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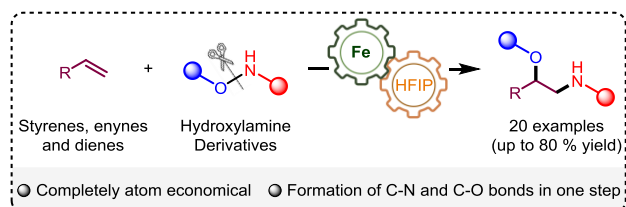
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Iron-catalyzed intermolecular oxyamination of terminal alkenes promoted by HFIP using hydroxylamine derivatives.

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Supporting Information Placeholder



ABSTRACT: An atom-economical intermolecular iron-catalyzed oxyamination of alkenes is described. The insertion of the oxygenated and nitrogenated moieties from the hydroxylamine substrate was observed with full regio- and chemoselectivity for terminal alkenes in good yields. HFIP as a solvent appeared to have a synergistic effect with the iron catalyst to promote the formation of the oxyaminated products. Preliminary mechanistic studies suggest a pathway going through an aziridination reaction followed by the in situ ring opening.

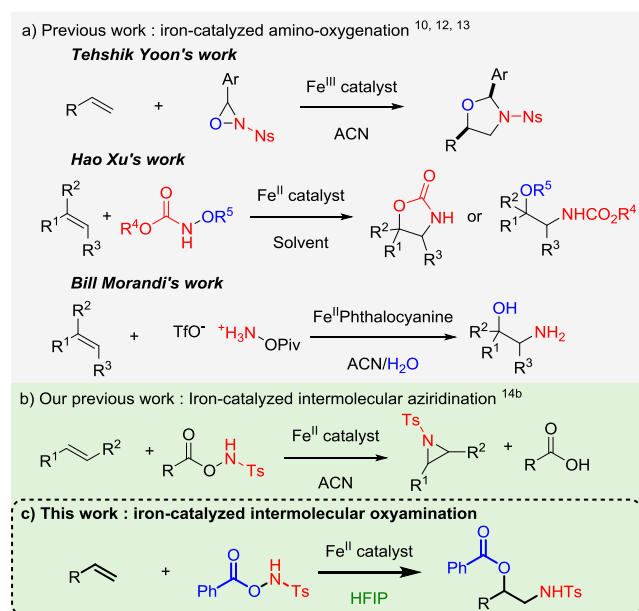
INTRODUCTION

Molecules containing vicinal amino alcohols are of great importance in chemistry. This structural motif is frequently found in many biologically active compounds, natural products and in a variety of chiral auxiliaries.¹ The classical strategies employed for the formation of 1,2-amino alcohols are based traditionally on the alkylation/reduction of β -amino aldehydes and β -hydroxyl imines, or on the ring opening of epoxides/aziridines with nitrogen/oxygen based nucleophiles.^{1b} The most appealing method certainly remains the direct oxyamination of olefins, allowing for the one-step installation of both oxygenated and aminated groups, using readily available alkenes.² Pioneering work in this area had been reported by Sharpless and co-workers using osmium as a catalyst and chloramine-T derivatives as nitrogen sources.³ Despite its effectiveness, particularly for enantioselective versions, the high toxicity of osmium limits the application of this method. Therefore, many groups have developed alternative protocols using different families of amine precursors and catalysts, mainly based on palladium,⁴ rhodium⁵ and copper.^{6,7} In order to promote a more sustainable approach, the development of methods based on the use of iron as a cheap, highly abundant, and non-toxic metal appears highly desirable. Iron-catalyzed oxyamination procedures have thus been recently investigated. Intramolecular versions of such a process were reported by Hao Xu in 2013 followed by our group.⁸ These tethered strategies have the advantage of being completely atom-economical and allow a full control of the regioselectivity.⁹ The selective intermolecular installation of the oxygen and the nitrogen atoms, catalyzed by iron, remains in contrast more ambitious and poorly explored. Tehshik Yoon

reported in 2010 the formation of 1,3-oxazolidines, as precursors of amino alcohols, using Davis' oxaziridine derivatives (scheme 1a).¹⁰ Interestingly, the regioselectivity obtained was complementary to the copper-catalyzed version described a few years earlier by the same group.^{6a, 6b} The investigation for a cleaner source of amine precursors in the field of metal-nitrenoids has led to a growing interest in the use of hydroxylamine derivatives.¹¹ In 2014, Hao Xu described an intermolecular iron-catalyzed olefin amino-oxygenation reaction with benzyloxycarbamate substrates. Depending on the reaction conditions used, and the alkene partner involved, two products can be formed, a protected amino alcohol or the corresponding oxazolidinone. Good to excellent yields were obtained, however the selectivity between the products was not rationalized (scheme 1a).¹² In 2016, Bill Morandi exploited the *O*-pivaloyl hydroxyl ammonium trifluoromethane sulfonate reagent for the intermolecular iron-catalyzed amino-hydroxylation of alkenes using a phthalocyanine as ligand. This process efficiently provided the unprotected amino alcohol products, but the isolated yields were generally obtained after Boc derivatization (scheme 1a).¹³ To the best of our knowledge, these methods represent the only examples reported so far in this field. Thus, following our research program dedicated to iron-catalyzed functionalization of alkenes,^{8b, 14} we investigated a novel sustainable oxyamination process. Our approach was focused on the reactivity of hydroxylamine derivatives from which insertion of both the oxygen and the nitrogen moieties was expected. This strategy would give access to the protected amino alcohols, which are easy to isolate and handle, with full atom economy. We reported recently an iron-catalyzed aziridination of olefins using *N*-tosyl *O*-acyl hydroxylamines as nitrogen sources. In this transformation,

the oxidative addition of the hydroxylamine to the iron complex leads to the reactive nitrene species that reacts with the alkene to get the aziridine, forming carboxylic acid as a by-product (scheme 1b).^{14b} Thenceforth, we envisioned to deviate the observed reactivity to an oxyamination reaction by the *in situ* ring opening of the aziridine with the released carboxylic acid through judicious activation. In the context of the development of sustainable methods, we were keen to avoid the addition of another reagent such as a Lewis acid and were attracted by the potential of an acidic non nucleophilic solvent. In particular hexafluoroisopropanol (HFIP) was appealing based on its high polarity, low nucleophilicity and its strong hydrogen-bond donor ability allowing for the stabilization of cationic species which promotes efficient addition or substitution reactions.¹⁵ This appeal for HFIP was also reinforced by a related intermolecular diamination reaction based on rhodium-nitrene species reported by the Rovis Group.¹⁶ We report herein our results for a novel intermolecular iron-catalyzed oxyamination process using hydroxylamine substrates which is facilitated by HFIP (scheme 1c).

Scheme 1. Context of the work



RESULTS AND DISCUSSION

In a first trial, the *N*-tosyl *O*-benzoyl hydroxylamine substrate **1a** and the styrene **2a** were mixed together with iron diacetate (10 mol %) and the PyBox ligand **L1** at 70 °C. We already reported that in acetonitrile after 18 h those conditions afforded the corresponding aziridine **A** in 83 % yield.^{14b} To our delight, keeping the same reaction conditions with a switch of solvent to HFIP led after only 2 h to the desired oxyaminated product **3a** in 63 % yield with a complete consumption of hydroxylamine **1a** (table 1, entry 1). Worthy of note, replacing HFIP with trifluoroethanol completely suppressed the formation of the oxyaminated product **3a** (table 1, entry 2).¹⁷ A mixture of tosylamine and other by-products was observed in this case. Using HFIP, a slight increase of the yield up to 67 % was observed with the use of iron(II) triflate as the metal source (table 1, entry 3) setting the conditions for the evaluation of the influence of the ligand. Classical bidentate, tridentate and tetradentate nitrogen-based ligands were then tested. The bidentate phenanthroline **L2** and bipyridine **L3** yielded

the desired product in moderate yields of 47 and 54 % respectively (table 1, entries 4-5). The use of the tetradentate bis-pyridine diamine ligand **L4**, had a dramatic influence with an almost complete inhibition of the reaction (3 % yield, table 1, entry 6). Tridentate ligands were found to be the most effective and the PyBox **L1** was not outperformed by the terpyridine **L5** (respectively 67 and 59 % yield table 1, entries 3 and 7). The nature of the metal salt was next studied keeping PyBox **L1** as the ligand. The use of iron(II) chloride gave comparable results to iron(II) acetate and iron(II) triflate (66, 63 and 67 % respectively, see table 1, entries 8 and 1 and 3), while iron(III) bromide provided the product **3a** with a lower 45 % yield (table 1, entry 9). The best result was finally obtained with iron(II) sulfate heptahydrate, the cheapest iron(II) catalyst tested, from which product **3a** was isolated in a 73 % yield (table 1, entry 10). The tosyl group appeared to have a significant impact on the reactivity, as the analogous *N*-nosyl *O*-benzoyl substrate provided the corresponding oxyaminated product in a moderate 40 % yield (table 1, entry 11). The yield could be increased to 50 % using the *N*-nosyl *O*-4-fluoro benzoyl derivative.¹⁷ A control experiment was then tried without the metal catalyst and ligand. In these conditions no conversion was observed, confirming thereby that HFIP alone does not induce the transformation (table 1, entry 12). In comparison with iron complexes, copper(I) iodide and copper(II) acetate gave no reaction in the same conditions, confirming that the iron complex is involved in the formation of the product **3a** (table 1, entries 13 and 14). Different protected hydroxylamine substrates were also evaluated as well as different polar solvents but none of the conditions tested outperformed the best conditions found (table 1, entry 10).¹⁷

