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Manganese-Catalyzed *N*-Alkylation of Sulfonamides Using Alcohols

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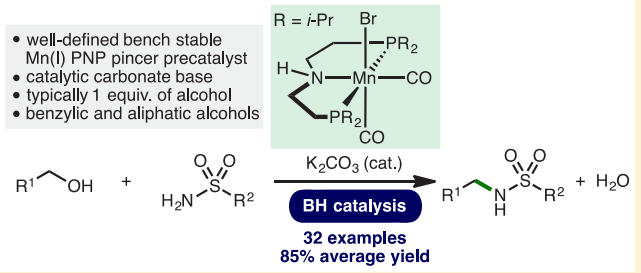
Supporting Information

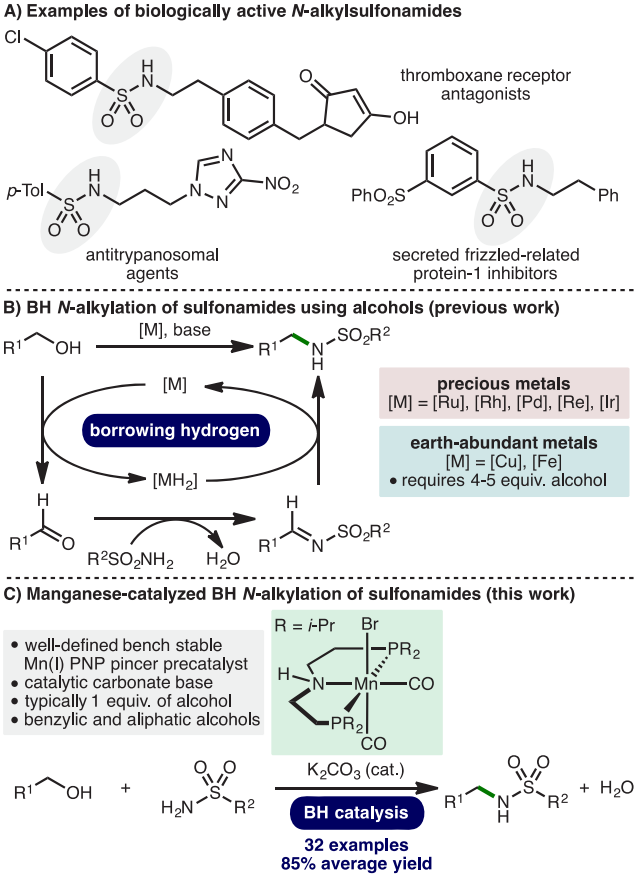
ABSTRACT: An efficient manganese-catalyzed *N*-alkylation of sulfonamides has been developed. This borrowing hydrogen approach employs a well-defined and bench-stable Mn(I) PNP pincer precatalyst, allowing benzylic and simple primary aliphatic alcohols to be employed as alkylating agents. A diverse range of aryl and alkyl sulfonamides undergoes mono-*N*-alkylation in excellent isolated yields (32 examples, 85% average yield).



The sulfonamide functional group is present in a diverse array of bioactive compounds.[1] More specifically, *N*-alkylsulfonamides are commonly employed in drug discovery programs, with examples including the development of thromboxane receptor antagonists,[2a] antitrypanosomal agents,[2b] and secreted frizzled-related protein-1 inhibitors (Scheme 1A).[2c] Classical methods for *N*-alkylsulfonamide synthesis include the reaction of amines with activated sulfonyl derivatives (commonly sulfonyl chlorides),[3] *N*-alkylation of primary sulfonamides with alkyl halides,[4] and reductive amidation using aldehydes.[5] Drawbacks of these methods include limited availability and stability of specific sulfonyl chlorides, the use of toxic alkylating agents, and the stoichiometric generation of undesired byproducts. In contrast, the borrowing hydrogen (BH) approach allows commodity alcohols to be employed as alkylating agents, with water generated as the only byproduct.[6] Traditionally, BH processes have employed precious metal catalysts. However, as part of ongoing efforts to reduce our dependence on precious metal catalysts,[7] recent advances have demonstrated the use of earth-abundant first-row transition-metal catalysts across a variety of borrowing hydrogen processes.[8]

