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# Iodine(V)/Ruthenium(III)-Cocatalyzed Oxidations: A Highly Efficient Tandem Catalytic System for the Oxidation of Alcohols and Hydrocarbons with Oxone

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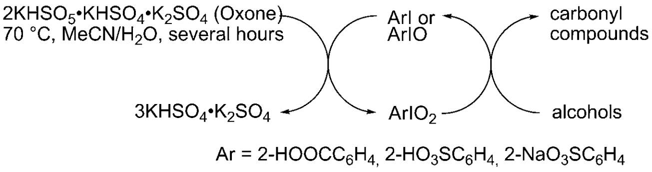
Hypervalent iodine compounds have found wide application as versatile and environmentally friendly oxidizing reagents in synthetic organic chemistry.[1,2] One of the most impressive recent achievements in the field of organoiodine chemistry is the development of catalytic systems based on hypervalent iodine.[2–4] In particular, the iodine(I)/iodine(III) catalytic cycle based on the oxidation of ArI in situ by using peracids has been utilized for the α functionalization of carbonyl compounds,[3a–d] the oxidative cleavage of alkenes and alkynes,[3e] the TEMPO-mediated oxidation of benzylic alcohols (TEMPO = 2,2,6,6-tetramethylpiperidine-1-oxyl),[3f] as well as for various intramolecular cyclizations.[3 g–n] Likewise, the iodine(V)-based catalytic cycles that employ Oxone as a stoichiometric oxidant have been used for the oxidation of alcohols,[4a–c] the oxidation of *p*-alkoxyphenols to quinones,[4d] and the oxidation of benzylic C–H bonds (Scheme 1).[4e] However, the synthetic value of the iodine(V)-based catalytic cycle is limited by the reoxidation step of iodine(I) or iodine(III) to the iodine(V) species, which proceeds relatively slowly even at temperatures above 70 °C.[4]



Scheme 1. Iodine(V)-catalyzed oxidations by using Oxone.[4]

Recently we reported a facile experimental procedure for the preparation of iodylarenes through the $RuCl_3$-catalyzed oxidation of iodoarenes with peracetic acid.[5] Further studies have demonstrated that the use of Oxone as the oxidant instead of peracetic acid leads to even milder reaction conditions. In a typical procedure, treatment of iodobenzene with Oxone in aqueous acetonitrile at room temperature in the presence of $RuCl_3$ (0.16 mol %) results in the formation of iodylbenzene, which can be isolated from the reaction mixture in a 59 % preparative yield (Scheme 2).

$$\mathrm{PhI}\ \xrightarrow[\mathrm{MeCN/H_2O\ (1{:}1\ v/v),\ RT}]{\mathrm{Oxone,\ RuCl_3\ (0.16\ mol\%)}}\ \mathrm{PhIO_2}$$

Scheme 2. $RuCl_3$-catalyzed preparation of iodylbenzene.

Taking into account that the Ru(III)-catalyzed oxidation of alcohols usually occurs only at temperatures above 80 °C,[6] whereas iodylarenes are effective oxidants at room temperature,[1f,h] we investigated the oxidation of alcohols by using an ArI/$RuCl_3$ tandem catalytic system. The reaction was optimized by using 1-phenylethanol (**1**) as a model substrate (Table 1). As expected, in the absence of PhI and in the presence of $RuCl_3$ (0.16 mol %), or in the presence of PhI without $RuCl_3$, the oxidation of substrate **1** at room temperature proceeded very slowly (Table 1, entries 1 and 2). The combined application of PhI and $RuCl_3$ resulted in almost instantaneous oxidation of **1** to acetophenone (**2**) with a 100 % conversion reached in less than 20 min (Table 1, entry 3). The optimized reaction required at least 1 mol equiv of Oxone (2 equiv of active oxygen); the use of smaller amounts of Oxone led to incomplete conversion owing to its noticeable decomposition with loss of oxygen gas under reaction conditions (Table 1, entry 4). Several

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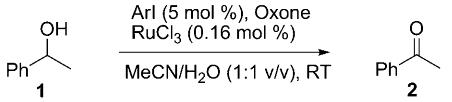
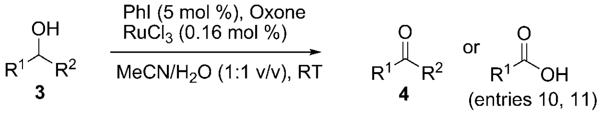
Table 1. Effect of ArI and $RuCl_3$ on the oxidation of 1-phenylethanol to acetophenone with Oxone.[a]

