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Development of new recyclable reagents and catalytic systems based on hypervalent iodine compounds

Mekhman S. Yusubov^{*a,b*} and Viktor V. Zhdankin^{**c*}

^a Siberian State Medical University, 634050 Tomsk, Russian Federation

^b Tomsk Polytechnic University, 634050 Tomsk, Russian Federation

^c Department of Chemistry and Biochemistry, University of Minnesota Duluth, Duluth,

MN 55812, USA. Fax: +1 218 726 7394; e-mail: vzhdanki@d.umn.edu

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Recent advances in the development of polymer-supported iodine(V) oxidants, recyclable monomeric hypervalent iodine(III) reagents and catalytic systems based on hypervalent iodine compounds are discussed. These efficient and environmentally friendly reagents and catalysts are particularly useful for oxidative transformations of alcohols to carbonyl compounds and for oxidations at the benzylic position.

During the past decade, the chemistry of hypervalent iodine compounds has attracted a significant research interest.¹⁻¹³ Hypervalent iodine reagents are used extensively in organic synthesis as efficient oxidizing reagents whose chemical properties are similar to those of mercury(II), thallium(III), lead(IV) and chromium(VI) derivatives but without the toxicity and environmental problems of these heavy metal congeners. Among hypervalent iodine compounds, pentavalent iodine derivatives (λ^5 -iodanes) are especially important as efficient oxidants.¹⁻⁴ In particular, heterocyclic λ^5 -iodane, 1-hydroxy-1-oxo-1*H*-1 λ^5 -benzo[*d*][1,2]iodoxol-3-one 1, known under the name of its tautomeric form of 2-iodoxybenzoic acid (IBX), has received widespread application in organic synthesis as an efficient and mild oxidant that can be used for selective oxidation of primary and secondary alcohols and for other important oxidations.¹⁻⁴ However, the explosive character and low solubility of IBX in common organic solvents restrict the practical application of this reagent. The low solubility and unfavorable physical and chemical properties of IBX 1 arise from strong intermolecular secondary bonding observed for this compound in a solid state.14,15



Earlier, we have developed a series of stable and soluble IBX analogues: IBX-amides **2**,¹⁶ IBX-esters **3**,^{17,18} *N*-(2-iodylphenyl)-acylamides (NIPA) **4**,¹⁹ 2-iodylphenyl ethers **5**,²⁰ 2-iodylbenzenesulfonamides **6**,²¹ 2-iodylbenzenesulfonate esters **7**²² and *N*-(2-iodylphenyl)tosylamides **8**.²³ According to X-ray data,



Viktor V. Zhdankin (right) received his M.S. (1978), Ph.D. (1981), and Doctor of Chemical Sciences (1986) degrees at M. V. Lomonosov Moscow State University in the research laboratories of Professor N. S. Zefirov. He moved to the University of Utah in 1990, where he worked for three years as instructor of organic chemistry and senior research associate with Professor P. J. Stang. In 1993, he joined the faculty of the University of Minnesota Duluth, where he is currently a professor of chemistry. He published over 220 scientific papers, edited several books and co-authored the *Handbook of Heterocyclic Chemistry* (3rd edn., 2010) with Professors A. R. Katritzky, C. A. Ramsden and J. A. Joule. His main research interests are in the fields of synthetic and mechanistic

organic chemistry of hypervalent main-group elements (iodine, xenon, selenium, sulfur and phosphorus) and organofluorine chemistry. Professor Zhdankin is a member of the Editorial Board of *Mendeleev Communications* and a scientific editor of *ARKIVOC*.

Mekhman S. Yusubov (left) received his M.S. (1985), Ph.D. (1991), and Doctor of Chemical Sciences (1998) degrees at Tomsk Polytechnic University in the laboratory of Professor V. D. Filimonov. He is a head of Chemistry Department at Siberian State Medical University and a professor at Tomsk Polytechnic University. Since 1994, he has been involved in intense international collaborative research programs with leading research laboratories in South Korea, Germany and the United Kingdom. In 2004, he started a joint research in the area of recyclable hypervalent iodine reagents with Professor V. V. Zhdankin in University of Minnesota Duluth. His main research interests are in the fields of chemistry of natural products and hypervalent iodine reagents. Professor Yusubov has published over 100 scientific papers.

a pseudocyclic moiety due to the intramolecular nonbonding iodine-oxygen interaction with *ortho*-substituent is a key structural feature present in these compounds.^{15–23} The presence of *ortho*-coordination in compounds **2–8** leads to partial disruption of the polymeric network, and consequently enhances their solubility and reactivity. Among these pseudocyclic IBX analogues, readily available, non-explosive and thermally stable hypervalent iodine reagents **2–5** have proved to be particularly useful, selective oxidizing reagents towards alcohols and sulfides.^{16–20,24}

Despite their useful reactivity, enhanced stability, and environmentally benign nature, reagents **2–5** are not perfect with respect to the Green Chemistry principles.²⁵ According to a basic principle of Green Chemistry, catalytic or recyclable reagents are superior to stoichiometric reagents. Here, we survey our recent research efforts on the development of recyclable oxidants and catalytic systems based on hypervalent iodine compounds.

