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Direct Sulfonamidation of Primary and Secondary Benzylic Alcohols Catalyzed by a Boronic Acid/Oxalic Acid System

Tristan Verdelet,[a] Robert M. Ward,[a] and Dennis G. Hall*[a]

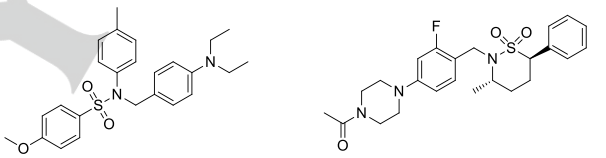
Abstract: The direct sulfonamidation of primary and secondary benzylic aclohols catalyzed by a 1,2,3,4-tetrafluorophenylboronic acid/oxalic acid co-catalytic system has been examined. The reaction proceeds under mild conditions with readily available starting materials and has been shown to be gram-scalable without significant decrease of yield. Both primary and secondary benzylic alcohols were evaluated and afforded the desired sulfonamide products with good to excellent yields.

Introduction

Sulfonamides and their derivatives are versatile compounds that can be used in various areas of organic and medicinal chemistry. In organic synthesis, they are often employed as amine protecting groups[1] or as reaction intermediates.[2] In medicinal chemistry, they have been found to possess interesting properties over a broad variety of diseases and as a consequence, many important drugs contain a sulfonamide unit.[3] In particular, N-benzyl sulfonamides are a sub-class of sulfonamides that are commonly employed in drug discovery[4] (Figure 1).

A common general way to access sulfonamides is the nucleophilic reaction between an amine and a sulfonyl halide partner.[5] The toxicity of the starting materials and the need for a stoichiometric quantity of a base render this process less attractive on the point of view of atom-economy and safety. Consequently, other routes have been widely investigated.[6] Among these alternatives, N-alkylation of sulfonamides with benzylic alcohols has gained great attention from the organic chemistry community.[7-11] A notable advantage of this approach is that alcohols are broadly available from commercial sources. In an ideal reaction design, the alcohol would be activated by a reusable catalyst, avoiding a pre-activation step, and the only by-product would be a molecule of water. During the last decade, considerable efforts have been committed to hydrogen autotransfer[8] or relay race[9] strategies for the preparation of sulfonamides. These elegant approaches, however often suffer from the need for expensive catalysts and high reaction temperatures. Several procedures based on Lewis[10] and Brønsted[11] acid activation of benzylic alcohols have also been reported for the synthesis of N-benzylsulfonamides, however the substrate scope of these methodologies is often quite limited.

Boronic acid catalysis[12] (BAC) has emerged as a promising tool for the mild activation and transformation of carboxylic acids,[13] alcohols[14] and carbonyls.[15] In a practical point of view, arylboronic acid catalysts exhibit many advantages: they are usually stable to air and moisture, possess a relatively low toxicity, are compatible with a broad range of chemical functionalities and their properties can be easily tuned via the introduction or replacement of substituents on the aryl moiety. Besides, arylboronic acids are now broadly commercially available at a moderate cost. Herein, by exploiting BAC, we developed a new carbon-nitrogen bond forming process starting from readily available benzylic alcohols and sulfonamides.



Cannabinoid receptor 2 inverse agonist[4a]

Retinoic acid receptor-related orphan receptor C inverse agonist[4b]

Figure 1. Benzylic sulfonamides in drug discovery.

Results and Discussion

Our reaction optimization study is shown in Table 1. 4-Bromobenzyl alcohol **1** and *para*-toluene sulfonamide **2** were used as model substrates for the catalytic sulfonamidation of benzylic alcohols. A relatively short reaction time of one hour was employed in order to obtain a more accurate comparison of the efficiency of different reaction conditions. We started the evaluation of boronic acids with tetrafluoroboronic acid **BA1** because it was previously reported as an efficient catalyst for the activation of allylic and benzylic alcohols in Friedel-Crafts reactions.[14g] When **BA1** (10 mol%) was employed as catalyst with one equivalent of *para*-toluene sulfonamide, only trace quantity of the desired sulfonamide product **3a** was obtained after one hour at 80 °C in a 4:1 mixture of hexafluoroisopropanol (HFIP) and nitromethane (entry 1). Intrigued by the work of Moran and co-workers concerning the crucial effect of oxalic acid as an additive in boronic acid catalyzed Friedel-Crafts reactions,[16] we examined its use in our model reaction. We were pleased to observe the formation of the desired product with a yield of 42% when both **BA1** and oxalic acid were employed

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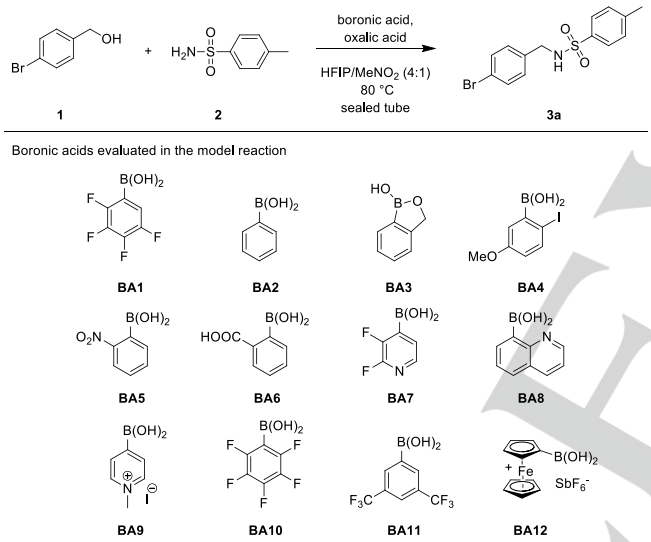
(entry 2). The use of two equivalents of **2** led to an improved yield of 65% of product **3a** (entry 3). As expected, the absence of the boronic acid partner only provided trace amount of product (entry 4). After these initial results, we turned our attention to the arylboronic acid component of this catalytic system (entries 5 to 14). Phenylboronic acid **BA2** and benzoxaborole **BA3** were found to be less efficient than **BA1**, with only 28% and 11% yield, respectively (entries 5 and 6). Use of 2-iodo-5-methoxyphenylboronic acid **BA4**, a known amidation catalyst,[13j,k] resulted in 35% of desired product **3a** (entry 7). Electron poor arylboronic acids **BA5** and **BA6**, bearing respectively a nitro group and a carboxylic acid at the ortho position of the arylboronic acid, did not demonstrate much activity for this transformation (entries 8 and 9). Hetero-arylboronic acids **BA7**, **BA8** and **BA9** were also evaluated but did not afford satisfactory results (entries 10 to 12). Finally, polyfluorinated arylboronic acids **BA10** and **BA11** provided similar results to **BA1** with respective yields of 64 and 62% (entries 13 and 14).



Scheme 1. Reaction model used for the optimization study (top) and list of boronic acids evaluated (bottom).

