Recyclable Hypervalent Iodine Reagents in Modern Organic Synthesis

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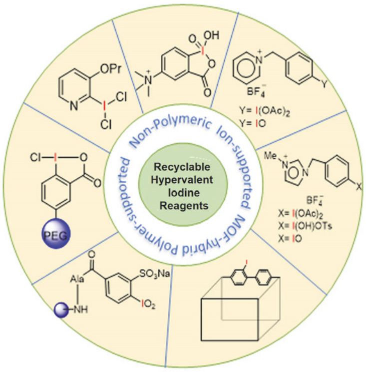

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Abstract Hypervalent iodine (HVI) reagents have gained much attention as versatile oxidants because of their low toxicity, mild reactivity, easy handling, and availability. Despite their unique reactivity and other advantageous properties, stoichiometric HVI reagents are associated with the disadvantage of generating non-recyclable iodoarenes as waste/co-products. To overcome these drawbacks, the syntheses and utilization of various recyclable hypervalent iodine reagents have been established in recent years. This review summarizes the development of various recyclable non-polymeric, polymer-supported, ionic-liquid-supported, and metal–organic framework (MOF)-hybridized HVI reagents.

Key words hypervalent iodine, recyclable reagents, polymer-supported, non-polymeric, ionic-liquid-supported, MOF hybrid

1 Introduction

Hypervalent iodine (HVI) compounds have emerged as versatile and eco-friendly reagents for organic synthesis. Owing to their mild oxidizing properties and favorable electrophilic character, these compounds have gained significant interest in organic synthesis. Their reactivity generally resembles that of transition-metal derivatives.[1] HVI compounds are used for C–H functionalization,[2] alcohol[3] and sulfide[4] oxidation, and oxidative coupling reactions,[5] among others. However, despite their wide application in organic synthesis, stoichiometric HVI reagents are associated with some major drawbacks. One limitation is the production of non-recyclable aryl iodides or similar waste products after the reaction. To overcome this drawback, various recyclable HVI reagents have been developed. Recyclable hypervalent reagents are commonly defined in the literature[1b,6,7] as polyvalent iodine compounds whose reduced form can be conveniently and efficiently separated from the reaction mixture in almost quantitative yield and re-oxidized to the initial reagent without any significant loss of activity. Common hypervalent iodine(III) reagents, such as (diacetoxyiodo)benzene, iodosylbenzene, [hydroxy(tosyloxy)iodo]benzene, 2-iodoxybenzoic acid (IBX), and others, are not considered as recyclable reagents. The reactions of these reagents with organic substrates produce stoichiometric amounts of iodobenzene or other iodoarenes as waste products, requiring column chromatography for separation and purification. The present review encompasses the development of recyclable HVI reagents over the past 10 years. In this review, a comprehensive discussion on the structure, synthesis, reactivity, and use of recyclable HVI reagents is presented. The review itself is divided into four sections based on the type of recyclable HVI reagent being employed.

- Polymer-supported hypervalent iodine reagents.
- Non-polymeric hypervalent iodine reagents.
- Ionic-liquid/ion-supported hypervalent iodine reagents.
- Metal–organic framework (MOF)-hybridized hypervalent iodine reagents.

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Biographical Sketches

Rimi received her M.Sc. in 2014 from Dyal Singh College, Karnal (Kurukshetra University, Kurukshetra). She passed the national-level examination CSIR-UGC (NET) and qualified for a Lectureship in Chemical Sciences in 2018. In 2021, she joined the research group of Dr. Ravi Kumar and Dr. Bhawna Uttam at the J.C. Bose University of Science and Technology, YMCA, Faridabad to pursue her doctoral studies. Her current research interests include the development and applications of new hypervalent iodine reagents.

Sakshi Soni received her M.Sc. in 2018 from the Department of Chemistry, Indira Gandhi University, Meerpur (Rewari). She passed the national-level examination GATE in Chemical Sciences in 2019. In 2021, she joined the research group of Dr. Ravi Kumar and Dr. Vinod Kumar at J.C. Bose University of Science and Technology, YMCA, Faridabad to pursue her doctoral studies. Her current research interests include the synthesis of heterocyclic compounds and studying their photophysical and biological properties.

Bhawna Uttam has been an assistant professor at the Department of Chemistry at the J.C. Bose University of Science and Technology, YMCA, Faridabad since April 2021. She obtained her Ph.D. from the Department of Chemistry at IIT Bombay under the supervision of Prof. C. P. Rao in 2020. She has gained significant experience working in the field of supramolecular organic chemistry. She is currently investigating metal–organic frameworks and their applications towards various catalytic reactions.

Hidehyasu China is an assistant professor at the Nagahama Institute of Bio-Science and Technology. He received his Ph.D. in 2015 from Ritsumeikan University under the supervision of Prof. Y. Okada. After working as a postdoctoral researcher for the Ritsumeikan Global Innovation Research Organization Project (Development of Electronic and Photonic Materials Based on Organic and Biotic Resources) with Prof. T. Dohi, he was promoted to assistant professor at the Nagahama Institute of Bio-Science and Technology in October 2019. He received the Heterocycles Award in 2019 from The Japan Institute of Heterocyclic Chemistry. His research interests include the development of methods for the synthesis of cyclic hypervalent iodine compounds and their applications.

Toshifumi Dohi is a professor at Ritsumeikan University. He received his M.S. degree in 2002 (Prof. S. Murai) from the Graduate School of Engineering of Osaka University, Japan, and his Ph.D. in 2005 (Prof. Y. Kita) from the Graduate School of Pharmaceutical Sciences of Osaka University, where he studied new reactivities of transition-metal catalysts and synthetic chemistry using hypervalent iodine reagents. After finishing his Ph.D. work, he became an assistant professor at Osaka University and was promoted to associate professor (PI) in 2014 at Ritsumeikan University. His current research interests are focused on reagent/catalyst design and the development of new reactions using hypervalent iodine reagents. He has received the IUPAC-ICOS 15 Poster Award for the most excellent presentation, the Pharmaceutical Society of Japan (PSJ) Award for Young Scientists (2009), the Banyu Chemist Award (2013), the Thieme Chemistry Journal Award (2014), the GSC Encouragement Award (2015), and the International Congress on Pure & Applied Chemistry (ICPAC) Lecture Award (2019).

Viktor V. Zhdankin was born in Ekaterinburg, Russian Federation. His M.S. (1978), Ph.D. (1981), and Doctor of Chemical Sciences (1986) degrees were earned at Moscow State University in the laboratory of Nikolay S. Zefirov. He moved to the University of Utah in 1990, where he worked for three years as an Instructor of Organic Chemistry and Senior Research Associate with Peter J. Stang. In 1993, he joined the faculty of the University of Minnesota Duluth, where he is currently a Professor of Chemistry. He has published more than 300 research papers, has given over a hundred research presentations in many countries, has edited several books, has co-authored the *Handbook of Heterocyclic Chemistry* (3rd edition) with Professors A. R. Katritzky, C. A. Ramsden, and J. A. Joule, and authored a book on *Hypervalent Iodine Chemistry*. His main research interests are in the areas of synthetic and mechanistic organic chemistry of hypervalent main-group elements and organofluorine chemistry. In 2011, he received the National Award of the American Chemical Society for *Creative Research & Applications of Iodine Chemistry*.

Ravi Kumar is an associate professor at the J.C. Bose University of Science and Technology, YMCA, Faridabad, India. He received his M.Sc. in 2000 and his Ph.D. in 2005 (Prof. Om Prakash and Prof. Pawan K Sharma) from the Department of Chemistry, Kurukshetra University. He subsequently joined the research group of Prof. Thomas Wirth at the School of Chemistry, Cardiff University, UK as a postdoctoral research fellow, where he explored asymmetric synthesis with hypervalent iodine reagents. He was awarded research grants under the Fast Track Scheme for Young Scientists by the Department of Science and Technology, India to work on hypervalent iodine reagents, the Commonwealth Academic Staff Fellowship by the Commonwealth Scholarship Commission, UK and the INSA-Visiting Scientist Fellowship by the Indian National Science Academy. His research areas include oxidative transformations using hypervalent iodine reagents and heterocyclic chemistry.

2 Polymer-Supported Hypervalent Iodine Reagents

Polymer-supported hypervalent iodine (PS-HVI) reagents are generally prepared by the reaction of polymer-supported iodides with a suitable oxidant. The reactivities of these reagents are comparable to those of their non-polymeric analogs. They are widely applicable in industry as well as in organic synthesis because of their low toxicity and low explosive hazard, particularly IBX derivatives.[7c]

2.1 Polymer-Supported Hypervalent Iodine(III) Reagents

In 1961, Okawara and co-workers reported the first polymer-bound HVI reagent, poly[(diacetoxyiodo)styrene] (PSDIB) (**1a**).[8] Several other polymer-supported reagents, such as poly[bis(trifluoroacetoxyiodo)styrene] (**2**), polystyrene-supported (hydroxytosyloxyiodo)arenes **3**, and resin-bound alkynyl iodonium salts **4** have also been reported.[9–26] Examples of polymer-supported HVI(III) compounds **1**–**11** are shown in Figure 1.

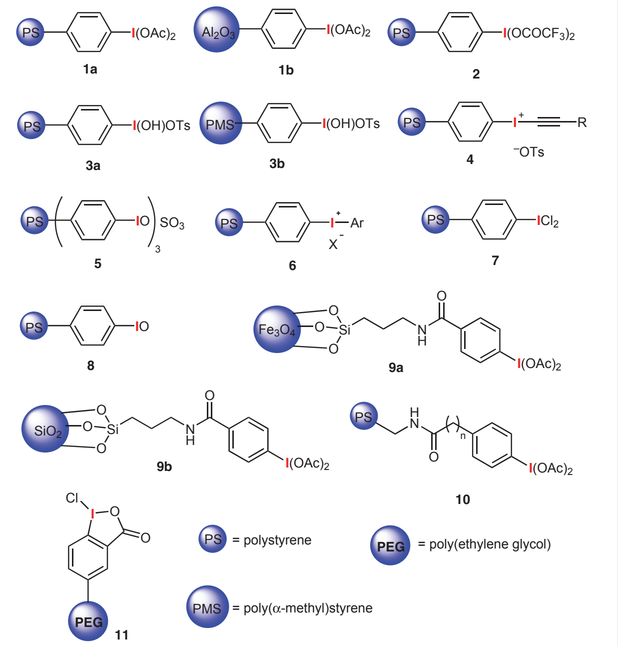
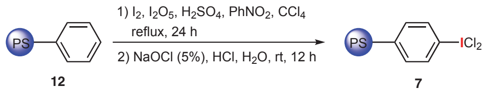
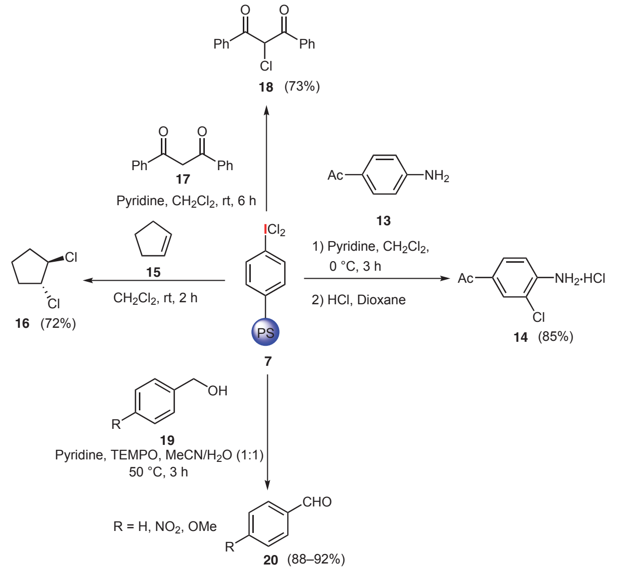


