

Hypervalent Halogen Compounds in Electrochemical Reactions: Advantages and Prospects

Bethan Winterson,^a Dhananjay Bhattacharjee,^a and Thomas Wirth^{a,*}

^a School of Chemistry, Cardiff University, Park Place, Main Building, Cardiff, Cymru/Wales, UK
E-mail: wirth@cf.ac.uk

Manuscript received: April 25, 2023; Revised manuscript received: June 12, 2023;
Version of record online: July 4, 2023

© 2023 The Authors. Advanced Synthesis & Catalysis published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Abstract: The clean and facile electrochemical synthesis of hypervalent iodine reagents is a fast growing field. In the past 5 years, a diverse number of reaction types have been established, from fluorinations, oxidative cyclizations, C–N and C–H couplings and oxidations. Electrochemistry is beneficial in terms of sustainability as the requirement for chemical oxidants is eliminated. This contributes to cleaner processes with limited by-product waste. Often, the purification of iodine(III) compounds is simple, since electrolysis is performed in the absence stoichiometric oxidants. Significant breakthroughs have been made recently, including the first asymmetric application, electrocatalytic applications, and even the synthesis of bromine(III) reagents using similar methodologies.

1. Introduction
2. Mechanistic Aspects
3. Diaryliodonium Compounds
4. [Bis(alkoxy)iido]arene Compounds
5. Iodine(V) Reagents
6. (Difluoroiodo)arenes
7. Stereoselective Applications
8. Electrocatalysis with Iodine(III)
9. Hypervalent Bromine Compounds
10. Conclusions

Keywords: Electrochemistry; Hypervalent; Iodine; Mediator; Synthesis

1. Introduction

The use of hypervalent iodine reagents in organic synthesis has regained much of its interest in the past decades. These reagents are non-metallic, environmentally friendly and offer a broad range of reactivities whilst, at the same time, typically being mild and highly efficient.^[1] Yet, despite the popularity of hypervalent iodine reagents in organic synthesis, the inherent demand for stoichiometric oxidizing reagents for their preparation diminishes their sustainable prospects as they remain a source of often toxic stoichiometric waste. For instance, Willgerodt used elemental chlorine for the synthesis of the first reported iodine(III) compound,^[2] but other oxidants such as bromates, perborates, peracids or persulfates are frequently employed in their synthesis.^[3] Discovering the correct chemical oxidant can also be somewhat challenging

owing to possible side reactions and by-product formation. Whilst *m*-chloroperbenzoic acid (*m*CPBA) is often the ‘go to’ oxidant in modern synthesis, undesired epoxidation, as opposed to alkene difunctionalization by fluorine or acetate, is commonly encountered when electron rich alkenes are present.^[4] This often results in the reliance on more expensive oxidants, typically Selectfluor[®]. In the same premise, the purification of subsequent products can also be problematic as large quantities of oxidant side products, such as *m*-chlorobenzoic acid when *m*CPBA is used, must be removed. This problem is typically exacerbated in large scale reactions. In this respect, Ochiai and Miyamoto^[5] and Powers^[6] established the use of molecular oxygen to generate peracids *in situ* which, in turn, can then be used to generate iodine(III) reagents. The use of oxygen for iodine(III) synthesis can be very attractive, as it is relatively cheap,



Thomas Wirth is professor of organic chemistry at Cardiff University. He received his PhD after studying chemistry at Bonn and the Technical University of Berlin. After a postdoctoral stay at Kyoto University as a JSPS fellow, he worked independently at the University of Basel before taking up his current position at Cardiff University in 2000. His main inter-

ests of research concern stereoselective electrophilic reactions, oxidative transformations with hypervalent iodine reagents and flow chemistry performed in microreactors.



Dhananjay Bhattacharjee is a Marie Skłodowska-Curie post-doctoral fellow at Cardiff University in the Wirth research group since 2023. After obtaining his MSc in Chemistry from Assam University, Silchar (2011) and his PhD in chemical sciences from the CSIR-Institute of Himalayan Bioresource Technology, Palampur, Himachal Pradesh under Academy

of Scientific and Innovative Research (AcSIR), New Delhi in the year 2019, he moved to Ural Federal University, Russian Federation, for a postdoctoral research position. His current research interest encompasses the electrochemical oxidation of Group 17 elements and exploration of their reactivities in organic synthesis.



Bethan Winterson is a PhD student at Cardiff University in the Wirth research group. After obtaining her MChem degree from Cardiff University (2019), she remained in Cardiff University to complete her doctorate under the supervision of Prof. Thomas Wirth. Her research interests are primarily focussed on the synthesis and application of hypervalent iodine reagents using electrochemical methods.

of Scientific and Innovative Research (AcSIR), New Delhi in the year 2019, he moved to Ural Federal University, Russian Federation, for a postdoctoral research position. His current research interest encompasses the electrochemical oxidation of Group 17 elements and exploration of their reactivities in organic synthesis.

environmentally greener, and by-product formation is less significant. The electrochemical generation of hypervalent iodine reagents, through the anodic oxidation of iodine(I) precursors, is also a highly promising alternative.^[7] In 1925, the first electrochemical synthesis of iodine(III) compounds was reported,^[8] but only in the last decades this methodology has been further developed.^[9] Indeed, the electrogeneration of iodine(III) has seen substantial growth in the past 10 years, which coincides with the introduction of commercially available electrochemical reactors and equipment.

Often, purification of the subsequent iodine(III) reagents is not necessary given the reaction is performed in the absence of all other reagents. They are typically used without further purification^[10] or can be dried and stored.^[11] The electrogeneration of iodine(III) requires a sequential two-electron anodic oxidation of iodine(I) to iodine(III), with a nucleophilic solvent or electrolyte providing the ligands. To date, only a limited number of nucleophiles have been used, including acetate, fluoride, fluorinated alcohols and

arenes (Figure 1).^[7] Ex-cell applications, where the electrochemical generation of iodine(III) reagents is performed in the absence of a substrate, are the most prevalent approach. This circumvents the relatively high oxidation potentials of aryl iodides.^[12] The groups of Hara, Waldvogel, Francke, Lennox and Wirth have

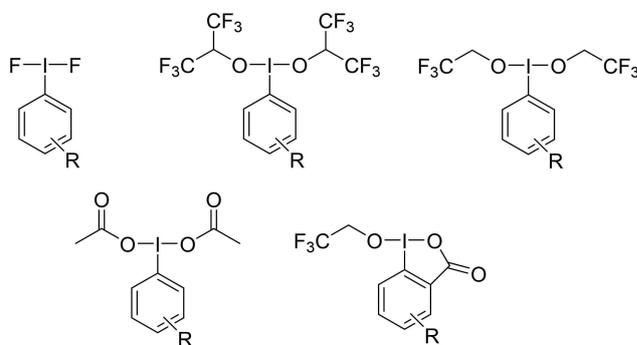
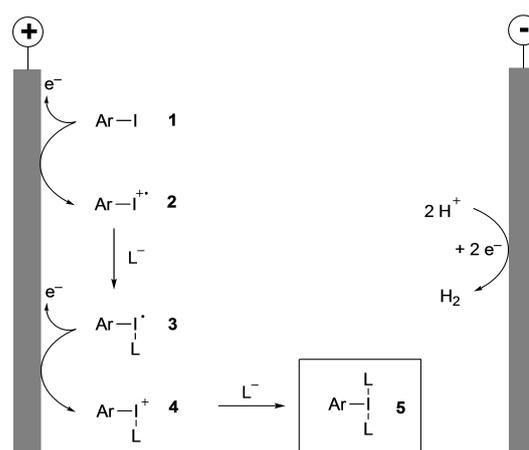


Figure 1. Common electrochemically generated iodine(III) reagents.

disclosed efficient electrochemical methods for the generation of iodine(III) reagents, including (difluoroiodo)arenes, (diacetoxyiodo)arenes and (dialkoxyiodo)arenes. Most of these applications rely on ex-cell methodology. Although favourable in terms of reaction selectivity, simplicity and versatility, this methodology is not compatible with the catalytic application of iodine(III) reagents. This is a shortfall given the high preference for catalytic quantities of iodine(I) in the field. In-cell procedures, whereby the substrate and iodine(I) precursor are present during the electrolysis, facilitate the use of sub-stoichiometric quantities of aryl iodides. In this respect, electron rich aryl iodides are often favoured attributed to their lower oxidation potential.^[13] Though, too much electron density can lead to decomposition of the aryl iodide,^[11] polymerization and passivation. Powers disclosed one of the first electrocatalytic applications of aryl iodides based on an anodically generated (diacetoxyiodo)-arene.^[13] Potentiostatic electrolysis (CPE) is often key to achieving selective aryl iodide oxidation in preference to the substrate. Though, electrocatalytic applications remain a few in the literature. Electrochemical applications of chiral iodine(III) reagents is also an underdeveloped area in the field, with Wirth disclosing the only procedure to date.^[14] Such techniques are often challenging in the electrochemistry owing to the increased complexity of the iodine(I) scaffold. In this respect, the functional group tolerance of electrochemistry must be considered when designing potential asymmetric mediators. Nevertheless, with the on-going and rapid development of electrochemically generated iodine(III) chemistry, electrochemistry is sure to advance the field tremendously.