Having found optimal boronic acid partners, a panel of different additives bearing carboxylic acids and/or alcohol functions were evaluated. This study confirmed that oxalic acid is the best co-catalyst (see SI). Any changes in the solvent system or in the HFIP/$MeNO_2$ ratio were found to be detrimental to the product yield (see SI). In order to probe the effect of water, an experiment was conducted in the presence of molecular sieves (entry 15). A complete inhibition of the reaction was observed in these conditions, suggesting that water may play a crucial role in this sulfonamidation reaction by preventing off-cycle dehydration of the boronic acid into inactive boronic anhydrides. A cautious analysis of the crude NMR spectra of the reaction (entry 2) revealed the presence of a small proportion of the dibenzylated sulfonamide product **3aa** (see SI for structure) resulting from the reaction of **3a** with **1**. To disfavor this undesired side reaction, the number of molar equivalents of *para*-toluene sulfonamide was increased from two to five. This modification led to an improved isolated yield after six hours of reaction, from 69 to 82% (entry 16). Depending on specific substrates used, it may be possible to fine tune reaction conditions and decrease the relative stoichiometry of the sulfonamide partner.

Table 1. Optimization study of the direct sulfonamidation reaction of **1** and **2** (Scheme 1).[a]

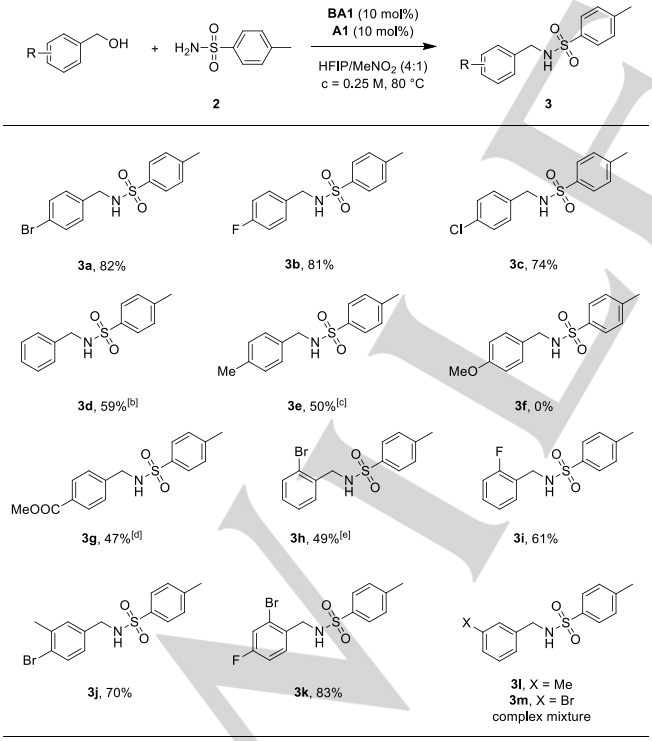
Entry	Boronic acid	Eq. of $TsNH_2$	NMR yield of **3a** (%)
1	BA1	1	trace[b]
2	BA1	1	42
3	BA1	2	65
4	-	2	trace
5	BA2	2	28
6	BA3	2	16
7	BA4	2	35
8	BA5	2	11
9	BA6	2	trace
10	BA7	2	15
11	BA8	2	trace
12	BA9	2	trace
13	BA10	2	64
14	BA11	2	62
15	BA1	2	trace[c]
16	BA1	5	82[d] [e]

[a] Reaction conditions: 0.50 mmol of *para*-bromobenzyl alcohol, *para*-toluene sulfonamide, 0.05 mmol of catalyst and 0.05 mmol of oxalic acid dihydrate were stirred in a mixture of HFIP and nitromethane (4:1, 1.0 mL) at 80 °C in a sealed tube for 1 hour and the crude product was analyzed by ^1H NMR with *para*-dinitrobenzene as an internal standard. [b] Without oxalic acid dihydrate. [c] With 500 mg of M.S. 4Å. [d] Isolated yield after a reaction time of 6 hours. [e] 2.0 mL of solvent.

With the optimal conditions in hand, we investigated the scope of the direct sulfonamidation of benzylic alcohols, starting with various primary alcohols (Scheme 2). As indicated above, para-bromobenzyl alcohol resulted in the formation of the desired sulfonamide **3a** with a good yield of 82%. The corresponding chloro- and fluoro- derivatives also provided good reactivity with 81 and 74% yield, respectively. Benzyl alcohol afforded product **3d** with a moderate yield of 59%. Although a

complete conversion of the starting material was observed, it is likely that more nucleophilic arenes like benzyl alcohol can undergo a Friedel-Crafts self-reaction competing with the desired sulfonamidation. Consequently, it was not surprising to observe a moderate yield of 50% of product **3e** when para-methylbenzyl alcohol was subjected to the reaction conditions. Likewise, no trace of desired product was observed with the para-methoxy substrate **3f**. For the latter, the ^{1}H NMR spectrum of the crude product revealed a complete polymerization of the starting material. With electron poor methyl-4-(hydroxymethyl)benzoate, a very low conversion was observed when the optimal conditions were applied. However, by using harsher reaction conditions and a 20 mol% catalyst loading of the recently described ferrocenium boronic acid[14h,i] **BA12** (see Scheme 1) with oxalic acid, a moderate yield of 47% of **3g** was obtained. Ortho-bromobenzyl alcohol provided 49% of the desired benzylsulfonamide **3h** while its fluoro analog afforded 61% of product **3i**. We were pleased to observe the formation of products **3j** and **3k** from the corresponding disubstituted benzylic alcohols, with 70 and 80% yield, respectively. These halogenated products are useful toward further derivatization by cross-coupling chemistry. Unfortunately, methyl- and bromo-*meta*-monosubstituted benzyl alcohols **3l** and **3m** failed to provide a clean reaction with the expected products.

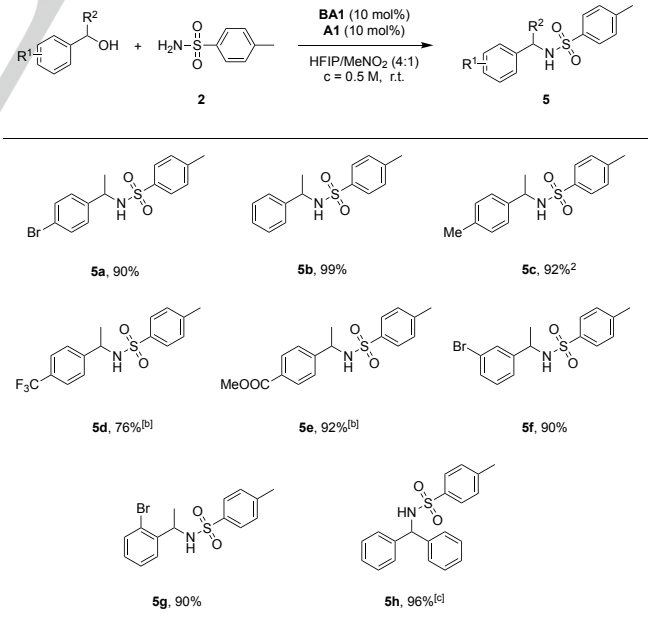
Table 2. Substrate scope for primary benzylic alcohols (isolated yields).[a]



[a] Reaction conditions : 0.50 mmol of benzylic alcohol, 2.50 mmol of *para*-toluene sulfonamide **2**, 0.05 mmol of tetrafluorophenylboronic acid **BA1** and 0.05 mmol of oxalic acid dihydrate **A1** were stirred in a mixture of HFIP and nitromethane (4:1, 2.0 mL) at 80 °C in a sealed tube for 6 hours. [b] Reaction time of 3 hours. [c] Reaction performed at 50°C for 3 hours. [d] 20 mol% of **BA12** and oxalic acid dihydrate **A1**, 100 °C for 24 h. [e] Reaction time of 24 hours. **BA12**: ferroceniumboronic acid hexafluoroantimonate.