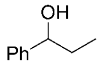
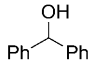
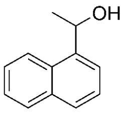
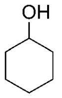
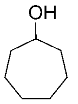
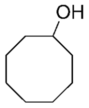
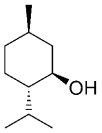
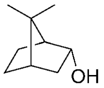
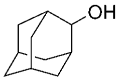
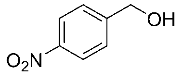
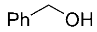


| Entry | ArI | Oxone [mol equiv] | $T$ [h] | Conversion [%][b] |
|---|---|---|---|---|
| 1 | none | 1.5 | 0.3 | 12[c] |
| 2 | PhI[d] | 1.0 | 1.0 | 0 |
| 3 | PhI | 1.0 | 0.3 | 100 |
| 4 | PhI | 0.67 | 1.0 | 83 |
| 5 | 2-$IC_6H_4SO_3H$ | 1.25 | 0.3 | 100 |
| 6 | 4-$IC_6H_4SO_3H$ | 1.15 | 0.3 | 100 |
| 7 | 4-$IC_6H_4SO_3Na$ | 1.25 | 0.6 | 100 |
| 8 | 3-$IC_6H_4CO_2H$ | 1.22 | 1.0 | 99 |

[a] All reactions were performed at room temperature by using 1-phenylethanol (0.1 mmol), $RuCl_3$ (0.16 mol %), and ArI (5 mol %) in MeCN/$H_2O$ (1:1 v/v) unless otherwise noted. [b] The conversion was determined by GC analysis. [c] Also contains styrene (8 %) and unreacted alcohol (80 %). [d] No $RuCl_3$ added.

Table 2. $PhI/RuCl_3$-cocatalyzed oxidation of alcohols.[a]



| Entry | Alcohol **3** | Oxone [mol equiv] | $T$ [h] | Yield of **4** [%][b] |
|---|---|---|---|---|
| 1 |  | 1.2 | 0.3 | 100 |
| 2 |  | 1.2 | 10 | 96 |
| 3 |  | 2.0 | 7 | 100 |
| 4 |  | 1.0 | 2 | 92 |
| 5 |  | 1.2 | 0.8 | 100 |
| 6 |  | 1.0 | 0.5 | 100 |
| 7 |  | 1.05 | 0.5 | 100 |
| 8 |  | 1.0 | 0.8 | 99 |
| 9 |  | 1.0 | 0.8 | 100 |
| 10 |  | 2.4 | 4 | 96[c] |
| 11 | $CH_3(CH_2)_7OH$ | 1.1 | 16 | 100[d] |
| 12 |  | 1.25 | 1.5 | 80[e] |

[a] All reactions were performed at room temperature by using alcohol (1 mmol), $RuCl_3$ (0.16 mol %), and PhI (5 mol %) in MeCN/$H_2O$ (1:1 v/v) unless otherwise noted. [b] Yields of isolated pure products **4** are shown. [c] 4-$NO_2C_6H_4CO_2H$ was the only product formed under these conditions. [d] $CH_3(CH_2)_6CO_2H$ was the only isolated product. [e] Isolated yield of 2,4-dinitrophenylhydrazone of benzaldehyde.

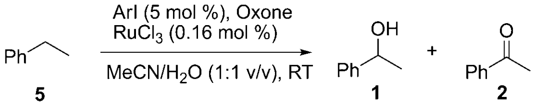
other iodoarenes tested in this reaction showed high catalytic activity that was comparable to PhI (Table 1, entries 5–8).

A variety of alcohols **3** were smoothly oxidized under optimized reaction conditions to afford the respective oxidation products **4** in excellent isolated yields at room temperature (Table 2). Similar to the high-temperature ArI/Oxone procedure,[4a] our protocol afforded ketones from the secondary alcohols (Table 2, entries 1–9) and mainly carboxylic acids from primary alcohols (Table 2, entries 10 and 11). Shorter reaction times, however, allowed the oxidation of benzyl alcohol predominantly to benzaldehyde (Table 2, entry 12). The use of smaller quantities of Oxone and decreasing the reaction time in the oxidation of other primary alcohols (Table 2, entries 10 and 11) also led to the predominant formation of aldehydes.

