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## Reactivity under mechanochemical conditions: a new and more sustainable era for hypervalent iodine?

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Hypervalent iodine reagents can mediate or catalyze a wide variety of organic reactions, and have hence become important tools in the synthetic toolbox of organic chemists. Recent developments in the field include reactions under mechanochemical conditions, ranging from reports on similar or improved reactivity compared to the solution-phase, to papers describing novel reaction pathways. As mechanochemistry has the potential to improve the sustainability profile of reactions by, for instance, avoiding reaction solvents and shortening reaction times, this critical review provides a sustainability comparison of mechanochemical and solution-phase reactions with iodine(III) compounds. The sustainability profiles were evaluated by comparing reaction yields, solvent properties and calculated *E*-factors, based on data available in the literature. Overall, the comparison provides strong support that mechanochemical hypervalent iodine reactions have improved sustainability compared to solution-phase, often with more than ten-fold decrease in waste production, and avoid a range of solvents with major issues according to the GSK solvent guide.

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### Green foundation

1. Hypervalent iodine reactions are popular in synthesis, as their reactions often display high selectivity under mild reaction conditions, without the need for inert conditions or transition metal catalysts. The low-toxicity and stable nature of these compounds is attractive, but the sustainability profile is hampered by the need for solvents that are often classed as highly hazardous. In this critical review, we evaluate their reactivity under mechanochemical conditions, which avoid the use of solvents.
2. The review describes the reaction performance, as well as the waste profile, of selected mechanochemical iodine(III) reactions in comparison to the corresponding solution-phase reactions, highlighting sustainability benefits as well as novel reactivity, providing guidance to readers on which reaction setups are more sustainable for each type of reaction.
3. The growing field of mechanochemistry has the potential to make organic synthesis more sustainable, and the green chemistry analysis used in this review should be applicable beyond iodine(III) reactions, providing further insight into sustainable organic synthesis.

## 1 Introduction

Hypervalent iodine chemistry has in recent decades developed into a flourishing field of research, with a wide variety of application areas ranging from organic synthesis to polymer chemistry.<sup>1</sup> Hypervalent iodine reagents are generally bench-stable, display low toxicity, and do not require inert reaction conditions, which are beneficial properties from a sustainability point of view. Drawbacks of this type of chemistry include the production of stoichiometric iodoarene (ArI) waste, and the common use of hazardous solvents both for reagent synthesis and use.<sup>1a,b</sup>

While the stoichiometric ArI waste can in some cases be avoided through the development of catalytic reactions,<sup>2</sup> the solvent use remains problematic. Due to the polarized structure of common hypervalent iodine reagents (Fig. 1), solubility can be challenging.<sup>3</sup> Beyond the polymeric structures PhIO and 2-iodoxybenzoic acid (IBX), also (diacetoxyiodo)benzene (DIB), [hydroxy(tosyloxy)iodo]benzene (HTIB), many iodonium salts, and benziodoxolones are sparingly soluble in most aprotic organic solvents. DMP and the fluorinated reagents [bis(trifluoroacetoxy)iodo]benzene (PIFA) and benziodoxoles display better solubility. The synthesis and application of hypervalent iodine reagents are frequently executed in the halogenated solvents dichloromethane (DCM), dichloroethane (DCE), chloroform, trifluoroethanol (TFE) and hexafluoroisopropanol (HFIP). Other solvents are dimethylformamide (DMF), tetrahydrofuran (THF) and rarely diethyl ether.<sup>1a</sup> Common solvent sustainability guides categorize all of these as “Red – major issues/hazardous”,<sup>4</sup> except for HFIP, which

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has not been evaluated in the guides but has a toxicity profile similar to that of TFE.<sup>5</sup>

The increasing use of acetonitrile (MeCN) and toluene, both listed as “Amber – some issues/problematic” in the solvent guides,<sup>4</sup> is an important step in the right direction. However, solvent-free methodology for synthesis and applications of hypervalent iodine compounds would be very attractive from a sustainability point of view.

Pioneering studies combining mechanochemistry with synthetic organic chemistry have demonstrated that mechanochemical organic reactions alleviate the need for a reaction solvent, can be high-yielding and time-efficient, can be less sensitive to air and moisture, and can sometimes give different reaction selectivity.<sup>6</sup> The use of liquid-assisted grinding (LAG), *i.e.*, the addition of a minimal amount of a liquid to the reaction vessel, can often facilitate mechanochemical reactions. While common solvents are often utilized as LAG additives, the volumes are considerably smaller and less of a sustainability concern.

Early reports on solvent-free reactions with hypervalent iodine reagents highlight that reactivity can be achieved through simple stirring under neat conditions,<sup>7</sup> and the combination with mechanochemical activation through grinding with a pestle and mortar or ball-milling is becoming more common. While many papers focus on reproducing reactions described in solution, the potential of combining mechanochemistry with hypervalent iodine chemistry is illustrated by several recent reports focusing on novel reactions that are unreported in solution.

## 2 Methodology and literature selection

### 2.1 Methods

In this critical review, we describe the synthesis and use of hypervalent iodine compounds in mechanochemical reactions. For a selected set of iodine(III) reactions, we have performed a

#### Iodine(III) compounds

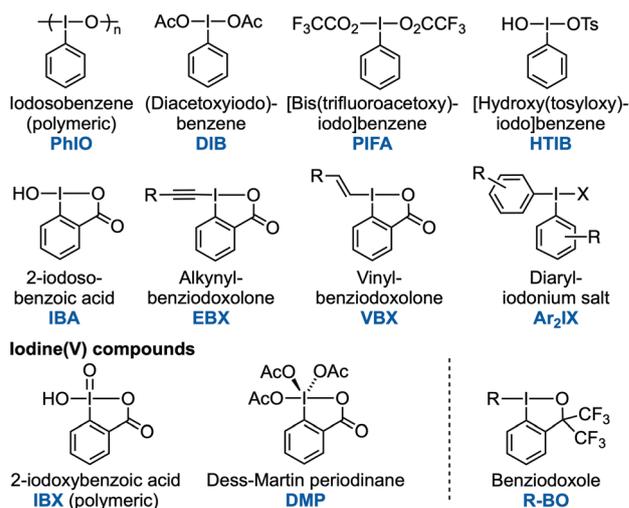


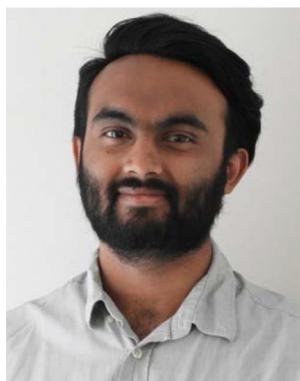
Fig. 1 Common hypervalent iodine reagents. Ts = *p*-toluenesulfonyl.

sustainability analysis, comparing the mechanochemical reactions to the corresponding solution-phase methods. The latter were selected to be as similar as possible to the mechanochemical reactions and refer only to transformations using hypervalent iodine reagents. The comparison includes yields for selected products, a sustainability assessment of the toxicity of the reaction solvent *vs.* LAG using the GSK solvent guide,<sup>4a</sup> and waste formation quantified using *E*-factors.<sup>8</sup> As few literature reports contain such data, we have calculated the *E*-factors for the transformations that have sufficient data to do so. We decided to calculate the *E*-factors *without purification*,<sup>5</sup> both to focus on the reactivity differences between mechanochemistry and solution-phase, and because of insufficient data on workup and purification in the reviewed papers. Solution-phase reactions performed on a much larger scale than the mechanochemical versions are presented without *E*-factors, as such comparisons are of limited use.



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Many methods have been demonstrated across a broader substrate range in solution, and later with a smaller mechanochemical scope. It is unclear whether this difference reflects an inherent advantage of the solvent-based method, or merely the extent of the substrates investigated, and so we have refrained from in-depth discussions of the scope and limitations of the methods.

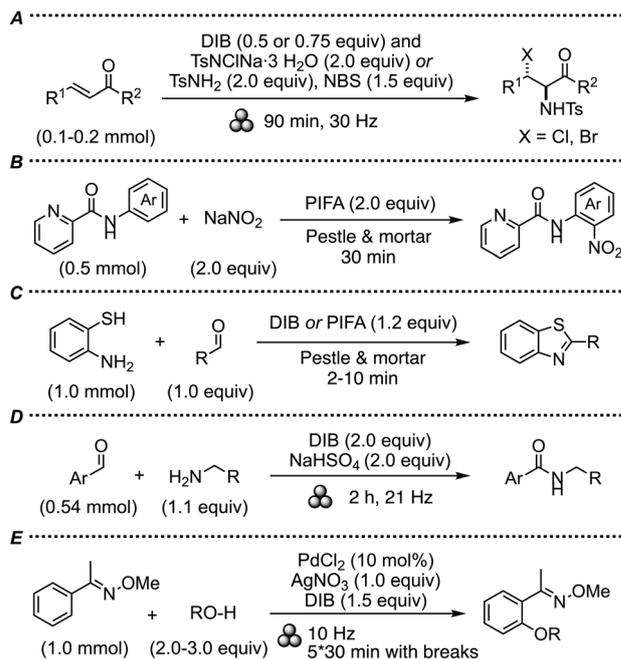
We have limited the solution-phase comparison and sustainability analysis to reactions utilizing the unique reactivity of the iodine(III) core to form new bonds, beyond simple oxidation. Other mechanochemical reactions with hypervalent iodine compounds are briefly described below.