The direct sulfonamidation of secondary benzylic alcohols was studied next (Table 3). 1-(4-Bromophenyl)ethanol was successfully transformed into sulfonamide **5a** after 3 hours at room temperature with an excellent yield of 90%. 1-Phenylethanol gave the desired sulfonamide **5b** with a near quantitative yield. In contrast with the primary benzylic alcohol series, electronically enriched 1-(p-tolyl)ethanol led to an excellent yield of 92% of product **5c** after a reaction time of only 10 minutes. In the case of electron poor arenes, an examination of the crude product by ^{1}H NMR spectroscopy showed the presence of remaining starting material after 24 hours at room temperature, consequently the temperature was set at 50 °C for those substrates. With these slightly modified conditions, 1-(4-(trifluoromethyl)phenyl)ethanol afforded the desired sulfonamide **5d** with a satisfying yield of 76% and methyl 4-(1-hydroxyethyl)benzoate provided an excellent yield of 92% of product **5e**. As shown with the high isolated yield of products **5f** and **5g**, the position of a bromide substituent had little influence on the reaction. Finally, an excellent yield of 96% of product **5h** was obtained from diphenylmethanol after a reaction time of just a few minutes.

Table 3. Substrate scope of secondary benzylic alcohols (isolated yields).[a]

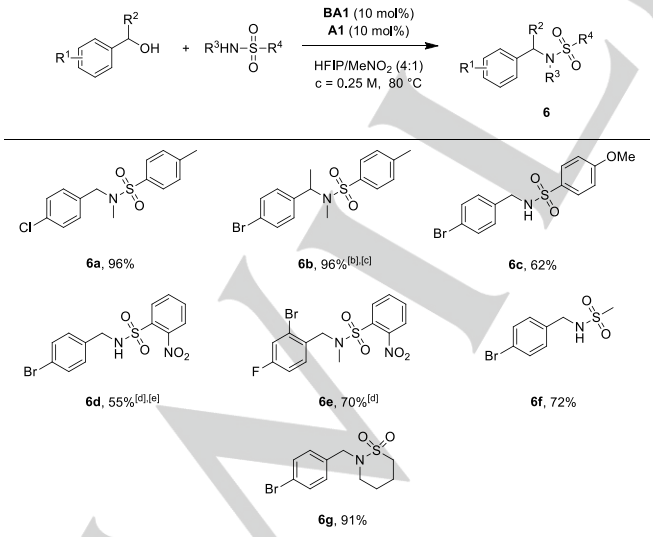


[a] Reaction conditions : 0.50 mmol of benzylic alcohol, 2.50 mmol of *para*-toluene sulfonamide **2**, 0.05 mmol of tetrafluorophenylboronic acid **BA1** and 0.05 mmol of oxalic acid dihydrate **A1** were stirred in a mixture of HFIP and nitromethane (4:1, 1.0 mL) at room temperature until complete conversion of

the starting benzylic alcohol (monitored by TLC). [b] Reaction performed at 50 °C. [c] 2 mL of a (4:1) HFIP/nitromethane mixture.

A variety of different sulfonamide nucleophiles were evaluated in the direct sulfonamidation of benzylic alcohols. First, N-methylated-*para*-toluenesulfonamide was reacted with 4-chlorobenzyl alcohol to furnish **6a** with an excellent yield of 96%. A similar yield was obtained when 1-(4-bromophenyl)ethanol was engaged with the same sulfonamide nucleophile. The electron rich para-methoxy-benzenesulfonamide afforded a moderate yield of 62% when reacted with **1**. Because of the convenience of its removal, the *o*-nosyl group is a widely used protecting group for primary and secondary amines. The Fukuyama amine synthesis[2] is a well established method for amination of alcohols, however, it suffers from the drawbacks of low atom economy associated with the Mitsunobu reaction. Consequently, we attempted the reaction of 2-nitrobenzenesulfonamide with primary benzylic alcohol **1**. Although harsher reaction conditions were needed due to the presence of a nitro group that decreases the nucleophilicity of the sulfonamide nitrogen, we were pleased to isolate 55% of desired product **6d** after 24 hours at 100 °C and with 20% co-catalysts loading. Likewise, a good yield of 70% of product **6e** was obtained when N-methyl-2-nitrobenzenesulfonamide was reacted with (2-bromo-4-fluorophenyl)methanol for 24 hours with the standard reaction conditions. Disappointing results were observed when the reactions between secondary benzyl alcohols with nosylamines were investigated. In contrast, alkyl sulfonamides provided excellent yields of 72% and 91% of **6f** and **6g**, respectively, when subjected to the reaction with benzylic alcohol **1**.

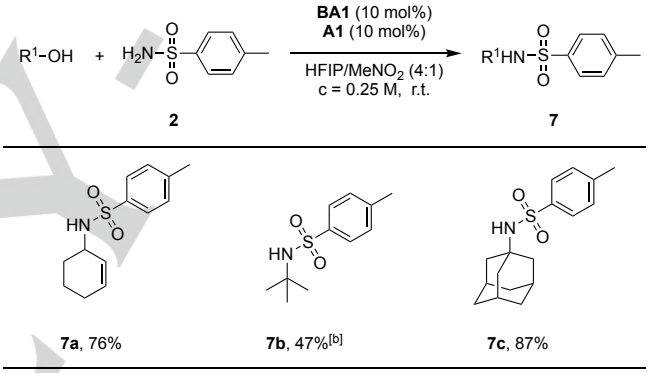
Table 4. Substrate scope of sulfonamide reagents (isolated yields).[a]



[a] Reaction conditions : 0.50 mmol of benzylic alcohol, 2.50 mmol of sulfonamide, 0.05 mmol of tetrafluorophenylboronic acid **BA1** and 0.05 mmol of oxalic acid dihydrate **A1** were stirred in a mixture of HFIP and nitromethane (4:1, 2.0 mL) at 80 °C in a sealed tube for 6 hours. [b] 2 mL of a (4:1) HFIP/nitromethane mixture were used. [c] Reaction performed at room temperature. [d] Reaction time of 24 hours. [e] Reaction performed at 100 °C, 20 mol% of **BA1** and oxalic acid dihydrate **A1**.

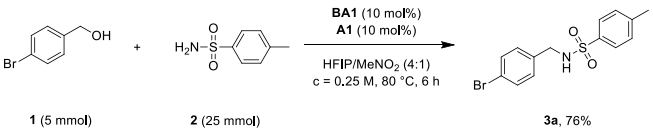
In order to demonstrate that our catalytic system is suitable with alcohol substrates other than benzylic alcohols, hexen-1-ol, *iso*-butanol and 1-adamantanol, were subjected to the reaction conditions with *para*-toluenesulfonamide **2**. Satisfactorily, all three alcohols afforded the corresponding sulfonamide products **7a**, **7b** and **7c** with 76%, 47% and 87% yield, respectively. The successful isolation of products **7b** and **7c** is remarkable because the corresponding tertiary alcohol substrates cannot form π-stabilized carbocations.