Figure 1 Structures of polymer-supported hypervalent iodine(III) reagents **1**–**11**

Chen, Zhdankin, and co-workers reported the one-pot synthesis of polystyrene-supported (dichloroiodo)benzene (PSDCIB) (**7**) via the iodination of polystyrene followed by oxidation with NaOCl (Scheme 1). Reagent **7** has been used effectively for the α-chlorination of dibenzoylmethane (**17**), the aryl chlorination of 4-aminoacetophenone (**13**), the dichlorination of cyclopentene (**15**), and the oxidation of benzyl alcohols **19** (Scheme 2). However, in the case of 2-thiophenemethanol, the corresponding oxidized product, 2-thiophenecarboxaldehyde, was obtained in only 20% yield, even after a reaction time of 12 hours. The reduced form of reagent **7** can be separated from the reaction mixture by simple filtration. Treatment of the reduced form with bleach and aqueous HCl regenerated PSDCIB (**7**) in approximately 90% overall yield.[27]

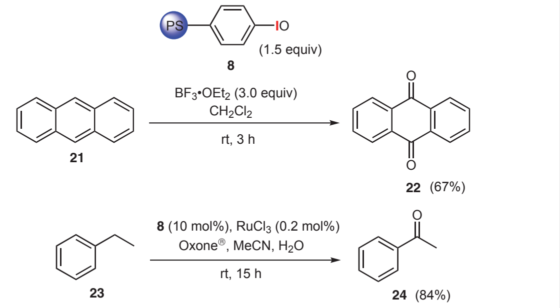


Scheme 1 Synthesis of polystyrene-supported PSDCIB (**7**)



Scheme 2 Reactions using hypervalent iodine reagent PSDCIB (**7**)

Chen and Zhdankin's group synthesized polystyrene-supported iodosyl benzene (PSISB) (**8**) under solvent-free conditions. PSISB (**8**) can be used effectively in the presence of Lewis acids, such as $BF_3{\cdot}Et_2O$, and the metal catalyst $RuCl_3$, for the oxidation of a variety of substrates, including alcohols, anthracenes, and alkylbenzenes. The oxidation of anthracene (**21**) with **8** in the presence of $BF_3{\cdot}Et_2O$ afforded anthraquinone (**22**) in 67% yield, while oxidation of ethylbenzene (**23**) in the presence of $RuCl_3$ gave acetophenone (**24**) in 84% yield (Scheme 3).[28]



Scheme 3 Oxidation of anthracene (**21**) and ethylbenzene (**23**) using polystyrene-supported iodosylbenzene (**8**)

Zhdankin et al. synthesized bifunctional silica-supported iodoarene-$RuCl_3$ catalysts **25** and **26** (Figure 2). Both **25** and **26** can be utilized for the efficient oxidation of alcohols and aromatic hydrocarbons using Oxone® as a stoichiometric oxidant. Catalyst **26** was more reactive than **25** in the oxidation of anthracene and indane. These catalysts were recoverable from the reaction mixture by simple filtration and could be reused, whereupon their reactivity decreased somewhat.[29]

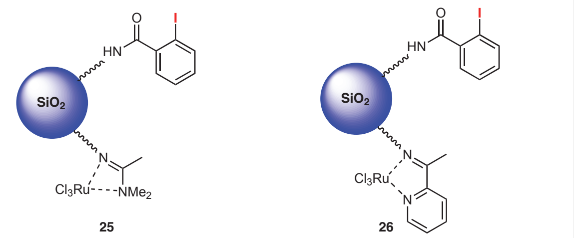
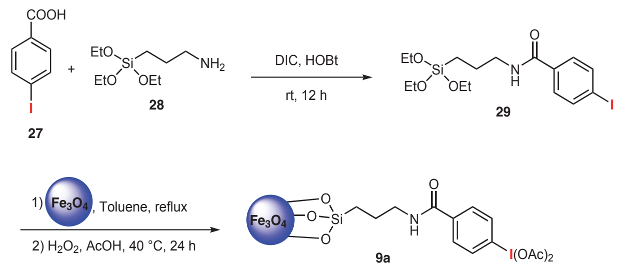
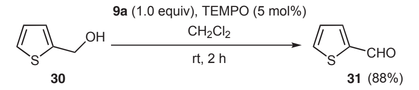


Figure 2 Structures of bifunctional silica-supported iodoarene-$RuCl_3$ catalysts **25** and **26**

In 2012, Wei and Zhu synthesized magnetic iron oxide (Fe_3O_4)-nanoparticle-supported (diacetoxyiodo)benzene **9a**.[30] Condensation of 4-iodobenzoic acid (**27**) and organosilane **28** in the presence of *N*,*N*′-diisopropylcarbodiimide (DIC) and 1-hydroxybenzotriazole (HOBt) afforded amide **29**. Amide **29** was refluxed with magnetite, and subsequent oxidation with hydrogen peroxide and acetic acid produced iodine reagent **9a** (Scheme 4). Organosilanes **28** have been used for immobilization because of their high affinity toward under-coordinated surface sites of iron oxide particles. In the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), **9a** efficiently oxidized alcohols to the corresponding carbonyl compounds in 78–96% yield. In particular, the reaction of 2-thiophenemethanol (**30**) with **9a** in the presence of TEMPO resulted in the formation of 2-thiophenecarboxaldehyde (**31**) in 88% yield (Scheme 5). The reduced form of **9a** can be recycled approximately eight times without a marked decrease in reactivity. The same group also synthesized silica-supported (diacetoxyiodo)benzene **9b** using a similar procedure.[30]



Scheme 4 Synthesis of magnetic-nanoparticle-supported (diacetoxyiodo)arene derivative **9a**



Scheme 5 Oxidation of 2-thiophenemethanol (**30**) with magnetic-nanoparticle-supported reagent **9a**

In 2016, Yakura and co-workers reported readily recoverable and recyclable magnetic-nanoparticle-supported iodoarene catalysts **32** and **33** (Figure 3). The utility of these catalysts for the oxidation of 4-alkoxyphenols **34** to their respective quinones **35** has been well established, affording yields of 68–95% (Scheme 6). It was found that phosphonic acid coated catalyst **33** showed better reactivity and recyclability due to its higher stability under acidic conditions. Iodoarene catalyst **33** can be recycled up to eight times, albeit resulting in a decrease in the activity of the catalyst and necessitating a longer reaction time.[31]

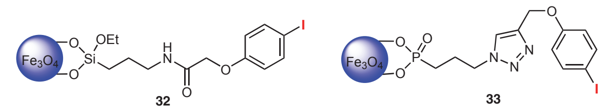
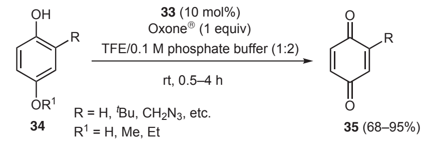
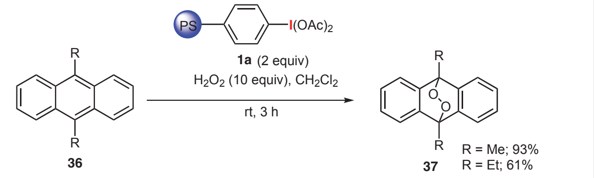


Figure 3 Magnetic-nanoparticle-supported iodoarene catalysts **32** and **33**



Scheme 6 Oxidation of 4-alkoxyphenols **34** using magnetic-nanoparticle-supported iodoarene catalyst **33**

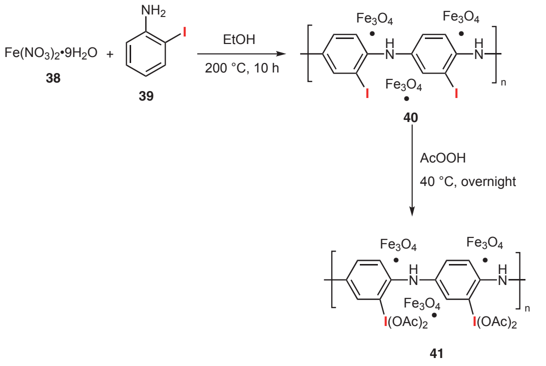
Çatir reported that PSDIB (**1a**) induced the generation of singlet oxygen from hydrogen peroxide for the peroxidation of various organic substrates, such as electron-rich alkenes, and conjugated and aromatic hydrocarbons. As a notable example, disubstituted anthracene derivatives **36** were treated with PSDIB/H_2O_2 to afford the corresponding peroxides **37** (Scheme 7).[32]



Scheme 7 Peroxidation of disubstituted anthracenes **36** using a PS-DIB/H_2O_2 system

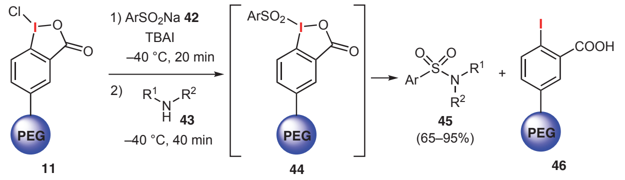
A variety of alcohols can be oxidized using a graphene-oxide-supported HVI (GO-HVI) reagent. The GO-HVI catalyst can be recovered via filtration and reused up to six times. Moreover, after completion of the sixth cycle, the reduced form of GO-HVI can be recovered by simple filtration. After recovery, the reduced form can be readily converted into GO-HVI by treatment with peracetic acid.[33]

