Electrochemistry and Reactivity of Chelation-stabilized Hypervalent Bromine(III) Compounds


Abstract: Hypervalent bromine(III) reagents possess a higher electrophilicity and a stronger oxidizing power compared to their iodine(III) counterparts. Despite the superior reactivity, bromine(III) reagents have a reputation of hard-to-control and difficult-to-synthesize compounds. This is partly due to their low stability, and partly because their synthesis typically relies on the use of the toxic and highly reactive BrF₃ as a precursor. Recently, we proposed chelation-stabilized hypervalent bromine(III) compounds as a possible solution to both problems. First, they can be conveniently prepared by electro-oxidation of the corresponding bromoarenes. Second, the chelation endows bromine(III) species with increased stability while retaining sufficient reactivity, comparable to that of iodine(III) counterparts. Finally, their intrinsic reactivity can be unlocked in the presence of acids. Herein, an in-depth mechanistic study of both the electrochemical generation and the reactivity of the bromine(III) compounds is disclosed, with implications for known applications and future developments in the field.

Introduction

The chemistry of hypervalent halogen species has experienced tremendous progress in recent decades, with hypervalent iodine(III) compounds playing an increasingly important role in modern organic synthesis.[11] The related isoelectronic hypervalent bromine(III) reagents exhibit stronger electrophilicity, better nucleofugality of the bromanyl unit, and more driving force for oxidations,[2–4] as evidenced by a series of unprecedented synthetic transformations involving oxidative coupling of alkenes and primary alcohols to conjugated enones.[5] Hofmann rearrangement of sulfonamides to the corresponding N-arylsulfonylamoyl fluorides,[6] regioselective C–H functionalization of non-activated alkenes,[7,8a] and a rare Bayer-Villiger-type oxidation of open-chain aliphatic aldehydes.[9] Recently, the application of diaryl-λ³-bromanes in catalysis[10] and in cycloaddition reactions[11] was also reported. Although these notable achievements underscore the remarkable synthetic potential of this reagent class, hypervalent bromine(III) chemistry appears to be underdeveloped in comparison to that of the iodine(III) counterparts. This notable disparity has been ascribed to two unfavorable factors. First, bromine(III) reagents exhibit poor stability and high oxidizing power, which has led to the general perception of difficult-to-control reactivity and poor compatibility with functional groups.[2,11] Second, conventional routes to λ³-bromane reagents rely eventually on the use of BrF₃, a highly toxic and extremely reactive liquid that demands for specific equipment and experimental techniques for its safe handling.[8]

Recently, a chelation-stabilized λ³-bromane reagent[12] (Martin's bromane 2, Scheme 1) was proposed as a possible solution to both the stability and the accessibility issue. Inspired by the successful in situ generation of reactive hypervalent iodine species via anodic oxidation of iodoarene precursors,[13,14] we presented a convenient electrochemical approach toward synthesis of 2.[15] The method is based on the anodic oxidation of parent aryl bromides 1 containing two coordinating hexafluoro-2-hydroxy-propanoyl substituents under galvanostatic conditions in an undivided cell (Eq. (1) in Scheme 1). The protocol was used to prepare a series of para-substituted derivatives of...
Martin’s bromane 2 that revealed remarkably high redox potentials covering a range from 1.86 V to 2.60 V versus Ag/AgNO₃. The compounds are benchtop-stable and have proven useful as reagents in various transformations. Thus, λ₃-bromane 2a (R = H) was shown to be sufficiently reactive to effect clean oxidative amidation of aniline derivatives (Eq. (2a) in Scheme 1). Furthermore, the intrinsic reactivity of hypervalent bromine(III) species can be unlocked by addition of Brønsted or Lewis acids, for example to achieve dehydrogenative homocoupling of substituted anisoles (Eq. (2b) in Scheme 1). Herein, mechanistic insights into both the electrochemical generation and the reactivity of chelation-stabilized bromine(III) compounds are disclosed.

