

# Iodine and iodic acid: an efficient reagent combination for iodination of aryl hydroxy ketones

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**Abstract**—A variety of *ortho*-hydroxy substituted aromatic carbonyl compounds were regioselectively iodinated with iodine and iodic acid in excellent yields.

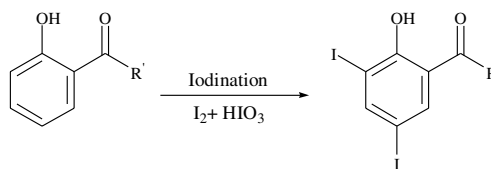
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## 1. Introduction

The iodination of aromatic carbonyl compounds has been the subject of numerous studies due to the potential of the products to serve as intermediates in organic synthesis and to act as bacterial and fungicidal agents.<sup>1</sup> The direct introduction of iodine into aromatic compounds under mild conditions requires an additive to increase the reactivity of iodine. Iodination of aromatic compounds has been carried out using molecular iodine together with a strong oxidizing agent such as nitric acid, sulfuric acid, iodic acid, sulfur trioxide and hydrogen peroxide.<sup>2a–c</sup> Recently, iodination methods have been intensively developed using iodonium donating systems, such as iodine nitrogen dioxide,<sup>3</sup> iodine-F-TEDA-[1-chloromethyl-4-fluoro-1,4-diazonia-bicyclo[2,2,2]octane-bis-(tetrafluoroborate)],<sup>4</sup> bis-*N*-iodosuccinimide,<sup>5</sup> iodine-di-iodine pentoxide,<sup>6</sup> mercury(II)-oxide-iodine,<sup>7</sup> iodine monochloride,<sup>8</sup> bis(pyridine) iodonium(I) tetrafluoroborate CF<sub>3</sub>SO<sub>3</sub>H,<sup>9</sup> NIS-CF<sub>3</sub>SO<sub>3</sub>H,<sup>10</sup> iodine silver sulfate,<sup>11</sup> iodine–mercury salts,<sup>12</sup> NaOCl–NaI,<sup>13</sup> iodine/Na<sub>2</sub>S<sub>2</sub>O<sub>8</sub><sup>14</sup> and iodine–(NH<sub>4</sub>)<sub>2</sub>S<sub>2</sub>O<sub>8</sub>–CuCl<sub>2</sub>–Ag<sub>2</sub>SO<sub>4</sub>.<sup>15</sup> However, some of these methods are hazardous and some of the reagents are toxic.

We report here a practical and regioselective aromatic iodination. A combination of iodine and iodic acid has been found to be an excellent reagent for the efficient iodination of aromatic carbonyl compounds such as hydroxy  $\alpha$ -chloroacetophenones, hydroxy propiophenones, hydroxybutyrophenones, hydroxybenzophenones and  $\alpha,\beta$ -unsaturated carbonyl compounds such as chalcones (Scheme 1). These reactions are carried out at 35–40 °C using commercial 95% aqueous ethanol as the solvent.

A variety of aromatic carbonyl compounds were investigated for the reaction with iodine and iodic acid (Table 1). The product was obtained in a regioselective manner, with iodination occurring at the electron rich *ortho* or *para* positions. When the *o*-position was blocked with a substituent, only iodination took place at the *p*-position. Iodination did not occur on the side chains, that is, –CO–CH<sub>2</sub>–R or –CH<sub>3</sub>. The iodination reaction only occurred on the hydroxy-substituted aromatic ring due to the electron density at the *ortho/para* positions, and



Scheme 1.

**Keywords:** Iodination; *o*-Hydroxy aromatic ketones; Molecular iodine; Iodic acid.

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**Table 1.** Iodination of hydroxy aromatics by iodine and iodic acid

Entry	Starting material	Product	Yield <sup>a,b</sup> (%)
1			81
2			87
3			82
4			86
5			85
6			86
7			82
8			87
9			84
10			83

<sup>a</sup> Refers to the isolated yield.<sup>b</sup> All the products exhibited expected analytical and spectral data.

not on another aromatic centre (Table 1, entries 7–10). The double bond remained intact during the iodination of  $\alpha,\beta$ -unsaturated carbonyl compounds.

The iodination procedure is very simple; the required reagents are easily handled without any special apparatus.

## 2. General procedure for the iodination of hydroxy aromatic ketones

To a mixture of 2-hydroxyaryl ketone (50 mmol), iodine (20 mmol) dissolved in ethanol (30 mL), iodic acid (10 mmol) dissolved in water (1 mL) was added with

stirring over 5 min and then the reaction mixture was stirred for 1.5 h at 35–40 °C. A solid separated out on dilution with water (15–20 mL). The solid product was filtered, washed with saturated sodium thiosulfate solution to remove excess iodine and then with cold water. The product was recrystallized from ethanol (80–87% yield) Table 1. Spectral data for 2-chloro-1-(3-chloro-2-hydroxy-5-iodophenyl) ethanone (entry 1). IR (Nujol)  $\nu$  3450, 1659, 1570  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.70 (s, 2H,  $\text{CH}_2\text{-Cl}$ ), 7.80 (s, 1H, Ar-H), 7.60 (s, 1H, Ar-H); EIMS ( $m/z$ ): 330 ( $\text{M}^+$ ), 281, 126, 91, 63. Anal. Calcd for  $\text{C}_8\text{H}_5\text{Cl}_2\text{IO}_2$ : C, 29.03; H, 1.57; Cl, 21.43; I, 38.35. Found: C, 28.92; H, 1.44; Cl, 21.35; I, 38.22.

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