Table 5. Versatility of the direct sulfonamidation reaction (isolated yields).[a]



[a] Reaction conditions : 0.50 mmol of alcohol, 2.50 mmol of sulfonamide, 0.05 mmol of tetrafluorophenylboronic acid **BA1** and 0.05 mmol of oxalic acid dihydrate **A1** were stirred in a mixture of HFIP and nitromethane (4:1, 2.0 mL) at room temperature until complete conversion of the starting material (monitored by TLC).[b] 1 mL of a (4:1) HFIP/nitromethane mixture were used.

To further assess the versatility of this sulfonamidation method, a gram-scale experiment was conducted starting with 5 mmol (935 mg) of **1**. We were pleased to obtain a 76% yield of desired product **3a** similar to that obtained when the reaction was performed on a 0.5 mmol scale (82%). Remarkably, the unreacted tosylamine **2** was almost quantitatively recovered during the flash chromatographic purification and could thus be re-used.



Scheme 1. Gram scale experiment.

As described before,[14g] this BAC system is thought to be conducive to an S_N1 mechanism involving carbocationic intermediates. This proposal is supported by the reactions of secondary alcohols (cf. Table 3), which are more facile and higher yielding compared to the reactions of primary alcohols. Moreover, sulfonamide partners of sufficient nucleophilicity are required in order to avoid side-reactions such as the 'self' Friedel-Crafts condensation between the transient benzylic carbocation and the arene unit of the benzylic alcohol substrate.

Conclusions

In summary, we developed a catalytic method to effect the direct transformation of primary and secondary benzylic alcohols into various sulfonamide products using a mixture of 2,3,4,5-tetrafluorophenylboronic acid and oxalic acid as a co-catalytic system. The reaction proceeds under mild conditions with acceptable to excellent yields using relatively benign starting materials. We showed that the reaction is gram-scalable and the excess of sulfonamide reagent can be recovered after purification. Furthermore, we demonstrated that this catalytic system can potentially be used with other alcohol substrates like allylic or tertiary alcohols.

Experimental Section

The following materials include representative experimental procedures and details for the synthesis and isolation of products. Full characterization of all new compounds and partial characterization of known compounds presented in the article are described. Unless otherwise stated, all reactions were performed in capped regular glassware with no further precautions. Tetrahydrofuran (THF) and dichloromethane (DCM) were purified using a cartridge solvent purification system prior to use. Acetone was dried with magnesium sulfate before use. All other solvents were purchased as ACS reagents and used without further purification. Unless otherwise noted, all other chemicals were purchased from commercial sources and used as received. Chromatographic separations were performed on silica gel 60 using ACS grade hexanes, ethyl acetate, dichloromethane, diethylether and toluene as eluents. Thin layer chromatography (TLC) was performed on silica gel 60 F254 plates, which were visualized under UV light and with $KMnO_4$ or phosphomolybdic acid (PMA) stains. ^1H NMR and ^{13}C NMR spectra were recorded on 400 MHz or 500 MHz instruments. The residual solvent protons (^1H / $CHCl_3$) or the solvent carbon (^{13}C) were used as internal references. ^1H NMR data is presented as follows: chemical shifts in ppm downfield from tetramethylsilane (multiplicity, coupling constant, integration). The following abbreviations are used in reporting NMR data: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; quin, quintet; dd, doublet of doublets; ddd, doublet of doublet of doublets; td, triplet of doublets; m, multiplet. The error of coupling constants from high-field ^1H NMR spectra is estimated to be 0.3 Hz. High-resolution mass spectra were recorded on a oaTOF analyzer. Infrared (IR) spectra frequencies are expressed in cm^{-1}. The resolution of the IR instrument is 4 wavenumber.

General procedure A for the catalytic sulfonamidation of primary benzylic alcohols: Without any other specification, the reaction conditions for the direct catalytic sulfonamidation of primary benzylic alcohols were the following ones. Benzylic alcohol derivative (0.50 mmol), *para*-toluenesulfonamide (430 mg, 2.50 mmol), 2,3,4,5-tetrafluorophenylboronic acid **BA1** (10.0 mg, 0.050 mmol) and oxalic acid dihydrate (6.3 mg, 0.050 mmol) were added to a mixture of HFIP (1.60 mL) and nitromethane (0.40 mL) in a sealed tube equipped with a magnetic stirring bar. The temperature was set to 80 °C and the reaction media was stirred at this temperature for 6 hours. The mixture was then allowed to cool down at room temperature and the solvent was evaporated. The crude product was purified by flash chromatography on silica gel using a solid deposit technique (silica).

N-(4-Bromobenzyl)-4-methylbenzenesulfonamide (3a).[10f] The title compound was prepared from (4-bromophenyl)methanol (94 mg) following the general procedure A and was purified with a hexane/DCM (25:75) eluent to afford an amorphous white solid. 140 mg (82%). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.74-7.71 (m, 2 H), 7.40-7.37 (m, 2 H), 7.30-7.28 (m, 2H), 7.08-7.06 (m, 2 H), 4.84 (t, *J* = 5.0 Hz, 1 H), 4.07 (d, *J* = 5.0 Hz, 2 H), 2.46 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 143.8, 137.0, 135.5, 131.9, 129.9, 129.7, 127.3, 122.0, 46.8, 21.7 ppm.

N-(4-Fluorobenzyl)-4-methylbenzenesulfonamide (3b).[10f] The title compound was prepared from (4-fluorophenyl)methanol (64 mg) following the general procedure A and was purified with a hexane/DCM (25:75) eluent to afford an amorphous white solid. 103 mg (74%). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.74-7.72 (m, 2 H), 7.29-7.28 (m, 2 H), 7.18-7.15 (m, 2 H), 6.95-6.91 (m, 2 H), 5.27 (t, *J* = 6.3 Hz, 1 H), 4.08 (d, *J* = 6.3 Hz, 2 H), 2.44 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 162.4 (J_{C-F} = 246.0 Hz), 143.6, 136.9, 132.3, 129.8, 129.7 (J_{C-F} = 7.5 Hz), 127.2, 115.5 (J_{C-F} = 21.0 Hz), 46.6, 21.6 ppm.

N-(4-Chlorobenzyl)-4-methylbenzenesulfonamide (3c).[10f] The title compound was prepared from (4-chlorophenyl)methanol (71 mg) following the general procedure A and was purified with a hexane/DCM (25:75) eluent to afford an amorphous white solid. 121 mg (82%). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.74-7.72 (m, 2 H), 7.30-7.28 (m, 2 H), 7.23-7.21 (m, 2 H), 7.14-7.12 (m, 2 H), 5.11 (t, *J* = 6.4 Hz, 1 H), 4.09 (d, *J* = 6.3 Hz, 2 H), 2.44 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.8, 136.9, 135.0, 133.8, 129.9, 129.3, 128.9, 127.2, 46.6, 21.6 ppm.