Results and Discussion

Anodic bromane generation

To better understand the mechanism of bromane formation, we intended to combine detailed electroanalytical studies with quantum chemical modeling. In our previous work,¹⁵ we have already obtained some information about bromoarene oxidation by performing preliminary electroanalytical experiments. Thus, voltammetric analysis of 1 at 10 mV s⁻¹ between 0 and 2.7 V versus Ag/0.01 M AgNO₃ (E_ref = +87 mV vs. Fc/Fc⁺ couple)⁶ using an electrolyte consisting of 0.1 M NBu₄BF₄ in HFIP showed that each of the bromoarenes exhibits a single irreversible anodic feature. The corresponding half-peak potentials (E_P/2) are situated between 1.86 V (1 e, R = OMe) and 2.60 V (1 g, R = NO₂), which means that the potential of 1 is flexibly tunable within a range of 0.74 V (see Table 1). A linear relationship between E_P/2 and σ⁺ substituent coefficients showed that the oxidizability is dependent on the electron donating or withdrawing ability of the substituent R and that the redox potential of the 1/2 couple thus exhibits a somewhat predictable behavior.

For the present study, one of the aims was to learn more about the mechanism of the formation of 2. For this purpose, the scan rate v was increased stepwise from 10 mV s⁻¹ to 1 V s⁻¹. The observed voltammetric responses of 1a are characteristic for the bromoarene series with the signal shape indicating that one or more chemical steps are coupled to the electron transfer (“chemical irreversibility”, see representative CVs in Figure 1A). Bromoarenes 1b-d, 1f and 1g exhibit analogous behavior (see the Supporting Information), whereas the voltammetry of 1e (R = OMe) is rather exceptional (Figure 1B). Initially, 1e displays irreversible behavior at low scan rates (dashed curve), followed by a gradual change to almost full reversibility with increasing v (dotted and solid lines, for j_p,ox/j_p,red ratios see Table S2 in the Supporting Information).
indicating that the intermediate formed upon electron transfer is stable on the voltammetry time scale.

Another striking difference between 1e and the other bromoarenes is that the anodic peak current density, \(j_p\), of the 4-OMe-substituted compound is significantly smaller. Both \(j_p\) and the slope of the linear fit of \(j_p\) versus \(v^{0.5}\) are approximately half as high as the average values for the other compounds (see Figure 1C and Table 1). One-electron oxidation of 1e and two-electron oxidation of the other bromoarenes, provide a reasonable rationale for this difference. In fact, it is well-established that a \(j_p\) value (and a \(j_p\) vs. \(v^{0.5}\) slope, respectively) twice as high as for a comparable one-electron transfer is characteristic of a two-electron process in which \(i_1\), the second oxidation is energetically more favorable than the first one and \(i_1i_2\), in which a fast chemical reaction is interposed between the two electrochemical steps.\(^{[14]}\)

A mechanism consistent with the observations described above is shown in Figure 2. Accordingly, bromanes 2 are generally formed via two electrochemical oxidation steps in an EEC pathway, which includes initial electron abstraction, deprotonation, further oxidation, and a second deprotonation (leading to \(1^{*+}, 1^*, 2^+,\) and 2, respectively). Competitive homogeneous disproportionation of \(1^*\) (or between \(1^{*+}\) and \(1^*\)) within the diffusion layer would also be in agreement with the diagnostic criteria (EEC\(_{\text{disp}}\) pathway).\(^{[17]}\) However, when the deprotonation step \(1^{*+}\rightarrow 1^*\) is slow due to a stabilization of \(1^{*+}\), the radical cation has sufficient time to diffuse into the bulk solution, where \(1^*\) is slowly formed (Figure 2, pathway highlighted in blue). Subsequent disproportionation again leads to the formation of 2 and 1 (2\(^+\) and 1, respectively). Such a delayed disproportionation would explain the distinct behavior of 1e, as it is in agreement both with the one electron peak in the CV and the observed formation of 2e in the preparative-scale electrolysis. Here, the electron-donating ability of the 4-methoxy substituent seems to be responsible for the enhancement of the lifetime of 1e\(^+\).