2. Mechanistic Aspects

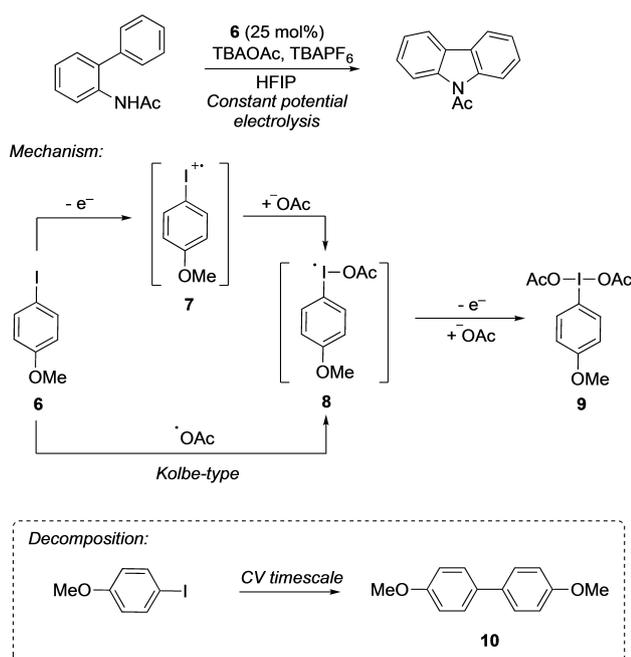
All electrochemical reactions will either proceed or will have to be initiated at the electrode surface. Early investigations into the direct oxidation of iodoarenes indicate that iodoarenes **1** must be pre-adsorbed on the electrode surface before the one electron oxidation to the radical cation **2** can proceed (Scheme 1).^[15] This is typically the rate-limiting step. The next reaction, the addition of a nucleophilic ligand, provided by the electrolysis solvent or supporting electrolyte, to intermediate **3**, is a fast process. It should be noted that not all nucleophiles are compatible as the iodoarene must have a lower oxidation potential than the nucleophile. A sequential one electron oxidation to intermediate **4**, followed by the addition of another ligand completes the electrochemical generation of the iodine(III) species **5**. Overall, this represents an ECEC mechanism. The cathodic half reaction is usually the reduction of protons rendering hydrogen as the sole by-product of the process. The formation of (dihaloiodo) or (dialkoxyiodo) arenes are usually observed in the presence of



Scheme 1. Electrochemical generation of iodine(III) reagents.

nucleophilic solvents, though co-ordinating *ortho*-substituents lead to the formation of cyclic structures.^[16] In contrast, trapping with an electron-rich arene results in the cyclic or acyclic diaryliodonium species.^[17] Also, homo-coupling, *via* electrophilic aromatic substitution in aprotic non-nucleophilic systems, renders a diaryliodonium species. Powers and Lennox both carried out mechanistic experiments into the electrogeneration of hypervalent iodine species. Powers *et al.* disclosed a iodine(III) electrocatalytic approach for C–H/C–N coupling which displayed high acetate dependency due to the stabilization of a transient iodine(II) intermediate (Scheme 2).^[13] Due to the dependency on acetate ions, two mechanistic pathways were investigated, either *via* iodine(III) formation or from an interrupted Kolbe electrolysis (*via* OAc^- to OAc^\bullet). Though, Kolbe electrolysis could not occur in the electrolysis solvent (hexafluoro isopropanol, HFIP) indicated by the absence of an oxidation peak in CV. This is consistent with the strong hydrogen bonding of acetate to HFIP ($\text{pK}_a = 9.3$).^[18] Therefore, *in situ* generated (diacetoxyiodo)arenes were responsible for their reaction. To study the stability of the electrochemically generated iodine(III) species, cyclic voltammetry experiments were carried out.

While the anodic oxidation of **6** was irreversible at low scan rates (< 100 mV/s), reversibility emerged at higher scan rates (> 250 mV/s). Since anodically generated (dialkoxyiodo)arenes, ligated with HFIP or trifluoroethanol (TFE), could also perform the C–N bond forming reaction,^[11] the authors investigated the identity of the iodine(III) reagents. But, no product could be observed in the absence of acetate, so the authors propose an active (diacetoxyiodo)arene. The addition of TBAOAc results in a loss of electrochemical reversibility for the oxidation of iodine(I) to iodine(III) which is key to their in-cell application. This method represents a powerful method for generat-



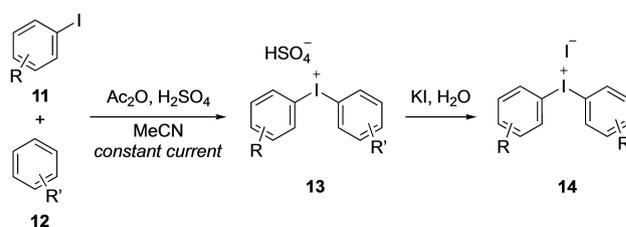
Scheme 2. Proposed mechanism for the generation of (diacetoxyiodo)arenes. TBAOAc: tetra-*n*-butylammonium acetate; TBAPF₆: tetra-*n*-butylammonium hexafluorophosphate; HFIP: 1,1,1,3,3,3-hexafluoroisopropanol.

ing (diacetoxyiodo)arenes *in situ*. More recently, the group disclosed an extensive cyclic voltammetry analysis for a family of 70 aryl iodide mediators.^[12] The results revealed the potential for the one electron oxidation of 4-substituted aryl iodides is well-correlated with standard Hammet parameters. For example, the oxidation of electron deficient aryl iodides occurs at higher potentials ($E_{p/2} = 2.0$ V *vs.* Fc/Fc⁺ for 4-nitroiodobenzene), as opposed to lower potentials for electron rich iodoarenes ($E_{p/2} = 1.32$ V *vs.* Fc/Fc⁺ for 4-iodoanisole). The application of aryl iodides in electrochemistry is plagued by high iodoarene loading, typically stoichiometric or ≥ 25 mol%, so potential chemical and electrochemical decomposition pathways were probed as a reason for this. At low scan rates, the CV of **6** displayed a shoulder with a peak potential of 1.39 V (*vs.* Fc/Fc⁺) which is indicative of chemical degradation of the catalyst. Indeed, the CV of **10** displayed the same peak potential (1.39 V *vs.* Fc/Fc⁺) as the shoulder peak observed in the CV of **6**, suggesting deiodinative coupling is operational on the timescale of the CV of **6**. Treating **6** with [bis(trifluoroacetoxy)iodo]benzene and BF₃·OEt also resulted in the deiodinative coupling product **10**. Importantly, the electrolysis of **6** in the presence of TBAOAc did not result in the formation of the biaryl **10**, indicating the importance of TBAOAc for practical application. These results are highly useful in guiding the design of iodoarene catalysts as electrochemical

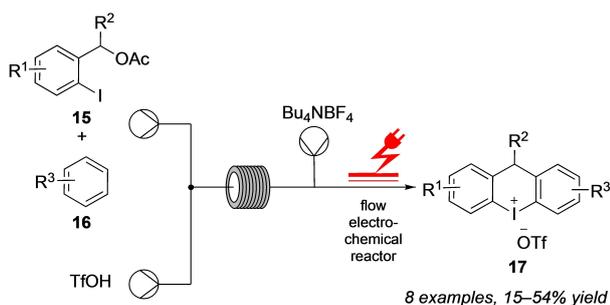
mediators. Likewise, Lennox *et al.* carried out mechanistic experiments for the electrochemical generation of (difluoroiodo)toluene. The anodic oxidation of 4-iodotoluene in dichloromethane and 5.6HF·amine (made by diluting 9HF·Py with 3HF·Et₃N), displayed 2 oxidation peaks consistent with each single-electron transfer event (Scheme 1).^[19] When lower concentrations of HF·amine were used or in the absence of HF, a single peak potential was observed indicating that fluoride stabilizes the formation of an iodine(II) radical. In the absence of fluoride, it undergoes rapid further oxidation to iodine(III) at a higher potential. Powers and co-workers later disclosed that it is even possible to isolate the iodonium radicals (iodine(II) species), generated by a single one-electron oxidation of aryl iodides.^[20] Thus, confirming they are likely intermediates in the anodic oxidation of iodoarenes. The iodine(II) reagent was also a competent reagent and its synthetic utility was demonstrated for the formation of carbazoles, oxidative dearomatization, lactone cyclization and benzylic acetoxylation.

3. Diaryliodonium Compounds

The electrochemical anodic oxidation of iodoarenes in the presence of arenes is a sustainable, single-step approach for the synthesis of diaryliodonium compounds. This was first described by Miller and Hoffmann in 1966.^[21] Using an electrochemical microreactor,^[17] Wirth *et al.* developed a flow protocol for the synthesis of diaryliodonium salts (Scheme 3). The microreactor consisted of two platinum electrodes separated by a thin (250 μ m) spacer. A solvent system of sulfuric acid (2 M), acetic anhydride and acetonitrile was employed in the synthesis. The sulfuric acid plays three integral roles, it provides the counter ion for the positively charged iodonium salt **13**, it is the supporting electrolyte, and it provides the proton for the balancing cathodic half reaction. Up to 72% yield for symmetric or asymmetric iodonium salts were obtained. Higher current densities are often preferred in flow synthesis since the flow rate and thereby productivity can be increased. Though, increased current densities in this case led to the undesired formation of the (diacetoxyiodo)arenes. Treatment of



Scheme 3. Flow electrochemical synthesis of diaryliodonium salts.

