m-Iodosylbenzoic Acid as a Convenient Recyclable Reagent for Highly Efficient $RuCl_3$-Catalyzed Oxidation of Alcohols to Carbonyl Compounds

Mekhman S. Yusubov,[a,b] Marina P. Gilmkhanova,[a,b] Viktor V. Zhdankin,[c] Andreas Kirschning*[d]

[a] The Tomsk Polytechnic University, 30 Lenin St., 634050 Tomsk, Russian Federation

[b] The Siberian State Medical University, 2 Moskovsky Trakt, 634050 Tomsk, Russian Federation

[c] Department of Chemistry and Biochemistry, University of Minnesota Duluth, Duluth, MN 55812, USA

[d] Institut für Organische Chemie, Leibniz Universität Hannover, Schneiderberg 1b, 30167 Hannover, Germany
E-mail: andreas.kirschning@uni-hannover.de

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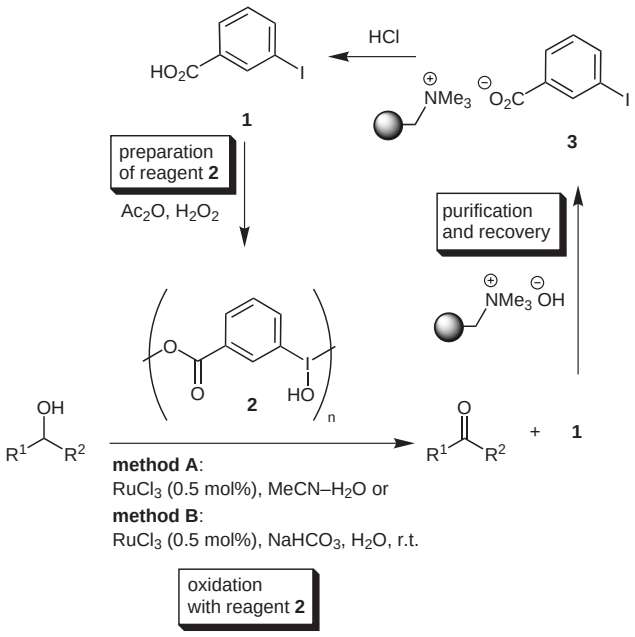
Abstract: *m*-Iodosylbenzoic acid selectively oxidizes primary and secondary alcohols to the respective carbonyl compounds in the presence of $RuCl_3$ (0.5 mol%) at room temperature in aqueous acetonitrile. Separation of pure products is conveniently achieved by scavenging any aryl iodide by ion exchange with IRA-900 (hydroxide form) or by simple extraction of the basic aqueous solution with water. The reduced form of the reagent, *m*-iodobenzoic acid, can be easily recovered from the ion-exchange resin or from the basic aqueous solution by simple acidification with HCl.

Key words: hypervalent iodine, *m*-iodosobenzoic acid, oxidation, catalysis, scavenger

During the past decade hypervalent iodine compounds have attracted a significant interest as mild and selective oxidizing reagents in synthetic organic chemistry.[1] Lately, the combination of transition-metal catalysis with hypervalent iodine reagents have proven to be powerful oxidizing system in various reactions.[1–4] In particular, iodosylbenzene is widely used as an oxidant in the transition-metal-catalyzed epoxidation of alkenes and hydroxylation of hydrocarbons.[1] Likewise, (diacetoxyiodo)arenes are efficient oxidizers in the $Pd(OAc)_2$-catalyzed selective acetoxylations of arene and alkene C–H bonds.[2] Recently, Yusubov et al. reported a $RuCl_3$-catalyzed oxidation of alcohols using (diacetoxyiodo)benzene (DIB) as oxidant.[5] Evidence was collected that this reaction proceeds via an initial instantaneous Ru-catalyzed disproportionation of DIB to iodobenzene and iodylbenzene with the latter acting as the actual stoichiometric oxidant.

In this report we describe a practical improvement of this oxidation protocol as far as purification of the products and recycling of the oxidizing reagent are concerned. In addition, the concept disclosed should be of broad importance for any iodine(III)-mediated reaction.

