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# Radical Truce-Smiles reactions on an isoxazole template: Scope and limitations

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ABSTRACT

The use of $TiCl_3$-HCl as promotor in the radical Truce-Smiles reactions of 2-(((3,5-dimethylisoxazol-4-yl) sulfonyl)oxy)benzenediazonium salts has been investigated in detail. During these reactions the desired Truce-Smiles rearrangement (*via* an *ipso*-substitution reaction) is accompanied by the formation of a number of by-products including dihydrobenzo[5,6][1,2]oxathiino[3,4-*d*]isoxazole 4,4-dioxides, dioxidobenzo[e][1,2]oxathiin-3-yl)ethan-1-ones, anilines and chloroaromatics. Replacing $TiCl_3$-HCl by $Cu(NO_3)_2$-$Cu_2O$ as reductant in these reactions was found to afford broadly comparable product distributions. Competition and radical clock experiments also provide an indication of the relative susceptibility of the isoxazole nucleus towards attack by aryl radicals.



## 1. Introduction

The Truce-Smiles rearrangement represents a general reaction which, in its original form, results in the intramolecular *ipso*-substitution reaction of a suitably activated aromatic ring system by a pendant nucleophile [1]. The versatility of this reaction is due, in part, to the broad range of substrates that are found to participate in this transformation, which leads to the generation of new aryl C-C, C-O and C-N bonds (Scheme 1) [2].

More recently, Smiles-type rearrangements have been shown to proceed on seemingly unactivated substrates, an advance which has found particular application in the synthesis of sterically hindered, quaternary, centres where it has been found that the rearrangements proceed with some degree of stereochemical control [3]. In addition, the invention of new cascade sequences in which Smiles-type reactions are integral, as cogently adumbrated by Greaney [4], has much synthetic potential. While most Smiles-type rearrangements were restricted to anionic, $S_NAr$-processes, the seminal observation by Speckamp [5a] concerning a free-radical[5b-d] variant has recently become an area of resurgent interest. Most notably, advancements in this area include the development of tandem cyclization-displacement cascades which enable the synthesis of polycyclic systems from simple, acyclic, starting materials [6]. Germaine to the present study is Motherwell's [7] report of radical Truce-Smiles reactions leading to the synthesis of bi-aryls, a process which is devoid of the now ubiquitous transition-metal-catalyzed cross-coupling cycle. Pivotal to this transformation is the generation of an aryl radical, most commonly from a suitably functionalized aryl halide, *via* the auspices of a one-electron reducing agent. At the time of Speckamp's and Motherwell's initial investigations the use of reducing agents such as tri-*n*-butyltin hydride was commonplace [8a], however environmental considerations have meant that the use of this reagent is now frowned upon, and is often replaced by more environmentally friendly reagents such as tris(trimethylsilyl)silane (TTMSS) [8b,c]. Given the facile reduction of diazonium salts to aryl radicals [9] we wished to capitalize on Motherwell's observation that radical-mediated Truce–Smiles rearrangements can be triggered by the reaction between an aryl diazonium salt and a benign reducing agent such as Ti(III)-HCl [10]. To our knowledge, the use of diazonium salts, as radical precursors, in Truce-smiles rearrangements has only one other citation, that by Lesur and co-workers [11a,b], in

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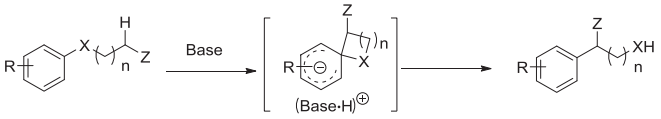



**Scheme 1.** A generalized Truce-Smiles rearrangement reaction.

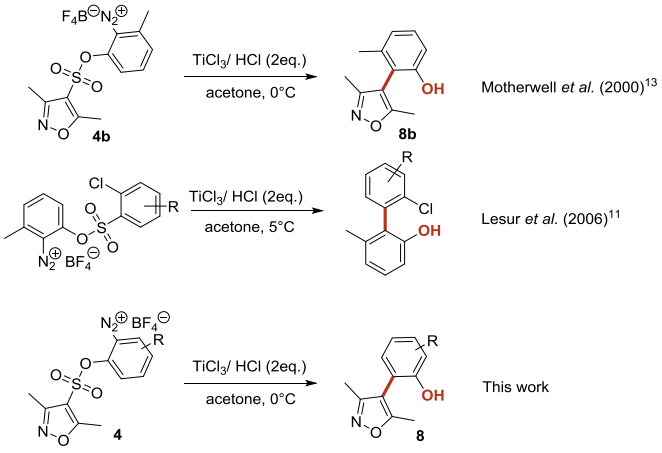
the patent literature, where it is reported that *ortho*-hydroxybiaryls were accessible using Motherwell's chemistry, Scheme 2. The phlegmatic development of this variant of the Truce-Smiles rearrangement [12a] is all the more surprising given the intense interest in the use of related Meeerwein arylation [12b–e] and palladium-catalyzed reactions [12f,g].

## 2. Results and discussion

In 2000 Motherwell reported [13], as a sole example, that exposure of the isoxazole-derived diazonium salt **4b** to commercially available $TiCl_3$-HCl resulted in the isolation of hetero-biaryl **8b**, an outcome that can best be described as a radical Truce-Smiles rearrangement reaction (Scheme 2). Given the ready availability of diazonium salts we wished to determine the scope and limitations of this radical-mediated rearrangement reaction. Specifically we required access to a variety of aryl-substituted isoxazoles [14] for biological testing and the Motherwell protocol appeared to be ideal for this purpose, even though there is only limited precedent for the use of isoxazoles as "acceptors" in radical-mediated Truce-Smiles rearrangements, Scheme 2. In this paper we present our initial findings concerning the use of aqueous $TiCl_3$ as a promotor for radical Truce-Smiles rearrangements in which aryl diazonium salts are employed as the radical precursors.

### 2.1. Synthesis of radical precursors

As an initial survey, a series of *ortho*-aminoarenesulfonate esters **3a-e** was prepared by reaction of sulfonyl chloride **1** [15] with amino phenols **2a-e** in the presence of a suitable base (using either aqueous NaOH or $Et_3N$) and their conversion into the stable arenediazonium salts **4a-e** was successfully accomplished upon reaction with $HBF_4$ in the presence of *iso*-amyl nitrite (Fig. 1) [16]. For completeness sake the regioselectivity in the initial ester-formation step was confirmed, in the case of **3a**, **3b**, **3c** and **3e**, by way of single crystal X-ray structure determinations, as depicted in Fig. 2.




**Scheme 2.** The Motherwell modification of the radical Truce-Smiles rearrangement.

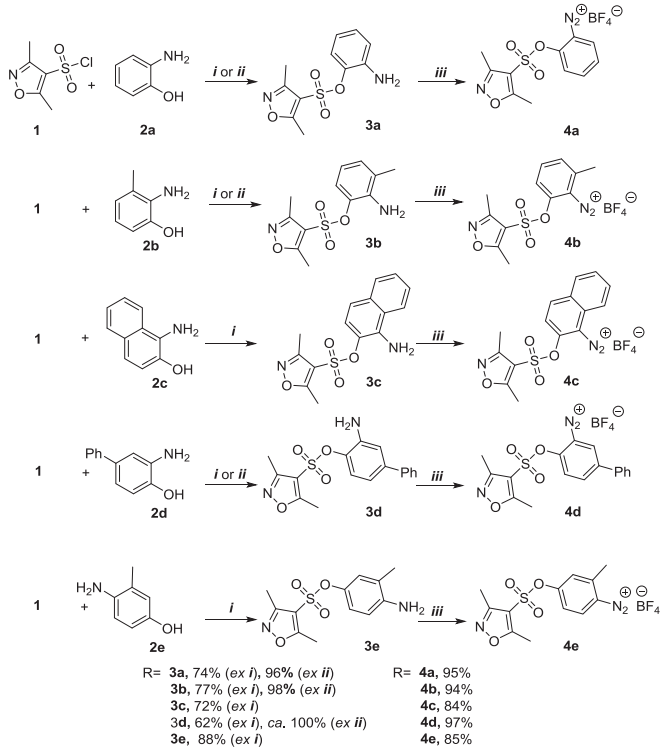



**Fig. 1.** Preparation of substrates **4a**-**4e**. Reagents and conditions: ***i*** NaOH (1 eq.); **1** (1 eq.); $CH_2Cl_2$; 0 °C; ***ii*** $Et_3N$ (1.1 eq.); **1** (1 eq.); $CH_2Cl_2$; 0 °C; ***iii*** $HBF_4$ (2.6 eq.); *iso*-amyl nitrite (1.2 eq.); EtOH; 0 °C.

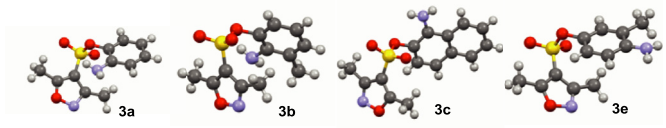


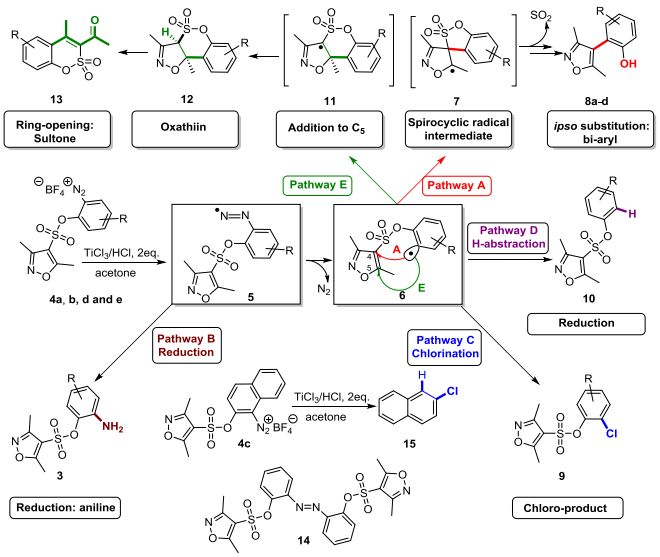

**Fig. 2.** Single crystal X-ray structures of **3a**, **3b**, **3c** and **3e**.

### 2.2. $TiCl_3$-HCl promoted reactions of diazonium salts *4a-e*

Having gained access to a representative selection of diazonium salts we then embarked upon an investigation into the pivotal Ti-induced rearrangement reaction. In practice, addition of commercially available $TiCl_3$-HCl (1.29 M $TiCl_3$ in 2 M HCl; 2 eq) to **4a-d** in acetone at 0 °C, under an atmosphere of nitrogen, resulted in the generation of complex reaction mixtures [16]. Apart from the desired rearrangement process these reactions were accompanied by the isolation of a number of by-products, in which the exact product profile was highly dependent upon substrate and reaction conditions, as summarized in Scheme 3.

#### 2.2.1. Pathway A: [1, 5] ipso-substitution reaction leading to rearranged products

It is understood that the reduction of diazonium salts such as **4a-e** by $TiCl_3$ proceeds by way of a single electron transfer (SET) process [17] producing aryldiazenyl radicals, Aryl-N=N•, **5** and that subsequent partitioning of these intermediates then dictates the observed product distribution. In the present case, fragmentation of **5** to the aryl radicals [18] **6** ultimately results in the Truce-Smiles rearrangement. This outcome is observed when the intermediate radicals **6** are able to undergo intramolecular *ipso*- substitution at the $C_4$-sulfonyl-bearing carbon in the acceptor, isoxazole, ring




**Scheme 3.** Products derived from the reaction between **4a-d** with $TiCl_3$.

(Scheme 3: pathway **A**) in preference to other competing processes (Scheme 3, pathways **B** to **E**). From the results that we have generated so far it appears that the incorporation of a bulky group, close to the radical centre of **6**, promotes 1,5-*ipso*-substitution *via* spirocyclic intermediates **7** which upon re-aromatization, by extrusion of $SO_2$, followed by H-atom abstraction, led to the formation of isoxazoles **8a** (14%), **8b** (68%), **8c** (20%) and **8d** (26%), (Pathway **A**, Scheme 3). These observations are in accord with those reported by Motherwell where bulky substituents positioned close to the reacting centre promote the formation of a hindered biaryl axis by way of the "enforced orthogonality" concept [19]. Support for this hypothesis is manifested in the single crystal X-ray structures of **8b**, **8c** and **8d**, the products of Truce-Smiles rearrangement, which possess torsion angles about the biaryl axis of 92.38°, −114.05° and 92.57° respectively in the solid state (Fig. 3). In those cases where *ipso*-substitution does not appear to be favoured alternate reaction pathways intervene, as discussed below.

### 2.2.2. Pathway B: $TiCl_3$ - mediated reduction: aniline formation

During our screening of the use of $TiCl_3$ as a trigger for the Truce-Smiles rearrangement we were somewhat surprised to note occasional complications in the generation of radicals **6** from **5**. For example, in the case of **4a** reaction with $TiCl_3$-HCl led to the formation of **3a** in low, but reproducible, yield (10%), Scheme 4. In addition to the isolation of aniline **3a**, this rearrangement was also accompanied by the formation of **10a**, **12a** and **13a** whose structures were confirmed by single crystal X-ray diffraction studies. The reductive cleavage reaction leading to **3a** appears to be substrate dependent and was not observed in the case of **4b**-**4e**. However we later observed that this reduction process can become the major reaction pathway which may ultimately limit the generality of the Ti(III)-methodology for the generation of aryl radicals from diazonium salts (see section 2.2.6, Schemes 14 and 15). Somewhat surprisingly, prior to our observations we were not aware of any other reports concerning the generation of anilines during the $TiCl_3$ – mediated reduction of diazonium salts, although it had been noted by Heinrich and co-workers [20] that aryldiazenes can disproportionate to anilines, along with other products, under acidic conditions. In passing we also note that the generation of **3a** could also proceed *via* the intermediacy of the azo-aromatic **14** (Scheme 3), derived from the initial coupling of **5a** with **6a,** followed by reduction [21] with $TiCl_3$, a possibility which has yet to be scrutinized in this context.

### 2.2.3. Pathway C: chlorination

During the course of these investigations we also observed that reaction of **4b** with $TiCl_3$-HCl afforded the chlorinated product **9b** in 11% isolated yield in addition to the desired Truce-Smiles product **8b** in 68% yield (Scheme 5). Although the transformation of aryl diazonium salts into aryl halides, *via* the auspices of metal salts, principally those derived from copper, is embodied in the classical Sandmeyer reaction [22], the interception of aryl radicals by titanium halides in such a fashion has, to our knowledge little literature precedent, although Beringer noted similar SET-ligand transfer processes during the reaction between aryliodonium salts and aqueous $TiCl_3$ [23]. In the case of **4b** we presume that SET from $TiCl_3$ resulted in the generation of radical intermediate **6b** whose partitioning, either *via* a Truce-Smiles manifold (Scheme 3, pathway A) or halogen transfer process (Scheme 3, pathway C) could ultimately lead to the isolation of **9b**, a process which competes favourably with the formation of **8b**. The generation of **8b** and **9b** was also

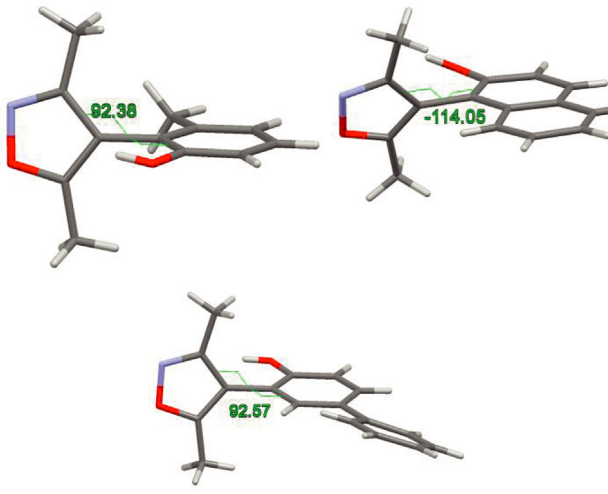
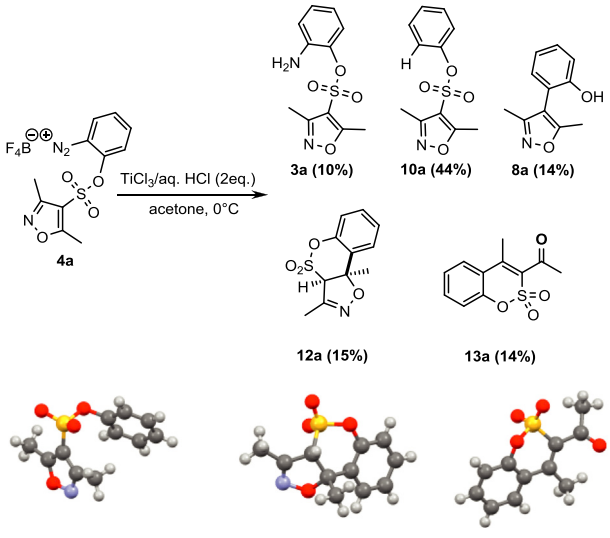
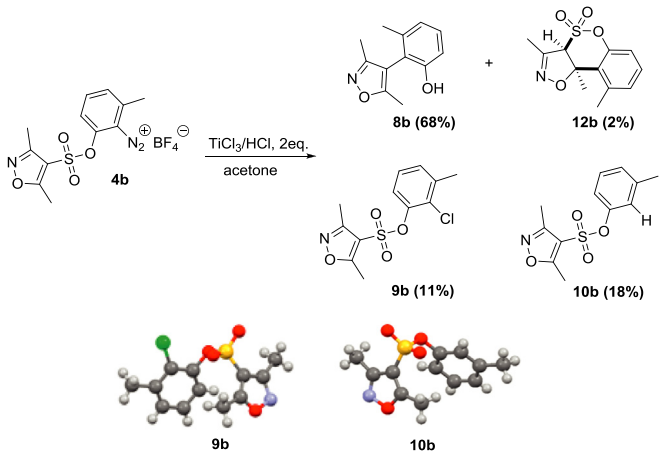


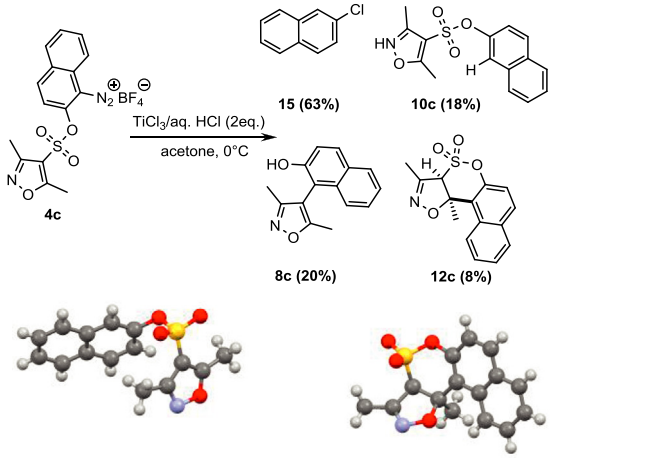

**Fig. 3.** Single crystal X-ray structures of **8b**, **8c** and **8d**.




**Scheme 4.** Product distribution from the reduction of **4a** with $TiCl_3$ together with the X-ray structures of **10a**, **12a** and **13a**.