Selective oxidation of activated and unactivated C−H bonds is of particular interest for organic chemists. The pentavalent iodine reagent, IBX, has been demonstrated to be a reagent of choice for the oxidation of benzylic C−H bonds.[7] Recently, the oxidation of benzylic C−H bonds has been performed under catalytic conditions by the IBX formed in situ by using Oxone as a terminal oxidant at 70–80 °C for 8–48 h.[4e] We investigated the oxidation of C−H bonds by using the $ArI/RuCl_3$ tandem catalytic system. The reaction was optimized by using ethylbenzene (**5**) as a model substrate (Table 3). As expected, in the absence of PhI and in the presence of $RuCl_3$, or in the presence of PhI and in the absence of $RuCl_3$ the oxidation of substrate **5** at room temperature did not occur or proceeded very slowly (Table 3, entries 1, 2, and 11). The combined application of PhI and $RuCl_3$ resulted in a 27 % conversion of **5** to **2** (Table 3, entry 3). The optimized reaction conditions that led to 80 % conversion of substrate **5** to product **2** required the addition of 4.2 mol equiv of Oxone in small portions over 11 h and the use of PhI (10 mol %; Table 3, entry 12). Out of several other iodoarenes tested in this reaction, 2-iodosulfonic acid and 2-iodobenzoic acid showed slightly better catalytic effects than iodobenzene (Table 3, entries 4–9), however, a noticeable amount of byproduct **1** was observed with these catalysts.

The results of the oxidation of several other hydrocarbons under optimized catalytic conditions are summarized in Table 4. In general, moderate to high isolated yields of aromatic ketones were obtained in these oxidations under very mild reaction conditions (Table 4, entries 1–6). Compared with the high-temperature IBX/Oxone procedure,[4e] our protocol was much more selective and generally did not

Table 3. Effect of ArI and $RuCl_3$ on the oxidation of **5** with Oxone.[a]

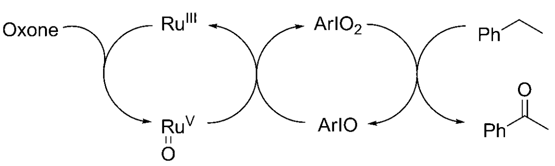


| Entry | ArI | Oxone [mol equiv] | $T$ [h] | Products (yield [%])[b] |
|---|---|---|---|---|
| 1 | none | 1.05 | 3.3 | **1** (1), **2** (8) |
| 2 | PhI[c] | 1.05 | 24 | **1** (0), **2** (0) |
| 3 | PhI | 1.05 | 3.3 | **1** (0.5), **2** (27) |
| 4 | 2-$IC_6H_4SO_3H$ | 1.05 | 3.3 | **1** (1), **2** (31) |
| 5 | 4-$IC_6H_4SO_3H$ | 1.05 | 3.3 | **1** (0.5), **2** (17) |
| 6 | 2-$IC_6H_4CO_2H$ | 1.05 | 3.3 | **1** (1), **2** (30) |
| 7 | 3-$IC_6H_4CO_2H$ | 1.03 | 3.3 | **1** (0), **2** (18) |
| 8 | 4-$IC_6H_4CF_3$ | 1.05 | 3.3 | **1** (0), **2** (13) |
| 9 | 4-$IC_6H_4Br$ | 1.05 | 3.3 | **1** (0), **2** (21) |
| 10 | PhI | 2.10[d] | 4.0 | **1** (0), **2** (50) |
| 11 | none | 2.10[d] | 4.0 | **1** (0), **2** (14) |
| 12 | PhI[e] | 4.2[f] | 11.5 | **1** (0), **2** (80) |

[a] All reactions were performed at room temperature by using **5** (0.1 mmol), ArI (5 mol %), and of $RuCl_3$ (0.16 mol %) in $MeCN/H_2O$ (1:1 v/v) unless otherwise noted. [b] Product yields were determined by GC analysis. Unreacted **5** was also present in all entries. [c] No $RuCl_3$ added. [d] Oxone (1.05 mol equiv) was initially added and the second portion (1.05 mol equiv) was added after 2 h. [e] PhI (10 mol %) was used. [f] Oxone (0.9 mol equiv) was initially added, the second portion (1.1 mol equiv) was added after 2 h, the third portion (1.1 mol equiv) was added 4 h later, and the final portion (1.1 mol equiv) was added 3 h later.