## 2.2 Mechanochemical iodine(III) reactions

DIB is often utilized both as a substrate in the synthesis of more complex iodine(III) reagents, and as a potent oxidant.<sup>1a,b</sup> In this fashion, the synthesis of oligomeric iodosobenzene sulfate (PhIO)<sub>3</sub>·SO<sub>3</sub> was initiated by grinding DIB with NaHSO<sub>4</sub> in a mortar, followed by stirring in water.<sup>9</sup> Early reports from Ando and co-workers detailed that pulverization of iodosobenzene and HCl-treated silica gel in a mortar provided an oxidative chlorinating reagent, presumably PhI(OH)Cl, which was utilized *in situ* for reactions with alkenes and sulfides.<sup>10</sup>

DIB was also utilized in halogenation of arenes through grinding with NaCl, NaBr or I<sub>2</sub>,<sup>11</sup> and in the synthesis of oxadiazoles from acylhydrazones.<sup>12</sup> Wang and co-workers described aminohalogenation of the alkene moiety of α,β-unsaturated ketones through ball-milling with DIB in the presence of chloramine-T (TsNClNa) or *N*-bromosuccinimide (NBS, Scheme 1A).<sup>13</sup> Furthermore, fused N-heterocycles could be halogenated or thiocyanated by grinding with DIB and the corresponding alkali metal or ammonium salt.<sup>14</sup>

PIFA is a fluorinated and often more reactive analogue of DIB. A regioselective nitration of anilides was achieved



Scheme 1 Examples of mechanochemical iodine(III) reactions.

through grinding with PIFA and sodium nitrite, likely through a radical reaction (Scheme 1B).<sup>15</sup> A series of papers details oxidative transformations with DIB, PIFA, or HTIB to yield heterocycles by grinding with a pestle and mortar. In this fashion, the oxidative aromatization of 1,4-dihydropyridines, as well as an oxidative cyclization of 2-pyridyl- or 2-quinolylhydrazones, were realized.<sup>16</sup> The DIB-mediated cyclization of chalcone oximes gave diarylisoxazoles through grinding with DIB,<sup>17</sup> and benzothiazoles were synthesized from 2-aminothiophenols and aldehydes, using DIB or PIFA (Scheme 1C).<sup>18</sup>

Mal and co-workers reported a DIB-mediated oxidative amidation of aryl aldehydes and benzylamines, with sodium bisulfate added to control the reactivity of this otherwise explosive combination (Scheme 1D).<sup>19</sup> Alkynyl- and vinyl selenides were synthesized by grinding DIB with carboxylic acids and diaryldiselenides, resulting in a selenodicarboxylation.<sup>20</sup>

There are several reports on multicomponent reactions utilizing an iodine(III) reagent under mechanochemical conditions. Wang and co-workers demonstrated an elegant synthesis of dihydropyrroles through a sequential ball-milling reaction of amines, alkyne esters and chalcones, promoted by iodine and DIB.<sup>21</sup> Likewise, a multicomponent reaction with dihydrazinopyridazines and aromatic aldehydes yielded bis-triazolopyridazines through grinding with DIB.<sup>22</sup> Also, the one-pot synthesis of triazoles from hydralazines and aldehydes, through oxidative cyclization of the corresponding hydrazones with DIB or PIFA, could be achieved in a planetary ball-mill.<sup>23</sup> The authors highlighted that the sustainability metrics were considerably improved compared to the corresponding solution-phase reaction.



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Berit Olofsson did her PhD in asymmetric synthesis at KTH, Sweden, followed by postdocs with Prof. Aggarwal at Bristol University, UK and Prof. Bäckvall at Stockholm University (SU). She started her independent career at SU in 2006, and was promoted to full Professor in 2013. She serves as the Co-Director of Stockholm University Center for Circular and Sustainable Systems (SUCCESS), and is an Advisory Board

member of Chem and Angew. Chem. Olofsson's research focuses on development of synthetic methodology towards iodine(III) reagents and their applications in metal-free and sustainable methodology for organic synthesis, including the recent focus on mechanochemistry. Website link: <https://www.organ.su.se/bo/>



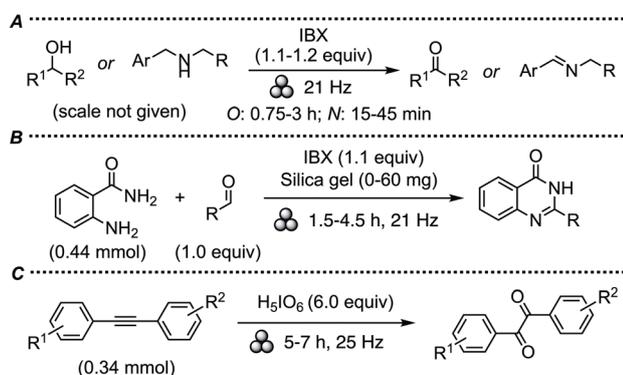
Transition metal-catalyzed reactions with DIB as oxidant are common in solution<sup>1a,b</sup> and mechanochemical versions of such reactions indicate that inert conditions are not required. A Pd-catalyzed *ortho*-C–H etherification of aryl oximes with a range of aliphatic alcohols proceeded well in the presence of DIB under ball-milling conditions (Scheme 1E).<sup>24</sup> In a DIB-mediated, Rh-catalyzed C–H amination with sulfamides, the catalyst was found to be much more stable than in solution-phase reactions.<sup>25</sup> Finally, a recent paper utilized DIB as a Lewis acid in a pestle and mortar-activated Pictet–Spengler-type reactions.<sup>26</sup>

Diaryliodonium salts (Ar<sub>2</sub>IX) are frequently used either as efficient arylation reagents<sup>27</sup> (see Section 5.1) or as aryl radical initiators in polymerization reactions.<sup>1c</sup> Recently, Golder and co-workers demonstrated that Ph<sub>2</sub>IPF<sub>6</sub> could be used under mechanoredox catalysis with the piezoelectric catalyst BaTiO<sub>3</sub> for free-radical polymerization (FRP) or reversible addition–fragmentation chain transfer (RAFT) polymerization to provide poly(meth)acrylates.<sup>28</sup>

### 2.3 Mechanochemical iodine(v) reactions

In 2014, Mal and co-workers performed an interesting study of the oxidative power of IBX under ball-milling conditions compared to reported solution-phase reactions.<sup>29</sup> Mechanochemical oxidation was efficient in a variety of reactions, including alcohol and amine oxidations to the corresponding aldehydes, ketones, or imines, as well as the one-pot synthesis of benzimidazoles, dithiane deprotection, and  $\alpha$ -haloketone synthesis from olefins (Scheme 2A).<sup>29</sup> Furthermore, the stoichiometric iodine(III) waste, 2-iodosobenzoic acid (IBA), could be re-oxidized *in situ* with Oxone to IBX, highlighting that iodine(v) compounds can both be formed and used under ball-milling conditions without explosions.

Another study demonstrated that while mechanochemical reactions between anilines and IBX caused explosions, the corresponding 2-aminobenzamides could be reacted with aldehydes and IBX to form quinazolinones (Scheme 2B).<sup>30</sup> IBX was also found to be the best oxidant in a mechanochemical synthesis of azo-based polymers.<sup>31</sup>



**Scheme 2** Examples of mechanochemical iodine(v) and iodine(vii) reactions.

### 2.4 Mechanochemical iodine(vii) reactions

The inorganic iodine(vii) reagent periodic acid (H<sub>5</sub>IO<sub>6</sub>) was demonstrated to be an efficient and divergent oxidant for polycyclic aromatic hydrocarbons, providing C–H oxidation under mechanochemical conditions and C–H iodination in solution.<sup>32</sup> Furthermore, it was utilized in the oxidation of internal alkynes to provide a large scope of 1,2-diketones under ball-milling conditions (Scheme 2C).<sup>33</sup>

The remainder of this review is focused on highlighting novel mechanochemical transformations with iodine(III) compounds, as well as providing a critical sustainability comparison with the corresponding solution-phase methodologies, where they exist.

## 3 Ligand exchange reactions

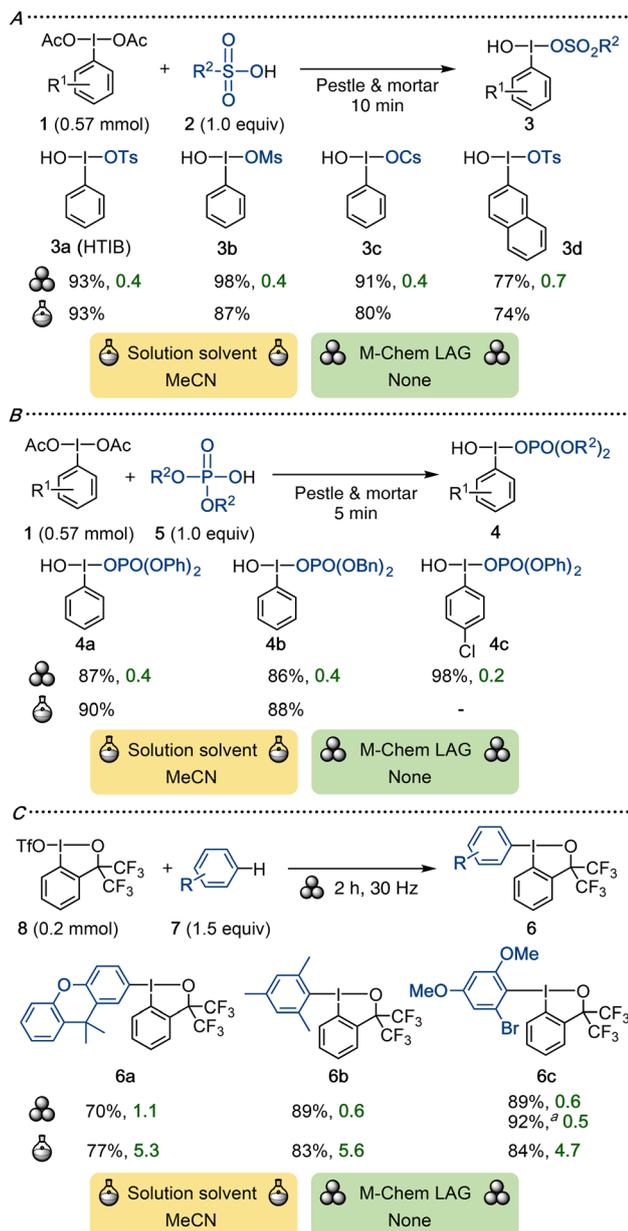
Reactions whereby hypervalent iodine compounds exchange an iodine ligand are called ligand exchanges. Such reactions are generally straightforward with heteroatom ligands, whereas introduction of carbon ligands can be more difficult.<sup>1a</sup>

DIB and HTIB are often used as substrates in ligand exchanges to reach more complex iodine(III) reagents in solution.<sup>1a,b</sup> In one of the early reports combining mechanochemistry with hypervalent iodine reagents, Yusubov and Wirth described the synthesis of HTIB derivatives by reacting (diacetoxyiodo)arenes **1** and sulfonic acid **2** *via* grinding with a pestle and mortar (Scheme 3A).<sup>34</sup> Evaporation of the liberated acetic acid afforded products **3** in good to excellent yields and with excellent waste profiles (*E*-factors < 1). In solution, the same transformation typically utilizes acetonitrile,<sup>1a</sup> classified as “Amber” by the GSK solvent guide, and proceeds in similarly high yields.<sup>35</sup> As the reported reaction scales are much larger than the mechanochemical ones, *E*-factor comparisons offer limited insight.<sup>5</sup> Eliminating the need for a problematic solvent enables a greener approach to these species, albeit reported here only on a small scale. By contrast, multi-gram syntheses of HTIB are well established in solution and are of commercial relevance.

[Hydroxy(phosphoryloxy)iodo]arenes **4** are structurally similar to HTIB, bearing a phosphate ligand in lieu of a tosylate. They were conveniently prepared in a solvent-free manner by grinding equimolar quantities of DIB **1** and phosphate ester **5** in a pestle and mortar. This efficiently provided the desired products **4** in high to excellent yields (Scheme 3B).<sup>36</sup> The corresponding reaction can be performed in aqueous acetonitrile with similar efficiency.<sup>37</sup> While direct comparison of *E*-factors is precluded due to the differences in reported reaction scale,<sup>5</sup> the mechanochemical reaction has impressively low *E*-factors, reflecting the minimal waste generated in the absence of solvent.