Further probing into the mechanism of bromane formation was carried out with a series of quantum chemical calculations using a state-of-the-art combination of density functional theory and coupled cluster methods (see computational details in the Supporting Information). The obtained results presented in Table 2 confirm the feasibility of the reaction sequence \(1\rightarrow 1^{*+}\rightarrow 1^*\rightarrow 2^+\rightarrow 2\) in terms of reaction free energies for all investigated derivatives. For all proton transfer reactions, cathodically generated HFIP anions have been assumed as proton acceptors, as has been established previously.\(^{[16]}\) The investigated deprotonations occur spontaneously without any barrier in silico. Similarly, the outer sphere electron transfer is expected to be associated with reaction barriers that are readily overcome under the given reaction conditions, since the redox-active sites are well accessible in all cases.

A closer look at the individual reaction steps yields interesting insight into certain aspects of the observed reactivity and provides further support for the proposed reaction mechanism (Table 2). For example, in good agreement with the experimental observations, the calculated ionization energy of \(1^*\) is lower than that of 1, rendering the second electron transfer more favorable than the first one. In contrast, the ionization free energy of \(1^{*+}\) is predicted to be significantly higher. On the basis of these results, the possibility for formation of 2 via an EEC mechanism appears unlikely.

It is furthermore interesting to consider the calculated free energy of the disproportionation reactions \(1^{*+}\rightarrow 1^*\rightarrow 2^+\rightarrow 2\) as well as 2 \(1^*\rightarrow 1^*+2\), which are favorable for all investigated derivatives with predicted free energies of approx. \(-30\) kcal mol\(^{-1}\). Only for 1e\(^+\) + 1e\(^*\) \(\rightarrow 2e + 2e^+\) the reaction free energy is significantly less negative (\(-14.5\) kcal mol\(^{-1}\)). This finding can be attributed to the relative stability of 1e\(^+\) that originates from the electron-donating character of the 4-methoxy group. The spin density plots shown in Figure 3 reflect this assessment. Moreover, our calculations indicate that 1e\(^+\) is less prone to deprotonation than all other 1\(^+\) derivatives (\(-34.0\) kcal mol\(^{-1}\) vs. approx. \(-50\) kcal mol\(^{-1}\)) and thereby cor-

![Figure 2. Proposed mechanism for anodic bromane formation.](image)

| Table 2. Calculated [DFT + DLPNO-CCSD(T)] reaction free energies (in kcal mol\(^{-1}\)) for all elementary steps of the electrochemical conversion of 1 to 2. |
|---|---|---|---|---|---|---|
| Derivative | 1\(\rightarrow\)1\(^*\) | 1\(^*\)\(\rightarrow\)1* | 1*\(\rightarrow\)1\(^{*+}\) | 1\(^{*+}\)\(\rightarrow\)1* | 2\(^+\)\(\rightarrow\)2 | 2\(\rightarrow\)1 | 2\(\rightarrow\)1 + 2 | 1\(^*\)\(\rightarrow\)1* + 1\(^{*+}\)\(\rightarrow\)2 + 2 |
| a | 169.9 | -49.2 | 180.3 | 139.2 | -49.5 | 210.5 | -31.1 | -30.7 |
| b | 170.8 | -49.8 | 181.4 | 141.4 | -50.1 | 212.4 | -29.6 | -29.4 |
| c | 170.4 | -40.2 | 180.8 | 141.8 | -51.3 | 211.5 | -30.5 | -28.1 |
| d | 169.0 | -48.0 | 178.9 | 139.7 | -49.1 | 211.6 | -30.3 | -29.3 |
| e | 154.5 | -34.0 | 169.6 | 140.0 | -50.0 | 210.5 | -30.5 | -14.5 |
| f | 170.9 | -50.5 | 180.5 | 143.0 | -52.7 | 210.7 | -30.1 | -28.0 |
| g | 171.5 | -51.3 | 182.2 | 143.5 | -52.3 | 211.4 | -29.1 | -28.1 |
roborate the proposed mechanism for the formation of 2e. Considering the significant driving force for both disproportionation reactions, we assume that the predominant reaction type will most likely be determined by the availability of the involved species (1e\textsuperscript{**} vs. 1e\textsuperscript{*}) rather than by thermodynamic factors.

