Progress in organocatalysis with hypervalent iodine catalysts

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Hypervalent iodine compounds as environmentally friendly and relatively inexpensive reagents have properties similar to transition metals. They are employed as alternatives to transition metal catalysts in organic synthesis as mild, nontoxic, selective and recyclable catalytic reagents. Formation of C–N, C–O, C–S, C–F and C–C bonds can be seamlessly accomplished by hypervalent iodine catalysed oxidative functionalisations. The aim of this review is to highlight recent developments in the utilisation of iodine(III) and iodine(V) catalysts in the synthesis of a wide range of organic compounds including chiral catalysts for stereoselective synthesis. Polymer-, magnetic nanoparticle- and metal organic framework-supported hypervalent iodine catalysts are also described.

1. Introduction

The major challenge of synthetic organic chemistry in the 21st century is the selective synthesis of target compounds in an efficient and economical way using mild reaction conditions. The most striking approach in environmentally benign organic synthesis.

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reactions is the development of catalytic strategies in the synthesis of organic molecules. Over the past few decades, hypervalent iodine reagents have emerged as efficient organocatalysts for the oxidative transformations of a wide range of organic substrates.\textsuperscript{1–5} These reagents are mild, non-toxic, moisture resistant, inexpensive and often recyclable. These properties make them ideal eco-friendly reagents to be employed for various organic transformations.\textsuperscript{6,7} Several reviews,\textsuperscript{6,8–22} book chapters\textsuperscript{23–27} and books\textsuperscript{28–31} have been published in the past years emphasising the progress and development of hypervalent iodine chemistry.

Prominent features of hypervalent iodine compounds are their oxidising properties and their electrophilic nature. They are commonly used as stoichiometric oxidants which makes them attractive candidates for the replacement of toxic heavy-metal oxidants.\textsuperscript{6} Moreover, hypervalent iodine reagents have been extensively used in the total synthesis of natural products and their intermediates.\textsuperscript{32} Representative examples of various hypervalent iodine reagents are shown in Fig. 1. For example, (diacetoxyiodo)benzene 1 and [bis(trifluoroacetoxy)iodo]benzene 2 are used as efficient oxidants in many organic transformations such as oxidation of alcohols, alkenes or organosulfides,\textsuperscript{33,34} rearrangements,\textsuperscript{35} cyclisations\textsuperscript{36,37} and transition metal-catalysed C–H bond functionalisations\textsuperscript{38,39} and alkene difunctionalisations.\textsuperscript{40,41}

(Dichloroiodo)benzene 3 is a chlorinating reagent\textsuperscript{7} while [hydroxy(tosyloxy)iodo]benzene 4 (Koser’s reagent) can be used for \(\alpha\)-oxytosylations of ketones.\textsuperscript{42–44} Owing to the electrophilic and excellent leaving nature of diaryliodonium salts 5, they are employed as versatile arylating agents in coupling reactions by reacting with suitable nucleophile.\textsuperscript{45} Cyclic hypervalent iodine(\textit{iii}) reagents such as 2-iodosobenzoic acid 6 (IBA) is synthesised by the oxidation of 2-iodobenzoic acid and less explored due to its poor reactivity.\textsuperscript{46} Trifluoromethyl benziodoxolone 7 was developed by Togni’s research group as

![Fig. 1 Examples of hypervalent iodine(\textit{ii})/(\textit{v}) reagents 1–14.](image-url)
trifluoromethylation reagent for the transfer of CF₃ moiety to the organic molecules. Zhdankin and coworkers reported the synthesis of 1-[[trisopropylsilyl]ethylnyl]-1-x,2-benziodoxol-3(1H) TIPS-EBX 8 as an efficient alkyne transfer reagent to various substrates. Later on Waser and coworkers published a review article in which they have compiled the application of other benziodoxole-based reagents.

Chiral hypervalent iodine reagents in stereoselective synthesis have made important developments in recent times. The first chiral reagent was prepared by Pribram in 1907 followed by many more optically active iodine(III)/(V) compounds which have been employed in asymmetric transformations. For example, Ishihara and his team reported compounds which have been employed in asymmetric aminations of 1-naphthol derivatives with high selectivities. Furthermore, pseudocyclic hypervalent iodine compounds is another interesting class containing additional non-covalent coordination at the iodine center. Iodine(v) reagents such as 2-iodoxybenzoic acid (IBX) 10a and FBX 10b, 2-iodoxybenzenesulfonic acid (IBS) 11 and Dess–Martin periodinane (DMP) 12 are routinely used as oxidising agents in a variety of oxidative transformations including oxidation of alcohol moieties and other functional groups.

Recently, Wirth and his team synthesised pseudocyclic iodine(III) reagents containing furan and thiophene units and proved their oxidising nature in various oxidative transformations. Very recently, Zhdankin and co-workers reported the synthesis of a powerful iodine(v) oxidant, 2-iodoxybenzoic acid bistriflate 14, by reacting IBX with trifluoromethanesulfonic acid and illustrated its potential application in the direct oxidation of hydrocarbons.

Hypervalent iodine reagents have properties resembling those of transition metals and can be employed as environmentally sustainable alternatives to transition metal catalysts such as mercury, lead and thallium reagents. Within this context, copious synthetic procedures have been developed using achiral or chiral iodine(III)/(V) pre-catalysts in the presence of stoichiometric oxidants such as CPBA, oxone, peracetic acid and molecular O₂, etc. which play a significant role in the in situ generation of active catalytic species such as hypohalite, trivalent, or pentavalent hypervalent iodine species. The utility of hypervalent iodine reagents as catalyst in the presence of peracetic acid was developed by Antonchick and co-workers.

2. Aminations

Amines have widespread uses in many facets of our lives and are present not only in natural products, but also play a vital role in medicinal chemistry. Metal-free approaches for the synthesis of amines through C–H aminations using hypervalent iodine reagents as catalysts were initially developed by the research groups of Chang, DeBoef and Antonchick.

2.1. C–H amination of arenes

2.1.1. Intermolecular C–H amination of arenes. C–H Aminations of arenes is a common reaction catalysed by an active hypervalent iodine catalytic species under mild reaction conditions. A novel metal-free route for the amination of simple electron-rich arenes 16 with 3-aminopyridine derivatives 15 using iodobenzene 17 as catalyst in the presence of peracetic acid as oxidant was developed by Antonchick and co-workers (Scheme 1). The desired arylated 3-aminopyridines 18 were formed in good yields. Notably, the amination of electron-deficient arenes was not observed.

Later, Muñiz and coworkers employed 1,2-diiodobenzene 20 as the precatalyst for an intermolecular C–H amination of substituted arenes 16 using N-disubstituted amines 19 as nitrogen sources and peracetic acid as oxidant (Scheme 2).
The reaction performed remarkably well even at reduced catalyst loadings of 3–4 mol%. The interesting feature of this catalytic approach is the successful amination of electron-deficient arenes. However, the amination products of electron-deficient arenes 16 were obtained in poor yields compared to other arenes. Mechanistic studies revealed the formation of μ-oxo-bridged bisiodine(III) derivative 22 upon oxidation of 1,2-diiodobenzene with peracetic acid.

The concept of soft-hard acid–base (SHAB) theory was introduced in the N–H arylation of sulfanilides 23 by Mal and Maiti. The catalytic system comprises of iodobenzene 17 as the pre-catalyst and mCPBA as oxidant (Scheme 3). Sulfanilides with electron donating and sulfonyl groups like –SO₂Ph, –Ts were tolerated and amination products 24 were isolated in moderate to excellent yields.

The proposed catalytic cycle for the N-arylation of 23 with 16 is shown in Scheme 4. Nitrenium ion 25 is a soft electrophile and generated from the interaction between sulfanilide 23 and iodine(III) species [A]. The newly generated nitrenium ion 25 interacts with electron rich arenes and undergoes an electrophilic aromatic substitution to furnish aminated amines 24 via generating carbocation intermediate 26. The regenerated iodobenzene 17 is further oxidised to the iodine(III) compound [A] re-entering the catalytic cycle.

### 2.1.2. Intramolecular C–H Amination of Arenes

Tanimori’s research group reported an iodine(III)-catalysed intramolecular oxidative C–H amination of aryl hydrazones 27 to provide N-aryl substituted 1H-indazoles 28 with iodobenzene 17 as pre-catalyst in the presence of Oxone® and TFA (Scheme 5). Aryl hydrazones 27 with electron withdrawing as well electron donating groups afforded the desired products 28 in moderate to good yields. However, hydrazones with terminal nitrogen atom without substituents or with substituents that destabilize the nitrenium ion intermediate were not tolerated. They also successfully demonstrated a one pot process for the synthesis of indazoles without isolating the intermediate hydrazone 27 using benzophenone and phenyl hydazine as precursors in the presence of acid catalyst under the optimal conditions.

In 2022, Kita and co-workers designed an efficient method to synthesize benzolactams 32 via an intramolecular C–H amination of aryl amides 29 using biaryl-based iodoarene precatalyst 30. The reaction involves the in situ generation of μ-oxo hypervalent iodine compound 31 through the oxidation of iodoarene 30 using mCPBA as oxidant (Scheme 6). When 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) was used as solvent, the desired benzolactams 32 were obtained in higher yields. Addition of CF₃COOH (2.0 eq.) significantly boosted the production of 32. Notably, other pre-catalysts such as iodobenzene, 4-iodotoluene and 4-iodoanisole were found unsuitable to catalyse this oxidative C–H amination reaction. Aryl amides 29 substituted with nitro, trifluoromethyl or ester functionalities were tolerant to the catalytic conditions. Moreover, the synthesis of five-, seven- and eight-membered benzolactams was achieved successfully in excellent to good yields using this protocol.

An interesting intramolecular C–H amination of aryl substituted amides 33 to functionalized lactams 35 was developed.

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**Scheme 3** Iodine(III)-catalysed N-arylation of 23 with 16 using iodobenzene 17 as pre-catalyst.

**Scheme 4** Catalytic cycle for the iodine(III)-catalysed N-arylation of 23 with 16 to 24 using iodobenzene 17 as pre-catalyst.

**Scheme 5** Iodine(III)-catalysed intramolecular oxidative C–H amination of aryl hydrazones 27 to 28.

**Scheme 6** Hypervalent iodine-catalysed C–H amination of aryl amides 29 for the synthesis of benzolactams 32.
by involving chiral diiodospirobiindane precatalyst 34 in the presence of mCPBA by Cai and co-workers (Scheme 7). The key feature of the reaction was the amination of amides along with desymmetrisation. Amides with cyclopentoxy substituents on the nitrogen gave the desired lactams 35 with better enantioselectivities than with other alkoxy substituents. The substrate scope was further corroborated with other functional groups R² on the aryl moiety.

2.2. Amination of alkenes

2.2.1. Intermolecular amination of alkenes. The amination of alkenes is a useful reaction providing easy access to different aliphatic amines. In 2022, a methodology of group-assisted purification (GAP) was adopted by Ali and co-workers for the regioselective and stereoselective synthesis of vicinal chloroamines 39 from electron-deficient cinnamates and cinnamamides 36 tethered with benzyldiphenylphosphine oxide (Bndpp) group as the GAP candidate (Scheme 8). The reaction was carried out by refluxing GAP anchored substrates 36 in the presence of 4 Å molecular sieves, PhI(OAc)₂ as catalyst, 4-TsNH₂ and 4-TsNCl₂ as the nitrogen and chlorine source, respectively, in dichloromethane under argon atmosphere. This protocol tolerated an array of functional groups providing products 39 in good yields. The benefits of this method are the simple and cost-effective purification technique which requires only a wash of the crude mixture with inexpensive solvents such as petroleum ether, as well as the recyclability and reusability of GAP auxiliary.