The broad use of hypervalent iodine reagents is still hampered by tedious purification and recycling protocols. Common byproducts are the corresponding reduction products, namely aryliodides which often are chromatographically removed. This also applies to the iodine(III) oxidant if it is not fully consumed or employed in excess. Recently, tagging strategies for reagents and catalysts have widely been investigated that allow easy purification by means of specific phase separation or scavenging.[6] We found that *m*-iodosylbenzoic acid (**2**) is an excellent iodosyl reagent which can be removed at the end of the reaction by treatment with anion-exchange resin or by addition of $NaHCO_3$ and can be easily recycled by simple acidification with HCl. Several other approaches to recyclable hypervalent iodide reagents have previously been reported.[7–9] These approaches usually involve polymeric or molecular species,[7] which require multistep syntheses, or employ fluorous alkyl iodides and fluorous solvents for separation of products.[8] In contrast to the previously reported protocols, *m*-iodosylbenzoic acid is an inexpensive and readily available reagent that can be easily recycled from the reaction mixture.



Scheme 1 Preparation and regeneration of *m*-iodosylbenzoic acid (**2**) and its use as tagged reagent in alcohol oxidation.

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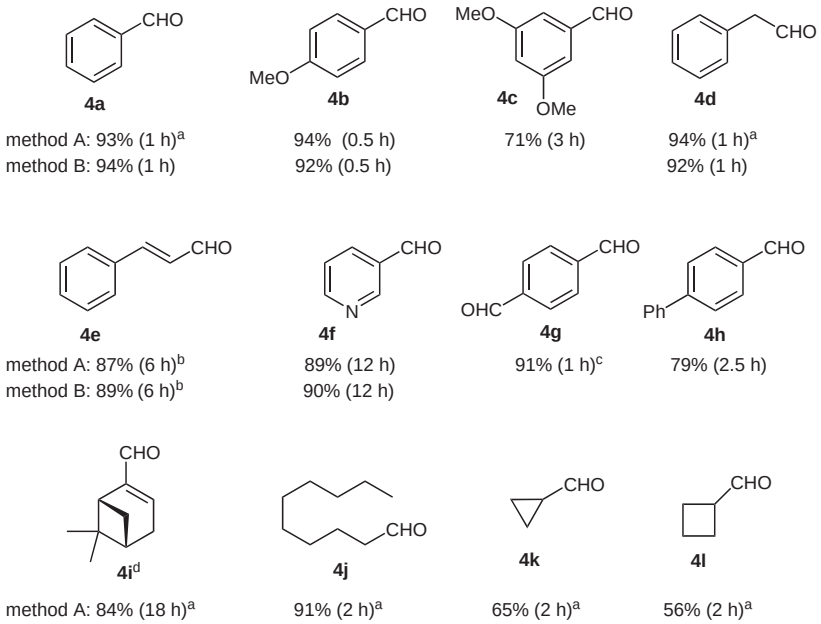

Figure 1 [a] Isolated and characterized (melting point) as 2,4-dinitrophenyl hydrazone; [b] *E*/*Z* mixture (ca. 1:1); [c] compound **2** (3.0 equiv) was employed; [d] (–)-myrtenol was used.

Surprisingly, *m*-iodosylbenzoic acid (**2**) has very rarely been employed since its first description by Wilgerodt in 1894.[10] A detailed spectroscopic investigation of *m*-iodosylbenzoic acid and its sodium salt supported a polymeric structure for these compounds.[10b] The known procedure for the preparation of *m*-iodosylbenzoic acid includes chlorination of *m*-iodobenzoic acid (**1**) followed by hydrolysis of the dichloride with a dilute sodium hydroxide solution.[9] As it was shown in a later work,[10b] this procedure affords a product contaminated with *m*-iodylbenzoic acid, the iodine(V) derivative which is formed due to disproportionation of *m*-iodosylbenzoic acid under conditions of basic hydrolysis. The explosive decomposition of the product at 175–180 °C,[10a] is also indicative of the presence of *m*-iodylbenzoic acid in the samples of *m*-iodosylbenzoic acid prepared according to Wilgerodt's procedure. We have developed an improved, one-step procedure affording analytically pure *m*-iodosylbenzoic acid (**2**) by simple oxidation of *m*-iodobenzoic acid (**1**) with peracetic acid followed by crystallization from ice-water.[11] This procedure affords uncontaminated *m*-iodosylbenzoic acid (**2**) in 72–80% yields in the form of a light yellow powder which melts without explosion at 168–169 °C. Pure *m*-iodosylbenzoic acid (**2**) is stable at room temperature and can be stored for at least six months without noticeable decomposition. However, in aqueous basic solutions *m*-iodosylbenzoic acid (**2**) (in the form of its salt) is unstable and disproportionates at room temperature. From NMR spectroscopic experiments we found that a solution of *m*-iodosylbenzoic acid (**2**; 1 equiv) and NaOH (3 equiv) in D_2O after one hour contains about equal amounts of the salts of *m*-iodosylbenzoic acid, *m*-iodobenzoic acid (**1**) and *m*-iodylbenzoic acid and completely disproportionates within 24 hours at room temperature.