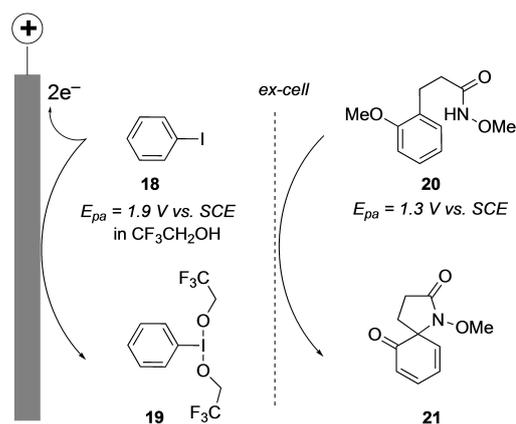


Scheme 4. Flow electrochemical synthesis of cyclic iodonium compounds **17**.

compounds **13** with potassium iodide in H₂O facilitated anion exchange and the resulting diaryliodonium salts **14** could be purified by simple filtration and washing. This highlights the benefits of the electrochemical synthesis as in the absence of chemical oxidants the products **14** could be easily purified. Moran and co-workers disclosed an improved protocol for the electrochemical synthesis of unsymmetrical diaryliodonium salts.^[22] Here, the addition of triflic acid (TfOH) during electrolysis directly yielded the more synthetically useful triflic anion bearing salts. Whilst fairly electron deficient iodoarenes could be oxidized successfully (4-fluoroiodobenzene), the reaction could not tolerate electron-deficient arene counterparts. A mixture of MeCN:HFIP (1:4) was used which was optimal for the solubility of the reagents providing sufficient conductivity to prevent high cell potentials. In this case, the aforementioned side products, namely the generation of (diacetoxy)arenes, could be completely prevented. The reaction was expanded to synthesis of cyclic diaryliodonium salts with high yields (up to 96%) and broad substrate applicability. More recently, Wirth in a collaboration with Nachtsheim developed an advanced synthetic method for the generation of cyclic iodonium compounds using flow electrolysis (Scheme 4).^[23] In a multi-step continuous-flow procedure, benzyl acetates **15** are submitted to a two-step procedure as readily available and cheap starting materials. An acid-catalyzed Friedel-Crafts alkylation of **15** with arenes **16** in the first reactor is followed by an anodic oxidative cyclization in the second electrochemical reactor, yielding cyclic iodonium compounds **17** in a highly substrate-dependent yield. Also, other researchers have employed electrochemical methods for the batch synthesis of diaryliodonium salts.^[16,24]

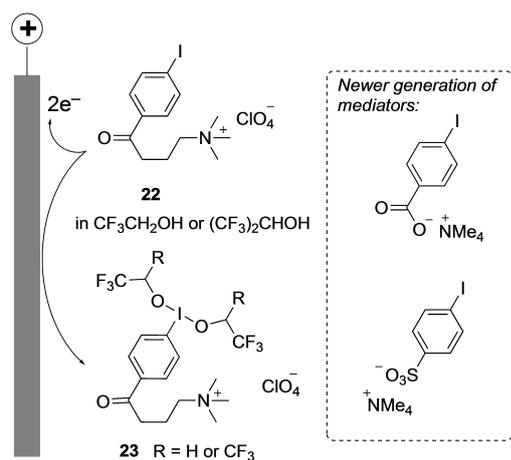
4. [Bis(alkoxy)iodo]arene Compounds

The electrochemically generated hypervalent iodine reagent [bis(trifluoroethoxy)iodo]benzene **19** (Scheme 5) was introduced by the Nishiyama group as



Scheme 5. Electrochemical generation of the hypervalent iodine reagent **19** and its application in spirocyclization.

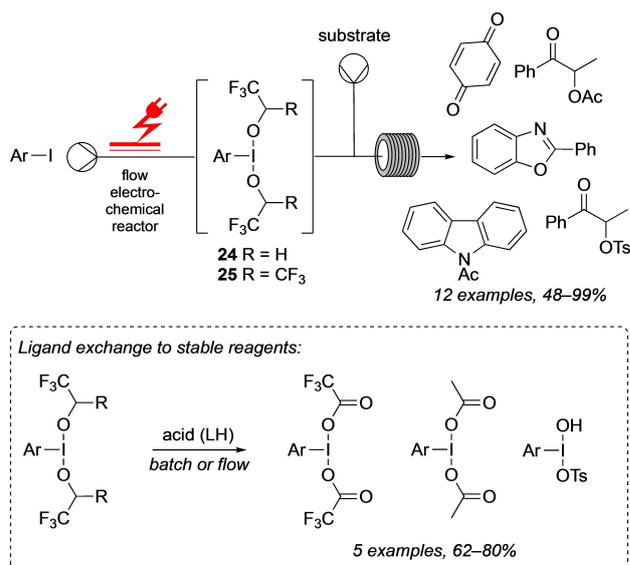
an unconventional substitute to the commercially available iodine(III) reagents such as [bis(trifluoroacetoxy)iodo]benzene (PIFA).^[10] Compound **19** cannot be isolated but its reactivity *in situ* is comparable and sometimes superior to PIFA. This is illustrated by its successful applications in the construction of a variety of oxygen and nitrogen-containing scaffolds such as **21**,^[25] natural products and the oxidation of naturally occurring xanthone derivatives.^[26] An ex-cell methodology was key to the successful application of compound **19**, given the higher oxidation potential of the iodobenzene mediator (1.9 V vs. SCE) compared to substrate oxidation (1.3 V vs. SCE). Although isolation of the active iodine(III) reagent **19** was not possible due to its instability, EI mass spectrometry revealed a fragment ion at $m/z = 303$ (PhIOCH₂CF₃) consistent with the proposed structure **19**. This is similar to the fragment mass of PIFA, $m/z = 317$ (PhICO₂CF₃). Francke *et al.* designed a recyclable iodine(I)/iodine(III) redox mediator **22** for electrosynthesis (Scheme 6).^[27] An ionically tagged aryl iodide is electrochemically oxidized either in the presence of trifluoroethanol (TFE) or 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) to the corresponding hypervalent iodine reagents **23**. Compound **23** is effective for inter/intramolecular C–N coupling^[27] and for the synthesis of benzoxazoles.^[28] The ionic substituent in **22** facilitates the recovery and recycling of the iodine(I) precursor, in addition to eliminating the need for supporting electrolytes. For several reasons, HFIP has emerged as the most prevalent and ideal solvent for the electrogeneration of iodine(III). In particular, HFIP exhibits high polarity, high anodic stability, low nucleophilicity and a relatively low pKa for facile proton reduction. Coordination of HFIP to an anodically oxidised iodine atom directly provides a useful iodine(III) reagent, without the requirement for additional reagents for ligands, such as acetic acid, therefore making the reaction simple and clean. It also



Scheme 6. Synthesis and anodic oxidation of ionically tagged mediators.

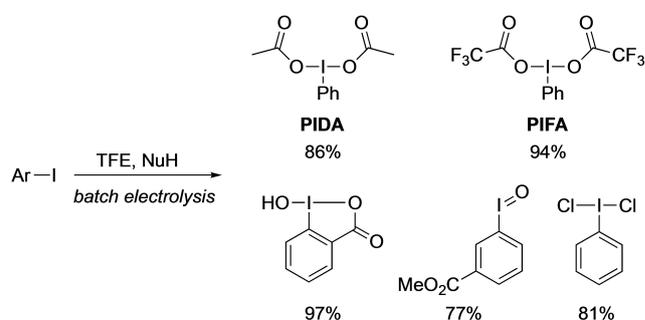
exhibits favorable radical stabilization effects in oxidative transformations^[29] and is therefore increasingly adopted in both electrochemistry and iodine(III) chemistry. Voltametric data even demonstrates the enhanced reactivity of commercially available reagents, like PIDA, in HFIP, attributed to its increased oxidizing power in this solvent.^[30] Further developments towards ionically tagged mediators was later disclosed by the Francke group,^[31] which simplifies the synthetic route to the iodine(I) precursors (Scheme 6). By producing iodophenylsulfonates or iodobenzoates, the ionic mediators could be accessed in one synthetic step (as opposed to 3 steps for **22**). Based on these discoveries, Wirth and co-workers developed an efficient flow procedure for the electrogeneration of similar (dialkoxyiodo)arenes (Scheme 7).^[11] The electrochemical oxidation of iodoarenes was carried out in TFE or HFIP, leading to the chemically unstable intermediates of type **24** and **25**. Such compounds undergo decomposition upon removal of solvent and are highly susceptible to ligand exchange.^[28] Whilst carrying out the reaction in HFIP led to passivation of the electrodes over time, no passivation of the electrodes was observed when using TFE. Because passivation leads to high voltages over the course of the flow procedure, the iodine(III) reagents bearing TFE ligands **24** were used for further downstream reactions.