Table 1. Optimization of the reaction conditions^a

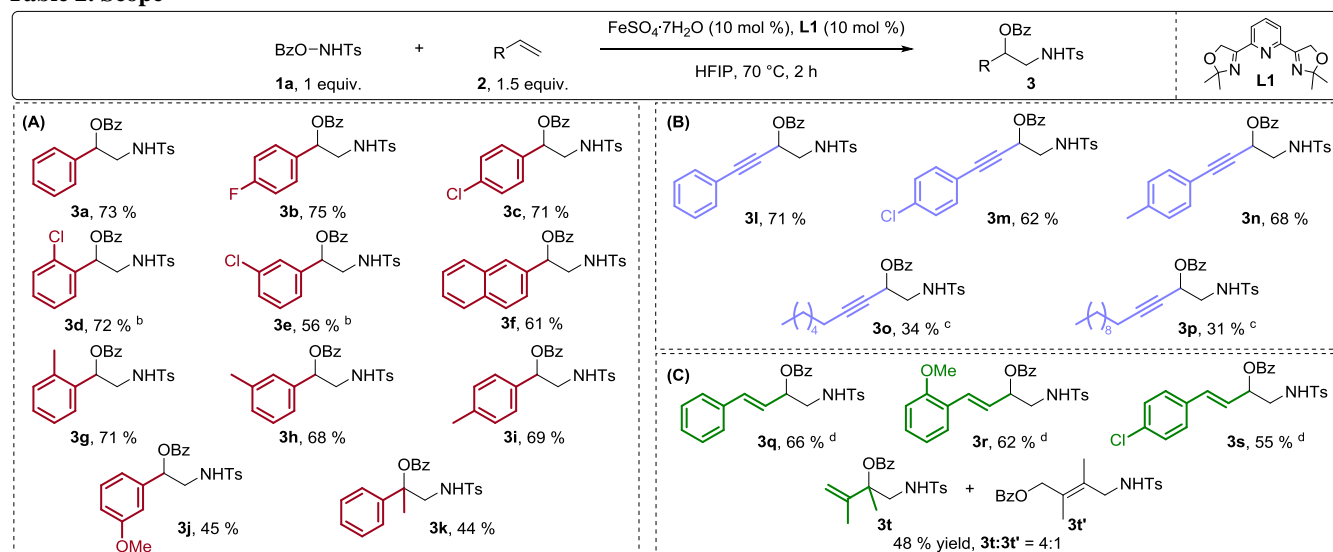
Entry	[M]	Ligand	Yield ^b
1	Fe(OAc) ₂	L1	63 %
2 ^c	Fe(OAc) ₂	L1	0 %
3	Fe(OTf) ₂	L1	67 %
4	Fe(OTf) ₂	L2 (20 mol %)	47 %
5	Fe(OTf) ₂	L3 (20 mol %)	54 %
6	Fe(OTf) ₂	L4	3 %
7	Fe(OTf) ₂	L5	59 %
8	FeCl ₂	L1	66 %
9	FeBr ₃	L1	45 %
10	FeSO ₄ ·7H ₂ O	L1	73 %
11 ^d	FeSO ₄ ·7H ₂ O	L1	40 %
12	---	---	0 %
13	CuI	L1	Trace
14	Cu(OAc) ₂	L1	Trace

(a) **1a** (0.23 mmol, 1 eq), **2a** (0.35 mmol, 1.5 eq), [M] (0.023 mmol, 10 mol %) and ligand (0.023 mmol, 10 mol %) were mixed in HFIP (C = 0.2

M) before stirring at 70 °C for 2 h. (b) Isolated yields. (c) TFE used instead of HFIP. (d) BzO-NHNs substrate used instead of **1a** to give the corresponding *N*-Ns oxyaminated product.

Having in hand the best reaction conditions, we next explored the scope of this transformation. The oxyamination of styrene derivatives worked smoothly with full regioselectivity. Compounds **3b** and **3c** bearing a fluoro- and a chloro- substituent at the para position were obtained in a 75 % and 71 % yield respectively (table 2-A). By comparison the 2-chloro and 3-chloro styrene reagents required a longer reaction time to reach a full conversion and to obtain products **3d** and **3e** with satisfying yields (72 % and 56 % respectively, table 2-A). The naphthyl functionalized product **3f** was obtained after 2 h in a good 61 % yield. The reaction was also tolerant to electron-donating substituents. Negligible effects were observed for the 2-methyl, 3-methyl and 4-methyl styrene derivatives, the products **3g**, **3h** and **3i** being isolated with yields similar to product **3a** (71 %, 68 % and 69 %, table 2-A). These examples demonstrate that the steric hindrance carried by the aromatic ring does not seem to have any effect on the reactivity. 3-methoxy styrene and α -methyl styrene were found to be less efficient substrates, the products **3j** and **3k** being obtained with

Table 2. Scope^a

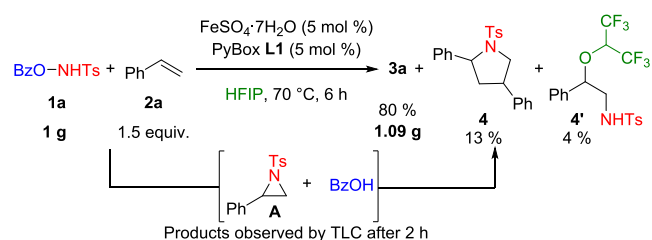


(a) Reaction conditions: in a sealed tube, **1a** (0.23 mmol, 1 eq), the proper alkene (0.35 mmol, 1.5 eq), $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (0.023 mmol, 10 mol %) and ligand **L1** (0.023 mmol, 10 mol %) were mixed with HFIP (C = 0.2 M) before stirring at 70 °C for 2 h. (b) Reaction time 72 h. (c) Reaction time 24 h. (d) Reaction conditions modification: $\text{Fe}(\text{OAc})_2$ (10 mol %), ligand **L1** (10 mol %), diene substrate (2.5 eq) with ACN (C = 0.2 M), stirring at 70 °C for 18 h.

To demonstrate the robustness of this methodology, a 1 g scale experiment was conducted decreasing the catalyst loading to 5 mol %. The product **3a** was isolated with an excellent 80 % yield, after the reaction time was extended to 6 h to achieve a complete conversion (scheme 2). The side-products **4** and **4'** were also isolated in 13 % and 4 % yield respectively (scheme 2).¹⁸ Compound **4** could result from a formal [3 + 2] dipolar cycloaddition between the aziridine **A** and the styrene **2a** while **4'** could be formed by addition of the HFIP solvent onto an activated aziridine species.¹⁹

Scheme 2. Gram-scale experiment

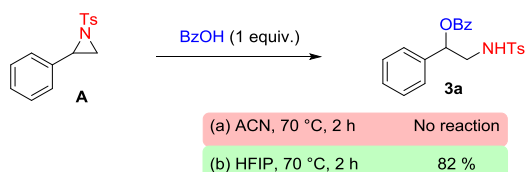
45 % and 44 % yield. The reactivity of enyne derivatives was then investigated. Gratifyingly, aryl functionalized compounds **3l**, **3m** and **3n** were produced with good results (71 %, 62 % and 68 % respectively, table 2-B). In contrast, alkyl enynes were poorly efficient in these conditions, the products **3o** and **3p**, which diverge from each other by the size of the alkyl chain, were isolated with 34 % and 31 % yield respectively after 24 h (table 2-B). Interestingly, the chemoselectivity for enynes was completely in favor of the double bond. Dienes also undergo a rather efficient oxyamination reaction, although the formation of product **3q**, bearing a phenyl ring and products **3r** and **3s** bearing 2-methoxy phenyl and 4-chloro phenyl substituents required a readjustment of the reaction conditions (table 2-C). A complete regioselectivity for the terminal alkene was observed in these examples. Finally, the 2,3-dimethyl butadiene substrate provided a mixture of the two regioisomers **3t** and **3t'** in a ratio 4:1 and a moderate 48 % yield (table 2-C). Aliphatic alkenes in contrast did not provide the oxyaminated product, the corresponding aziridines were obtained for the substrates tested.