Another experimental observation supports the proposed ECE\textsubscript{disp} mechanism for 1e \textrightarrow 2e. During preparative-scale electrolysis of 1, the electrolyte solution usually remains colorless or, sometimes, becomes slightly yellowish. Only the oxidation of 1e leads to a deep red coloration of the electrolyte solution, which disappears shortly after switching off the current. This prompted us to perform a spectroelectrochemical (SEC) analysis of the oxidation of 1e (see Figure 4). After applying a potential of 2.0 V, two bands arise simultaneously at 336 nm and 534 nm (Figure 4, bottom) in addition to the band of 1e at 288 nm. An apparent increase of the latter can be assigned to formation of 2e, which absorbs at similar wavelengths (284 nm, see pure component spectrum in Figure 4, top). The new features are in good agreement with the bands predicted by quantum chemical calculations (321 nm and 487 nm). Noteworthy, no bands in the respective energy regimes are predicted for 1e\textsuperscript{*} and 2e\textsuperscript{**} (see Table S8 in the Supporting Information). After switching off the potential, the bands at 336 nm and 534 nm rapidly disappear, while the signal for 2e continues to increase, which is further evidence for the proposed disproportionation mechanism.

Cathodic reduction of bromanes

As described in the previous section, the CVs of the bromoar- enes recorded in HFIP show that with the exception of 1e, the compounds are irreversibly oxidized, meaning that there is no associated reduction peak in the reverse scan. Thus, the anodically generated bromanes appear to be surprisingly robust toward reduction at the cathode. Knowledge of the cathodic behavior is still desirable, as it allows conclusions to be drawn about the properties of 2 as a chemical oxidant (see below). In this regard, an electroanalytical study demands for employing solvents that were used in the synthetic applications, that is, acetonitrile for C–H amidations and dichloromethane for arene-arene homocouplings (Eq. (2a) and (2b) in Scheme 1)\textsuperscript{[15]}. CV studies of the cathodic reduction were thus carried out in each of these solvents using a glassy carbon working electrode and NBu\textsubscript{4}BF\textsubscript{4}, as the supporting electrolyte, whereby both the shape of the profiles and the half-peak potentials are quite similar.

In the range between 0.1 and −0.9 V, each of the bromanes exhibits a single irreversible feature, indicating that electron transfer is followed by a rapid chemical step. The forward scans are shown in Figure 5 exemplarily for acetonitrile (for full CVs, see the Supporting Information). The corresponding E\textsubscript{1/2} values are situated in the range between −0.35 V (2g, R=NO\textsubscript{2}) and −0.53 V (2e, R=OMe; see table in Figure 5). It follows that i) the electrochemical reduction of 2 is relatively difficult, ii) with 0.18 V, the range of reduction potentials covered by series 2 is relatively narrow compared to the range of oxidation potentials of 1 (0.74 V). A good match was found between the experimental half-peak potentials and E\textsubscript{1/2} values predicted on the basis of a two-parameter correlation with \(\sigma\text{R}\) and \(\sigma\text{P}\) substituent constants (Figure 5, bottom right; for details see Tables S5 and S6 in the Supporting Information), the latter two explicitly accounting for inductive (\(\sigma\text{P}\)) and resonance effects (\(\sigma\text{R}\))\textsuperscript{[19]}. Accordingly, there is a correlation between E\textsubscript{1/2} and electron-donating/withdrawing ability of R, indicating the inclusion of the aromatic ring in the reduction process (albeit, apparently, to a much lesser extent than for the oxidation of 1).

Surprisingly, further analysis of the reduction peaks shows that the process, both in CH\textsubscript{3}CN and CH\textsubscript{2}Cl\textsubscript{2}, is associated with merely a single electron exchange (see the Supporting Information). To better understand the underlying mechanism, 2a was subjected to controlled potential electrolysis (CPE, Scheme 2). In acetonitrile, bromoarene 1a could be isolated in 74% yield after passing 1.0 F at −0.78 V versus Ag/AgNO\textsubscript{3} (11% recovered 2a). This result is in agreement with the one electron peak observed in the CV experiments, and can be explained by initial formation of radical anion 2a\textsuperscript{*}, followed by
For applications in synthetic organic chemistry, 2-bromobenzene \(2a\) can thus be considered a poor single electron oxidant. This important finding prompted us to study mechanisms of the recently published reactions involving \(2a\), such as oxidative amination of \(N,N\)-dimethylanilines 3 (Eq. (1), Scheme 3). \(^{[11]}\) The oxidative amination apparently proceeds through the addition of phthalimide 5 to iminium ion \(4a\) that is formed in situ from parent aniline \(3a\) and hypervalent bromine(III) reagent \(2a\). A calculated free energy of \(-19.3\) kcal mol\(^{-1}\) confirms the thermodynamical feasibility of iminium \(4a\) formation induced by \(2a\).