Vicinal diamines are a significant class of compounds in the biopharmaceutical field. Enantioselective diaminations of alkenes is typically performed with palladium, copper and titanium catalysts, and lately Muñiz and colleagues have established an inexpensive route for the intermolecular diamination of styrenes 40 with bissulfonimides 41 as nitrogen source utilizing achiral as well as chiral aryl iodides as catalysts (Scheme 9). They described the first iodine(III)-catalysed enantioselective intermolecular diamination of styrenes 40 using chiral aryl iodide 42 as catalyst. anti-Diamines 44 were obtained in moderate to good yields with high enantiomeric excess from both terminal as well as substituted styrenes. Using achiral aryl iodides 43a or 43b, irrespective of the position of substituents, styrenes 40 with various electron donating and electron withdrawing groups afforded diamine products 45 in good yields. In addition to styrenes, diamination of (E)-stilbene proceeded to afford diamines in moderate yield while allylbenzene produced the corresponding diamine in excellent yield.

Later, the same group developed a scale-up protocol for the synthesis of aryl iodine pre-catalysts 47 and successfully applied it to the diamination of functionalised terminal styrenes 46 using HNMs₂ 48 as nucleophile and mCPBA as oxidant (Scheme 10). Amination products 49 were obtained in moderate to good yields with high enantiomeric excess (up to 99% ee).

2.2.2. Intramolecular amination of alkenes. Wirth and co-workers employed a novel pyridine-based chiral iodine(I) catalyst 51 in the enantioselective intramolecular diamination of homoallylic guanidine and diaminosulfone derivatives 50 to bicyclic products 52 in the presence of sodium perborate and

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Scheme 7 Intramolecular C–H amination of aryl substituted amides 33 followed by desymmetrisation using 34 as chiral pre-catalyst.

Scheme 8 Iodine(III)-catalysed stereoselective amino chlorination of GAP anchored cinnamates and cinnamamides 36.

Scheme 9 Iodine(III)-catalysed vicinal diamination of styrenes 40 to 44 and 45 using pre-catalysts 42 and 43, respectively.

Scheme 10 Iodine(III)-catalysed vicinal diamination of terminal styrenes 46 using C₂-symmetric chiral iodoarene 47 as pre-catalyst and HNMs₂ 48 as nitrogen source.
acetic acid in acetonitrile (Scheme 11).\(^{82}\) Lactate-based catalysts of type 9 were found to be inefficient in this reactions. The protecting group in 52 could be removed to provide free diamines through reduction using lithium aluminium hydride.

### 2.3. Oxyamination of alkenes

#### 2.3.1. Intermolecular oxyamination of alkenes

During the last years, attention has been focused on the development of oxyamination reactions using hypervalent iodine catalysis. Wata and Hashimoto developed a protocol for an enantioselective oxyamination of aryl- or alkyl-substituted alkenes 40 using organoiodine(\(\text{II/III}\)) catalysis.\(^{83}\) The use of N-(fluorosulfonyl)carbamate 53 as bifunctional \(N,O\)-nucleophile was considered as a critical element in this reaction. Chiral organoiodine catalyst 54 was found indispensable to achieve good turnover and high enantioselectivity. Notably, the use of magnesium monoperoxyphthalate hexahydrate (MMPP) as oxidant gave high product yields for electronically neutral or slightly electron-poor vinylarenes whereas Selectfluor was found optimal for electron-deficient or \(o\)-halogenated vinylarenes. The reaction proceeds via formation of intermediates 56-58 (Scheme 12). Carbamate 53 reacts with \(in\ situ\) generated hypervalent iodine to form intermediate 56, which converts into intermediate 58 via formation of an alkene-coordinated iodonium intermediate 57. Finally, the intermediate 58 cyclises intramolecularly to yield product 55 by the nucleophilic attack of oxygen and regenerates the chiral iodoarene 54.

#### 2.3.2. Intramolecular oxyamination of alkenes

In 2021, Deng et al. reported an iodine(\(\text{III}\))-catalysed intramolecular oxyamination of alkenes 63 containing an amide functionality using Ts\(_2\)NH 41 as an external nitrogen source. Optimisation results showed that 2,6-dimethoxy iodobenzene 64 provided the best catalytic activity in the presence of mCPBA as an oxidant (Scheme 15).\(^{85}\) A variety of \(N\)-aryl, \(N\)-benzyl and \(N\)-methoxyl substituted pentenamides smoothly underwent this transformation, affording desired oxyamination products 65 in good yields and with high regioselectivity. Additionally, substrates with cycloalkyl rings provided spiro-tetrahydrofuranyl methanamine products in high yields.

An intramolecular oxyamination of \(\gamma,\delta\)- and \(\delta,\epsilon\)-unsaturated esters 66 and \(N\)-allyl amides 70 was developed with benzyl \(N\)-(fluorosulfonyl)carbamate 67 as an exogenous nitrogen source using hypervalent iodine catalysis (Scheme 16).\(^{86}\) Selectfluor...
was found as the best oxidant for these aminations. Various functional groups were tolerated under the given reaction conditions and the corresponding lactones and oxazolines in good yields with up to 77% enantiomeric excess. Moreover, the protecting group of the aminated products was removed to make free amino compounds under acidic conditions without losing any selectivity.

2.4. C–H amination at sp^3 carbon

Shi and co-workers developed an intramolecular sp^3 C–H amination of ortho-substituted N-methoxy benzamides 72 for the synthesis of γ-lactams 74 catalysed by an iodine(III) species generated in situ by using catalytic amounts of iodoarene 73. Among the various iodoarenes investigated, 2-iodobiphenyl 73 emerged as a good pre-catalyst. The reaction proceeded smoothly with electron-neutral and electron-deficient substrates, while electron-rich substrates gave poor yield. The amination reaction worked well for cyclic as well as acyclic tertiary C–H bonds and due to the high energy barrier, a direct amination of secondary C–H bonds was not observed. Notably, the amination at chiral centres worked smoothly and it was found to be stereospecific.

The mechanism for the amination of ortho-substituted N-methoxy benzamides 72 to γ-lactams 74 is given in Scheme 18. The mechanism was proposed based on the DFT calculations for the reaction of benzamides 72a with PIDA. Reaction is initiated with the formation of an iodonium intermediate 75 which converts into the protonated lactam 76 via the transition state TS 76 involving a hydride shift, followed by C–N bond formation. Finally, the protonated lactam 76 undergoes deprotonation to give amination product 74a.

2.5. Imination of benzylic C–H

In 2019, Mal and co-workers reported an intramolecular oxidative C–N bond formation via C–H imination reaction at sp^3 carbon centre. During these imination reactions, the synthesis of 1,2-disubstituted benzimidazoles 78 was achieved from dibenzyl amines 77 using two different catalytic systems, one with the conventional iodobenzene 17 as precatalyst (Scheme 19, Method A) and the second with tetrabutylammonium iodide as precatalyst (Scheme 19, Method B). The amination reaction proceeded through hydrogen elimination, two hydrogens from the highly acidic benzylic C(sp^3) and the remaining two from the aryl-N(sp^3). Symmetrical dibenzyl amines afforded a single isomer of benzimidazoles but unsymmetrical dibenzyl amines produced a mixture of isomers as major product being the imination at benzylic centre substituted with electron rich arenes.

3. Oxidation reactions

3.1. Oxidation of alcohols

3.1.1. Oxidation of primary and secondary alcohols. Oxidation of alcohols is traditionally an indispensable reaction of
organic synthesis as it provides synthetically valuable carbonyl compounds. Hypervalent iodine catalysis was employed for the oxidation of alcohols for the first time in 2005.90 Since that first report, various iodine(III) and iodine(V) catalysts have been developed for the oxidation of alcohols.3 An eco-friendly protocol for the oxidation of primary and secondary alcohols was developed at room temperature by using 2-iodo-N-isopropyl-5-methoxybenzamide 80 as a catalyst with Oxone86 and Bu4NHSO4.91 Secondary benzylic and aliphatic alcohols 81 afforded the corresponding ketones 82 in good to excellent yields and primary alcohols 83 were converted to the corresponding carboxylic acids 84 in moderate to excellent yields (Scheme 20). During the oxidation of primary alcohols, the corresponding aldehydes were not observed probably due to the presence of water in the reaction.

In another report, an iodine(V)-catalysed aerobic oxidation of secondary alcohols 81 to the corresponding ketones 82 was achieved in good to excellent yields catalysed by 2-tert-butylsulfonyl-iodobenzene 85 in the presence of n-butyraldehyde 86 and CoCl2·6H2O (Scheme 21).92 The role of CoCl2·6H2O was to initiate the aldehyde-promoted aerobic oxidation of precatalyst 85 to generate the iodine(V) species in situ. In case of aromatic secondary alcohols, both electron rich and electron deficient derivatives were tolerated. The oxidation of primary alcohols 83 gave the carboxylic acids 84.

The proposed catalytic cycle for the above oxidation process is shown in Scheme 22. Initially, the aldehyde-promoted aerobic oxidation of precatalyst 85 occurred to form iodosylbenzene 87 followed by disproportionation to generate iodylbenzene 88. Iodine(V) intermediate 88 then oxidises the alcohol 81 to ketone 82 and regenerates 87, which on disproportionation forms the active catalytic iodine(V) species 88.91 Polymer-supported hypervalent iodine pre-catalysts 89 and 90 were synthesised by Kirsch and Ballaschk and revealed their potential application in the oxidation of secondary alcohols 81 to corresponding ketones 82 (Scheme 23).93 The primacy of this
green synthesis is the multiple reusability of the catalyst without losing much catalytic activity and easy work-up. A wide range of secondary alcohols including cyclic, bicyclic and benzylic alcohols were tolerated. Phenols and amines are vulnerable to these catalytic conditions. Furthermore, the catalytic oxidation with IBS-derived catalyst proceeds faster and cleaner compared to IBX-derived catalyst.

In 2020, Enderlin and co-workers demonstrated a simple and extremely efficient iodine(V)-catalysed gram scale synthesis of 2,5-diformylfuran using sodium 2-iodobenzenesulfonate as precatalyst, Oxone as oxidant and nitromethane as solvent. A notable feature of this process is its simple work-up procedure involving only filtrations and extractions to obtain in high purity (Scheme 24).

Nemati and co-workers designed and developed a hypervalent iodine(m) based heterogeneous nano-catalyst using magnetic polyiodoaniline nano-composite, Fe₃O₄-PANI-I(OAc)₂ for the selective oxidation of functionalised benzyl alcohols to corresponding aldehydes in the presence of TEMPO as oxidant and acetonitrile as solvent. A wide range of electron-withdrawing and donating groups were tolerated to give the corresponding benzaldehydes in desirable yields without the formation of any by-product. The key feature of this nano-composite precatalyst is its stability and reusability for five consecutive cycles.

3.1.2. Oxidation of allylic alcohols. Rao and co-workers described the catalytic use of 2-iodoxybenzoic acid (IBX) generated in situ by the oxidation of 2-iodosobenzoic acid (IBA) using Oxone as an oxidant. During these oxidations, allylic alcohols are oxidised to the corresponding ketones. Various electron-withdrawing and donating groups were tolerated to give the corresponding benzaldehydes in desirable yields without the formation of any by-product. The key feature of this nano-composite precatalyst is its stability and reusability for five consecutive cycles.

3.1.3. Oxidation of 1,2-diols. Hypervalent iodine catalysis in the presence of molecular oxygen was used for glycol scission of 1,2 diols by Uchiyama and coworkers. By optimizing the reaction conditions, isobutyraldehyde, pentamethyldiobenzene and acetonitrile emerged as the best O₂ mediator, catalyst and solvent, for the cleavage of diols. Mono- and di-substituted diols (R₁ = H; R₂ = aryl, alkyl) and various dihydrobenzoins were smoothly cleaved to give the corresponding carboxylic acids. Notably, tri- and tetra-substituted diols (R₁, R₂ = aryl, alkyl) afforded desired ketones even in air or in the dark (Scheme 27). The efficiency of the reaction can be enhanced by premixing the aldehyde and O₂ before the addition of the substrate.