**Scheme 5.** Product distribution from the reduction of **4b** with $TiCl_3$ together with the X-ray structures of **9b** and **10b**.



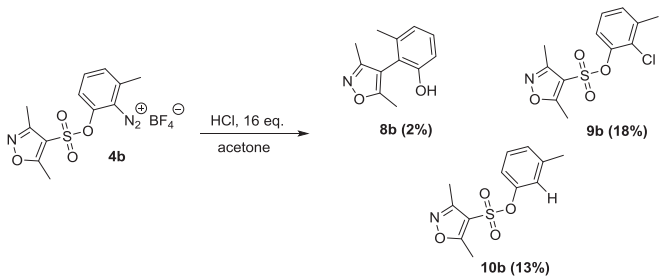

**Scheme 7.** Product distribution from the reduction of **4c** with $TiCl_3$ together with the X-ray structures for **10c** and **12c**.

accompanied by the formation of **10b** (18% isolated yield), presumably the result of H-abstraction from solvent (acetone) and a minor quantity of the oxathiin **12b** (2%; stereochemistry by analogy) whose generation of which is discussed in section 2.2.5. Unambiguous structural assignments for **8b**, **9b** and **10b** were obtained by way of single crystal X-ray structure determinations (Scheme 5 and Fig. 3).

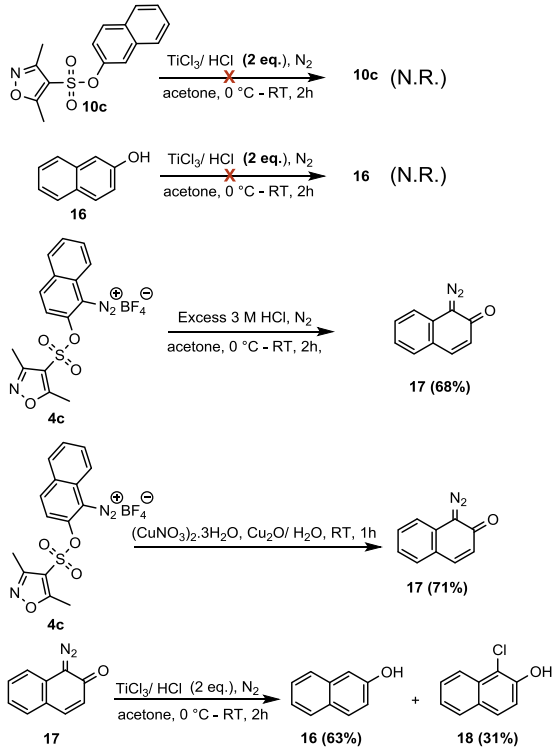
Interestingly the blank reaction between **4b** with an excess (16 eq) of HCl (3 M) in acetone also afforded the chloro-aromatic **9b** (18%), plausibly *via* an $S_N1$-type process [24a], together with the reduced product **10b** (13%) and the rearranged bi-aryl **8b** (2%), Scheme 6. Evidently radical generation is therefore still operative in this case to a limited extent, even in the absence of titanium(III). However, it is not possible therefore at the present stage to determine whether the isolation of the chlorinated product **9b**, during the $TiCl_3$-promoted rearrangement reaction of **4b**, is the result of a ligand transfer reaction[24b,c] of a Ti(IV) species or through the interception of an aryl cation with the HCl that is present in the reaction medium.

As noted above (section 2.2.1), the $TiCl_3$-promoted rearrangement of **4c** afforded the biaryl **8c** in only meagre yield (20%). Quite unexpectedly (Scheme 7), the major product of this reaction proved to be 2-chloronaphthalene, **15** (63%) which was isolated together with minor quantities of the reduction product **10c** (18%) and the sultone **12c** (8%), whose structures were again confirmed by single crystal X-ray analysis, Scheme 7.

Intrigued as to the formation of **15** we again embarked upon a series of blank reactions in order to gain insights into the mechanism of its generation (Scheme 8). It was quickly established that both sulphonate **10c** and 2-naphthol **16** were isolated, unchanged,




**Scheme 6.** Product distribution from the blank reaction between **4b** and HCl.




**Scheme 8.** Conversion of **4c** into **15**: blank reactions.

upon exposure to the standard reduction conditions using $TiCl_3$. Somewhat surprising however, reaction of **4c** with 3 M HCl in the absence of $TiCl_3$ resulted in the isolation of the known [25] diazo-ketone **17** in good overall yield (68%). Diazo-ketone **17** was also isolated, again in good yield (71%), from the reaction between **4c** and $Cu(NO_3)_2$-$Cu_2O$, a system which usually promotes hydroxy-dediazotization [26] ("phenolverkochung") of aryl diazonium salts to phenols. That diazo-ketone **17** was not an intermediate in the $TiCl_3$-promoted conversion of **4c** into **15** was shown to be the case as reaction between a purified sample of **17** and $TiCl_3$-HCl afforded a mixture of 2-naphthol, **16** and 1-chloro-2-naphthol, **18** in 63% and 31% isolated yield respectively. Further blank experiments also indicated that diazo-ketone **17** is relatively stable towards 3 M

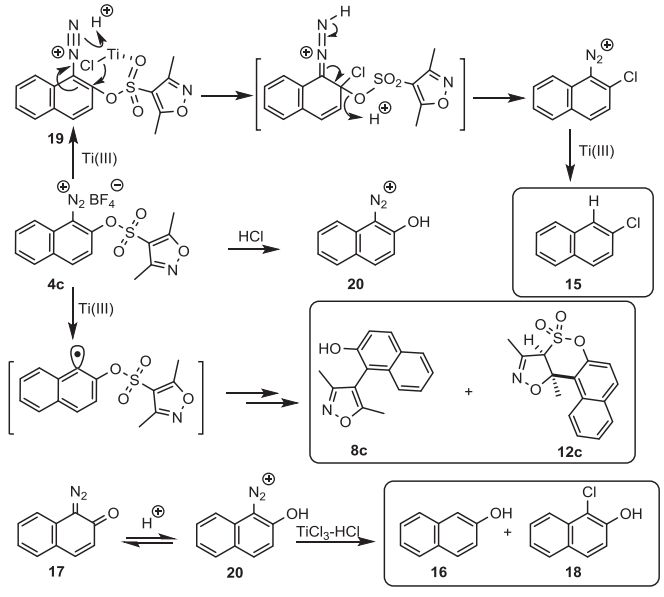
HCl in the absence of $TiCl_3$. Evidently, reaction of **4c** with either 3 M HCl or $Cu(NO_3)_2$-$Cu_2O$ results in hydrolysis of the sulfonate ester and ultimately leads to the generation of **17** [27].

In terms of the conversion of **4c** into **15** the activating ("nuisance") [28] effect of the diazonium group in Sandmeyer-type reactions is in fact a documented, but often overlooked, complication. It is not uncommon to observe the formation of products arising from displacement reactions of aryl diazonium salts bearing nucleofugal groups at the *ortho*- and *para*-positions with nucleophilic species present in the reaction medium. In this instance we posit that reaction between **4c** with $TiCl_3$-HCl proceeds *via* an addition elimination reaction, plausibly by way of a complex such as **19**, Scheme 9 [29]. In addition, the conversion of **17** into **16** and **18** presumably proceeds *via* initial, reversible, protonation [30] to the diazonium salt **20** which on further reaction with $TiCl_3$-HCl leads to the isolation of **16** and **18**, Scheme 9.

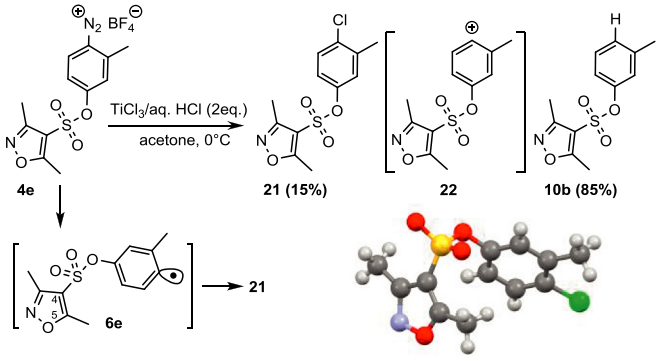
In a further set of blank experiments it was decided to study the fate of the diazonium salt **4e** under our standard reaction conditions with a view to determining the efficiency of the halogen transfer process in a substrate that was unable to participate in an intramolecular Truce-Smiles rearrangement. In the event, reaction of **4e** with $TiCl_3$-HCl resulted in the isolation of the reduced species **10b** (identical to that also generated in Scheme 6) as the major product (85%), together with minor amounts of the chlorinated aromatic **21** (15%). The structure assigned to **21** was also subsequently confirmed by way of single crystal X-ray structure determination, and presumably arose *via* the intermediacy of the cation **22**, Scheme 10. Overall, this outcome infers that H-abstraction from solvent by **6e**, affording **10b**, proceeds at a faster rate than incorporation of halogen.

### 2.2.4. Pathway D: H-atom abstraction from the reaction medium

As noted with **4a** (Scheme 4) and **4e** (Scheme 10) a common side-reaction observed during these Ti(III)-mediated rearrangement reactions is one of H-atom abstraction, where the hydrogen atom is presumed to be derived from the co-solvent, acetone [17,18]. In certain cases, as with **4e**, the hydrogen abstraction pathway leading to **10b** (85% yield) becomes the major pathway, Scheme 10. Similarly reaction of **4d** with $TiCl_3$-HCl resulted in the isolation of **10d** in 40% yield, together with lesser quantities of the




**Scheme 9.** Reaction pathways involving **4c**.



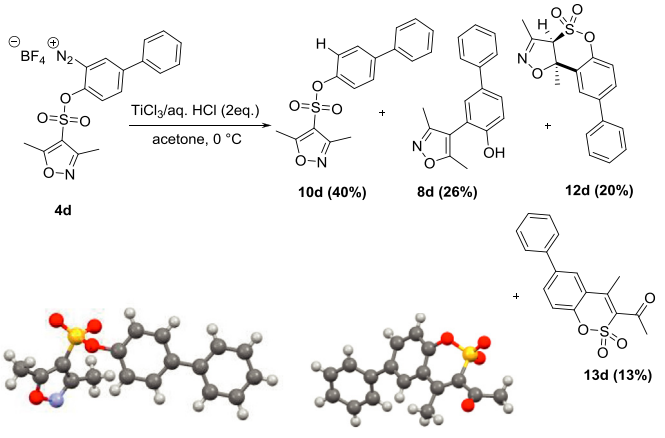

**Scheme 10.** Reaction of **4e** with Ti(III) together with the X-ray structure of **21.**

rearranged product **8d** (26%), the oxathiin **12d** (20%) and its hydrolysis product, sultone **13d**, in 13% yield, Scheme 11.

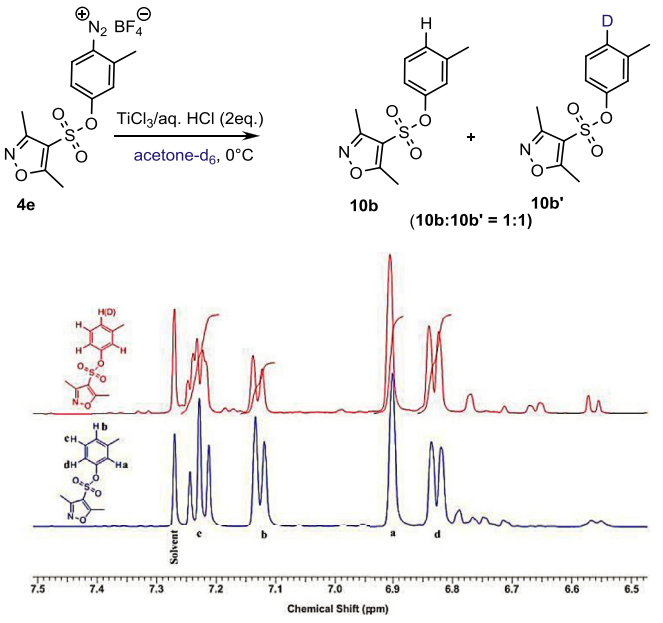
While the degree of H-abstraction *vs* rearrangement in these reactions was found to be dependent, to some degree, on steric effects (*e.g.* **4a** [3:1] *vs* **4b** [1:3.7]) the rate of addition of $TiCl_3$-HCl to the substrate also appeared to be critical in this regard. In the case of substrate **4b** for example, the rapid addition of $TiCl_3$-HCl (over 3 min when compared to 15 min) resulted in an increase in the yield of **10b** from 18% to 42%, an outcome which was at the expense in the yield of **8b**, which depreciated from 68% to 44%. Similar effects have been reported by Heinrich et al. where reaction of diazonium salts with $TiCl_3$-HCl resulted in the isolation of reduction products during the intermolecular capture of aryl radicals with trapping agents such as furan [31]. These outcomes may infer that the H-transfer is in fact derived from water that is coordinated to the titanium centre [32], an issue that we have briefly examined. In this case we observe that repeating the reaction between **4e** with $TiCl_3$-HCl in acetone-$d_6$ as solvent resulted in the generation of a 50:50 mixture of **10b** and the deuterated analogue **10b′** as the major products as judged by an analysis of the $^1$H NMR spectrum of the crude reaction mixture (Scheme 12.). This outcome indicates that abstraction of H(D) from solvent by **6e is** partially operative in this case.

### 2.2.5. Pathway E: [1,6]-addition reactions

In addition to the desired *ipso*-substitution process (Scheme 3, pathway A), which results in bi-aryl formation, we also noted that aryl radicals **6** also undergo "[1,6]-addition" at $C_5$ of the isoxaole




**Scheme 11.** Assessment of the reactivity profile of **4d** towards Ti(III) together with the X-ray structure of **10d** and **13d**.




**Scheme 12.** Reaction of **4e** with $TiCl_3$-HCl in acetone-$d_6$ (upper); expansion of the aromatic region of $^1$H NMR spectra for **10b** and **10b′** (lower).

ring (Scheme 3, pathway E) leading to the isolation of oxathiins **12a**, 15%, **12b**, 2%, **12c**, 8% and **12d**, 20% (Schemes 4, 5, 7 and 11 respectively) [33]. The identity of these 1-6 addition by-products is readily apparent from an examination of their $^1$H NMR spectra (Fig. 4), where $H_4$ appears as a characteristic, broadened, multiplet at $\delta$ 4.5–4.65 ppm which exhibit long range coupling ($J \approx 1$ Hz) with the methyl group at $C_5$ ($\delta$ 2.2–2.3 ppm). These "[1,6]-addition" reactions proceed regioselectively by intramolecular attack of the aryl radical **6** at $C_5$ of the isoxazole ring; the formation of alternate, regioisomeric, products arising from attack at $C_3$ were not observed [34]. We presume that the overall stereochemical outcome of these reactions results from the approach of the H-donor, R′-H, from the less hindered, *exo*-face, of the intermediate radical **23** (Scheme 12). In addition to the isolation of **12a-d** we also observed the formation of sultones **13a** (14%) and **13d** (13%), Schemes 4 and 11 respectively. Once again structural assignments were initially based on spectroscopic data ($\bar{\nu}_{max}$ 1691 cm$^{-1}$; $\delta$ [$^{13}$C NMR] 192 ppm) and were confirmed by way of single crystal X-ray analysis for both of these compounds. The formation of **13a** and **13d** presumably arises (Scheme 13) *via* initial reductive cleavage [35] of the N-O bond in isoxazolines **12a** and **12d** by Ti(III), followed by hydrolysis of the resultant β-hydroxy imine **24** and finally elimination of water [36].

### 2.2.6. Inter-intramolecular competition experiments

Given that there is scant information in the literature concerning the addition of free radicals to isoxazoles [34] we wished to gauge the relative reactivity of the isoxazole nucleus towards aryl radicals. Hence the relative reactivity of aryl radicals **6** towards intramolecular capture was compared to that of a reaction whose absolute rate had been previously determined. Furan, being an electron rich aromatic, is known to react efficiently with electron deficient aryl radicals at a rate ($k = \sim 2.7 \times 10^6$ M$^{-1}$ s$^{-1}$) which is intermediate to that observed for the same reaction with benzene ($k = \sim 4.5 \times 10^5$ M$^{-1}$ s$^{-1}$) and simple alkenes ($k = \sim 2.8 \times 10^8$ M$^{-1}$ s$^{-1}$) at 25 °C [37], and was therefore chosen as a reference point.