However, a literature survey returns controversial mechanisms for iminium \(4a\) formation from aniline \(3a\) and hypervalent iodine(III) species, related to \(2a\). Thus, a single electron transfer (SET) from aniline \(3a\) to hydroxybenziodoxole\(^{[22]}\) or PIDA\(^{[23]}\) was proposed to generate transient radical cation \(3a^{++}\) en route to the iminium ion \(4a\) (Eq. (2), Scheme 3). An alternative mechanistic scenario towards iminium ion \(4a\) involves \(\beta\)-deprotonation of transient aniline-containing iodine(III) species \(T5-2\) (Eq. (3), Scheme 3). \(^{[24]}\) Given the apparent inconsistency in the mechanism of the iodine(III)-mediated oxidative amination reaction, we decided to examine in more detail the reaction of aniline \(3a\) with \(\lambda^2\)-bromobenzene \(2a\).

The comparison of the measured oxidation potential for aniline \(3a\) \((E_{P/2} = 0.40\) V) with the reduction potential of \(\lambda^2\)-bromobenzene \(2a\) \((E_{P/2} = -0.50\) V) in MeCN shows a large potential gap of 0.9 V, suggesting that SET oxidation of aniline \(3a\) by \(2a\) is thermodynamically unfavorable. This assessment is supported by calculations showing that the formation of \(2a^+\) and \(3a^+\) is endergonic \((\Delta G = 20.1\) kcal mol\(^{-1}\)). Of note, electrochemically generated radical cation \(3a^{++}\) was found to be highly unstable and short-lived in MeCN with a half-life on the order of microseconds. \(^{[25]}\) Furthermore, radical cation \(3a^{++}\) was reported to undergo rapid dimerization to \(N,N,N\)-tetramethylbenzidine (TMB; see Scheme 2, Eq. (2)) with an extremely high rate constant \((k = 2.5 \times 10^9\) M\(^{-1}\) s\(^{-1}\)). \(^{[26]}\) The lack of evidence for the formation of TMB upon mixing the equimolar amounts of \(2a\) and \(3a\) in MeCN (in absence of \(S\)) renders highly unlikely the involvement of radical cation \(3a^{++}\) in the oxidative amination. \(^{[27]}\)

Additional experimental evidence against the intermediacy of radical cation \(3a^{++}\) in the oxidative amination was obtained by a control experiment using aniline \(3b\) as the radical clock probe. \(^{[28]}\) Assuming that SET between \(3b\) and \(\lambda^2\)-bromobenzene \(2a\) is feasible, the generated radical cation \(3b^{++}\) should feature any radical character (shown are only two resonance forms for \(3b^{++}\); see Eq. (4), Scheme 3). The O-allyl-substituted aryI radicals such as \(3b^{++}\) are well-known to undergo the radical 5-exo cyclization to \(7^{++}\) with an extremely high rate constant \((k = 6.3 \times 10^9\) s\(^{-1}\) at 30°C). \(^{[29]}\) Subsequent deprotonation and hydrogen atom transfer from MeCN would furnish 2,3-dihydrobenzofuran \(8\). Notably, the formation of \(8\) was not observed in the crude reaction mixture of the oxidative amination. Instead, the desired oxidative amination product 6b was isolated in 63% yield (Eq. (1), Scheme 3). Finally, important evidence against the intermediacy of radical cation \(3a^{++}\) was obtained by EPR studies. Specifically, the formation of radicals could not be observed upon mixing \(\lambda^2\)-bromobenzene \(2a\) (0.1 M solution in MeCN)

**Chemical versus radical reactivity**

The results of the cathodic scans and CPE suggest that although formation of \(2a^+\) is in principle feasible, the one electron reduction is unfavorable and proceeds at negative potentials. 