Nemati et al. developed a magnetic nanocomposite containing the HVI(III) reagent Fe_3O_4-PANI (polyaniline)-$I(OAc)_2$ (**41**) as a green, low-cost nanocomposite catalyst with good efficiency. Catalyst **41** was synthesized by the reaction of ferric nitrate nonahydrate (**38**) and 2-iodoaniline (**39**) to form **40**, followed by oxidation with preheated peracetic acid (Scheme 8). Catalyst **41** effectively oxidized benzyl alcohols bearing electron-withdrawing and electron-donating groups under mild conditions to produce the corresponding benzaldehyde derivatives. However, electron-withdrawing groups such as Br, Cl, and NO_2 on the benzene ring of the substrate decreased the reaction rate, thereby increasing the reaction time. Moreover, catalyst **41** could be regenerated five times without remarkable deactivating. This was attributed to the good bonding of active catalytic partial with the polymeric support.[34]



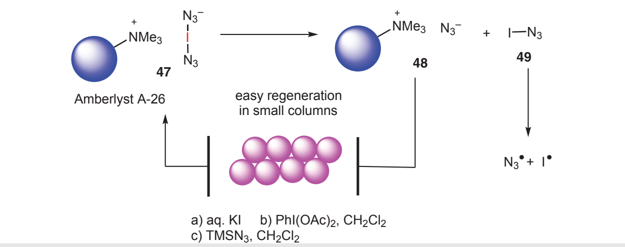
Scheme 8 Synthesis of magnetic nanocomposite catalyst **41**

In 2021, Macara and co-workers reported the synthesis of polyethylene glycol (PEG)-supported hypervalent iodine reagent **11**. They also performed the sulfonylation of various amines **43**, such as morpholine, diethylamine, and piperidine, using sodium aryl sulfinate (**42**) and **11** to form the corresponding sulfonamides **45** in 65–95% yield (Scheme 9). This method does not require chromatographic separation for further product purification. Reagent **11** can be regenerated by oxidizing **46** using trichloroisocyanuric acid (TCICA).[35]



Scheme 9 Synthesis of sulfonamides **45** using PEG-supported HVI reagent **11**

Various polymer-bound iodine-ate(I) complexes have been synthesized by Kirschning and co-workers,[36] and their reactivity has already been discussed in a review published by Zhdankin and Yusubov.[7b,c] Recently, Kirschning reported the use of a polymer-bound bisazido iodate(I) complex for photochemical transformations, such as 1,2-functionalization of alkenes and chemoselective oxidation of secondary alcohols in the presence of primary alcohols. The polymer support can be regenerated after the generation of an azide radical.[36f,g] The recycling procedure toward the Amberlyst A-26 resin is shown in Scheme 10.[36f]



Scheme 10 Polymer-bound bisazidoiodate(I) **47**, release of iodine azide **49**, the proposed photochemical generation of the azide radical and resin regeneration

2.2 Polymer-Supported Hypervalent Iodine(V) Reagents

The groups of Giannis and Rademann independently synthesized polymer-supported IBX reagents. Giannis produced silica-gel-supported IBX **50**, and Rademann synthesized Merrifield-resin-supported IBX **51b**, respectively.[37,38] Recently, several polymer-supported pseudocyclic iodylarene derivatives, such as IBX-amides, IBX-esters, IBX-ethers, and N-(2-iodyl-phenyl)-acylamide (NIPA) resins have also been synthesized.[39–49] Chemical inertness to the solvent and the swelling tendency of the polymer-support are key factors behind the efficient activity of polymer-supported reagents.[50] The structures of polymer-supported HVI(V) reagents **50–61** are shown in Figure 4.

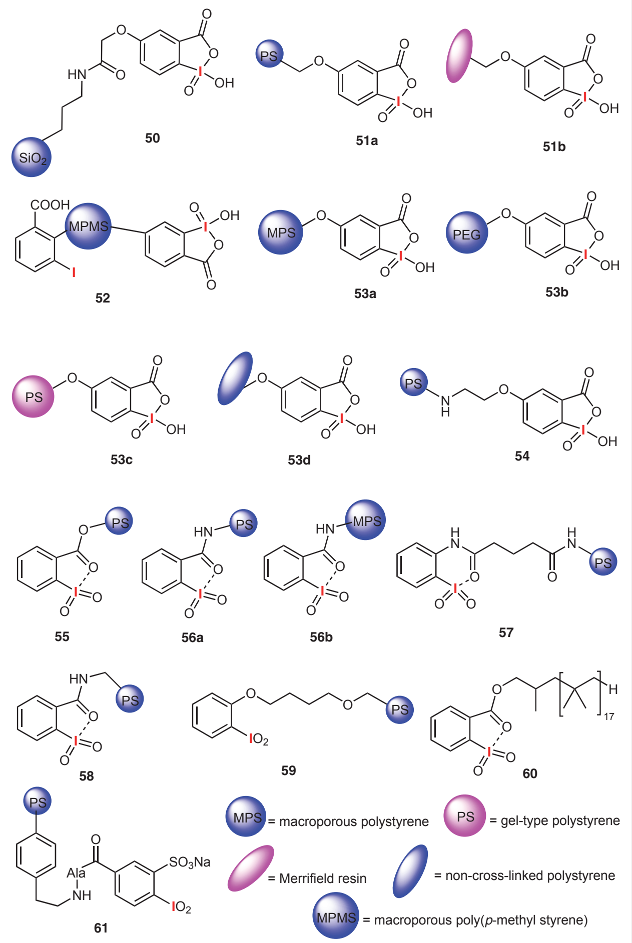
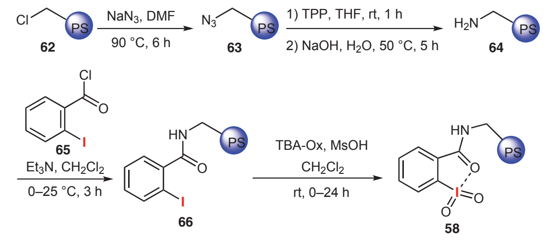


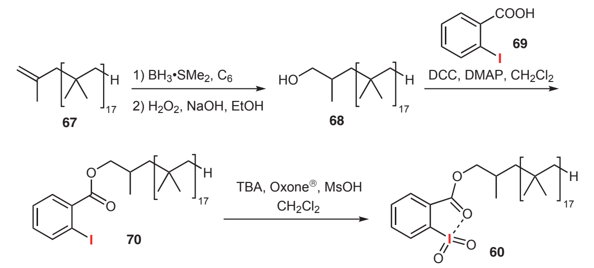
Figure 4 Structures of polymer-supported HVI(V) reagents **50–61**

Lee's group developed a straightforward method for the synthesis of polymer-supported IBX-amide **58**, with a stable linkage and a high loading capacity of up to 1.40 mmol g^{-1}, for the efficient oxidation of various alcohols, phosphites, and sulfides in dichloromethane to access the corresponding carbonyl, phosphate, and sulfoxide products. Chloromethyl polystyrene resin **62** was heated with sodium azide to form azidomethyl polystyrene **63**, which was then treated with triphenylphosphine (TPP) followed by hydrolysis with sodium hydroxide to produce aminomethyl polystyrene **64**. The coupling of **64** with **65** followed by oxidation with tetrabutylammonium Oxone® (TBA-Ox) afforded **58** (Scheme 11). Reagent **58** can be recycled a minimum of five times without any loss in reactivity. After the fifth cycle, the activity of IBX amide decreases slowly due to the possible degradation of the polystyrene backbone after repetitive activation.[50]



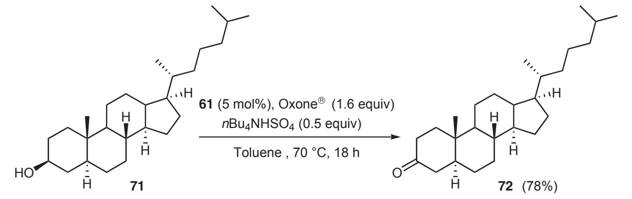
Scheme 11 Synthesis of polymer-supported IBX amide **58**

Samunual and Bergbreiter synthesized polyisobutylene (PIB)-bound IBX derivative **60**. Alkene-terminated polyisobutylene **67** was explored in hydroboration–oxidation, resulting in the formation of PIB-supported alcohol **68**, which upon esterification using 2-iodobenzoic acid (**69**) gave 2-iodoester **70**. Ester **70** was treated with TBA-Ox and methanesulfonic acid to afford the pseudocyclic iodine(V) reagent **60** (Scheme 12). Reagent **60** can be recycled five times by employing biphasic separation followed by oxidation with TBA-Ox.[51]



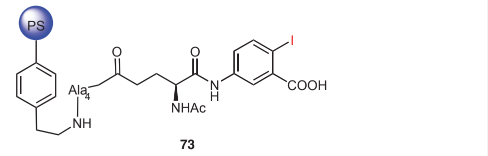
Scheme 12 Synthesis of polyisobutylene-bound IBX reagent **60**

Ballaschk and Kirsch synthesized solid-supported hypervalent iodine compound **61**, which is based on 2-iodoxybenzenesulfonic acid (IBS). Catalyst **61** was used for the effective oxidation of secondary alcohols. For example, the oxidation of 5α-cholestan-3β-ol **71** using IBS-derived reagent **61** and Oxone® at 70 °C in toluene delivered 5α-cholestan-3-one **72** in 78% yield (Scheme 13).[52]



Scheme 13 Oxidation of 5α-cholestan-3β-ol **71** with **61**

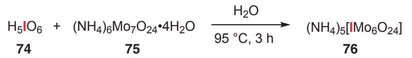
Moreover, the same group also synthesized solid-supported catalyst **73** (Figure 5), which is based on an IBX derivative, for the oxidation of secondary alcohols. They found that catalyst **73** showed inferior activity to catalyst **61**. Catalysts **61** and **73** can be readily separated from reaction mixtures by filtration and reused several times without any significant loss in catalytic activity.[52]



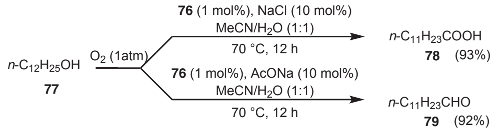
73

Figure 5 Structure of solid-supported IBX-derived catalyst **73**

In 2018, Wei et al. developed inorganic ligand-coordinated polyoxametallate (POM) iodine catalyst **76** by treating ammonium heptamolybdate (**75**) with orthoperiodic acid (**74**) in an aqueous medium at 95 °C for 3 hours (Scheme 14).[53] This catalyst selectively oxidizes various alcohols, including primary, secondary, allylic, and benzylic, under aerobic conditions without the use of toxic oxidants such as Oxone®, or sensitive organic ligands. Oxidation of lauryl alcohol (**77**) by employing iodine catalyst **76** under an oxygen atmosphere (balloon) in the presence of NaCl gave lauric acid (**78**) in 93% yield. When sodium acetate was used as an additive instead of sodium chloride, selective oxidation to lauraldehyde (**79**) occurred in a yield of 92% (Scheme 15). Upon reaction completion, catalyst **76** was precipitated by the addition of ether to the reaction mixture. The catalyst can be reused without any further purification at least six times.[53] It is noteworthy that this oxidation cycle involves iodine(VII)–iodine(V) catalysis.