Polymer-supported iodine(V) oxidants

Polymer-supported reagents have found broad application in organic synthesis since the development of the solid-phase and combinatorial high throughput synthesis techniques. Attachment of a chemical reagent to an insoluble polymer matrix enables easy reaction work-up by simple filtration, automated parallel synthesis and fast reaction optimization.^{26–28} A number of polymer-supported hypervalent iodine(III) reagents have also been reported.^{2–5}

The presence of a functional group in the ortho-position of pseudocyclic iodylarenes 2-5 provides a convenient opportunity of linking a hypervalent iodine(V) reagent to the polymeric backbone. Shortly after our preparation of IBX-amides 2¹⁶ and IBX-esters 3,¹⁷ Lee and co-workers have reported the synthesis of polymer-supported IBX-amides 9, 10 and IBX-ester 11 starting from commercially available hydroxy or amino polystyrene in two steps.²⁹ Oxidant resins 9-11 were prepared with loadings of 0.65–1.08 mmol g⁻¹, and they were evaluated with a series of alcohol substrates. Polymer supported IBX-amide 10 exhibited particularly fast and efficient oxidative activities toward alcohols under mild reaction conditions.²⁹ IBX-amide resin 10 is also an efficient oxidant for the oxidative bromination of activated aromatic compounds using tetraethylammonium bromide.³⁰ Linclau and co-workers reported an improved synthesis of solidsupported IBX-amide resins 12 and 13 using inexpensive and commercially available 2-iodobenzoyl chloride and Merrifield resin.³¹ Oxidation of alcohols to the corresponding carbonyl compounds can be accomplished using 1.2 equiv. of resins 12 and 13. Recycling of the resin is also possible with a minimal loss of activity after two reoxidations.³¹



In the context of these findings, we considered the development of a polymer-supported *N*-(2-iodylphenyl)acylamide reagent (NIPA resin).³² In order to furnish a pseudo benziodoxazine scaffold and to assure proper immobilization to the resin through

an amide function, the carbamoylbutanoic acid moiety was chosen as a linker. Commercially available 2-iodoaniline 14 was reacted with glutaric anhydride to give acid 15, which was subsequently coupled to aminomethylpolystyrene with 1-hydroxy-1H-benzotriazole/diisopropylcarbodiimide (HOBt/DIC) to give resin 16. To block any possible free amino groups, the resin was subsequently treated with an excess of acetic anhydride and pyridine (Scheme 1). The loading of resin 16 was determined by elemental analysis and corresponded to 82% conversion. Oxidation of resin 16 to NIPA resin 17 was initially performed with 3,3-dimethyldioxirane, as it was described for a solutionphase synthesis.¹⁹ The obtained resin was characterized by IR spectroscopy and elemental analysis. Oxidizing activity of NIPA resin 17 was measured by GC analysis with an excess of benzyl alcohol as a test substrate and was found to be 0.31 mmol g⁻¹ with respect to IO₂ groups. Much higher loading levels (0.7–0.8 mmol g⁻¹) have been reached by the oxidation of resin 16 using an equimolar mixture of tetrabutylammonium $Oxone^{\otimes} [2Bu_4NHSO_5 \cdot Bu_4NHSO_4 \cdot (Bu_4N)_2SO_4]$ with methanesulfonic acid. To avoid the supplementary preparation of tetrabutylammonium Oxone[®], we have performed the oxidation of polymer 16 in the CH₂Cl₂-H₂O biphasic system using Oxone® (2KHSO₅·KHSO₄·K₂SO₄), Bu₄NHSO₄ and MeSO₃H (Scheme 1). Overall, our synthesis of NIPA resin 17 employs commercially available aminomethylated polystyrene; it includes three simple steps and affords the resin with good loading of 0.70-0.80 mmol g⁻¹. Combined with straightforward synthesis and cheap starting materials, NIPA resin 17 represents a good alternative to previously reported IBX resins 9-13.29-31



Scheme 1 Preparation of NIPA resin. *Reagents and conditions:* i, glutaric anhydride (1.1 equiv.), PhMe, reflux, 3 h; ii, **15** (1 equiv.), HOBt (1.1 equiv.), DIC (1.0 equiv.), DMF, 105 °C, 8 h, then room temperature, 8 h; iii, Ac₂O (2.0 equiv.), pyridine (2.0 equiv.), 80 °C, 3 h; iv, Oxone[®] (10 equiv.), MsOH (10 equiv.), Bu₄NHSO₄ (5 equiv.), CH₂Cl₂–H₂O, room temperature, 36 h.

Carbonyl compounds are important intermediates for the preparation of a wide variety of organic substances. Hence, there is an ensuing interest in developing new mild and selective methods for the oxidation of alcohols, especially using solid-supported reagents.^{33,34} Hypervalent iodine based oxidants do not rely on heavy metal salts or additional co-oxidants, thus meeting scalable, economical and environmentally friendly requirements put forth by the contemporary chemical industry. In this context, NIPA resin **17** appears to be an apt reagent, since its synthesis, in contrast to IBX resins,^{29–31} does not contain multiple labor-intensive and time-consuming steps. Based on solution-phase

Entry	Alcohol	Product	Conver- sion (%) ^a	Entry	Alcohol	Product	Conver- sion (%) ^a
1	ОН	0	> 99	11	ОН		> 99
2	МеО	MeO	> 99	12 [ОН		$> 99^{b}$
3	ОН И И И И И И И И И И И И И И И И И И И	NO ₂	> 99	13	ОН		94 ^{<i>b</i>,<i>c</i>}
4	ОН		98	14	- OH		61
5	ОН		> 99	15	ОН	0	> 99
6	₩ ₆ OH	$\forall f_6 = 0$	> 99	16	Н	, o	96
7	ОН	0	> 99	17 N	MeS	MeS	85 ^d
8	Сурон	√o	> 99	18	ОН		> 99 (89%) ^e
9	С SОН		> 99	19	OH	F ⁰	> 99 (86%) ^e
10	ОН	O N	> 99	20	ОН	О	90 ^f

Table 1 Oxidations of alcohols with NIPA resin 17.