N-Benzyl-4-methylbenzenesulfonamide (3d).[10f] The title compound was prepared from benzyl alcohol (54 mg) following the general procedure A with a reaction time of 3 hours and was purified with a hexane/DCM (25:75) eluent to afford an amorphous white solid. 77 mg (59%). ^1H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.80-7.77 (m, 2 H), 7.34-7.32 (m, 2 H), 7.30-7.27 (m, 3 H), 7.23-7.21 (m, 2 H), 7.72 (t, *J* = 6.2 Hz, 1 H), 4.14 (d, *J* = 6.2 Hz, 2 H), 2.46 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 143.5, 136.9, 136.3, 129.8, 128.7, 127.9, 127.9, 127.2 47.3, 21.6 ppm.

4-Methyl-N-(4-methylbenzyl)benzenesulfonamide (3e).[10f] The title compound was prepared from p-tolylmethanol (61 mg) following the general procedure A. The temperature of the reaction was set to 50 °C with a reaction time of 3 hours. The crude product was purified with a hexane/DCM (25:75) eluent to afford an amorphous white solid. 69 mg (50%). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.77-7.74 (m, 2 H), 7.30-7.28 (m, 2 H), 7.07 (m, 4 H), 4.84 (t, *J* = 6.0 Hz, 1 H), 4.08 (d, *J* = 6.4 Hz, 2 H) 2.45 (s, 3 H), 2.42 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.4, 137.6, 136.9, 133.3, 129.7, 129.3, 127.9, 127.2, 47.0, 21.5, 21.1 ppm.

N-(2-Bromobenzyl)-4-methylbenzenesulfonamide (3h).[17] The title compound was prepared from (2-bromophenyl)methanol (94 mg) following the general procedure A with a reaction time of 24 hours, and was purified with a hexane/DCM (25:75) eluent to afford a viscous oil. 83 mg (47%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.72-7.70 (m, 2 H), 7.47-7.45 (m, 1 H), 7.31-7.29 (m, 1 H), 7.26-7.24 (m, 2 H), 7.23-7.20 (m, 1 H), 7.13-7.09 (m, 1 H), 4.92 (t, *J* = 6.6 Hz, 1 H), 4.24 (d, *J* = 6.3 Hz, 2 H), 2.41 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.4, 136.9, 135.6, 132.7, 130.4, 129.6, 129.4, 127.7, 127.1, 123.4, 47.4, 21.5 ppm.

N-(2-fluorobenzyl)-4-methylbenzenesulfonamide (3i). The title compound was prepared from (2-fluorophenyl)methanol (64 mg) following the general procedure A and was purified with an hexane/DCM (35:65) eluent to afford a white amorphous solid. 85 mg (61%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.75-7.73 (m, 2 H), 7.28-7.22 (m, 4 H), 7.08-7.05 (m, 1 H), 6.99-6.96 (m, 1 H), 4.81 (t, *J* = 5.0 Hz, 1 H), 4.22 (d, *J* = 5.0 Hz, 2 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 160.7 ($J_{C\text{-}F}$ = 246.6 Hz), 143.4, 136.9, 130.1, 129.6, 129.6, 127.1, 124.7, 123.6 ($J_{C\text{-}F}$ = 14.5 Hz), 115.3 ($J_{C\text{-}F}$ = 21.1 Hz), 41.2, 21.5 ppm; IR (solid) 3253, 1493, 1419, 1346, 1238, 1162, 804, 760 cm^{-1}; HRMS [M–H]$^-$ calcd for $C_{14}H_{13}FNO_2S$ 278.0657, found 278.0652.

N-(4-Bromo-3-methylbenzyl)-4-methylbenzenesulfonamide (3j). The title compound was prepared from (4-bromo-3-methylphenyl)methanol (101 mg) following the general procedure A and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 124 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.74-7.71 (m, 2 H), 7.40 (d, J = 8.1 Hz, 1 H), 7.30-7.27 (m, 2 H), 7.03 (d, *J* = 2.1 Hz, 1 H), 6.87 (dd, *J* = 8.1, 2.1 Hz, 1 H), 5.06 (t, *J* = 6.2 Hz, 1 H), 4.05 (d, *J* = 6.2 Hz, 2 H), 2.45 (s, 3 H), 2.30 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.6, 138.1, 136.9, 135.6, 132.5, 130.3, 129.7, 127.1, 126.8, 124.2, 46.6, 22.7, 21.5 ppm; IR (cast film, DCM) 3254, 1597, 1444, 1318, 1155, 1090, 1027, 815 cm^{-1}; HRMS (ESI) [M+Na]$^+$ calcd for $C_{15}H_{16}BrNNaO_2S$ 375.9983, found 375.9979.

N-(2-Bromo-4-fluorobenzyl)-4-methylbenzenesulfonamide (3k). The title compound was prepared from (2-bromo-4-fluorophenyl)methanol (102 mg) following the general procedure A and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 149 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.73-7.70 (m, 2 H), 7.31 (dd, *J* = 8.7, 5.9 Hz, 1 H), 7.28-7.26 (m, 2 H), 7.21 (dd, *J* = 7.9, 2.3 Hz, 1 H), 6.94 (ddd, *J* = 8.5, 8.0, 2.6 Hz, 1 H), 5.09 (t, *J* = 6.6 Hz, 1 H), 4.21 (d, *J* = 6.6 Hz, 2 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 161.9 ($J_{C\text{-}F}$ = 251.6 Hz), 143.6, 136.9, 131.6 ($J_{C\text{-}F}$ = 3.7 Hz), 131.5 ($J_{C\text{-}F}$ = 8.6 Hz), 129.6, 127.1, 123.5 ($J_{C\text{-}F}$ = 9.6 Hz), 120.0 ($J_{C\text{-}F}$ = 24.6 Hz), 114.7 ($J_{C\text{-}F}$ = 21.0 Hz), 46.7, 21.5 ppm; IR (neat) 3263, 1592, 1482, 1325, 1230, 1159, 1053, 778 cm^{-1}; HRMS (ESI) [M+Na]$^+$ calcd for $C_{14}H_{13}BrFNNaO_2S$ 379.9732, found 379.9731.

Methyl 4-((4-methylphenylsulfonamido)methyl)benzoate (3g).[8p] Methyl 4-(hydroxymethyl)benzoate (83 mg, 0.50 mmol), *para*-toluenesulfonamide (430 mg, 2.50 mmol), ferroceniumboronic acid hexafluoroantimonate salt **BA12** (47 mg, 0.10 mmol) and oxalic acid dihydrate (12.6 mg, 0.10 mmol) were added to a mixture of HFIP (1.60 mL) and nitromethane (0.40 mL) in a sealed tube equipped with a magnetic stirring bar. The temperature was set to 100 °C and the reaction media was stirred at this temperature for 24 hours. The mixture was then allowed to cool down to room temperature and the solvent was evaporated. The crude product was purified by flash chromatography on silica gel using a solid deposit technique (silica) and with a cyclohexane/EtOAc (90:10 to 80:20) eluent to afford the title compound as an amorphous white solid. 75 mg (47%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.95-7.93 (m, 2 H), 7.76-7.74 (m, 2 H), 7.31-7.27 (m, 4 H), 4.82 (t, *J* = 6.2 Hz, 1 H), 4.19 (d, *J* = 6.5 Hz, 2 H), 3.90 (s, 3 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 166.7, 143.8, 141.5, 136.8, 130.0, 129.8, 129.7, 127.7, 127.2, 77.3, 77.2, 77.0, 76.8, 52.2, 46.9, 21.6 ppm.