Yoshikai and co-workers reported a regioselective synthesis of arylbenziodoxoles **6** from arenes **7** and benziodoxole triflate **8** under both solution-phase and ball-milling conditions (Scheme 3C).<sup>38</sup> Reactions in acetonitrile for 24 h were performed in a glove-box and applied to a broad scope of arenes





**Scheme 3** Mechanochemical ligand exchange reactions. <sup>a</sup>2 mmol scale. Ms = methanesulfonyl; Cs = (1*R*)-10-camphorsulfonyl; Tf = trifluoromethylsulfonyl.

in high yields. While the mechanochemical reaction was only demonstrated across four substrates, the authors highlighted the utility of the method through a gram-scale synthesis of **6c** in 92% yield. The mechanochemical setup is attractive due to both the shorter reaction times and the excellent *E*-factors, which are 5–9 times lower than in solution.

## 4 Oxidative reactions

Iodine(III) compounds with two heteroatom ligands on iodine are widely employed oxidants under transition metal-free or

transition metal-catalyzed solution-phase conditions.<sup>1a,b</sup> Reactions commonly employ DIB (**1a**), PIFA (**9**) or HTIB (**3a**), and sometimes involve direct ligand transfer from iodine(III) to the substrate. Section 4 describes selected mechanochemical methods, including sustainability comparisons with the corresponding solution-phase methods.

### 4.1 Tosyloxylation

Carbonyl compounds readily undergo  $\alpha$ -oxidation upon treatment with various iodine(III) compounds, with  $\alpha$ -tosyloxylation using HTIB as the most well-known transformation. This reactivity is well-established under inert conditions in solution, either utilizing stoichiometric amounts of iodine(III) or combining catalytic amounts of iodoarene with a stoichiometric oxidant such as *m*CPBA.<sup>1a,39</sup>

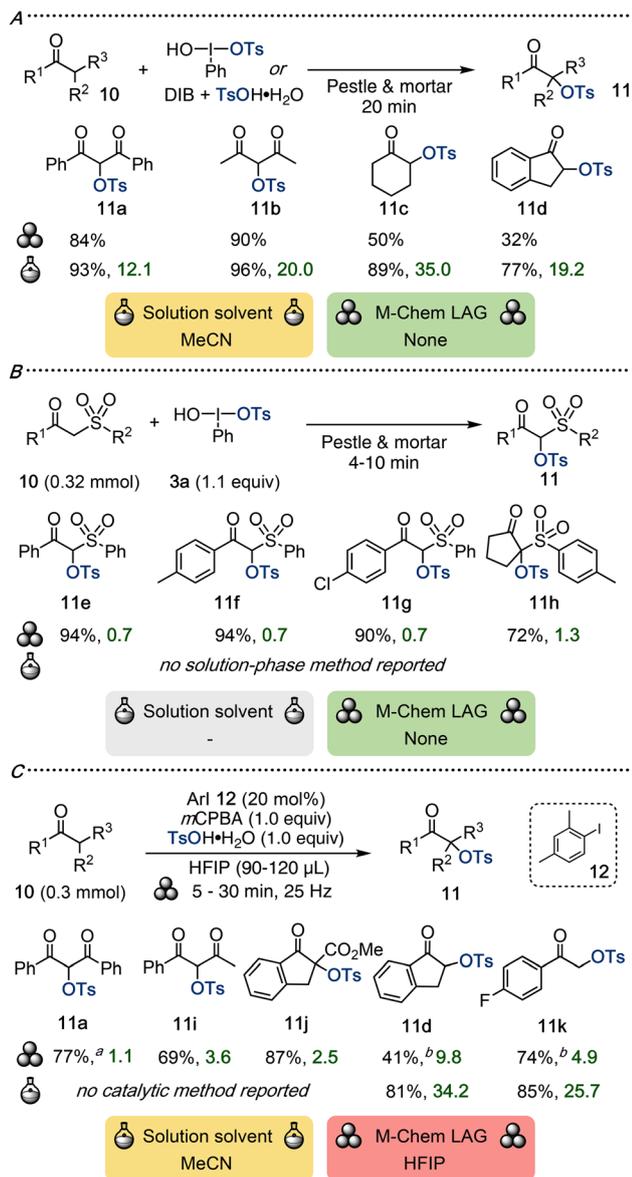
In 2005, Yusubov and Wirth demonstrated the first mechanochemical  $\alpha$ -sulfonyloxylation of carbonyl compounds **10** to yield products **11** (Scheme 4A).<sup>34</sup> The reactions were performed in a pestle and mortar, either using isolated HTIB or *in situ* formed reagent from DIB and tosic acid. Tosyloxylation of dicarbonyl substrates proceeded in good yields, whereas reactions with ketones or transfer of alternative sulfonyl groups gave reduced yields. Reactions performed in acetonitrile required increased temperatures to access such products,<sup>40</sup> which is unfeasible through simple grinding, highlighting an inherent limitation of this methodology. Unfortunately, the *E*-factors could not be calculated for the mechanochemical setup due to a lack of experimental data.

Varma and co-workers subsequently extended the mechanochemical tosyloxylation scope to include the facile synthesis of  $\alpha$ -tosyloxy  $\beta$ -keto sulfones **11e–11h** from HTIB (Scheme 4B).<sup>41</sup> Grinding of the substrates in a pestle and mortar produced a scope of nine products in good to excellent yields. A range of electronics, including aryl and cyclic alkyl substituents, were well tolerated. This singular mechanochemical procedure constitutes the only synthesis of  $\alpha$ -tosyloxy  $\beta$ -keto sulfones, and the low *E*-factors demonstrate a minimal environmental footprint.

Recently, our group investigated the efficiency of a range of iodine(III) reactions under ball-milling conditions. Within that study, we carried out tosyloxylation of carbonyl compounds **10** to give products **11** using a catalytic amount of 2,4-dimethyliodobenzene (**12**), with *m*CPBA and tosic acid as stoichiometric reagents and HFIP as LAG (Scheme 4C).<sup>42</sup> While catalytic iodine(III) reactions are prevalent in solution, this report constitutes the first example of a catalytic system with hypervalent iodine under mechanochemical conditions, highlighting that fast oxidation from iodine(I) to iodine(III) is feasible through ball-milling. The mechanochemical yields of **11d** and **11k** could be improved by preheating the ball-milling vessel and increasing the reagent amounts to partially overcome the limitations observed with less reactive substrates in the pestle and mortar reaction in Scheme 4A.

Comparison to solution-phase results for the catalytic reaction can only be performed for **11d** and **11k**, due to differing product scopes. Both products showcase considerably lower





**Scheme 4**  $\alpha$ -Tosyloxylations of carbonyl compounds. <sup>a</sup>No HFIP added. <sup>b</sup>1.5 equiv. *m*CPBA and tosic acid, preheated vessel.

*E*-factors in the mechanochemical protocol, despite lower yields being obtained with that method. While the need for toxic HFIP as LAG lowers the sustainability profile, the minimal volume needed (0.3–0.4 mL mmol<sup>-1</sup>) should be compared to solution-phase reactions in acetonitrile (10 mL mmol<sup>-1</sup>), which is also a problematic solvent. Furthermore, the synthesis of **11a** proceeded efficiently without use of HFIP.

To conclude, sulfonyloxylations of carbonyl compounds proceed well under both mechanochemical and solution-phase conditions. The catalytic method in Scheme 4C gives similar yields to the stoichiometric iodine(III) method in Scheme 4A, as illustrated by products **11a** (77% vs. 84%) and **11c** (41% vs. 32%). Though the *E*-factors of individual tosyloxylations may be lower for reactions using stoichiometric iodine

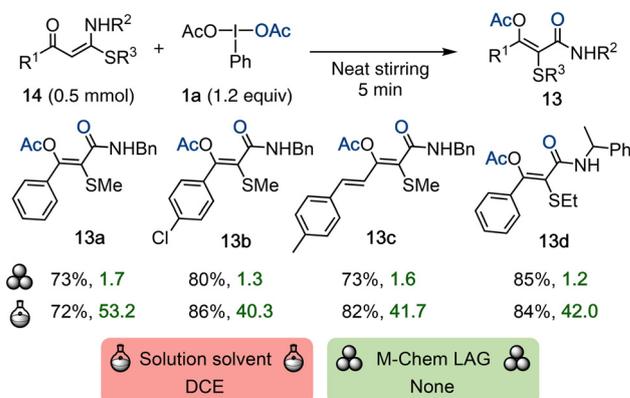
(III), the waste generated during reagent synthesis is not considered in such calculations. In addition to the consistently lower *E*-factors achieved with mechanochemistry, most examples proceed without need for any toxic additive. However, large-scale applications of the mechanochemical approach remain unreported.

## 4.2 Oxidative rearrangement

Yu and co-workers reported the synthesis of  $\alpha,\beta$ -unsaturated amides **13** through a DIB-mediated oxidation and alkythio migration of alkythio-functionalized enaminones **14** (Scheme 5).<sup>43</sup> The reaction was initiated by manually stirring the substrates with a glass rod in a glass vial for 5 minutes, and the resultant liquid was left under ambient conditions for an additional two hours until complete conversion of **14** was observed. This highlights that, while mechanochemical activation of the reaction was necessary, the continued reaction took place without it. The target compounds **13** were isolated in moderate to good yields across ten substrates of varying electronics. The authors also reported a solution-phase version with a substrate scope of 42 amides, which required the use of DCE, designated “Red – highly hazardous” by the GSK solvent guide<sup>4</sup> due to its toxicity and probable carcinogenicity. Furthermore, the DIB loading in solution was increased from 1.2 to 1.5 equiv. The solvent-free route is thus more favorable from a green chemistry perspective, both based on *E*-factor score and solvent toxicity.