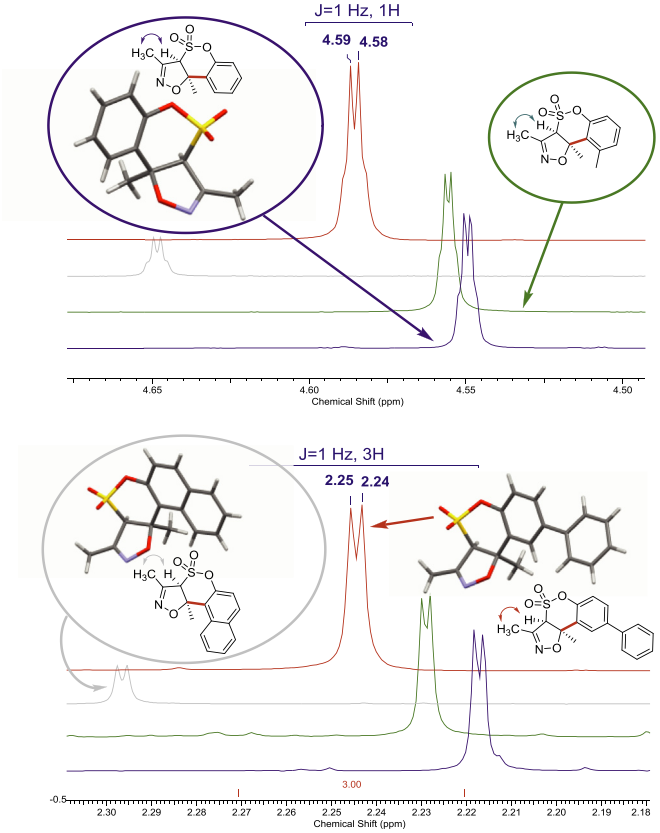
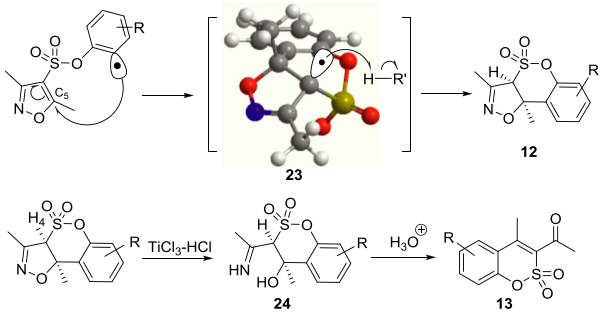
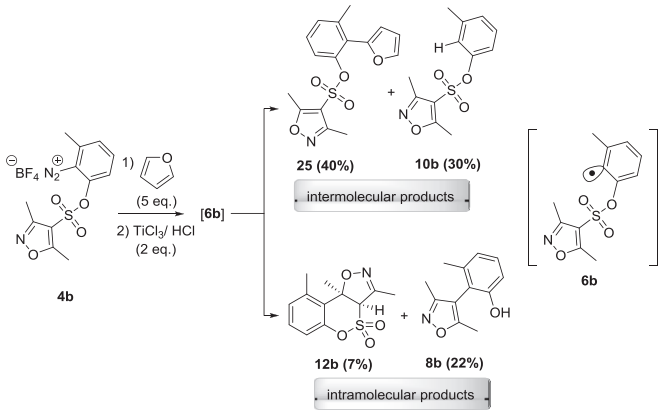


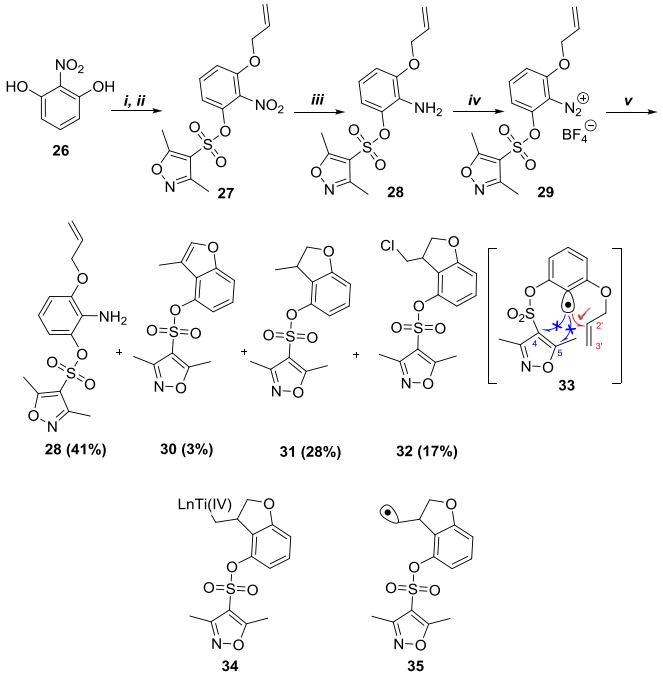

**Fig. 4.** Characteristic $^1$H NMR spectral data for **12a - 12d**.




**Scheme 13.** Generation of **12** and **13** *via* a "[1,6]-addition" process.




**Scheme 14.** *Inter- vs intra*molecular arylation of **6b**.



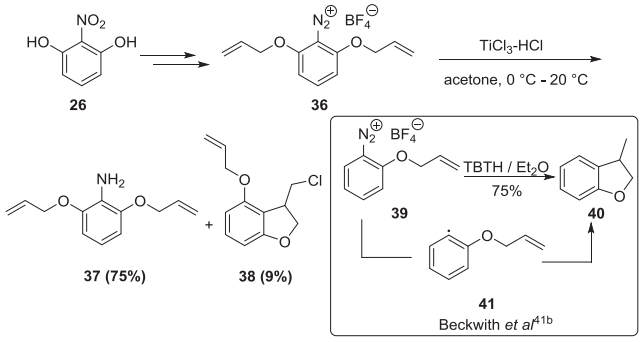

**Scheme 15.** Radical–clock reactions involving **29**. Reagents and conditions: ***i*** $K_2CO_3$ (1 eq.); $CH_3CN$; 70 °C; 57%; ***ii*** $Et_3N$ (1.1 eq.); **1** (1.1 eq.); $CH_2Cl_2$; 0 °C; *ca*. 100%; ***iii*** Zn dust (5 eq.); $NH_4Cl$; MeOH/THF; 98%; ***iv*** $HBF_4$ (2.5 eq.); *iso*-amyl nitrite (1.1 eq.); EtOH; 95%; ***v*** $TiCl_3$-HCl (2 eq.); acetone; 0 °C.

In an initial competition experiment the diazonium salt **4b** was reacted with $TiCl_3$ (2 eq) in the presence of an excess of furan (5 eq.), under our standard reaction conditions. Purification of the products from this reaction by column chromatography and then preparative HPLC afforded the substituted furan **25** (40%), the result of an intermolecular addition of aryl radical **6b** to furan, together with **8b** (22%) and **12b** (7%) *via* intramolecular isoxazole addition, and the reduced product **10b** (30%), Scheme 14. These results clearly demonstrate that the hindered aryl radical **6b** competes effectively for furan, in an intermolecular process, when compared to the alternate, intramolecular addition reaction, suggesting that the isoxazole moiety of **4b** is less reactive towards radical attack than the unsubstituted furan nucleus.

As an extension to this study the synthesis of diazonium salt **29** was also accomplished from *bis*-phenol **26** using well established chemistry (Scheme 15). Here an allylloxy-residue, situated *ortho*- to the incipient aryl radical centre, was to be used as an internal radical clock [38a] enabling an estimation of the efficiency of addition to the isoxazole ring versus reaction with the alkene moiety.[1] In the event, exposure of **29** to $TiCl_3$-HCl, as described previously, generated a complex reaction mixture which was purified by preparative HPLC (Scheme 15).

Surprisingly, the single largest component of this reaction was one of non-productive reduction resulting in the isolation of the aniline **28** (41%) together with the benzofuran **30** (3%), dihydrobenzofuran **31** (28%) and chloride **32** (17%), Scheme 15. All three of the latter products are the result of a 5-*exo*-*trig*- addition of the aryl radical **33** to the C2′- C3′ double bond of the allyl ether moiety, a process that is evidently more favourable than attack at C4- or C5- of the isoxazole ring. It is not clear, at this stage, whether the final,

[1] Cyclization of aryl radicals, such as **39** to **40**, *via* a 5-*exo*-*trig*-pathway (Scheme 16) is known to proceed rapidly [38b] ($k \approx 6.3 \times 10^9\ s^{-1}$ at 30 °C).




**Scheme 16.** Attempted cyclization using **36** as starting material.

isolated, products, **30**–**32**, arises from the intermediacy of a discrete Ti(IV) complex **34**, or free radical intermediate **35** [39].

In order to gauge the efficiency of 5-*exo*-*trig*-cyclization reactions in this system the synthesis of the 2,6-bis(allyloxy)benzenediazonium salt **36**, which is devoid of an isoxazole appendage, was undertaken and its reaction with Ti(III) was investigated, Scheme 16. Somewhat unexpectedly, exposure of **36** to $TiCl_3$-HCl afforded the aniline **37** in high yield (75%) together with the dihydrobenzofuran **38** as a minor by-product (9%) [40,41a]. Clearly, the introduction of functionality, which may exert either a steric or electronic effect, *ortho*- to the diazonium moiety, has a major influence on the outcome of the initial electron transfer reaction which precedes aryl radical formation. These results are also in stark contrast to the chemistry of the diazonium salt **39**, which is known to undergo cyclization to the dihydrobenzofuran **40** in good yield when conducted under reaction conditions that promote the generation of aryl radicals such as **41** [41b].

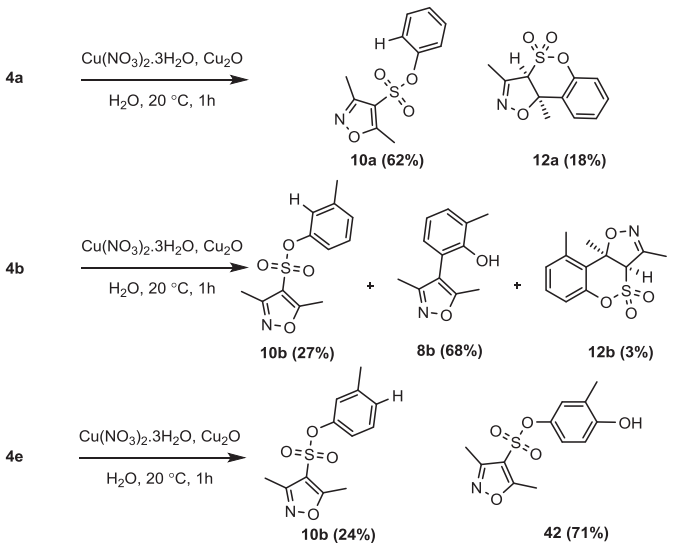
### 2.2.7. Effect of metal on product distribution

We previously noted the effect of changing the reductant $(Cu(NO_3)_2$-$Cu_2O$ [26] instead of $TiCl_3$-HCl) on the outcome of the rearrangement reactions of **4c** (see Scheme 8) and wished to investigate these effects further. The outcome of the reaction between **4a**, **4b** or **4e** with $(Cu(NO_3)_2$-$Cu_2O$ was found to be substrate dependent but largely mirrored the results obtained using $TiCl_3$-HCl although the isolation of products arising from hydroxydediazoniation, as expected [26], now become apparent, Scheme 16.

In a control experiment reaction of **4e** with $Cu(NO_3)_2$-$Cu_2O$ afforded, as expected, phenol **42** as the major product (71%) together with the ester **10b** (24%), Scheme 17. This outcome is to be compared with that from the reaction of **4e** with $TiCl_3$-HCl which afforded **10b** as the major product (85%) together with relatively minor quantities of the chloro-compound **21** (15%). Encouragingly, rearrangement of **4b** in the presence of $(Cu(NO_3)_2$-$Cu_2O$ led to **8b** in 68**%** yield, together with **10b** (27%) and **12b** (3%) rather than to hydroxylation products, which indicates that radical formation and subsequent capture is faster than hydroxyl incorporation in this instance.

### 2.2.8. Comparison with related methodology: attempted fluoride-promoted Truce-Smiles reactions

We recently reported [42] a fluoride induced Truce-Smiles rearrangement of *ortho*-(trimethylsilyl)aryl sulphonate esters leading to bi-aryls and wondered whether this particular process could be applied to the synthesis of functionalized isoxazoles, Scheme 17. Unfortunately all attempts to induce rearrangement of **42** into **8a**, using a range of fluoride sources, under various conditions, met with failure. For example, reaction of **43** with TBAF in

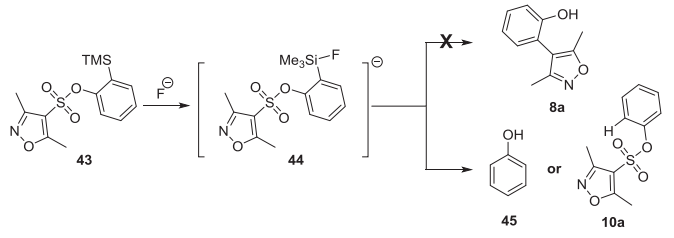



**Scheme 17.** Effect of metal additives on the radical Truce-Smiles rearrangement.

THF-acetonitrile merely promoted protodesilylation and resulted in the isolation of the ester **10a** (78%). Alternatively, reaction of **42** with caesium fluoride in THF led to the isolation of phenol, **45** in 92% yield, Scheme 18. Evidently the hypervalent silicon species **44**, the presumed intermediate in these protodesilylation reactions, is either insufficiently reactive or too sterically encumbered to participate in either *ipso*-substitution or addition reactions with the isoxazole template. This outcome underscores the differing electronic and steric demands of the radical Truce-Smiles rearrangements when compared to its anionic variant, subtleties which are currently the focus of further investigation.

## 3. Conclusion

A detailed analysis of the product distribution resulting from $TiCl_3$-HCl – promoted, radical, Truce Smiles rearrangements of functionalized diazonium salts is reported. The intended outcome from these reactions – the preparation of isoxazoles substituted at $C_4$- with aromatic residues – was only partially accomplished, because the desired rearrangement reaction (*via* an *ipso*-substitution mechanism) is highly dependent on structural features within the substrate and the nature of the radical promoter. That said it would appear that this methodology may find application in the synthesis of bi-aryls which are sterically congested about the newly formed bi-aryl axis. As such our observations are in keeping with Motherwell's "enforced orthogonality" concept. In certain cases *ipso*-substitution is also accompanied by addition, and subsequent fragmentation of the isoxazoline ring resulting in the isolation of a variety of oxathiins and sultones. The isolation of reduction products and chloroaromatics are also observed in a number of these reactions. We have shown, using "radical clock" reactions, that the isoxazole nucleus is less reactive than furan towards radical addition. The course of the initial diazonium salt reduction by Ti(III) is also heavily influenced by neighbouring functionality: in certain cases a previously unreported reduction of diazonium salts to anilines, rather than to aryl radicals, becomes the major reaction pathway. These radical Truce-Smiles rearrangements are also promoted by other reductants such as $Cu(NO_3)_2$-$Cu_2O$ and efforts are currently underway in order to define agents which promote cyclization without the intervention competing side reactions. Anionic variants [42] of the Truce-Smiles rearrangements were unsuccessful when using an isoxazole nucleus as acceptor.




**Scheme 18.** Attempted fluoride-mediated, "anionic-", Truce-Smiles rearrangement reaction of **43**.

## 4. Experimental section

### 4.1. General experimental

All air-sensitive reactions were carried out under an atmosphere of nitrogen in oven-dried glassware unless stated otherwise. All reagents were used as received from commercial sources commercially unless stated otherwise. Infrared spectra were recorded using a Bruker-Alpha- FT-IR spectrometer. Reactions were monitored by thin layer chromatography (TLC) on 0.25 mm precoated plastic sheets Merck silica gel 60 $F_{254}$ polyester backed plates. Visualization of TLC plates was achieved by either viewing under a UV lamp ($\lambda_{max}$ 254 nm) or by thermal development after dipping into an aqueous solution of potassium permanganate. Column chromatography was conducted on Merck silica gel SDS (particle size 40–63 μm) as the stationary phase. HPLC separations were conducted on an Agilent 1260A preb HPLC. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. $^1$H NMR, $^{13}$C NMR, $^{13}$C DEPT90, $^{13}$C DEPT135, $^{13}$C DEPTQ and COSY spectra were recorded on Bruker-DRX 300 MHz, Bruker-B12–400 ultrashield/Avance III 400 (BBO 400 MHz S15mm), Bruker-B14-Ascend 500 MHz/Avance III HD (CPPBBO 5 mm), Bruker-B11-Avance III HD/Ascend 400 MHz (CPPBBO 5 mm), Bruker-B11-Avance II 500/500 Ultrashield (BBO 500 MHz S2 5 mm), Bruker-B07 - DRX Avance 500/500 Ultrashield (BBI 500 MHz SB 5 mm) spectrometers operating at ambient temperature. Chemical shifts values are given in parts per million (ppm); peak patterns are indicated as follows: br.s, broad singlet; s, singlet; d, doublet; t, triplet; q, quadruplet; qui, quintuplet; m, multiplet. DEPTQ refer to $^{13}$CNMR signal, while signals were separated as (CH, $CH_3$ "up") and ($C_{qua.}$, $CH_2$ "down"). NMR assignments were made with the aid of DEPT135, DEPT90, COSY pulse sequences. Low resolution mass (LRMS) and high resolution (HRMS) spectra were recorded on a Waters SQD2 and Waters Q-TOF micro mass spectrometers respectively. All mass spectrometry results are reported in the form *m/z*. Elemental analysis was performed by Mr. Ian Jennings in the Microanalytical Laboratory within the School of Chemistry, The University of Manchester. X-ray crystallographic data for selected compounds was recorded in the X-ray Crystallography Laboratory, School of Chemistry, University of Manchester (Supplementary information).

### 4.2. General synthetic procedures (GP)

#### 4.2.1. Synthesis of radical precursors

*4.2.1.1. General procedure 1 (GP1): sulfonate esters using aqueous NaOH as base.* In a 100 mL round bottom flask with proper magnetic stirrer, a mixture of the phenol (1.1 eq.) 3,5-dimethylisoxazole-4-sulfonyl chloride **1**(1 eq.), in $CH_2Cl_2$ (50 mL) was stirred vigorously for 5 min. To this stirred solution, excess of aqueous NaOH solution (2 M, 8 mL) was added, followed by

addition of water (2–3 mL) and allowed to stir for 24 h. The reaction mixture was diluted with water (5 mL) and extracted with $CH_2Cl_2$ (3 x 30 mL). The combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo* to afford the crude product which was purified by recrystallization or column chromatography as indicated.

*4.2.1.2. General procedure 2 (GP2): sulfonate ester using $Et_3N$ as base.* To an ice-cold solution of the phenol (1.1 eq.), triethylamine(1.1 eq.), $CH_2Cl_2$ (75 mL) under an $N_2$ atmosphere, a solution of 3,5-dimethylisoxazole-4-sulfonyl chloride **1**(1.1 eq.) in 10 mL $CH_2Cl_2$ was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 24 h. The reaction mixture was quenched with water and the $CH_2Cl_2$ layer was separated, dried over $MgSO_4$ and concentrated *in vacuo.* The crude was purified by flash column chromatography using $CH_2Cl_2$ to afford pure sulfonate esters or sulfonamides.

*4.2.1.3. General procedure 3 (GP3): synthesis of diazonium salts.* A slurry of aniline **3(a–e)** (1 eq.) in ethanol (5 mL) was stirred for 5 min. To this stirred solution at 0 °C, was added an aqueous solution of $HBF_4$ (48%, 2.6 eq.), followed by the dropwise addition of *iso*-amyl nitrite (1.2 eq.) over 15 min. The resulting reaction mixture was stirred for 30 min at temperature 0–5 °C and then allowed to stir at room temperature for 30 min. The precipitated product was carefully filtrated and washed with a small amount of the ethanol. The crude diazonium product was dried at room temperature and purified by dissolving it in minimum amount of acetone followed by precipitation by dropwise addition of cold diethyl ether.