The BH alkylation of sulfonamides using alcohols has been reported employing various homogeneous precious metal catalyst systems based on ruthenium, rhodium, palladium, rhenium, and iridium (Scheme 1B).[9−11] The work of Xu and co-workers[10d] provides a particularly relevant comparison to the present work with MnO_2-catalyzed chemistry that proceeds at 135 °C for a number of sulfonamide substrates. With respect to earth-abundant first-row transition metals, Shi and Beller reported the $Cu(OAc)_2$-catalyzed *N*-alkylation of sulfonamides.[12] Interestingly, the reaction performs best in an air atmosphere, with the in situ formation of bis-sulfonylated amidines observed, which may serve as ligands to stabilize the catalyst. Subsequently, Shi and Deng described the $FeCl_2$-catalyzed *N*-alkylation of sulfonamides.[13] Despite these notable advances, both approaches largely employ benzylic alcohols and require an excess of the alkylating agent (4−5 equiv).

Scheme 1. Sulfonamide Importance and Project Overview



Furthermore, the development of an efficient catalytic BH *N*-alkylation of sulfonamides using well-defined complexes based

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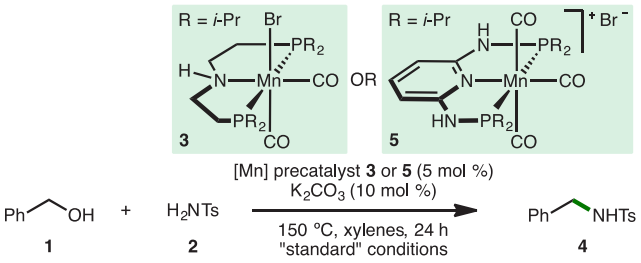
J. Org. Chem. 2019, 84, 3715−3724

on earth-abundant first-row transition metals remains an unsolved problem. To this end, herein we report the use of PNP pincer complexes based on manganese for the *N*-alkylation of sulfonamides using both benzylic and simple primary aliphatic alcohols (Scheme 1C).[14]

For optimization, the *N*-alkylation of *p*-toluenesulfonamide **2** with benzyl alcohol **1** was selected as a model system (Table 1). After extensive optimization,[15] it was found that a BH

Table 1. Optimization of Mn-Catalyzed *N*-Benzylation[a]



entry	variation from "standard" conditions	yield[b] (%)
1	none	98 (86)
2	no [Mn] precatalyst	<2
3	no K_2CO_3	5
4	[Mn] precatalyst **5** (5 mol %) instead of **3**	<2
5	Cs_2CO_3 (10 mol %) instead of K_2CO_3	94
6	KOH (10 mol %) instead of K_2CO_3	5
7	KO*t*-Bu (10 mol %) instead of K_2CO_3	41
8	[**1**] = 0.5 M	92
9	[**1**] = 2 M	92
10	110 °C	18
11	reaction time = 6 h	82
12	[Mn] precatalyst **3** (4 mol %)	94
13	[Mn] precatalyst **3** (3 mol %)	42

[a]Reactions performed using **1** (1 mmol), **2** (1 mmol), and bench-grade xylenes. [**2**] = 1 M. [b]Yield after 24 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. Isolated yield given in parentheses.

system composed of bench-stable Mn(I) PNP pincer precatalyst **3** (5 mol %)[16] and K_2CO_3 (10 mol %) as base in xylenes ([**2**] = 1 M) at 150 °C for 24 h enabled the *N*-benzylation of **2**, giving **4** in 98% NMR yield and 86% isolated yield (entry 1). Importantly, only 1 equiv of the alkylating agent and catalytic quantities of base were required for complete conversion, giving a high atom economy process.[17] No alkylation occurs in the absence of the manganese precatalyst **3**,(entry 2), with only 5% conversion observed in the absence of K_2CO_3 (entry 3). It was found that manganese precatalyst **5**, introduced by Sortais and co-workers,[14d] was ineffective for the desired transformation, resulting in no observable formation of sulfonamide **4** (entry 4). When Cs_2CO_3, KOH, or KO-*t*-Bu was used as base, lower conversions to **4** (entries 5−7) was observed. Furthermore, altering the reaction concentration (entries 8 and 9), lowering reaction temperature (entry 10), reducing the reaction time (entry 11), or reducing the catalyst loading (entries 12 and 13) all lowered the efficiency of the *N*-benzylation of **2**.