^{*a*}All oxidations were carried out with 1.0 equiv. of NIPA resin **17** in dry dichloroethane at reflux (85 °C) for 60 min, unless otherwise noted. The resin was removed by filtration and washed with dry dichloroethane. The resulting filtrates were analyzed by GC-MS. For product isolation, combined filtrates from several resin washings were passed through small pad of silica gel, silica gel washed with DCE, and the combined DCE fractions were evaporated to yield the respective carbonyl compound, pure by ¹H NMR. ^{*b*}Oxidation was performed for 30 min. ^{*c*}(*Z*)-isomer (6%) was detected. ^{*d*}Oxidation was carried out with 0.5 equiv. of NIPA resin **17**. 4-(Methylsulfinyl)benzaldehyde (7%) and [4-(methylthio)phenyl]methanol (8%) were detected. ^{*e*}Isolated yields. ^{*f*}Oxidation was carried out with 2.0 equiv. of NIPA resin **17** in dry DCE at 60 °C for 180 min.

NIPA chemistry, no acidic additives (in contrast to IBX-amide resins)^{29–31} are required to effect fast conversion to the corresponding alcohol.

We tested NIPA resin **17** with a variety of alcohol substrates: benzylic, allylic, primary and secondary alcohols, a diol and a thioalcohol (Table 1).³² Most alcohols were oxidized to the respective aldehyde or ketone products in excellent purities and yields. Interestingly, oxidation of *cis*-cyclohexane-1,2-diol yielded only the respective hydroxycyclohexanone and, in contrast to IBX amides, no C–C bond cleavage was observed. The polymeric material, resulting from the reduction of NIPA resin **17** with alcohols, can be collected and reoxidized according to the procedure described above (Scheme 1). A moderate decline in oxidative activity was observed after multiple recovery steps, putatively due to iodine loss in the course of resin reoxidation under acidic conditions.

At the next step, we have investigated the preparation of polymer-supported 2-iodylphenol ethers **5**, which are readily available and stable IBX analogues having a pseudocyclic fourmembered ring motif.²⁰ To create a 2-iodylphenol ether scaffold and to ensure proper immobilization to resin through amide and ether bonds, 4-hydroxybutanoic acid and 1,4-butanediol moieties, respectively, were chosen as linkers.³⁵ Preparation of these linkers was achieved through easy steps with excellent yields. Thus, the reaction of commercially available 2-iodophenol **18** with ethyl 4-bromobutanoate gave ester **19**, which was afterwards saponified to afford acid **20**. Acid **20** was subsequently coupled to aminomethylated polystyrene with HOBt/DIC to yield resin **22** (Scheme 2). To block any possible free amino groups, the resin was treated with an excess of acetic anhydride and pyridine.

Since 2-iodophenol can be easily attached to the halomethylated polymers through a simple nucleophilic substitution, we have also investigated Merrifield resin as a solid support. This resin is cheaper than aminomethylated polystyrene and is more stable to the typical acidic oxidation conditions that have previously been used for the oxidation of known polymersupported reagents. Although direct attachment of 2-iodophenol **18** to Merrifield resin was unsuccessful, readily available alcohol **21** was successfully coupled to the Merrifield resin *via* an ether link to yield polymer **23** (Scheme 2).

The loadings of resins 22 and 23 were determined by elemental analysis and corresponded to 89 and 70% conversions, respectively. Oxidation of polymers 22 and 23 was initially performed with 3,3-dimethyldioxirane (Scheme 2, method A), as described for the solution phase synthesis of monomeric



room temperature, 3 days



2-iodylphenol ethers 3.²⁰ Resins 24 and 25 were characterized by IR spectroscopy and elemental analysis. The oxidizing activity of reagents 24 and 25 was measured by GC-MS analysis using an excess of 4-methoxybenzyl alcohol as the test substrate under reflux in 1,2-dichloroethane for 3 h. Based on these measurements, the loadings of resins 24 and 25 were found to be 1.23 and 0.81 mmol g⁻¹, respectively, on a IO_2 group basis. Since the dioxirane oxidation was effective but not very practical (3,3-dimethyldioxirane is unstable and not readily available), we have tested the *in situ* generated dioxirane as the oxidizing agent. The modified protocol (Scheme 2, method B) consists of treatment of resins 22 and 23 with Oxone[®], NaHCO₃, and acetone at room temperature and affords resins 24 and 25 with only slightly lower loading levels $(0.74-0.86 \text{ mmol g}^{-1} \text{ for})$ polymer 24 and 0.50–0.55 mmol g^{-1} for polymer 25). We have used this practical procedure (method B) for the preparation of numerous batches of resins 24 and 25 in gram quantities.