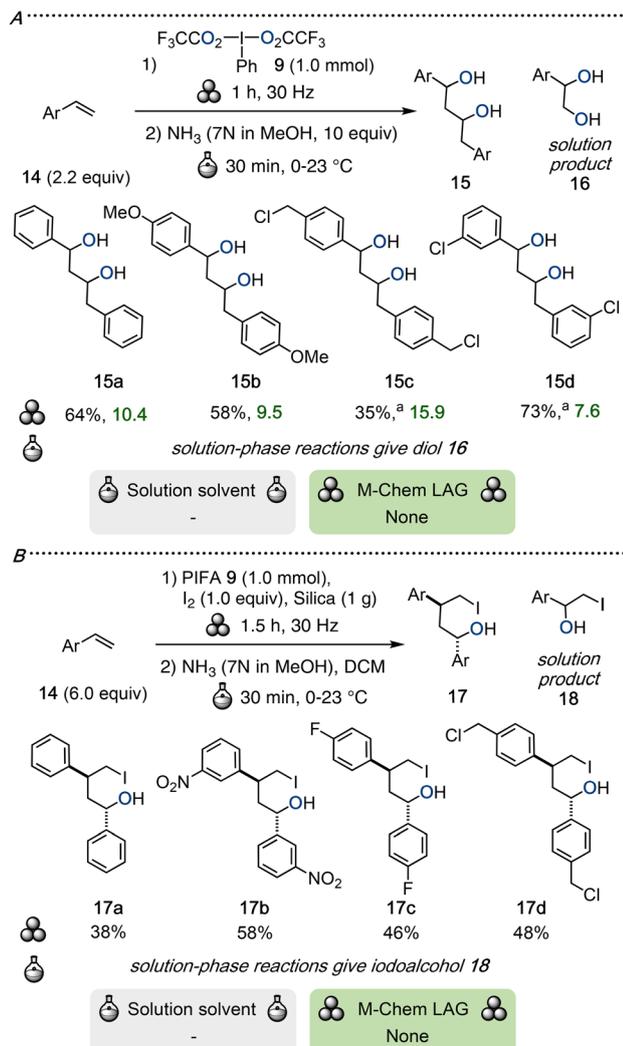
## 4.3 Oxidative functionalization of alkenes

Mechanosynthesis can proceed *via* pathways distinct from conventional solution-phase methods, giving access to products with different regio- or stereoselectivity. The groups of Yeung and Ke demonstrated that the mechanochemical dioxxygenation of styrenes **14** with PIFA yielded dimeric 1,3-diol **15** as the major product and monomeric 1,2-diol **16** as the side-product (Scheme 6A).<sup>44</sup> The reaction was conducted in a horizontal ball-mill and the *in situ* formed diester was subsequently treated with ammonia in methanol to give the corresponding diol **15**. In contrast, a one-pot reaction performed in dichloro-



**Scheme 5** DIB-mediated synthesis of conjugated amides.





**Scheme 6** PIFA-mediated oxidative dimerizations of alkene. <sup>a</sup>3.0 equiv. of 14.

methane (DCM) under reflux afforded the 1,2-diol **16** as sole product.<sup>45</sup> Mechanistic studies suggest that strong mechanical impact forces may induce dimerization of PIFA, thereby reducing the concentration of the active monomeric species and promoting an intramolecular cascade reaction between olefins to furnish the 1,3-disubstituted product. In solution, dissociated trifluoroacetate anions may instead selectively favor a direct substitution mechanism, thus following the conventional dioxygenation pathway to selectively give 1,2-diols.<sup>44</sup>

The calculated *E*-factors are relatively poor, which stem from side-product formation and the need for treatment with ammonia in methanol. Nonetheless, this method provides a novel synthetic route to 1,3-diols through the direct dioxygenation of styrenes, whereas conventional solution-phase routes to 1,3-diols require several steps.<sup>46</sup>

A mechanochemical 1,4-iodohydroxylation strategy was also developed by treating styrenes **14** with PIFA and molecular iodine under ball-milling conditions with silica as solid-

assisted grinding agent (SAG).<sup>44</sup> Quenching with ammonia in methanol furnished the corresponding 1,4-iodoalcohols **17** as single diastereomers in moderate yields (Scheme 6B). The same mechanistic rationale as above was employed to explain the observed selectivity in favor of **17** over the solution-phase product **18**. Though insufficient details are provided to accurately calculate *E*-factors, this protocol remains the only reported route to access these novel products.

Hypervalent iodine reagents are frequently employed in fluorinations to reach pharmaceutically relevant characteristics, such as increased metabolic stability and potency in medicines. In this vein, the groups of Stuart and Browne reported a mechanochemical fluorocyclization of functionalized alkenes *via* ball-milling.<sup>47</sup> Fluoroiodoxole **19** was employed as a fluorine source in reactions with alkenyl hydrazones **20** to yield 5-fluoro-tetrahydropyridazines **21** in high yields when activated by the use of HFIP as LAG (Scheme 7A). While the reaction could also be performed in similar yields with HFIP as solvent under inert conditions, the mechanochemical protocol affords much-improved *E*-factors through an 8-fold reduction of toxic HFIP.

In a similar fashion, treatment of alkenyl oximes **22** with fluoroiodoxole **19** produced 5-fluorodihydrooxazines **23** with DCM as LAG (Scheme 7B).<sup>47</sup> Notably, mechanochemical activation afforded higher yields than conventional synthesis in DCM due to suppressed side-product formation.<sup>47</sup> The mechanochemical *E*-factors are comparatively high due to the use of excess  $\text{AgBF}_4$  as reaction additive. However, the use of DCM is markedly reduced, along with the environmental footprint of the reaction.

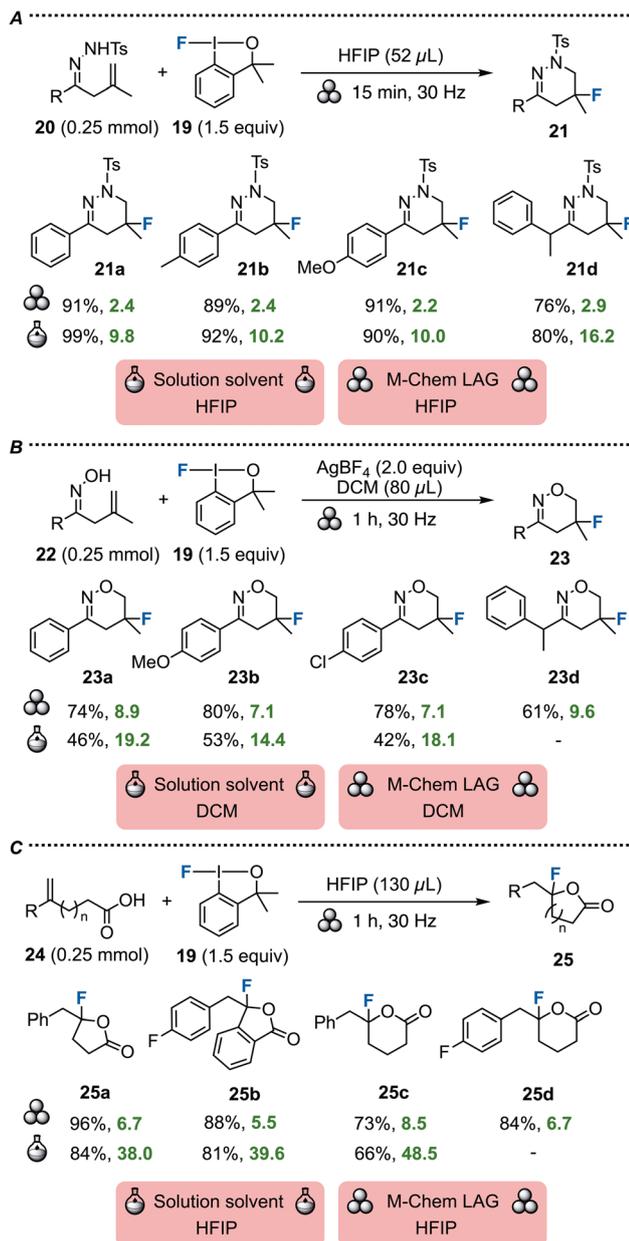
Finally, the authors reported an intramolecular fluorolactonization protocol under ball-milling conditions, using HFIP as LAG (Scheme 7C).<sup>47</sup> Fluoroiodoxole **19** was applied to unsaturated carboxylic acids **24** to furnish  $\gamma$ - and  $\delta$ -lactones **25**.

Compared to their previously reported solution-based method in HFIP solvent,<sup>48</sup> higher yields were obtained. Furthermore, the volume of toxic HFIP was reduced by a factor of 6, thereby leading to much-improved *E*-factor scores indicative of a more sustainable process by mechanochemistry.

#### 4.4 Oxidative sulfonylation

Sulfonylation of imidazothiazoles and related scaffolds is frequently copper-catalyzed and often involves harmful solvents such as DMF, elevated temperatures, and long reaction times.<sup>49</sup> In 2025, Hamze and co-workers developed a PIFA-mediated mechanochemical route towards the regioselective C5-sulfonylation of imidazothiazoles.<sup>50</sup> For this purpose, imidazo[2,1-*b*]thiazoles **26** were ground with aryl methyl sulfides **27** and PIFA in a vibrational ball-mill to produce a broad scope of arylthiolated products **28** (Scheme 8). The procedure was also upscaled to afford 1.36 g of the desired product **28a** after recrystallization. A mechanistic investigation indicated an ionic pathway with a highly electrophilic iodine(III)-S(Me)Ar intermediate that is attacked by the imidazothiazole, whereas related methods proposed radical mechanisms.<sup>51</sup> The authors compared the environmental impact of their method to per-



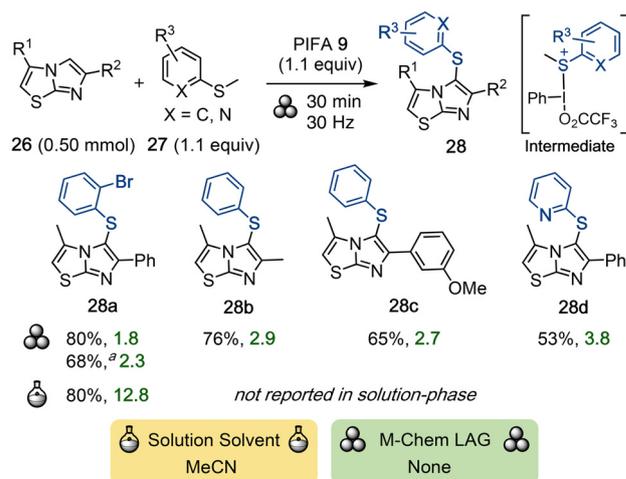


**Scheme 7** Oxidative fluorinations with fluorobenziodoxole **19**.

forming the synthesis of **28a** in acetonitrile at 50 °C. The *E*-factor of the solution-based reaction is 100 times higher due to the need for excess reagents, solvent waste, and an aqueous/DCM workup to quench residual PIFA.