The mechanism of the reaction was next investigated. Our initial hypothesized involvement of an aziridine intermediate was confirmed via three observations. During the gram scale experiment a complete conversion of the starting material **1a** to the corresponding aziridine **A** was observed after 2 hours of stirring (scheme 2). The formation of aziridine intermediates were also observed after 2 h for the 2-chloro and 3-chloro styrene reagents leading after a few more hours to the corre-

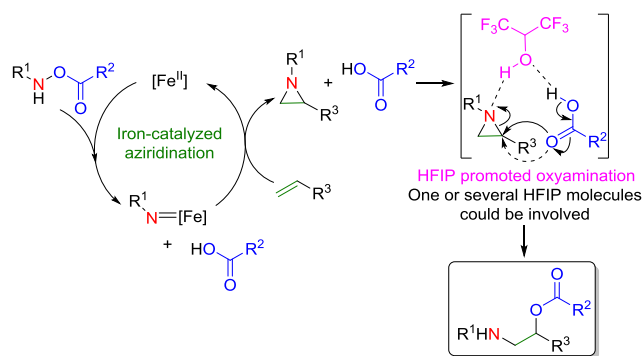
spending oxyaminated products **3d** and **3e** (see table 2-A). To confirm the role of HFIP in this transformation, aziridine ring opening experiments were next performed. Compound **A** in acetonitrile in the presence of 1 equivalent of benzoic acid did not give any further transformation, as already observed in our previous work (scheme 3-a).^{14b} In comparison, the reaction of the aziridine, in HFIP, with 1 equivalent of benzoic acid provided the product **3a** in 82 % yield (scheme 3-b).

Scheme 3. Aziridine ring opening reactions



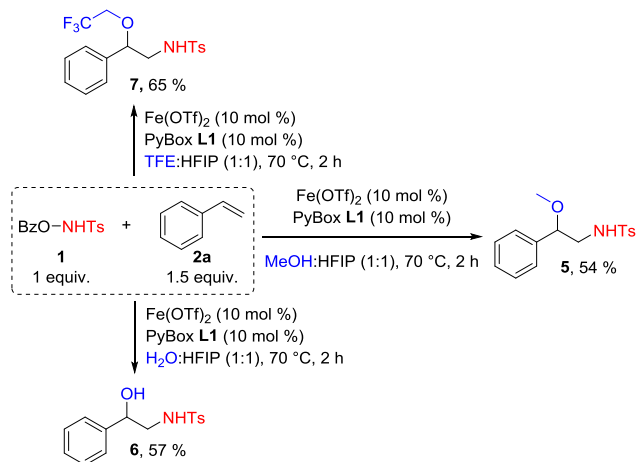
Therefore, the mechanism likely involves a stepwise process starting with the rapid iron-catalyzed aziridination, followed by the slow ring opening of the formed aziridine. The latter is induced by the released benzoic acid and mediated by the acidic HFIP (scheme 4). This solvent also has a strong influence in the kinetic of the reaction by accelerating the aziridination step compared to acetonitrile.^{14b} Our proposition of the proton-promoted aziridine ring-opening mechanism is supported by the work of Xie, Xu and Lu who reported a computational study to prove this type of pathway.²⁰

Scheme 4. Plausible mechanism



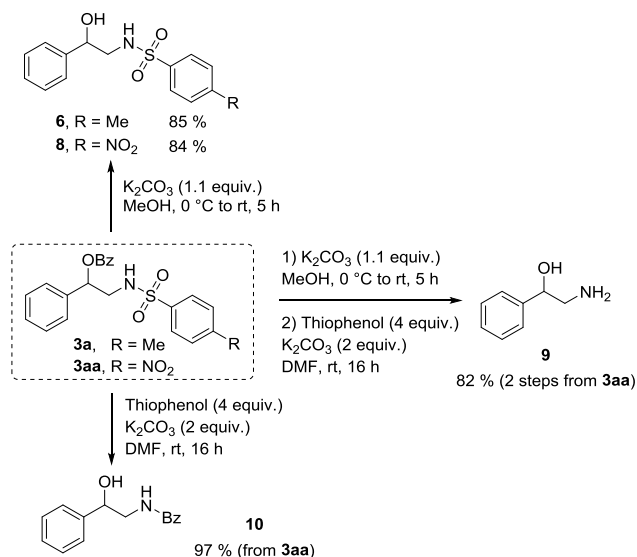
To further explore the scope of this transformation, the addition of nucleophilic co-solvents in a 1:1 mixture ratio with HFIP was evaluated using substrates **1a** and **2a**. Iron(II) sulfate heptahydrate appeared to be ineffective unlike iron(II) triflate which produced the targeted compounds smoothly. The addition of methanol and water yielded the formation of the amino ether **5** and the amino alcohol **6** in 54 % and 57 % respectively. Additionally, the amino trifluoroethyl ether **7** was isolated in 65 % yield with TFE as co-solvent (scheme 5).

Scheme 5. Addition of nucleophilic co-solvents



Post-functionalization reactions were next investigated. The selective cleavage of the ester moiety was easily realized on the *N*-tosyl and *N*-nosyl compounds **3a** and **3aa** in the presence of potassium carbonate in methanol, yielding the mono-protected amino alcohol products **6** and **8** in 85 % and 84 % respectively. The free hydroxyl amine **9** could be obtained with an excellent 82 % yield in two steps by first deprotection of the alcohol followed then by the cleavage of the sulfonamide group. Interestingly, the compound **3aa** could be transformed to the hydroxyl *N*-benzoyl product **10** in almost quantitative yield using thiophenol and potassium carbonate in DMF (scheme 6).

Scheme 6. Synthetic transformations



CONCLUSION

To conclude, we have developed a novel atom-economical oxyamination reaction mediated by iron complexes and HFIP using hydroxylamine derivatives as both the nitrogen and oxygen functional groups which are introduced. The process is fully regioselective and chemoselective towards terminal alkenes, yielding protected amino alcohols which could be easily isolated and then converted to the corresponding free

hydroxyl amine products. This process is complementary to the methods reported by the groups of Hao Xu and Bill Morandi and could be used as a convenient retrosynthetic disconnection in the field of multistep synthesis.

EXPERIMENTAL SECTION

General Information. All commercially available reagents were purchased from chemical suppliers. Styrene derivatives were used without further purification. Reactions were performed under an argon atmosphere. Anhydrous solvents were purchased from chemical suppliers and used without further purification. Analytical thin layer chromatography was performed on commercial silica gel plates 60F254. Flash column chromatography was performed on silica gel 60 (40–63 μm). NMR spectra were recorded on a 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (δ 0.00 ppm) or the CHCl_3 residual peak (δ 7.26) or the MeOH residual peak (δ 3.31) for ^1H NMR. Chemical shifts of $^{13}\text{C}\{^1\text{H}\}$ NMR are reported relative to CDCl_3 (δ 77.16) or CD_3OD (δ 49.00). Coupling constant (J) are reported in Hertz unit (Hz). Multiplicities are described with standard following abbreviations: s = singlet, br = broad, d = doublet, t = triplet, q = quadruplet, dd = doublet of doublet, dt = doublet of triplet, td = triplet of doublet, m = multiplet. High resolution mass spectra (HRMS) were recorded with a TOF mass analyzer under electrospray ionization (ESI) in positive or negative ionization mode detection, atmospheric pressure chemical ionization or atmospheric pressure photoionization (APPI). Melting points were measured on a K \ddot{o} fler bench or Buchi B-545 melting point apparatus. IR spectra were recorded on a FT-IR spectrophotometer, and the wavelengths reported in cm^{-1} .