The full scope of the Mn-catalyzed BH *N*-alkylation of sulfonamides was explored, starting with the *N*-alkylation of *p*-toluenesulfonamide **2** (Scheme 2A/B).[18] When the optimized reaction conditions (Table 1, entry 1) are used, various substituted benzylic alcohols can be employed as alkylating agents, giving the corresponding mono-*N*-alkylated sulfonamides in excellent isolated yields (products **4** and **6**−**15**, 84% average yield). Within the aryl unit, 4-Me, 3-Me, and 2-Me substitution is tolerated in addition to electron-donating (4-OMe) and electron-withdrawing (4-CF_3) substituents. However, the sterically congested 2,4,6-trimethylbenzyl alcohol was unreactive. 4-Iodobenzyl alcohol can be employed as the alkylating agent, incorporating an additional functional handle into sulfonamide **11** for subsequent elaboration via established cross-coupling methods. Interestingly, thiophene-3-ylmethanol can be converted to sulfonamide **12** in 87% isolated yield, but thiophene-2-ylmethanol gives no conversion to the corresponding sulfonamide, suggesting that it may inhibit catalysis via coordination to Mn. The catalytic system exhibits chemoselectivity, tolerating the reducible benzyl ether, olefin, and ester moieties present within products **13**−**15**. We were pleased to discover that less activated simple primary aliphatic alcohols can also be employed as alkylating agents in this process (products **16**−**19**, 84% average yield). In each case, the alcohol was used as solvent in order to obtain high isolated yields of the *N*-alkylated sulfonamides. Methanol is challenging to employ as the alkylating agent in borrowing hydrogen processes, which can partly be attributed to the increased energy of dehydrogenation compared to higher alcohols (e.g., ΔH (MeOH) = +84 kJ mol^{-1}, cf. ΔH (EtOH) = +68 kJ mol^{-1}).[19] In this system employing 1 equiv of K_2CO_3, *N*-methylation of *p*-toluenesulfonamide proceeds efficiently, affording **19** in 89% isolated yield.[20] Unfortunately, despite examining a range of alternative reaction conditions, we found that allylic and propargylic alcohols produce multiple unidentified products whereas secondary alcohols are unreactive in this *N*-alkylation procedure.

Next, we explored the scope of the reaction with respect to variation within the sulfonamide component (Scheme 2C/D). When the optimized reaction conditions (Table 1, entry 1) are employed, a variety of aryl sulfonamides undergo efficient mono-*N*-alkylation with benzyl alcohol (products **20**−**32**, 85% average yield). Sulfonamides containing sterically encumbered aryl units such as *o*-tolyl, mesityl, trisyl, and 1-naphthyl were all well tolerated. Within the aryl unit, electron-donating (4-OMe) substituents are readily accommodated, whereas solvent quantities of benzyl alcohol and 1 equiv of K_2CO_3 were required when less nucleophilic 4-(trifluoromethyl)-benzenesulfonamide was used, accessing **28** in 61% isolated yield. In line with this observation, employing 4-nitrobenzenesulfonamide and 4-cyanobenzenesulfonamide gave no observable *N*-alkylation products, with starting materials returned in both cases. 4-Bromobenzenesulfonamide was readily tolerated, incorporating an additional functional handle into product **29**. Thiophene-2-sulfonamide underwent efficient *N*-benzylation, giving **30** in 73% isolated yield. However, a sulfonamide containing a pyridine ring did not give any observable conversion to the corresponding *N*-alkylated product, which may be attributed to coordination to the catalyst. Reducible functionalities within the sulfonamide nucleophile are conserved, providing products **31** and **32** in 95% and 70% isolated yields, respectively. A selection of alkyl sulfonamides was also tolerated, giving products **33**−**36** in excellent isolated yields. Employing benzamide and methyl-carbamate as nucleophiles resulted in recovered starting materials in both cases, despite examining a range of reaction conditions.