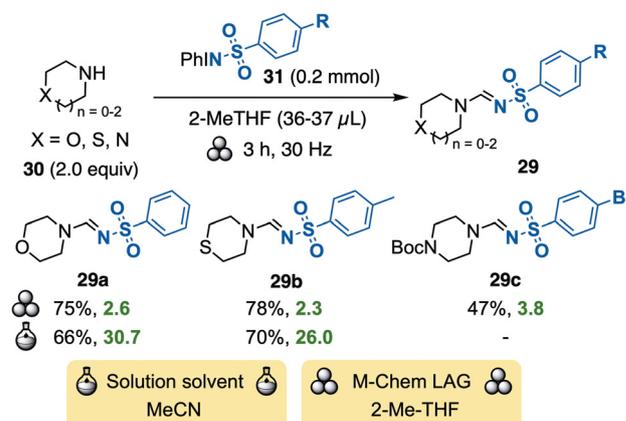
#### 4.5 Reactions with iodonium sulfonimides

Iodonium sulfonimides (PhINSO<sub>2</sub>R) are iodine(III) reagents commonly used in nitrogen-transfer reactions, *e.g.*, imination or aziridination reactions.<sup>1a</sup> They were recently applied in a metal-free imination to provide sulfondiimines, where mechanochemical conditions proved less efficient than reactions in MeCN.<sup>52</sup> The same year, Sen & co-workers reported a



**Scheme 8** Regioselective sulfenylation of imidazothiazoles. <sup>a</sup>5 mmol scale.

synthesis of *N*-sulfonyl amidines **29** by ball-milling cyclic amines **30** with the iodine(III) reagents *N*-sulfonyl iminoiodinanes **31** and 2-methyl-THF as LAG (Scheme 9).<sup>53</sup> The substrate scope included several types of heterocyclic amines, giving C–N coupled products **29** in moderate to good yields. The proposed mechanism is complex and involves a ring contraction step to provide the added carbon in **29**, motivating the need for 2 equiv. of amines **30**. The method can be compared with the previously reported DIB-mediated transformation in acetonitrile, which has a large scope and similar yields.<sup>54</sup> While the *E*-factors of the mechanochemical reactions are considerably lower, they do not show the waste formed in the synthesis of iminoiodinanes **31** from sulfonamides, DIB, and KOH in methanol, which is not required in the solution-phase reaction. A fair comparison would be based upon the entire two-step process, but the *E*-factors for the synthesis of iminoiodinanes **31** cannot be calculated due to a lack of experimental details.



**Scheme 9** Synthesis of *N*-sulfonyl amidines.



## 5 Transfer of carbon ligands

Iodine(III) reagents with two carbon ligands are efficient reagents for the transfer of a carbon ligand to a nucleophile under metal-free or transition metal-catalyzed conditions. The most common reagents are diaryliodonium salts, alkynyliodonium salts, and vinyliodonium salts, as well as the cyclic reagents ethynylbenziodoxolones (EBX), vinylbenziodoxolones (VBX) and trifluoromethylbenziodoxol(on)es (called Togni's reagents).<sup>1a</sup>

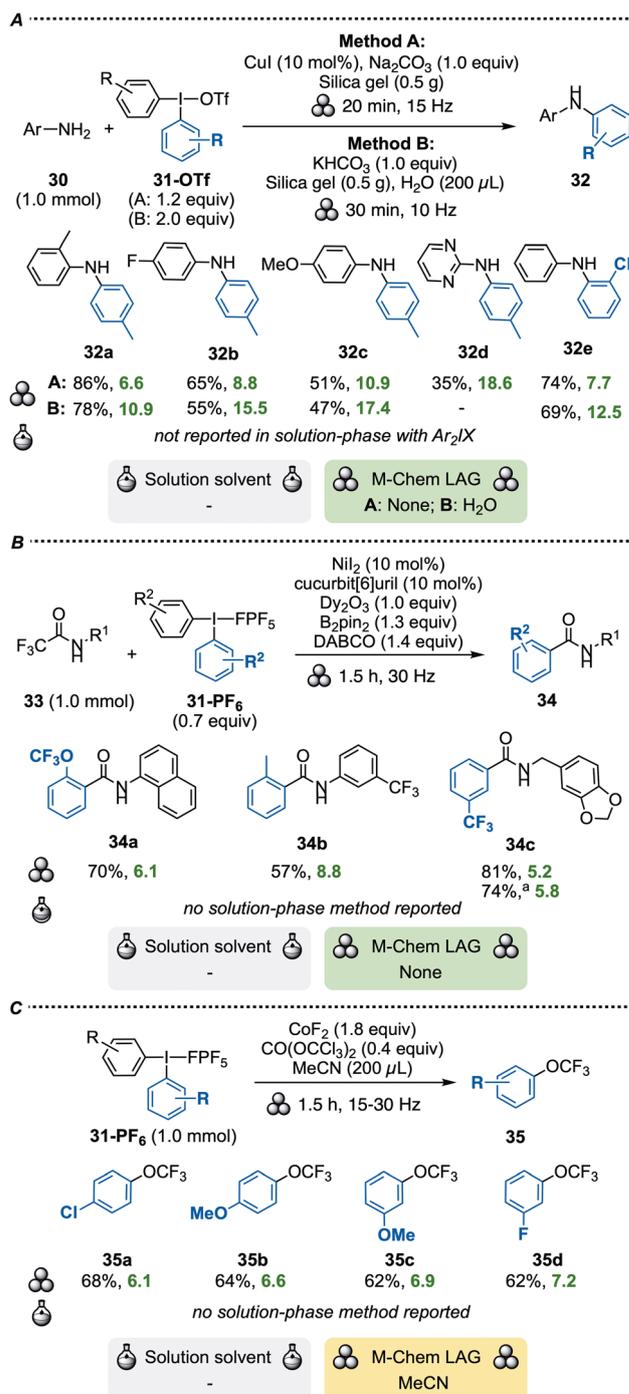
### 5.1 Arylations

Diaryliodonium salts ( $\text{Ar}_2\text{IX}$ ) are efficient electrophilic arylation reagents under both transition metal-catalyzed and metal-free conditions, and have found broad applications in solution-phase reactions.<sup>27</sup> In 2020, Li and co-workers disclosed the first mechanochemical reactions with  $\text{Ar}_2\text{IX}$ , in which arylation of anilines **30** with diaryliodonium triflates **31-OTf** was achieved by ball-milling either under copper-catalyzed or metal-free conditions to provide diarylamines **32** (Scheme 10A, methods A & B).<sup>55</sup> Interestingly, both reaction setups utilized silica gel as SAG, and the metal-free method also employed water as LAG. Method A delivered slightly higher yields than method B and could also be applied for the arylation of heterocyclic amines in moderate yields. Aliphatic amines proved to be poor substrates with both methods. Method A is also superior in terms of *E*-factors, as method B requires excess reagent usage and LAG.

While there are reports with limited scope for metal-free arylation of anilines with  $\text{Ar}_2\text{IX}$  in DMF or toluene,<sup>56</sup> as well as a Cu-catalyzed method in DCM/DMSO,<sup>57</sup> those products do not overlap with Li's product scope,<sup>55</sup> making a direct comparison unfeasible.

The groups of Iaroshenko and Mkrtychyan reported the mechanochemical activation of trifluoroacetamides **33** to achieve defluorinative arylation to amides **34** (Scheme 10B).<sup>58</sup> Several aryl sources were suitable for this transformation under ball-milling conditions, ranging from boronic acids and siloxanes to dimethylsulfonium salts and  $\text{Ar}_2\text{IPF}_6$  **31-PF<sub>6</sub>**. The arylation required nickel-catalysis combined with stoichiometric amounts of lanthanide additive and  $\text{B}_2\text{pin}_2$  to furnish the products in moderate to high yields. A range of electronics and sterics, as well as aliphatic amides, were tolerated. A large-scale reaction was also demonstrated, providing 2.39 g of **34c**. Considering the many additives required for the reaction, the associated *E*-factors are quite low. We did not find any equivalent reactions in solution, and the authors state that the corresponding solution-phase reactions failed to produce the target product. On the other hand, conventional amide coupling methodologies to amides **34** may be more accessible than the use of substrates **33**.

Iaroshenko and co-workers subsequently developed a trifluoromethoxylation protocol utilizing a combination of  $\text{CoF}_2$  and triphosgene to produce an  $\text{OCF}_3$  source *in situ* under ball-milling conditions. This system was applied to a number of different aryl sources, including  $\text{Ar}_2\text{IPF}_6$  **31-PF<sub>6</sub>** to produce 4



**Scheme 10** Arylations with diaryliodonium salts. <sup>a</sup>10 mmol scale. DABCO = (1,4-diazabicyclo[2.2.2]octane).

examples of products **35** (Scheme 10C).<sup>59</sup> While there is no solution-phase methodology for this reaction with hypervalent iodine reagents to allow for comparison, there is a plethora of methodologies to conduct this transformation.<sup>60</sup>

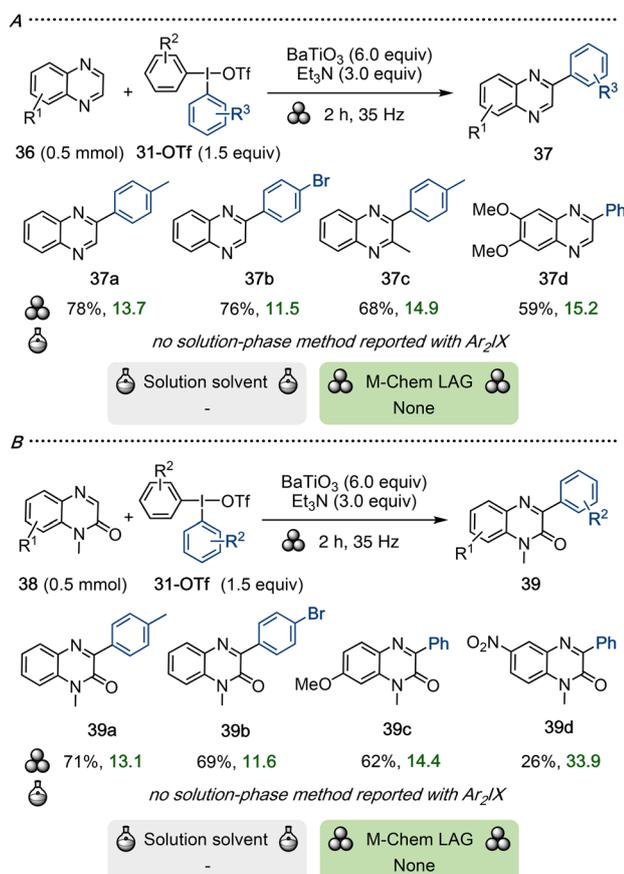
In 2019, Ito and co-workers pioneered the use of piezoelectric materials to carry out mechanochemical methodologies with redox-sensitive compounds, where aryldiazonium salts were