General procedure A - Synthesis of enyne substrates 2l, 2m, 2n, 2o and 2p. (Styrene reagents 2a–2k and the dimethyl butadiene 2t are commercially available). In a round bottom flask, $\text{PdCl}_2(\text{PPh}_3)_2$ (42 mg, 0.06 mmol, 4 mol %), CuI (17 mg, 0.09 mmol, 6 mol %), PPh_3 (16 mg, 0.06 mmol, 4 mol %), NEt_3 (2.1 mL, 15 mmol, 10 equiv.), the desired phenyl acetylene (1.5 mmol, 1 equiv.), and vinylbromide (3 mL, 3 mmol, C = 1 M in THF, 2 equiv.) were placed successively in dry THF (7.5 mL, C = 0.2 M) under argon. The reaction was put in a PTFE coated aluminum heat block and stirred at 50 $^\circ\text{C}$ for 2 h. The solvent was then removed under reduced pressure and a saturated aqueous NH_4Cl solution was added to the resulting residue. The aqueous layer was then extracted with DCM (3 times). The combined organic phases were dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography using pure pentane as eluent to afford the corresponding product as a colorless oil.

General procedure B - Synthesis of diene substrates 2q, 2r and 2s. In a round bottom flask, methyltriphenylphosphonium bromide (1 equiv.) was suspended in anhydrous THF (C = 0.2 M) and cooled to -78 $^\circ\text{C}$. Then, $n\text{-BuLi}$ (1.6 M in THF, 1.5 equiv.) was added dropwise, and the mixture warmed to room temperature was stirred for 30 mn to give a clear orange-red solution. Trans-cinnamaldehyde (1.5 equiv.) was added in one portion and the mixture was stirred

for 18 h at room temperature. The reaction was then evaporated under reduced pressure without heating, and the crude residue was purified by silica gel flash column chromatography using pure pentane as eluent to afford the diene product as a colorless oil.

The enyne and diene substrates are all known compounds and the analytical data were in accordance with the literature.²¹

General procedure C - Iron-catalyzed oxyamination reaction. In a sealed tube were placed $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (6.45 mg, 0.023 mmol, 10 mol %) and PyBox ligand **L1** (6.34 mg, 0.023 mmol, 10 mol %) under argon in HFIP (1.15 mL, C = 0.2 M). The suspension was stirred at room temperature for 10 mn. Then, *N*-(benzoyloxy)-4-methylbenzenesulfonamide **1a** (67.6 mg, 0.23 mmol, 1 equiv.) was added to the solution followed by the desired alkene (0.35 mmol, 1.5 equiv.). The tube was immediately sealed and placed in an oil bath at 70 $^\circ\text{C}$ to stir for 2 h. The reaction was quenched with a saturated aqueous NaHCO_3 solution and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic phases were dried over MgSO_4 and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography using cyclohexane/ethyl acetate as eluent (from 100:0 to 80:20) to afford the corresponding oxyaminated products.

The following oxyaminated products were prepared using the general procedure C, deviation from these conditions are specified for each corresponding products.

2-((4-methylphenyl)sulfonamido)-1-phenylethyl benzoate **3a**. Known compound²²

White solid; m = 67.2 mg, 73 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 122–129 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 8.00 (d, J = 7.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.59–7.57 (m, 1H), 7.45–7.42 (m, 2H), 7.36–7.31 (m, 5H), 7.24–7.22 (m, 2H), 6.00–5.93 (m, 1H), 4.79 (br s, 1H), 3.56–3.43 (m, 2H), 2.39 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.7, 143.7, 137.1, 137.0, 133.5, 129.9, 129.8, 129.6, 129.0, 128.9, 128.6, 127.1, 126.5, 74.7, 48.0, 21.7; IR ($\nu = \text{cm}^{-1}$) 3674, 3335, 3067, 2972, 2903, 1713, 1600, 1271, 1155; HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 418.1084, found 418.1079.

2-((4-nitrophenyl)sulfonamido)-1-phenylethyl benzoate **3aa**. Known compound²²

Slightly yellow solid; (general procedure C on 0.62 mmol scale using the corresponding BzO-NHNs substrate) m = 107 mg, 40 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 134–136 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 8.16 (d, J = 8.5 Hz, 2H), 7.93 (t, J = 8.5 Hz, 4H), 7.61–7.54 (m, 1H), 7.41 (t, J = 8 Hz, 2H), 7.39–7.30 (m, 5H), 6.02 (t, J = 6 Hz, 1H), 5.16–5.08 (m, 1H), 3.62 (t, J = 6 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.7, 149.9, 146.1, 136.5, 133.8, 129.8, 129.1, 128.6, 128.1, 126.4, 124.5, 74.3, 48.4; IR ($\nu = \text{cm}^{-1}$) 3290, 3106, 2927, 1721, 1530, 1349, 1271, 1165; HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{17}\text{N}_2\text{O}_6\text{S}$ [$\text{M} - \text{H}^+$] 425.0802, found 425.0817.

1-(4-fluorophenyl)-2-((4-methylphenyl)sulfonamido)ethyl benzoate 3b.

Slightly yellow solid; m = 71.2 mg, 75 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 134-136 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 8.01-7.96 (m, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.61-7.56 (m, 1H), 7.47-7.42 (m, 2H), 7.32-7.28 (m, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.02 (t, *J* = 8.5 Hz, 2H), 5.93 (dd, *J* = 4.5 Hz, 7.5 Hz, 1H), 4.71 (t, *J* = 6.5 Hz, 1H), 3.54-3.41 (m, 2H), 2.40 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.6, 162.9 (d, *J* = 21.8 Hz), 143.8, 137.0, 133.6, 133.0 (d, *J* = 3.6 Hz), 129.9, 129.8, 129.5, 128.6, 128.4 (d, *J* = 8.2 Hz), 127.1, 116.0 (d, *J* = 21.8 Hz), 74.1, 48.0, 21.7; ¹⁹F{¹H} NMR (CDCl₃, 500 MHz, ppm) δ = -112.6; IR (ν = cm⁻¹) 3286, 2927, 2859, 1724, 1602, 1513, 1271, 1161; HRMS (ESI): m/z calcd for C₂₂H₂₀FNO₄SNa [M + Na⁺] 436.0989, found 436.0983.

1-(4-chlorophenyl)-2-((4-methylphenyl)sulfonamido)ethyl benzoate 3c. Known compound²²

White solid; m = 71.3 mg, 71 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 135-137 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.99 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.61-7.56 (m, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.31-7.28 (m, 2H), 7.25-7.21 (m, 4H), 5.93 (dd, *J* = 5 Hz, 7 Hz, 1H), 4.79 (t, *J* = 6.5 Hz, 1H), 3.54-3.42 (m, 2H), 2.40 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.5, 143.8, 136.9, 135.6, 134.8, 133.7, 129.9, 129.8, 129.4, 129.2, 128.6, 127.9, 127.1, 74.1, 47.9, 21.7; IR (ν = cm⁻¹) 3288, 2988, 1722, 1600, 1269, 1160, 1092; HRMS (ESI): m/z calcd for C₂₂H₁₉ClNO₄S [M - H⁺] 428.0719, found 428.0729.

1-(2-chlorophenyl)-2-((4-methylphenyl)sulfonamido)ethyl benzoate 3d.

Amorphous solid; (general procedure C after 72 h of reaction) m = 71.6 mg, 72 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 8.03 (d, *J* = 8 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.62-7.57 (m, 1H), 7.48-7.39 (m, 3H), 7.35-7.31 (m, 1H), 7.25-7.22 (m, 2H), 7.20 (d, *J* = 8 Hz, 2H), 6.31 (dd, *J* = 3.5 Hz, 8 Hz, 1H), 4.96 (t, *J* = 6.5 Hz, 1H), 3.62-3.55 (m, 1H), 3.51-3.44 (m, 1H), 2.37 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.4, 143.6, 137.1, 134.9, 133.6, 132.2, 130.0, 129.9, 129.8, 129.7, 129.4, 128.6, 127.4, 127.1, 71.8, 46.4, 21.7; IR (ν = cm⁻¹) 3286, 3065, 2986, 1725, 1600, 1269, 1160; HRMS (ESI): m/z calcd for C₂₂H₂₀ClNO₄SNa [M + Na⁺] 452.0694, found 452.0688.

1-(3-chlorophenyl)-2-((4-methylphenyl)sulfonamido)ethyl benzoate 3e.