General procedure B for the catalytic sulfonamidation of secondary benzylic alcohols: without any other specification, the reaction conditions for the direct catalytic sulfonamidation of secondary benzylic alcohols were the following ones. benzylic alcohol derivative (0.50 mmol), *para*-toluenesulfonamide (430 mg, 2.50 mmol), 2,3,4,5-tetrafluorophenylboronic acid **BA1** (10.0 mg, 0.050 mmol) and oxalic acid dihydrate (6.3 mg, 0.050 mmol) were added to a mixture of HFIP (0.8 mL) and nitromethane (0.2 mL) in a sealed tube equipped with a magnetic stirring bar. The reaction media was stirred at room temperature until complete conversion of the starting material (monitored by TLC). The solvent was then evaporated and the crude product was purified by flash chromatography on silica gel using a solid deposit technique (silica).

N-(1-(4-Bromophenyl)ethyl)-4-methylbenzenesulfonamide (**5a**).[18] The title compound was prepared from 1-(4-bromophenyl)ethanol (102 mg) following the general procedure B and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 160 mg (90%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.55-7.54 (m, 2 H), 7.28-7.26 (m, 2 H), 7.16-7.15 (m, 2 H), 6.96-6.93 (m, 2 H), 4.85 (d, *J* = 6.9 Hz, 1 H), 4.41 (app quin, *J* = 6.9 Hz, 1 H), 2.38 (s, 3H), 1.36 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 143.4, 141.0, 137.5, 131.5, 129.5 127.9, 127.1, 121.3, 53.1, 23.4, 21.5 ppm.

4-Methyl-N-(1-phenylethyl)benzenesulfonamide (**5b**).[18] The title compound was prepared from 1-phenylethanol (61 mg) following the general procedure B and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 137 mg (99%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.64-7.60 (m, 2 H), 7.20-7.16 (m, 5 H), 7.11-7.09 (m, 2 H), 4.96 (d, *J* = 7.0 Hz, 1 H), 4.46 (app quin, *J* = 6.9 Hz, 1 H), 2.38 (s, 3 H), 1.42 (d, *J* = 6.9 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.1, 142.0, 137.7, 129.4, 128.5, 127.4, 127.1, 126.1, 53.6, 23.5, 21.5 ppm.

4-Methyl-N-(1-(p-tolyl)ethyl)benzenesulfonamide (**5c**).[19] The title compound was prepared from 1-(p-tolyl)ethanol (68 mg) following the general procedure B with a 2 mL mixture of HFIP and nitromethane (4:1) as solvent. The crude product was then purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 133 mg (92%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.64-7.62 (m, 2 H), 7.20-7.17 (m, 2 H), 7.02-6.97 (m, 2 H), 4.91 (d, *J* = 6.9 Hz, 1 H), 4.41 (app quin, *J* = 6.9 Hz, 1 H), 1.41 (d, *J* = 6.8 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.0, 139.1, 137.7, 137.2, 129.4, 129.2, 127.1, 126.0, 53.4, 23.5, 21.5, 21.0 ppm.

4-Methyl-N-(1-(4-(trifluoromethyl)phenyl)ethyl)benzenesulfonamide (**5d**).[20] The title compound was prepared from 1-(4-(trifluoromethyl)phenyl)ethanol (95 mg) following the general procedure B with a reaction temperature set to 50°C. The crude product was then purified with a gradient of hexane/DCM eluent (from 50:50 to 25:75) to afford an amorphous white solid. 131 mg (76%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.55-7.53 (m, 2 H), 7.40-7.38 (m, 2 H), 7.21-7.19 (m, 2H), 7.12-7.11 (m, 2 H), 5.31 (d, *J* = 7.0 Hz, 1 H), 4.54 (app quin, *J* = 7.0 Hz, 1 H), 2.36 (s, 3 H), 1.42 (d, *J* = 6.9 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 145.9, 143.4, 137.3, 129.6 ($J_{C\text{-}F}$ = 32.8 Hz), 129.4, 127.0, 126.6, 125.3 ($J_{C\text{-}F}$ = 4.0 Hz), 124.0 ($J_{C\text{-}F}$ = 272.2 Hz), 53.3, 23.5, 21.3 ppm.

Methyl 4-(1-(4-methylphenylsulfonamido)ethyl)benzoate (**5e**). The title compound was prepared from methyl 4-(1-hydroxyethyl)benzoate (90 mg) following the general procedure B with a reaction temperature set to 50°C. The crude product was then purified with a hexane/EtOAc eluent (80:20) to afford an amorphous white solid. 153 mg (92%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.83-7.79 (m, 2 H), 7.60-7.57 (m, 2 H), 7.19-7.16 (m, 2 H), 7.13-7.11 (m, 2 H), 5.67 (d, *J* = 7.4 Hz, 1 H), 4.49 (app quin, *J* = 7.0 Hz, 1 H), 3.88 (s, 3 H), 2.34 (s, 3 H), 1.38 (d, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 166.8, 147.3, 143.3, 137.5, 129.8, 129.5, 129.1, 127.0, 126.2, 53.4, 52.1, 23.5, 21.4 ppm; IR (neat) 3252, 1721, 1432, 1322, 1285, 1153, 1115, 1083 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd for $C_{17}H_{19}NNaO_4S$ 356.0932, found 356.0925.

N-(1-(3-Bromophenyl)ethyl)-4-methylbenzenesulfonamide (**5f**). The title compound was prepared from 1-(3-bromophenyl)ethanol (102 mg) following the general procedure B and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 161 mg (90%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.58-7.56 (m, 2 H), 7.29-7.26 (m, 1 H), 7.18-7.17 (m, 2 H), 7.10 (app s, 1 H), 7.06-7.06 (m, 2 H), 4.84 (d, *J* = 6.9 Hz, 1 H), 4.45 (app quin, *J* = 6.9 Hz, 1 H), 2.39 (s, 3 H), 1.40 (d, *J* = 6.9 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 144.2, 143.4, 137.3, 130.4, 130.0, 129.5, 129.4, 127.0, 124.9, 122.5, 53.2, 23.5, 21.5 ppm; IR (cast film, DCM) 3273, 1597, 1433, 1325, 1160, 1091, 813, 666 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd for $C_{15}H_{16}BrNNaO_2S$ 375.9983, found 375.9974.