The oxidative properties of resins 24 and 25 were evaluated by the reactions with benzylic, allylic, primary and secondary alcohols. With all tested alcohols, a 100% conversion to the respective carbonyl products has been reached in 0.5–3 h at room temperature, which is indicative of a higher oxidative reactivity of reagents 24 and 25 compared to NIPA resin 17. Although both reagents gave corresponding carbonyl compounds with high conversion and purity, resin 24 performed these oxidations faster in most cases. Both reagents showed good selectivity towards the oxidation of a hydroxy group in the presence of a sulfide group. The reduced polymeric materials formed in the reactions of resins **24** and **25** with alcohols can be collected and reoxidized according to the procedure described above (Scheme 2). A slow decline in oxidative activity was observed after multiple recovery steps, possibly, due to iodine loss in the course of resin reoxidation.³⁵

In summary, a series of polymer-supported hypervalent iodine(V) oxidants based on *ortho*-substituted iodylarenes linked to a polystyrene backbone has been developed. These new recyclable reagents have the advantage of easy reaction work-up by simple filtration, and they can find practical applications in the solid-phase and combinatorial high throughput synthesis techniques.

Recyclable monomeric hypervalent iodine(III) reagents

Despite the utility of the polymer-supported reagents, they still have several drawbacks. These reagents require a multistep preparation, they are insoluble and, therefore, have lower reactivity compared to the corresponding monomeric analogues. Moreover, the repeated use of these polymers leads to significant degradation due to the benzylic oxidation of the polystyrene chain. The other previously reported approaches to recyclable hypervalent iodide reagents involve complex molecular species,^{36,37} which require multistep syntheses, or employ fluorous alkyl iodides and fluorous solvents for separation of products.³⁸

In the last few years, much effort has been devoted to the development of simple, nonpolymeric, recyclable iodanes, which show reactivities similar to those of the original hypervalent iodine(III) reagents. We have found that 3-iodosylbenzoic acid 27 (Scheme 3) is an excellent oxidizing reagent whose reduced form, 3-iodobenzoic acid 26, can be removed at the end of the reaction by treatment with an anion-exchange resin or by addition of NaHCO₃, and it can be easily recycled.³⁹ Likewise, 3-(dichloroiodo)benzoic acid is an excellent chlorinating reagent that can be similarly recycled via 3-iodobenzoic acid.⁴⁰ In contrast to the previously reported protocols,³⁶⁻³⁸ hypervalent iodine reagents derived from 3-iodobenzoic acid are inexpensive and readily available compounds that can be easily recovered from the reaction mixture. Recently, we have reported the preparation and X-ray crystal structure of two new recyclable nonpolymeric hypervalent iodine reagents derived from 3-iodobenzoic acid, namely, 3-[bis(trifluoroacetoxy)iodo]benzoic acid 28 and 3-[hydroxy(tosyloxy)iodo]benzoic acid 29.41 Compounds 28 and 29 were conveniently prepared in high yield by treatment of 3-iodosylbenzoic acid 27 with trifluoroacetic acid or p-toluenesulfonic acid, respectively (Scheme 3).



Scheme 3 Preparation of 3-iodosylbenzoic acid 27 and its derivatives 28 and 29.

Products **28** and **29** were isolated as white, stable, microcrystalline compounds and analyzed by NMR spectroscopy, elemental analysis, and X-ray crystallography.⁴¹ The structural features and reactivity patterns of compounds **28** and **29** are similar to those of [bis(trifluoroacetoxy)iodo]benzene PhI(OCOCF₃)₂ and [hydroxy(tosyloxy)iodo]benzene PhI(OH)OTs, which belong to the most important and widely used hypervalent iodine reagents.¹⁻⁵ The oxidative properties of reagents 28 and 29 were evaluated in the most typical reactions previously reported for PhI(OCOCF₃)₂ and PhI(OH)OTs, such as the oxidation of sulfides,³⁶ the oxidative iodination of arenes,⁴² the α -tosyloxylation of ketones³⁶ and the Hofmann-type rearrangement³⁶ (Scheme 4). The products of these reactions (Scheme 4) were conveniently separated from the by-product, 3-iodobenzoic acid 26, by simple treatment with ion-exchange resin IRA-900. 3-Iodobenzoic acid 26 can be easily regenerated from IRA-900 resin by treatment with aqueous HCl, and it can be reoxidized to reagent 27 without additional purification.³⁹ An alternative procedure for product separation involves basic aqueous work-up followed by acidification with HCl.40



Scheme 4 Representative reactions of reagents 28 and 29.

In summary, we have reported the preparation, X-ray structural characterization, and reactivity of 3-[bis(trifluoroacetoxy)iodo]benzoic acid **28** and 3-[hydroxy(tosyloxy)iodo]benzoic acid **29**, new recyclable iodine(III) reagents derived from 3-iodosylbenzoic acid. Compounds **28** and **29** have a reactivity pattern similar to the most common non-recyclable hypervalent iodine reagents, PhI(OCOCF₃)₂ and PhI(OH)OTs; however, their reduced form, 3-iodobenzoic acid **26**, can be easily recovered from reaction mixture and reused. In contrast to the polymer-supported recyclable reagents, compounds **28** and **29** are soluble in organic solvents, and they can be recovered from reaction mixtures without any loss of activity.