White solid; (general procedure C after 72 h of reaction) m = 56.5 mg, 56 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 103-108 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.99 (d, *J* = 7.5 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.59-7.54 (m, 1H), 7.45-7.39 (m, 2H), 7.28-7.24 (m, 3H), 7.23-7.19 (m, 3H), 5.91 (dd, *J* = 4.5 Hz, 7.5 Hz, 1H), 5.28-5.10 (m, 1H), 3.52-3.38 (m, 2H), 2.38 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.5, 143.9, 139.2, 136.9, 134.9, 133.7, 130.3, 130.0, 129.9, 129.3, 129.1, 128.7, 127.1, 126.6, 124.8, 74.1, 47.9, 21.7; IR (ν = cm⁻¹) 3674, 3336, 2988, 2968, 2901, 1714, 1600, 1274, 1066; HRMS (ESI): m/z calcd for C₂₂H₂₀ClNO₄SNa [M + Na⁺] 452.0694, found 452.0688.

2-((4-methylphenyl)sulfonamido)-1-(naphthalen-2-yl)ethyl benzoate 3f. Known compound²²

White solid; m = 63 mg, 61 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 107-113 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 8.03 (d, *J* = 7 Hz, 2H), 7.83-7.77 (m, 3H), 7.76 (s, 1H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.61-7.57 (m, 1H), 7.51-7.48 (m, 2H), 7.47-7.39 (m, 3H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.12 (dd, *J* = 5 Hz, 7.5 Hz, 1H), 4.89-4.77 (br m, 1H), 3.67-3.52 (m, 2H), 2.36 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.7, 143.7, 137.0, 134.4, 133.5, 133.4, 133.1, 129.9, 129.8, 129.6, 129.0, 128.6, 128.2, 127.8, 127.1, 126.7, 126.1, 123.7, 74.9, 47.9, 21.7; IR (ν = cm⁻¹) 3273, 2928, 1721, 1600, 1272, 1154; HRMS (ESI): m/z calcd for C₂₆H₂₃NO₄SNa [M + Na⁺] 468.1240, found 468.1236.

2-((4-methylphenyl)sulfonamido)-1-(*o*-tolyl)ethyl benzoate 3g. Known compound²²

White solid; m = 67.8 mg, 71 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 119-126 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.99 (dd, *J* = 1 Hz, 8 Hz, 2H), 7.70 (d, *J* = 8 Hz, 2H), 7.59-7.54 (m, 1H), 7.42 (t, *J* = 8 Hz, 2H), 7.33-7.29 (m, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.20-7.12 (m, 3H), 6.14 (dd, *J* = 4 Hz, 8 Hz, 1H), 5.16-5.09 (m, 1H), 3.48-3.36 (m, 2H), 2.38 (s, 3H), 2.37 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.7, 143.7, 137.1, 135.6, 135.4, 133.4, 130.9, 129.9, 129.8, 129.6, 128.6, 128.5, 127.1, 126.6, 125.6, 72.1, 47.2, 21.6, 19.2; IR (ν = cm⁻¹) 3301, 2963, 2928, 1700, 1600, 1283, 1158; HRMS (ESI): m/z calcd for C₂₃H₂₃NO₄SNa [M + Na⁺] 432.1240, found 432.1234.

2-((4-methylphenyl)sulfonamido)-1-(*m*-tolyl)ethyl benzoate 3h.

White solid; m = 64.6 mg, 68 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 108-109 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.99 (dd, *J* = 1.5 Hz, 8 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.58-7.53 (m, 1H), 7.44-7.39 (m, 2H), 7.24-7.18 (m, 3H), 7.13-7.08 (m, 3H), 5.92 (dd, *J* = 4.5 Hz, 8 Hz, 1H), 5.23-5.06 (m, 1H), 3.55-3.39 (m, 2H), 2.38 (s, 3H), 2.31 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.6, 143.6, 138.6, 137.1, 137.0, 133.4, 129.8, 129.6, 129.5, 128.8, 128.5, 127.2, 127.1, 123.4, 74.8, 48.0, 21.6, 21.5; IR (ν = cm⁻¹) 3276, 2963, 2927, 1720, 1599, 1268, 1160; HRMS (ESI): m/z calcd for C₂₃H₂₃NO₄SNa [M + Na⁺] 432.1240, found 432.1236.

2-((4-methylphenyl)sulfonamido)-1-(*p*-tolyl)ethyl benzoate 3i. Known compound²²

Amorphous solid; m = 65.5 mg, 69 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.98 (d, *J* = 7.5 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.25-7.19 (m, 4H), 7.13 (d, *J* = 8 Hz, 2H), 5.91 (dd, *J* = 4.5 Hz, 8 Hz, 1H), 4.90 (br s, 1H), 3.57-3.39 (m, 2H), 2.38 (s, 3H), 2.32 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 165.7, 143.6, 138.7, 137.0, 134.1, 133.4, 129.9, 129.7, 129.6, 128.5, 127.1, 126.5, 74.7, 48.0, 21.7, 21.3; IR (ν = cm⁻¹) 3288, 3052, 2924, 1721, 1600, 1270, 1160; HRMS (ESI): m/z calcd for C₂₃H₂₃NO₄SNa [M + Na⁺] 432.1240, found 432.1229.

1-(3-methoxyphenyl)-2-((4-methylphenyl)sulfonamido)ethyl benzoate 3j.

Amorphous solid; m = 44 mg, 45 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 8.00 (dd, J = 1.5 Hz, 8 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 8 Hz, 2H), 7.28-7.20 (m, 3H), 6.90 (d, J = 7.5 Hz, 1H), 6.86-6.82 (m, 2H), 5.92 (dd, J = 4.5 Hz, 7 Hz, 1H), 4.71 (br s, 1H), 3.78 (s, 3H), 3.54-3.43 (m, 2H), 2.39 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.6, 160.1, 143.7, 138.7, 137.2, 133.5, 130.1, 129.9, 129.7, 128.6, 127.2, 118.7, 114.1, 112.4, 74.6, 55.4, 48.1, 21.6; IR ($\nu = \text{cm}^{-1}$) 3305, 3072, 2928, 1724, 1602, 1271, 1163; HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{23}\text{NO}_5\text{SNa}$ [$\text{M} + \text{Na}^+$] 448.1189, found 448.1193.

1-((4-methylphenyl)sulfonamido)-2-phenylpropan-2-yl benzoate 3k.

White solid; m = 42 mg, 44 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 147-157 °C; ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 7.98 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.45 (d, J = 8 Hz, 2H), 7.36-7.27 (m, 5H), 7.25 (d, J = 8 Hz, 2H), 4.86-4.79 (m, 1H), 3.50 (d, J = 6.5 Hz, 2H), 2.40 (s, 3H), 2.00 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.0, 143.6, 141.6, 137.1, 133.3, 130.6, 129.9, 129.8, 128.9, 128.6, 128.1, 127.1, 124.9, 83.2, 53.2, 23.1, 21.7; IR ($\nu = \text{cm}^{-1}$) 3274, 3087, 2971, 2913, 1724, 1599, 1153, 1089; HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{23}\text{NO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 432.1240, found 432.1230.

1-((4-methylphenyl)sulfonamido)-4-phenylbut-3-yn-2-yl benzoate 3l.

Yellow oil; m = 68.5 mg, 71 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 8.00 (dd, J = 1.5 Hz, 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H), 7.60-7.55 (m, 1H), 7.46-7.39 (m, 4H), 7.34-7.27 (m, 3H), 7.21 (d, J = 8.0 Hz, 2H), 5.79 (dd, J = 5 Hz, 6.5 Hz, 1H), 5.13 (t, J = 6.5 Hz, 1H), 3.61-3.51 (m, 2H), 2.36 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.3, 143.8, 137.1, 133.6, 132.1, 130.0, 129.9, 129.2, 128.5, 128.4, 127.1, 121.5, 87.3, 83.2, 63.7, 46.6, 21.7; IR ($\nu = \text{cm}^{-1}$) 3295, 3063, 2970, 2926, 2234, 1724, 1600, 1265, 1159, 1092; HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{21}\text{NO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 442.1084, found 442.1079.

4-(4-chlorophenyl)-1-((4-methylphenyl)sulfonamido)but-3-yn-2-yl benzoate 3m.