By treating the electrochemically generated (dialkoxyiodo)arenes with the corresponding acid, (diacetoxyiodo)arenes, [bis(trifluoroacetoxy)iodo]arenes or Koser's reagents could be generated in excellent yields. Given the oxidation was carried out in the absence of all other reagents, the isolation of these compounds was simple, either by precipitation, crystallization or by removal of the solvent. Depending on the aromatic substitution on the arene and solvent, the yields of the (dialkoxyiodo)arenes (**24** and **25**) ranged



Scheme 7. Continuous flow electrochemical generator of hypervalent iodine reagents.

from 42% to 99%. The electrochemically generated **24** could also be used without further modification in further downstream flow reactions. For example, intramolecular cyclizations, the synthesis of benzoxazoles, dearomatization of phenols or the oxidation of sulfides to sulfoxides. Carrying out an *in situ* ligand exchange of **24** in flow followed by combination with a ketone provided the α -functionalized products. The combination of electrochemistry and flow chemistry largely improves the ecological footprint of the overall process compared to conventional approaches. The requirement for high concentrations of supporting electrolytes (typically 0.1 M in batch) is removed, which reduces the waste and cost implication of the procedure. A similar approach was later reported by He *et al.* where the synthesis of hypervalent iodine(III) compounds has been performed in batch mode (Scheme 8).^[16a] Anodic oxidation of aryl iodides in an undivided batch cell using TFE in the presence of excess nucleophiles



Scheme 8. Electrochemical generation of stable I(III) reagents by He *et al.*

(NuH) furnished common hypervalent iodine reagents such as PIDA, (dichloroiodo)arenes, iodosylbenzenes and benziodoxoles. Other researchers have synthesized analogous iodine(III) reagents in the absence of fluorinated alcohols.^[16b]

5. Iodine(V) Reagents

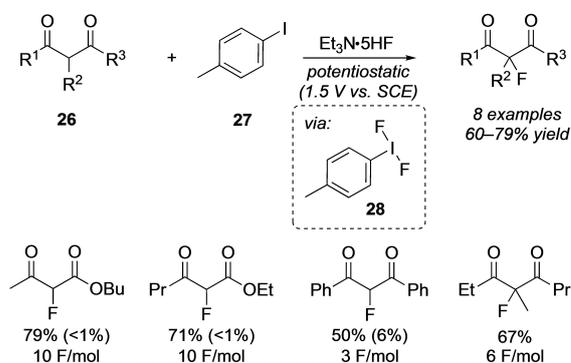
Although the synthesis of iodine(III) reagents has been well-established, electrochemical routes to iodine(V) reagents are sparse. Since the oxidation states of iodine increase in the order iodine(I) < iodine(III) < iodine(V), this phenomena could be attributed to the typically higher oxidation potentials needed to access iodine(V) compared to iodine(III). Moreover, these electrochemical methods are often riddled with selectivity issues and mixtures of iodine(III) and iodine(V) products are common. Bystron and co-workers investigated the electrochemical generation of 2-iodoxybenzoic acid (IBX).^[32] The reaction followed a sequential anodic oxidation of 2-iodobenzoic acid (1.58 V vs. SCE) to 2-iodosobenzoic acid, followed by oxidation 2-iodosobenzoic acid (1.95 V vs. SCE) to IBX, in 0.2 M H₂SO₄. The reaction could be tailored to access either the iodine(III) or iodine(V) product using potentiostatic electrolysis. At an electrode potential of 1.83 V (SCE), 2-iodobenzoic acid was exclusively converted to 2-iodosobenzoic acid. Higher electrode potentials (1.93 V vs. SCE) gave mixtures of iodine(III) and iodine(V), whilst further increases (2.03 V vs. SCE) gave IBX as the sole product.

Although the reaction was only carried out on an analytical scale, the team showed that high yields (99% by potentiometric titration) could be obtained. Miyake and co-workers also investigated the electrochemical production of iodine(V) reagents in aqueous conditions,^[33] although mixtures of iodine(III) and iodine(V) products were obtained. Recently, Powers and colleagues discovered that the disproportionation of electrochemically generated iodosylarenes can give the corresponding iodoxyarenes.^[34] The selectivity for the iodine(V) : iodine(III) products was 4.2:1.0 under the optimal conditions. Other hypervalent iodine reagents in oxidation states above +3 can also be obtained *via* electrochemical methods, particularly periodate.^[35]

6. (Difluoroiodo)arenes

The principle of generating chemically sensitive or hazardous hypervalent iodine reagents has been long established in electrochemistry, particularly in the field of fluorine chemistry. Special focus has also been paid on the synthesis of (difluoroiodo)arenes due to their diverse fluorine chemistry, well established electro-generation, and the great importance of C–F bond formation in pharmaceuticals, agrochemicals and mate-

rials industry.^[36] The first electrochemical synthesis was established early on in the field of iodine(III) chemistry, by Schmidt and Meinert in 1960.^[37] Electrolysis of iodobenzene in acetonitrile was performed in the presence of silver fluoride, serving as both the fluoride donor and fluorine source. Albeit, Rozhkov found that this electrochemistry could not be reproduced since such a solution was non-conductive.^[38] Improvements were made by Fuchigami in 1994, but the authors found that electrolysis of iodobenzene, in a mixture of Et₃N·3HF and MeCN (divided cell), led to the formation of a dimeric iodonium salt.^[39] Meanwhile, the oxidation of 4-iodotoluene gave mainly benzylic fluorination, which can be a common problem in these electrochemical processes.^[40] It should be noted that in combinations of Et₃N·3HF and MeCN, anodic passivation, which suppress anodic current, is a regularly encountered problem in electrochemistry.^[41] Only the (difluoroiodo)arene from 4-nitroiodobenzene (2.3 V vs. SCE) could be purified, but in low yields of 53% attributed to the high oxidation potential. Low faradaic efficiencies were also obtained, as the oxidation required 4.4 F/mol to perform compared to the theoretical amount of 2 F/mol. 4-Iodoanisole (1.9 V vs. SCE) could also be oxidized to the corresponding (difluoroiodo)arene, but it could not be isolated due to its instability. The electrocatalytic application is presented later in this review. Given the high oxidation potentials of these mediators was problematic for anodic oxidation, the same authors proposed a chloride mediated oxidation of iodoarenes.^[42] Although, only the chlorofluoride iodine(III) reagents were obtained (discussed later). Since then, much improvement has been made towards the electrogeneration of iodine(III) difluorides. A breakthrough synthesis was disclosed by Hara and Yoneda (Scheme 9).^[43] By changing the electrolyte system from Et₃N·3HF to Et₃N·5HF, (difluoroiodo)toluene **28** could be generated and applied in an in-cell manner for the mono-fluorination



Scheme 9. Synthesis of (difluoroiodo)toluene and application to the fluorination of β -keto esters. Yields of the difluorinated products in parenthesis.

of β -keto esters. Since $\text{Et}_3\text{N}\cdot 3\text{HF}$ is not suitable for the fluorination of molecules bearing high oxidation potentials^[41] (around 2 V vs. Ag/Ag^+), it is likely the solvent is not ideal, *i.e.* anodically stable enough, for the oxidation of iodoarenes (1.8 V vs. Ag/Ag^+ for iodobenzene).^[11] The electrolysis was performed under potentiostatic reaction conditions (1.5 V vs. Ag/Ag^+) with a 1:1 mixture of 4-iodotoluene and the dicarbonyl substrate in an undivided cell. This set-up represents an improvement to the previous methods,^[39] as undivided cells are beneficial in terms simplicity and reproducibility. Mono-fluorinated β -keto esters were obtained as the major product in all cases, with small impurities of the difluorinated products observed in a few cases. It is notable that high faradaic equivalents are needed for the conversion of most compounds (3–10 F/mol in all cases). Further advancements were made by Fuchigami in 2010 with the development of recyclable iodoarene mediators for fluorinations, one representing polystyrene supported iodobenzene **29**,^[44] whilst the other is described as a task-specific ionic liquid **30** (Figure 2).^[45] Modification of the iodoarene by these charged or polymer moieties did not affect their mediator capabilities. Compounds **29** and **30** could successfully be applied in the fluorination of various organosulfur compounds in high yields, and then be recycled with no detriment to the yield. Cyclic voltammetry analysis of **30** in 0.1 M $\text{Et}_4\text{N}\cdot 4\text{HF}/\text{MeCN}$ displayed an oxidation peak at 1.9 V vs. SCE, which is not dissimilar to an iodoarene devoid of the charged imidazolium cation. In recent years, the synthesis of (difluoroiodo)arenes has been well-established by Waldvogel, Lennox and Wirth and applied in various types of fluorinations. In 2019, Waldvogel re-ignited the interest in the electrochemical generation of iodine(III) difluorides with two sequential publications for the synthesis of oxazolines^[46] and oxazoles^[47] (Scheme 10). The electrolysis of 4-iodotoluene was carried out in a 1:1 *v/v* mixture of the commercially available $5\text{HF}\cdot\text{Et}_3\text{N}$ and dichloromethane, under galvanostatic conditions. The reactions were performed in an in-cell manner meaning the substrates were present during electrolysis. It should be noted that surprisingly high current densities were tolerated ($j=50\text{ mA}/\text{cm}^2$) which represents just 30 minutes electrolysis time for 0.5 mmol. This is distinct from most iodine(III) chemistry where current densities are usually 5–10 mA/cm^2 .^[40a] Though, in both cases, a reaction time of 15 h (30 minutes electrolysis followed by stirring

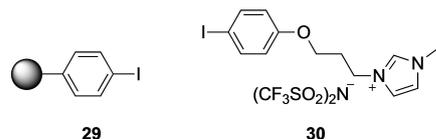
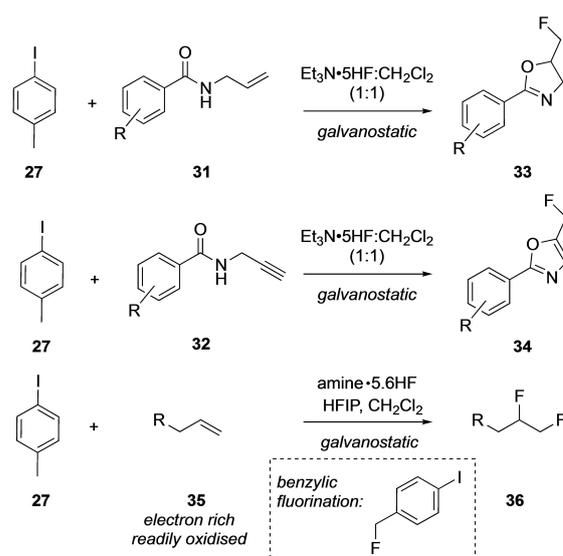


Figure 2. Recyclable ionic mediators designed by Fuchigami.