Scheme 14 Preparation of inorganic ligand-supported iodine catalyst **74**



Scheme 15 Selective oxidation of lauryl alcohol (**77**) in the presence of catalyst **76**

3 Non-Polymeric Recyclable Hypervalent Iodine Reagents

The reuse of polymer-supported HVI reagents causes oxidative degradation of the polymer backbone, which leads to a decrease in the catalytic efficiency. Several non-polymeric recyclable HVI reagents have thus been synthesized to overcome this drawback.

3.1 Non-Polymeric Recyclable Hypervalent Iodine(III) Reagents

Kita and co-workers reported the synthesis of highly reactive recyclable hypervalent iodine reagents **80–82** containing an adamantane ring.[54] In addition, several other non-polymeric recyclable tetraphenylmethane reagents **83–85**[55] were developed by the same research group. The main reason for the high reactivity of these reagents is that the iodine sites are well controlled in the tetrahedral structure and are sufficiently far apart from each other. These reagents are widely used for the oxidation of alcohols, biaryl coupling, and α-tosyloxylation.[54,55] The reduced form of adamantane and methane-based reagents can be readily recovered in nearly quantitative yield by quenching the reaction with methanol followed by simple filtration. The recovered product was re-oxidized back to the respective reagent by reaction with *m*-chloroperbenzoic acid (*m*-CPBA). Certain non-polymeric HVI(III) reagents such as **86–89**, biphenyl-based HVI(III) reagents **90–93**, as well as terphenyl-based HVI(III) reagents **94** and **95** have also been synthesized;[54–68] their reactivity patterns have already been discussed in previous reviews.[1b,6,7] The structures of these non-polymeric recyclable HVI(III) reagents are shown in Figure 6.

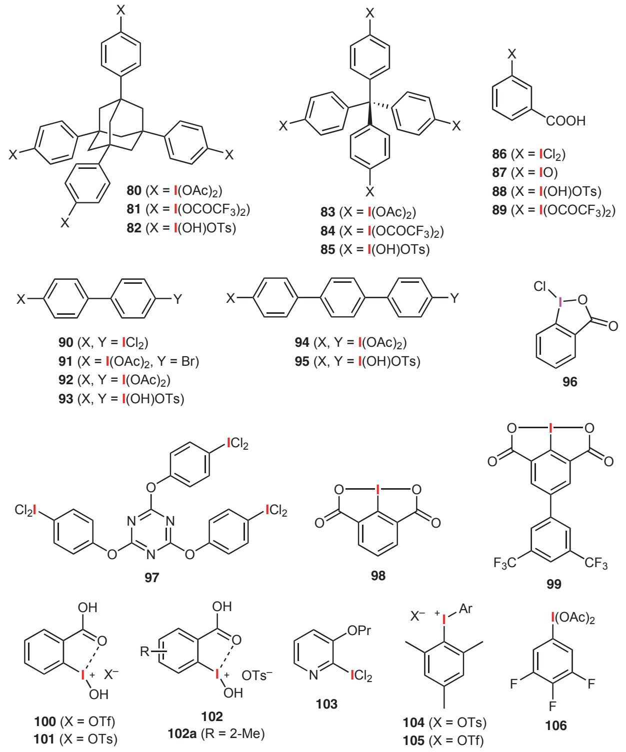
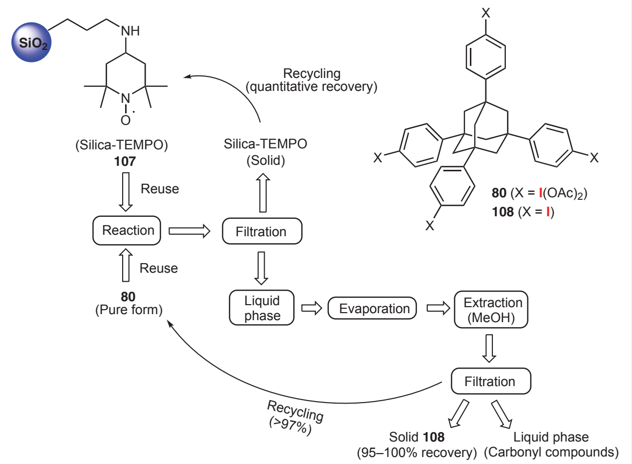


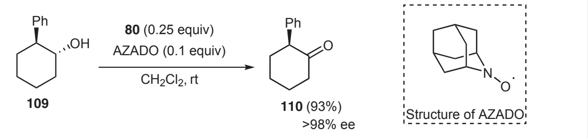
Figure 6 Structures of non-polymeric recyclable HVI(III) reagents **80–106**

In 2011, Zhdankin et al. carried out the efficient oxidation of alcohols and sulfides using a recyclable catalytic system based on silica-supported $RuCl_3$ and 3-(dichloroiodo)benzoic acid (**86**).[68] Furthermore, Kita et al. developed an excellent dual recycling strategy for hypervalent iodine reagent **80** and silica-supported TEMPO **107**, as shown in

Scheme 16.[69a] Recyclable reagent **80** was applied in the oxidation of optically active alcohol **109** to the enolizable ketone **110** by using the less-hindered nitroxyl radical 2-azaadamantane-*N*-oxyl (AZADO), without racemization (Scheme 17).[69]

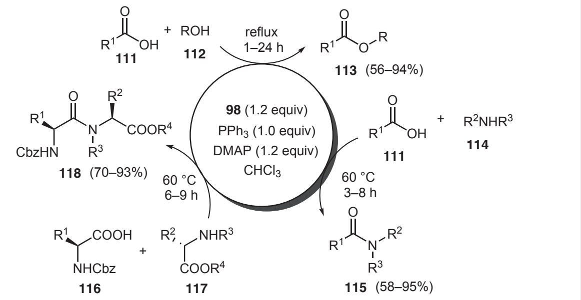


Scheme 16 A dual recycling strategy involving **80** and silica-supported TEMPO **107**



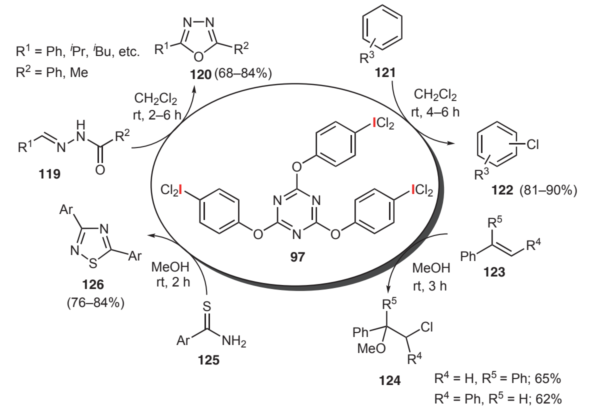
Scheme 17 Oxidation of alcohol **109** using **80** and AZADO

In 2012, Zhang and co-workers found that the HVI(III) iodosodilactone reagent **98** (Figure 6) was applicable for esterification, amidation, and peptide coupling reactions (Scheme 18). The reaction of carboxylic acid **111** with alcohol **112** in the presence of **98**, DMAP, and PPh$_3$ afforded the corresponding esters **113** in 56–94% yield. Reagent **98** has also been utilized for the synthesis of acid derivatives, such as amides **115** and peptides **118** (Scheme 18). Condensation of the chiral secondary alcohol L-menthol and *n*-hexanoic acid afforded the corresponding ester with retention of the stereochemistry (>99% ee). Furthermore, reagent **98** can be recovered from the reaction mixture without any loss in reactivity.[70]

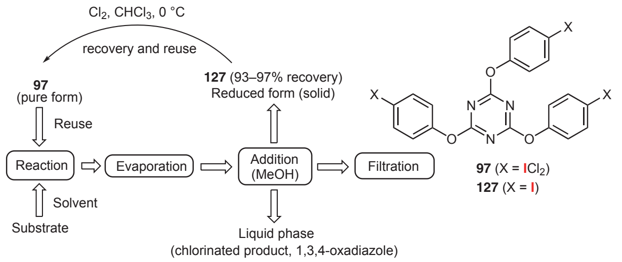


Scheme 18 Direct esterification, amidation and peptide coupling using hypervalent reagent **98**

Karade et al. synthesized a new recyclable reagent, 2,4,6-tris[(4-dichloroiodo)phenoxy]-1,3,5-triazine (**97**) using 2,4,6-trichloro-1,3,5-triazine, 4-iodophenol and KOH. The reaction was conducted in acetone for 48 hours at room temperature to form 2,4,6-tris[(4-iodo)phenoxy]-1,3,5-triazine **127** (see Scheme 20), which was further treated with chlorine gas in chloroform to afford 2,4,6-tris[(4-dichloroiodo)phenoxy]-1,3,5-triazine (**97**). Iodine reagent **97** is useful for the chlorination of various organic substrates, such as the electrophilic chlorination of benzene derivatives **121** and the chloromethoxylation of olefins **123**. Furthermore, **97** can be effectively used for the intramolecular oxidative cyclization of *N*-acylhydrazones **119** in the synthesis of 1,3,4-oxadiazoles **120** (68–84% yield). Dimerization of **125** can also be performed using this reagent to afford 3,5-diaryl-1,2,4-thiadiazoles **126** (Scheme 19). In the case of chlorination and oxidative cyclization reactions, the reduced form of **97** can be recovered by evaporating the solvent, followed by methanol addition and filtration (Scheme 20); however, for the synthesis of thiadiazoles, recovery can be achieved by simple filtration.[71] Recently, alcohol oxidation using reagent **97** and TEMPO has also been reported.[72] α-



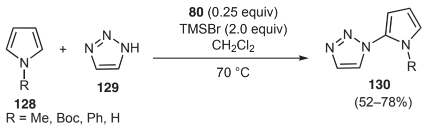
Scheme 19 Synthetic utility of 2,4,6-tris[(4-dichloroiodo)phenoxy]-1,3,5-triazine (**97**)



Scheme 20 Procedure for the recovery and reuse of **97**

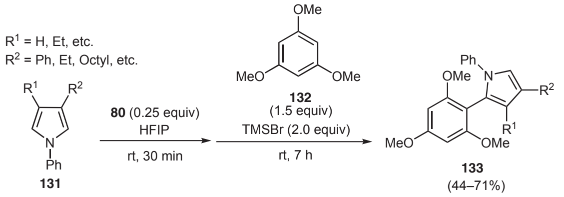
Tosyloxylation of ketones in 63–84% yield can be performed using 2,4,6-tris[(4-iodo)phenoxy]-1,3,5-triazine (**127**) as the catalyst.[73]