3.2. Oxidation of phenols

The oxidation of phenolic compounds is usually known as the de aromatisation of phenols. The oxidative de aromatisation of phenols is one of the common reaction of hypervalent iodine(m) reagents. Both internal and external nucleophiles have been employed during these oxidation reactions which the precatalyst can be recovered by simple filtration and there was no side product observed during these oxidations.

Scheme 24 Iodine(v)-catalysed selective oxidation of HMF to using 92 as precatalyst.

Scheme 25 Iodine(vi)-catalysed selective oxidation of benzylalcohols to aldehydes in the presence of Fe₃O₄-PANI-I(OAc)₂ nano-composite.

Scheme 26 Iodine(vi)-catalysed oxidation of terminal allylic alcohols and internal allylic alcohols to corresponding carbonyl compounds and , respectively.

Scheme 27 Iodine(III)-catalysed oxidation of 1,2-diols using penta-methyl iodobenzene as precatalyst in the presence of molecular O₂ as oxidant.
lead to dearmourised products such as highly functionalised quinolines, quinols and spiranlanes.\textsuperscript{21,30,98}

A general reaction pathway for the hypervalent iodine mediated oxidation of phenols is shown in Scheme 28. The phenolic compound 105 reacts with the hypervalent iodine(III) compound 1 or 2 through a ligand exchange and forms intermediate 106, which then undergoes a nucleophilic attack by an external nucleophile and forms either ortho-cyclohexadiene 107 or para-cyclohexadiene 108 via a dearmourisation process. In case of phenols 105 having an internal nucleophile, dearmourisation to ortho-spirocycles 109 and para-spirocycles 110 are taking place.

3.2.1. Intermolecular dearmourisation of phenols. In recent years, the iodine[III]-catalysed dearmourisation of phenols has received a particular attention by various hypervalent iodine chemists around the world.\textsuperscript{3,21} Dearmourisations of phenols have been developed using hypervalent iodine catalysis in past two decades.\textsuperscript{3} An eco-friendly protocol was reported by Yakura and co-workers for the oxidation of 4-alkoxyphenols 111 to p-benzoquinones 113 in good yields using magnetic nanoparticle-supported iodoarene catalyst 112 in the presence of Oxone\textsuperscript{K} (Scheme 29).\textsuperscript{99,100} The catalyst consists of phosphonate groups connecting a magnetic \( \text{Fe}_3\text{O}_4 \) nanocatalyst. After the completion of reaction, the catalyst can be easily separated by applying an external magnetic field and reused several times.

Muniz and Fra described an enantioselective hydroxylative dearmourisation of 4-substituted phenols 105 using the lactic amide motif-based chiral aryliodide catalyst 114 in the presence of \( m \)CPBA as an oxidant (Scheme 30).\textsuperscript{101} Two different solvent mixtures (A and B) were used during these dearmourisation reactions. The dearmourised products 115 were obtained in almost similar yields in both reaction conditions. However, the chiral catalyst could not transfer the chirality successfully and products were obtained in only up to 5% enantiomeric excess.

Hypervalent iodine(V)-mediated hydroxylative dearmourisation of 2-substituted phenols 105 to their cyclodimers 117 via [4+2] cycloaddition was developed by Ishihara and co-workers.\textsuperscript{102} The catalytic system comprises of precatalyst 116a or 116b which generates the catalytic species 2-iodoxenesulfonyl acid \textit{in situ} in the presence of Oxone\textsuperscript{K} as oxidant (Scheme 31). Inclusion of a trialkylsilylmethyl substituent at the ortho-position of phenols facilitates the reaction and use of buffered Oxone\textsuperscript{K} suppresses silanol elimination. The reaction was performed with various (2-(silylmethyl)phenols) 105 (R\textsuperscript{2} = CH\textsubscript{3}SiMe\textsubscript{3}) requiring the addition of K\textsubscript{2}CO\textsubscript{3} (0.375 eq.). Under similar catalytic conditions, oxidation of \( o \)-substituted 1- or 2-naphthols 118 provided ortho naphthoquinols 119 in excellent yields (Scheme 31). The same catalytic approach was employed for the synthesis of the natural products biscarvacrol and lacinilene C methyl ether in high yields.

Over the past few years, metal–organic frameworks (MOFs) have emerged as a support to catalyse organic reactions by offering high reactant selectivity and reusability. Various multivariate Al and Zr-MOF supported iodine catalysts 120 and 121, that can be recovered and recycled several times, were developed by Cozzolino and co-workers for the oxidation of hydroquinones 111 to \( p \)-quinones 113 in the presence of \( m \)CPBA and MeNO\textsubscript{2} (Scheme 32).\textsuperscript{103} These catalysts were prepared by treating the appropriate amount of linkers with zirconium(IV)chloride or aluminiumchloride and catalysts with 25% linkers were found to be ideally suited to achieve the
optimal balance between catalyst loading and catalyst accessibility. 2-Iodoterephthalic acid was used as iodine linker in UiO-66 25%-I \(^{120}\) and MIL-53 25%-I \(^{121}\). The same group prepared two novel expanded-pore iodine-functionalized UiO-67 (Zr) \(^{122}\) and DUT-5 (Al) \(^{123}\) catalysts and employed them in the oxidation of hydroquinones \(^{111}\) to \(p\)-quinones \(^{113}\) and catechol derivatives \(^{114}\) to \(o\)-quinones \(^{125}\), respectively using Al and Zr-MOF supported iodine catalysts \(^{120–123}\).

Hashimoto and co-workers introduced a coherent procedure for the asymmetric catalysis of \(para\)-hydrative intermolecular deariomatisation of functionalised phenols \(^{105}\) and naphthols \(^{118}\).

An environmentally friendly hypervalent iodine-catalysed oxidation of alkoxyarenes \(^{127a,b}\) to \(p\)-quinones \(^{129}\) was developed using 2-iodobenzoic acid \(^{128}\) as precatalyst and Oxone\(^{\text{R}}\) as oxidant in acetonitrile–water (Scheme 34).\(^{106}\) This approach provides \(p\)-quinones \(^{129}\) in excellent yields in a short reaction time at room temperature. Usually, these oxidation reactions suffer from the formation of \(o\)-quinones as side products, but this reaction provides \(p\)-quinones exclusively. Earlier studies\(^{107}\) using Oxone\(^{\text{R}}\)-generated hypervalent iodine oxidants for the deariomatisation of phenols have indicated a preference for \(p\)-quinones \(^{129}\) formation over \(o\)-quinones \(^{130}\), which made Oxone\(^{\text{R}}\) as the oxidant of choice in this procedure (Scheme 34). Notably, the \(in\ situ\) generated cyclic iodine(\(m\)) compound IBA \(^{6}\) was acting as catalytic species.

3.2.2. \textbf{Intramolecular deariomatisation of phenols.} Intramolecular deariomatisation of phenols using hypervalent iodine reagents provides various biologically active cyclic and spirocyclic scaffolds.\(^{18}\) Several hypervalent iodine-catalysed approaches are now available for the intramolecular deariomatisation of phenols.\(^{3,21}\)

The first hypervalent iodine-catalysed intramolecular deariomatisation of phenols was investigated in 2005 by Kita and co-workers.\(^{108}\) Kita and few other research groups employed hypervalent iodine catalysis to construct different spirocyclic scaffolds \(via\) intramolecular deariomatisation of phenols and naphthols.\(^{109–116}\) All these reports are covered in our previous review on hypervalent iodine catalysis published in 2014.\(^{3}\)

Ishihara and co-workers developed the spiro lactonisation of phenols \(^{131}\) with a propionic acid functionality in the \(ortho\)-position to enantiomerically rich \(ortho\)-dioxolanones \(^{133}\) using \(p\)-iodoarene \(^{132}\) as the oxidant of choice in this procedure (Scheme 34). Notably, the \(in\ situ\) generated cyclic iodine(\(m\)) compound IBA \(^{6}\) was acting as catalytic species.

![Scheme 31](https://example.com/scheme31.png)

**Scheme 31** Iodine(\(v\))-catalysed deariomatisation of functionalised phenols \(^{105}\) and naphthols \(^{118}\).

![Scheme 32](https://example.com/scheme32.png)

**Scheme 32** Iodine(\(v\))-catalysed oxidation of hydroquinones \(^{111}\) and catechols \(^{124}\) to \(p\)-quinones \(^{113}\) and \(o\)-quinones \(^{125}\), respectively using Al and Zr-MOF supported iodine catalysts \(^{120–123}\).

![Scheme 33](https://example.com/scheme33.png)

**Scheme 33** Iodine(\(ii\))-catalysed enantioselective deariomatisation of functionalized phenols \(^{105}\) to \(p\)-quinones \(^{115}\) using \(^{126}\) as precatalyst.

![Scheme 34](https://example.com/scheme34.png)

**Scheme 34** Iodine(\(ii\))-catalysed oxidation of alkoxyarenes \(^{127}\) to \(p\)-quinones \(^{129}\) using \(^{128}\) as precatalyst.
The absolute configuration of products (with excellent selectivity (up to 93% ee) (Scheme 35). Interemployed for the oxidation of phenols at room temperature while the same catalytic system was assigned based on single crystal X-ray analysis.

Lactonisation of phenols

Interestingly, same precatalyst was not found suitable for the lactonisation of phenols 136 substituted with acetic acid in the para-position to para-dioxolanones 138. Another conformationally flexible chiral iodoarene based precatalyst 137 was used for the lactonisation of phenols 136 and para-dioxolanones 138 were obtained with up to 89% ee (Scheme 35).

The same group accomplished an enantioselective hypervalent iodine(m)-catalysed intramolecular oxidative dearomatisation of naphthols 139 by generating conformationally flexible λ,1 iodine catalysts in situ from 2-aminoalcohol based aryl iodide 132 in the presence of mCPBA as oxidant (Scheme 36). High functionalized spirilactones 140 were obtained in moderate to high yields with up to 98% ee. Use of HFIP as an additive along with the solvent DCE facilitated the oxidation of less reactive 2-naphthols whereas ethanol was used as additive in the case of 1-naphthols. The current protocol tolerates electron-donating as well as electron-withdrawing substituents in 139.

Similarly, an iodine(m)-catalysed enantioselective spirilactonisation of 4-substituted 1-naphthols 139a was developed by Nachtsheim et al. using a novel triazole-based chiral iodoarene precatalyst 141 in the presence of mCPBA (Scheme 37). During these oxidations, spirilactones 140a with electron-drawing and donating groups were prepared in moderate to good yields. Notably, the precatalyst 141 was not found equally effective compare to the C2-symmetric chiral precatalyst 132 for the same reaction and enantiomeric excess was reduced to < 72% (Scheme 37).

Atropisomers play a crucial role as catalyst in asymmetric catalysis. In 2017, Ogasawara and co-workers developed a novel C2-symmetric conformationally rigid atropisomeric chiral diiododiene 142 from 1,2-bis(4,4-dimethyl-2-pentynyl)benzene and Cp2ZrCl2/Mg. Design and synthesis of low-cost and reliable chiral iodoarene reagents for asymmetric catalysis is of tremendous interest nowadays, two research groups recently succeeded in constructing novel chiral organoiodanes based on carbohydrates and helicenes. Ziegler and Imrich reported d-glucose-based chiral iodoarene 143. Helicene-based chiral iodoarene catalyst 144 was designed and synthesised by Quideau and co-workers through a double Wittig olefination followed by the double photo-cyclisation from inexpensive starting materials. These novel chiral aryl iodide reagents served as interesting catalysts for the spirilactonisation of naphthols 139b to afford chiral spirilactone 140b employing mCPBA as oxidant (Scheme 38). The reaction catalysed by 142 yielded 140b as (S)-isomer in 73% ee whereas 143 or 144 provided 140b as (R)-isomer with up to 60% ee. Notably, the

Scheme 35 Hypervalent iodine(m)-catalysed enantioselective dearomatisation of phenolic compounds 131, 134 and 136.

Scheme 36 Iodine(m)-catalysed enantioselective spirilactonisation of naphthols 139 to 140 using conformationally flexible chiral iodoarene 132 as precatalyst.