Scheme 10. The synthesis of oxazolines and oxazoles by Waldvogel, and *vic*-difluorination by Lennox.

overnight without electricity) was required, as the fluorocyclisation was slower than the anodic oxidation of 4-iodotoluene (C step). A broad range of 16 oxazolines and 15 oxazoles could be synthesized in good to excellent yields, including those displaying aromatic methoxy substituents, electron withdrawing groups and heterocycles like thiophene and furan. As opposed to an in-cell application by Waldvogel, Lennox *et al.* implemented an ex-cell methodology for the application of (difluoroiodo)arenes which improves substrate tolerance.^[40a] In this respect, electron rich substrates ($E_{\text{ox}} < 1.8\text{ V}$) bearing lower oxidation potentials than iodoarenes ($E_{\text{ox}} = 1.9\text{ V}$) can be easily tolerated. The reaction was applied for the *vicinal* difluorination of electron rich alkenes. In contrast to Waldvogel's reports, the authors chose to use a 'home-made' $\text{HF}\cdot\text{amine}$ source, made by diluting $9\text{HF}\cdot\text{Py}$ with $3\text{HF}\cdot\text{Et}_3\text{N}$, because of the beneficial cost implications. This also allowed fine tuning of the $\text{HF}:\text{amine}$ ratio which played a role in the selectivity of the reaction. At low HF concentrations, primarily the benzylic fluorination of iodotoluene was observed. At the optimal $5.6\text{HF}\cdot\text{amine}$, no benzylic fluorination was detected and only iodine(III) was formed. A broad range of over 50 alkenes could be successfully fluorinated in low to good yields (<5%–93%). The group later used a similar methodology for the fluoroarylation of phenolic ethers, instead opting for a divided cell technique over ex-cell methodology.^[19] Since (difluoroiodo)arenes are toxic and suffer from low chemical stability, Wirth and colleagues proposed a flow procedure could be beneficial. Flow chemistry could be easily integrated into an automated system, therefore it would facilitate 'hands-free' handling of

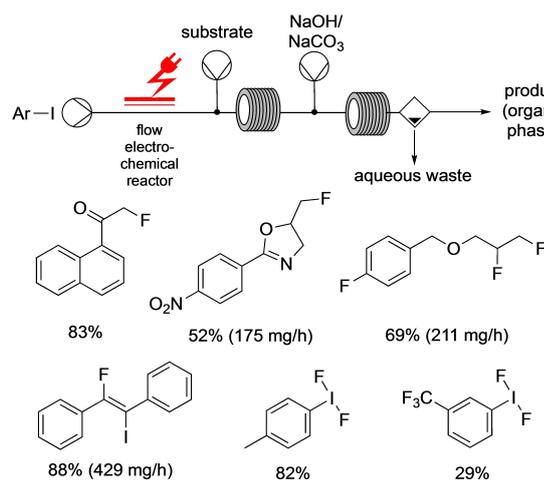
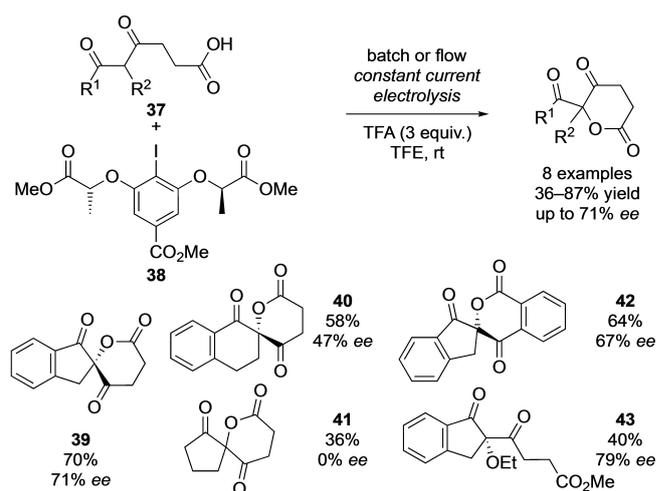


Figure 3. Flow electrochemical synthesis and use of iodine(III) difluorides.

toxic HF reagents. Based on previous research, Wirth *et al.* developed a flow chemical synthesis of iodine(III) difluorides and showed their direct use in fluorination reactions (Figure 3).^[40b] The flow synthetic approach gave increased yields in most cases in much shorter reaction times compared to batch. The spatial separation between the electrochemical and chemical step in the flow system meant a diverse number of reaction types could be performed. High flow rates facilitated productivities of up to 834 mg/h with vastly reduced reaction times. The isolation of the iodoarene difluorides was also simple and in good yields, since the electrolysis is performed in the absence of chemical oxidants. The system also integrated an in-line quenching technique, consisting of a base to quench HF, to remove any safety concerns to the experimentalist. In-line quenching could be coupled with in-line liquid-liquid extraction to perform the aqueous organic work-up.

7. Stereoselective Applications

The use of chiral iodine(III) reagents is arguably the most underdeveloped area in iodine(III) electrochemistry, with only one procedure published to date. Indeed, stereoselective electrochemical reactions on a whole are notably lacking in the literature, and as such, remains a major synthetic challenge for electrochemists.^[48] Such techniques are challenging owing to the increased complexity of the systems. For instance, chiral mediators are inherently more ‘decorated’ than their achiral counterparts, thereby the electrochemical procedure must be carefully designed to avoid undesirable activation/racemization of the newly introduced chiral functionalities. Often, solvent choice is highly specific in electrochemistry (for instance the reliance of HFIP in many procedures), and



Scheme 11. Electrochemical synthesis of chiral iodine(III) reagents for stereoselective synthesis.

the best electrolysis solvent could be incompatible with achieving high enantioselectivity. Nonetheless, Wirth *et al.* demonstrated the first use of chiral iodine(I) precursors for the electrochemical generation of chiral iodine(III) reagents (Scheme 11).^[14] The enantioselective electrochemical α -lactonization of diketo acids using chiral iodoarenes as redox mediators led to the formation of cyclized products in up to 71% *ee*. The electrolysis was performed in an undivided batch cell, using two platinum electrodes and TFE as the solvent. Even though the reaction proceeded without the use of trifluoroacetic acid (TFA), the addition of small amounts of acid (3 equiv.) were found to increase the efficiency and enantioselectivity of the reaction (*i.e.* 51% yield, 61% *ee* in the absence of TFA, and 70% yield, 71% *ee* with additional TFA for compound **39**). Cyclic voltammetry analysis of the chiral mediator **38** displayed a peak at 1.83 V vs. Ag/Ag⁺, which is crucially lower than the direct oxidation of the substrates (2.07 V vs. Ag/Ag⁺ for the substrate of **39**). Adapting this enantioselective process in an electrochemical flow microreactor facilitated a 10-fold reduction in the concentration of the electrolyte, from 0.05 M in batch, to 0.005 M in flow. When the carboxylic acid was protected as an ester, β -functionalization of the dicarbonyl took place. For example, with the addition of ethanol under identical electrolysis conditions, the product **43** could be obtained in high enantioselectivity.