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**Figure 5.** Top: Background and drift corrected linear sweep voltammograms (LSV) of bromanes \(2a-g\) \((c = 5\) mM) recorded at 10 mVs\(^{-1}\) in CH\(_2\)CN. Bottom left: Half-peak potentials \(E_{\text{pr}}\) (obs.) measured in CH\(_2\)CN and the values predicted using \(\sigma_i\) and \(\sigma_j\) substituent constants \(E_{\text{pr}}\) (pred.), for details see the Supporting Information. Bottom right: Correlation between \(E_{\text{pr}}\) (obs.) and \(E_{\text{pr}}\) (pred.) for 2 in CH\(_2\)Cl\(_2\) and CH\(_2\)CN.

**Scheme 2.** Results of preparative-scale cathodic reduction of \(2a\) in CH\(_2\)CN.
with aniline 3a (0.1 M solution in MeCN) at room temperature. In striking contrast, the formation of a persistent radical intermediate from 2a and 3a was clearly observed when HFIP was used as the solvent at room temperature (for details see Figure S5 in the Supporting Information). Furthermore, the oxidative amination experiment in HFIP using aniline 3b as the radical clock probe (Eq. (4), Scheme 3) returned a highly complex mixture of unidentified products. This result implies a change of the reaction mechanism upon replacing MeCN by HFIP as the solvent. Consequently, the combined mechanistic evidence suggests the SET oxidation of anilines to radical cations $3^+$ by $\lambda^3$-bromane 2a is unlikely under the published oxidative amination conditions in MeCN as the solvent. [15]

The formation of iminium ion 4a in MeCN apparently follows an ionic pathway, involving intramolecular $\beta$-deprotonation within a transient [12-Br-4] complex TS-1 between aniline 3a and Lewis acidic $\lambda^3$-bromane 2a (Eq. (3), Scheme 3). In agreement with the abundant experimental evidence, quantum chemical calculations suggest that an ionic pathway to 6a via 4a is thermodynamically well feasible as illustrated by Figure S8 in the Supporting Information.

Acidic bromane activation

In contrast to the efficiency of $\lambda^3$-bromane 2a in the oxidative amination of anilines, the activation of bromine(III) reagent 2a by the addition of Lewis or Brønsted acids was found to be necessary to accomplish the homocoupling of arenes such as 9 to biaryl 10 in CH$_2$Cl$_2$ (Eq. (1), Scheme 4). [15] Importantly, the closely related hypervalent iodine(III)-mediated oxidative biaryl coupling was shown to proceed through SET oxidation of electron-rich arenes to the corresponding cation radicals $11^+$ (Eq. (2), Scheme 4), [30] and Lewis acid additives such as BF$_3$·OEt$_2$ were required to enhance the SET oxidizing ability of PhI(OCOCF$_3$)$_2$. [31,32] Assuming a similar mechanism for iodine(III) and bromine(III)-mediated biaryl coupling, the requirement for a Lewis acid additive to enhance the SET oxidizing ability of $\lambda^3$-bromane 2a becomes evident given its more negative reduction potential ($E_{P/2} = 0.57$ V) compared to PhI(OCOCF$_3$)$_2$ ($E_{P/2} = 0.20$ V, see the Supporting Information).

TMS-OTf was chosen as Lewis acid additive for the bromine(III)-mediated biaryl coupling. [33] A nearly quantitative formation of biaryl 10 (98% yield) was observed after 3 h at $-30^\circ$C (Eq. (1), Scheme 4), when 2a was used together with 1 equiv. TMS-OTf. TMS-OTf. It should be noted that the formation of 10 was not observed with added TMS-OTf in the absence of 2a. Importantly, TfOH as the additive (1.05 equiv) also resulted in the 2a-mediated formation of biaryl in DCM as the solvent (93% yield of 10). This observation led us to hypothesize that partial hydrolysis of TMSOTf by traces of water under the biaryl coupling conditions may take place to form TFOH, which is the actual activator of 2a. [33] To verify this hypothesis, the TMSOTf-mediated biaryl coupling was performed under standard

Scheme 3. Mechanistic studies of oxidative aminations induced by 2a (calculated free energies in kcal mol$^{-1}$).