Scheme 37 Iodine(m)-catalysed enantioselective spirilactonisation of 4-substituted 1-naphthols 139a to spirilactones 140a.
lower reaction temperature resulted in longer reaction times with improved yield and enantioselectivity.

In 2017, Ciufolini and co-workers described an enantioselective intramolecular oxidative spiroetherification of naphthoic alcohols 145 employing chiral aryl iodide 146 as precatalyst in the presence of mCPBA (Scheme 39). A wide range of spirocyclic ethers 147 bearing electron donating and withdrawing substituents were synthesized in high yields with up to 93% enantiomeric excess. Like in other spirocyclisations, the active iodine(III) catalytic species was generated in situ by oxidation of the chiral precatalyst 146 with 3-chloroperbenzoic acid. The absolute configuration of product 147 was assigned as (R)-isomer by its single crystal X-ray analysis.

In 2020, Tariq and Moran performed an oxidative dearomatization of amide-tethered phenols 148 mediated by λ3-iodanes generated in situ from the 4-iodotoluene 149/mCPBA catalytic system (Scheme 40). The intramolecular dearomatisation protocol furnished spirooxazolines 151 in 30–94% yields with excellent functional group compatibility. The reaction scope was investigated with a range of aryl, alkyl and heteroaryl amide-based phenols under optimised conditions. Notably, methoxy and alkyl substituted phenyl amides 148 yielded spirocycles 151 in moderate yields whereas the fluoro-substituted substrates led to the higher yields of the products. It was suggested that the activation of phenolic oxygen by λ3-iodane and subsequent cyclisation of pendent amide on to the aromatic ring results in the formation of dearomatised product 151. Further oxidative dearomatization of naphthols 152 was performed with 40 mol% of 4-iodotoluene 149 to produce spirocycles 153 in moderate yields. Moreover, triptycene based pre-catalysts 154–156 were also employed in the same reaction but could achieved only very limited success.

Wirth and co-workers developed the synthesis of novel iodoctropyanes 154–156 and employed them as precatalyst for the intramolecular dearomatisation of naphthols 152. The spirocyclic product 153 was obtained in moderate yields with only up to 6% ee (Scheme 41).

Gong and co-workers described an elegant method for the construction of spirooxindoles 159 by an intramolecular dearomatisation of 1-hydroxy-N-aryl-2-naphthamides 158 using chiral iodoarene 157 as precatalyst (Scheme 42). This is the first example of an enantioselective dearomatisation of 1-hydroxy-N-aryl-2-naphthamides 158 providing a facile access to a library of spirooxindoles 159 in good yields with up to 92% ee. The dearomatisation involves the oxidation of chiral iodoarene 157 to generate the active chiral hypervalent λ3-iodane in situ, which catalyses the oxidative of spirocyclisation.
Notably, an all-carbon stereogenic centre in the products is generated during these oxidation reactions.

In another report, the same research group developed a highly enantioselective approach for the spirocarboxylation of N,N-diphenylmalonamides 160 using hypervalent iodine catalysis. Oxidation reactions were performed by using (S)-proline-derived chiral iodoarene 161 as precatalyst in the presence of peracetic acid leading to the synthesis of spiroindoles 162 in variable yields with up to 90% ee (Scheme 43). Once again a quaternary carbon stereogenic centre is generated.

In 2020, Xiong and co-workers developed an enantioselective intramolecular alkox-yoxylactonisation following by dearomatisation of 3'-hydroxy-[1,1'-biphenyl]-2-carboxylic acids 163 employing chiral C2-symmetric iodoarene 164 as precatalyst using mCPBA and MeOH (Scheme 44). Functionalised cyclohexadienones 165 were prepared in moderate yields in up to 52% ee. The size of the alkyl group in the alcohols played a significant role as the yields of the products were decreased with an increased size while the ee was improved significantly. Moreover, the dearomatisation of 2-bromoanilides 166 substituted with ethyl, methyl, acetoxy and methoxycarbonyl functional groups at *para* position of the phenyl ring were also accomplished successfully under these conditions.

### 3.4. Oxidation of sulfides and sulfoxamides

Various hypervalent iodine reagents have been used as oxidants for the oxidation of organosulfur compounds under mild reaction conditions. The role of hypervalent iodine catalysis in the oxidation of organosulfur compounds is very limited. In 2021, Shimazaki et al. developed a highly enantioselective hydrative *para*-dearomatisation of anilides 166 with water as nucleophile using indanol-based chiral organoiodine precatalyst 167. This oxidation approach offers functionalised *p*-quinol imines 168 in poor to excellent yields with up to 93% enantiomeric excess (Scheme 45). In general, 4-methyl sulfonanilides with different 2-substituents such as chloro, bromo, methyl, phenyl, silyl and amide groups were tolerated. Moreover, the dearomatisation of 2-bromoanilides 166 substituted with ethyl, methyl, acetoxy and methoxycarbonyl functional groups at *para* position of the phenyl ring were also accomplished successfully under these conditions.

### 3.3. Oxidation of aromatic amines

Hypervalent iodine reagents have been employed successfully for the dearomatisation of aromatic amines but there is paucity of the literature to achieve similar oxidations using hypervalent iodine catalysis. In 2021, Shimazaki et al. developed a highly enantioselective hydrative *para*-dearomatisation of anilides 166 with water as nucleophile using indanol-based chiral organoiodine precatalyst 167.
Furthermore, an electrochemical oxidation of [1,1′-biaryl]-2-sulfonamides provided the corresponding dibenzothiazines in good yields (Scheme 46).

3.5. Oxidation of alkenes

Oxidation of alkenes with hypervalent iodine reagents is one of the key reactions of hypervalent iodine reagents. Usually, hypervalent iodine reagents activates the olefinic double bond and lead to different oxidations such as epoxidations, hydroxylations, acetoxylations or oxidative cleavages. Oxidation of alkenes achieved by involving hypervalent iodine catalysis until 2014 are compiled in our previous review article.

3.5.1. Acetoxylation of alkenes. Muñiz and co-workers developed iodine(III)-catalysed enantioselective diacetoxylation of styrenes using chiral precatalyst and as precatalyst, peracetic acid as an oxidant and acetic anhydride as the acetylating agent (Method A, Scheme 47). Various substituted styrenes gave the desired diacetoxylation products in good yields with high enantioselectivities (up to 94% ee). Another iodine(III)-catalysed approach was developed by using chiral precursor in the presence of Selectfluor as a terminal oxidant and diacetoxylation of styrenes was achieved in high yields with up to 88% ee (Method B, Scheme 47).

A proposed mechanism for the diacetoxylation of styrenes using chiral iodoarene is shown in Scheme 48. Peracetic acid oxidises the iodoarene to the iodine(III) species. One of the acetate group in dissociates to create a free coordination site at iodine(III) in the presence of triflic acid while the other acetate group participates in hydrogen bonding to generate intermediate. Subsequently, styrene coordinates to intermediate followed by nucleophilic attack of acetate to the exposed re-face of to form intermediate. Intramolecular nucleophilic addition of the acetyl group provides Woodward dioxolonium intermediate and regenerates the iodine(i) catalyst. Dioxolonium intermediate gives two regioisomeric alcohols and on hydrolysis, which on further treatment with acetic anhydride generates the desired product.

Pyridine-based iodoarene was developed and employed as precatalyst for the iodine(III)-catalysed vicinal diacetoxylation of trisubstituted alkenes in the presence of peracetic acid (Scheme 49). The acetoxylation exhibited good functional group tolerance and afforded vicinal diacetoxylation products in good yields. This catalyst acts as a kinetically excellent catalyst due to the Lewis base adduct formation between the pyridine nitrogen and electrophilic iodine(III) centre.

3.5.2. Fluorination of alkenes. In recent years, several research groups have established different methodologies for
of Selectfluor as the oxidant and in combination of an amine and HF as fluorine source (Scheme 52).\textsuperscript{138} Fluorinations proceeded smoothly and vicinal difluorinated products 192 were obtained in good yields. The percentage of geminal fluorination was enhanced on increasing the ratio of HF/amine and the geminal fluorination was observed when amine–HF was used in a 1:9.2 ratio. Additionally, an enantioselective catalytic fluorination of styrenes 48 to 192 was also developed by employing the chiral iodoarene 193 (Scheme 52).\textsuperscript{139} Similar to racemic fluorinations, enantioselective fluorinations proceeded smoothly and vicinal difluorinated products are obtained in good yields in up to 88% enantiomeric excess. The major enantiomer was assigned to have syn configuration based on X-ray analysis. Brønsted acidity of the HF-amine source and assistance of Lewis basic groups adjacent to the reaction site are significant factors which favour the formation of vicinal difluorination over the geminal by subduing the 1,2-aryl shift. The effect of electronic factors were further validated by computing correlations of the enantioselectivity versus the $^{13}$C NMR shift of ipso carbon of the aryl ring and log(ee) versus the Hammett value $\sigma$.

Jacobsen’s research group reported a novel method for the catalytic 1,2-difluorination of trisubstituted olefins 186 using aryl iodide catalyst 194 in the presence of HF–pyridine as the nucleophilic fluoride source and mCPBA as the stoichiometric oxidant (Scheme 53).\textsuperscript{139} Terminal and internal alkene, especially with substituents such as amino and nitrogen containing heterocycles, were tolerated under the reaction conditions. **anti**-Difluorination products 197 and 199 were observed with o-nitro styrenes 196 and acrylamides 198 due to the anchimeric assistance of Lewis basic groups adjacent to the reaction site (Scheme 53).\textsuperscript{139}

A stereoselective version of this reaction was endeavoured by using the chiral catalyst 200 with the same oxidant and fluorine source to afford vicinal **anti**-difluorination product 199 in 51% yield with 93% ee (Scheme 54).\textsuperscript{139} The reaction using the chiral catalyst was much slower compared to the achiral catalyst. The ester moiety of 200 was modified to form another catalyst 202 for an enantioselective geminal difluorination of tetra-substituted olefins 201 to 203.\textsuperscript{144} Reactions were performed at relatively at low temperate (–50 °C to –20 °C) and...
fluorinated products 203 were obtained in good yields with up to 97% ee (Scheme 55).140 Introducing a substituent at benzylic position of the styrenes provided high enantioselectivity. Notably, the cinnamamides and cinnamate esters afforded the desired products 203 in excellent yields (Scheme 55). Tertiary and quaternary stereocenters were generated during these geminal difluorination and cation /C1/C1/C1 interactions played a vital role in achieving the high selectivity. Absolute configuration of the product was assigned based on the single crystal X-ray analysis.

The same research group reported an enantiocontrolled synthesis of vicinal 1,2-difluorinated products 205 from secondary cinnamamides using hypervalent iodine catalysis.141 Vicinal difluorinated products were obtained in moderate to high yields with up to 98% ee (Scheme 56). Interestingly, anchimeric assistance by the neighbouring tert-butyl amide group suppresses the competing 1,1-difluorination reaction via a rearrangement pathway thereby increasing chemoselectivity towards the formation of vicinal 1,2-difluorinated products 206. Notably, the ratio of geminal difluorination was increased in case of neighbouring Me or Et instead of t-Bu in the substrates.

Another novel chiral precatalyst 208 was synthesized by Jacobsen and co-workers and employed in the iodine(iii)-catalysed enantioselective geminal difluorination of α-bromostyrenes 207 to afford β,β-difluoroalkyl bromides 209 in moderate to excellent yields with up to 93% enantiomeric excess (Scheme 57).142 Electron-deficient bromo styrenes with meta- and para-substituents were tolerated whereas ortho-substituted as well as electron-rich styrenes were not tolerated due to the proclivity of the substrates to engage in selective π interactions with the catalyst in the enantio-determining transition state as revealed by SAPT studies.

A general mechanism for iodine(iii)-catalysed vicinal and geminal difluorination of alkenes is shown in Scheme 58.138,143 The catalytic cycle is initiated by the iodoarene oxidation to the active catalytic species 210. The catalytic cycle is initiated by the iodoarene oxidation to the active catalytic species 210. This activates the olefinic substrate to afford an iodonium intermediate 211. Iodonium intermediate 211

configuration of the product was assigned based on the single crystal X-ray analysis.