In 2015, Kita and co-workers achieved the cross-coupling of pyrroles **128** and azoles **129** to afford coupling product **130** in 52–78% yield using 1,3,5,7-tetrakis[4-(diacetoxyiodo)phenyl]adamantane (**80**) in combination with bromotrimethylsilane at 70 °C (Scheme 21).[74]



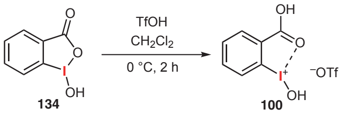
Scheme 21 Oxidative cross-coupling of pyrroles **128** with triazoles **129** using reagent **80**

In 2018, Kita et al. reported the cross-coupling reaction of pyrroles **131** with the electron-rich arene **132** using adamantane-core-based reagent **80** in hexafluoroisopropanol (HFIP) at room temperature (Scheme 22).[75]



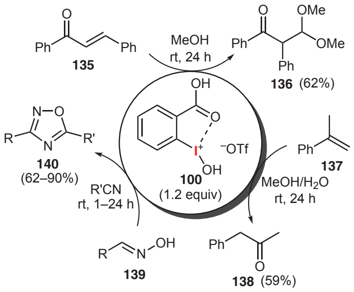
Scheme 22 Metal-free oxidative cross-coupling of pyrroles **131** with **132** using reagent **80**

Zhdankin and co-workers reported the synthesis, structure, and reactivity of pseudocyclic benziodoxole triflate (IBA-OTf) (**100**). Treatment of iodosylbenzoic acid **134** with trifluoromethanesulfonic acid (TfOH) in CH_2Cl_2 for 2 hours at 0 °C resulted in IBA-OTf (**100**) in 93% yield (Scheme 23). X-ray crystallographic analysis revealed the exceptional stability of **100** owing to the strong intramolecular attraction between the carboxy oxygen and iodine atoms. IBA-OTf (**100**) acts as an electrophilic reagent for various nucleophilic organic substrates, as well as terminal oxidants.[76]



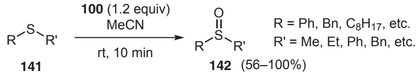
Scheme 23 Conversion of 2-iodobenzoic acid **134** into pseudocyclic benziodoxole triflate (**100**)

Diaryliodonium triflates were also synthesized by the same group via the reaction of **100** and mesitylene in 2,2,2-trifluoroethanol (TFE) for 24 hours at room temperature.[76] Furthermore, the versatility of IBA-OTf (**100**) was established for various substrates, as shown in Scheme 24. The reduced form of reagent **100** (i.e., 2-iodobenzoic acid) can be readily recovered from the reaction mixture by a simple acid–base liquid–liquid biphasic protocol. Re-oxidation of the recovered 2-iodobenzoic acid followed by treatment with trifluoromethanesulfonic acid regenerates **100**.[76]



Scheme 24 Reaction of **100** with various organic substrates

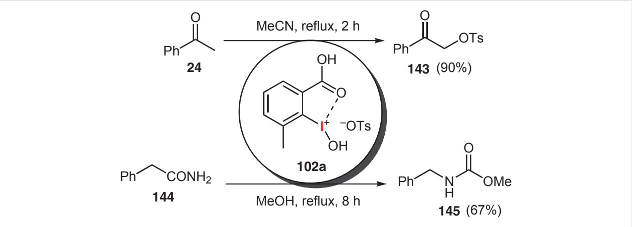
Treatment of various sulfides **141** with **100** at room temperature for 10 minutes resulted in controlled oxidation to give the corresponding sulfoxides **142** in 56–100% yield (Scheme 25), except in the case of 2-(phenylthio)ethanol, which was oxidized to 2-(phenylsulfinyl)ethanol under similar conditions in 24% yield.[77]



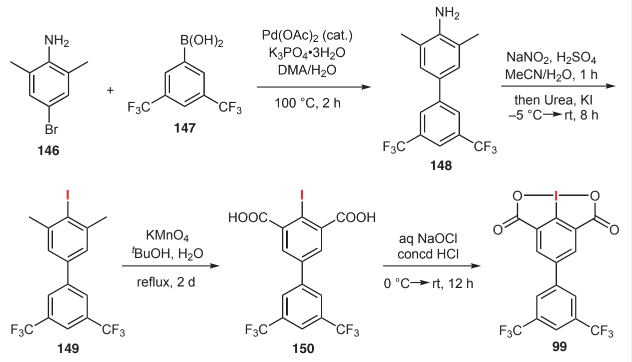
Scheme 25 Sulfide oxidation using reagent **100**

Zhdankin and co-workers prepared pseudocyclic benziodoxole tosylates **101** and **102** by treating 1-hydroxybenziodoxolones with *p*-toluenesulfonic acid in dichloromethane. Salts **101** and **102** can also be synthesized by a ligand-transfer reaction between substituted 2-iodobenzoic acids and [hydroxy(tosyloxy)iodo]benzene (Koser's reagent). Pseudocyclic benziodoxole tosylates **101** and **102** can be used for the oxidation of sulfides, the Hoffmann rearrangement of phenylacetamides, the tosyloxylation of acetophenones, and the iodination of mesitylene. The presence of a methyl group at the *ortho* position of **102a** leads to increased reactivity towards α-tosyloxylation of acetophenone (**24**) and Hoffmann rearrangement of phenylacetamide (**144**) (Scheme 26).[78]

Zhang et al. reported the synthesis of 6-(3,5-bis(trifluoromethyl)phenyl)-1H,4H-2aλ^3-ioda-2,3-dioxacyclopenta[*hi*]indene-1,4-dione (FPID) (**99**) by employing the palladium-catalyzed coupling of 4-bromo-2,6-dimethylaniline (**146**) with 3,5-bis(trifluoromethyl)phenyl boronic acid (**147**), followed by diazotization and iodination to form iodinated product **149**. Subsequent oxidation of **149** using $KMnO_4$ and sodium hypochlorite (NaOCl) gave iodine(III) reagent **99** (Scheme 27).[79]

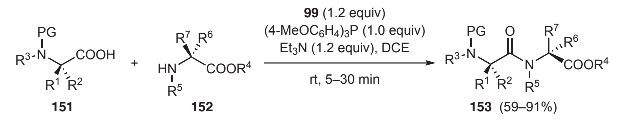


Scheme 26 Reactions mediated by *o*-methyl-substituted pseudocyclic benziodoxole tosylate **102a**



Scheme 27 Synthesis of FPID (**99**)

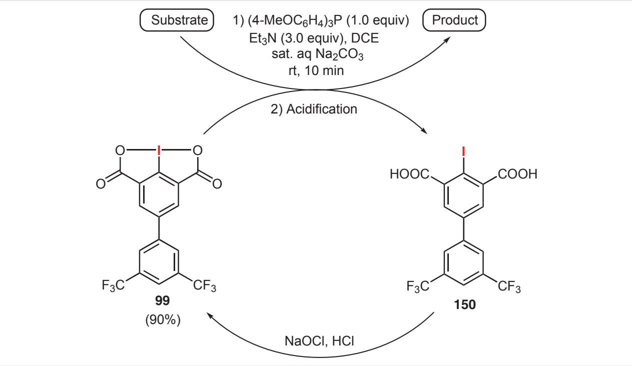
Reagent **99** in combination with tris(4-methoxyphenyl)phosphine can be utilized for the rapid synthesis of dipeptides **153** in 59–91% yield from standard and sterically hindered amino acids (Scheme 28).[79] It is worth mentioning that a similar reaction using iodine reagent **98** requires 3–4 hours for completion to afford the dipeptides.



Scheme 28 FPID-mediated peptide synthesis from sterically hindered amino acids **151** and **152**

The reduced form of **99** can be recovered by diluting the reaction mixture with ethyl acetate, followed by washing with a saturated solution of sodium carbonate and acidification of the aqueous layer with HCl. Diacid **150** can be oxidized back to **99** by treatment with NaOCl/HCl, as shown in Scheme 29.[79]

Various peptides, such as protected Leu-enkephalin **154** (Figure 7),[78] the cyclic heptapeptide pseudostellarin D (**155**) (Figure 7), and bioactive peptides **156–159** (Figure 8) have been synthesized via peptide coupling using **99** and tris(4-methoxyphenyl)phosphine. FPID (**99**) can be recovered following peptide coupling.[80]



Scheme 29 Recycling procedure for **99**

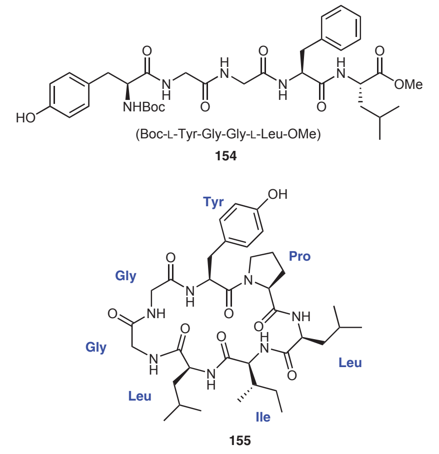


Figure 7 Structures of N/C-protected Leu-enkephalin **154** and pseudostellarin D (**155**)

H2N-Tyr-Gly-Gly-Phe-Leu-OH
156 (42%)

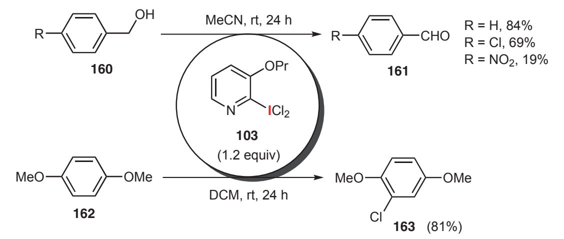
H2N-Gly-Gly-Tyr-Pro-Leu-Ile-Leu-OH
157 (53%)

H2N-Lys-Leu-Pro-Ala-Gly-Thr-Leu-Phe-OH
158 (30%)

H2N-Trp-Val-Pro-Ser-Val-Tyr-OH
159 (21%)

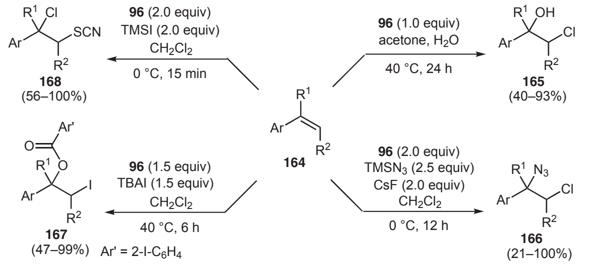
Figure 8 FPID-mediated preparation of bioactive peptides **156–159** accessed via solid-phase peptide synthesis