Catalytic application of hypervalent iodine reagents

The catalytic use of hypervalent iodine reagents is one of the most impressive recent developments in organoiodine chemistry.^{5,8–10} Numerous examples of catalytic utilization of the iodine(III) species have been reported.^{43–57} In particular, the iodine(I)/iodine(III) catalytic cycle based on the *in situ* oxidation of ArI using peracids has been utilized for the α -functionalization of carbonyl compounds,^{43–46} the oxidative cleavage of alkenes and alkynes,⁴⁷ the TEMPO-mediated oxidation of benzylic alcohols,⁴⁸ and various intramolecular cyclizations.^{49–57} Likewise, the iodine(V) based catalytic cycles employing Oxone[®] as a stoichiometric oxidant have been used for the oxidation of alcohols,^{58–60} the oxidation of *p*-alkoxyphenols to quinones⁶¹ and the oxidation of benzylic C–H bonds.⁶² For example,

Ishihara *et al.*⁵⁸ have developed an optimized procedure for the catalytic oxidation of alcohols by using 2-iodylbenzenesulfonic acid⁶³ as an extremely active catalyst and Oxone[®] as a terminal oxidant (Scheme 5). However, the synthetic value of the iodine(V)-based catalytic cycle is limited by the reoxidation step of iodine(I) or iodine(III) to iodine(V) species, which proceeds relatively slowly even at temperatures above 70 °C.^{58–62}



Scheme 5 Iodine(V)-catalyzed oxidations using Oxone[®].^{58–60}

Based on our studies of RuCl₃-catalyzed disproportionation of iodine(III) species to iodobenzene and iodylbenzene,64,65 we have developed an extremely mild and efficient tandem catalytic system for the oxidation of alcohols and hydrocarbons via a Ru^{III}-catalyzed reoxidation of ArIO to ArIO₂ using Oxone® as a stoichiometric oxidant.⁶⁶ Taking into account that the Ru^{III}catalyzed oxidation of alcohols usually occurs only at temperatures above 80 °C, while iodylarenes are effective oxidants at room temperature,²⁻⁴ we investigated the oxidation of alcohols using the PhI/RuCl₃ tandem catalytic system. The reaction was optimized using 1-phenylethanol as a model substrate. As expected, in the absence of PhI and in the presence of RuCl₃ (0.16 mol%), or in the presence of PhI without RuCl₃ the oxidation of 1-phenylethanol at room temperature proceeds very slowly. The combined application of PhI and RuCl₃ results in the almost instantaneous oxidation of 1-phenylethanol to acetophenone with a 100% conversion reached in less than 20 min. Alcohols 30 are smoothly oxidized under these reaction conditions to afford respective oxidation products 31 in excellent isolated yields at room temperature (Scheme 6).

$$\begin{array}{ccc} OH \\ R^{1} \\ \hline R^{2} \\ 30 \end{array} \xrightarrow[room temperature]{} PhI (5 mol%), Oxone^{\textcircled{0}} \\ \hline RuCl_{3} (0.16 mol\%) \\ \hline MeCN-H_{2}O (1:1, v/v), \\ room temperature \\ \hline 31 \\ \hline \end{array} \xrightarrow[room temperature]{} R^{1} \\ \hline R^{2} \\ \hline R^{1} \\ \hline R^{2} \\ \hline R^{$$

Scheme 6 PhI/RuCl₃-cocatalyzed oxidation of alcohols.⁶⁶

Selective oxidation of activated and unactivated C-H bonds is of particular interest for organic chemists. The pentavalent iodine reagent, IBX 1, has been demonstrated to be a reagent of choice for the oxidation of benzylic C-H bonds.67,68 Recently, the oxidation of benzylic C-H bonds has been performed under catalytic conditions by the in situ formed IBX using Oxone® as a terminal oxidant at 70-80 °C for 8-48 h.62 We investigated the oxidation of C-H bonds using the PhI/RuCl₃ tandem catalytic system. The reaction was optimized using ethylbenzene as a model substrate. As expected, in the absence of PhI and in the presence of RuCl₃ or in the presence of PhI and in the absence of RuCl₃ the oxidation of ethylbenzene at room temperature does not occur or proceeds very slowly. The combined application of PhI and RuCl₃ results in up to 80% conversion of ethylbenzene to acetophenone. The optimized reaction conditions require the addition of 4.2 mole-equiv. of Oxone® in small portions over 11 h and the use of 10 mol% PhI (Table 2, entry 1).

The results of the oxidation of hydrocarbons under catalytic conditions are summarized in Table 2. In general, moderate to high yields of aromatic ketones are obtained in these oxidations under very mild reaction conditions (entries 1–8). Compared to the high-temperature IBX/Oxone[®] procedure,⁶² our protocol is

Table	2	PhI/RuCl ₂	-cocatalyzed	oxidation of hydrogenetic and hydrogenet	rocarbons.a
			, ,	2	



^{*a*}All reactions were performed at room temperature in MeCN–H₂O (1:1, v/v) using 1.0 mmol of a hydrocarbon, 2–6 mmol of Oxone[®], 0.16 mol% of RuCl₃ and 5 mol% of PhI unless otherwise noted. ^{*b*}Yields of isolated products are shown; unreacted hydrocarbons were also present in all entries. ^{*c*}10 mol% of PhI was used.

much more selective and generally does not afford products of C–C bond cleavage and carboxylic acids. The oxidation of an unactivated C–H bond in adamantane under these conditions proceeds with a low conversion affording 1-adamantanol in only 1.5% yield (entry 9).