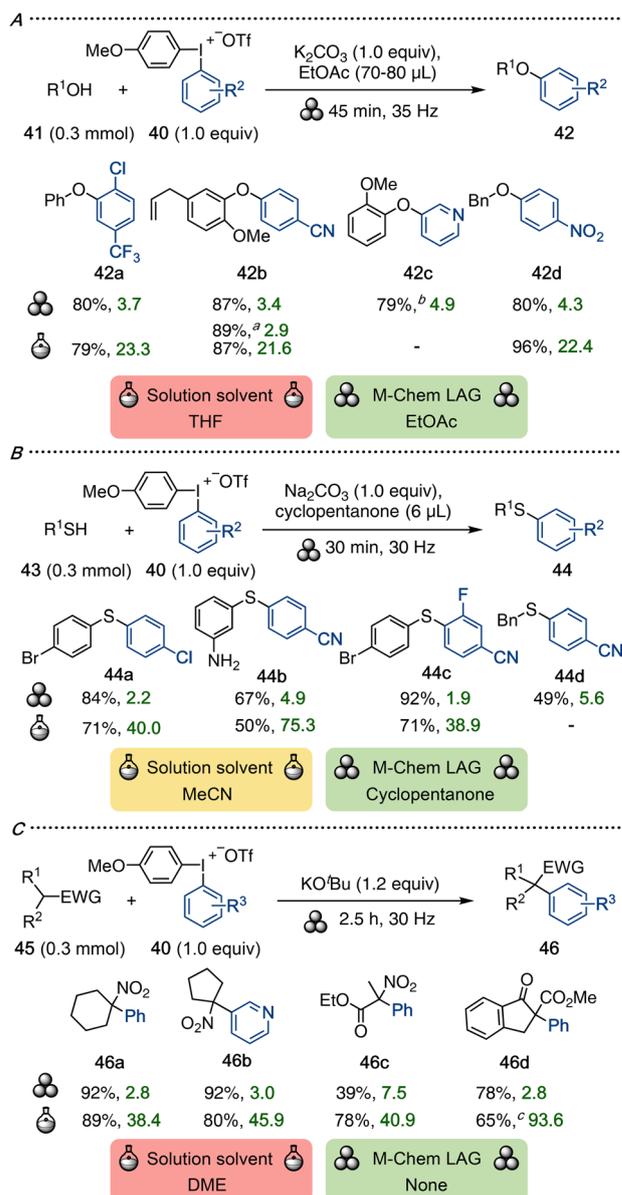
utilized as an aryl radical source for arylation and borylation reactions.<sup>61</sup> In this sense, mechanical force from milling causes a polarity within the material, similar to an excited state of a photo-excitabile material.<sup>6a</sup> Li and co-workers subsequently showed that diaryliodonium triflates **31-OTf** could be used as an alternative aryl source in C–H arylation of quinoxalines **36** through a mechanoredox reaction with the piezoelectric material BaTiO<sub>3</sub> (Scheme 11A).<sup>62</sup> Ball-milling efficiently delivered products **37** in moderate to good yields.

The authors extended this strategy towards quinoxalinones **38**, which delivered the corresponding products **39** in similar yields (Scheme 11B).<sup>62</sup> The *E*-factors for these reactions are higher than for previous arylation examples due to the required excess of piezoelectric material and triethylamine. However, the BaTiO<sub>3</sub> could be reused several times without marked loss of activity. As there is no solution-phase method to generate the targeted products, a comparison cannot be made.

Our group recently reported mechanochemical arylations of a range of *O*-, *S*- and *C*-nucleophiles (Scheme 12).<sup>42</sup> Using known solution-phase methods as a starting point,<sup>63</sup> we investigated the reactivity under ball-milling conditions in the presence of LAGs that were selected based on the GSK solvent guide. Unsymmetric diaryliodonium salts (Ar<sup>1</sup>Ar<sup>2</sup>IOTf, **40**) were utilized to chemoselectively transfer the more electron-poor aryl moiety, giving iodoanisole as waste.<sup>64</sup>



**Scheme 11** Piezoelectric mechanoredox arylations.



**Scheme 12** Transition-metal free arylations. **40** is drawn as an ion pair as it is unsymmetric. <sup>a</sup>3.0 mmol scale with 0.45 mL LAG; <sup>b</sup>milling time: 15 min with **41** and base, then 2 h after addition of **40**; <sup>c</sup>with chiral Ar<sub>2</sub>I<sup>+</sup>X<sup>-</sup>, 37% ee.

A LAG was imperative for arylations of phenols and alcohols **41**, and ethyl acetate was hence used as a LAG in the synthesis of aryl ethers **42** (Scheme 12A). The scope included a large-scale synthesis of **42b** in 89% yield. Arylation of *S*-nucleophiles **43** to products **44** required minimal amounts of a LAG, and the green solvent cyclopentanone was selected for this purpose (Scheme 12B). *C*-Arylations of nitroalkenes and other alkanes with EWG (**44**) proceeded well without a LAG (Scheme 12C).

A range of electronics and sterics were tolerated on the explored nucleophiles. Aryl groups decorated with electron-withdrawing groups (EWGs) and/or *ortho*-substituents were efficiently transferred, whereas electron-rich aryl groups were



more challenging.<sup>42</sup> The article also contained a benchmarking section where reported solution-phase methodology under inert conditions<sup>63</sup> was utilized to synthesize selected products in the mechanochemical scope. Interestingly, yields were similar under standard reaction conditions, whereas more concentrated or neat reactions gave considerably lower yields, indicating the importance of mechanochemical activation.<sup>42</sup>

The sustainability analysis highlights that the problematic solvents THF, dimethoxyethane (DME) and MeCN were avoided through the ball-milling approach, which instead used small amounts of green solvents as LAGs. Furthermore, the mechanochemical *E*-factors were consistently lower, ranging from a 5- to 20-fold reduction in waste, signifying a much-improved environmental footprint.

## 5.2 Alkynylations

Ethynylbenziodoxolones (EBX) are commonly used as electrophilic alkynylation reagents, often allowing for more chemoselective and predictive reactions than alkynyl(aryl)iodonium salts due to the stabilizing benziodoxolone core.<sup>1a</sup> Waser and co-workers have popularized EBX chemistry under both transition metal-catalyzed and metal-free conditions, including the gold-catalyzed C–H alkynylation of indole derivatives.<sup>65</sup> The C2-selective alkynylation of indoles with EBX has been reported under Rh- or Co-catalyzed inert conditions.<sup>66</sup>

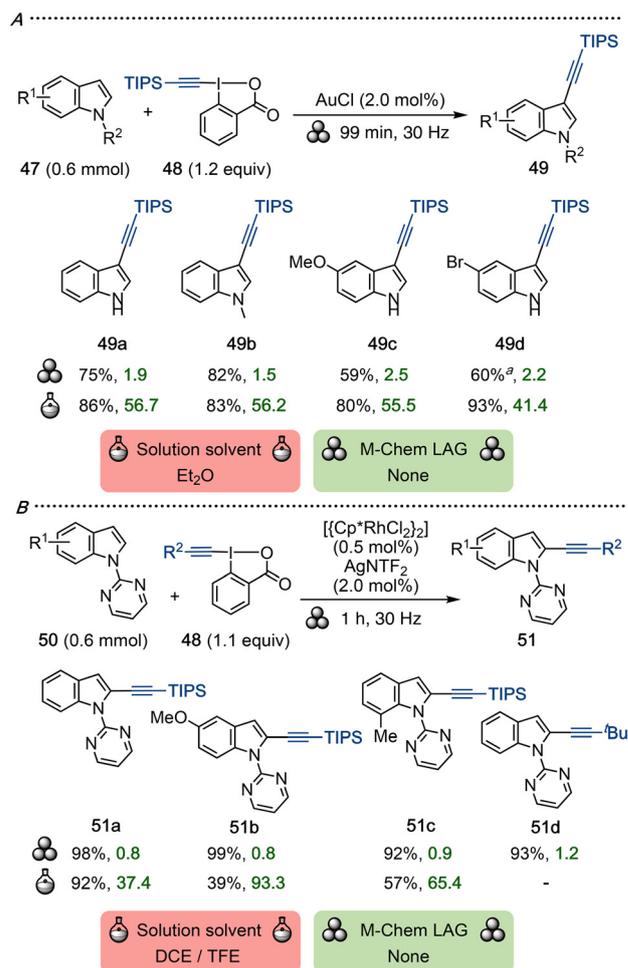
Bolm and co-workers developed mechanochemical versions of these transformations using two different transition metal-catalyzed systems to achieve C3- or C2-selective alkynylation under ball-milling conditions.<sup>67</sup> Following Waser's precedent in solution-phase,<sup>65a</sup> indoles **47** were regioselectively alkynylated with TIPS-EBX **48** to yield products **49** using AuCl as catalyst (Scheme 13A). The reaction proceeded well with both NH- and *N*-alkyl indoles, and a C3-methylated substrate was instead alkynylated in the C2 position, following Waser's observations.

To reach a general method for C2 alkynylation, a Rh-catalyzed method was developed for *N*-pyrimidyl indoles **50** (Scheme 13B). The reaction occurred within one hour, and the scope of **51** includes a variety of substituted indoles, although EWG-decorated indoles were formed in lower yield. Silylated EBX as well as alkyl-EBX reagents were tolerated in the reaction.

While solution-based methods work well for both types of alkynylation,<sup>65a,66</sup> the catalyst loadings and the reaction times were reduced in the mechanochemical setup. Furthermore, it avoids the handling of the hazardous solvents diethyl ether, DCE and TFE, and does not require inert conditions. The calculated *E*-factors for the ball-milling method are excellent and dramatically improved compared to the solution-phase reactions, signifying a greener and more resource-efficient process.

## 5.3 Synthesis of alkenes

Vinylbenziodoxolones (VBX) and vinylbenziodoxoles (VBO) were recently demonstrated as electrophilic vinylation reagents under both transition metal-free and transition metal-catalyzed conditions.<sup>68</sup> They offer more tunable reactivity than acyclic vinyl(aryl)iodonium salts, and the three reagent types can be screened to fine-tune the reactivity in vinylation.



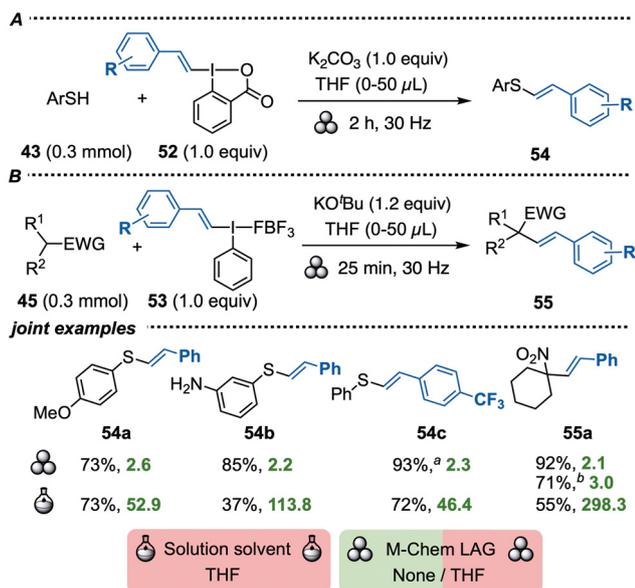
**Scheme 13** Transition metal-catalyzed alkynylations with EBX. <sup>a</sup>AuCl 3.0 mol%.