2-(Dichloroiodo)-3-propoxypyridine (**103**) was developed by Zhdankin et al. as an efficient reagent for the oxidation of benzylic alcohols **160** and the monochlorination of 1,4-dimethoxybenzenes **162** (Scheme 30). Moreover, **103** was also used for the monochlorination of 1,3-diketones.[81] The reduced form of **103** can be readily regenerated from the reaction mixture by employing an acid–base liquid–liquid biphasic protocol.[81]



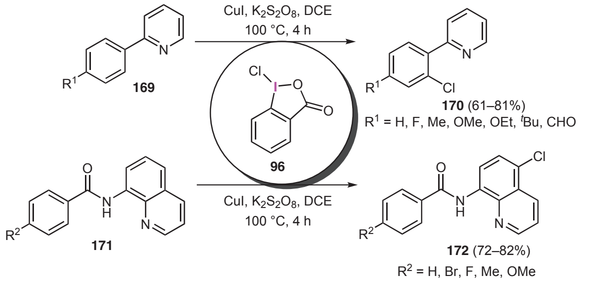
Scheme 30 2-(Dichloroiodo)-3-propoxypyridine (**103**) as an oxidant

1-Chloro-1,2-benziodoxol-3-one (**96**) is useful for the α-chlorination of β-keto esters and 2-acetyl-1-tetralones,[82] the difunctionalization of alkenes through oxychlorination, dichlorination, chlorothiocyanation, iodoesterification and azidochlorination,[83] and for the synthesis of various nitrogen-containing heterocycles and boron dipyrrole methylene (BODIPY) dyes.[84] Various olefins **164** were treated with a range of nucleophiles, such as acetone/water, trimethylsilyl azide, tetra-*n*-butylammonium iodide (TBAI), and (trimethylsilyl)isothiocyanate (TMSI) in the presence of 1-chloro-1,2-benziodoxol-3-one (**96**) to form the corresponding products **165–168** (Scheme 31).[83]



Scheme 31 Difunctionalization of olefins **164** using HVI(III) reagent **96**

In 2017, Parvathaneni and Perumgani performed the highly regioselective copper-catalyzed chlorination of aromatic compounds **169** and **171** using 1-chloro-1,2-benziodoxol-3-one (**96**) and $K_2S_2O_8$ as additives in dichloromethane at 100 °C (Scheme 32).[85] The recycling of reagent **96** involves the recovery of its reduced form by simple solid–liquid-phase separation followed by re-oxidation.[67]



Scheme 32 Chlorination of various aromatic substrates **169** and **171** using **96**

Electrosynthesis is a well-established, safe, and eco-friendly synthetic approach that involves either the replacement of toxic redox reagents by electric current, or the in situ generation of these reagents. Many reports have been published regarding the electrochemical generation of hypervalent iodine reagents that are extensively used as ex-cell or in-cell mediators in different chemical transformations. However, the mediators used were not recyclable. In 2010, Fuchigami and co-workers carried out the electrocatalytic fluorination of organosulfur compounds using recyclable polymer-supported iodobenzene **173** in an ionic liquid. Indirect anodic fluorination of xanthates and phenyl sulfides was carried using the task-specific ionic liquid **174** synthesized from iodophenol. Both of these mediators can be easily recovered and reused several times without losing their activity. The structures of the recyclable mediators synthesized by Fuchigami et al. are shown in Figure 9.[86a,b] The reactivity of electrochemically generated HVI reagents has already been covered in a review by Wirth et al.[87]

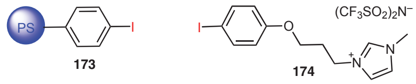
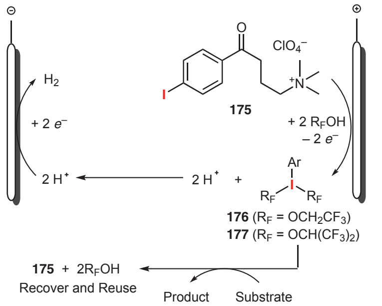


Figure 9 Structures of recyclable mediators **173** and **174** reported by Fuchigami et al.

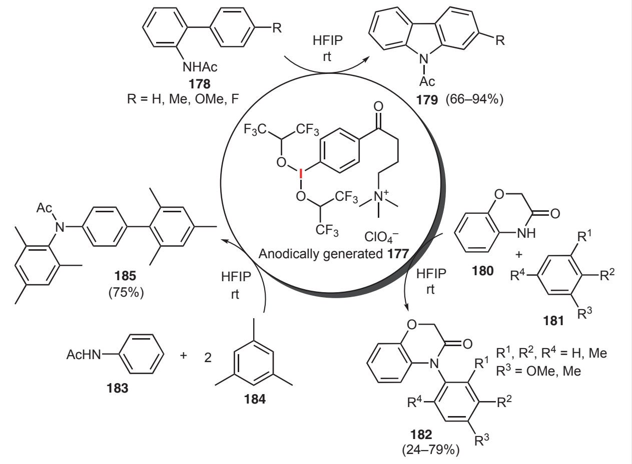
In 2016, Broese and Francke reported the electrosynthesis of I(III) species using fluorinated alcohols, such as HFIP, as the solvent due to their excellent electrochemical properties (Scheme 33).[86c] They performed inter- and intramolecular C–N and C–C coupling reactions using the recyclable mediator salt **177**. Intramolecular cyclization of 2-(*N*-acetylamino)biphenyls **178** and intermolecular C–N coupling of **180** with substituted arenes **181** using **177** resulted in the formation of the corresponding products **179** and **182**. Moreover, **177** was utilized for the coupling of acetanilide (**183**) with mesitylene (**184**) to generate the C–N and C–C coupled product **185** (Scheme 34). In the case of amides reacting with di-and trimethoxybenzene, a complex reaction mixture was obtained, without the amide component being affected.[86c]



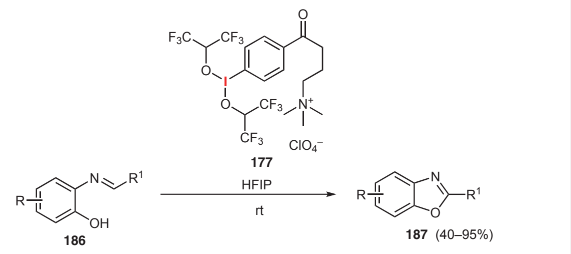
Scheme 33 Electrosynthesis of iodine(III) species **176** and **177**

Francke et al. reported the synthesis of benzoxazoles **187** starting from *ortho*-iminophenols **186** using electrochemically generated dialkoxyiodane **177** and HFIP as the solvent (Scheme 35). This protocol is compatible with various redox-sensitive functional groups, such as alkenes, bromine, and carboxylic acids.[86d]

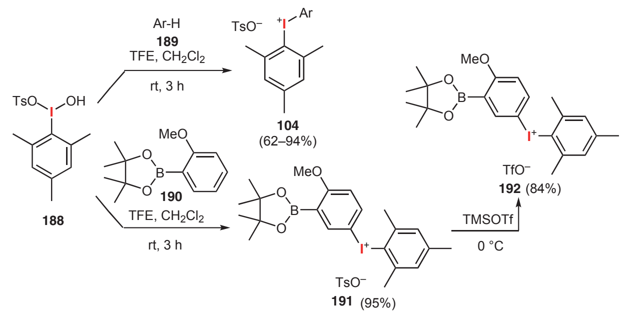
Recyclable syntheses of mesityl iodonium salts **104** and **105** have been achieved using a dehydrative condensation approach. Treatment of electron-rich aromatic compounds **189**, bearing alkyl and alkoxy substituents, with [hy-



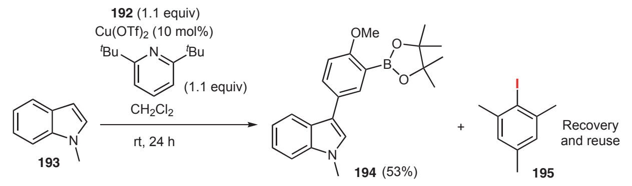
Scheme 34 Various C–N coupling reactions using electrochemically generated I(III) reagent **177**



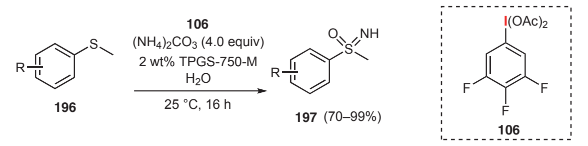
Scheme 35 Synthesis of benzoxazoles **187** using pre-generated **177**



Scheme 36 Recyclable synthesis of mesityl iodonium salts **104**, **191** and **192** using a dehydrative condensation approach



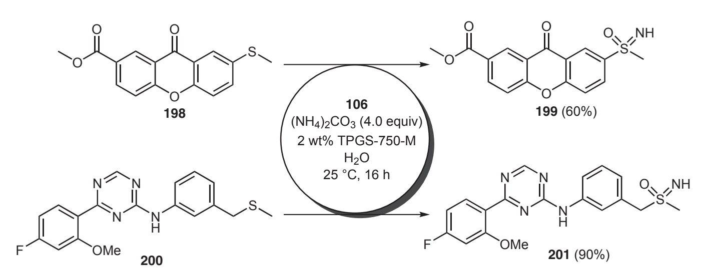
Scheme 37 The C–H arylation of *N*-methylindoles **193** using boron-functionalized mesityl iodonium salt **192**



Scheme 38 Synthesis of sulfoximines **197** using **106**

droxy(tosyloxy)iodo]mesitylene (**188**) in 2,2,2-trifluoroethanol (TFE) afforded *para*-substituted iodonium salts **104** with high selectivity in 62–94% yield (Scheme 36). In addition, the synthesis of boron-functionalized iodonium salts **191** and **192** in yields of 95% and 84%, respectively, has also been reported. Diaryliodonium salt **192** was found to be useful for the C–H arylation of *N*-substituted indoles **193** without releasing the boron functional moiety (Scheme 37). Recovered mesityl iodide **195** can be reused to regenerate mesityl iodonium salts via recyclable synthesis involving dehydrative condensation.[88]

In 2020, Xu et al. synthesized NH-sulfoximines **197** using various HVI(III) reagents and observed that diacetoxyiodo-3,4,5-trifluorobenzene **106** showed the best reactivity under mild conditions (Scheme 38). Treatment of xanthone derivative **198** with **106** using ammonium carbonate (as the nitrogen source) and the surfactant TPGS-750M (as the catalyst) resulted in xanthone sulfoximines **199** in 60% yield. The same group also synthesized BAY-1143572 (a PTEFb-inhibitor) (**201**) from **200** in racemic form and 90% yield using similar reaction conditions (Scheme 39). Reagent **106** can be regenerated by treating the recovered reduced form with sodium perborate tetrahydrate and trifluoromethane sulfonic acid.[89]



Scheme 39 Synthesis of xanthone sulfoximines **199** and BAY-1143752 (**201**) using diacetoxyiodo-3,4,5-trifluorobenzene **106**

3.2 Recyclable Non-Polymeric Hypervalent Iodine(V) Reagents

IBX and Dess–Martin periodinane (DMP) are examples of commonly used stoichiometric non-polymeric hypervalent iodine(V) reagents, although the recovery of these reagents from their reaction mixtures is low yielding. To overcome this limitation, various recyclable HVI(V) reagents have been reported in the literature.[90–99] The structures of these reagents are shown in Figure 10.