*4.2.1.4. General procedure 4 (GP4): $TiCl_3$ reactions.* A solution of aqueous $TiCl_3$ (1.29 M in HCl, 2 eq.) was added dropwise to a solution of diazonium salt (1eq.) in acetone (3–5 mL) in sealed vial and under ($N_2$) atmosphere at 0 °C. After the addition, the reaction mixture was stirred for 0.5 h at 0 °C and then 1 h at RT, water was added and it was extracted with $CH_2Cl_2$. The organic layer was washed with brine, dried over $MgSO_4$ and evaporated *in vacuo* to afford various products. The crude products were purified by column chromatography on silica gel or by Preparative-HPLC.

*4.2.1.5. General procedure 5 (GP5): Allylation of phenols.* To an oven-dried 100 mL round flask containing 2-nitroresorcinol (2 eq.) and $K_2CO_3$ (2.0 eq.) in $CH_3CN$, allyl bromide (1.1 eq.) was added and the reaction mixture was stirred for 24 h at 70 °C. After completion the reaction mixture was cooled to room temperature, diluted with water and extracted with DCM. The combined organic layers were dried over $MgSO_4$ and purified by flash chromatography on silica gel.

*4.2.1.6. General procedure 6 (GP6): reduction of nitro group to anilines.* Nitro compound (1 eq.) and zinc dust (5 eq.) were suspended in mixed solvent of (MeOH: THF, 1:1; v/v) and an excess of saturated $NH_4Cl$ solution was added carefully. The reaction mixture became warm. There was an obvious change in the zinc suspension. The reaction was finished in 10 min. The reaction mixture was filtered through a silica plug and diluted with EtOAc and saturated $NaHCO_3$. The layers were separated and the combined organics dried over $MgSO_4$ and concentrated under reduced pressure.

*4.2.1.7. General procedure 7 (GP7): TBAF-promoted rearrangements reactions.* Under nitrogen atmosphere, (TBAF, 3 eq.) was added slowly to a stirred solution of 2-(trimethylsilyl)phenyl 3,5-dimethylisoxazole-4-sulfonate **49** (1 eq.) in dry solvent ($CH_3CN$/THF, 1 M). The reaction mixture was stirred at (RT/70 °C) for sixteen hours and then poured into ether (25 mL). The resulting mixture was washed with dilute HCl (3 M, 10 mL) and then with water ($2 \times 10$ mL), dried over $MgSO_4$ and the reaction mixture taken to dryness *in vacuo.* The crude product was purified by column chromatography.

*4.2.1.8. General procedure 8 (GP8): CsF-promoted rearrangement reactions.* To an oven-dried 25 mL round-bottom flask equipped with a magnetic stir bar was added CsF (3 eq.). The reaction flask was connected to an oven-dried condenser and sealed well with proper rubber septum. A balloon was linked on top, evacuated and backfilled with $N_2$ gas (three times). 10 mL of solution (0.1 M) aryl anion precursor **49** (1eq.) in dry (THF/MeCN) was added to the CsF. The resulting mixture was stirred in (RT/70 °C) for 16 h and then poured into ether (20 mL). The mixture was washed with dilute HCl (3 M, 10 mL) and with water ($2 \times 10$ mL). Dried over $MgSO_4$ and the crude was taken to dryness *in vacuo*. The crude product was purified by flash column chromatography.

*4.2.1.9. General procedure 9 (GP9): effect of metal ($Cu(NO_3)_2{\cdot}3H_2O$-$Cu_2O$) [26].* **4(a–e)** (1 eq.) was added to a solution of copper (II) nitrate trihydrate (57 eq.) and copper (I) oxide (3 eq.) in water (108 mL/mmol), the reaction mixture was vigorously stirred at room temperature for 70 min. The solid was filtered and washed with dichloromethane. The filtrate was extracted three times with dichloromethane, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The crude was purified on silica gel column chromatography (2:8 ethyl acetate: petroleum ether; v/v).

### 4.3. Syntheses of sulfonate esters

#### 4.3.1. 2-Aminophenyl 3′,5′-dimethylisoxazole-4′-sulfonate, *3a*

**Using GP1:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (2 g, 10.22 mmol, 1 eq.), 2-amino phenol **2a** (1.22 g, 11.24 mmol, 1.1 eq.), NaOH (2 M, 25 mL, 50 mmol). Recrystallization by petroleum ether gave the *title compound* as a brown-coloured crystalline solid. Yield 2.03 g (74%).

**Using GP2**: Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (1 g, 5.11 mmol, 1.1 eq.), 2-amino phenol **2a** (506.3 mg, 4.64 mmol, 1 eq.), $Et_3N$ (0.712 mL, 5.11 mmol, 1.1 eq.). Yield 1.19 g (96%); **mp.** 99–101 °C; $\bar{\nu}_{max}$**/cm$^{-1}$** (ATR) 3473, 3386, 3075, 1623, 1587, 1502, 1436, 1377, 1161, 1362, 1314, 1269, 1205, 1115, 1030, 878, 804, 758, 710. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.26 (s, 3 H), 2.35 (s, 3 H), 3.79 (br. s., 2 H), 6.56–6.63 (m, 1 H), 6.69 (dd, $J = 8.0$, 1.0 Hz, 1 H), 6.80 (dd, $J = 8.0$, 1.0 Hz, 1 H), 6.98–7.04 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.7, 12.5, 112.3, 117.5, 118.6, 122.9, 128.5, 136.1, 139.8, 158.2, 175.7. **LRMS (ES$^+$)** $C_{11}H_{12}N_2O_4S$ requires 268; found **(ES$^+$)** 269 $[M+H]^+$, **(ES$^-$)** 267 $[M-H]^-$; **HRMS (ES$^+$)** $C_{11}H_{12}N_2O_4SNa$ $[M+Na]^+$ requires 291.0415; found 291.0425 ($\Delta = 3.3$ ppm). **Microanalysis** $C_{11}H_{12}N_2O_4S$ requires: C, 49.25, H, 4.51, N, 10.44, S, 11.95%; found: C, 49.45, H, 4.76, N, 10.37, S, 11.78%.

#### 4.3.2. 2-Amino-3-methylphenyl 3′,5′-dimethylisoxazole-4-sulfonate, *3b*

**Using GP1:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (2 g, 10.22 mmol, 1 eq.), 2-amino-3-methylphenol **2b** (1.38 g, 11.24 mmol, 1.1 eq.), NaOH (2 M, 25 mL, 50 mmol). Recrystallization by petroleum ether gave the *title compound* as brown-coloured, crystalline solid. Yield 2.2 g (77%).

Using **GP2:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (1 g, 5.11 mmol, 1.1 eq.), 2-amino-3-methylphenol **2b** (571.46 mg, 4.64 mmol, 1 eq.), $Et_3N$ (0.712 mL, 5.11 mmol, 1.1 eq.). Yield 1.3 g (98%); **mp.** 94–96 °C; $\bar{\nu}_{max}$**/cm$^{-1}$** (ATR): 3464, 3381, 3029), 2977, 2941, 2905, 1626, 1584, 1482, 1437, 1405, 1361, 1118,

1268, 1196, 911, 794, 770. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.12 (s, 3 H), 2.25 (s, 3 H), 2.37 (s, 3 H), 3.63 (br. s., 2 H), 6.59 (d, $J$ = 8.0 Hz, 1 H), 6.66 (d, $J$ = 1.0 Hz, 1 H), 6.82 (dq, $J$ = 8.0, 1.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.7, 12.5, 17.3, 112.4, 117.5, 123.2, 128.5, 129.0, 136.1, 137.1, 158.2, 175.6. **LRMS (ES$^+$)** $C_{12}H_{14}N_2O_4S$ requires 282; found **(ES$^+$)** 283 $[M+H]^+$; **HRMS (ES$^+$)** $C_{12}H_{15}N_2O_4S$ $[M+H]^+$ requires 283.0312; found 283.0313 ($\Delta$ = 0.35 ppm).

*4.3.3. Synthesis of **3c***

**Using GP1:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (1 g, 5.11 mmol, 1 eq.), 1-aminonaphthalen-2-ol hydrochloride **2c** (1.1 g, 5.62 mmol, 1.1 eq.), NaOH (2 M, 12 mL, 24 mmol). Recrystallization by $CHCl_3$/petroleum ether gave *title compound* as yellow-brown coloured crystalline solid. Yield 1.2 g (72%); **mp.** 116–117 °C; **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3475, 3391, 3066, 3054, 2958, 2929, 1618, 1590, 1511, 1465, 1438, 1407, 1385, 1363, 1205, 1269, 1179, 1159, 1129, 1112, 1078, 1036, 976, 871, 707. **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta$ 2.24 (s, 3 H), 2.28 (s, 3 H), 4.31 (br. s., 2 H), 6.91 (d, $J$ = 9.0 Hz, 1 H), 7.08 (d, $J$ = 9.0 Hz, 1 H), 7.35–7.39 (m, 2 H), 7.63–7.69 (m, 2 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ 10.8, 12.6, 112.6, 118.5, 120.9, 121.2, 124.1, 125.8, 126.6, 128.6, 131.3, 132.8, 135.1, 158.1, 175.7. **LRMS (ES$^+$)** $C_{15}H_{14}N_2O_4S$ requires 318; found **(ES$^+$)** 319 $[M+H]^+$; **HRMS (ES$^+$)** $C_{15}H_{15}N_2O_4S$ $[M+H]^+$ requires 319.0753; found 319.0765 ($\Delta$ = 3.9 ppm).

*4.3.4. Synthesis of 3-amino-[1,1′-biphenyl]-4-yl 3″,5″-dimethylisoxazole-4″-sulfonate, **3d***

**Using GP1:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (960.08 mg, 4.90 mmol, 1 eq.), 3-amino-[1,1′-biphenyl]-4-ol, **2d** (1 g, 5.39 mmol, 1.1 eq.), NaOH (2 M, 12 mL, 24 mmol). Recrystallization by $CH_2Cl_2$/petroleum ether gave the *title compound* as feint brown-coloured crystalline solid. Yield 1.04 g (62%).

Using **GP2:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (1 g, 5.11 mmol, 1.1 eq.), 3-amino-[1,1′-biphenyl]-4-ol, **2d** (859.46 mg, 4.64 mmol, 1 eq.), $Et_3N$ (0.712 mL, 5.11 mmol, 1.1 eq.). Yield 1.59 g (100%); **mp.** 103–104 °C; **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3466, 3377, 3057, 3033, 3012, 1620, 1588, 1512, 1486, 1438, 1408, 1360, 1085, 1383, 1324, 1269, 1234, 1204, 1165, 1038, 913, 867, 829, 761, 695. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.22 (s, 3 H), 2.31 (s, 3 H), 3.86 (s, 2 H), 6.71–6.76 (m, 1 H), 6.81 (s, 1 H), 6.82 (d, $J$ = 2.0 Hz, 1 H), 7.18–7.23 (m, 1 H), 7.27 (t, $J$ = 7.0 Hz, 2 H), 7.34–7.38 (m, 2 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.8, 12.6, 112.4, 116.0, 117.3, 123.2, 127.0, 127.8, 128.9, 135.5, 139.9, 140.1, 141.7, 158.2, 175.9. **LRMS (ES$^+$)** $C_{17}H_{16}N_2O_4S$ requires 344; found **(ES$^+$)** 345 $[M+H]^+$, 367 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{17}H_{17}N_2O_4S$ $[M+H]^+$ requires 345.0909; found 345.0921 ($\Delta$ = 3.5 ppm). **Microanalysis** $C_{17}H_{16}N_2O_4S$ requires: C, 59.29, H, 4.68, N, 8.13, S, 9.31%; found: C, 59.56, H, 4.67, N, 8.08, S, 9.17%.

*4.3.5. 4-Amino-3-methylphenyl 3′,5′-dimethylisoxazole-4′-sulfonate, **3e***

Using **GP1:** Starting with 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (1 g, 5.11 mmol, 1 eq.), 4-amino-3-methylphenol **2e** (692.54 mg, 5.62 mmol, 1.1 eq.), NaOH (2 M, 13 mL, 26 mmol). Recrystallization by $CHCl_3$/petroleum ether gave the *title compound* as light brown-coloured crystalline solid. Yield 1.26 g (88%); **mp.** 96–97 °C; **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3473, 3374, 3083, 2986, 1644, 1586, 1528, 1498, 1438, 1356, 1198, 1306, 1272, 1150, 1117, 1052, 997, 935, 917, 874. **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta$ 2.09 (s, 3 H), 2.30 (s, 3 H), 2.36 (s, 3 H), 3.75 (s, 2 H), 6.52–6.56 (m, 1 H), 6.60–6.66 (m, 1 H), 6.74 (d, $J$ = 2.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ 10.7, 12.4, 17.4, 112.1, 114.9, 120.4, 123.4, 123.9, 140.4, 144.3, 158.2, 175.4. **LRMS (ES$^+$)** $C_{12}H_{14}N_2O_4S$ requires 282; found **(ES$^+$)** 283 $[M+H]^+$, 305 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{12}H_{15}N_2O_4S$ $[M+H]^+$ requires 283.0753; found 283.0740 ($\Delta$ = −4.6 ppm). **Microanalysis** $C_{12}H_{14}N_2O_4S$ requires: C, 51.05, H, 5.00, N, 9.92, S, 11.36%; found: C, 50.76, H, 5.19, N, 9.81, S, 11.04%.

*4.3.6. 2-(((3′,5′-dimethylisoxazol-4′-yl)sulfonyl)oxy)benzenediazonium tetrafluoroborate, **4a***

**Using GP3:** Starting with amine **3a** (1.30 g, 4.85 mmol, 1 eq.), ethanol (7 mL), isoamyl nitrite (0.782 mL, 5.82 mmol, 1.2 eq.), $HBF_4$ 48% (1.64 mL, 12.62 mmol, 2.6 eq.). The *title compound* was obtained as a colourless amorphous solid. Yield 1.691 g (95%); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3104, 2998, 2290), 1573, 1478, 1442, 1408, 1365, 1313, 1275, 1219, 1204, 1130, 1050, 1036, 853, 782, 733, 688, 651. **$^1$H NMR** (400 MHz, acetone-$d_6$): $\delta$ 2.46 (s, 3 H), 2.72 (s, 3 H), 8.01–8.12 (m, 2 H), 8.54 (td, $J$ = 8.0, 1.0 Hz, 1 H) 8.99 (dd, $J$ = 8.0, 1.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, acetone-$d_6$): $\delta$ 9.9, 12.4, 109.3, 110.6, 124.1, 129.9, 135.4, 144.6, 148.8, 157.8, 178.6. **Microanalysis** $C_{11}H_{10}BF_4N_3O_4S$, requires: C, 35.99, H, 2.75, N, 11.45, S, 8.73%; found: C, 36.24, H, 2.95, N, 11.40, S, 8.96%.

*4.3.7. (((3′,5′-dimethylisoxazol-4′-yl)sulfonyl)oxy)-6-methylbenzenediazonium tetrafluoroborate, **4b***

**Using GP3:** Starting with amine **3b** (800 mg, 2.83 mmol, 1 eq.), ethanol (8 mL), isoamyl nitrite (0.46 mL, 3.39 mmol, 1.2 eq.), $HBF_4$ 48% (0.96 mL, 7.36 mmol, 2.6 eq.). The *title compound* was obtained as colourless amorphous solid. Yield 1.01 g (94%); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3140, 3108, 3082, 2996, 2947, 2266, 1596, 1566, 1479, 1413, 1263, 1212, 1025, 962, 817, 793, 722, 682, 632. **$^1$H NMR** (400 MHz, Acetone-$d_6$): $\delta$ 2.46 (s, 3 H), 2.73 (s, 3 H), 2.97 (s, 3 H), 7.84 (d, $J$ = 8.0 Hz, 1 H), 7.93 (dt, $J$ = 8.0, 1.0 Hz, 1 H), 8.37 (t, $J$ = 8.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, acetone-$d_6$): $\delta$ 9.9, 12.4, 18.3, 109.4, 110.7, 121.2, 131.1, 143.5, 148.4, 148.9, 157.8, 178.5. **Microanalysis** $C_{12}H_{12}BF_4N_3O_4S$, requires: C, 37.82, H, 3.17, N, 11.03, S, 8.41%; found: C, 38.00, H, 2.92, N, 11.02, S, 8.21%.

*4.3.8. 1-(((3,5-dimethylisoxazol-4-yl)sulfonyl)oxy)naphthalene-2-diazonium tetrafluoroborate, **4c***

**Using GP3:** Starting with amine **3c** (606 mg, 1.9 mmol, 1 eq.), ethanol (5 mL), isoamyl nitrite (0.307 mL, 2.28 mmol, 1.2 eq.), $HBF_4$ 48% (0.64 mL, 4.95 mmol, 2.6 eq.). The *title compound* was obtained as yellowish-green coloured amorphous solid. Yield 668 mg (84%); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3120, 3081, 3069, 2984), 2242, 1625, 1578, 1563, 1510, 1405, 1368, 1273, 1245, 1227, 1207, 1174, 1126, 1060, 1043, 1019, 979, 873, 851, 833, 766. **$^1$H NMR** (400 MHz, acetone-$d_6$): $\delta$ 2.52 (s, 3 H), 2.79 (s, 3 H), 8.06 (ddd, $J$ = 8.0, 7.0, 1.0 Hz, 1 H), 8.20 (d, $J$ = 9.0 Hz, 1 H), 8.25 (ddd, $J$ = 8.0, 7.0, 1.0 Hz, 1 H), 8.54 (d, $J$ = 8.0 Hz, 1 H), 8.62 (dd, $J$ = 8.0, 1.0 Hz, 1 H), 9.20 (d, $J$ = 9.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, acetone-$d_6$): $\delta$ 10.0, 12.5, 111.0, 119.7, 122.3, 126.9, 130.3, 131.3, 134.4, 147.2, 153.8, 157.8, 178.8. **Microanalysis** $C_{15}H_{12}BF_4N_3O_4S$, requires: C, 43.19, H, 2.90, N, 10.07, S, 7.69%; found: C, 43.30, H, 3.06, N, 9.98, S, 7.57%.