A plausible, simplified mechanism for these catalytic oxidations is shown in Scheme 7, which includes two catalytic redox cycles. The reaction starts with the initial oxidation of PhI to PhIO and then to PhIO₂ by the Oxone[®]/Ru(III,V) system. The generated in situ, highly active monomeric PhIO₂ species are responsible for the actual oxidation of organic substrates by known mechanisms.^{62,67,68} We propose that the intermediate oxoruthenium complexes are responsible for the reoxidation of the initially formed PhIO to PhIO₂ (Scheme 7). The experimental evidence for the catalytic oxidation of PhIO to PhIO₂ mediated by the oxoruthenium species has previously been documented,⁶⁹ and the generation and identification of highly reactive ruthenium(V) oxo species was reported.⁷⁰ The oxidation of organic substrates with PhIO₂ in this system can be additionally catalyzed by ruthenium species. Several examples of transition-metal-catalyzed oxidations using ArIO₂ as a stoichiometric oxidant have been reported.39,71,72

Thus, we have developed an extremely mild and efficient tandem catalytic system for the oxidation of alcohols and hydrocarbons based on the Ru^{III}-catalyzed reoxidation of PhIO



Scheme 7 PhI/RuCl₃ tandem catalytic system for the oxidation of organic substrates with Oxone^{®,66}

to $PhIO_2$ using Oxone as a stoichiometric oxidant. Due to the mild reaction conditions, our protocol is highly selective, and it generally does not afford products of C–C bond cleavage.

Conclusions

A survey of current literature demonstrates that hypervalent iodine compounds attract significant interest as efficient and environmentally friendly oxidizing reagents, which can be used instead of the toxic derivatives of mercury(II), thallium(III), lead(IV), chromium(VI) and other heavy metals.¹⁻¹³ Our contribution to this area of research consists in the development of new hypervalent iodine reagents, 16-23,73-92 some of which have already found practical application in organic synthesis. The recent discovery of recyclable reagents and catalytic systems based on the iodine redox chemistry has initiated a major surge of research activity and added a new dimension to the field of hypervalent iodine chemistry. Taking into account the importance of Green Chemistry principles,²⁵ it can be anticipated that the current trend toward the synthetic application of recyclable reagents and catalytic systems based on hypervalent iodine chemistry will continue in the future. We hope that our recent studies described here will provide an added stimulus for the further development of the chemistry of hypervalent iodine compounds.

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References

- 1 Hypervalent Iodine Chemistry, ed. T. Wirth, Springer-Verlag, Berlin, 2003.
- 2 V. V. Zhdankin and P. J. Stang, Chem. Rev., 2008, 108, 5299.
- 3 U. Ladziata and V. V. Zhdankin, ARKIVOC, 2006, (ix), 26.
- 4 V. V. Zhdankin, Curr. Org. Synth., 2005, 2, 121.
- 5 V. V. Zhdankin, ARKIVOC, 2009, (i), 1.
- 6 U. Ladziata and V. V. Zhdankin, Synlett, 2007, 527.
- 7 R. D. Richardson and T. Wirth, Angew. Chem. Int. Ed., 2006, 45, 4402.
- 8 M. Uyanik and K. Ishihara, Chem. Commun., 2009, 2086.
- 9 T. Dohi and Y. Kita, Chem. Commun., 2009, 2073.
- 10 M. Ochiai and K. Miyamoto, Eur. J. Org. Chem., 2008, 4229.
- 11 G. F. Koser, Adv. Heterocycl. Chem., 2004, 86, 225.
- 12 R. M. Moriarty, J. Org. Chem., 2005, 70, 2893.
- 13 L. Pouysegu, D. Deffieux and S. Quideau, Tetrahedron, 2010, 66, 2235.
- 14 P. J. Stevenson, A. B. Treacy and M. Nieuwenhuyzen, J. Chem. Soc., Perkin Trans. 2, 1997, 589.
- 15 D. Macikenas, E. Skrzypczak-Jankun and J. D. Protasiewicz, Angew. Chem. Int. Ed., 2000, 39, 2007.
- 16 V. V. Zhdankin, A. Y. Koposov, B. C. Netzel, N. V. Yashin, B. P. Rempel, M. J. Ferguson and R. R. Tykwinski, *Angew. Chem. Int. Ed.*, 2003, 42, 2194.
- 17 V. V. Zhdankin, D. N. Litvinov, A. Y. Koposov, T. Luu, M. J. Ferguson, R. McDonald and R. R. Tykwinski, *Chem. Commun.*, 2004, 106.
- 18 V. V. Zhdankin, A. Y. Koposov, D. N. Litvinov, M. J. Ferguson, R. McDonald, T. Luu and R. R. Tykwinski, J. Org. Chem., 2005, 70, 6484.
- 19 U. Ladziata, A. Y. Koposov, K. Y. Lo, J. Willging, V. N. Nemykin and V. V. Zhdankin, Angew. Chem. Int. Ed., 2005, 44, 7127.
- 20 A. Y. Koposov, R. R. Karimov, I. M. Geraskin, V. N. Nemykin and V. V. Zhdankin, *J. Org. Chem.*, 2006, **71**, 8452.
- 21 A. Y. Koposov, D. N. Litvinov and V. V. Zhdankin, *Tetrahedron Lett.*, 2004, **45**, 2719.