reaction conditions in the presence of sub-stoichiometric amounts of DTBP (0.2 equiv) as a proton scavenger (Eq. (1), Scheme 4). The formation of 10 was not observed with the added DTBP. Furthermore, the biaryl coupling also did not proceed in the presence of 2,6-di-tert-butylpyridinium triflate (1.0 equiv; prepared in situ from equimolar amounts of TfOH and DTBP), a relatively weak Brønsted acid that is generated upon proton quench by DTBP. However, biaryl 10 was slowly formed in 79% yield using TMSOTf (1 equiv) with added DTBP (0.2 equiv) and water (0.2 equiv) at room temperature. Possibly, a small excess of TfOH (trace amounts of the acid present in TMSOTf combined with TfOH that was formed upon hydrolysis of TMSOTf) with respect to DTBP was sufficient to catalyze the formation of biaryl 10. Taken together, these experiments provide evidence favoring the activation of the biaryl coupling by TfOH that is generated in situ from TMS-OTf.

Additional support for the acid-base interactions between λ3-bromane 2a and Brønsted acid was obtained by NMR experiments. Thus, a downfield displacement of 1H NMR signals (δ = 0.03 and 0.04 ppm) and 19F NMR signal (δ = 0.19 ppm) for λ3-bromane 2a was observed upon addition of two equivalents of TfOH (see table, Figure 6B). In sharp contrast, the addition of TMSOTf (2 equiv) or BF3·OEt2 (2 equiv) did not lead to noticeable changes in the NMR spectra of 2a. Apparently, TMS-OTf is not a sufficiently strong Lewis acid to form a stable complex with the moderately Lewis basic oxygen atom of the bromaoxole subunit in 2a. Overall, the experiments above provide evidence that the activation of λ3-bromane 2a requires protonation by a strong Brønsted acid such as TfOH (Figure 6A).

Quantum chemical calculations were performed to provide additional insights into the protonation of λ3-bromane 2a with TfOH. According to our results on the local coupled cluster level of theory, the protonation of 2a to 2a-TfOH is associated with a free reaction energy of ΔG = 5.8 kcal mol⁻¹ and virtually no reaction barrier (see Figure 6A; the optimized geometry of the adduct is shown in Figure 6C). This implies that only a small fraction of 2a is protonated by added stoichiometric TfOH which agrees well with the relatively small displacements in chemical shifts observed in 19F and 1H NMR spectra for the 1:2 mixture of 2a-TfOH (Figure 6B). In contrast, the computed 19F and 1H chemical shift values for 2a-TfOH show more pronounced displacements; the calculated average displace-

![Scheme 4. Activation of 2a for oxidative biaryl homo-coupling.](image-url)
ment value for chemical shifts of the two protons at position 3 amounts to $\delta = 0.45$ ppm when going from 2a to 2a-TfOH, while that for a proton at position 4 amounts to 0.66 ppm. Furthermore, an average shift of $\delta = 3.12$ ppm is predicted for the $^{19}$F signals. When compared with the observed displacements of the $^1$H and $^{19}$F NMR shifts for a 1:2 mixture of 2a-TfOH, the computed values have the correct sign and roughly the correct relative size. Therefore, taking into account the small fraction of formed 2a-TfOH under these conditions and considering the progression of the signal position for higher acid concentrations shown in Figure 6D, the computed NMR shifts agree well with our experimental observations and thus support the proposed mechanistic picture of equilibrium protonation of 2a by the added TfOH. These findings, together with the absence of any displacement of the NMR shifts for a 1:2 mixture of 2a-TMOSOTf, provide further evidence for the indirect role of TMOSOTf in terms of activating 2.

The observed equilibrium protonation of $\lambda^1$-bromane 2a called for additional experiments to estimate the approximate acidity of the solution needed for protonating 2a, in terms of the unified pH ($pH_{lab}^{H^\bullet}$) scale. The term $pH_{lab}^{H^\bullet}$ stands for unified pH ($pH_{lab}^H$) "aligned" with the aqueous pH scale, that is, the $pH_{lab}^H$ values in any solvent are directly comparable with the conventional aqueous pH values. In other words, in a solution with a given $pH_{lab}^H$, made in any solvent, the chemical potential of the solvated proton is equal to the chemical potential of solvated proton in water at the same value of conventional pH.