*4.3.9. Synthesis of 4-(((3,5-dimethylisoxazol-4-yl)sulfonyl)oxy)-[1,1′-biphenyl]-3-diazonium tetrafluoroborate, **4d***

**Using GP3:** Starting with amine **3d** (1.15 g, 3.35 mmol, 1 eq.), ethanol (4 mL), isoamyl nitrite (0.54 mL, 4.03 mmol, 1.2 eq.), $HBF_4$ 48% (1.14 mL, 8.73 mmol, 2.6 eq.). The *title compound* was obtained as a yellow-coloured amorphous powder. Yield 1.24 g (97%); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3107, 3070, 3056, 3035, 2275, 1586, 1558, 1515, 1480, 1439, 1404, 1367, 1289, 1271, 1235, 1202, 1153, 1129, 1061, 1030, 884, 852. **$^1$H NMR** (400 MHz, acetone-$d_6$): $\delta$ 2.49 (s, 3 H), 2.74 (s, 3 H), 7.53–7.63 (m, 3 H), 7.82–7.88 (m, 2 H), 8.12 (d, $J$ = 9.0 Hz, 1 H), 8.77–8.81 (m, 1 H), 9.29 (d, $J$ = 2.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, acetone-$d_6$): $\delta$ 10.0, 12.4, 109.9, 110.5, 124.5, 127.2, 129.6, 130.0, 132.6, 135.2, 142.2, 142.3, 147.6, 157.8, 178.7. **Microanalysis**

$C_{17}H_{14}BF_4N_3O_4S$, requires: C, 46.07, H, 3.18, N, 9.48, S, 7.23%; found: C, 46.28, H, 2.92, N, 9.43, S, 7.40%.

*4.3.10. Synthesis of 4-(((3,5-dimethylisoxazol-4-yl)sulfonyl)oxy)-2-methylbenzenediazonium tetrafluoroborate, **4e***

**Using GP10:** Starting with amine **3e** (500 mg, 1.77 mmol, 1 eq.), Ethanol (6 mL), isoamyl nitrite (0.28 mL, 2.12 mmol, 1.2 eq.), $HBF_4$ 48% (0.60 mL, 4.60 mmol, 2.6 eq.). The *title compound* was obtained as a colourless, crystalline, solid. Yield 574 mg (85%); $\bar{\nu}_{max}$/**cm**$^{-1}$ (ATR) 3110, 3048, 3029, 2271, 1603, 1587, 1563, 1499, 1471, 1436, 1404, 1379, 1362, 1313, 1274, 1204, 1124, 946, 889. **$^1$H NMR** (400 MHz, acetone-$d_6$) $\delta$ 2.38 (s, 3 H), 2.58 (s, 3 H), 2.98 (s, 3 H), 7.78 (dd, $J$ = 9.0, 2.0 Hz, 1 H), 7.88 (d, $J$ = 2.0 Hz, 1 H), 8.91 (d, $J$ = 9.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, acetone-$d_6$) $\delta$ 9.9, 12.0, 18.1, 111.3, 114.8, 123.1, 126.5, 135.8, 148.5, 157.0, 157.6, 177.2. **Microanalysis** $C_{12}H_{12}BF_4N_3O_4S$, requires: C, 37.82, H, 3.17, N, 11.03, S, 8.41%; found: C, 37.67, H, 3.24, N, 10.98, S, 8.59%.

*4.4. $TiCl_3$ reactions*

*4.4.1. Reaction of **4a** using $TiCl_3$*

Using **GP4:** Starting with **4a** (1.32 g, 3.60 mmol, 1 eq.), acetone (6 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 5.59 mL, 7.21 mmol). The crude was purified by column chromatography (ethyl acetate: petroleum ether; 2:8 v:v) to afford **3a**, **8a**, **10a**, **12a** and **13a**.

*4.4.1.1. 2-Aminophenyl 3,5-dimethylisoxazole-4-sulfonate, **3a**.* Brown-coloured crystalline solid. Yield 35.4 mg (10%). **R$_f$** 0.21 (100% $CH_2Cl_2$); $\bar{\nu}_{max}$/**cm**$^{-1}$ (ATR) 3386, 3075, 3043, 1623, 1587, 1502, 1436, 1377, 1161, 1362, 1314, 1269, 1205, 1115, 1030, 878, 804, 758, 710. **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta$ 2.26 (s, 3 H), 2.35 (s, 3 H), 3.79 (br. s., 2 H), 6.56–6.63 (m, 1 H), 6.69 (dd, $J$ = 8.0, 1.0 Hz, 1 H), 6.80 (dd, $J$ = 8.0, 1.0 Hz, 1 H), 6.98–7.04 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.7, 12.5, 112.3, 117.5, 118.6, 122.9, 128.5, 136.1, 139.8, 158.2, 175.7. **LRMS (ES$^+$)** $C_{11}H_{12}N_2O_4S$ requires 268; found **(ES$^+$)** 269 $[M+H]^+$, **(ES$^-$)** 267 $[M-H]^-$; **HRMS (ES$^+$)** $C_{11}H_{12}N_2O_4SNa$ $[M+Na]^+$ requires 291.0415; found 291.0423 ($\Delta$ = 2.74 ppm).

*4.4.1.2. Phenyl 3,5-dimethylisoxazole-4-sulfonate, **10a**.* Colourless crystalline solid. Yield 146.94 mg (44%). **R$_f$** 0.60 (2:8 ethyl acetate: petroleum ether; v:v); **m.p.** 65.5–66.5 °C; $\bar{\nu}_{max}$/**cm**$^{-1}$ (ATR): 3066, 2970 1584, 1486, 1436, 1406, 1363, 1268, 1204, 1178, 1152, 1121; **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.29 (s, 3 H), 2.34 (s, 3 H), 7.02–7.07 (m, 2 H), 7.27–7.38 (m, 3 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.6, 12.3, 112.1, 122.4, 127.8, 130.0, 148.9, 158.0, 175.5. **LRMS (EI)** $C_{11}H_{11}NO_4S$ requires 253; found **(EI)** 253 $[M^{+\cdot}]$; **HRMS (EI)** $C_{11}H_{11}NO_4S$ $[M^{+\cdot}]$ requires 253.0723; found 253.0723, ($\Delta$ = 0 ppm).

*4.4.1.3. 2-(3,5-Dimethylisoxazol-4-yl)phenol, **8a**.* Colourless, crystalline, solid. Yield 95.25 mg (14%). **R$_f$** 0.67 (100% $CH_2Cl_2$); **m.p.** 61–62 °C; $\bar{\nu}_{max}$/**cm**$^{-1}$ (ATR) 3515-3328, 3128, 3072, 3039, 2992, 2971, 2931, 1642, 1607, 1576, 1504, 1479, 1456, 1436, 1419, 1331, 1238, 1169, 1147, 1096, 1037, 1014, 994, 951, 828. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.10 (s, 3 H), 2.26 (s, 3 H), 3.90–6.55 (br.s., 1 H), 6.88–6.96 (m, 2 H), 7.00 (dd, $J$ = 7.0, 2.0 Hz, 1 H), 7.20–7.25 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ 10.5, 11.6, 112.1, 116.1, 116.2, 120.7, 130.0, 131.3, 154.1, 160.0, 167.0. **LRMS (ES$^-$)** $C_{11}H_{11}NO_2$ requires 189; found **(ES$^-$)** 188 $[M-H]^-$; **HRMS (ES$^+$)** $C_{11}H_{12}NO_2$ $[M+H]^+$ requires 190.0868; found 190.0873 ($\Delta$ = 2.6 ppm).

*4.4.1.4. (3aR*,9bR*)-3,9b-Dimethyl-3a,9b dihydrobenzo[5,6][1,2]oxathiino[3,4-d]isoxazole-4,4-dioxide, **12a**.* Colourless, crystalline solid. Yield 50.1 mg (15%). **R$_f$** 0.63 (100% $CH_2Cl_2$); **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta$ 1.87 (s, 3 H), 2.31 (d, $J$ = 1.0 Hz, 3 H), 4.65 (br.m, 1 H), 7.16 (dd, $J$ = 8.0, 1.4 Hz, 1 H), 7.37–7.41 (m, 1 H), 7.43–7.47 (m, 1 H), 7.64 (dd, $J$ = 8.0, 2.0 Hz, 1 H). **$^{13}$CNMR** (125 MHz, $CDCl_3$) $\delta$ 13.2, 27.8, 74.0, 87.0, 119.5, 125.4, 127.4, 128.3, 131.1, 148.5, 148.8. **LRMS (ES$^+$)** $C_{11}H_{11}NO_4S$ requires 253; found **(ES$^+$)** 254 $[M+H]^+$, 276 $[M+Na]^+$, **(ES$^-$)** 252 $[M-H]^-$; **HRMS (ES$^+$)** $C_{11}H_{11}NO_4SNa$ $[M+Na]^+$ requires 276.0301; found 276.0295 ($\Delta$ = −2.17 ppm).

*4.4.1.5. 1-(4-Methyl-2,2-dioxidobenzo[e][1,2]oxathiin-3-yl)ethan-1-one, **13a**.* Colourless, crystalline solid. Yield 43.98 mg (14%). **R$_f$** 0.38 (100% $CH_2Cl_2$); $\bar{\nu}_{max}$/**cm**$^{-1}$ (ATR) 2926, 2851), 1691, 1584 1553, 1485, 1447, 1426, 1365, 1354, 1313, 1279, 1203, 1170, 1118, 1089, 1034, 1018, 958, 870, 794, 764. **$^1$HNMR** (400 MHz, $CDCl_3$) $\delta$ 2.54 (s, 3 H), 2.68 (s, 3 H), 7.34 (dd, $J$ = 8.0, 1.0 Hz, 1 H), 7.40–7.45 (m, 1 H), 7.56–7.61 (m, 1 H), 7.74 (dd, $J$ = 8.0, 1.0 Hz, 1 H). **$^{13}$CNMR** (100 MHz, $CDCl_3$) $\delta$ 16.7, 31.7, 119.4, 122.0, 126.5, 127.8, 133.4, 134.1, 146.9, 150.1, 192.6. **LRMS (ES$^+$)** $C_{11}H_{10}O_4S$ requires 238; found **(ES$^+$)** 239 $[M+H]^+$, 261 $[M+Na]^+$, **(ES$^-$)** 237 $[M-H]^-$; **HRMS (ES$^+$)** $C_{11}H_{11}O_4SNa$ $[M+Na]^+$ requires 261.0192; found 261.0184 ($\Delta$ = −3.07 ppm).

*4.4.2. Reaction of **4b** with $TiCl_3$*

According to **(GP4)** the starting materials were mixed: **4b** (1.2 g, 3.14 mmol, 1 eq.), acetone (5 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 4.9 mL, 6.29 mmol). The crude material was purified by column chromatography (2:8 ethyl acetate: petroleum ether; v/v) and then preparative HPLC resulting in the isolation of the following products:

*4.4.2.1. 3,5-Dimethylisoxazole-4-sulfonate, **9b**.* The *title compound* was isolated by preparative HPLC (ACE-127-2546, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 1.0 mL/min, retention time (t) = 6.217 min) as a colourless, crystalline solid. Yield 85.06 mg (9%). **R$_f$** 0.72 (2:8 ethyl acetate: petroleum ether; v/v); **$^1$H NMR** (400 MHz, $CD_2Cl_2$) $\delta$ 2.22 (s, 3 H), 2.28 (s, 3 H), 2.34 (s, 3 H), 7.11–7.19 (m, 3 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.8, 12.7, 20.3, 112.9, 121.8, 127.0, 129.7, 139.0, 145.0, 158.3, 175.6. **LRMS (ES$^+$)** $C_{12}H_{12}ClNO_4S$ requires 301; found **(ES$^+$)** 302 $[M+H]^+$ for $^{35}$Cl, 304 $[M+H]^+$ for $^{37}$Cl, 324 $[M+Na]^+$ for $^{35}$Cl; **HRMS (ES$^+$)** $C_{12}H_{13}ClNO_4S$ $[M+H]^+$ requires 302.0244; found 302.0246 for $^{35}$Cl ($\Delta$ = - 0.662 ppm).

*4.4.2.2. m-Tolyl 3,5-dimethylisoxazole-4-sulfonate, **10b**.* The *title compound* was isolated by preparative HPLC (ACE-127-2546, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 1.0 mL/min, retention time (t) = 5.808 min) as a colourless, crystalline solid. Yield 150.9 mg (18%). **R$_f$** 0.82 (2:8 ethyl acetate: petroleum ether; v/v); **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.26 (s, 3 H), 2.27 (s, 3 H), 2.32 (s, 3 H), 6.75 (dd, $J$ = 8.0, 2.0 Hz, 1 H), 6.83 (s, 1 H), 7.05 (d, $J$ = 7.0 Hz, 1 H), 7.13–7.18 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ = 10.7, 12.5, 21.3, 112.3, 119.1, 122.9, 128.5, 129.6, 140.5, 148.9, 158.1, 175.4. **LRMS (ES$^+$)** $C_{12}H_{13}NO_4S$ requires 267; found **(ES$^+$)** 268 $[M+H]^+$; **HRMS (ES$^+$)** $C_{12}H_{13}NO_4SNa$ $[M+Na]^+$ requires 290.0463; found 290.0477 ($\Delta$ = 4.8 ppm).

*4.4.2.3. 2-(3,5-Dimethylisoxazol-4-yl)-6-methylphenol, **8b**.* Colourless crystalline solid. Yield 433 mg (68%). **m.p.** 51–52 °C; **R$_f$** 0.25 (3:7 ethyl acetate: petroleum ether; v/v); $\bar{\nu}_{max}$/**cm**$^{-1}$ (ATR) 3521-3269, 3034, 2976, 2924, 1633, 1603, 1574, 1464, 1437, 1411, 1378, 1318, 1288, 1253, 1235, 1155, 1086, 1014, 994, 945, 893, 869, 787, 769. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 1.97 (s, 3 H), 1.99 (s, 3 H), 2.18 (s, 3 H), 5.81 (s, 1 H), 6.76–6.80 (m, 2 H), 7.13 (t, $J$ = 8.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.5, 11.5, 20.0, 110.3, 113.2, 115.1, 121.9, 129.7, 139.2, 154.8, 160.4, 167.41. **LRMS (ES$^+$)** $C_{12}H_{13}NO_2$ requires 203; found **(ES$^+$)** 204 $[M+H]^+$, **(ES$^-$)** 202 $[M-H]^-$; **HRMS (ES$^+$)** $C_{12}H_{14}NO_2$ $[M+H]^+$ requires 204.1025; found 204.1028 ($\Delta$ = 1.7 ppm).

*4.4.2.4. (3aR*,9bR*)-3,9,9b-Trimethyl-3a,9b-dihydrobenzo[5,6][1,2]oxathiino[3,4-d]isoxazole-4,4-dioxide,* ***12b****.* Colourless foam. Yield 24 mg (2%). $\mathbf{R_f}$ 0.45 (3:7 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta$ 1.74 (s, 3 H), 2.23 (d, $J$ = 1.0 Hz, 3 H), 2.58 (s, 3 H), 4.56 (br.m, 1 H), 6.92 (dd, $J$ = 8.0, 1.0 Hz, 1 H), 7.10 (dd, $J$ = 7.0, 1.0 Hz, 1 H), 7.18–7.23 (m, 1 H). **$^{13}$C NMR** (125 MHz, $CDCl_3$): $\delta$ = 12.9, 21.3, 27.9, 76.1, 88.5, 117.4, 124.0, 129.9, 131.1, 139.5, 147.5, 148.7. **LRMS (ES$^+$)** $C_{12}H_{13}NO_4S$ requires 267; found **(ES$^+$)** 268 $[M+H]^+$; **HRMS (EI)** $C_{12}H_{14}NO_4S$ $[M^{+\cdot}]$ requires 267.0463; found 267.0473, ($\Delta$ = 3.74 ppm).

*4.4.3. Reaction of* ***4c*** *with $TiCl_3$*

According to **(GP4)** the starting materials were mixed: **4c** (180 mg, 0.43 mmol, 1 eq.), acetone (3 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 0.66 mL, 0.86 mmol). The crude product was purified by column chromatography (2:8 ethyl acetate: petroleum ether; v/v) which afforded **15**, **10c**, **8c** and **12c** as shown below.

*4.4.3.1. 2-Chloronaphthalene,* ***15****.* Colourless, crystalline solid. Yield 44 mg (63%). $\mathbf{R_f}$ 0.92 (2:8 ethyl acetate: petroleum ether; v/v); **$^1$HNMR** (400 MHz, $CDCl_3$) $\delta$ 27.42–7.57 (m, 3 H), 7.76–7.88 (m, 4 H). **$^{13}$CNMR** (100 MHz, $CDCl_3$): $\delta$ = 126.1, 126.6, 126.8, 126.9, 127.1, 127.8, 129.5, 131.6, 131.6, 134.0. This data is essentially identical to that reported in the literature [43].

*4.4.3.2. Naphthalen-2-yl 3,5-dimethylisoxazole-4-sulfonate,* ***10c****.* Off-white coloured crystalline solid. Yield 23 mg (18%). $\mathbf{R_f}$ 0.66 (2:8 ethyl acetate: petroleum ether; v/v); **$^1$HNMR** (400 MHz, $CDCl_3$) $\delta$ 2.39 (d, $J$ = 3.0 Hz, 6 H), 7.20 (dd, $J$ = 9.0, 2.4 Hz, 1 H), 7.53–7.60 (m, 3 H), 7.80–7.91 (m, 3 H). **$^{13}$CNMR** (100 MHz, $CDCl_3$) $\delta$ 10.8, 12.5, 120.0, 120.7, 126.9, 127.3, 127.9, 127.9, 130.2, 132.1, 133.4, 146.4, 158.1, 175.5. **LRMS (ES$^+$)** $C_{15}H_{13}NO_4S$ requires 303; found **(ES$^+$)** 326 $[M+Na]^+$, **(ES$^-$)** 302 $[M-H]^-$; **HRMS (EI)** $C_{15}H_{13}NO_4S$ $[M^{+\cdot}]$ requires 303.0557; found 303.0558 ($\Delta$ = - 0.594 ppm).

*4.4.3.3. 1-(3,5-Dimethylisoxazol-4-yl)naphthalen-2-ol,* ***8c****.* Off-white crystalline solid. Yield 21 mg (20%). **m.p.** 86–87 °C; $\mathbf{R_f}$ 0.12 (100% $CH_2Cl_2$); $\bar{\nu}_{\mathbf{max}}$**/cm$^{-1}$** (ATR) 3384, 3210, 3146, 3060, 2926, 2799, 1616, 1592, 1502, 1469, 1439, 1404, 1374, 1358, 1333, 1302, 1267, 1220, 1184, 1122, 1083, 1039, 1027, 965, 919, 828, 754. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.10 (s, 3 H), 2.29 (s, 3 H), 5.32–5.54 (br.s, 1H), 7.33 (dt, $J$ = 8.0, 1.0 Hz, 1 H), 7.37–7.49 (m, 2 H), 7.84–7.91, (m, 2 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.5, 11.6, 107.8, 117.5, 123.6, 123.7, 127.2, 128.5, 129.0, 130.8, 132.9, 133.4, 152.3, 161.1, 168.6. **LRMS (ES$^+$)** $C_{15}H_{13}NO_2$ requires 239; found **(ES$^+$)** 240 $[M+H]^+$, 262 $[M+Na]^+$, **(ES$^-$)** 238 $[M-H]^-$; **HRMS (ES$^+$)** $C_{15}H_{14}NO_2$ $[M+H]^+$ requires 240.1019; found 240.1013 ($\Delta$ = −2.52).