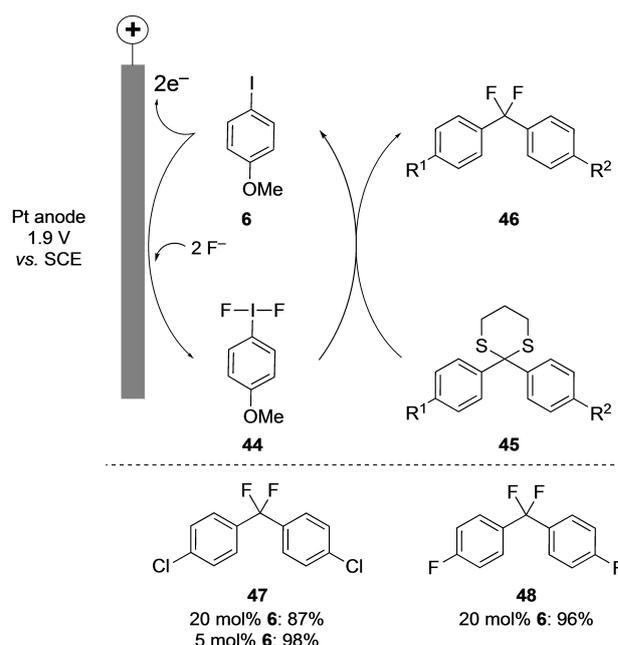
8. Electrocatalysis with Iodine(III)

Electrochemical applications of iodine(III) reagents has been largely limited to stoichiometric applications and only a few electrocatalytic reports are known to date. Since the oxidation of aryl iodides typically

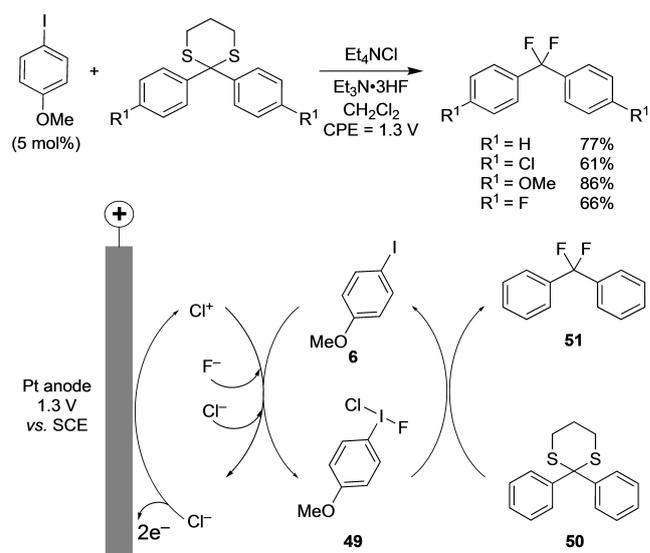
requires substantial overpotentials, electrochemically generated iodanes are frequently used in an excellent manner. In this aspect, the high oxidation potentials of aryl iodides are circumvented by spatial separation of the substrate from the electrolysis step. Although excellent methods are highly efficient, they obviate some of the sustainability advantages of electrochemistry. Especially, the atom economic prospects. Achieving selective aryl iodide oxidation in preference to direct substrate activation is often challenging, which results in this deficiency of electrocatalytic procedures. Furthermore, if there is a mismatch of reaction-rates between the electrochemical and chemical steps, whereby the reaction between the mediator and product is slower than anodic oxidation of the iodine(I) compound, this can complicate matters further. ‘Pulsed’ electrolysis, where electrolysis is carried out in cycles, can obviate some of these issues. In this process, the reaction mixture is stirred periodically in the absence of electricity in-between each electrical pulse, until the iodine(I) compound is regenerated, and the electricity can be applied again. Although, this process often has inherent disadvantages such as vastly increased reaction times compared with the corresponding stoichiometric application.^[40a] Potentiostatic electrolysis is more prevalent in these electrocatalytic approaches, as opposed to the galvanostatic conditions typically adopted in stoichiometric procedures. This is useful in terms of avoiding direct substrate activation/decomposition if the substrate is activated at similar potentials to the iodoarene. But long reaction times are often a problem caused by inefficient current densities with decreasing substrate concentration.^[49]

Despite these complications, a few groups have successfully demonstrated the use of sub-stoichiometric iodine(I) compounds in electrochemistry. One of the earliest examples is disclosed by Fuchigami for the anodic *gem*-difluorination of dithioketals (Scheme 12).^[39] The electrolysis was performed under constant potential conditions (1.9 V) using 4-iodoanisole as mediator, in a mixture of 0.67 M Et₃N·3HF in MeCN, in an in-cell manner. Since the oxidation potential of the dithioketal (2.1 V vs. SCE, in Et₃N·3HF and DME)^[50] is higher than that of 4-iodoanisole, selective oxidation of **6** occurred at 1.9 V (vs. Ag/Ag⁺) to form **44**, which could immediately react with the dithioketal to provide the *gem*-difluorinated products. Indeed, oxidizing only the thioketal **45** at 1.9 V (vs. Ag/Ag⁺) did not give any desired product. Only 5 mol% of 4-iodoanisole **6** was sufficient to give the products in high yields.

Two years later, Fuchigami and co-workers demonstrated another electrocatalytic approach for the *gem*-difluorination of dithioketals.^[42] Here, rather than the direct oxidation of the aryl iodine, the authors show an indirect oxidation with chloride ions. The active hypervalent iodine reagent was generated *via* chloride ion



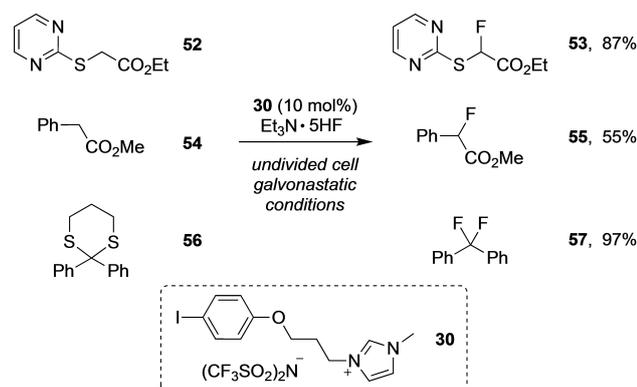
Scheme 12. Mechanism for the *gem*-difluorination of dithioketals by sub-stoichiometric quantities of **6**.



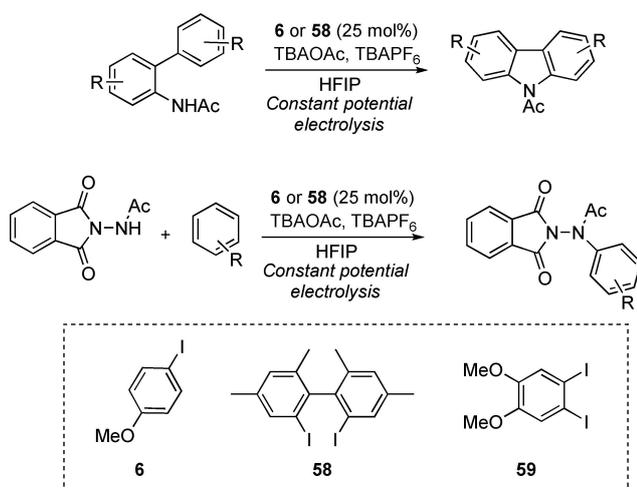
Scheme 13. Aryl iodide oxidation *via* chloride ion mediators and their subsequent in-cell reaction.

mediation (Et₄NCl as a source of chloride ions) (Scheme 13). However, rather than the desired iodoarene difluorides being obtained, the authors obtained the chlorofluoro derivative **49** which was also an active fluorinating reagent. Applying just 20 mol% of 4-iodoanisole in the system under potentiostatic reaction conditions (1.3 V) gave the desired product **51** in 81% yield. A further reduction to 5 mol% resulted in a slight decrease to 77% yield for **51**.

Anodic passivation is a problem with the direct anodic *gem*-difluorination of dithioketals,^[50] however this mediatory system obviates any passivation. Compound **30** can also be used in sub-stoichiometric quantities for electrochemistry (Scheme 14).^[45] It has been shown as an effective catalyst for *gem*-difluorination, benzylic fluorination and the mono-fluorination of organosulfur compounds. More recently, Powers *et al.* demonstrated the use of iodoarenes in sub-stoichiometric quantities for the electrosynthesis of carbazoles and oxidative amide-arene coupling in HFIP (Scheme 15).^[13] Similar to the above mentioned procedures, the use of electron rich arenes (onset potential ~1.40 V vs. Ag/Ag⁺) and **58** (1.68 V vs. Ag/Ag⁺), and potentiostatic electrolysis were the key to the success of this procedure, to avoid direct substrate oxidation. Mediator **58** was designed to increase the oxidizing power of the iodine(III) reagent. Just 25 mol% of the iodoarene mediators were necessary to generate the products in good yields. The procedure showed extremely good functional group tolerance,



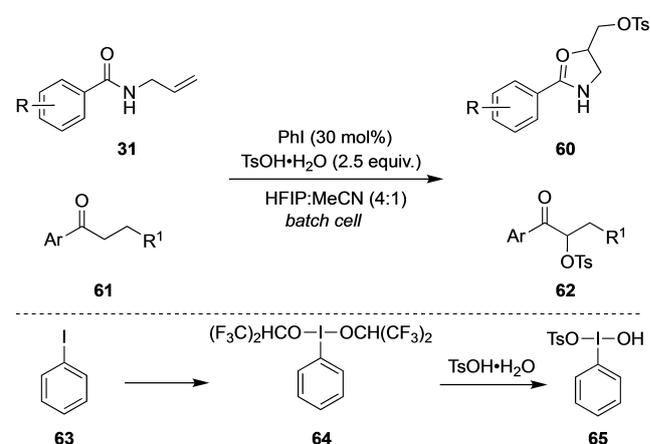
Scheme 14. In-cell, electrocatalytic application of a recyclable mediator.



Scheme 15. Electrocatalytic process for C–N/C–H coupling.

with a series of 22 carbazoles and 9 amide-arene coupled products obtained with excellent yields in most cases.