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A general mechanism for iodine(iii)-catalysed vicinal and geminal difluorination of alkenes is shown in Scheme 58.138,143 The catalytic cycle is initiated by the iodoarene oxidation to the active catalytic species 210. This activates the olefinic substrate 48 to afford an iodonium intermediate 211. Iodonium intermediate 211
undergoes ring opening by the nucleophilic attack of fluoride ion to form a common intermediate 212. Intermediate 212 leads the formation of two different reaction products through path ‘a’ and ‘b’. In path ‘a’, intermediate 212 undergoes a nucleophilic substitution reaction with fluoride ion to yield vicinal difluorination product 192. In path ‘b’, intermediate 212 undergoes an aryl migration via formation of phenonium intermediate 213 to provide the geminal fluorination product 189. The mechanism is well supported by theoretical studies.143

3.5.3. Fluoroaziridination of alkenes. Hypervalent iodine catalysis can also be efficiently used for the development of aziridinations of electron deficient alkenes.144 Previously, chiral aryl iodide 202 was employed for the iodine(III)-catalysed fluoroaziridination of cinnamyl amines 214 to enantiomerically enriched fluoroaziridines 215 in moderate to good yields (Scheme 59).143


3.5.4. Epoxidation of alkenes. Hypervalent iodine catalysis was employed for the epoxidation of electron deficient alkenes 218 using iodobenzene 17 in the presence of terminal oxidant Oxone using TFA as an additive. Reactions were completed in a short reaction time by using ultrasound as energy source and afforded the epoxides 219 in good yields (Scheme 60).145 Oxone was particularly selected as oxidant to generate the hypervalent iodine catalytic species in this reaction because of its inertness towards the alkene epoxidation. Substrates with electron-donating substituents gave excellent yields compared to hindered substrates and arenes with electron-withdrawing groups. The scope of the reaction was also extended to styrenes with ester functionality.

A possible catalytic cycle for the epoxidation of alkenes 218 to epoxides 219 is given in Scheme 61.145 The catalytic cycle is initiated with the formation of an iodine(III) species 2 by in situ oxidation of iodobenzene 17. The iodine(III) species 2 activates the olefinic double bond and forms an iodonium intermediate 220 which converts to intermediate 221 on the ring opening by the nucleophilic attack by trifluoroacetoxy anion. Finally, intermediate 221 cyclizes intramolecularly to epoxides 219 along with the formation of precatalyst 17. The active catalytic
hypervalent iodine species 2 is regenerated by the oxidation of precatalyst 17 to continue the catalytic cycle.

3.5.5. Epoxidation of hydroperoxides. Hypervalent iodine catalysis was used for the dehydration of hydroperoxides.\textsuperscript{146} Hydroperoxides are useful substrates and provide the corresponding carbonyl compounds through oxidation. Hydroperoxides 222 were oxidized to \( \alpha, \beta \)-unsaturated carbonyl compounds 223 when treated with 10 mol\% of IBX 11 as dehydration catalyst in the presence of \( p \)-TsOH hydrate in DMSO at room temperature (Scheme 62).\textsuperscript{147} The iodine(v)-catalysed dehydration of hydroperoxides worked well and both acyclic and cyclic allylic hydroperoxides are successfully converted during these catalytic reactions. In most of the oxidation reactions, enones were obtained in good yields except with acetal based hydroperoxides, which decomposed and formed the products in low yields. It is quite challenging to use allylic hydroperoxides due to their explosive nature.\textsuperscript{147} To overcome this issue, a promising one pot methodology was developed for the direct conversion of alkenes 224 into enones 225 using C\textsubscript{60} as a photosensitizer in an O\textsubscript{2} atmosphere using a fluorescent lamp in the presence of IBX 11 (Scheme 62).\textsuperscript{147} Enones were obtained in good yields except the amino based cyclic olefins. Acyclic enones were obtained in only moderate yields probably due to the low selectivity of singlet oxygen in ene reactions of acyclic alkenes. Low concentration of hydroperoxides in \( ^1 \)H NMR studies clearly supports the better safety profile of this one pot oxidation compared to the direct oxidation of hydroperoxides generated by singlet oxygen.\textsuperscript{147}

3.6. Oxidation of benzylic C–H bonds

Oxidation of benzylic C–H bonds is an important reaction in organic synthesis and a number of hypervalent iodine mediated approaches have been used to achieve these oxidation reactions.\textsuperscript{148,149} In 2020, Maruoka and co-workers reported the application of a hypervalent iodine(\( \mu \)) reagent as redox-neutral catalyst for the selective benzylic C–H oxidation of various arenes 226 to the corresponding carbonyl derivatives 228 at room temperature by employing polymeric iodosylbenzene (PhIO\(_m\), 86 as catalyst and Al(NO\textsubscript{3})\(_3\) as oxidant.\textsuperscript{150} Monomeric PhIO, the active iodine(\( \mu \)) species, is generated in situ by the depolymerisation of PhIO\(_n\), 228 using aluminium nitrate as reagent (Scheme 63). Interestingly, only arenes that are moderately activated by electron-donating groups were reactive in these oxidations. The current protocol is inefficient for arenes which are strongly activated with electron-rich groups and N-heterocycles, the former leads the over-oxidation products (benzoic acids) and the latter was unreactive due to the Lewis basicity of nitrogen.

Another catalytic approach for benzylic C–H oxidation was developed by Nachtsheim and co-workers.\textsuperscript{151} An enantioselective hydroxylation of alkyl arenes 229 to 231 with a newly designed triazole substituted chiral precatalyst 230 was communicated, which acts not only as a halogen donor for the nonstereoselective radical halogenation but also as a chiral ligand during these enantioselective oxidations. This methodology involved irradiation of alkyl arenes 229 with blue LED’s in the presence of chiral aryl iodide 230 (15 mol\%), mCPBA (2.5 eq.), CuBr (20 mol\%) in combination with NaBr (1.5 eq.) in acetonitrile at room temperature (Scheme 64).\textsuperscript{151} Various substrates were found to be compatible with this current protocol to afford the corresponding benzyl alcohols in moderate to good yields with excellent enantioselectivities.

4. \( \alpha \)-Functionalisations of ketones

Functionalisation of carbonyl compounds in the \( \alpha \)-position employing hypervalent iodine reagents is another key reactions of organic synthesis.\textsuperscript{21} Additionally, hypervalent iodine catalysis has been proved a quite useful approach for the developing these reactions.\textsuperscript{3} In this section, various \( \alpha \)-functionalisations of carbonyl compounds will be discussed.

4.1. \( \alpha \)-Oxytosylation of ketones

Basdevant and Legault achieved the \( \alpha \)-oxytosylation of acetyl enol ether 232 using hypervalent iodine catalysis in the presence of PhI 17, mCPBA and \( p \)-TsOH-H\(_2\)O. It was required...
to add the precursor 232 in portions and only then α-tosyloxy ketone 233 was obtained in 74% yield (Scheme 65).\(^{152}\) It was observed that the catalytic reaction was quite slow compared to the stoichiometric reaction. Under catalytic reaction conditions, acetyl enol ethers 232 served as suitable substrates due to their low nucleophilicity and easy availability.\(^{151}\)

Furthermore, Whitehead and coworkers designed and synthesised a series of iodoarenes 235 coupled with diamino acids and the reactivity of these catalysts was assessed for α-oxytosylation of propiophenone 234 (Scheme 65). These precatalysts 235 allow the α-oxytosylation of propiophenone 234 in 35–93% yield. Notably, there was no asymmetric induction observed during these reactions.\(^{153}\)

In the continuation of searching for high selectivities during these reactions, a novel C₂-symmetric chiral iodoarene 236 was synthesised and used as precatalyst to transfer the chirality in the presence of terminal oxidant during the α-oxytosylation of acetyl enol ether 232.\(^{154}\) Once again, the catalytic reaction was found slower than the stoichiometric reaction, but the α-oxytosylated product 233 was obtained as (S)-isomer in 90% ee (Scheme 66). Notably, the same precatalyst 236 showed moderate selectivity in the direct oxytosylation of propiophenone 234.\(^{154}\)

Recently, the concept of “hypervalent twist” was effectively used to develop more reactive hypervalent iodine reagents.\(^{155-159}\) In case of twisted hypervalent iodine reagents, the presence of ortho-substituents leads to an out-of-plane distortion that destabilises the hypervalent iodine reagents.\(^{160}\)

The same concept was used to design and synthesis of N-heterocyclic substituted iodoarene precatalyst (NHIA) 238 which was used for α-oxytosylation of ketones 237 in the presence of mCPBA (Scheme 67).\(^{161}\) Notably, very low catalytic loadings (1 mol%) were efficient to catalyse these reactions successfully and in good yields. The reaction showed tolerance for both aromatic and aliphatic ketones but α-oxytosylation of aromatic ketones provided better yields. Aromatic ketones bearing electron donating functionalities exhibited lower yields during these transformations. Moreover, the same reaction condition was applied for the α-oxytosylation of cyclic ketones.

### 4.2. α-Acetoxylation of ketones

In 2020, Wirth and Hokamp reported an iodine(III)-catalysed enantioselective α-acetoxylation of acetyl enol ethers 232 with high enantioselectivities (up to 88% ee) using hypervalent iodine catalysis (Scheme 68).\(^{162}\) This methodology required resorcinol/lactamide-based chiral aryl iodide 112 as precatalyst in the presence of mCPBA and the additive BF₃·OEt₂. Aromatic moieties with substituents such as halogens, nitro, alkyl and methoxy groups were well tolerated but substrates having electron withdrawing groups at the aromatic ring gave higher yields. The enantioselectivity was influenced by the nature and position of the functional group present in the aromatic ring. High selectivities were observed in case of substrates with electron withdrawing groups while enantiomeric excess was reduced drastically when the substitution was present at the sterically more demanding ortho-position.

A plausible mechanism for the iodine(III)-catalysed α-acetoxylation of acetyl enol ethers 232 is shown in Scheme 69. The catalytic cycle is initiated by the formation of an active iodine(III) catalytic species 241 through oxidation of the chiral aryl iodide catalyst 112 with the terminal oxidant. The catalytic species 241 is further activated by boron trifluoride etherate and undergoes a ligand exchange with the substrate 232 to

[Scheme 65](image)

Scheme 65 Iodine(III)-catalysed α-oxytosylation of acetyl enol ether 232 and propiophenone 234 to α-tosyloxy ketone 233.

[Scheme 66](image)

Scheme 66 Iodine(III)-catalysed α-oxytosylation of acetyl enol ether 232 to enantiomerically enriched α-tosyloxy ketone 233.

[Scheme 67](image)

Scheme 67 Iodine(III)-catalysed α-oxytosylation of ketones 237 by using N-heterocyclic substituted iodoarene precatalyst (NHIA) 238.

[Scheme 68](image)

Scheme 68 Enantioselective α-acetoxylation of acetyl enol ethers 232 to α-acetoxylated ketones 240 using iodine(III) catalysis.
form another intermediate 242. The subsequent Sn2 displacement provides α-acetoxylation of acetyl enol ethers 240 with regeneration of precatalyst 112.162

4.3. α-Fluorination of ketones

Fluorination of carbonyl compounds is an interesting reaction for the formation of C–F bonds.43 Shibata and co-workers reported the α-fluorination of 1,3-dicarbonyl compounds 243 catalysed by 4-iodotoluene 149 using mCPBA as oxidant and HF/pyridine as fluorine source (Scheme 70).163 The targeted tertiary α-fluorinated compounds 244 were obtained in moderate to excellent yields. In the case of α-fluorination, aromatic compounds with electron-withdrawing as well as electron-donating substituents, aliphatic and heteroaromatic substrates were tolerated. In addition, the reaction of cyclic/acyclic tertiary β-ketoesters provided α-fluorinated-β-ketoesters with a quaternary stereogenic centre in good yields.