- 22 V. Zhdankin, R. N. Goncharenko, D. N. Litvinov and A. Y. Koposov, *ARKIVOC*, 2005, (iv), 8.
- 23 A. K. Mailyan, I. M. Geraskin, V. N. Nemykin and V. V. Zhdankin, J. Org. Chem., 2009, 74, 8444.
- 24 A. Y. Koposov and V. V. Zhdankin, Synthesis, 2005, 22.
- 25 Green Chemistry Education: Changing the Course of Chemistry, eds. P. T. Anastas, I. J. Levy and K. E. Parent, ACS Symposium Series, 2009.
- 26 C. A. McNamara, M. J. Dixon and M. Bradley, *Chem. Rev.*, 2002, **102**, 3275.
- 27 P. Hodge, Curr. Opin. Chem. Biol., 2003, 7, 362.
- 28 N.-H. Nam, S. Sardari and K. Parang, J. Comb. Chem., 2003, 5, 479.
- 29 W.-J. Chung, D.-K. Kim and Y.-S. Lee, *Tetrahedron Lett.*, 2003, 44, 9251.
- 30 D.-K. Kim, W.-J. Chung and Y.-S. Lee, Synlett, 2005, 279.
- 31 P. Lecarpentier, S. Crosignani and B. Linclau, *Mol. Diversity*, 2005, 9, 341.
- 32 U. Ladziata, J. Willging and V. V. Zhdankin, Org. Lett., 2006, 8, 167.
 33 S. Weik, G. Nicholson, G. Jung and J. Rademann, Angew. Chem. Int.
- *Ed.*, 2001, **40**, 1436. 34 B. Hinzen and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1907.
- 35 R. R. Karimov, Z.-G. M. Kazhkenov, M. J. Modjewski, E. M. Peterson and V. V. Zhdankin, *J. Org. Chem.*, 2007, **72**, 8149.
- 36 H. Tohma, A. Maruyama, A. Maeda, T. Maegawa, T. Dohi, M. Shiro, T. Morita and Y. Kita, *Angew. Chem. Int. Ed.*, 2004, 43, 3595.
- 37 A. Moroda and H. Togo, *Tetrahedron*, 2006, **62**, 12408.
- 38 V. Tesevic and J. A. Gladysz, J. Org. Chem., 2006, 71, 7433.
- 39 M. S. Yusubov, M. P. Gilmkhanova, V. V. Zhdankin and A. Kirschning, Synlett, 2007, 563.
- 40 M. S. Yusubov, L. A. Drygunova and V. V. Zhdankin, *Synthesis*, 2004, 2289.
- 41 M. S. Yusubov, T. V. Funk, K.-W. Chi, E.-H. Cha, G. H. Kim, A. Kirschning and V. V. Zhdankin, J. Org. Chem., 2008, 73, 295.
- 42 T. Muraki, H. Togo and M. Yokoyama, J. Org. Chem., 1999, 64, 2883.
- 43 M. Ochiai, Y. Takeuchi, T. Katayama, T. Sueda and K. Miyamoto, J. Am. Chem. Soc., 2005, 127, 12244.
- 44 J. Sheng, X. Li, M. Tang, B. Gao and G. Huang, Synthesis, 2007, 1165.
- 45 Y. Yamamoto, Y. Kawano, P. H. Toy and H. Togo, *Tetrahedron*, 2007, 63, 4680.
- 46 R. D. Richardson, T. K. Page, S. Altermann, S. M. Paradine, A. N. French and T. Wirth, *Synlett*, 2007, 538.
- 47 K. Miyamoto, Y. Sei, K. Yamaguchi and M. Ochiai, J. Am. Chem. Soc., 2009, 131, 1382.
- 48 C. I. Herrerias, T. Y. Zhang and C.-J. Li, Tetrahedron Lett., 2006, 47, 13.
- 49 T. Dohi, A. Maruyama, M. Yoshimura, K. Morimoto, H. Tohma and Y. Kita, Angew. Chem. Int. Ed., 2005, 44, 6193.
- 50 T. Dohi, A. Maruyama, Y. Minamitsuji, N. Takenaga and Y. Kita, *Chem. Commun.*, 2007, 1224.
- 51 T. Dohi, Y. Minamitsuji, A. Maruyama, S. Hirose and Y. Kita, *Org. Lett.*, 2008, **10**, 3559.
- 52 A. Moroda and H. Togo, Synthesis, 2008, 1257.
- 53 H. Liu and C.-H. Tan, Tetrahedron Lett., 2007, 48, 8220.
- 54 S. Quideau, G. Lyvinec, M. Marguerit, K. Bathany, A. Ozanne-Beaudenon, T. Buffeteau, D. Cavagnat and A. Chenede, *Angew. Chem. Int. Ed.*, 2009, 48, 4605.
- 55 T. Dohi, A. Maruyama, N. Takenage, K. Senami, Y. Minamitsuji, H. Fujioka, S. Caemmerer and Y. Kita, *Angew. Chem. Int. Ed.*, 2008, **47**, 3787.
- 56 M. Uyanik, T. Yasui and K. Ishihara, Angew. Chem. Int. Ed., 2010, 49, 2175.
- 57 M. Ngatimin and D. W. Lupton, Aust. J. Chem., 2010, 63, 653.
- 58 M. Uyanik, M. Akakura and K. Ishihara, J. Am. Chem. Soc., 2009, 131, 251.
- 59 A. P. Thottumkara, M. S. Bowsher and T. K. Vinod, *Org. Lett.*, 2005, 7, 2933.
- 60 A. Schulze and A. Giannis, Synthesis, 2006, 257.
- 61 T. Yakura and T. Konishi, Synlett, 2007, 765.
- 62 L. R. Ojha, S. Kudugunti, P. P. Maddukuri, A. Kommareddy, M. R. Gunna, P. Dokuparthi, H. B. Gottam, K. K. Botha, D. R. Parapati and T. K. Vinod, *Synlett*, 2009, 117.