Yellow solid; m = 65.1 mg, 62 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 140-150 °C; ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 8.00 (dd, J = 1.5 Hz, 8.0 Hz, 2H), 7.75 (d, J = 8.5 Hz, 2H), 7.62-7.57 (m, 1H), 7.44 (d, J = 8 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8 Hz, 2H), 5.78 (dd, J = 4.5 Hz, 6.5 Hz, 1H), 5.01 (br s, 1H), 3.61-3.50 (m, 2H), 2.37 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.3, 143.9, 137.1, 135.4, 133.7, 133.4, 130.0, 129.9, 129.1, 128.8, 128.6, 127.1, 120.0, 86.2, 84.2, 63.6, 46.5, 21.7; IR ($\nu = \text{cm}^{-1}$) 3297, 2958, 2923, 1718, 1600, 1325, 1270, 1152; HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{20}\text{ClNO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 476.0694, found 476.0689.

1-((4-methylphenyl)sulfonamido)-4-(*p*-tolyl)but-3-yn-2-yl benzoate 3n.

Brown solid; m = 68.1 mg, 68 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 97-103 °C; ^1H NMR (CDCl_3 , 500 MHz,

ppm) δ = 8.0 (dd, J = 1.5 Hz, 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H), 7.61-7.57 (m, 1H), 7.44 (t, J = 8 Hz, 2H), 7.30 (d, J = 8 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8 Hz, 2H), 5.78 (dd, J = 4.5 Hz, 6.5 Hz, 1H), 4.93 (t, J = 6.5 Hz, 1H), 3.60-3.50 (m, 2H), 2.37 (s, 3H), 2.34 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.3, 143.8, 139.5, 137.1, 133.6, 132.0, 130.0, 129.9, 129.2, 128.6, 127.2, 118.4, 87.6, 82.5, 63.7, 46.7, 21.7; IR ($\nu = \text{cm}^{-1}$) 3306, 2963, 2927, 2235, 1723, 1702, 1326, 1268, 1158; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{23}\text{NO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 456.1240, found 456.1234.

1-((4-methylphenyl)sulfonamido)dec-3-yn-2-yl benzoate 3o.

Yellow solid; (general procedure C after 24 h of reaction) m = 33.7 mg, 34 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 69-70 °C; ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 7.95 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8 Hz, 2H), 7.60-7.55 (m, 1H), 7.43 (d, J = 8 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 5.55-5.51 (m, 1H), 4.92-4.85 (m, 1H), 3.48-3.37 (m, 2H), 2.38 (s, 3H), 2.17 (td, J = 1.5 Hz, 7.0 Hz, 2H), 1.51-1.43 (m, 2H), 1.36-1.22 (m, 6H), 0.87 (t, J = 7.0 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.4, 143.7, 137.1, 133.5, 130.0, 129.9, 129.4, 128.5, 127.1, 89.0, 74.5, 63.5, 46.8, 31.4, 28.6, 28.3, 22.6, 21.7, 18.8, 14.2; IR ($\nu = \text{cm}^{-1}$) 3674, 3334, 2993, 2971, 2901, 2228, 1705, 1600, 1273, 1165, 1092; HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 450.1710, found 450.1706.

1-((4-methylphenyl)sulfonamido)tetradec-3-yn-2-yl benzoate 3p.

Yellow oil; (general procedure C after 24 h of reaction) m = 34.8 mg, 31 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 7.96 (dd, J = 1 Hz, 8 Hz, 2H), 7.74 (d, J = 8.5 Hz, 2H), 7.60-7.55 (m, 1H), 7.43 (d, J = 8 Hz, 2H), 7.23 (d, J = 8 Hz, 2H), 5.56-5.51 (m, 1H), 4.84 (t, J = 6.5 Hz, 1H), 3.49-3.37 (m, 2H), 2.38 (s, 3H), 2.17 (td, J = 2.0 Hz, 7 Hz, 2H), 1.51-1.44 (m, 2H), 1.36-1.25 (m, 14H), 0.88 (t, J = 7.0 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.4, 143.7, 137.1, 133.5, 130.0, 129.9, 129.4, 128.5, 127.1, 89.0, 74.4, 63.5, 46.8, 32.0, 29.7, 29.6, 29.5, 29.2, 29.0, 28.4, 22.8, 21.7, 18.8, 14.3; IR ($\nu = \text{cm}^{-1}$) 3674, 3286, 2988, 2971, 2925, 2901, 2241, 1727, 1601, 1265, 1163, 1067; HRMS (ESI): m/z calcd for $\text{C}_{28}\text{H}_{37}\text{NO}_4\text{SNa}$ [$\text{M} + \text{Na}^+$] 506.2336, found 506, 2333.

(*E*)-1-((4-methylphenyl)sulfonamido)-4-phenylbut-3-en-2-yl benzoate 3q.

Amorphous solid; (general procedure C on 0.2 mmol scale, reaction conditions modification: $\text{Fe}(\text{OAc})_2$ (10 mol %), **L1** (10 mol %), diene substrate (2.5 equiv.) in ACN ($\text{C} = 0.2 \text{ M}$), stirring at 70 °C for 18 h) m = 55.4 mg, 66 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); ^1H NMR (CDCl_3 , 500 MHz, ppm) δ = 8.00-7.97 (m, 2H), 7.73 (d, J = 8.5 Hz, 2H), 7.60-7.55 (m, 1H), 7.43 (t, J = 8 Hz, 2H), 7.35-7.27 (m, 5H), 7.21 (d, J = 8 Hz, 2H), 6.68 (d, J = 15.5 Hz, 1H), 6.11 (dd, J = 7.0 Hz, 16.0 Hz, 1H), 5.68-5.62 (m, 1H), 5.02-4.95 (m, 1H), 3.41 (t, J = 6 Hz, 2H), 2.37 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 126 MHz, ppm) δ = 165.7, 143.7, 136.9, 135.7, 134.9, 133.5, 129.9, 129.8, 129.7, 128.7, 128.5, 127.1, 126.9, 123.6, 73.5, 46.5, 21.7; IR ($\nu = \text{cm}^{-1}$) 3322, 2969, 2926, 2901, 1715, 1695, 1600, 1326,

1263, 1157, 1070; HRMS (ESI): m/z calcd for $C_{24}H_{22}NO_4S$ [$M - H^+$] 420.1264, found 420.1287.

(E)-4-(2-methoxyphenyl)-1-((4-methylphenyl)sulfonamido)but-3-en-2-yl benzoate 3r.

White solid; (general procedure C on 0.2 mmol scale, reaction conditions modification: $Fe(OAc)_2$ (10 mol %), **L1** (10 mol %), diene substrate (2.5 equiv.) in ACN ($C = 0.2$ M), stirring at 70 °C for 18 h) $m = 56$ mg, 62 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 108-119 °C; 1H NMR ($CDCl_3$, 500 MHz, ppm) $\delta = 7.98$ (dd, $J = 1.5$ Hz, 8 Hz, 2H), 7.73 (d, $J = 8.5$ Hz, 2H), 7.60-7.54 (m, 1H), 7.42 (t, $J = 8$ Hz, 2H), 7.34 (dd, $J = 1.5$ Hz, 8 Hz, 1H), 7.26-7.22 (m, 1H), 7.20 (d, $J = 8.5$ Hz, 2H), 6.99 (d, $J = 16.0$ Hz, 1H), 6.90 (t, $J = 7.5$ Hz, 1H), 6.85 (d, $J = 8$ Hz, 1H), 6.16 (dd, $J = 7.0$ Hz, 16.0 Hz, 1H), 5.66-5.60 (m, 1H), 5.02-4.92 (m, 1H), 3.83 (s, 3H), 3.41 (t, $J = 6.0$ Hz, 2H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz, ppm) $\delta = 165.8$, 157.1, 143.6, 137.0, 133.3, 130.1, 129.9, 129.6, 128.5, 127.5, 127.1, 124.6, 124.2, 120.7, 110.9, 74.0, 55.5, 46.7, 21.6; IR ($\nu = cm^{-1}$) 3675, 3297, 2988, 2970, 2925, 2901, 1716, 1697, 1597, 1324, 1252, 1153, 1067; HRMS (ESI): m/z calcd for $C_{25}H_{24}NO_5S$ [$M - H^+$] 450.1370, found 450.1390.

(E)-4-(4-chlorophenyl)-1-((4-methylphenyl)sulfonamido)but-3-en-2-yl benzoate 3s.