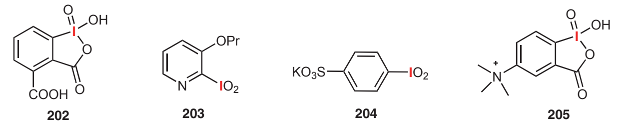
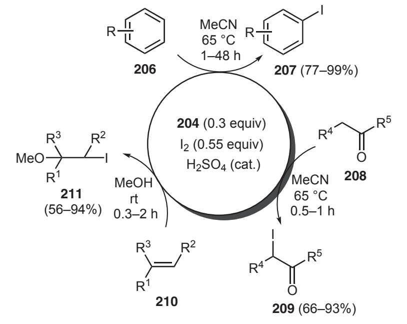


Figure 10 Structures of non-polymeric recyclable HVI(V) reagents **202**–**205**

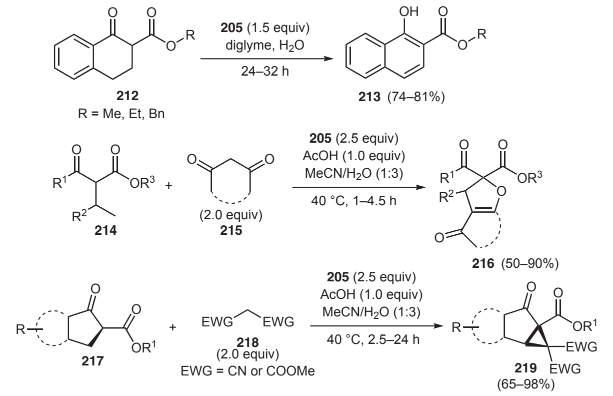
In 2002, Thottumkara reported modified 2-iodoxybenzoic acid (*m*IBX) (**202**) as an efficient reagent for the oxidation of allylic and benzylic alcohols in water, affording the corresponding aldehydes in 60–96% yield. The reduced form of **202** is insoluble in water and can be separated by simple filtration. The recovered product can be re-oxidized to *m*IBX, resulting in an eco-friendly and cost-effective synthetic protocol.[90] Zhdankin et al. reported the synthesis of 3-propoxy-2-iodylpyridine **203** via the oxidation of 2-iodylpyridine with 3,3-dimethyldioxirane. Reagent **203** displays good solubility in organic solvents because of the interaction between the nitrogen and the solvent molecules. The reduced form of **203** can be readily separated from the reaction mixture by treatment with sulfuric acid and recovered in 95–99% yield by neutralization with sodium hydroxide.[93]

Zhdankin et al. also reported the synthesis of the recyclable and water-soluble I(V) reagent potassium 4-iodylbenzenesulfonate (PIBS) (**204**) via the oxidation of 4-iodobenzenesulfonic acid using Oxone® in water.[94] This water-soluble reagent can be used for the oxidative iodination of arenes,[94] alkenes,[95] alkynes,[95] and ketones[95] (Scheme 40). Unreacted PIBS (**204**) and its reduced form PIBS-H can be recovered from the reaction mixture.[94,95]

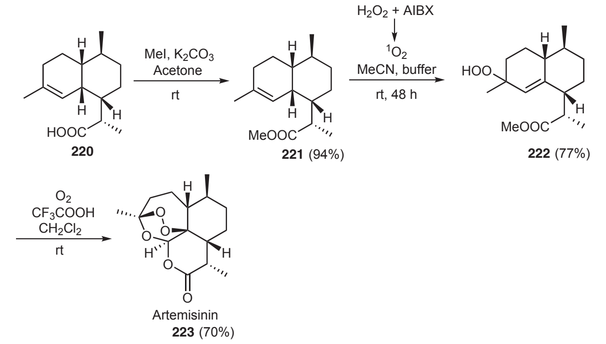
In an example reported by Sharma and co-workers, the HVI(V) reagent IBX and choline chloride/urea solvent were recycled in a three-component Ugi reaction. The reduced form of IBX can be recovered from the reaction mixture by filtration and converted back into IBX by treatment with aqueous Oxone®. The catalytic efficiency of IBX decreased after three cycles.[96]



Scheme 40 PIBS (**204**)-mediated iodination of arenes **206**, aromatic ketones **208** and iodomethoxylation of alkenes **210**



Scheme 41 AIBX (**205**)-promoted reactions of various β-keto esters



Scheme 42 Synthesis of the antimalarial drug artemisinin (**223**) using the AIBX/H_2O_2 system

Zhang et al. synthesized a water-soluble I(V) reagent, 5-trimethylammonio-1,3-dioxo-1,3-dihydro-$1\lambda^5$-benziodoxole anion (AIBX) (**205**). AIBX is a useful reagent for the aromatization of **212**,[97] the oxidative addition of β-keto esters **214** and **215**,[98] and the dehydrogenative cyclopropanation of **217**,[99] enabling access to the corresponding products **213**, **216**, and **219** (Scheme 41). AIBX, which is soluble in water, can be regenerated after extraction of the organic component with ethyl acetate followed by evaporation of the aqueous layer to produce the reduced form of **205**, which can be oxidized using dimethyl dioxirane.[99]

Recently, Zhang et al. developed an efficient method for the generation of singlet oxygen by treating water-soluble AIBX (**205**) with hydrogen peroxide. This system can be used to perform various reactions, such as Schenck-ene, cycloaddition, and heteroatom oxidation. This strategy was also applied to the synthesis of the antimalarial drug artemisinin. Esterification of dihydroartemisinic acid (**220**) followed by the Schenck-ene reaction afforded **222** in 77% yield. Treatment of **222** with O_2 in the presence of trifluoroacetic acid finally resulted in the formation of artemisinin (**223**) in 70% yield (Scheme 42).[100]

3.3 Fluorous Hypervalent Iodine Reagents

Fluorous HVI(III) reagents are useful oxidants and chlorinating agents. In general, fluorous hypervalent iodine compounds can be synthesized via the iodination of fluorous arenes using periodic acid and iodine in the presence of sulfuric acid, followed by oxidation. Fluorous hypervalent iodine reagents are useful for the oxidation of alcohols[101] and phenols,[102,103] as well as for the chlorination of alkenes.[104] The structures of fluorous HVI compounds **224**–**230** are shown in Figure 11.

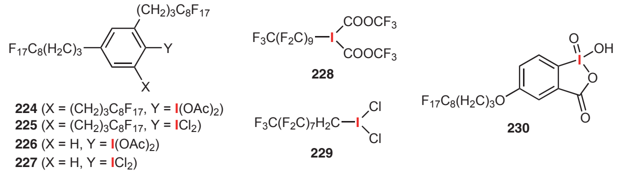
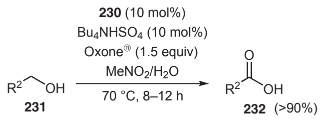


Figure 11 Structures of fluorous hypervalent reagents **224**–**230**

Miura and co-workers reported the fluorous IBX **230**-catalyzed oxidation of alcohols to the corresponding aldehydes or ketones. However, alcohols **231** resulted in the formation of carboxylic acids **232** in >90% yield (Scheme 43). Fluorous iodine reagents, except for **230**, can be recovered using a simple liquid–liquid biphasic protocol. Insoluble fluorous IBX **230** can be removed by simple filtration and can be recycled without a significant decrease in reactivity.[105]

4 Ionic-Liquid/Ion-Supported Hypervalent Iodine Reagents

Ion-supported HVI(III) reagents are widely used for the oxidation of alcohols and sulfides without over-oxidation. Various ionic-liquid or (ion-supported) HVI(III) reagents **233**–**244** have been reported in the literature, as shown in Figure 12.[106–119] In 2005, Handy and Okello reported the synthesis of **234**, a room-temperature ionic-liquid supported HVI(III) reagent (Koser's salt) for the tosyloxylation of ketones in good yields.[106]



Scheme 43 Conversion of alcohols **231** into carboxylic acids **232** using fluorous IBX reagent **230**

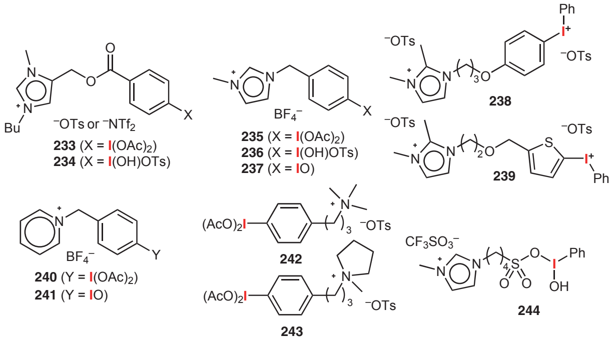


Figure 12 Structures of ionic-liquid and ion-supported hypervalent iodine reagents **233**–**244**

In 2011, Zhang et al. reported that alkaline hydrolysis of room temperature ionic liquid (RTIL)-supported hypervalent iodine reagents **235** and **240** afforded RTIL iodosylbenzenes **237** and **241**, respectively, at room temperature. Both these reagents are efficient oxidants, and no polymerization was observed with RTIL-supported iodosylbenzene.[114]

Zhdankin and co-workers reported bifunctional ionic-liquid-supported reagents **245** and **246** bearing iodoarene and TEMPO moieties as two active sites (Figure 13).[115] In the presence of peracetic (PAA) and HFIP, these reagents have been used for the oxidation of various alcohols **247** at room temperature to give the corresponding aldehydes or ketones **248** (Scheme 44). The presence of two catalytic sites facilitates alcohol oxidation because the reaction mode can be switched from intermolecular to intramolecular. Bifunctional ionic-liquid-supported reagent **246** showed superior reactivity and recyclability without significant loss in activity.[115]

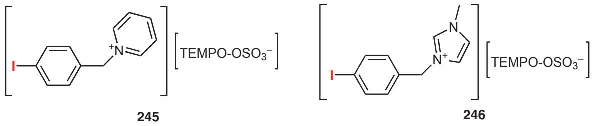
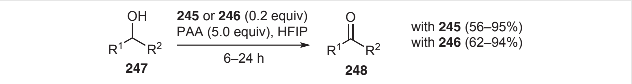
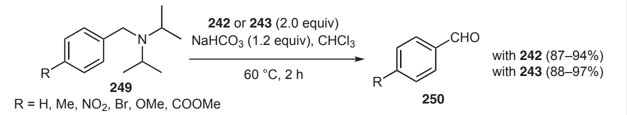