*4.4.3.4. (3aR*,11 cR*)-3,11c-Dimethyl-3a,11c-dihydronaphtho[1′,2′:5,6][1,2]oxathiino[3,4-d]isoxazole-4,4-dioxide,* ***12c****.* The title compound was isolated by column chromatography as a colourless, crystalline, solid. Yield 10 mg (8%). $\mathbf{R_f}$ 0.24 (100% $CH_2Cl_2$). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 1.93 (s, 3 H), 2.30 (d, $J$ = 1.0 Hz, 3 H), 4.65 (br.m, 1 H), 7.17 (d, $J$ = 9 Hz, 1 H), 7.45–7.51 (m, 1 H), 7.58 (s, 1 H), 7.79–7.85 (m, 2 H), 8.49 (d, $J$ = 1.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ = 13.1, 28.7, 75.9, 89.1, 118.2, 126.3, 126.9, 127.8, 129.1, 132.4, 132.9, 146.2, 147.6. **LRMS (ES$^+$)** $C_{15}H_{13}NO_4S$ requires 303; found **(ES$^+$)** 304 $[M+H]^+$, **(ES$^-$)** 302 $[M-H]^-$; **HRMS (ES$^+$)** $C_{15}H_{14}NO_4S$ $[M+H]^+$ requires 304.0638; found 304.0636 ($\Delta$ = - 0.67 ppm).

*4.4.4. Reaction of* ***4d*** *with $TiCl_3$*

According to **(GP4)** the starting materials were mixed: **4d** (1.03 g, 2.32 mmol, 1 eq.), acetone (9 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 3.6 mL, 4.65 mmol). The crude product was purified by column chromatography (2:8 ethyl acetate: petroleum ether; v/v) to afford **8d**, **10d**, **12d** and **13d**.

*4.4.4.1. [1,1′-Biphenyl]-4-yl 3,5-dimethylisoxazole-4-sulfonate,* ***10d****.* Colourless crystalline solid. Yield 305 mg (40%). **m.p.** 97–98 °C; $\mathbf{R_f}$ 0.69 (2:8 ethyl acetate: petroleum ether; v/v); $\bar{\nu}_{\mathbf{max}}$**/cm$^{-1}$** (ATR) 3078, 3059, 3039, 2987, 1584, 1517, 1484, 1439, 1405, 1392, 1361, 1272, 1215, 1201, 1185, 1162, 1122, 1045, 1016, 982, 945, 864, 847, 758. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.40 (s, 3 H), 2.45 (s, 3 H), 7.38–7.44 (m, 1 H), 7.45–7.51 (m, 2 H), 7.54–7.63 (m, 4 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.8, 12.5, 112.2, 122.7, 127.1, 128.5, 129.0, 139.4, 140.9, 148.2, 158.1, 175.5. **LRMS (ES$^+$)** $C_{17}H_{15}NO_4S$ requires 329; found **(ES$^+$)** 330 $[M+H]^+$, 352 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{17}H_{16}NO_4S$ $[M+H]^+$ requires 330.0795; found 330.0791 ($\Delta$ = −1.08 ppm).

*4.4.4.2. 2-(3,5-Dimethylisoxazol-4-yl)-[1,1′-biphenyl]-3-ol,* ***8d****.* Colourless crystalline solid. Yield 160 mg (26%). **m.p.** 87–88 °C; $\mathbf{R_f}$ 0.35 (2:8 ethyl acetate: petroleum ether; v/v); $\bar{\nu}_{\mathbf{max}}$**/cm$^{-1}$** (ATR) 3406 br., 3068, 3031, 2925, 2856, 1642, 1589, 1479, 1439, 1378, 1361, 1269, 1206, 1169, 1125, 1075, 1044, 864, 832, 762, 694. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.14 (s, 3 H), 2.30 (s, 3 H), 5.34–6.53 (m, 1 H), 7.02 (d, $J$ = 8.0 Hz, 1 H), 7.23 (d, $J$ = 2.0 Hz, 1 H), 7.25 (dt, $J$ = 7.0, 2.0 Hz, 1 H), 7.32–7.37 (m, 2 H), 7.44–7.49 (m, 3 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ = 10.7, 11.7, 112.2, 116.6, 116.7, 126.7, 127.0, 128.7, 128.9, 129.8, 133.9, 140.3, 153.8, 160.1, 167. **LRMS (ES$^+$)** $C_{17}H_{15}NO_2$ requires 265; found **(ES$^+$)** 266 $[M+H]^+$, **(ES$^-$)** 264 $[M-H]^-$; **HRMS (EI)** $C_{17}H_{15}NO_2$ $[M]^{+\cdot}$ requires 265.1097; found 265.1087 ($\Delta$ = −3.999 ppm).

*4.4.4.3. (3aR*,9bR*)-3,9b-dimethyl-8-phenyl-3a,9b-dihydrobenzo[5,6][1,2]oxathiino[3,4-d]isoxazole-4,4-dioxide,* ***12d****.* Colourless crystalline solid Yield 153 mg (20%). $\mathbf{R_f}$ 0.29 (2:8 ethyl acetate: petroleum ether; v/v); **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta$ 1.92 (s, 3 H), 2.34 (d, $J$ = 1.0 Hz, 3 H), 4.68 (br.m, 1 H), 7.24 (d, $J$ = 8.0 Hz, 1 H), 7.40–7.45 (m, 1 H), 7.46–7.52 (m, 2 H), 7.57–7.61 (m, 2 H), 7.63 (dd, $J$ = 8.0, 2.3 Hz, 1 H) 7.82 (d, $J$ = 2.0 Hz, 1 H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta$ 13.2 ($\underline{C}H_3$), 28.0 ($\underline{C}H_3$), 74.0, 87.1, 119.9, 125.6, 127.0, 127.2, 128.1, 129.0, 129.8, 139.3, 140.8, 147.8, 148.8. **LRMS (ES$^+$)** $C_{17}H_{15}NO_4S$ requires 329; found **(ES$^+$)** 352 $[M+Na]^+$, **(ES$^-$)** 328 $[M-H]^-$; **HRMS (ES$^+$)** $C_{17}H_{15}NO_4SNa$ $[M+Na]^+$ requires 352.0614; found 352.0617 ($\Delta$ = 0.85 ppm).

*4.4.4.4. 1-(4-Methyl-2,2-dioxido-6-phenylbenzo[e][1,2]oxathiin-3-yl)ethan-1-one,* ***13d****.* Colourless, crystalline solid; yield 95 mg (13%). $\mathbf{R_f}$ 0.52 (2:8 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 22.50 (s, 3 H), 2.61 (s, 3 H), 7.32 (d, $J$ = 8.0 Hz, 1 H), 7.34–7.39 (m, 1 H), 7.39–7.45 (m, 2 H), 7.46–7.50 (m, 2 H), 7.68 (dd, $J$ = 8.0, 2.0 Hz, 1 H), 7.78 (d, $J$ = 2.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ = 16.7, 31.7, 119.7, 122.1, 126.4, 127.2, 128.3, 129.2, 132.1, 139.2, 140.1, 146.9, 149.3, 192.7. **LRMS (ES$^+$)** $C_{17}H_{14}O_4S$ requires 314; found **(ES$^+$)** 337 $[M+Na]^+$, **(ES$^-$)** 313 $[M-H]^-$; **HRMS (ES$^+$)** $C_{17}H_{15}O_4SNa$ $[M+Na]^+$ requires 337.0505; found 337.0505, ($\Delta$ = - 0.89 ppm).

*4.4.5. Reaction of* ***4e*** *with $TiCl_3$*

*4.4.5.1. Using acetone as solvent.* According to **(GP4)** the starting materials were mixed: **4e** (312 mg, 0.81 mmol, 1 eq.), acetone (3 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 1.27 mL, 1.63 mmol). The crude product was purified by preparative HPLC to afford **10b** and **21**.

*4.4.5.1.1. 4-Chloro-3-methylphenyl 3,5-dimethylisoxazole-4-sulfonate,* ***21****.* The *title compound* was isolated by Preparative HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 8.038 min) as a colourless crystalline solid. Yield 36.57 mg (15%). $\mathbf{R_f}$ 0.76 (2:8 ethyl

acetate: petroleum ether; v/v); **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.38 (s, 3 H), 2.38 (s, 3 H), 2.46 (s, 3 H), 6.82–6.87 (m, 1 H), 7.01 (dd, $J = 2.0$, 1.0 Hz, 1 H), 7.34 (d, $J = 9.0$ Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.7, 12.6, 20.3, 112.2, 120.7, 124.6, 130.2, 133.6, 138.4, 147.1, 158.0, 175.5. **LRMS (ES$^+$)** $C_{12}H_{12}ClNO_4S$ requires 301; found **(ES$^+$)** 302 $[M+H]^+$ for $^{35}$Cl, 304 $[M+H]^+$ for $^{37}$Cl, 324 $[M+Na]^+$ for $^{35}$Cl; **HRMS (ES$^+$)** $C_{12}H_{13}ClNO_4S$ $[M+H]^+$ requires 302.0244; found 302.0245 for $^{35}$Cl, ($\Delta = 0.331$ ppm). **Microanalysis** $C_{12}H_{12}ClNO_4S$ requires: C, 47.77; H, 4.01; Cl, 11.75; N, 4.64; S, 10.63%; Found: C, 47.96, H, 4.32, N, 4.57, S, 10.49, Cl, 11.30%.

*4.4.5.1.2. m-Tolyl 3,5-dimethylisoxazole-4-sulfonate,* ***10b****.* The *title compound* was isolated by preparative HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 8.721 min) as a colourless, crystalline solid. Yield 183.82 mg (85%). **$R_f$** 0.82 (2:8 ethyl acetate: petroleum ether; v/v). The spectral data for this compound was identical to that recorded for compound **10b**, obtained from the reaction of **4b** with $TiCl_3$, experiment 4.4.2.

*4.4.5.2. Using acetone-$d_6$ as solvent.* According to **(GP4)** the starting materials were mixed: **4e** (200 mg, 0.52 mmol, 1 eq.), acetone-$d_6$ (5 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 0.8 mL, 1.03 mmol).

Examination of the $^1$H NMR spectrum (in $CDCl_3$) of the crude reaction mixture indicated the presence of **10b** and **10b´** (**10b**:**10b´** = 1:1) as the major products.

### *4.5. Radical clock experiments*

#### *4.5.1. Synthesis and reactions of 2-(allyloxy)-6-(((3′,5′-dimethylisoxazol-4′-yl)sulfonyl)oxy)benzenediazonium tetrafluoroborate, 29 with $TiCl_3$*

*4.5.1.1. 3-(Allyloxy)-2-nitrophenol.* According to **(GP5)** the starting materials were mixed: 2-nitroresorcinol **26**(21 g, 135.38 mmol, 2 eq.) and $K_2CO_3$ (9.31 g, 67.69 mmol, 2.0 eq.), $CH_3CN$ (300 mL), allyl bromide **27**(6.43 mL, 74.41 mmol, 1.1 eq.). The crude product was purified by gradient elution column chromatography (using long silica column, 100% petroleum ether; to 5:5 $CH_2Cl_2$: petroleum ether; v/v) to afford *3-(allyloxy)-2-nitrophenol* as an orange-coloured, viscous oil. Yield 7.52 g (57%). **$R_f$** 0.57 (7:3 $CH_2Cl_2$: petroleum ether; v/v); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3547-3330, 3089, 3080, 3027, 2988, 2937, 1607, 1586, 1531, 1459, 1424, 1352, 1278, 1256, 1196, 1173, 1110, 1075, 1019, 990, 961, 929, 853, 788, 758. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 4.6 (dt, $J = 5.0$, 1.0 Hz, 2 H), 5.29 (dq, $J = 10.0$, 1.0 Hz, 1 H), 5.49 (dq, $J = 17.0$, 1.0 Hz, 1 H), 6.00 (ddt, $J = 17.0$, 10.0, 5.0 Hz, 1 H), 6.49 (dd, $J = 8.0$, 1.0 Hz, 1 H) 6.62–6.65 (m, 1 H), 7.30–7.35 (m, 1 H), 9.99 (br. s., 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 70.1, 104.9, 110.6, 118.0, 127.5, 131.6, 135.5, 154.4, 155.11. **LRMS (ES$^+$)** $C_9H_9NO_4$ requires 195; found **(ES$^-$)** 194 $[M-H]^-$; **HRMS (ES$^-$)** $C_9H_8NO_4$ $[M-H]^-$ requires 194.0453; found 194.0462 ($\Delta = 4.6$ ppm).

*4.5.1.2. 3-(Allyloxy)-2-nitrophenyl 3,5-dimethylisoxazole-4-sulfonate,* ***27****.* According **(GP2)**, the starting materials were mixed: **1** (1.15 g, 5.90 mmol, 1.1 eq.), 3-(allyloxy)-2-nitrophenol (1.05 g, 5.36 mmol, 1 eq.), $Et_3N$ (0.82 mL, 5.9 mmol, 1.1 eq.). The *title compound*, *3-(allyloxy)-2-nitrophenyl 3,5-dimethylisoxazole-4-sulfonate*, **27** was obtained as a yellow-coloured, crystalline, solid. Yield 1.90 g (100%); **mp.** 129–130 °C; **$R_f$** 0.62 (100% $CH_2Cl_2$); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3099), 2997, 2943, 2877, 1610, 1581, 1533, 1480, 1464, 1408, 1357, 1294, 1272, 1232, 1204, 1126, 1108, 1040, 955, 940, 924, 852, 788. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.28 (s, 3 H), 2.51 (s, 3 H), 4.63 (dt, $J = 5.0$, 1.0 Hz, 2 H), 5.27 (dq, $J = 10.0$, 1.0 Hz, 1 H), 5.34 (dq, $J = 17.0$, 1.0 Hz, 1 H), 5.92 (ddt, $J = 17.0$, 10.0, 5.0 Hz, 1 H), 7.03 (dd, $J = 8.0$, 1.0 Hz, 1 H), 7.13 (dd, $J = 8.0$, 1.0 Hz, 1 H), 7.45 (t, $J = 8.0$ Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.6, 12.7, 70.3, 111.9, 112.9, 115.0, 118.7, 131.1, 131.5, 134.9, 140.5, 151.1, 158.0, 176.3. **LRMS (ES$^+$)** $C_{14}H_{14}N_2O_7S$ requires 354; found **(ES$^+$)** 355 $[M+H]^+$, 377 $[M+Na]^+$, 393 $[M+K]^+$, **(ES$^-$)** 353 $[M-H]^-$; **HRMS (ES$^+$)** $C_{14}H_{14}N_2O_7SNa$ $[M+Na]^+$ requires 377.0419; found 377.0423 ($\Delta = 0.9$ ppm). **Microanalysis** $C_{14}H_{14}N_2O_7S$ requires: C, 47.46; H, 3.98; N, 7.91; S, 9.05%; Found: C, 47.31, H, 3.97, N, 7.77, S, 9.05%.

*4.5.1.3. 3-(Allyloxy)-2-aminophenyl 3,5-dimethylisoxazole-4-sulfonate,* ***28****.* According **(GP6)**, the starting materials were mixed: 3-(allyloxy)-2-nitrophenyl 3,5-dimethylisoxazole-4-sulfonate **27** (1.95 g, 5.50 mmol, 1 eq.), zinc dust (1.8 g, 27.54 mmol, 5 eq.), MeOH/THF (1:1, 25 mL) and saturated $NH_4Cl$ (25 mL) was added. The *title compound*, 3-*-(allyloxy)-2-aminophenyl 3,5-dimethylisoxazole-4-sulfonate*, **28** was obtained as colourless oil and was pure enough (judged by: $^1$H NMR spectra, and TLC), and directly used for next reaction without any further purification. Yield 1.74 g (98%). **$R_f$** 0.45 (100% $CH_2Cl_2$); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3472, 3382, 3084, 2981, 2939, 2870, 1619, 1587, 1497, 1471, 1408), 1384, 1360, 1114, 1288, 1269, 1223, 1201, 1162, 1078, 1033, 920, 789, 770. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.23 (s, 3 H), 2.35 (s, 3 H), 3.95 (br. s., 2 H), 4.46 (dt, $J = 5.0$, 1.0 Hz, 2 H), 5.20 (dq, $J = 10.0$, 1.0 Hz, 1 H), 5.29 (dq, $J = 17.0$, 1.0 Hz, 1 H), 5.94 (ddt, $J = 17.0$, 10.0, 5.0 Hz, 1 H), 6.43–6.52 (m, 2 H) 6.63 (dd, $J = 7.8$, 1.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta = 10.6$, 12.5, 69.5, 110.6, 112.2, 115.0, 116.4, 117.8, 130.8, 132.9, 135.9, 147.3, 158.1, 175.7. **LRMS (ES$^+$)** $C_{14}H_{16}N_2O_5S$ requires 324; found **(ES$^+$)** 325 $[M+H]^+$, 347 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{14}H_{16}N_2O_5SNa$ $[M+Na]^+$ requires 347.0678; found 347.0688 ($\Delta = 3$ ppm).

*4.5.1.4. 2-(Allyloxy)-6-(((3′,5′-dimethylisoxazol-4′-yl)sulfonyl)oxy)-benzenediazonium tetrafluoroborate,* ***29****.* According to **(GP3)** the starting materials were mixed: **28** (473 mg, 1.45 mmol, 1 eq.), ethanol (5 mL), isoamyl nitrite (0.23 mL, 1.74 mmol, 1.2 eq.), $HBF_4$ 48% (0.49 mL, 3.79 mmol, 2.6 eq.). The *title compound, 2-(allyloxy)-6-(((3′,5′-dimethylisoxazol-4′-yl)sulfonyl)oxy)benzenediazonium tetrafluoroborate* ***29*** was obtained as colourless, crystalline, solid. Yield 583 mg (95%); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3099, 2985, 2944, 2249, 1600, 1570, 1490, 1450, 1408, 1397, 1381, 1363, 1306, 1263, 1210, 1132, 1099, 1051, 948, 927, 792, 744, 702, 677. **$^1$H NMR** (400 MHz, acetone-$d_6$) $\delta$ 2.46 (s, 3 H), 2.74 (s, 3 H), 5.22 (dt, $J = 5$, 1 Hz, 2 H), 5.46 (dq, $J = 10$, 1 Hz, 1H), 5.62 (dq, $J = 17$, 1 Hz, 1 H), 6.11–6.24 (m, 1 H), 7.51 (dd, $J = 8.6$, 1 Hz, 1 H), 7.76 (d, $J = 9$ Hz, 1 H), 8.41 (dd, $J = 9$, 8 Hz, 1 H). **$^{13}$CNMR** (100 MHz, acetone-$d_6$) $\delta$ 9.9, 12., 73.3, 110.6, 114.2, 114.91, 120.1, 130.5, 145.8, 148.1, 157.8, 161.8, 164.3, 178.5. **Microanalysis** for $C_{14}H_{14}BF_4N_3O_5S$, require: C, 39.74; H, 3.34; N, 9.93; S, 7.58%; Found: C, 39.76, H, 3.17, N, 9.81, S, 7.76%.

