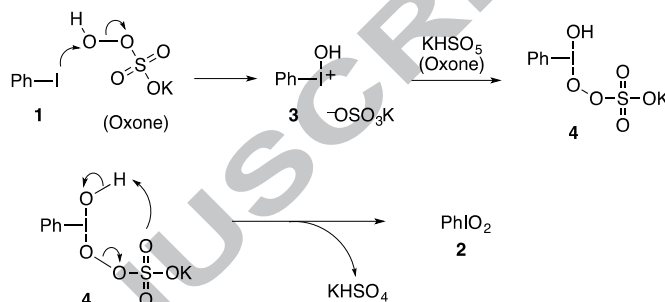
Our new procedure works well for the preparation of iodylarenes with either electron-donating or electron-withdrawing substituents in the aromatic ring (Table 1). The yields of isolated products in general are similar or higher compared to the previously reported procedures,<sup>6</sup> with the advantages of very mild reaction conditions and convenience of Oxone as the oxidant. The procedure is very simple and affords analytically pure products after simple filtration and additional washing of solid products on the filter, which is especially important when handling such potentially explosive compounds as iodylarenes. Most of iodylarenes decompose with explosion at their melting points above 200 °C; however, we have not experienced any unexpected explosions while handling these compounds at room temperature. We were even able to prepare products **2a**, **2d**, **2e**, **2i** and **2o** in a larger scale of 2-3 grams (see Supporting Information for details). **CAUTION: A safety shield must be always used while preparing and handling iodylarenes. It is also recommended to avoid using metal spatulas and sintered glass filters.**

Using this simple protocol we have synthesized the previously unknown iodylarenes **2e**, **2f**, **2m** and the novel 1,2-diiodylbenzene **2l** (Table 1, entry 12). In contrast to the monoiodylarenes, compound **2l** is a shock-sensitive explosive at room temperature and should be handled with especial precautions. We were able to reliably characterize this product by high-resolution mass-spectrometry and NMR spectroscopy in DMSO solution.

Our procedure allows the preparation of iodylarenes bearing strong electron-withdrawing substituents such as nitro, trifluoromethyl, and carboxylic groups (entries 11, 13-15). However, no oxidation was observed in the case of pentafluoriodobenzene, C<sub>6</sub>F<sub>5</sub>I, even after several hours at 50 °C. The oxidation of 2-iodobenzoic acid with Oxone at room temperature affords 2-iodosylbenzoic acid (IBA) because of the high stability of the initially formed iodine(III) benziodoxole ring. It is known from the literature that the preparation of 2-iodoxybenzoic acid (IBX) requires heating of 2-iodobenzoic acid with Oxone in water to 70 °C.<sup>8</sup>

Almost all previously reported procedures for the preparation of iodylarenes involve initial formation of iodosylarenes, e.g. PhIO, followed by disproportionation to PhI and PhIO<sub>2</sub> at high temperature.<sup>6</sup> The very mild reaction conditions of the oxidation of ArI with Oxone suggest that this reaction does not involve the ArIO disproportionation step. The proposed mechanism for the oxidation of PhI to PhIO<sub>2</sub> with Oxone is shown in Scheme 2. The reaction starts from the oxidation of PhI to hydroxyiodonium species **3** with Oxone. In our earlier work,<sup>9</sup> we confirmed the presence of [PhI(OH)]<sup>+</sup> in the PhI/Oxone mixture in aqueous acetonitrile by ESI mass-spectrometry; however, we were not able to isolate PhIO<sub>2</sub> from the reaction mixture in this work. The second step of the mechanism consists of the formation of iodine(III) peroxysulfate **4** by ligand exchange of hydroxyiodonium species **3** with Oxone. The formation of iodine(III) peroxides is a known reaction, and the cyclic peroxides - derivatives of benziodoxole have been even characterized by X-ray diffraction.<sup>10</sup> Finally, the heterolytic

cleavage of the peroxy bond in iodine(III) peroxysulfate **4** results in elimination of hydrosulfate anion with formal oxidation of iodine(III) to iodine(V) and the formation of PhIO<sub>2</sub> (Scheme 2). The excellent leaving group ability of hydrosulfate anion facilitates this process.



**Scheme 2.** Plausible mechanism of the oxidation of iodoarenes with Oxone.

It is likely that the previously reported oxidation of iodoarenes with sodium hypochlorite in acetic acid at room temperature<sup>3e,6g</sup> also occurs by a mechanism not involving the ArIO disproportionation step.

In conclusion, we have developed a mild and efficient method for the preparation of iodylarenes by oxidation of iodoarenes with Oxone in aqueous acetonitrile at room temperature. This new procedure allows the preparation of various iodylarenes with electron-donating or electron-withdrawing substituents in the aromatic ring including the previously unknown 1,2-diiodylbenzene.

## Acknowledgments

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## Supplementary Material

Supplementary data (these data include experimental details, analytical data, <sup>1</sup>H, <sup>13</sup>C and <sup>19</sup>F NMR spectra of products **2**) associated with this article can be found, in the online version, at <http://>

## References and notes

- For selected books and reviews on hypervalent iodine chemistry, see: (a) Zhdankin, V. V. *Hypervalent Iodine Chemistry: Preparation, Structure and Synthetic Application of Polyvalent Iodine Compounds*, John Wiley & Sons Ltd, Chichester, **2014**; (b) Kaiho, T. Editor, *Iodine Chemistry and Applications*, John Wiley & Sons, Inc., Hoboken, New Jersey, **2015**; (c) Yoshimura, A.; Zhdankin, V. V. *Chem. Rev.* **2016**, *116*, 3328-3435; (d) Charpentier, J.; Fruh, N.; Togni, A. *Chem. Rev.* **2015**, *115*, 650-682; (e) Dohi, T.; Kita, Y. *Curr. Org. Chem.* **2016**, *20*, 580-615; (f) Kita, Y.; Dohi, T. *Chem. Rec.* **2015**, *15*, 886-906; (g) Li, Y.; Hari, D. P.; Vita, M. V.; Waser, J. *Angew. Chem., Int. Ed.* **2016**,

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## Highlights

- Iodylarenes are prepared by oxidation of iodoarenes with Oxone at room temperature
- Various iodylarenes including previously unknown 1,2-diiodylbenzene were prepared
- New mechanism for the oxidation of iodoarenes by Oxone has been proposed