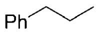
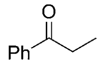
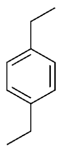
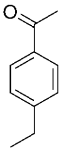
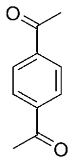
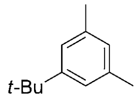
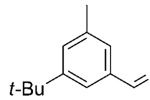
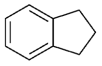
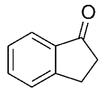
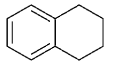
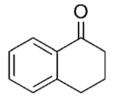
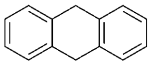
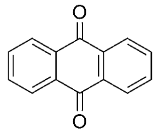
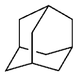
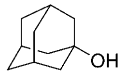
afford products of C–C bond cleavage and carboxylic acids. The oxidation of an unactivated C–H bond in adamantane under these conditions proceeded with a low conversion, affording 1-adamantanol in only 1.5 % yield (Table 4, entry 7).

A plausible, simplified mechanism for these catalytic oxidations is shown in Scheme 3, which includes two catalytic redox cycles. The reaction starts with the initial oxidation of ArI to ArIO and then to $ArIO_2$ by the Oxone/Ru(III,V) system as inferred from Schemes 1 and 2. The in situ generated, highly active monomeric $ArIO_2$ species are responsible for the actual oxidation of organic substrates by known mechanisms.[7a] We propose that the intermediate oxoruthenium complexes are responsible for the reoxidation of the initially formed ArIO to $ArIO_2$ (Scheme 3). Experimental evidence towards catalytic oxidation of PhIO to $PhIO_2$ mediated by the oxoruthenium species has previously been documented,[8a] and the generation and identification of highly reactive ruthenium(V)-oxo species was reported in the literature.[8b–d] The initiation step of this catalytic mechanism, that is, an oxygen atom transfer from an oxo transition-metal complex to the iodine atom of the starting iodoarene, has previously been observed in the reaction of oxoiron(IV) porphyrin and iodobenzene.[9]



Scheme 3. Tandem catalytic system for the oxidation of organic substrates with Oxone.

Table 4. $PhI/RuCl_3$-cocatalyzed oxidation of hydrocarbons.[a]

| Entry | Substrate | Oxone [mol equiv] | $T$ [h] | Products | Yield [%][b] |
|---|---|---|---|---|---|
| 1 |  | 6.1[c] | 26 |  | 80 |
| 2 |  | 2.06 | 3 |  | 77 |
|  |  |  |  |  | 11 |
| 3 |  | 1.2 | 6 |  | 23 |
| 4 |  | 2.0[c,d] | 1 |  | 95 |
| 5 |  | 1.2[d] | 1 |  | 69 |
| 6 |  | 8.2[d] | 20 |  | 72 |
| 7 |  | 2.5[d] | 8 |  | 1.5[e] |

[a] All reactions were performed at room temperature by using a hydrocarbon (1.0 mmol), $RuCl_3$ (0.16 mol %), and PhI (5 mol %) in $MeCN/H_2O$ (1:1 v/v) unless otherwise noted. [b] Yields of isolated products are shown. Unreacted hydrocarbons were also present in all entries. [c] Oxone was added in small portions during the indicated time period. [d] PhI (10 mol %) was used. [e] The yield of 1-adamantanol was determined by GC analysis.

In summary, we have reported an extremely mild and efficient tandem catalytic system for the oxidation of alcohols and hydrocarbons based on a Ru(III)-catalyzed reoxidation of ArIO to $ArIO_2$ by using Oxone as a stoichiometric oxidant. Owing to the mild reaction conditions, our protocol is highly selective and generally does not afford products of C–C bond cleavage.

## Experimental Section

**Typical procedure of the $PhI/RuCl_3$-cocatalyzed oxidation of propylbenzene**: Oxone (3.74 g; 6.1 mmol) was added to a mixture of propylbenzene

(120 mg, 1 mmol), PhI (0.5 mL of a 0.1 M solution in MeCN, 0.05 mmol, 5 mol %), and RuCl$_3$ (10 µL of 0.16 M solution in water, 0.0016 mmol, 0.16 mol %) in acetonitrile (3 mL) and water (3 mL) in five portions over 22 h under stirring at room temperature. The reaction mixture was stirred for an additional 4 h (the reaction was monitored by TLC by the disappearance of propylbenzene). Then ethyl acetate (15 mL) and water (20 mL) were added and the mixture was stirred for 5 min. The organic solution was separated and the aqueous phase was extracted with ethyl acetate (2 × 15 mL). The organic phases were combined, washed with NaCl (saturated solution, 20 mL), and dried over Na$_2$SO$_4$ (anhydrous). Removal of the solvent under vacuum afforded propiophenone (107 mg, 80 %). The oxidation of the other hydrocarbons (Table 4) was performed by using a similar procedure.

## Acknowledgements

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**Keywords:** catalysis · hypervalent compounds · oxidation · Oxone · ruthenium

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