A versatile asymmetric α-fluorination of cyclic β-keto esters 245 using the C2-symmetric aryl iodide catalyst 246a or 246b in the presence of mCPBA and triethylamine pentafluoride as fluoride source was developed by Rueping and co-workers.164 Enantioselectively enriched α-fluorinated carbonyl compounds 247 bearing quaternary stereocenter were obtained in good yields with up to 83% ee (Scheme 71).165 It was observed that the enantioselectivity increases with the size of the ester group of the β-ketoesters.

5. Cyclisation reactions

In past decades, a number of cyclisation reactions have been developed using hypervalent iodine reagents.23 These reactions constitute an integral part of organic synthesis as they lead to the formation of several biologically important heterocycles.15 More importantly, hypervalent iodine catalysis has played a significant role in the progress of these reactions.3 In this section, both intramolecular cyclisations and intermolecular annulations with hypervalent iodine catalysis are highlighted.

5.1. Intramolecular cyclisations

Intramolecular cyclisation reactions have been extensively used to achieve different oxygen- and nitrogen-containing heterocyclic scaffolds. Synthesis of three-membered N- and O-heterocycles144,145 was already discussed in the oxidation of alkenes (Section 3.5). Herein, the application of hypervalent
iodine catalysis for the construction of five- and six-membered heterocycles will be discussed.

5.1.1. Synthesis of O-heterocycles

5.1.1.1. Synthesis of lactones. The synthesis of chiral 4-fluoroisochromanones 251 was achieved by Jacobsen and co-workers with excellent enantio- and diastereoselectivities.\(^ {166}\) The reaction involves catalytic fluorolactonisation of vinyl benzoates 249 with the aid of chiral aryl iodide 250 in the presence of mCPBA by taking HF-py in the ratio 1:9 as the fluoride source (Scheme 72). A syn diastereoisomer with 35–86% yield and up to 96% ee is formed in this reaction by the nucleophilic displacement of the aryliodonium group in the intermediate 252 with the aid of anchimeric assistance of the carboxylate functionality. Various electron-withdrawing and electron-donating groups at the aryl moiety are tolerated. Furthermore, an enantioselective sulfonyloxylactonisation and phosphoryloxylactonisation of 4-pentenoic acid derivatives 253 was reported by Masson and co-workers using C\(_2\)-symmetric chiral iodoarene 254 as precatalyst in the presence of mCPBA as oxidant (Scheme 73).\(^ {167}\) This method enabled a straightforward synthesis of sulfonyloxy- and phosphoryloxy-γ-butyrolactones 256 and 258 in good yields with moderate to high enantioselectivities. Both, 4-pentenoic acids and 1-allylcycloalkane carboxylic acids afforded γ-lactones and spirrolactones, respectively, in good yields.

A possible catalytic cycle for the sulfonyloxylactonisation of iodine(III) catalysis is shown in Scheme 74. The catalytic cycle is initiated with the oxidation of chiral aryl iodide 254 to iodine(III) species 259 by mCPBA in the presence of sulfonic acid 255. The iodine(III) intermediate 259 activates the double bond of olefinic acid 253 to form the chiral iodonium intermediate 260. Iodonium intermediate 260 undergoes an intramolecular cyclisation to form the lactone intermediate 261. Finally, lactone intermediate 261 provides sulfonylated lactones 256 and regenerates the catalyst to continue the catalytic cycle.\(^ {167}\)

Later, Hilt and co-workers developed an electrochemical approach for the lactonisation of vinyl benzoates 249 mediated by hypervalent iodine(III) catalysis using PhI 17 as precatalyst in the presence of lithium perchlorate as electrolyte and trifluoroacetic acid to form trifluoroethoxy-substituted isochromanes 263 in moderate to good yields (Scheme 75).\(^ {168}\) The scope of the reaction was expanded by changing the steric and electronic components of the substrates; only functional groups labile to oxidative conditions show low yields. Moreover, N-heterocyclic substituted iodoarene precatalyst (NHIA) 238 was also employed to achieve similar lactonisations.\(^ {164}\)

5.1.1.2. Synthesis of cyclic ethers. He and co-workers employed hypervalent iodine catalysis to develop the synthesis of various benzoimino lactones 265 through iodine(III)-catalysed intramolecular oxy-cyclisation of 2-vinylbenzamides 265.\(^ {169}\)}
catalysis has been used to synthesise fluorinated piperidines.

Scheme 78 Iodine(III)-catalysed enantioselective fluorocyclisation

Iodine(III)-catalysed lactonisation of vinyl benzoates

Iodine(III)-catalysed intramolecular oxy-cyclisation of 2-vinylbenzamides with eq.) to accelerate the oxidation process. Various 2-

An environmental friendly synthesis of 2-arylbenzofurans was developed by indine(III)-catalysed intramolecular cyclisation of 2-

The proposed catalytic cycle for the hypervalent iodine-catalysed cyclisation of alkenes 271 to fluorinated piperidines 272 is shown in Scheme 80. The oxidant oxidises the precatalyst 149 to ArIO 273 which, in turn, reacts with HF to form the electrophilic hypervalent iodine species ArIF 274. ArIF 274 reacts with alkenes 271 to form intermediate 275 with the liberation of HF. Furthermore, the intermediate 275 converts into aziridinium intermediate 277 via formation of intermediate 276. Final nucleophilic attack of fluoride ion to aziridinium intermediate 277 affords the fluoropiperidine 278 along with the regeneration of precatalyst 149 to continue the catalytic cycle.

The fluorocyclisation of para-substituted styrenes 269 proceeded with high selectivity compared to meta-substituted derivatives, whereas low selectivities and a decreased reactivity was observed in ortho substituted styrenes. Optimisation of various chiral catalysts revealed that increasing the steric demand of the α-substituent R1 in 269 improved the stereo-selectivity of the fluorocyclisation. Both catalysts 269 were able to induce high enantioselectivities, particularly the newly developed 1-naphthyllactate catalyst (R,R)-269b yielded higher ee values than the mesityl analogue (R,R)-269a. Additionally, the synthesis of fluorinated pyrrolidines via an aminofluorination of styrenes was achieved under similar conditions.

5.1.2. Synthesis of N-heterocycles

5.1.2.1. Synthesis of piperidines. Hypervalent iodine cyclisation has been successfully used to synthesise fluorinated piperidines 272 by involving an intramolecular aminofluorination of α-aminoalkenes 271 using 4-MeC6H4I 149/nHF-pyridine/ mCPBA catalytic system (Scheme 79).163 Cyclisations proceeded smoothly and various fluorinated piperidines 272 with alkyl, aryl and cyclic substituents were obtained in 31–77% yield. Notably, efforts were made to develop an asymmetric variant of this reaction, but only moderate enantiomeric excesses were obtained (not shown).

The proposed catalytic cycle for the hypervalent iodine-catalysed cyclisation of alkenes 271 to fluorinated piperidines 272 is shown in Scheme 80. The oxidant oxidises the precatalyst 149 to ArIO 273 which, in turn, reacts with HF to form the electrophilic hypervalent iodine species ArIF 274. ArIF 274 reacts with alkenes 271 to form intermediate 275 with the liberation of HF. Furthermore, the intermediate 275 converts into aziridinium intermediate 277 via formation of intermediate 276. Final nucleophilic attack of fluoride ion to aziridinium intermediate 277 affords the fluoropiperidine 278 along with the regeneration of precatalyst 149 to continue the catalytic cycle.
cycle. To improve the yield, HF has to be used in excess because of the reversible nature of the reaction from ArIF₂ 274 to ArIO 273 and then due to a competitive hydroxylation reaction. 163 Furthermore, N-heterocyclic substituted iodoarene precatalyst (NHIA) 238 was employed for the hypervalent iodine-catalysed cyclisation of ortho-phenyl acetanilide 278 to N-acyl carbazole 280 (Scheme 81). 161 Notably, the ‘twisted’ hypervalent iodine species was generated during the progress of this reaction and N-acyl carbazole 280 was obtained in 77% yield. Moreover, another precatalyst 279 of the same series was also used and gave carbazole 280 in 49% yield (Scheme 81). 161 Peracetic was used as terminal oxidant to generate active catalytic species.

5.1.3.3. Synthesis of O,N-heterocycles

5.1.3.1. Synthesis of oxazoles. Punniyamurthy and co-workers developed a simple and efficient catalytic procedure for the synthesis of benzoazoles 283 and benzothiazoles 285 by intramolecular cyclisation of arylanilides 281 and arylthioanilides 284, respectively (Scheme 82). 174 This transformation employed 1-iodo-4-nitrobenzene 282 as precatalyst, Oxone® as oxidant in the presence of HFIP at room temperature. Anilides with halogen substituents afforded the desired products in good to excellent yields whereas nitro substituents were not compatible with the reaction. Amide groups with aryl, heteroaryl and alkyl substituents were tolerated. This protocol was successfully extended to gram scale.

The proposed catalytic cycle for the iodine(III)-catalysed cyclisation of arylanilides 281 to benzoazoles 283 is shown in Scheme 83. As usual, the active hypervalent iodine species 286 is generated by the oxidation of aryl iodide 282 which reacts with substrate 281 to form new hypervalent iodine species 287. Furthermore, species 287 undergo an intramolecular cyclisation to form a cationic intermediate 288. Finally, the cationic intermediate 288 gave benzoazoles 283 through deprotonation and releases aryl iodide 282 to re-enter into the catalytic cycle. 174

In 2015, Moran and co-workers developed an intramolecular cyclisation of N-alkenylamides 289 for the synthesis of five to seven membered ring systems 291 containing both nitrogen and oxygen atoms (Scheme 84). 175 The catalytic system employed 2-iodoanisole 290 as precatalyst, Selectfluor as oxidant and TFA as additive. The cyclisation was not effective when mCPBA or Oxone® were used as oxidants. An array of electron rich and electron poor aryl amides were cyclised to obtain the corresponding products in good yields. Moreover, an enantioselective synthesis of isoxazoline 291a from 289a (R¹ = Ph; R² = H and n = 1) was accomplished by the use of 47 as chiral iodine precatalyst, but the product was obtained in low yield with 69% ee (Scheme 84). 175

Scheme 80  Catalytic cycle for the hypervalent iodine-catalysed cyclisation of alkenes 271 to piperidines 272 using 149 as precatalyst.

Scheme 81  Iodine(III)-catalyzed cyclisation of ortho-phenyl acetanilide 278 to N-acyl carbazole 280 using N-heterocyclic substituted iodoarene precatalyst (NHIA) 238 and 279.

Scheme 82  Iodine(III)-catalysed synthesis of benzoxazoles 283 and benzothiazoles 285.

Scheme 83  The proposed catalytic cycle for iodine(III)-catalysed intramolecular cyclisation of arylanilides 281 to benzoazoles 283.
Similar substrates 289 were cyclised to 2-oxazolines 292 with an exocyclic fluoromethyl group in the presence of p-methyliodobenzene 149 as precatalyst, Selectfluor and a mixture of triethylamine tris(hydrogenfluoride) (Et3N/C13 HF) and Olah’s reagent (Py/C1 HF) as fluoride source (Scheme 85).176 This cyclisation reaction was compatible with several functional groups and extended to prepare six-membered rings.