Since high catalyst loadings, i.e. ≥ 10 mol%, are largely necessary for good yields in these electrocatalytic methods, Powers *et al.* designed a new class of aryl iodide mediators for electrocatalytic application.^[20] The newly designed mediator **59** was an efficient electrocatalyst for C–H/E–H coupling that operated at as low as 0.5 mol% catalyst loading (compound **59**). Compared to **6**, improved product yields and high faradaic efficiencies were observed using **59** even at lower catalyst loadings. In a similar fashion, Xu and co-workers found **6** was an effective electrocatalyst for the synthesis of NH-sulfoximines and NH-sulfonimidamides.^[51] Here, galvanostatic electrolysis was employed in preference to potentiostatic electrolysis. Just 10 mol% of the catalyst was enough to generate the products in good to excellent yields in all cases. The electrocatalytic hydroxylation of arenes with a rhodium catalyst and the use of catalytic amounts of iodine(III) reagents was reported by Ackermann.^[52] The reaction took place in an undivided cell and provided high yields of the reaction products. The rhodium catalytic cycle (not shown) has been investigated in detail in which the rhodium catalyst is re-oxidized with electrogenerated [(bistrifluoroacetoxy)iodo]benzene. Moran and Elsherbini very recently disclosed some further developments in iodine(I)/iodine(III) catalytic processes in which cyclizations and α -oxytosylations have been investigated (Scheme 16).^[53] Initially, iodobenzene **63** is oxidized in the presence of HFIP to **64**, which undergoes ligand exchange with tosylic acid to form the more stable Koser's reagent **65**. Compound **65** is the active iodine(III) reagent which interacts with the corresponding substrate. Using 30 mol% of iodobenzene facilitates good yields for a broad range of substrates of

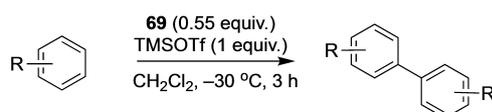
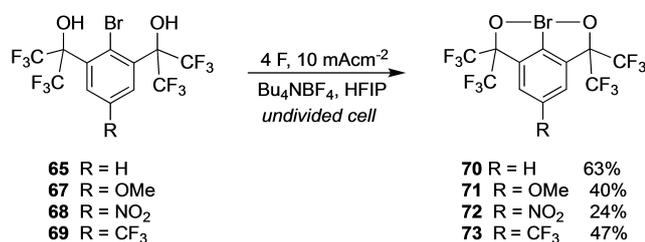


Scheme 16. Electrogeneration of Koser's reagent and its electrocatalytic application.

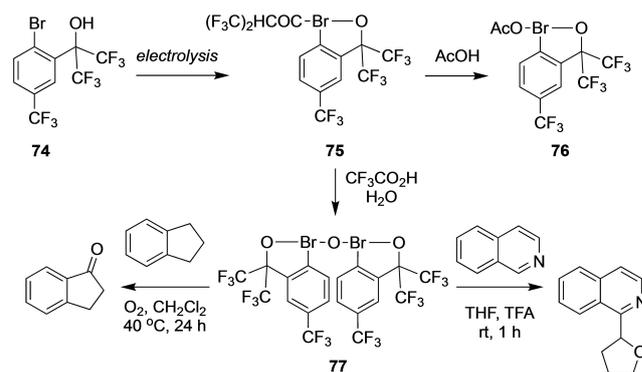
type **31** and **61**. A similar electrocatalytic oxytosylation with **63** was reported by He and co-workers, employing 20 mol% of the mediator.^[16]

9. Hypervalent Bromine Compounds

Hypervalent bromine compounds often exhibit superior reactivity compared to the analogous hypervalent iodine reagents owing to their higher ionization potential, greater electrophilicity and nucleofugality.^[54] Though, there is a notable lack of reports for their synthesis, especially in electrochemistry, due to the higher thermodynamic barrier for the oxidation of bromine. For instance, the oxidation potential of aryl bromides (2.3 V for 2-Br-C₆H₄-CO₂Et vs. Ag/Ag⁺) is significantly higher than the corresponding aryl iodide (1.9 V for *o*-(CO₂Et)C₆H₄I vs. Ag/Ag⁺).^[55] In this respect, stronger oxidizing reagents are required for their synthesis and the breath of oxidants available is far more limited than in hypervalent iodine chemistry. For a long time, the most reliable method for their synthesis followed a ligand exchange of BrF₃, a highly toxic, pyrophoric and reactive compound, which circumvented the unfavorable oxidation process. Though in very recent years, BrF₃ free approaches have emerged.^[56] Electrochemistry is a powerful tool for oxidation chemistry as the narrow redox potential of chemical oxidants can be avoided by finely tuning the electrolysis parameters. In 2021, Francke, Suna and co-workers developed a ground breaking synthesis for bromine(III) reagents by using electrochemical oxidation (Scheme 17).^[57] The anodic oxidation of an aryl bromide, bearing two coordinating hexafluoro-2-hydroxypropenyl substituents, delivered the stable bromine(III) derivatives analogous to Martin's reagent.^[58] Electrolysis was carried out in a simple undivided batch cell bearing a glassy carbon anode and platinum cathode, with HFIP as the solvent and TBABF₄ as the electrolyte under galvanostatic conditions. The corresponding half peak potentials ($E_{p/2}$)



Scheme 17. An electrochemical procedure for the synthesis of bromine(III) reagents.



Scheme 18. Second generation of electrochemically generated bromine(III) reagents.

were situated in a range of between 1.86 V (for **67**) and 2.6 V (for **68**). Such reagents displayed broad synthetic applicability and were demonstrated in oxidative diaryl coupling, oxidative amidations and benzoxazole formation with good yields. Although the bromine reagents were electrochemically synthesized, they were extracted from the electrolysis mixture before further use (ex-cell type application). Francke and Suna also published mechanistic studies for the electrochemical production of the bromane analogue.^[59] The reaction proceeds *via* parallel ECEC (Figure 1) and ECE_{disp} mechanisms.

Building on this knowledge, Suna and co-workers expanded this platform for the electrochemical synthesis of dimeric bromine(III) compounds (Scheme 18).^[60] The anodically generated benzbromoxole **75** serves as a versatile platform to access diverse bromine(III) congeners, including acetoxy-, alkoxy-, ethynyl- and diaryl bromanes. Compound **75** is a crystalline solid that can be stored in the freezer for 8 weeks. It is stable in organic solvents such as deuterated chloroform ($\tau_{1/2}=96 \text{ h}$) and deuterated acetonitrile ($\tau_{1/2}=168 \text{ h}$) at room temperature, but the stability can be improved by exchanging the HFIP ligand for acetate ($\tau_{1/2}=520 \text{ h}$ in MeCN-d₃ for compound **76**). The aryl bromine **74** exhibits a single irreversible oxidation peak ($E_{p/2}=2.62 \text{ V}$) which is higher than that of the aryl bromide **69** ($E_{p/2}=2.54 \text{ V}$). Product **77**, obtained by the hydrolysis of **75**, was synthetically useful for benzylic oxidation and Minisci-type arylations. Homolytic cleavage of the Br–O bond provides a convenient source of electrophilic radicals.

10. Conclusions

The electrochemical generation of hypervalent iodine reagents has seen rapid development over the past 5 years. Considerable diversity in the reactions and reagents that can be accessed has been reported

throughout the literature. Although electrochemistry has benefits in terms of sustainability, the other benefits are often overlooked, including, the simplicity for the purification of iodine(III) reagents in the absence of chemical oxidants. With the growing number of procedures for the electrosynthesis of hypervalent iodine reagents, electrochemical methods are becoming increasingly popular in the field. Though, there are still some methodological deficits. For instance, the catalytic application of hypervalent iodine reagents using chemical oxidants is well-established in the field, but few electrocatalytic approaches are reported. Moreover, asymmetric reactions with chiral iodoarenes have only been reported once, which is surprising given the plethora of asymmetric chemistry available to iodine(III) chemistry. Nevertheless, ground-breaking advances have been made in the past 5 years which is sure to continue the advance of hypervalent iodine electrochemistry.