#### *4.5.2. Reaction of* ***29*** *with $TiCl_3$*

According to **(GP4)** the starting materials were mixed: **29** (466 mg, 1.10 mmol, 1 eq.), acetone (5 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 1.7 mL, 2.2 mmol). Purification of the crude reaction mixture by reparative HPLC afforded **28**, **30**, **31** and **32**.

*4.5.2.1. 3-Methylbenzofuran-4-yl 3′,5′-dimethylisoxazole-4′-sulfonate,* ***30****.* Purified by Preparative HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 9.180 min). The *title compound* was obtained as a colourless, crystalline, solid. Yield 10 mg (3%). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.28 (s, 3 H), 2.29 (d, $J = 1.0$ Hz, 3 H), 2.35 (s, 3 H), 6.58–6.60 (m, 1 H), 7.07–7.12 (m, 1 H), 7.33–7.37 (m, 2 H). **LRMS (ES$^+$)** $C_{14}H_{13}NO_5S$ requires 307; found **(ES$^+$)** 330 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{14}H_{13}NO_5S$ $[M+Na]^+$ requires 330.0412; found 330.0410 ($\Delta = 0.605$ ppm).

*4.5.2.2. (±)-3-methyl-2,3-dihydrobenzofuran-4-yl 3′,5′-dimethylisoxazole-4′-sulfonate,* ***31***. Purified by Preparative HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 10.599 min) gave the *title compound* as a colourless, crystalline, solid. Yield 95 mg (28%). $\mathbf{R_f}$ 0.62 (3:7 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta = 1.30$ (d, $J = 7$ Hz, 3 H), 2.29 (s, 3 H), 2.37 (s, 3 H), 3.53 (dt, $J = 9.0$, 6.7 Hz, 1 H), 4.07 (dd, $J = 9.0$, 6.3 Hz, 1 H), 4.59 (t, $J = 9.0$ Hz, 1 H), 6.31 (dd, $J = 8.0$, 1.0 Hz, 1 H), 6.67 (d, $J = 8.0$ Hz, 1 H), 6.91–7.07 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta = 10.7$ ($\underline{C}H_3$), 12.6 ($\underline{C}H_3$), 18.5 ($\underline{C}H_3$), 35.9, 78.9, 109.2, 112.9, 113.9, 125.7, 129.4, 145.9, 158.1, 161.9, 175.4. **LRMS (ES$^+$)** $C_{14}H_{15}NO_5S$ requires 309; found **(ES$^+$)** 310 $[M+H]^+$; **HRMS (ES$^+$)** $C_{14}H_{16}NO_5S$ $[M+H]^+$ requires 310.0732; found 310.0744 ($\Delta = -3.77$ ppm).

*4.5.2.3. (±)-3-(Chloromethyl)-2,3-dihydrobenzofuran-4-yl 3′,5′-dimethylisoxazole-4′-sulfonate,* ***32***. Purified by Preparative HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 12.411 min) gave the *title compound* as a colourless, crystalline, solid; Yield 64 mg (17%). $\mathbf{R_f}$ 0.56 (3:7 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 12.39 (s, 3 H), 2.49 (s, 3 H), 3.68 (dd, $J = 11.0$, 9.0 Hz, 1 H), 3.92–4.04 (m, 2 H), 4.61–4.73 (m, 2 H), 6.40 (dd, $J = 8.0$, 1.0 Hz, 1 H), 6.80 (d, $J = 8.0$ Hz, 1 H) 7.13–7.19 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.7, 12.6, 43.8, 44.6, 75.3, 109.7, 112.6, 113.9, 120.5, 130.7, 145.9, 158.1, 162.6, 175.7. **LRMS (ES$^+$)** $C_{14}H_{14}ClNO_5S$ requires 343; found **(ES$^+$)** 344 $[M+H]^+$, 308 $[M\text{-}Cl]^-$; **HRMS (ES$^+$)** $C_{14}H_{14}NO_5S$ $[M\text{- }Cl]^-$ requires 308.0587; found 308.0583 ($\Delta$ = - 1.36 ppm).

*4.5.2.4. 3-(Allyloxy)-2-aminophenyl 3,5-dimethylisoxazole-4-sulfonate,* ***28***. Purified by Preparative HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 17.208 min) gavr the title compound as a colourless oil; Yield 146 mg (41%). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.27 (s, 3 H), 2.38 (s, 3 H), 3.94 (br. s., 2 H), 4.48 (dt, $J = 5.0$, 1 Hz, 2 H), 5.23 (dq, $J = 10.0$, 1.0 Hz, 1 H), 5.31 (dq, $J = 17.0$, 1.0 Hz, 1 H), 5.91–6.02 (m, 1 H) 6.44–6.47 (m, 1 H), 6.49–6.54 (m, 1 H) 6.64 (dd, $J = 8.0$, 1.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.7 ($CH_3$), 12.6 ($CH_3$), 69.7, 110.7, 112.4, 115.0, 116.6, 118.1, 130.8, 132.8, 136.1, 147.5, 158.2, 175.6. **LRMS (ES$^+$)** $C_{14}H_{16}N_2O_5S$ requires 324; found **(ES$^+$)** 325 $[M+H]^+$, 347 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{14}H_{16}N_2O_5SNa$ $[M+Na]^+$ requires 347.0678; found 347.0685 ($\Delta = 2$ ppm). The spectral data for this compound was identical to that observed earlier for **28**.

### *4.5.3. Intramolecular radical clock reactions: reaction of 1,3-bis(allyloxy)benzenediazonium tetrafluoroborate, 36 with $TiCl_3$*

*4.5.3.1. Synthesis of 1,3-bis(allyloxy)-2-nitrobenzene.* According to **(GP5)**, and after separation of 3-(allyloxy)-2-nitrophenol **28**. The crude mixture of unreacted 2-nitroresorcinol and 1,3-bis(allyloxy)-2-nitrobenzene was stirred overnight with excess NaOH (2 M, 100 mL) and the mixture was extracted by $CH_2Cl_2$ (50 mL x 3). The organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The *title compound* was isolated as a yellowish green oil. Yield 5 g (29%). $\mathbf{R_f}$ 0.70 (5:5 $CH_2Cl_2$: petroleum ether; v/v); $\bar{\nu}_{max}$/**cm$^{-1}$** (ATR) 3097, 3087, 3019, 2990, 2938, 2886, 2874, 1649, 1610, 1584, 1530, 1477, 1423, 1370, 1303, 1262, 1237, 1117, 1092, 987, 927, 850, 775, 669. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 4.4 (dt, $J = 5$, 1 Hz, 4 H), 5.09 (dq, $J = 10$, 1 Hz, 2 H), 5.21 (dq, $J = 17$, 1 Hz, 2 H), 5.78 (ddt, $J = 17$, 10, 5, 5 Hz, 2 H), 6.47 (d, $J = 1$ Hz, 2 H), 7.10 (t, $J = 8$ Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 69.7, 105.9, 118.0 (2 x = $\underline{C}H$), 131.1, 131.8, 132.6, 150.7. **LRMS (ES$^+$)** $C_{12}H_{13}NO_4$ requires 235; found **(ES$^+$)** 236 $[M+H]^+$, 258 $[M+Na]^+$, 274 $[M+ K]^+$; **HRMS (EI)** $C_{12}H_{13}NO_4$ $[M^{+\cdot}]$ requires 235.0839; found 235.0841 ($\Delta = 0.81$ ppm).

*4.5.3.1.1. Synthesis of: 1,3-bis(allyloxy)aniline,* ***37***. According **(GP6)**, the starting materials were mixed: 1,3-bis(allyloxy)-2-nitrobenzene **35** (1.025 g, 4.35 mmol, 1 eq.), zinc dust (1.42 g, 21.78 mmol, 5 eq.), MeOH/THF (1:1, 8 mL) and saturated $NH_4Cl$ (8 mL) was added. The *title amine* was obtained as brown oil, was pure enough (judged by: NMR spectra, and TLC), and directly used for next reaction without any further purification. Yield 840 mg (94%). $\mathbf{R_f}$ 0.68 (100% $CH_2Cl_2$); $\bar{\nu}_{max}$/**cm$^{-1}$** (ATR) 3471, 3372, 3080, 3016, 2981, 2920, 2911, 2864, 1648, 1599, 1566, 1422, 1362, 1291, 1175, 1139, 1047, 990, 920, 757, 713. **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 3.71 (br. s., 2 H), 4.40 (dt, $J = 5$, 1 Hz, 4 H), 5.12 (dq, $J = 11.0$, 1.0 Hz, 2 H), 5.26 (dq, $J = 17$, 1 Hz, 2 H), 5.87–5.99 (m, 2 H), 6.35–6.40 (m, 2 H), 6.46–6.51 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 69.5, 105.9, 116.7, 117.3, 126.4, 133.8, 146.6. **LRMS (ES$^+$)** $C_{12}H_{15}NO_2$ requires 205; found **(ES$^+$)** 206 $[M+H]^+$; **HRMS (EI)** $C_{12}H_{16}NO_2$ $[M^{+\cdot}]$ requires 205.1097; found 205.1097 ($\Delta = 0$ ppm).

*4.5.3.2. Synthesis of 1,3-bis(allyloxy)benzenediazoniumtetrafluoroborate, 36.* According to **(GP3)** the starting materials were mixed: 2,6-*bis*(allyloxy)aniline **36** (319 mg, 1.56 mmol, 1 eq.), ethanol (4 mL), *iso*amyl nitrite (0.25 mL, 1.87 mmol, 1.2 eq.), $HBF_4$ 48% (0.53 mL, 4.05 mmol, 2.6 eq.). The *title compound* was obtained as yellow solid. Yield 421 mg (89%); $\bar{\nu}_{max}$/**cm$^{-1}$** (ATR) 3176, 3105, 3025, 2962, 2272, 2243, 1579, 1490, 1466, 1426), 1319, 1272, 1246, 1136, 1033, 995, 933, 888, 788, 714, 653, 623, 520. **$^1$H NMR** (400 MHz, acetone-$d_6$) $\delta$ 4.59 (dt, $J = 5$, 1 Hz, 4 H), 4.97 (dq, $J = 10$, 1 Hz, 2 H), 5.09 (dq, $J = 17$, 1 Hz, 2 H), 5.64 (ddt, $J = 17$, 10, 5, 5 Hz, 2 H), 6.70 (d, $J = 1$ Hz, 2 H), 7.71 (t, $J = 8$ Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 71.8, 92.2, 106.8, 119.8, 131.0, 145.2, 160.8. **Microanalysis** for $C_{12}H_{13}BF_4N_2O_2$, require: C, 47.40; H, 4.31; N, 9.21%; Found: C, 46.63, H, 4.12, N, 9.05%.

### *4.6. Reaction of* ***36*** *with $TiCl_3$ leading to* ***37*** *and* ***38***

According to **(GP4)** the starting materials were mixed: **37** (300 mg, 0.986 mmol, 1 eq.), acetone (4 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 1.5 mL, 1.97 mmol). Purification of the crude reaction mixture by column chromatography (6:4 $CH_2Cl_2$: hexane; v/v) and afforded **37** and **38**.

*4.6.1. (±)-6-(Allyloxy)-3′-(chloromethyl)-2′,3′-dihydrobenzofuran,* ***38***

Colourless, crystalline, solid. Yield 20 mg (9%). $\mathbf{R_f}$ 0.35 (6:4 $CH_2Cl_2$: hexane; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 3.59 (dd, $J = 10.0$, 11.0 Hz, 1 H), 3.92–4.00 (m, 1 H), 4.04 (ddd, $J = 10.0$, 3.0, 1.0 Hz, 1 H), 4.59 (dt, $J = 5.0$, 1.0 Hz, 2 H), 4.63 (dd, $J = 10.0$, 5.0 Hz, 1 H), 4.66 (dd, $J = 10.0$, 9.0 Hz, 1 H), 5.32 (dq, $J = 10.0$, 1.0 Hz, 1 H), 5.41 (dq, $J = 17.0$, 1.0 Hz, 1 H), 6.04–6.06 (m, 1 H), 6.42 (d, $J = 8.0$ Hz, 1 H), 6.48 (d, $J = 8.0$ Hz, 1 H), 7.13 (t, $J = 8.0$ Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 43.6, 45.4, 68.7, 75.2, 103.3, 104.1, 117.6, 130.5, 133.0. **LRMS (ES$^+$)** $C_{12}H_{13}ClO_2$ requires 224; found GC-MS **(EI)**: 224 $[M]^{+\cdot}$ for $^{35}$Cl; **HRMS (EI)**; $C_{12}H_{14}ClO_2$ $[M]^{+\cdot}$ requires 224.0598 for $^{35}$Cl; found 224.0593 ($\Delta$ = - 2.23 ppm).

### *4.7. 1,3-Bis(allyloxy)aniline,* ***37***

Brown-coloured oil. Yield 151 mg (75%). $\mathbf{R_f}$ 0.68 (100% $CH_2Cl_2$). **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta = 3.73$ (br. s., 2 H), 4.41 (dt, $J = 5.0$, 1.0 Hz, 4 H), 5.10 (dq, $J = 11.0$, 1.0 Hz, 2 H), 5.28 (dq, $J = 17.0$, 1.0 Hz, 2 H), 5.88–6.00 (m, 2 H), 6.36–6.41 (m, 2 H), 6.48–6.53 (m, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 69.6, 105.8, 116.9, 117.4, 126.4, 133.7, 146.7. **LRMS** Calculated $C_{12}H_{15}NO_2$, 205, observed **LRMS (ES$^+$)** 206 $[M+H]^+$. The spectral data for this compound was identical to that previously for this compound.

### 4.8. Intermolecular vs intramolecular radical capture experiments: reaction of **4b** with $TiCl_3$ in the presence of furan

To a solution of 2-(((3′,5′-dimethylisoxazol-4-yl)sulfonyl)oxy)-6-methylbenzenediazonium tetrafluoroborate **4b** (435 mg, 1.36 mmol, 1 eq.) in acetone (5 mL) containing furan (0.5 mL, 6.84 mmol, 5 eq.) was added $TiCl_3$ (2.1 mL, 2.72 mmol, 2 eq.) using our standard procedure (GP4).

Purification of the crude product by flash column chromatography and then HPLC afforded **10b**, **12b,** and **25**.

#### 4.8.1. 2-(Furan-2′-yl)-3-methylphenyl 3″,5″-dimethylisoxazole-4″-sulfonate, **25**

Purified by Prep HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 9.355 min) to give *title compound* as a pale yellow crystal. Yield 181 mg (40%); **mp**. 88–90; $\mathbf{R_f}$ 0.69 (3:7 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 1.91 (s, 3 H), 2.12 (s, 3 H), 2.16 (s, 3 H), 6.28 (dd, $J$ = 3.0, 1.0 Hz, 1 H), 6.35 (dd, $J$ = 3.0, 2.0 Hz, 1 H), 7.14–7.18 (m, 1 H), 7.25–7.27 (m, 2 H), 7.33 (dd, $J$ = 2.0, 1.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.5, 12.4, 20.6, 110.7, 111.2, 112.4, 121.5, 125, 129.4, 129.8, 140.6, 142.9, 146.8, 147.2, 157.8, 174.9. **LRMS (ES$^+$)** $C_{16}H_{15}NO_5S$ requires 333; found **(ES$^+$)** 334 $[M+H]^+$, 356 $[M+Na]^+$; **HRMS (ES$^+$)** $C_{16}H_{16}NO_5SNa$ $[M+Na]^+$ requires 356.0563; found 356.0562 ($\Delta$ = - 0.32 ppm).

#### 4.8.2. m-Tolyl 3,5-dimethylisoxazole-4-sulfonate, **10b**

Purified by Prep HPLC (ACE-137-2520, 254 nm, n-hexane/ethyl acetate = 90/10, flow rate = 15 mL/min, retention time (t) = 8.851 min) to afford *title compound* as a colourless, crystalline solid. Yield 109 mg (30%). The spectral data for this compound was identical to that recorded for compound **10b** obtained from the reaction between **4b** and $TiCl_3$, experiment 4.4.2.

#### 4.8.3. (3aR*,9bR*)-3,9,9b-trimethyl-3a,9b-dihydrobenzo[5,6][1,2]oxathiino[3,4-d]isoxazole-4,4-dioxide, **12b**

Purified by column chromatography to give *title compound* as a white solid; Yield 25 mg (7%). $\mathbf{R_f}$ 0.45 (3:7 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 1.84 (s, 3 H), 2.33 (d, $J$ = 1 Hz, 3 H), 2.68 (s, 3 H), 4.65 (br.m, 1 H), 7.00–7.04 (m, 1 H), 7.18–7.22 (m, 1 H), 7.28–7.33 (m, 12 H). **LRMS (ES$^+$)** $C_{12}H_{13}NO_4S$ requires 267; found **(ES$^+$)** 268; **HRMS (EI)** $C_{12}H_{13}NO_4S$ $[M^{\cdot+}]$ requires 267.0463; found 267.0474, ($\Delta$ = 4.11 ppm). The spectral data for this compound was identical to that previously recorded for **12b**.

### 4.9. Synthesis of 2-(3′,5′-dimethylisoxazol-4′-yl)-3-methylphenol, **8b**

Purified by column chromatography afforded the *title compound* as a white crystal; Yield 60 mg (22%). $\mathbf{R_f}$ 0.25 (3:7 ethyl acetate: petroleum ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 1.96 (s, 3 H), 1.99 (s, 3 H), 2.16 (s, 3 H), 5.81 (s, 1 H), 6.75–6.79 (m, 2 H), 7.12 (t, $J$ = 8.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 10.5, 11.5, 20.0, 110.3, 113.2, 115.1, 121.9, 129.7, 139.2, 154.8, 160.4, 167.4. **LRMS (ES$^+$)** $C_{12}H_{13}NO_2$ requires 203; found **(ES$^+$)** 204 $[M+H]^+$, **(ES$^-$)** 202 $[M-H]^-$; **HRMS (ES$^+$)** $C_{12}H_{14}NO_2$ $[M+H]^+$ requires 204.1025; found 204.1029, ($\Delta$ = 1.95 ppm). The spectral data for this compound was identical to a sample of **8b** previously prepared in experiments 4.4.2 and 4.6.