We have found that *m*-iodosylbenzoic acid (**2**) can serve as an efficient recyclable reagent in $RuCl_3$-catalyzed oxidation of primary alcohols to aldehydes in very good yields.[12,13] Two different experimental procedures have been developed for this oxidation: method A for oxidation under slightly acidic conditions, and method B under slightly basic conditions (Scheme 1). Method A consists in the addition of $RuCl_3$ (0.5 mol%) to the mixture of a primary alcohol and 1.0–1.5 equivalents of reagent **2** in MeCN–H_2O (5:1), while according to method B the alcohol is oxidized with an aqueous solution of sodium salt of reagent **2** in the presence of $NaHCO_3$ at room temperature.

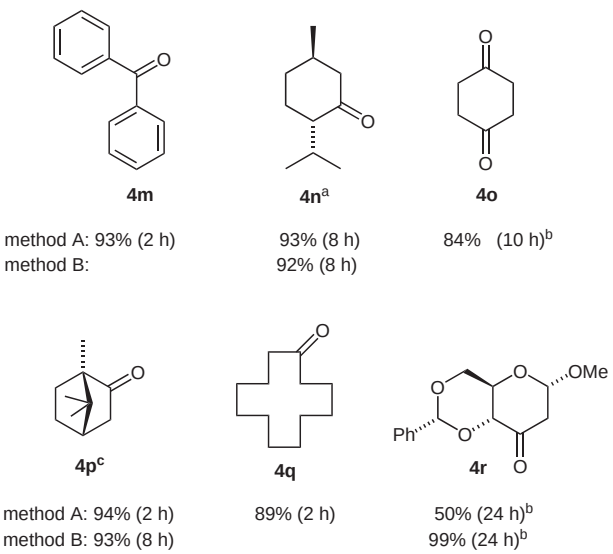

Figure 2 [a] (–)-Menthol was used; [b] compound **2** (3.0 equiv) was employed, [c] (–)-borneol was used.

Method B is particularly useful for the oxidation of acid-sensitive substrates. Product yields and reaction times for the oxidation of a series of primary alcohols are shown in Figure 1.

In method A, the reaction is terminated by addition of IRA 900 (hydroxide form) which traps the reduction product *m*-iodobenzoic acid (**1**) by ion exchange (as polymer **3**). Also any remaining oxidant **2** is removed in this way. *m*-Iodobenzoic acid (**1**) can be easily regenerated (> 95%) from polymer **3** in pure form by treatment with aqueous HCl. When the oxidation is performed in the presence of $NaHCO_3$ (method B), the carbonyl compound is conveniently extracted from the reaction mixture with diethyl ether, while the sodium salt of *m*-iodobenzoic acid remains in the aqueous solution and can be easily recycled and reused.

Also secondary alcohols can be oxidized furnishing the corresponding ketones (Figure 2). Method B gave better results in the oxidation of the acid-sensitive protected sugar derivative (product **4r**),[14] while in the oxidation of borneol, method A afforded a much higher yield of the respective product **4p**.

It can be assumed that *m*-HO_2CPhIO_2 and aryl iodide **1** are initially formed as a result of the Ru-catalyzed disproportionation of reagent **2**, and *m*-iodylbenzoic acid serves as the actual oxidizer in the oxidation of alcohols.[5] In practical use, however, the readily available and stable iodosyl compound **2** is a more convenient oxidizer compared to the explosive iodylarene.

In conclusion, we have disclosed that the rarely employed *m*-iodosylbenzoic acid is an ideally tagged iodine(III) reagent which in our view allows the easiest purification protocol for aryliodine reagents known so far. This tagging concept was utilized in the $RuCl_3$-catalyzed oxidation of alcohols but should also be applicable for most iodine(III)-mediated reactions.