We investigated the vinylation of *S*- and *C*-nucleophiles under ball-milling conditions, and found that VBX **52** was suitable for the *S*-vinylation of thiols to give products **54** (Scheme 14A). Vinylidonium salts **53** were preferred in the *C*-vinylation of nitroalkenes and  $\beta$ -ketoesters to yield products **55**, here exemplified with the synthesis of **55a** on both small and large scales (Scheme 14B).<sup>42</sup>

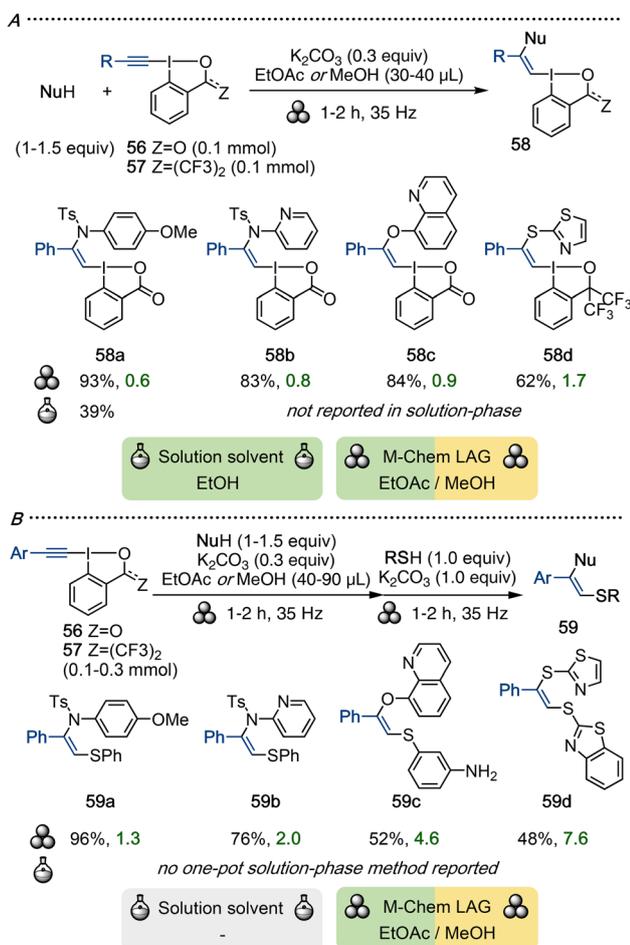
The corresponding solution-phase vinylation reactions require inert conditions in anhydrous THF and give similar or lower yields.<sup>68a,69</sup> The *E*-factors in solution are very high, which further highlights the benefits of the mechanochemical transformation.

VBX compounds with a  $\beta$ -heteroatom substituent (X-VBX) are formed through  $\beta$ -addition of various heteroatom nucleophiles to EBX. This transformation was demonstrated in solution-phase by Waser and co-workers,<sup>70</sup> and Yoshikai's group developed the corresponding transformation from ethynylbenziodoxoles (EBO) to yield X-VBO.<sup>71</sup> This type of reactivity was unexplored under mechanochemical conditions, which inspired our group to embark upon the investigation depicted in Scheme 15A.<sup>72</sup> A wide variety of *N*- and *O*-nucleophiles





**Scheme 14** Transition metal-free vinylation with VBX. <sup>a</sup>0.2 mmol scale with LAG. <sup>b</sup>3.0 mmol scale, milling time: 15 + 10 min.



**Scheme 15** Synthesis of X-VBX/VBO and one-pot synthesis of complex alkenes.

underwent efficient addition to EBX **56** under ball-milling conditions when ethyl acetate was utilized as LAG. Reactions with electron-rich nucleophiles proceeded smoothly in a 1.5 mL vessel, whereas weaker nucleophiles required a 5 mL vessel with a larger ball to ensure sufficient reactivity. *S*-Nucleophiles were too reactive in reactions with EBX, resulting in byproduct formation. Reactions with EBO **57** were, on the other hand, selective for mono-addition, and yielded a range of *S*-VBO products (exemplified by **58d**) with methanol as LAG.

A one-pot reaction combining the synthesis of X-VBX/VBO **58** with a subsequent *S*-vinylation to reach bis(hetero)-substituted *Z*-alkenes **59** was subsequently developed (Scheme 15B).<sup>72</sup> A large scope was demonstrated by variation of the first nucleophile and the thiol, and moderate to excellent yields of **59** were obtained within 2–4 hours of ball-milling.

Comparing the first method with solution-phase methodology<sup>69</sup> highlights that improved yields and *E*-factors were obtained under mechanochemical conditions, while the major influence on the solution-phase *E*-factor originates from the use of sustainable solvent ethanol. The one-pot reaction for the synthesis of alkenes **59** was also evaluated in the solution-phase, but failed under a range of conditions, which is likely due to the mismatch of solvents reported for the separate steps (EtOH vs. dry, degassed THF). To the contrary, the ball-milling method is fast, clean, and high yielding, illustrating the utility of mechanochemistry in organic synthesis.

## 6 Conclusions and outlook

The combination of mechanochemistry with hypervalent iodine chemistry has been investigated in a wide range of reactions. In this critical review, we highlighted several mechanochemical iodine(III) reactions where solution-phase reactions either fail or give different types of products. We also compared the reactivity between mechanochemical and solution-phase reactions when possible, and evaluated the methods from a sustainability perspective. We found that the calculated *E*-factors for solution-phase reactions were often dominated by solvent contributions, and moderate to great improvements in the waste profiles were observed under mechanochemical conditions. Furthermore, mechanochemical reactions avoid a range of hazardous reaction solvents and inert conditions that are required in the solution phase.

Mechanochemical activation of hypervalent iodine compounds holds the potential to open a new and more sustainable era of hypervalent iodine research, with novel reactivity to be discovered. Challenges of this growing research field include that the high energy environment can lead to leaching of trace metals from the reaction vessels, requiring careful control over reaction materials.<sup>73</sup> While transfer of the crude reaction from the reaction vessel can be difficult and require solvent in small scale reactions, such issues can be better handled at large scale. The development of large-scale or industrial processes could also allow alternative workup and



purification procedures, further amplifying sustainability benefits. We have highlighted a handful of up-scaled mechanochemical reactions in the review, but further investigations are needed, especially considering that up-scaling of hypervalent iodine reactions needs to be done with care both in solution and in the solid phase.<sup>74</sup>

To conclude, we believe that the demonstrated possibilities to reach different reaction pathways, or to develop one-pot reactions for systems that cannot be combined in solution, can be key to new discoveries in hypervalent iodine chemistry as well as in other parts of organic synthesis and catalysis.

## Author contributions

Conceptualization: SD, BO; investigation: PÖ, SD, BO; visualization: PÖ, SD, BO; project administration: BO; funding acquisition: BO; writing – original draft: PÖ, SD, BO; writing – review & editing: PÖ, BO.

## Conflicts of interest

There are no conflicts to declare.

## Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: method description and *E*-factor calculations. See DOI: <https://doi.org/10.1039/d6gc00367b>.

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## References

- (a) A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2024, **124**, 11108; (b) *The Chemistry of Hypervalent Halogen Compounds*, ed. B. Olofsson, I. Marek and Z. Rappoport, Wiley, 2019; (c) A. D. Asandei, *Chem. Rev.*, 2016, **116**, 2244.
- (a) K. Ishihara and K. Muniz, in *Iodine Catalysis in Organic Synthesis*, Wiley-VCH, Weinheim, Germany, 2022; (b) F. V. Singh, S. E. Shetgaonkar, M. Krishnan and T. Wirth, *Chem. Soc. Rev.*, 2022, **51**, 8102.
- V. V. Zhdankin and J. D. Protasiewicz, *Coord. Chem. Rev.*, 2014, **275**, 54.
- (a) C. M. Alder, J. D. Hayler, R. K. Henderson, A. M. Redman, L. Shukla, L. E. Shuster and H. F. Sneddon, *Green Chem.*, 2016, **18**, 3879; (b) D. Prat, A. Wells, J. Hayler, H. Sneddon, C. R. McElroy, S. Abou-Shehada and P. J. Dunn, *Green Chem.*, 2016, **18**, 288.
- See the SI for details.
- (a) J. L. Howard, Q. Cao and D. L. Browne, *Chem. Sci.*, 2018, **9**, 3080; (b) J.-L. Do and T. Friščić, *ACS Cent. Sci.*, 2017, **3**, 13; (c) V. Martinez, T. Stolar, B. Karadeniz, I. Brekalo and K. Užarević, *Nat. Rev. Chem.*, 2023, **7**, 51; (d) J. G. Hernández and C. Bolm, *J. Org. Chem.*, 2017, **82**, 4007.
- O. Prakash and V. Sharma, *Indian J. Chem.*, 1999, **38B**, 229.
- R. A. Sheldon, *Green Chem.*, 2023, **25**, 1704.
- A. Y. Kuposov, B. C. Netzel, M. S. Yusubov, V. N. Nemykin, A. Y. Nazarenko and V. V. Zhdankin, *Eur. J. Org. Chem.*, 2007, 4475.
- (a) H. Sohmiya, T. Kimura, P. Bauchat, M. Fujita and T. Ando, *Chem. Lett.*, 1991, **20**, 1391; (b) H. Sohmiya, T. Kimura, M. Fujita and T. Ando, *Chem. Lett.*, 1992, **21**, 891; (c) H. Sohmiya, T. Kimura, M. Fujita and T. Ando, *Tetrahedron*, 1998, **54**, 13737.
- N. N. Karade, G. B. Tiwari, D. B. Huple and T. A. J. Siddiqui, *J. Chem. Res.*, 2006, **2006**, 366.
- V. S. Rao and K. V. G. Chandra Sekhar, *Synth. Commun.*, 2004, **34**, 2153.
- (a) G.-W. Wang and X.-L. Wu, *Adv. Synth. Catal.*, 2007, **349**, 1977; (b) X.-L. Wu, J.-J. Xia and G.-W. Wang, *Org. Biomol. Chem.*, 2008, **6**, 548.
- D. R. Indukuri, G. R. Potuganti and M. Alla, *Synlett*, 2019, 1573.
- D. An, W. Song, Z. Peng, Y. Zhang and W. Dong, *ChemistrySelect*, 2018, **3**, 12946.
- (a) P. Kumar, *Chin. J. Chem.*, 2009, **27**, 1487; (b) P. Kumar, *Chem. Heterocycl. Compd.*, 2012, **47**, 1237.
- K. V. G. Chandra Sekhar, T. V. N. V. T. Sasank, H. N. Nagesh, N. Suresh, K. M. Naidu and A. Suresh, *Chin. Chem. Lett.*, 2013, **24**, 1045.
- P. Kumar, Meenakshi, S. Kumar, A. Kumar, K. Hussain and S. Kumar, *J. Heterocycl. Chem.*, 2012, **49**, 1243.
- T. Kumar Achar and P. Mal, *Adv. Synth. Catal.*, 2015, **357**, 3977.
- J. P. Das, U. K. Roy and S. Roy, *Organometallics*, 2005, **24**, 6136.
- H. Xu, H.-W. Liu, K. Chen and G.-W. Wang, *J. Org. Chem.*, 2018, **83**, 6035.
- R. Aggarwal, Mamta and G. Sumran, *ARKIVOC*, 2019, **2019**, 190.
- L. Gonnet, C. André-Barrès, B. Guidetti, A. Chamayou, C. Menendez, M. Baron, R. Calvet and M. Baltas, *ACS Sustainable Chem. Eng.*, 2020, **8**, 3114.
- K. Zhou, H.-Y. Hao, Y.-J. Mao, Q.-Z. Wu, L. Chen, S. Wang, W. Jin, Z.-Y. Xu, S.-J. Lou and D.-Q. Xu, *ACS Sustainable Chem. Eng.*, 2021, **9**, 4433.
- X. Lu, Y. Bai, J. Qin, N. Wang, Y. Wu and F. Zhong, *ACS Sustainable Chem. Eng.*, 2021, **9**, 1684.
- M. Panda, A. Bera, D. Dandapat, P. Barik, S. Dhara, M. Iqbal, K. Pramanik, S. Pramanik and S. Samanta, *Asian J. Org. Chem.*, 2025, **14**, e00118.
- (a) E. A. Merritt and B. Olofsson, *Angew. Chem., Int. Ed.*, 2009, **48**, 9052; (b) P. Villo and B. Olofsson, in *Patai's*