### 4.10. Attempted fluoride-mediated Truce-Smiles rearrangement reactions

#### 4.10.1. Synthesis of 2-(trimethylsilyl)phenyl 3′,5′-dimethylisoxazole-4′-sulfonate, **42**

*4.10.1.1. (2-Bromophenoxy)trimethylsilane [42].* In an oven dried flask, 2-bromophenol (57.09 mmol, 9.7 g, 6.5 mL, 1 eq.) in anhydrous THF (15 mL) was stirred at rt under nitrogen atmosphere. To this solution 1,1,1,3,3,3-hexamethyldisilazane (HMDS) (0.6 eq, 34.25 mmol, 7.18 mL) was added in dropwise by syringe and then heated under reflux for 4 h at 85 °C. After cooling to 20 °C the solvent, produced $NH_3$ and unreacted HMDS was evaporated under reduced pressure. The silyl ether was obtained as a colourless oil. Yield 13 g (94%). $^1$H NMR confirmed the purity of (2-bromophenoxy)trimethylsilane, so without further purification was used for next reaction; $\bar{\nu}_{max}$/**cm$^{-1}$**(ATR): 3061(=C–H str.), 2959 (–C–H str.), 2899, 1583 (C=C str.), 1474, 1439, 1408, 1283, 1251, 1155, 1120, 1046, 1028; **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta$ = 7.45 (1 H, dd, $J$ = 8.0, 1.0 Hz, Ar-$\underline{H}_3$), 7.10 (1H, td, $J$ = 8.0 Hz, 1.0 Hz, Ar-$\underline{H}_5$), 6.72–6.85 (2H, m, Ar-$\underline{H}_{6,4}$), 0.24 (9H, s, 3× C$\underline{H}_3$); **$^{13}$C NMR** (100 MHz, $CDCl_3$): $\delta$ = 152.0 ($C_1$), 132.9 ($C_3$), 127.9 ($C_5$), 122.3 ($C_4$), 120.4 ($C_6$), 115.2 ($C_2$), 0.0 ($CH_3$). **LRMS (EI)** $C_9H_{13}BrOSi$ requires 244; found **(EI)** 244 $[M^{+\cdot}]$ for $^{79}$Br, 246 $[M^{+\cdot}]$ for $^{81}$Br.

#### 4.10.2. Synthesis of 2-(trimethylsilyl)phenol [42]

2-Bromophenoxy)trimethylsilane, 10 g, 41 mmol, 1 eq.) was dissolved in dry THF (50 mL) and cooled to −78 °C under nitrogen with continuous stirring. To this solution dropwise of *n*-BuLi (38.5 mL of 1.6 M in hexane, 61.5 mmol, 1.5 eq.) was added by syringe. The reaction mixture was stirred for three hours in same temperature, then warmed to rt and stirred for one hour. The reaction mixture quenched by adding saturated ammonium chloride (10 mL). The reaction mixture was allowed to room temperature and then extracted it with ethyl acetate (3 × 25 mL). The organic phase was washed with water, brine, and dried over $MgSO_4$ and the reaction mixture taken to dryness *in vacuo*. The obtained light brown oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1) to give the *title compound* 2-(trimethylsilyl) phenol as colourless oil. Yield 6.31 g (93%). $\bar{\nu}_{max}$/**cm$^{-1}$**(ATR): 3600-3300 (broad, O–H str.), 3080 (=C–H str.), 2959 (–C–H str.), 1593 (C=C str.), 1436, 1241, 1122, 1072; **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta$ = 7.31 (d, $J$ = 7.0, 1 H), 7.11–7.17 (m, 1 H), 6.86 1H, tt, $J$ = 7.0, 1.0 Hz,1 H), 6.51 (1H, d, $J$ = 8.0 Hz, Ar-$\underline{H}_6$), 4.92 (1H, s, broad, O$\underline{H}$), 0.26 (s, 9H, C$\underline{H}_3$); **$^{13}$CNMR** (100 MHz, $CDCl_3$): $\delta$ = 161.3 ($C_2$), 136.2 ($C_6$), 131.6 ($C_4$), 126.4 ($C_1$), 121.6 ($C_5$), 115.4 ($C_3$). **LRMS (EI)** $C_9H_{14}OSi$ requires 166.0863; found **(EI)** 166.0864 $[M^{+\cdot}]$, ($\Delta$ = 0.87 ppm).

#### 4.10.3. Synthesis of 2-(trimethylsilyl)phenyl 3′,5;-dimethylisoxazole-4′-sulfonate, **42**

To the stirred solution of sodium hydride (1.156 g, 48.19 mmol, 4 eq.) in dry THF (75 mL) under nitrogen atmosphere *2-(trimethylsilyl)phenol* (2 g, 12.048 mmol, 1 eq.) was added. The reaction mixture was stirred for thirty minutes and then 3,5-dimethylisoxazole-4-sulfonyl chloride **1** (2.59, 13.25 mmol, 1.1 eq.) was added, reaction mixture was allowed to stir for three hour and then poured it into ether (100 mL). The organic phase was washed with water, brine, dried over $MgSO_4$, and then the reaction mixture taken to dryness *in vacuo*. The light yellow oil was purified by column chromatography (gradient elution, gradient 10 → 70% EtOAc/petroleum ether) to obtain pure colourless viscous oil of *title compound*. Yield 3.71 g (95%). $\mathbf{R_f}$ 0.48 (9:1 petroleum ether: EtOAc; v/v); **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 7.38(1H, dd, $J$ = 7, 2 Hz), 7.10–7.19 (2H, m), 6.78 (1H, dd, $J$ = 8, 1 Hz), 2.41 (s, 3H), 2.26 (s, 3H), 0.18 (s,

9H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 175.0, 158.5, 155.0, 136.8, 133.8, 131.1, 127.2, 120.0, 115.0, 13.2, 11.2, 0.0. **LRMS (ES$^+$)** $C_{14}H_{19}NO_4SSi$ requires 325; found **(ES$^+$)** 326 $[M+H]^+$, **(ES$^-$)** 324 [M-H]: **Microanalysis** $C_{14}H_{19}NO_4SSi$ requires: C, 51.67, H, 5.88, N, 4.3, S, 9.85%; Found: C, 52.00, H, 6.18, N, 4.15, S, 9.25%.

### 4.11. Attempted fluoride-induced Truce-Smiles rearrangements

#### 4.11.1. Using TBAF as fluoride source

According to **(GP7)** and at room temperature the starting materials were mixed, A solution of TBAF ($Bu_4NF$) (6 mL, 1 M in THF, 6 mmol, 3 eq.) was added to **42** (0.651 g, 2 mmol, 1 eq.) in dry acetonitrile (12 mL). The crude was purified by column chromatography (silica, 10% diethyl ether, petroleum ether) afforded *phenyl 3,5-dimethylisoxazole-4-sulfonate,* ***10a*** as a colourless crystalline solid. Yield 0.395 g (78%). **$R_f$** 0.65 (9:1 petroleum ether: ether; v/v). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 2.23 (s, 3H), 2.27 (s, 3H), 6.95–6.99 (2H, m), 7.17–7.33 (3H, m). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 176.8, 159.4, 150.2, 131.3, 129.1, 123.7, 113.4, 13.7, 11.9. **LRMS (EI)** $C_{11}H_{11}NO_4S$ requires 253; found **(EI)** 253 $[M^{+\cdot}]$. **Microanalysis** $C_{11}H_{11}NO_4S$ requires: C, 52.17, H, 4.38, N, 5.53, S, 12.66%; Found: C, 52.20, H, 4.29, N, 5.35, S, 12.14%. The spectral data for this compound was compatible to the same compound which previously reported **10a**.

#### 4.11.2. Using caesium flouride as a fluoride source

According to **(GP8)** the starting materials were mixed, CsF (456 mg, 3 mmol, 3 eq.) was added to a solution of **42** (325 mg, 1 mmol, 1 eq.) in dry THF (10 mL) and the mixture was refluxed at 70 °C for 16 h. The crude was purified by flash column chromatography (100% $CH_2Cl_2$-100% EtOAc) afforded *phenol* as a white solid. Yield 87 mg (92%). **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ = 6.08 (br. s., 1 H), 6.93–6.97 (m, 2 H), 7.02–7.06 (m, 1 H), 7.30–7.36 (m, 2 H); **$^{13}$C NMR** (125 MHz, $CDCl_3$): $\delta$ = 115.6, 121.1, 129.9, 155.2 (spectral data identical to a reference sample).

### 4.12. Effect of metal on product distribution of rearrangement reactions

#### 4.12.1. Reaction between 4a and $Cu(NO_3)_2{\cdot}3H_2O$-$Cu_2O$ leading to *10a* and *12a*

According to **(GP9)** the starting materials were mixed: **4a** (107 mg, 0.29 mmol, 1 eq.), $Cu(NO_3)_2\cdot 3H_2O$ (4.02 g, 16.64 mmol, 57 eq.), $Cu_2O$ (126 mg, 0.876 mmol, 3 eq.), $H_2O$ (32 mL). Purification by silica gel column chromatography gave the isolated products **10a** (white crystal, 45 mg, 62%), **12a** (white solid, 13 mg, 18%). The spectral data for these compounds were compatible to those compounds which previously reported.

#### 4.12.2. Reaction between *4b* and $Cu(NO_3)_2{\cdot}3H_2O$-$Cu_2O$ leading *8b*, *10b* and *12b*

According to **(GP9)** the starting materials were mixed: **4b** (250 mg, 0.65 mmol, 1 eq.), $Cu(NO_3)_2\cdot 3H_2O$ (9.03 g, 37.39 mmol, 57 eq.), $Cu_2O$ (281 mg, 1.97 mmol, 3 eq.), $H_2O$ (71 mL). Purification by silica gel column chromatography gave the isolated products **10b** (white crystal, 47 mg, 27%), **8b** (colourless, crystalline solid. Yield 90 mg (68%) and **12b** (white solid, 5 mg, 3%). The spectral data for these compounds was identical to that previously recorded for these compounds.

#### 4.12.3. Reaction of *4c* with $Cu(NO_3)_2{\cdot}3H_2O$-$Cu_2O$ leading to *17* [25]

According to **(GP9)** the starting materials were mixed: **4c** (135 mg, 0.32 mmol, 1 eq.), $Cu(NO_3)_2\cdot 3H_2O$ (4.40 g, 18.24 mmol, 57 eq.), $Cu_2O$ (137.35 mg, 0.96 mmol, 3 eq.), $H_2O$ (35 mL). Purification by silica gel column chromatography gave the *title compound* as reddish-brown solid. Yield 38.62 mg (71%). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 6.59 (d, $J$ = 9.0 Hz, 1 H), 7.17–7.23 (m, 2 H), 7.44 (ddd, $J$ = 8.0, 7.0, 1.0 Hz, 1 H), 7.51 (dd, $J$ = 1.0 Hz, 1 H), 7.57 (d, $J$ = 9.0 Hz, 1 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 77.2, 119.7, 124.7, 125.6, 125.9, 127.2, 129.8, 130.1, 140.3, 180.2. **LRMS** Calculated $C_{10}H_6N_2O$, 170, observed **LRMS (ES$^+$)** 171 $[M + H^+]$, 193 $[M + Na^+]$; **HRMS (ES$^+$)** calculated $C_{10}H_6N_2ONa$ $[M + Na^+]$ 193.0372, observed 193.0365 ($\Delta$ = - 3.8 ppm). This spectral data is in good agreement to that reported in the literature [25].

#### 4.12.4. Reaction of *4e* with $Cu(NO_3)_2{\cdot}3H_2O$-$Cu_2O$ leading to *10b* and *41*

According to **(GP9)** the starting materials were mixed: **4e** (333 mg, 0.87 mmol, 1 eq.), $Cu(NO_3)_2\cdot 3H_2O$ (12.03 g, 49.80 mmol, 57 eq.), $Cu_2O$ (375 mg, 2.62 mmol, 3 eq.), $H_2O$ (95 mL). Purification by silica gel column chromatography afforded **10b** and **41**.

*4.12.4.1. m-Tolyl 3,5-dimethylisoxazole-4-sulfonate,* ***10b***. Isolated as a colourless, amorphous solid. Yield 56 mg (24%). The spectral data for this compound was identical to that recorded for compound **10b**, obtained from the reaction between **4b** with $TiCl_3$, experiment 4.4.2 (Scheme 5).

*4.12.4.2. 4-Hydroxy-3-methylphenyl 3′,5′-dimethylisoxazole-4-sulfonate,* ***41***. Brown-coloured solid. Yield 175 mg (71%). **mp.** = 88–90 °C; **$R_f$** 0.27 (2:8 ethyl acetate: hexane; v/v); **$\bar{\nu}_{max}$/cm$^{-1}$** (ATR) 3613-3483, 3042, 2962, 1589, 1503, 1438, 1409, 1379, 1359, 1269, 1199, 1184, 1122, 1041, 999, 944, 911, 878, 826, 763. **$^1$H NMR** (500 MHz, CDCl3): $\delta$ = 2.14 (s, 3 H), 2.27 (s, 3 H), 2.34 (s, 3 H), 4.94 (br. s., 1 H), 6.60–6.67 (m, 2 H), 6.78 (d, $J$ = 3.0 Hz, 1 H); **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta$ 10.7, 12.5, 15.8, 112.2, 115.5, 120.5, 124.6, 125.7, 142.1, 153.1, 158.2, 175.3. **LRMS (ES$^+$)** $C_{12}H_{13}NO_5S$ requires 283; found **(ES$^+$)** 284 $[M+H]^+$, 306 $[M + Na^+]$**, (ES$^-$)** 282 $[M-H]^-$; **HRMS (ES$^+$)** $C_{12}H_{13}O_5SNNa$ $[M+Na]^+$ requires 306.0407; found 306.0407 ($\Delta$ = 0.12 ppm).

### 4.13. Blank reactions

#### 4.13.1. Reaction between *4b* with HCl

3 M HCl (2.4 mL, 6.4 mmol, 16 eq.) was added dropwise to a solution of **4b** (154 mg, 0.40 mmol, 1 eq.) in acetone (3 mL) in sealed vial and under ($N_2$) atmosphere at 0 °C. After the addition, the reaction mixture was stirred for 0.5 h at 0 °C and then 1 h at RT. Water (20 mL) was added to the reaction mixture and several time was extracted with $CH_2Cl_2$. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was obtained as sticky brown solid. Initial purification of the mixture by flash chromatography afforded a mixture of **7b**, **8b**, and **10b** where the product ratio was determined by **$^1$H NMR** analytical HPLC analysis against authentic materials (see supplementary information).

### 4.13. Reaction between *10c* and $TiCl_3$

According to (**GP4**) the starting materials were mixed: **10c** (200 mg, 0.657 mmol, 1 eq.), acetone (3 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 1.02 mL, 1.31 mmol). Work-up, as above, afforded **10c**, essentially unchanged, as judged by $^1$H NMR analysis.

#### 4.13.1. Reaction between 16 and $TiCl_3$

According to **(GP4)** the starting materials were mixed: 2-naphthol, **16** (250 mg, 1.73 mmol, 1 eq.), acetone (3 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 2.68 mL, 3.46 mmol). Work-up, as above, and chromatography of the residue (silica; 30% EtOAc: hexane) afforded **16** essentially unchanged, as judged by $^1$H NMR analysis.

*4.13.2. Reaction between 17 and $TiCl_3$ leading to 16 and 18*

According to (**GP4**) the starting materials were mixed: **17** (60 mg, 0.34 mmol, 1 eq.), acetone (0.54 mL), $TiCl_3$ (1.29 M in HCl, 2 eq., 1.02 mL, 1.31 mmol). Purification of the crude product by column chromatography silica; gradient elution: 10%–30% EtOAc:hexane) afforded **16** and **18**:

*4.13.2.1. Naphthalen-2-ol, **16**.* Colourless, crystalline solid. Yield 31 mg (63%). $R_f$ 0.87 (100% EtOAc). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 5.44 (br. s., 1 H), 7.13–7.20 (m, 2 H), 7.36–7.41 (m, 1 H), 7.48 (ddd, $J = 8.2$, 6.9, 1.3 Hz, 1 H), 7.71 (dd, $J = 8.3$, 0.50 Hz, 1 H), 7.78–7.84 (m, 2 H). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta$ 109.6, 117.8, 123.7, 126.4, 126.6, 127.8, 128.9, 129.9, 134.6, 153.3. This data was essentially identical to that recorded on an authentic sample (ex Aldrich).

*4.13.2.2. 1-Chloronaphthalen-2-ol, **18** [44].* Colourless, crystalline solid. Yield 19 mg (31%), **mp.** 67–68 °C (Lit [44]. 66 °C), **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta$ 6.35 (s, 1 H), 7.42 (d, $J = 8.0$ Hz, 1 H), 7.47–7.53 (m, 1 H), 7.67 (ddd, $J = 8.0$, 7.0, 1.0 Hz, 1 H), 7.73 (d, $J = 8.0$ Hz, 1 H), 7.84 (d, $J = 8.0$ Hz, 1 H), 8.19 (d, $J = 8.0$ Hz, 1 H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta$ 113.6, 117.4, 122.9, 124.3, 127.7, 128.4, 128.6, 129.6, 131.2, 149.5. **LRMS (EI)** $C_{10}H_7ClO$ requires 178; found GC-MS **(EI)** 178 $[M]^{+\cdot}$ for $^{35}$Cl, 180 for $^{37}$Cl. This data is essentially identical to that reported in the literature for this compound [44].

*4.13.3. Reaction between **4c** and HCl leading to **17***

To a solution of **4c** (84 mg, 0.20 mmol) in acetone (2 mL), (3 M, HCl, 3 mL) was added and stirred under ($N_2$) gas for 2 h. Water (10 mL) was added and extracted by $CH_2Cl_2$ (3 × 15 mL). Work-up as above and chromatography of the residue (silica gel: 30% EtOAc: hexane) afforded **17** as a reddish-coloured solid. Yield 23 mg (68%). The spectral data for this compound was identical to the material isolated in experiment 4.10.3.

## 5. X-ray data

Crystallographic data (excluding structure factors) for compounds **3a**, **3b**, **3c**, **3e**, **8b**, **8c**, **8d**, **9b, 10a**, **10b**, **10c**, **10d**, **12a, 12c**, **12d**, **13a**, **13d** and **21** have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data (CCDC nos. CCDC 1891090–1891107) can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

## Conflicts of interest

The authors declare no competing interests.

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## Appendix A. Supplementary data

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