Figure 13 Structures of bifunctional ionic-liquid-supported iodoarenes **245** and **246**



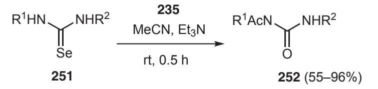
Scheme 44 Oxidation of alcohols using bifunctional ionic-liquid-supported iodoarene–TEMPO reagents **245** and **246**

Ion-supported (diacetoxyiodo)benzenes (DIBs) **242** and **243** are efficient reagents for the oxidation of various primary and secondary alcohols, the oxidation of *N*,*N*-diisopropyl arylamines, the oxidative 1,2-aryl migration of aryl ketones, and the synthesis of substituted oxazoles and methyl carbamates.[116] Treatment of *N*,*N*-diisopropyl arylamines **249** with ion-supported DIB reagents **242** and **243** in methanol under basic conditions afforded the respective aromatic aldehydes **250** in >87% yield (Scheme 45).[116]



Scheme 45 Oxidation of *N*,*N*-diisopropyl benzylamines **249** to aromatic aldehydes **250**

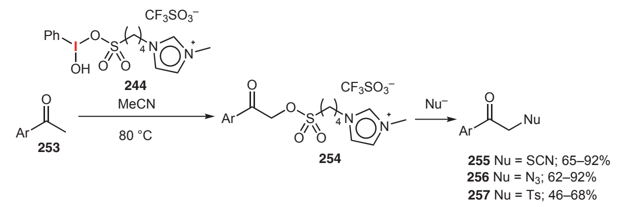
Xie and Pan reported the use of the ion-supported HVI(III) reagent $[\text{dibmim}]^+[\text{BF}_4]^-$ **235** as an *N*-acetylating agent for disubstituted selenoureas **251** under mild conditions to form *N*-acetylureas **252** in 55–96% yield (Scheme 46). In the case of unsymmetrical selenoureas, acetylation was regioselective, occurring at the amine with a lower pK_a value.[117]



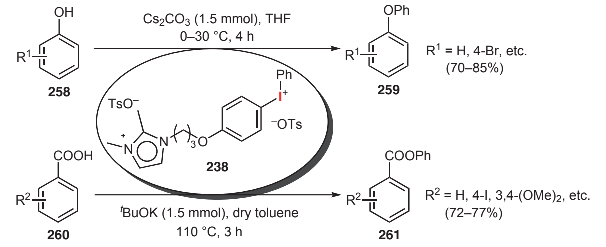
Scheme 46 *N*-Acetylation of selenoureas **251** using reagent **235**

Kumar and co-workers synthesized imidazole-based ionic-liquid-supported HVI reagent **244** and demonstrated its utility in the conversion of various substituted acetophenones **253** into α-substituted acetophenones **255**–**257** in good to excellent yields using three different nucleophiles, namely azide, thiocyanate, and *p*-toluenesulfonate ions (Scheme 47). This strategy avoids the use of chromatographic techniques for purification.[118]

Ionic-liquid-supported diaryliodonium salts **238** and **239** have been synthesized via the reaction of a HVI(III) reagent with ionic-liquid-supported arenes. Salt **238** was used for the metal-free *O*-phenylation of phenols **258** and carboxylic acids **260** to afford the corresponding ethers **259** and esters **261**, respectively (Scheme 48). Meanwhile, *O*-phenylation of phenols using **239** resulted in slightly lower yields (57–66%) of the desired products.[119]

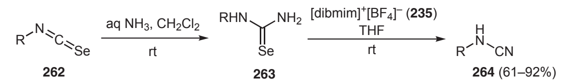


Scheme 47 Synthesis of α-substituted acetophenones **255**–**257** using **244**



Scheme 48 *O*-Phenylation of phenols **258** and carboxylic acids **260** using ionic-liquid-supported diaryliodonium salt **238**

Xie and co-workers synthesized cyanamides **264** from isoselenocyanates **262** using $[\text{dibmim}]^+[\text{BF}_4]^-$ **235** in 61–92% yield (Scheme 49). Selenium powder can be recovered from the reaction mixture by filtration, and the reduced form of reagent **235** can be recovered by concentrating the filtrate, followed by the addition of ethyl acetate and precipitation using petroleum ether. The recovered ionic-liquid-supported iodobenzene can be re-oxidized to **235** using peracetic acid.[120]

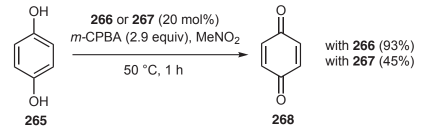


Scheme 49 Ion-supported **235**-mediated synthesis of cyanamides **264**

5 Metal–Organic-Framework (MOF)-Hybridized Hypervalent Iodine Reagents

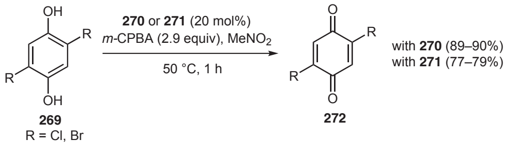
Various polymer-supported HVI compounds have been reported for the oxidation and coupling of diverse organic substrates and for the synthesis of heterocyclic compounds. However, the ambiguous geometry around the catalytic site limits systematic tuning as well as complete understanding of the active sites. To overcome these limitations, MOF-hybridized hypervalent iodine reagents have been prepared by treating appropriate metal salts with a suitable linker. Highly stable MOF multivariate MIL-53 (Al) and UiO-66 (Zr) supporting varying percentages of linker have been developed by Cozzolino and co-workers.[121] UiO-66 25%-I (**266**) is reportedly more efficient than MIL-53 25%-I (**267**) toward the oxidation of hydroquinone (**265**) (Scheme 50). Catalyst

266 can be readily recycled with high catalytic efficiency, whereas a sharp decrease occurs in the catalytic activity of **267** due to aggregation of catalyst particles during the reaction.[121]

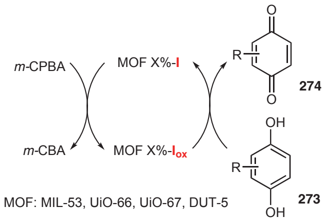


Scheme 50 Oxidation of hydroquinone (**265**) catalyzed by MOF-hybridized hypervalent iodine reagents **266** and **267**

Cozzolino prepared DUT-5 (Al) and UiO-67 (Zr) hybridized with iodine linkers as analogs of MIL-53 and UiO-66 via iso-reticular expansion and a multivariate approach. Both DUT-5 25%-I (**270**) and UiO-67 25%-I (**271**) exhibited superior reactivity toward the oxidation of dichloro- and dibromo-substituted hydroquinones **269** (Scheme 51) compared to their corresponding predecessors. These MOFs can be recycled without a significant decrease in efficiency. The general mechanism of the catalytic oxidation of hydroquinones **273** by heterogeneous iodine catalysts is shown in Scheme 52.[122]



Scheme 51 Oxidation of dichloro- and dibromo-substituted hydroquinones using MOF-hybridized hypervalent catalysts **270** and **271**



Scheme 52 General mechanism for the catalytic oxidation of various hydroquinones **273** by heterogeneous iodine catalysts in the presence of *m*-CPBA

Cardenal and co-workers investigated the coordination chemistry of iodosylbenzenes with transition-metal clusters, such as carboxylate-bridged Zn_2 complexes and Zr_6O_4 clusters, commonly encountered in MOFs. $(PhIO)_n$ participation was observed during ligand exchange with both clusters to form iodobenzene dicarboxylates; here, iodosylarene serves only as a ligand for Zr_6 clusters.[123] Recently, Richardson and Bryant reported the syntheses of iodine-supported IRMOF-9 (**275**) and UiO-67 (**276**) frameworks and their use in the oxidation of alcohols and sulfides (Figure 14).

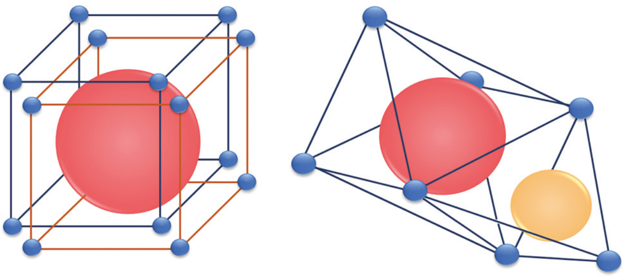
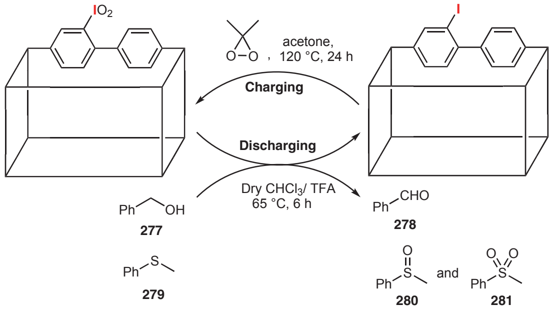


Figure 14 Schematic Structures of **275** (left) and **276** (right). The large red and yellow spheres are used to convey the pore space in the frameworks. Smaller blue spheres representing the metal nodes and the linking lines the linear bpdc-I bridging ligands

Treatment of benzyl alcohol (**277**) or thioanisole (**279**) with excess $Zr_6O_4(OH)_4(bpdc\text{-}IO_x)_6$ (**276**) in the presence of trifluoroacetic acid afforded the corresponding aldehyde **278** or sulfoxide **280**, respectively. In the case of sulfoxidation, sulfones **281** were also obtained, while no overoxidation was observed in the case of **277**. Iodine-based MOFs can be reused by the oxidation of their organic groups, facilitated by dimethyldioxirane (Scheme 53). Powder X-ray diffraction analysis confirmed that the crystallinity and porosity were maintained after post-synthetic oxidation.[124]



Scheme 53 Oxidation of benzyl alcohol (**277**) and thioanisole (**279**) with a MOF supported with HVI(V)

6 Conclusion

The literature summarized herein reflects a significant continuing interest in HVI chemistry, in particular, toward the development of recyclable hypervalent iodine reagents. This review summarizes the development of non-polymeric recyclable HVI reagents as well as polymeric-, MOF-, and ionic-liquid-supported iodine compounds. Recent discoveries of hypervalent recyclable reagents have led to remarkable achievements in the field of HVI chemistry. The development of diverse recyclable iodine compounds contributes to addressing significant synthetic challenges and provides a versatile tool for sustainable development.

Conflict of Interest

The authors declare no conflict of interest.

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