N-Propargyl amides 293 were cyclised to oxazoles 295 in good yields by iodine(III) species ArIF2, generated in situ from 4-iodoanisole 294 in the presence of Selectfluor and HF–pyridine as the fluoride source (Scheme 86).177 Aromatic as well as aliphatic amides were tolerated. Internal alkynes and amides containing haloarenes were found futile as substrates. Later, similar cyclisations were achieved in moderate yields by treating N-propargyl amides 293 with bisulfonyl(imides) 41 using PhI 17 as the precatalyst, Oxone as oxidant and TBAHSO4 (TBA: tetrabutylammonium) as a phase transfer reagent178 or by using precatalyst (2-IC6H4OMe)290 in combination with mCPBA.179

An one-pot protocol for the synthesis of oxazole-5-carbaldehydes 297 was developed by the cyclisation of N-propargylamides 293 using the PIDA/LiI catalytic system in the presence of oxygen under irradiation with visible light. This process involves an iodocyclisation followed by oxidative deiodination and cyclised products 297 were isolated in good to excellent yields (Scheme 87).180

The mechanism for PIDA-catalysed cyclisation of N-propargylamides 293 to oxazole-5-carbaldehydes 297 is given in Scheme 88. The reaction is initiated by the PIDA mediated oxidation of iodide to iodine monoacetate which induced the cyclisation of substrate 293 to cyclic intermediate 299. Under the visible light, C–I cleaves homolytically and forms radical 300 along with an iodine radical. The radical 300 reacts with oxygen to form peroxy radical intermediate 301 which is subsequently converted to another radical intermediate 302. Intermediate 302 rearranges to radical species 303 that gave the final aldehyde product 297 along with a hydroxyl radical. The hydroxyl radical reacts with iodine radical to form HIO that produced iodine on decomposition to continue the catalytic cycle.180 Moreover, the tetrabutylammonium iodide (TBAI) has been also employed as precatalyst in the presence of terminal oxidant to develop the synthesis of similar oxazole scaffolds.181

5.1.4. Synthesis of carbocycles. Polycyclic aromatic hydrocarbons 305 were easily prepared by Murphy and others via oxidative intramolecular C–H coupling of styrenes 304 containing arene and alkene functionalities. These cyclisations were achieved using 4-iodotoluene 149 as precatalyst, mCPBA as oxidant, BF3·OEt2 as additive and chlorobenzene as solvent (Scheme 89).182 Polysubstituted phenanthrene derivatives were...
successfully prepared in moderate to high yields. Among the various functional groups, only very strong electron-withdrawing substituents such as NO₂, Ac, COOMe and CF₃ on the vinyl as well as arene moiety were not found suitable during these cyclisations. The scope of the reaction was also expanded for the formation of tetra and pentacyclic aromatics.

5.2. Intermolecular annulations

Like intramolecular cyclisations, intermolecular reactions have been extensively used for developing the synthesis of various heterocycles under metal-free reaction conditions. Applications of hypervalent iodide catalysis to achieve intermolecular annihilations until 2013 are reviewed in our previous article.³

5.2.1. Synthesis of N-heterocycles. Various hypervalent iodine-catalysed intermolecular annihilations have been used to construct nitrogen-containing heterocycles. Isoquinolones 308 were synthesised by the cycloaddition of alkynes 307 and benzamides 306 using catalytic amounts of iodobenzene 17 in HFP/IP in the presence of peracetic acid (Scheme 90).¹⁸³ Notably, a significant increase in the yield was observed by the portion-wise addition of the oxidant. Electron-withdrawing and electron-donating groups in alkynes were tolerated and some regioselectivity was witnessed in the case of unsymmetrically substituted diarylacetylenes. Irrespective of the position and arenes with alkyl/aryl/alkoxy groups provided the desired products and sulfonyle or carbonyl groups on nitrogen atoms of the anilides were also tolerated. The catalytic pathway was found to be less effective compared to the stoichiometric one.

The synthesis of benzimidazoles 313 and quinoxalines 315 was developed by Kamal and co-workers using hypervalent iodine catalysis.¹⁸⁵ The condensation of o-phenyldiamines 312 with various aryl or heteroaryl aldehydes 97 afforded the corresponding benzimidazoles 313 in good to excellent yields (Scheme 91). Moreover, the condensation of o-phenyldiamines 312 with benzil 314 provides quinoxalines 315 in excellent yields (Scheme 92). During these annihilations, very low catalytic loading of Koser’s reagent 4 (1 mol%) was sufficient to achieve the products in high yields.

5.2.2. Synthesis of N,O-heterocycles. In the past years, organocatalysis involving hypervalent iodine catalysts has been used to construct various N,O-heterocycles.³ Zhdankin and co-workers developed a catalytic system using hypervalent iodine(Ⅲ) reagents for the oxidative cycloaddition of aldoximes 309 with various aryl or heteroaryl aldehydes 97 afford quinoxalines 315 via oxidative cycloaddition of aldoximes 316 with maleimide 319 (Scheme 93).¹⁸⁶ This catalytic protocol involves an in situ generation of the cyclic iodine(Ⅲ) species 318 (IBA-OTF) by oxidation of 2-iodobenzoic acid 317 with mCPBA in the presence of trifluoromethanesulfonic acid. Various substituted aromatic aldoximes 316 with electron-rich and electron-poor aryl rings were tolerated. The same research group reported also a similar catalytic protocol for the oxidative cycloaddition of styrenes 304 to polycyclic aromatic hydrocarbons 305.
of aldoximes 316 with organonitriles 321 to prepare 1,2,4-oxadiazoles 322 (Scheme 93). Moreover, similar substrates were employed in the annulations using modified reaction conditions. 2,4-Disubstituted and 2,4,5-trisubstituted oxazoles 325 were synthesised regioselectively through a [2+2+1] addition of internal as well as terminal alkynes 307, nitriles 321 and oxygen atoms employing iodine(III) catalysis. The scope of the reaction was examined by using two different precatalyst PhI 17 and 4-ClC₆H₄I 323 in the presence of mCPBA and Tf₂NH. All the cyclisation reactions were performed at room temperature and cyclised products were obtained in moderate to good yields (Scheme 94). Mechanistic studies showed the involvement of iodine(III) species in the catalytic cycle and the active catalytic iodine(III) intermediate PhI(OH)NTf₂ 324 was isolated. The hypervalent iodine catalysis was also employed for the construction of isoxazole systems. Moreover, a few other catalytic systems have been used to build similar scaffolds.

5.2.3. Synthesis of N,S-heterocycles. Wang and co-workers established a catalytic protocol for the preparation of various thiadiazole scaffolds 328 through an intermolecular oxidative annulation via the formation of an intermediate 327 formed from aldehydes 97 and thiosemicarbazide 326 employing iodine(III) catalysis (Scheme 95). Mono- and di-substituted aryl aldehydes irrespective of the position of functional groups gave moderate to excellent yields. Naphthyl, heteroaryl and alkyl aldehydes were also tolerated.

Kamal and co-workers described the synthesis of benzothiazoles 330 by the condensation of 2-aminothiophenol 329 with aromatic aldehydes 97 using Koser’s reagent 4 as catalyst in the presence of molecular oxygen. Reactions were completed in short reaction time and afforded the benzothiazoles 330 in excellent yields (Scheme 96). During these cyclisations, a very low catalytic loading (1 mol%) was sufficient for catalysis to the cyclised products in high yields. Notably, aromatic aldehydes bearing electron donating groups showed slightly better yields compare to substrates with electron withdrawing groups.

6. Oxidative rearrangements

Hypervalent iodine reagents are known for activating the olefinic double bonds and later they behave as good leaving groups. Additionally, they can participate in the formation of cationic intermediates that lead to variety of rearrangement reactions. Initially, the focus of hypervalent iodine chemists was on the developments of oxidative rearrangements using hypervalent iodine reagents in stoichiometric amounts but later rearrangements have been developed using hypervalent iodine catalysis. Some rearrangements have already been described in Section 3.5.2 discussing the geminal difluorination of alkenes. 6.1. 1,2-Aryl/alkyl migration reactions

In 2018, Mal and co-workers developed an iodine(III)-catalysed C–H functionalisation of N-(5-bromo-2',4',6'-triethyl[1,1'-biphenyl]-2-yl)methanesulfonamide 331 to carbazole 332 along with an 1,2-migration of an ethyl group. The reaction was carried out by using 20 mol% of iodobenzene 17 as an iodine(III) catalyst.
product 332 was obtained in 48% yield (Scheme 97). Notably, the stoichiometric version of the same reaction was also developed and rearranged products were obtained in better yields compared to the catalytic reaction.

An enantioselective rearrangement of allylic alcohols 333 using (S)-proline-derived chiral iodoarene 334 as precatalyst assisted by the Bronsted acid p-TsOH was described by Gong and co-workers.\(^{194}\) Bronsted acids promote the formation of ethers from allylic alcohols whereas the chiral aryl iodide catalyses the 1,2-aryl migration to afford chiral \(\alpha\)-arylated-\(\beta\)-alkoxylated ketones 335 in good yields and with excellent enantiomeric excess (Scheme 98).\(^{194}\) The presence of electron withdrawing and electron donating groups at para- or meta-position of the phenyl rings of allylic alcohols are well tolerated. Moreover, N-heterocyclic substituted chiral iodoarene precatalyst (NHA)\(^\text{230}\) was also employed to perform these rearrangements under almost similar catalytic reaction conditions and the selectivity was increased to up to 98% ee.\(^{195}\) The same rearrangement was also achieved by using another N-heterocyclic substituted achiral precatalyst 238 in moderate yields.\(^{160}\)

A plausible mechanistic pathway for the enantioselective 1,2-aryl migration in allylic alcohols 333 catalysed by \textit{in situ} generated chiral iodine(\textit{m}) reagent is shown in Scheme 99.\(^{193}\) Initially, the allylic alcohol 333 reacts with ROH 83 to form an alkoxylated product 337. Simultaneously, aryl iodide 334 is oxidized to iodine(\textit{m}) 336 which activates the double bond of diaryalkene 337 in presence of p-TsOH to give complex 338. Nucleophilic attack on 338 by \(\text{H}_2\text{O}\) generates the intermediate 339 which undergoes a semipinacol-type rearrangement to furnish intermediate 340 along with regeneration of the precatalyst 334. Finally, deprotonation of intermediate 340 gives the product 335.

In 2020, Tiwari and co-workers reported an iodine(\textit{m})-catalysed enantioselective 1,2-tolyl group migration with geminal diacetoxylation of aromatic alkene 342.\(^{196}\) The reaction was performed at low temperature with the rearranged product 344 obtained in 27% yield with up to 92% ee (Scheme 100). The catalytic system involved 20 mol% chiral iodine(\textit{m}) catalyst 343 and \text{mCPBA} in \text{CHCl}_3: AcOH (1 : 1). Some research groups have achieved a similar 1,2-aryl migration reactions by using ammonium iodide\(^{197}\) and molecular iodine\(^{198}\) as catalysts. Hypervalent iodine catalytic species are not generated during these two rearrangements but these transformations may be quite useful for the readers who are working in hypervalent iodine catalysis.

In 2015, Gulder and co-workers reported a novel rearrangement of imides 345 using catalytic amounts of iodobenzamide 346 in the presence of \(N\)-bromosuccinimide (NBS) 347 as oxidant in hexafluoro-2-propanol (HFIP) at room temperature.\(^{199}\) This metal-free route lead to the facile preparation of valuable \(\alpha,\alpha\)-disubstituted-\(\alpha\)-hydroxycarboxylamides 349 in good to excellent yields (Scheme 101).\(^{199}\) The reaction involved the formation of cyclic hypervalent iodine(\textit{m}) species (bromo benziodoxole) 348 by oxidation of iodobenzamide 346 with NBS 347. Notably, none of these reactions exhibited aryl bromination and longer reaction
times were observed with reduced catalyst loading and when bromo benziodoxole 348 was used instead of NBS 347.

In 2020, an iodine(III)-catalysed enantioselective Wagner–Meerwein rearrangement of β-substituted styrenes 350 involving aryl, alkyl and hydride migrations was published affording 1,3-difluorinated products 351 and 352 in good to excellent yields with an excellent enantiomeric excess (Scheme 102).200 The catalytic system comprises of chiral aryl iodide 200 as precatalyst, mCPBA as the oxidant and py/C19HF as the fluoride source. Notably, the 1,2-anti-diastereomers 351 were obtained when aryl is the migrating group and 1,2-syn diastereomers 352 were obtained when methyl is the migrating group (Scheme 102).