- Chemistry of Functional Groups: The Chemistry of Hypervalent Halogen Compounds*, ed. B. Olofsson, I. Marek and Z. Rappoport, 2019, p. 461.
- 28 (a) P. Chakma, S. M. Zeitler, F. Baum, J. Yu, W. Shindy, L. D. Pozzo and M. R. Golder, *Angew. Chem., Int. Ed.*, 2023, **62**, e202215733; (b) S. M. Zeitler, P. Chakma and M. R. Golder, *Chem. Sci.*, 2022, **13**, 4131.
- 29 T. K. Achar, S. Maiti and P. Mal, *RSC Adv.*, 2014, **4**, 12834.
- 30 M. T. Alam, S. Maiti and P. Mal, *Beilstein J. Org. Chem.*, 2018, **14**, 2396.
- 31 S. Hou, J. Xu, J. Wang, H. Wang and P. Zhang, *Chem. – Eur. J.*, 2024, **30**, e202303126.
- 32 H. Luo, F.-Z. Liu, Y. Liu, Z. Chu and K. Yan, *J. Am. Chem. Soc.*, 2023, **145**, 15118.
- 33 P. Nayek and P. Mal, *Chem. – Eur. J.*, 2024, **30**, e202401027.
- 34 M. S. Yusubov and T. Wirth, *Org. Lett.*, 2005, **7**, 519.
- 35 G. F. Koser and R. H. Wettach, *J. Org. Chem.*, 1977, **42**, 1476.
- 36 M. Zhu, C. G. Cai, W. Ke and J. Shao, *Synth. Commun.*, 2010, **40**, 1371.
- 37 G. F. Koser, J. S. Lodaya, D. G. Ray and P. B. Kokil, *J. Am. Chem. Soc.*, 1988, **110**, 2987.
- 38 W. Ding, C. Wang, J. R. Tan, C. C. Ho, F. León, F. García and N. Yoshikai, *Chem. Sci.*, 2020, **11**, 7356.
- 39 G. F. Koser, *Aldrichimica Acta*, 2001, **34**, 89.
- 40 (a) M. S. Yusubov, T. V. Funk, R. Y. Yusubova, G. Zholobova, A. Kirschning, J. Y. Park and K.-W. Chi, *Synth. Commun.*, 2009, **39**, 3772; (b) S. T. Handy and M. Okello, *Synlett*, 2002, 489; (c) J. S. Lodaya and G. F. Koser, *J. Org. Chem.*, 1988, **53**, 210.
- 41 D. Kumar, M. S. Sundaree, G. Patel, V. S. Rao and R. S. Varma, *Tetrahedron Lett.*, 2006, **47**, 8239.
- 42 S. Doobary, M. M. de Vries Ibáñez and B. Olofsson, *Green Chem.*, 2024, **26**, 11518.
- 43 Z. Liu, F. Huang, P. Wu, Q. Wang and Z. Yu, *J. Org. Chem.*, 2018, **83**, 5731.
- 44 L. Pan, L. Zheng, Y. Chen, Z. Ke and Y.-Y. Yeung, *Angew. Chem., Int. Ed.*, 2022, **61**, e202207926.
- 45 M. Çelik, C. Alp, B. Coşkun, M. S. Gültekin and M. Balci, *Tetrahedron Lett.*, 2006, **47**, 3659.
- 46 J. Cai, Y. Wen, W. Sheng, X. Huang, Y. Zheng, C. Song and J. Li, *Green Chem.*, 2023, **25**, 6618.
- 47 W. Riley, A. C. Jones, K. Singh, D. L. Browne and A. M. Stuart, *Chem. Commun.*, 2021, **57**, 7406.
- 48 H. K. Minhas, W. Riley, A. M. Stuart and M. Urbonaite, *Org. Biomol. Chem.*, 2018, **16**, 7170.
- 49 I. P. Beletskaya and V. P. Ananikov, *Chem. Rev.*, 2022, **122**, 16110.
- 50 X. Liu, V. Dorokhov, O. Provot, C. Tran, P. Retailleau, J.-F. Soulé and A. Hamze, *ChemSusChem*, 2025, **18**, e202500320.
- 51 M. Liu, K. Yan, J. Wen, N. Zhang, X. Chen, X. Li and X. Wang, *Asian J. Org. Chem.*, 2022, **11**, e202200381.
- 52 M. T. Passia, N. Bormann, J. S. Ward, K. Rissanen and C. Bolm, *Angew. Chem., Int. Ed.*, 2023, **62**, e202305703.
- 53 S. Guha, S. Maheshwari, M. K. Ravva, J. M. Jacob, S. Yadav and S. Sen, *Asian J. Org. Chem.*, 2023, **12**, e202300348.
- 54 C. S. Nishad, K. K. Haldar and B. Banerjee, *J. Org. Chem.*, 2022, **87**, 11644.
- 55 J. Jiang and J. Li, *ChemistrySelect*, 2020, **5**, 542.
- 56 (a) M. A. Carroll and R. A. Wood, *Tetrahedron*, 2007, **63**, 11349; (b) N. Purkait, G. Kervefors, E. Linde and B. Olofsson, *Angew. Chem., Int. Ed.*, 2018, **57**, 11427.
- 57 I. Sokolovs, D. Lubriks and E. Suna, *J. Am. Chem. Soc.*, 2014, **136**, 6920.
- 58 S. Mkrtchyan, M. Shkooor, M. Phanindrudu, M. Medved', O. Sevastyanova and V. O. Iaroshenko, *J. Org. Chem.*, 2023, **88**, 863.
- 59 S. Mkrtchyan, V. B. Purohit, J. Zapletal, O. Shalimov, J. Nociarová, G. Addová, J. Filo, M. G. Garcia, E. Kupcová, B. Benická and V. O. Iaroshenko, *Cell Rep. Phys. Sci.*, 2024, **5**, 102118.
- 60 T. Liang, C. N. Neumann and T. Ritter, *Angew. Chem., Int. Ed.*, 2013, **52**, 8214.
- 61 K. Kubota, Y. Pang, A. Miura and H. Ito, *Science*, 2019, **366**, 1500.
- 62 J. Jiang, S. Song, J. Guo, J. Zhou and J. Li, *Tetrahedron Lett.*, 2022, **98**, 153820.
- 63 (a) N. Jalalian, E. E. Ishikawa, L. F. Silva and B. Olofsson, *Org. Lett.*, 2011, **13**, 1552; (b) S. Sarkar, N. Wojciechowska, A. A. Rajkiewicz and M. Kalek, *Eur. J. Org. Chem.*, 2022, e202101408; (c) C. Dey, E. Lindstedt and B. Olofsson, *Org. Lett.*, 2015, **17**, 4554.
- 64 J. Malmgren, S. Santoro, N. Jalalian, F. Himmo and B. Olofsson, *Chem. – Eur. J.*, 2013, **19**, 10334.
- 65 (a) J. P. Brand, J. Charpentier and J. Waser, *Angew. Chem., Int. Ed.*, 2009, **48**, 9346; (b) E. Le Du and J. Waser, *Chem. Commun.*, 2023, **59**, 1589.
- 66 (a) F. Xie, Z. Qi, S. Yu and X. Li, *J. Am. Chem. Soc.*, 2014, **136**, 4780; (b) Z.-Z. Zhang, B. Liu, C.-Y. Wang and B.-F. Shi, *Org. Lett.*, 2015, **17**, 4094.
- 67 G. N. Hermann, M. T. Unruh, S.-H. Jung, M. Krings and C. Bolm, *Angew. Chem., Int. Ed.*, 2018, **57**, 10723.
- 68 (a) E. Stridfeldt, A. Seemann, M. J. Bouma, C. Dey, A. Ertan and B. Olofsson, *Chem. – Eur. J.*, 2016, **22**, 16066; (b) N. Declas, G. Pisella and J. Waser, *Helv. Chim. Acta*, 2020, **103**, e2000191.
- 69 L. Castoldi, E. M. Di Tommaso, M. Reitti, B. Gräfen and B. Olofsson, *Angew. Chem., Int. Ed.*, 2020, **59**, 15512.
- 70 (a) P. Caramenti, N. Declas, R. Tessier, M. D. Wodrich and J. Waser, *Chem. Sci.*, 2019, **10**, 3223; (b) T. Ura, D. Shimbo, M. Yudasaka, N. Tada and A. Itoh, *Chem. – Asian J.*, 2020, **15**, 4000; (c) J. Li, C. Zhou, L.-M. Chen, X.-Y. Chen, X.-Q. Guo and T.-R. Kang, *Synlett*, 2024, 307.
- 71 (a) J. Wu, X. Deng, H. Hirao and N. Yoshikai, *J. Am. Chem. Soc.*, 2016, **138**, 9105; (b) J. Wu, K. Xu, H. Hirao and N. Yoshikai, *Chem. – Eur. J.*, 2017, **23**, 1521.
- 72 S. Doobary, J. Braunreuther, A. K. Inge and B. Olofsson, *Angew. Chem., Int. Ed.*, 2026, **65**, e19049.
- 73 F. Basoccu, P. Caboni and A. Porcheddu, *ChemSusChem*, 2025, **18**, e202402547.
- 74 R. Obermüller, H. Tobisch, L. Stockhammer and M. Waser, *Org. Process Res. Dev.*, 2024, **28**, 3735.