Yellow solid; (general procedure C on 0.2 mmol scale, reaction conditions modification: $Fe(OAc)_2$ (10 mol %), **L1** (10 mol %), diene substrate (2.5 equiv.) in ACN ($C = 0.2$ M), stirring at 70 °C for 18 h) $m = 49.7$ mg, 55 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 141-150 °C; 1H NMR ($CDCl_3$, 500 MHz, ppm) $\delta = 8.01$ -7.97 (m, 2H), 7.73 (d, $J = 8.5$ Hz, 2H), 7.61-7.56 (m, 1H), 7.44 (t, $J = 8$ Hz, 2H), 7.27-7.25 (m, 4H), 7.23 (d, $J = 8$ Hz, 2H), 6.64 (d, $J = 16$ Hz, 1H), 6.10 (dd, $J = 7.0$ Hz, 16.0 Hz, 1H), 5.67-5.61 (m, 1H), 4.94 (t, $J = 6.5$ Hz, 1H), 3.44-3.37 (m, 2H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz, ppm) $\delta = 165.6$, 143.8, 136.9, 134.2, 133.6, 130.0, 129.8, 129.6, 128.9, 128.6, 128.1, 127.1, 124.4, 73.3, 46.5, 21.7; IR ($\nu = cm^{-1}$) 3324, 3042, 2927, 2854, 1711, 1600, 1319, 1271, 1148, 1094; HRMS (ESI): m/z calcd for $C_{24}H_{21}ClNO_4S$ [$M - H^+$] 454.0874, found 454.0896.

2,3-dimethyl-1-((4-methylphenyl)sulfonamido)but-3-en-2-yl benzoate (major) 3t and (E)-2,3-dimethyl-4-((4-methylphenyl)sulfonamido)but-2-en-1-yl benzoate (minor) 3t'.

Colorless oil; $m = 41.2$ mg, 48 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20), ratio (major:minor) = 4:1; 1H NMR ($CDCl_3$, 500 MHz, ppm) $\delta = 8.03$ -8.00 (m, 0.5H, minor), 7.95-7.90 (m, 2H, major), 7.78 (d, $J = 8.5$ Hz, 0.5H, minor), 7.74 (d, $J = 8$ Hz, 2H, major), 7.59-7.53 (m, 1H, major), 7.46 (d, $J = 8$ Hz, 0.5H, minor), 7.42 (t, $J = 8$ Hz, 2H, major), 7.30-7.24 (m, 3H), 5.03 (s, 1H, major), 5.01 (s, 1H, major), 4.97 (t, $J = 6.5$ Hz, 1H, major), 4.68 (s, 0.5H, minor), 3.62 (d, $J = 6.5$ Hz, 0.5H, minor), 3.40 (dd, $J = 6$ Hz, 13 Hz, 1H, major), 3.32 (dd, $J = 7$ Hz, 13 Hz, 1H, major), 2.41 (s, 0.8H, minor), 2.40 (s, 3H, major), 1.75-1.69 (m, 7.6H, minor + major); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz, ppm) $\delta = 166.8$, 165.1, 144.4, 143.6, 143.4, 137.0, 133.3, 133.2, 130.9, 130.5, 129.9, 129.8, 129.7, 128.6, 128.5, 127.3, 127.1, 113.4, 84.1, 65.3, 49.7, 45.5, 21.9, 21.7, 19.1, 17.9, 17.0; IR ($\nu = cm^{-1}$) 3288, 2987, 1718, 1600, 1317,

1278, 1161, 1093; HRMS (ESI): m/z calcd for $C_{20}H_{23}NO_4SNa$ [$M + Na^+$] 396.1240, found 396.1230.

Procedure for the gram scale iron-catalyzed oxyamination

reaction. In a sealed tube were placed $FeSO_4 \cdot 7H_2O$ (47.7 mg, 0.17 mmol, 5 mol %) and PyBox ligand **L1** (47 mg, 0.17 mmol, 5 mol %) under argon in HFIP (17.2 mL, $C = 0.2$ M). The suspension was stirred at room temperature for 10 mn. Then, *N*-(benzoyloxy)-4-methylbenzenesulfonamide **1a** (1 g, 3.43 mmol, 1 equiv.) was added to the solution followed by styrene **2a** (0.590 mL, 5.15 mmol, 1.5 equiv.). The tube was immediately sealed and placed in an oil bath at 70 °C to stir for 6 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution and the aqueous phase was extracted with DCM (3 times). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography using cyclohexane/ethyl acetate as eluent (from 100:0 to 80:20) to afford 2-(4-methylbenzenesulfonamido)-1-phenylethyl benzoate **3a** (1.09 g, 80 %) as a white solid.

2,4-diphenyl-1-tosylpyrrolidine 4. Known compound²³

Colourless oil; $m = 169.8$ mg, 13 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20), ratio (anti:syn) ~ 4:6; 1H NMR ($CDCl_3$, 500 MHz, ppm) $\delta = 7.73$ (d, $J = 8$ Hz, 1.4H, anti), 7.64 (d, $J = 8$ Hz, 2H, syn), 7.42-7.20 (m, 18H, mixture of syn and anti), 7.14-7.11 (m, 2H, syn), 7.04-7.01 (m, 1.4H, anti), 5.05 (d, $J = 8$ Hz, 0.7H, anti), 4.81 (dd, $J = 7$ Hz, 10.0 Hz, 1H, syn), 4.19-4.13 (m, 1H, syn), 4.03 (dd, $J = 7.5$ Hz, 9.5 Hz, 0.7H, anti), 3.52 (t, $J = 11.5$ Hz, 1H, syn), 3.50-3.42 (m, 0.7H, anti), 3.32-3.25 (m, 0.7H, anti), 2.99-2.90 (m, 1H, syn), 2.71-2.64 (m, 1H, syn), 2.45 (s, 2H, anti), 2.43 (s, 3H, syn), 2.17 (dd, $J = 6.5$ Hz, 12 Hz, 0.7H, anti), 2.12-2.01 (m, 1.8H, mixture of syn and anti); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz, ppm) $\delta =$ (mixture of syn and anti) 143.7, 143.5, 143.0, 142.6, 139.6, 139.1, 135.7, 134.7, 129.8, 129.7, 128.8, 128.7, 128.6, 128.5, 127.7, 127.6, 127.5, 127.3, 127.2, 127.1, 127.1, 126.5, 126.2, 126.1, 64.6, 63.1, 56.0, 55.2, 44.5, 43.8, 42.2, 41.5, 21.7; IR ($\nu = cm^{-1}$) 3309, 2972, 1599, 1162; HRMS (ESI): m/z calcd for $C_{23}H_{23}NO_2SNa$ [$M + Na^+$] 400.1342, found 400.1330.

***N*-(2-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-2-phenylethyl)-4-methylbenzenesulfonamide 4'.**

Colourless oil; $m = 57.5$ mg, 4 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); 1H NMR ($CDCl_3$, 500 MHz, ppm) $\delta = 7.73$ (d, $J = 8.5$ Hz, 2H), 7.42-7.37 (m, 3H), 7.32 (d, $J = 8$ Hz, 2H), 7.25-7.22 (m, 2H), 4.81 (dd, $J = 5$ Hz, 8.5 Hz, 1H), 4.76 (dd, $J = 4.5$ Hz, 8.5 Hz, 1H), 3.97 (sept, $J = 5.5$ Hz, 1H), 3.35-3.24 (m, 2H), 2.44 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz, ppm) $\delta = 143.9$, 136.9, 134.6, 130.1, 130.0, 129.3, 127.8, 127.2, 84.0, 72.9 (sep, $J = 32$ Hz), 48.6, 21.7; IR ($\nu = cm^{-1}$) 3673, 3289, 3071, 2987, 1599, 1287, 1221, 1194, 1162, 1103; HRMS (ESI): m/z calcd for $C_{18}H_{16}F_6NO_3S$ [$M - H^+$] 440.0750, found 440.0764.

General procedure D - Addition of nucleophilic co-

solvents. In a sealed tube were placed $Fe(OTf)_2$ (8.21 mg, 0.023 mmol, 10 mol %) and PyBox ligand **L1** (6.34 mg, 0.023 mmol, 10 mol %) under argon in a mixture of HFIP and the desired co-solvent (1.15 mL, $C = 0.2$ M, 1:1 ratio). The suspension was stirred at room temperature for 10 mn. Then, *N*-

(benzoyloxy)-4-methylbenzenesulfonamide **1a** (67.6 mg, 0.23 mmol, 1 equiv.) was added to the solution followed by styrene **2a** (40 μ L, 0.35 mmol, 1.5 equiv.). The tube was immediately sealed and placed in an oil bath at 70 °C to stir for 2 h. The reaction was quenched with a saturated aqueous NaHCO₃ solution and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography using cyclohexane/ethyl acetate as eluent (from 100:0 to 50:50) to afford the corresponding products.