The acidity necessary for protonation of 2a is expressed as a "buffer point pH$_{lab}^{H^\bullet}$", that is, pH$_{lab}^{H^\bullet}$, at which approximately half of 2a is free and half has TfOH added (2a-TfOH, Figure 6A). Experiments for determination of the buffer point were carried out in 1,2-dichloroethane, where a self-consistent acidity scale has been previously established and linked to the unified pH (pH$_{lab}^{H^\bullet}$) scale. The experiments consisted in titration of a mixture of 2a and a reference compound, for which the $pH_{lab}^{H^\bullet}$ and buffer point pH$_{lab}^{H^\bullet}$ estimates are available in 1,2-dichloroethane. Different reference compounds were tried. The titration experiments gave a clearly interpretable outcome only with 13 (monitored by $^{19}$F NMR) and 14 (monitored by UV-Vis spectrometry; see Figure 6E and the Supporting Information). The obtained buffer points are as follows: the buffer point pH$_{lab}^{H^\bullet}$ from titration of 13 was $-6.8$ and from titration of 14 was $-8.5$. Thus, the average value of the buffer point pH$_{lab}^{H^\bullet}$ together with an uncertainty estimate would be $(-7.7 \pm 1.2)$. This value has high uncertainty but allows qualitative interpretation: it means that by its acidity, in terms of the chemical potential of the solvated proton, such solution corresponds approximately to a hypothetical aqueous solution with pH $-7.7$. The uncertainty estimate embraces the full range of variability that we have seen in our experiments. Additional explanations, descriptions of experiments, and the obtained NMR and UV-Vis spectra are presented in the Supporting Information.

Conclusion

A combination of experimental and quantum chemical methods provided important insight into electrochemical properties and reactivity of chelation-stabilized $\lambda^1$-bromanes. Cyclic voltammetry studies in HFIP show that the anodic oxidation of parent bromoarenes that are equipped with coordinating hexafluoro-2-hydroxy-propanol units in positions 2 and 6 proceeds via parallel ECEC and ECE$_{disp}$ sequences, whereby the initially formed cation radical intermediate could be detected in the case of the para-methoxy-substituted bromoarene by UV-Vis spectroelectrochemistry. In contrast, cathodic conversion of the chelation-stabilized $\lambda^1$-bromanes to parent bromoarenes in acetonitrile occurs via single electron reduction, followed by hydrogen atom abstraction from the solvent and protonation. The corresponding half-peak potentials indicate that Martin’s-type $\lambda^1$-bromanes are rather poor single electron oxidants. This important finding was corroborated by mechanistic studies of bromine(III)-mediated oxidative amidation of N,N-dimethylanilines in MeCN that provided compelling evidence against the involvement of a SET mechanism. The oxidative amidation in MeCN apparently proceeds through an ionic mechanism, involving an inner-sphere redox process within a transient [12-Br-4] complex. On the other hand, chelation-stabilized $\lambda^1$-bromanes possess comparable SET oxidizing ability to that of hypervalent iodine(III) reagents such as PIFA. The latter requires activation by Lewis acid to effect SET oxidation in, for example, oxidative biaryl coupling, whereas the activation by a strong Bronsted acid such as TfOH turned out to be the most efficient for Martin’s-type $\lambda^1$-bromanes. The observed displacements of chemical shifts in $^1$H and $^{19}$F NMR spectra for $\lambda^1$-bromane suggests its equilibrium protonation by the added TfOH with a buffer point pH$_{lab}^{H^\bullet}$ determined to be $-7.7 \pm 1.2$ by titration experiments in 1,2-dichloroethane. The protonation presumably leads to the cleavage of benzbromooxole ring and the formation of more reactive bromonium(III) triflate that features enhanced [Ar-Br]$^-$ cationic character as reflected by a LUMO energy reduction of 1.01 eV and a slight increase of the Mulliken charge population by 0.07 units and, hence, increased Lewis acidity and oxidizing ability. Overall, we believe that the detailed mechanistic understanding of electrochemical properties and reactivity of the chelation-stabilized $\lambda^1$-bromanes will help to widen the use of hypervalent bromine(III) species in contemporary organic synthesis and accelerate the development of unprecedented synthetic transformations. Our ongoing work on the electrochemical synthesis of various bromine(III) species and their application in organic synthesis will be reported in due course.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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