6.2. Hofmann rearrangements

Also Hofmann rearrangements have been developed by using hypervalent iodine reagents in stoichiometric amounts.16,37 The first report on the Hofmann rearrangement appeared in 2012 by Ochiai and his research group.201 Later in the same year, the application of hypervalent iodine catalysis in Hofmann rearrangements was extended by Zhdankin and co-workers.202 In 2017, Hofmann rearrangements of primary amides 353 to carbamates 355 via the formation of isocyanate intermediate 354 was successfully achieved by Miyamoto and co-workers using precatalyst 103, molecular oxygen as an oxidant and isobutyaldehyde as the O2 mediator.97

The rearranged products were obtained in moderate to excellent yields (Scheme 103). A variety of aliphatic as well as aryl amides were tolerated.

7. Photoredox catalysis

Hypervalent iodine reagents have a unique property of producing free radicals that makes these reagents suitable for photochemical reactions.203 In past decade, a number of hypervalent iodine reagents have been successfully employed in photoredox catalysis.19 In the majority of these hypervalent iodine induced photoredox reactions, the iodine reagents have been used in stoichiometric amounts, but there are few photoredox reactions where these reagents play a role of co-catalysts in combination with photoredox catalysts. In this section, the photoredox reactions catalysed by both hypervalent iodine and photoredox catalysts are highlighted.

7.1. Alkynylations

In 2014, Chen and others reported the deboronative alkynylation of potassium alkyl trifluoroborates 356 with alkynyl benziodoxole 357 to alkynes 307 using photoredox catalysis in the presence of catalyst BI–OH 358.
This reaction was highly chemoselective and tolerated a wide range of functional groups.

Scheme 105 depicts the proposed catalytic cycle for the photoredox-catalysed deboronative alkynylation of potassium alkyl trifluoroborates 356 to alkynes 307 using photoredox catalysis.

Glorious and co-workers developed a hydrogen atom transfer (HAT) method for the selective alkynylation of sp$^3$ C(O)–H bond of aldehydes 97 via photoredox catalysis (Scheme 106). This process delineates effective synthesis of ynones 307 via formation of intermediate 363 and eliminates benziodoxole radical 360 which later oxidizes Ru(bpy)$_3^{2+}$ to Ru(bpy)$_3^{3+}$ and forms orthoiodobenzoic acid.

Glorys and co-workers developed a hydrogen atom transfer (HAT) method for the selective alkynylation of sp$^3$ C(O)–H bond of aldehydes 97 via photoredox catalysis (Scheme 106). This process delineates effective synthesis of ynones 307 via formation of intermediate 363 and eliminates benziodoxole radical 360 which later oxidizes Ru(bpy)$_3^{2+}$ to Ru(bpy)$_3^{3+}$ and forms orthoiodobenzoic acid.

7.2. Decarboxylative coupling of α-ketoacids

Wang and co-workers described the decarboxylative alkynylation of α-ketoacids 373 with functionalised bromoacetylenes 374 using BI–OH 358 as catalyst under sunlight irradiation. This method tolerated a wide range of functional groups and led to the energy-efficient synthesis of ynones 367 in good yields (Scheme 108). The substrate scope showed that bromoacetylenes functionalised with electron-withdrawing groups abstracts a hydrogen and forms the carbonyl radical of the substrates. The scope of the reaction was widely explored with different aliphatic and aromatic aldehydes and the corresponding alkynylation products were obtained in decent yields.

In 2021, Chen and others reported the synthesis of aminoaalkynes 372 from cycloalkylamides 368 via a selective C(sp$^3$)–C(sp$^3$) cleavage/alkynylation strategy using photoredox catalysis. The reaction employed Ph-Acr-MesBF$_4$ 370 as photocatalyst and catalytic amounts of cyclic iodine(III) reagent 3,4-Ome-BI-OAc 369 (Scheme 107). The photoredox catalyst 370 was quite effective at low catalyst loading. Notably, 369 non-covalently activates cycloalkylamide 368 thereby facilitating the single-electron oxidation and ring-opening alkynylation as governed by various mechanistic probing experiments. A variety of nucleophiles 371 such as n-butanol, methanol, water, p-tolueneethiol, 1-naphthol, TMSCN, indole and N-Me-indole were used to trap the iminium intermediate to give the desired aminoaalkyne products in decent yields. Additionally, the bifunctional aminoaalkynes were used to prepare indolizidine-fused azacycles via metal-catalysed cyclisations.

Scheme 106 Photoredox-catalysed alkynylation of aldehydes 97 with alkynyl benziodoxole 357 to ynones 367 using a catalytic amount of BI–OAc 366.

Scheme 105 Proposed catalytic cycle for iodine(III)-catalysed alkynylation of potassium alkyl trifluoroborates 356 to alkynes 307 using photoredox catalysis.
provided higher product yields while those with electron-donating groups showed inferior yields. Notably, the results of sunlight-driven reaction were comparable to those obtained by using blue light ($\lambda = 450–455$ nm).

The possible catalytic cycle for the decarboxylative coupling reaction is summarized in Scheme 109. Initially, BI–OH reacts with $\alpha$-ketoacid to form the intermediate, which upon sunlight irradiation generates iodanyl radical and acyl radical. The iodanyl radical reacts with bromoacetylene to give BI–alkyne intermediate along with the formation of a Br radical. Subsequently, the addition of acyl radical to the intermediate forms intermediate, which eventually releases the coupling product and regenerates intermediate. Finally, coupling of iodanyl radical with bromine radical produces bromobenziodoxole, which undergoes hydrolysis to regenerate BI–OH.

7.3. Synthesis of phenols

In 2015, an organo-photoredox catalysed activation of PhI(OAc)$_2$ was reported by Yadav and co-workers for the conversion of arylboronic acids to phenols. This transformation was performed with 1.0 mol% of Eosin Y as photoredox catalyst and K$_2$CO$_3$ as base in acetonitrile under visible light irradiation (Scheme 110). The reaction proceeded smoothly with substrates bearing electron-donating or electron-withdrawing substituents and the corresponding phenols were isolated in excellent yields. Notably, the photo-chemically excited Eosin Y activates PhI(OAc)$_2$ to form a methyl radical, which plays a key role for conversion of arylboronic acids to phenols.

7.4. Dearomatisation

Furthermore, photoredox catalysis was employed for the dearomatisation of $p$-substituted anisole derivatives to spiro lactams using Kita’s catalyst under blue light irradiation.

8. Photochemical reactions

There are several hypervalent iodine mediated reactions driven by light. Moreover, there are hypervalent iodine catalysed organic reactions that require light to proceed. The visible-light driven decarboxylative acylarylation of acrylamides with $\alpha$-ketoacids was developed using hypervalent iodine(III)-catalysis. This method led to the energy-efficient synthesis of 3,3-disubstituted 2-oxindoles in good yields without using any photoredox catalyst (Scheme 112). Hypervalent iodine reagent BI–OAc was employed as catalyst, which generates the radical species by cleavage of oxygen–iodine bond in the presence of blue LED (450–455 nm). The course of the reaction was examined with a diverse array of N-methyl-N-arylmethacrylamides, functionalised with electron-donating or withdrawing groups at the benzene ring and produced 2-oxindoles in good yields. Notably, ketoacids with electron-donating substituents in the aryl ring provided slightly higher yields.
A photocatalytic approach towards the synthesis of chiral ketones 392 was introduced by Maruoka and co-workers using hypervalent iodine catalysis. In this study, the diastereoselective radical hydroacylation of alkylidenemalonates 390 was developed with various linear and branched chain aldehydes under UV light irradiation using hypervalent iodine as catalyst. Chiral ketones were obtained in good yields with high diastereoselectivity accomplished by employing (−)-8-phenylmenthol as chiral auxiliary (Scheme 113). Acyl radical addition preferably takes place at the less sterically hindered face of the alkenes and thereby (S)-isomers forms predominantly because of the effective shielding of Re face by the phenyl group of the chiral auxiliary. Moreover, the same approach was successfully applied for the synthesis of (−)-methyleneolactocin.

9. Miscellaneous reactions

Hypervalent iodine catalysis is used to achieve many different organic transformation and it is not possible to categorise all of the published reactions. Yakura et al. developed a mild, efficient and eco-friendly iodine(ν)-catalysed oxidative cleavage of tetrahydrofuran-2-methanols 393 to form γ-lactones 395 using 2-iodobenzenamide 394 as precatalyst and Oxone® as co-oxidant (Scheme 114). The catalytic cycle for an iodine(ν)-catalysed oxidative cleavage of tetrahydrofuran-2-methanols 393 to γ-lactones 395 is explained in Scheme 115. The reaction begins with the oxidation of iodobenzenamide 394 by Oxone® to give iodine(ν) species 397 via formation of iodine(m) intermediate 396. Iodine(ν) species 397 oxidises the alcohol 393 to generate key aldehyde intermediate 398 along with the regeneration of iodine(m) species for the next cycle. Eventually, the aldehyde 398 reacts with Oxone® to form formate 399 via a Baeyer–Villiger type rearrangement which is oxidised to the desired lactone 395. Notably, the aldehyde 398 did not oxidise to the corresponding carboxylic acid.

Hu and colleagues developed an iodine(m)-catalysed Balz–Schiemann fluorination of aromatic diazonium salts 401 under mild reaction conditions where the iodine(m) species lowered the energy activation barrier of the reaction. A wide range of aromatic fluorides were prepared in good yields in the presence of 402–404 as iodine(m) catalysts and BF₃·Et₂O as additive (Scheme 116).

Cyclopropanes behave often similar to olefins and can be activated by hypervalent iodine compounds. In 2017, hypervalent iodine catalysis has been used for the oxidative ring opening of substituted cyclopropanes 407 to obtain 1,3-difluorinated...
compounds 408 using PhI 17 as precatalyst and Py·9HF as source of fluoride in the presence of mCPBA (Scheme 117).215 Arylcyclopropanes 407 with electron-withdrawing substituents were tolerated while those with electron-donating substituents were not. With increased catalytic loadings (20 mol%), non-conjugated mono-substituted cyclopropanes 407 bearing ether and amine functionalities afforded difluorinated products 408 in good to excellent yields. The reaction involves the formation of key intermediate 409 that converts into a fluoroiodine(III) species 410. Eventually, iodine(III) intermediate 410 gave the final product 408 either through a S_N1 route involving the formation of a tertiary carbocation or through a concerted backside fluoride substitution, the latter affords diastereomerically enriched products.

The acidic PIFA 2 was explored as catalyst for nucleophilic substitutions of internal and terminal propargylic alcohols 411.216 Aromatic and heteroaromatic propargyl alcohols 411 with electron-donating substituents reacted faster with allyl silyl ethers 412 to afford 1,5-enynes 413 in good yields using PIFA 2 as catalyst in the absence of any oxidant (Scheme 118).

The intermediate propargylic cation was generated by the reversible equilibrium between propargyl alcohol 417 and the PIFA 2 catalyst. Scheme 119 shows the proposed mechanism for the formation of an adduct 415 from the ligand exchange of PIFA 2 with propargyl alcohol 411, which decomposes into iodosobenzene 416 and propargylic carbocation 417. Propargylic carbocation 417 undergoes a nucleophilic substitution with allyl silyl ethers 412 to form substituted product 413. Iodosobenzene 416 binds with the eliminated TFA to regenerate the catalyst 2. The use of a stronger nucleophile would decrease the product yield due to the competition at the active site of PIFA 2 catalyst by the nucleophile and propargyl alcohol and anilines cannot be used as nucleophiles due to their Lewis basicity.215

Synthetically important E-vinyl boronates 420 were prepared by Wei and co-workers by the hydroboration of terminal alkynes 418 with bis(pinacolato)diboron (B_{2}pin_{2}) 419 using catalytic amounts of PhI(OAc)_{2} 1 in the presence of BuONa and EtOH as the hydrogen donor in air (Scheme 120).217 Aromatic as well as aliphatic terminal alkynes 418 gave moderate to good yields with good regio- and stereoselectivity.
is the need of more general applicable catalysts, especially when considering stereoselective reactions.

Conflicts of interest

There are no conflicts to declare.

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