The products **5**, **6** and **7** were prepared using the general procedure **D**.

***N*-(2-methoxy-2-phenylethyl)-4-methylbenzenesulfonamide **5**.** Known compound²⁴

Amorphous solid; m = 38.6 mg, 54 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 70:30); ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.72 (d, *J* = 8.5 Hz, 2H), 7.35-7.28 (m, 5H), 7.21-7.18 (m, 2H), 5.05-4.97 (m, 1H), 4.20 (dd, *J* = 3.5 Hz, 9.5 Hz, 1H), 3.24-3.18 (m, 1H), 3.17 (s, 3H), 2.98-2.91 (m, 1H), 2.42 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 143.6, 138.3, 137.0, 129.9, 129.0, 128.5, 127.2, 126.7, 82.1, 56.9, 49.5, 21.7; IR (ν = cm⁻¹) 3288, 3057, 2931, 2827, 1599, 1330, 1161, 1090; HRMS (ESI): m/z calcd for C₁₆H₁₉NO₃Na [M + Na⁺] 328.0978, found 328.0969.

***N*-(2-hydroxy-2-phenylethyl)-4-methylbenzenesulfonamide **6**.** Known compound²⁵

White solid; m = 38.3 mg, 57 % Yield from general procedure **D**; 85 % Yield from the deprotection procedure (a) (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 50:50); m.p. 113-120 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.73 (d, *J* = 8.5 Hz, 2H), 7.36-7.27 (m, 7H), 4.95 (dd, *J* = 4.5 Hz, 8.5 Hz, 1H), 4.80 (dt, *J* = 3.5 Hz, 9 Hz, 1H), 3.29-3.21 (m, 1H), 3.06-2.99 (m, 1H), 2.47-2.42 (m, 1H), 2.42 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 143.8, 140.9, 136.8, 129.9, 128.8, 128.4, 127.2, 125.9, 72.9, 50.3, 21.7; IR (ν = cm⁻¹) 3336, 3066, 2928, 1712, 1600, 1323, 1270, 1154, 1093; HRMS (ESI): m/z calcd for C₁₅H₁₆NO₃S [M - H⁻] 290.0845, found 290.0861.

***4*-methyl-*N*-(2-phenyl-2-(2,2,2-trifluoroethoxy)ethyl)benzenesulfonamide **7**.**

White solid; m = 56.4 mg, 65 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 80:20); m.p. 76-80 °C; ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.73 (d, *J* = 8 Hz, 2H), 7.40-7.33 (m, 3H), 7.31 (d, *J* = 8 Hz, 2H), 7.24-7.19 (m, 2H), 5.00-4.83 (m, 1H), 4.46 (dd, *J* = 3.5 Hz, 9 Hz, 1H), 3.71-3.61 (m, 1H), 3.60-3.51 (m, 1H), 3.30-3.22 (m, 1H), 3.15-3.06 (m, 1H), 2.43 (s, 3H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 143.8, 137.1, 136.6, 129.9, 129.3, 129.2, 127.2, 126.8, 123.7 (q, *J* = 276.5 Hz), 82.1, 66.0 (q, *J* = 34.25 Hz), 49.2, 21.7; ¹⁹F{¹H} NMR (CDCl₃, 500 MHz, ppm) δ = -73.9; IR (ν = cm⁻¹) 3290, 3033, 2933, 1599, 1331, 1280, 1161, 1129, 1093; HRMS (ESI): m/z calcd for C₁₇H₁₇F₃NO₃S [M - H⁻] 372.0876, found 372.0888.

Deprotection procedures.

(a) Removal of the benzoyl group: In a round bottom flask was placed compound **3a** or **3aa** (1 equiv.) under argon in

MeOH (C = 0.08 M). The solution was cooled at 0 °C then K₂CO₃ (1.1 equiv.) was added in one portion. The suspension was stirred at 0 °C for 4 h. The reaction was quenched with a saturated aqueous NH₄Cl solution and the aqueous phase was extracted with DCM (3 times). The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography using cyclohexane/ethyl acetate as eluent to afford the pure alcohol as a white solid.

(b) Removal of the sulfonamide group: In a round bottom flask was placed compound **8** (60 mg, 0.19 mmol, 1 equiv.) under argon in DMF (0.93 mL, C = 0.2 M). Then, thiophenol (76 μ L, 0.74 mmol, 4 equiv.) and K₂CO₃ (51.5 mg, 0.37 mmol, 2 equiv.) were successively added. The suspension was stirred at room temperature for 16 h. The crude residue was directly loaded and purified by silica gel flash column chromatography using ethyl acetate/MeOH as eluent to afford the pure amino alcohol **9** (25 mg, 98 % yield), as a white solid.

(c) Preparation of alcohol **10**: In a round bottom flask was placed compound **3aa** (75 mg, 0.18 mmol, 1 equiv.) under argon in DMF (0.94 mL, C = 0.2 M). Then, thiophenol (72 μ L, 0.70 mmol, 4 equiv.) and K₂CO₃ (48.6 mg, 0.35 mmol, 2 equiv.) were successively added. The suspension was stirred at room temperature for 16 h. The crude residue was directly loaded and purified by silica gel flash column chromatography using ethyl acetate/MeOH as eluent to afford the pure amino alcohol **10** (41 mg, 97 % yield), as a white solid.

***N*-(2-hydroxy-2-phenylethyl)-4-nitrobenzenesulfonamide **8**.** Known compound²²

White solid; (deprotection procedure (a)) m = 60 mg, 84 % Yield (purified by silica gel flash column chromatography, cyclohexane/ethyl acetate as eluent = 50:50); ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 8.33 (d, *J* = 9 Hz, 2H), 8.00 (d, *J* = 9.0 Hz, 2H), 7.37-7.26 (m, 5H), 5.19 (br s, 1H), 4.85 (dd, *J* = 4 Hz, 8.5 Hz, 1H), 3.40-3.33 (m, 1H), 3.15-3.06 (m, 1H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 150.2, 145.9, 140.5, 129.0, 128.8, 128.4, 125.9, 124.6, 72.9, 50.2.

***2*-amino-1-phenylethanol **9**.** Known compound²⁶

White solid; (deprotection procedure (a) then (b)) m = 25 mg, 82 % Yield from **3aa**; 98 % Yield from **8** (purified by silica gel flash column chromatography, ethyl acetate/methanol as eluent = 90:10); ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.32-7.13 (m, 5H), 4.78 (d, *J* = 6 Hz, 1H), 4.45 (br s, 3H), 3.06-2.92 (m, 1H), 2.91-2.77 (m, 1H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 141.8, 128.5, 127.8, 126.0, 72.7, 48.2.

***N*-(2-hydroxy-2-phenylethyl)benzamide **10**.** Known compound²²

White solid; (deprotection procedure (c)) m = 41 mg, 97 % Yield (purified by silica gel flash column chromatography, ethyl acetate/methanol as eluent = 80:20); ¹H NMR (CDCl₃, 500 MHz, ppm) δ = 7.75 (d, *J* = 7.5 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.45-7.39 (m, 4H), 7.37 (t, *J* = 8 Hz, 2H), 7.33-7.28 (m, 1H), 6.59 (br s, 1H), 4.97 (dd, *J* = 3.5 Hz, 7.5 Hz, 1H), 3.97-3.88 (m, 1H), 3.57-3.49 (m, 1H), 3.30 (br s, 1H); ¹³C{¹H} NMR (CDCl₃, 126 MHz, ppm) δ = 168.9, 141.9, 134.1, 131.9, 128.8, 128.1, 127.1, 126.0, 74.0, 48.0.

ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/>

Experimental details for the preparation of **L1**, TsNHOBz and NsNHOBz substrates; complementary table of optimization; characterization data for compounds **1a**, **2l** to **2p**; copies of ^1H , $^{13}\text{C}\{^1\text{H}\}$ NMR for products **3a** to **3t'**, **5**, **6**, **7**, **8**, **9** and **10**; copy of $^{19}\text{F}\{^1\text{H}\}$ NMR for product **7**.

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