N-(1-(2-Bromophenyl)ethyl)-4-methylbenzenesulfonamide (**5g**). The title compound was prepared from 1-(2-bromophenyl)ethanol (102 mg) following the general procedure B and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 159 mg (90%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.65-7.64 (m, 2 H), 7.37 (dd, *J* = 8.0, 1.3 Hz, 1 H), 7.24 (dd, *J* = 7.8, 1.7 Hz, 1 H), 7.14-7.12 (m, 2 H), 7.10 (dd, *J* = 7.6, 1.3 Hz, 1 H), 6.98 (td, *J* = 7.6, 1.7 Hz, 1 H), 5.72 (d, *J* = 7.4 Hz, 1 H), 4.88 (app quin, *J* = 7.0 Hz, 1 H), 2.34 (s, 3 H), 1.38 (d, *J* = 6.9 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 143.2, 141.3, 137.1, 132.8, 129.4, 128.5, 127.8, 127.7, 127.1, 122.0, 53.0, 23.0, 21.5 ppm. IR (cast film, DCM) 3279, 1444, 1324, 1161, 1092, 1024, 958, 756 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd for $C_{15}H_{16}BrNNaO_2S$ 375.9983, found 375.9972.

N-Benzhydryl-4-methylbenzenesulfonamide (**5h**).[10f] The title compound was prepared from diphenylmethanol (benzhydrol) (92 mg) following the general procedure B with 2 mL of a HFIP/nitromethane (4:1) solvent. It was then purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 163 mg (96%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.58-7.55 (m, 2 H), 7.22-7.19 (m, 6 H), 7.14-7.09 (m, 6 H), 5.57 (d, *J* = 7.0 Hz, 1 H), 5.10 (d, *J* = 7.1 Hz, 1 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.2, 140.5, 137.4, 129.4, 128.5, 127.6, 127.4, 127.2, 61.3, 21.5 ppm.

General procedure C for the catalytic sulfonamidation of benzyl alcohols with various sulfonamides: Without any other specification, the reaction conditions for the direct catalytic sulfonamidation of benzylic alcohols were the following ones. Benzylic alcohol derivative (0.50 mmol), sulfonamides (2.50 mmol), 2,3,4,5-tetrafluorophenylboronic acid **BA1** (10.0 mg, 0.050 mmol) and oxalic acid dihydrate (6.3 mg, 0.050 mmol) were added to a mixture of HFIP (1.6 mL) and nitromethane (0.4 mL) in a sealed tube equipped with a magnetic stirring bar. The reaction media was stirred at 80 °C for 6 hours. The solvent was then evaporated and the crude product was purified by flash chromatography on silica gel using a solid deposit technique (silica).

N-(4-Chlorobenzyl)-N,4-dimethylbenzenesulfonamide (6a).[21] The title compound was prepared from (4-chlorophenyl)methanol (71 mg) and N,4-dimethylbenzenesulfonamide (465 mg) following the general procedure C and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 148 mg (96%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.73-7.70 (m, 2 H), 7.36-7.34 (m, 2 H), 7.31-7.28 (m, 2 H), 7.26-7.23 (m, 2 H), 4.09 (s, 1 H), 2.57 (s, 1 H), 2.45 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.6, 134.3, 134.2, 133.7, 129.8, 129.7, 128.8, 127.5, 53.5, 34.4, 21.6 ppm.

N-(1-(4-Bromophenyl)ethyl)-N,4-dimethylbenzenesulfonamide (6b). The title compound was prepared from 1-(4-bromophenyl)ethanol (102 mg) and N,4-dimethylbenzenesulfonamide (460 mg) following the general procedure C. The reaction was performed at room temperature and monitored by TLC. The crude product was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 176 mg (96%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.76-7.73 (m, 2 H), 7.47-7.44 (m, 2 H), 7.35-7.33 (m, 2 H), 7.21-7.18 (m, 2 H), 5.25 (q, *J* = 7.0 Hz, 1 H), 2.58 (s, 3 H), 2.46 (s, 3 H), 1.28 (d, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 143.3, 139.1, 137.0, 131.5, 129.8, 129.0, 127.1, 121.6, 54.3, 28.4, 21.5, 15.1 ppm; IR (solid) 2983, 1485, 1337, 1167, 933, 818, 742, 656 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd for $C_{16}H_{18}BrNNaO_2S$ 390.0139, found 390.0132.

N-(4-Bromobenzyl)-4-methoxybenzenesulfonamide (6c). The title compound was prepared from (4-bromophenyl)methanol (95 mg) and 4-methoxybenzenesulfonamide (470 mg) following the general procedure C and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 111 mg (62%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.78-7.75 (m, 2 H), 7.39-7.37 (m, 2 H), 7.08-7.06 (m, 2H), 6.96-6.94 (m, 2 H), 4.89 (t, *J* = 6.3 Hz, 1 H), 4.06 (d, *J* = 6.3 Hz, 2 H), 3.87 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 163.0, 135.6, 131.6, 131.3, 129.6, 129.2, 121.6, 114.3, 55.7, 46.5 ppm; IR (solid) 3270, 1595, 1577, 1307, 1262, 1155, 1030, 804 cm^{-1}; HRMS (ESI) $[M–H]^–$ calcd for $C_{14}H_{13}BrNO_3S$ 353.9805, found 353.9799.

N-(4-Bromobenzyl)-2-nitrobenzenesulfonamide (6d). The title compound was prepared from (4-bromophenyl)methanol (94 mg) and 2-nitrobenzenesulfonamide (505 mg) following the general procedure C. The reaction was performed at 100 °C with a reaction time of 24 hours. The crude product was purified with an hexane/DCM (50:50 to 75:25) eluent to afford an amorphous white solid. 102 mg (55%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.97 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.83 (dd, *J* = 7.9, 1.4 Hz, 1 H), 7.71 (td, *J* = 7.7, 1.5 Hz, 1 H), 7.65 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.36-7.34 (m, 2 H), 7.11-7.10 (m, 2 H), 5.75 (t, *J* = 6.5 Hz, 1 H), 4.28 (d, *J* = 6.4 Hz, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 147.8, 134.9, 133.9, 133.5, 132.8, 131.8, 130.9, 129.5, 125.3, 122.0, 47.2 ppm; IR (solid) 3341, 3100, 1592, 1543, 1487, 1438, 1358, 1204, 1070, 1009, 738 cm^{-1}; HRMS (ESI) $[M–H]^–$ calcd for $C_{13}H_{10}BrN_2O_4S$ 368.9550, found 368.9547.

N-(2-Bromo-4-fluorobenzyl)-N-methyl-2-nitrobenzenesulfonamide (6e). The title compound was prepared from (2-bromo-4-fluorophenyl)methanol (103 mg) and N-methyl-2-nitrobenzenesulfonamide (540 mg) following the general procedure C with a reaction time of 24 hours. The crude product was then purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 140 mg (70%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 8.04-8.02 (m, 1 H), 7.76-7.69 (m, 2 H), 7.69-7.67 (m, 1 H), 7.50 (dd, *J* = 8.7, 5.9 Hz, 1 H), 7.30 (dd, *J* = 8.1, 2.6 Hz, 1 H), 7.07 (ddd, *J* = 8.7, 7.9, 2.6 Hz, 1 H), 4.55 (s, 2 H), 2.86 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 161.9 ($J_{C\text{-}F}$ = 251.5 Hz), 148.3 , 133.8 , 132.2 , 131.7 , 131.1 , 130.9 ($J_{C\text{-}F}$ = 8.6 Hz), 130.7 ($J_{C\text{-}F}$ = 3.5 Hz), 124.3 , 123.6 ($J_{C\text{-}F}$ = 9.6 Hz), 120.1 ($J_{C\text{-}F}$ = 24.5 Hz), 115.3 ($J_{C\text{-}F}$ = 21.1 Hz), 52.9, 34.7 ppm; IR (cast film, DCM) 3096, 2931, 1589, 1487, 1372, 1168, 925, 763 cm^{-1}; HRMS (ESI) $[M+Na]^+$ calcd for $C_{14}H_{12}BrFN_2NaO_4S$ 424.9583, found 424.9583.