- 63 A. Y. Koposov, D. N. Litvinov, V. V. Zhdankin, M. J. Ferguson, R. McDonald and R. R. Tykwinski, *Eur. J. Org. Chem.*, 2006, 4791.
- 64 M. S. Yusubov, K.-W. Chi, J. Y. Park, R. Karimov and V. V. Zhdankin, *Tetrahedron Lett.*, 2006, 47, 6305.
- 65 A. Y. Koposov, R. R. Karimov, A. A. Pronin, T. Skrupskaya, M. S. Yusubov and V. V. Zhdankin, J. Org. Chem., 2006, 71, 9912.
- 66 M. S. Yusubov, A. A. Zagulyaeva and V. V. Zhdankin, *Chem. Eur. J.*, 2009, **15**, 11091.
- 67 K. C. Nicolaou, T. Montagnon, P. S. Baran and Y. L. Zhong, J. Am. Chem. Soc., 2002, 124, 2245.
- 68 J. N. Moorthy, N. Singhal and K. Senapati, *Tetrahedron Lett.*, 2006, 47, 1757.
- 69 M. Bressan and A. Morvillo, *Inorg. Chem.*, 1989, 28, 950.
- 70 M. M. T. Khan, A. P. Rao and S. H. Mehta, J. Mol. Catal., 1993, 78, 263.
- 71 I. M. Geraskin, M. W. Luedtke, H. M. Neu, V. N. Nemykin and V. V. Zhdankin, *Tetrahedron Lett.*, 2008, 49, 7410.
- 72 I. M. Geraskin, O. Pavlova, H. M. Neu, M. S. Yusubov, V. N. Nemykin and V. V. Zhdankin, *Adv. Synth. Catal.*, 2009, **351**, 733.
- 73 V. V. Zhdankin, C. J. Kuehl, J. T. Bolz, M. S. Formaneck and A. J. Simonsen, *Tetrahedron Lett.*, 1994, 35, 7323.
- 74 V. V. Zhdankin, R. M. Arbit, B. J. Lynch, P. Kiprof and V. G. Young, J. Org. Chem., 1998, 63, 6590.
- 75 V. V. Zhdankin, M. McSherry, B. Mismash, J. T. Bolz, J. K. Woodward, R. M. Arbit and S. Erickson, *Tetrahedron Lett.*, 1997, **38**, 21.
- 76 C. J. Kuehl, J. T. Bolz and V. V. Zhdankin, Synthesis, 1995, 312.
- 77 V. V. Zhdankin, C. J. Kuehl and A. J. Simonsen, J. Org. Chem., 1996, 61, 8272.
- 78 V. V. Zhdankin, C. J. Kuehl, A. P. Krasutsky, J. T. Bolz, B. Mismash, J. K. Woodward and A. J. Simonsen, *Tetrahedron Lett.*, 1995, 36, 7975.
- 79 A. P. Krasutsky, C. J. Kuehl and V. V. Zhdankin, Synlett, 1995, 1081.
- 80 V. V. Zhdankin, A. P. Krasutsky, C. J. Kuehl, A. J. Simonsen, J. K. Woodward, B. Mismash and J. T. Bolz, *J. Am. Chem. Soc.*, 1996, **118**, 5192.
- 81 V. V. Zhdankin, R. M. Arbit, M. McSherry, B. Mismash and V. G. Young, J. Am. Chem. Soc., 1997, 119, 7408.
- 82 V. V. Zhdankin, J. T. Smart, P. Zhao and P. Kiprof, *Tetrahedron Lett.*, 2000, **41**, 5299.
- 83 V. V. Zhdankin, A. E. Koposov, J. T. Smart, R. R. Tykwinski, R. McDonald and A. Morales-Izquierdo, J. Am. Chem. Soc., 2001, 123, 4095.
- 84 V. V. Zhdankin, A. Y. Koposov, L. S. Su, V. V. Boyarskikh, B. C. Netzel and V. G. Young, *Org. Lett.*, 2003, 5, 1583.
- 85 V. V. Zhdankin, O. Maydanovych, J. Herschbach, R. McDonald and R. R. Tykwinski, *J. Am. Chem. Soc.*, 2002, **124**, 11614.
- 86 V. V. Zhdankin, O. Maydanovych, J. Herschbach, J. Bruno, E. D. Matveeva and N. S. Zefirov, J. Org. Chem., 2003, 68, 1018.
- 87 U. Ladziata, J. Carlson and V. V. Zhdankin, *Tetrahedron Lett.*, 2006, 47, 6301.
- 88 A. Y. Koposov, B. C. Netzel, M. S. Yusubov, V. N. Nemykin, A. Y. Nazarenko and V. V. Zhdankin, *Eur. J. Org. Chem.*, 2007, 4475.
- 89 V. V. Zhdankin, V. N. Nemykin, R. R. Karimov and Z.-G. Kazhkenov, *Chem. Commun.*, 2008, 6131.
- 90 V. N. Nemykin, A. Y. Koposov, B. C. Netzel, M. S. Yusubov and V. V. Zhdankin, *Inorg. Chem.*, 2009, 48, 4908.
- 91 M. S. Yusubov, R. Y. Yusubova, T. V. Funk, K.-W. Chi and V. V. Zhdankin, Synthesis, 2009, 2505.
- 92 A. A. Zagulyaeva, M. S. Yusubov and V. V. Zhdankin, J. Org. Chem., 2010, 75, 2119.

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