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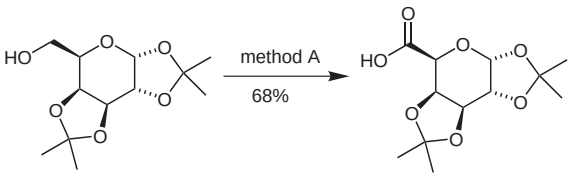
(11) **Improved Procedure for the Preparation of *m*-Iodosylbenzoic Acid (2)**: *m*-Iodobenzoic acid (**1**; 2.48 g, 10 mmol) was added at 40 °C to a freshly prepared solution of peracetic acid in AcOH [prepared by stirring a mixture of Ac_2O (60 mL) and 35% H_2O_2 (14 mL) at 40 °C for 4 h in dark] and the resulting mixture was stirred for 12 h at ambient temperature in dark. A spontaneous heating of the reaction mixture up to 45 °C and complete dissolution of *m*-iodobenzoic acid was observed during the first two hours of stirring. The reaction mixture was poured onto ice-water (150 mL), and allowed to crystallize. The precipitate was filtered on a Büchner funnel and washed with ice-water (200 mL). The solid was then dried, first by maintaining suction and then in vacuum, to afford product **2** as a light yellow powder. Yield: 1.90–2.11 g (72–80% yield); mp 168–169 °C. ^{1}H NMR (200 MHz, CD_3COOD): δ = 7.71 (t, 1 H), 8.35 (d, 1 H), 8.48 (d, 1 H), 8.89 (s, 1 H). Anal. Calcd for $C_7H_5IO_3$ (263.93): C, 31.84; H, 1.91. Found: C, 31.77; H, 1.84.

(12) **$RuCl_3$-Catalyzed Oxidation of Alcohols to Carbonyl Compounds**:
Method A: To a mixture of alcohol (0.05–0.20 mmol) and *m*-iodosylbenzoic acid (**2**; 0.075–0.300 mmol, 1.5 equiv) in aq MeCN (MeCN–H_2O, 5:1; 0.5–2 mL) an aqueous solution of $RuCl_3$ (1.0–4.0 μL of 0.25 M solution; 0.25–1.0 μmol) was added under stirring at r.t. An instantaneous formation of a cotton-like, off-white precipitate was observed. The reaction mixture was stirred for a period of time indicated in Figures 1 and 2 (the reactions were monitored by TLC). Then, CH_2Cl_2 (1.5 mL) and IRA 900 (hydroxide form; 160–620 mg) were added and the mixture was stirred for 5 min. The polymer was removed by filtration and the solution was

concentrated under vacuum to afford the NMR-pure carbonyl compound. Most products were additionally identified as 2,4-dinitrophenylhydrazones, prepared by the treatment of reaction mixtures with a standard solution of 2,4-dinitrophenylhydrazine. *m*-Iodobenzoic acid (**1**) can be easily regenerated (>95%) from IRA 900 by treatment with aq HCl and reused without additional purification.

Method B: *m*-Iodosylbenzoic acid (**2**; 40 mg, 0.15 mmol) was added to an aqueous solution of $NaHCO_3$ (63 mg in 1.0 mL of H_2O) and the mixture was stirred until the formation of a clear solution was observed. Then, the alcohol (0.1 mmol) and an aqueous solution of $RuCl_3$ (2.0 μL of 0.25 M solution; 0.5 μmol) were added under stirring at r.t. The reaction mixture was stirred for a period of time indicated in Figures 1 and 2 (the reactions were monitored by TLC via disappearance of the alcohol). After completion of the reaction, the solution was extracted with Et_2O. The final NMR-pure products were obtained by evaporation of Et_2O from the extract; most prepared carbonyl compounds were additionally identified as their 2,4-dinitrophenylhydrazones. The aqueous solution that was left after extraction was acidified with HCl, and the white precipitate of *m*-iodobenzoic acid was separated by filtration and used for regeneration of reagent **2**.

(13) In one case we encountered further oxidation to galacturonic acid when 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose was employed (Scheme 2).



Scheme 2

(14) This is particularly well demonstrated for the formation of ulose **4r** which can undergo facile elimination of methanol to the corresponding enulose.