References

- [1] T. Wirth, *Top. Curr. Chem.* **2003**, *224*, 1–4.
- [2] C. Willgerodt, *J. Prakt. Chem.* **1886**, *33*, 154–160.
- [3] V. V. Zhdankin, *Hypervalent Iodine Chemistry: Preparation, Structure, and Synthetic Applications of Polyvalent Iodine Compounds*, Wiley, Hoboken, **2013**, pp. 21–143.
- [4] a) T. H. Wöste, K. Muñoz, *Synthesis* **2016**, *48*, 816–827; b) F. Scheidt, M. Schäfer, J. C. Sarie, C. G. Daniliuc, J. J. Molloy, R. Gilmour, *Angew. Chem. Int. Ed.* **2018**, *57*, 16431–16435.
- [5] K. Miyamoto, J. Yamashita, S. Narita, Y. Sakai, K. Hirano, T. Saito, C. Wang, M. Ochiai, M. Uchiyama, *Chem. Commun.* **2017**, *53*, 9781–9784.
- [6] A. Maity, S.-M. Hyun, D. C. Powers, *Nat. Chem.* **2018**, *10*, 200–204.
- [7] a) R. Francke, *Curr. Opin. Electrochem.* **2021**, *28*, 100719; b) C. Chen, X. Wang, T. Yang, *Front. Chem.* **2022**, *10*, 883474.
- [8] F. Fichter, P. Lotter, *Helv. Chim. Acta* **1925**, *8*, 438–442.
- [9] a) M. Elsherbini, T. Wirth, *Chem. Eur. J.* **2018**, *24*, 13399–13407; b) T. Wirth, *Curr. Opin. Electrochem.* **2021**, *28*, 100701.
- [10] Y. Amano, S. Nishiyama, *Tetrahedron Lett.* **2006**, *47*, 6505–6507.
- [11] M. Elsherbini, B. Winterson, H. Alharbi, A. A. Folgueiras-Amador, C. Génot, T. Wirth, *Angew. Chem. Int. Ed.* **2019**, *58*, 9811–9815.
- [12] B. L. Frey, P. Thai, L. Patel, D. C. Powers, *Synthesis* **2023**, DOI: 10.1055/a-2029-0617.
- [13] A. Maity, B. L. Frey, N. D. Hoskinson, D. C. Powers, *J. Am. Chem. Soc.* **2020**, *142*, 4990–4995.
- [14] W.-C. Gao, Z.-Y. Xiong, S. Pirhaghani, T. Wirth, *Synthesis* **2019**, *51*, 276–284.
- [15] H. Höffelner, H. W. Lorch, H. Wendt, *J. Electroanal. Chem. Interfacial Electrochem.* **1975**, *66*, 183–194.
- [16] a) B. Zu, J. Ke, Y. Guo, C. He, *Chin. J. Chem.* **2021**, *39*, 627–632; b) T. Bystron, B. Devadas, K. Bouzek, J. Svoboda, V. Kolarikova, J. Kvicala, *ChemElectroChem* **2021**, *8*, 3755–3761.
- [17] K. Watts, W. Gattrell, T. Wirth, *Beilstein J. Org. Chem.* **2011**, *7*, 1108–1114.
- [18] R. Filler, R. M. Schure, *J. Org. Chem.* **1967**, *32*, 1217–1219.
- [19] S. Doobary, D. L. Poole, A. J. J. Lennox, *J. Org. Chem.* **2021**, *86*, 16095–16103.
- [20] B. L. Frey, M. T. Figgins, G. P. Van Trieste, R. Carmieli, D. C. Powers, *J. Am. Chem. Soc.* **2022**, *144*, 13913–13919.
- [21] L. L. Miller, A. K. Hoffmann, *J. Am. Chem. Soc.* **1967**, *89*, 593–597.
- [22] M. Elsherbini, W. J. Moran, *Org. Biomol. Chem.* **2021**, *19*, 4706–4711.
- [23] J. Spils, T. Wirth, B. J. Nachtsheim, *Beilstein J. Org. Chem.* **2023**, *19*, 27–32.
- [24] J. P. Martin, P. Derek, *J. Electrochem. Soc.* **2001**, *148*, D37.
- [25] a) D. Kajiyama, T. Saitoh, S. Nishiyama, *Electrochem.* **2013**, *81*, 319–324; b) Y. Amano, S. Nishiyama, *Heterocycles* **2008**, *75*, 1997–2003; c) T. Izawa, S. Nishiyama, S. Yamamura, *Tetrahedron* **1994**, *50*, 13593–13600.
- [26] Y. Nishihama, Y. Amano, T. Ogami, S. Nishiyama, *Electrochem.* **2006**, *74*, 609–611.
- [27] T. Broese, R. Francke, *Org. Lett.* **2016**, *18*, 5896–5899.
- [28] O. Koleda, T. Broese, J. Noetzel, M. Roemelt, E. Suna, R. Francke, *J. Org. Chem.* **2017**, *82*, 11669–11681.
- [29] a) Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujita, S. Mitoh, H. Sakurai, S. Oka, *J. Am. Chem. Soc.* **1994**, *116*, 3684–3691; b) Y. Kita, H. Tohma, M. Inagaki, K. Hatanaka, T. Yakura, *Tetrahedron Lett.* **1991**, *32*, 4321–4324; c) Y. Kita, M. Egi, T. Takada, H. Tohma, *Synthesis* **1999**, 885–897.
- [30] I. Colomer, C. Batchelor-McAuley, B. Odell, T. J. Donohoe, R. G. Compton, *J. Am. Chem. Soc.* **2016**, *138*, 8855–8861.
- [31] A. F. Roesel, T. Broese, M. Májek, R. Francke, *ChemElectroChem* **2019**, *6*, 4229–4237.
- [32] a) T. Bystron, A. Horbenko, K. Syslova, K. K. Hii, K. Hellgardt, G. Kelsall, *ChemElectroChem* **2018**, *5*, 1002–1005; b) B. Devadas, J. Svoboda, M. Krupička, T. Bystron, *Electrochim. Acta* **2020**, *342*, 136080.
- [33] S. J. Folkman, R. G. Finke, J. R. Galán-Mascarós, G. M. Miyake, *ACS Sustainable Chem. Eng.* **2021**, *9*, 10453–10467.
- [34] P. Thai, B. L. Frey, M. T. Figgins, R. R. Thompson, R. Carmieli, D. C. Powers, *Chem. Commun.* **2023**, *59*, 4308–4311.
- [35] a) S. Arndt, R. Rücker, A. Stenglein, S. R. Waldvogel, *Org. Process Res. Dev.* **2022**, *26*, 2447–2455; b) C. M. Kisukuri, R. J.-R. Bednarz, C. Kampf, S. Arndt, S. R. Waldvogel, *ChemSusChem* **2022**, *15*, e202200874.
- [36] S. Dehnen, L. L. Schafer, T. Lectka, A. Togni, *J. Org. Chem.* **2021**, *86*, 16213–16219.

- [37] H. Schmidt, H. Meinert, *Angew. Chem.* **1960**, *72*, 109–110.
- [38] I. N. Rozhkov, *Russ. Chem. Rev.* **1976**, *45*, 615–629.
- [39] T. Fuchigami, T. Fujita, *J. Org. Chem.* **1994**, *59*, 7190–7192.
- [40] a) S. Doobary, A. T. Sedikides, H. P. Caldora, D. L. Poole, A. J. J. Lennox, *Angew. Chem. Int. Ed.* **2020**, *59*, 1155–1160; b) B. Winterson, T. Rennigholtz, T. Wirth, *Chem. Sci.* **2021**, *12*, 9053–9059.
- [41] T. Fuchigami, S. Inagi, *Chem. Commun.* **2011**, *47*, 10211–10223.
- [42] T. Fujita, T. Fuchigami, *Tetrahedron Lett.* **1996**, *37*, 4725–4728.
- [43] S. Hara, T. Hatakeyama, S.-Q. Chen, K. Ishi-i, M. Yoshida, M. Sawaguchi, T. Fukuhara, N. Yoneda, *J. Fluorine Chem.* **1998**, *87*, 189–192.
- [44] T. Sawamura, S. Kuribayashi, S. Inagi, T. Fuchigami, *Adv. Synth. Catal.* **2010**, *352*, 2757–2760.
- [45] T. Sawamura, S. Kuribayashi, S. Inagi, T. Fuchigami, *Org. Lett.* **2010**, *12*, 644–646.
- [46] J. D. Haupt, M. Berger, S. R. Waldvogel, *Org. Lett.* **2019**, *21*, 242–245.
- [47] J. D. Herszman, M. Berger, S. R. Waldvogel, *Org. Lett.* **2019**, *21*, 7893–7896.
- [48] M. Ghosh, V. S. Shinde, M. Rueping, *Beilstein J. Org. Chem.* **2019**, *15*, 2710–2746.
- [49] D. Pollok, S. R. Waldvogel, *Chem. Sci.* **2020**, *11*, 12386–12400.
- [50] Y. Tomonori, F. Toshio, *Chem. Lett.* **1992**, *21*, 1995–1998.
- [51] X. Kong, L. Lin, X. Chen, Y. Chen, W. Wang, B. Xu, *ChemSusChem* **2021**, *14*, 3277–3282.
- [52] L. Massignan, X. Tan, T. H. Meyer, R. Kuniyil, A. M. Messinis, L. Ackermann, *Angew. Chem. Int. Ed.* **2020**, *59*, 3184–3189.
- [53] M. Elsherbini, W. J. Moran, *J. Org. Chem.* **2023**, *88*, 1424–1433.
- [54] M. Ochiai, A. Yoshimura, K. Miyamoto, S. Hayashi, W. Nakanishi, *J. Am. Chem. Soc.* **2010**, *132*, 9236–9239.
- [55] K. Miyamoto, M. Saito, S. Tsuji, T. Takagi, M. Shiro, M. Uchiyama, M. Ochiai, *J. Am. Chem. Soc.* **2021**, *143*, 9327–9331.
- [56] M. Lanzi, Q. Dherbassy, J. Wencel-Delord, *Angew. Chem. Int. Ed.* **2021**, *60*, 14852–14857.
- [57] I. Sokolovs, N. Mohebbati, R. Francke, E. Suna, *Angew. Chem. Int. Ed.* **2021**, *60*, 15832–15837.
- [58] T. T. Nguyen, J. C. Martin, *J. Am. Chem. Soc.* **1980**, *102*, 7382–7383.
- [59] N. Mohebbati, I. Sokolovs, P. Woite, M. Lõkov, E. Parman, M. Ugandi, I. Leito, M. Roemelt, E. Suna, R. Francke, *Chem. Eur. J.* **2022**, *28*, e20220097.
- [60] I. Sokolovs, E. Suna, *Org. Lett.* **2023**, *25*, 2047–2052.