N-(4-Bromobenzyl)methanesulfonamide (6f). The title compound was prepared from (4-bromophenyl)methanol (94 mg) and methanesulfonamide (238 mg) following the general procedure C and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 95 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.51-7.48 (m, 2 H), 7.25-7.21 (m, 2H), 4.78 (bs, 1 H), 4.27 (d, *J* = 6.2 Hz, 2 H), 2.88 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ 135.8, 132.0, 129.6, 122.1, 46.5, 41.3 ppm; IR (solid) 3250, 1489, 1452, 1311, 1145, 1083, 810, 758 cm^{-1}; HRMS (ESI) $[M–H]^-$ calcd for $C_8H_9BrNO_2S$ 261.9543, found 261.9541.

2-(4-Bromobenzyl)-1,2-thiazinane 1,1-dioxide (6g). The title compound was prepared from (4-bromophenyl)methanol (75 mg, 0.40 mmol) and 1,2-thiazinane 1,1-dioxide (270 mg, 2.0 mmol) following the general procedure C and was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 111 mg (91%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.49-7.46 (m, 2 H), 7.23-7.21 (m, 2 H), 4.25 (s, 2 H), 3.21-3.19 (m, 2 H), 3.10-307 (m, 2 H), 2.24-2.19 (m, 2 H), 1.64-1.60 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 135.2, 131.8, 130.2, 121.8, 49.5, 48.9, 48.5, 24.0, 21.9 ppm; IR (solid) 2947, 1487, 1330, 1143, 1094, 1009, 904, 760 cm^{-1}; HRMS (EI) $[M]^+$ calcd for $C_{11}H_{14}BrNO_2S$ 302.9929, found 302.9929.

General procedure D for the catalytic sulfonamidation of various alcohols with *para*-toluenesulfonamide: Without any other specification, the reaction conditions for the direct catalytic sulfonamidation of alcohols were the following ones. Alcohol derivative (0.50 mmol), *para*-toluenesulfonamide (430 mg, 2.50 mmol), 2,3,4,5-tetrafluorophenylboronic acid **BA1** (10.0 mg, 0.050 mmol) and oxalic acid dihydrate (6.3 mg, 0.050 mmol) were added to a mixture of HFIP (1.6 mL) and nitromethane (0.4 mL) in a round bottom flask equipped with a magnetic stirring bar. The reaction media was stirred at room temperature until completion of the reaction (monitored by TLC). The solvent was then evaporated and the crude product was purified by flash chromatography on silica gel using a solid deposit technique (silica).

N-(Cyclohex-2-en-1-yl)-4-methylbenzenesulfonamide (7a).[19] The title compound was prepared from cyclohex-2-enol (49 mg, 0.50 mmol) following the general procedure D with a reaction time of 5 minutes (it has been noticed that an extension of the reaction time had a detrimental effect on the reaction yield). The media was then diluted with 20 mL of DCM and washed successively with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered and evaporated. The crude product was purified with an hexane/DCM (25:75) eluent to afford an amorphous white solid. 96 mg (76%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.78-7.76 (m, 2 H), 7.29-7.27 (m, 2 H), 5.75-5.71 (m, 1 H), 5.36-5.32 (m, 1 H), 4.84 (d, *J* = 8.5 Hz, 1 H), 3.81-3.76 (m, 1 H), 2.41 (s, 3 H), 1.97-1.83 (m, 2 H), 1.77-1.69 (m, 1 H), 1.63-1.48 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 143.2, 138.4, 131.4, 129.7, 127.1, 127.0, 49.0, 30.2, 24.5, 21.5, 19.3 ppm.

N-(tert-Butyl)-4-methylbenzenesulfonamide (7b).[22] The title compound was prepared from *tert*-butanol (38 mg) following the general procedure D with 2 mL of HFIP/nitromethane (4:1) solvent. It was then purified with an hexane/DCM (50:50) eluent to afford an amorphous white solid. 53 mg (47%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.81-7.78 (m, 2 H), 7.29-7.27 (m, 2 H), 5.00 (s, 1 H), 2.42 (s, 3 H), 1.21 (s, 9 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 142.7, 140.6, 129.4, 127.0, 54.5, 30.1, 21.5 ppm.

N-((3s,5s,7s)-Adamantan-1-yl)-4-methylbenzenesulfonamide (7c).[23] The title compound was prepared from (3s,5s,7s)-adamantan-1-ol (76 mg) following the general procedure D and was purified with an hexane/DCM (75:25) eluent to afford an amorphous white solid. 133 mg (87%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.81-7.79 (m, 2 H), 7.29-7.27 (m, 2 H), 4.70 (s, 1 H), 2.43 (s, 3 H), 2.02-2.00 (m, 3 H), 1.80-1.79 (m, 6 H), 1.63-1.54 (m, 6 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 142.7, 141.1, 129.4, 126.9, 55.1, 43.1, 35.9, 29.5, 21.5 ppm.

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Keywords: boronic acids • sulfonamides • organocatalysis • benzylic alcohols • synthetic method

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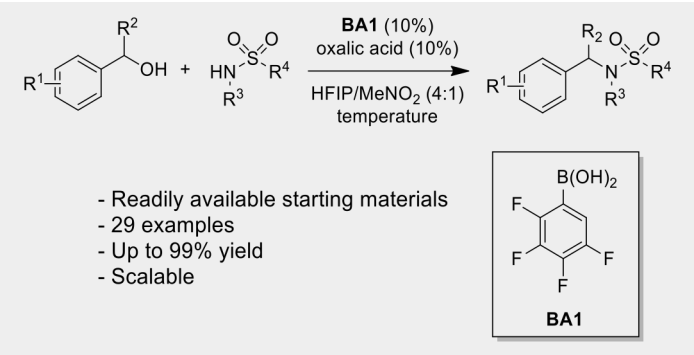

Direct sulfonamidation*

*Tristan Verdelet, Robert M. Ward and Dennis G. Hall**

Page No. – Page No.
Direct Sulfonamidation of Primary and Secondary Benzylic Alcohols Catalyzed by a Boronic Acid/Oxalic Acid System.

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TOC Text:

A catalytic method was developed to effect the direct transformation of primary and secondary benzylic alcohols into various sulfonamide products using a mixture of 2,3,4,5-tetrafluorophenylboronic acid and oxalic acid as a co-catalytic system. The reaction proceeds under mild conditions affords acceptable to excellent yields of products using relatively benign starting materials. The reaction is gram-scalable and the excess of sulfonamide reagent can be recovered after purification.