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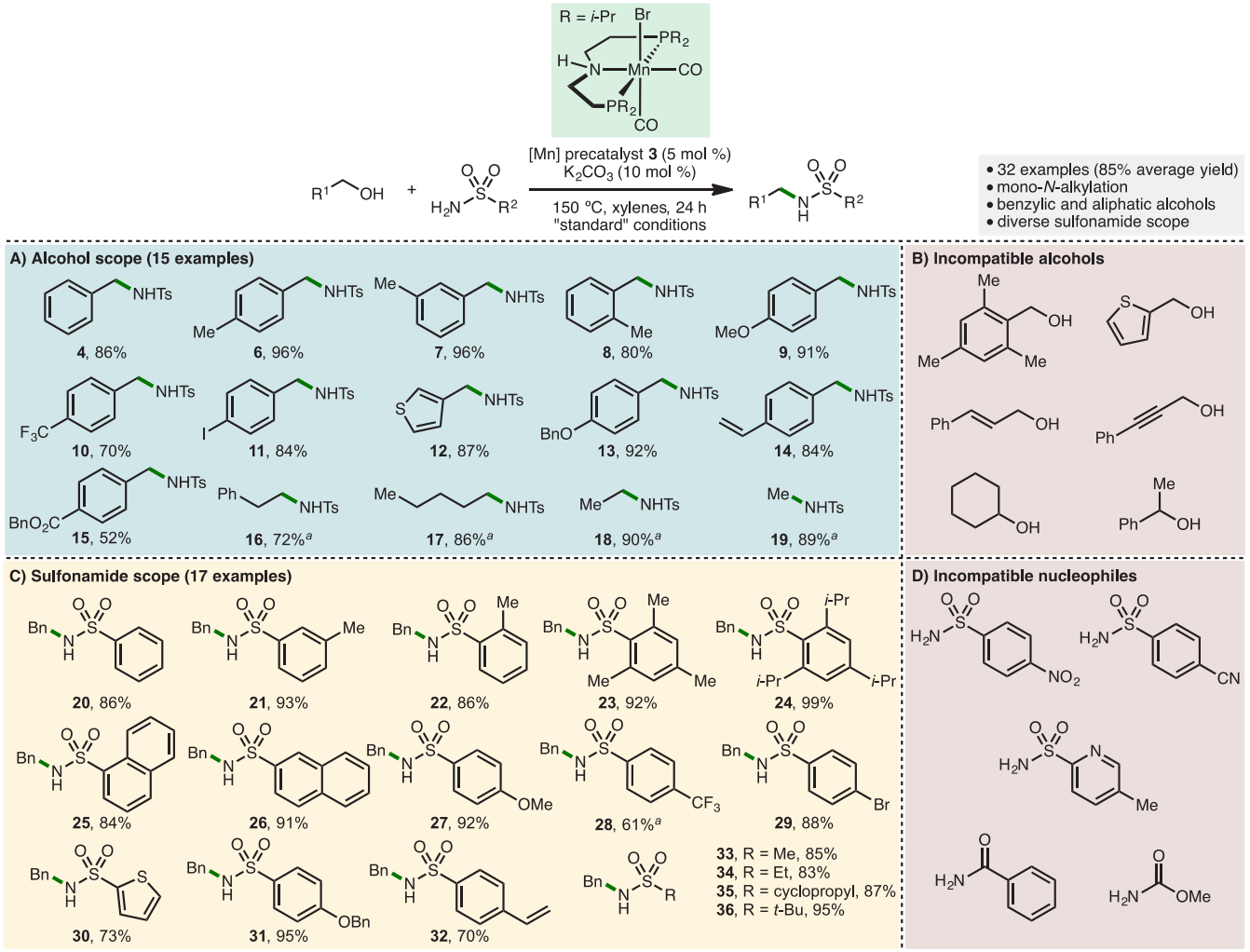
Scheme 2. Scope of the Mn-Catalyzed BH *N*-Alkylation of Sulfonamides*

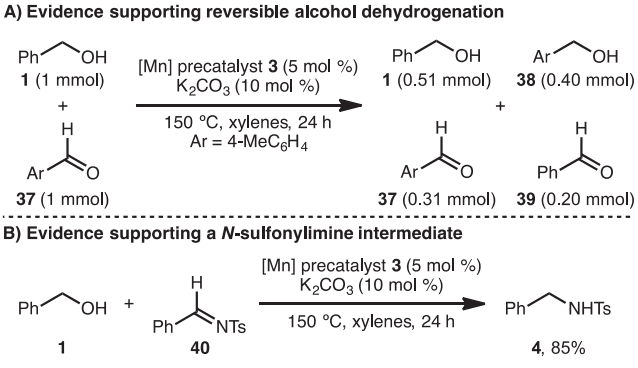


*Reactions performed using 1 mmol of alcohol and sulfonamide starting materials and bench-grade xylenes. All yields are isolated yields after chromatographic purification. [a]Alcohol used as solvent and K_2CO_3 (1 equiv).

To obtain insight into the reaction mechanism, equimolar quantities of benzyl alcohol **1** and *p*-tolualdehyde **37** were subjected to the "standard" reaction conditions, which gave a mixture of alcohols (**1** and **38**) and aldehydes (**37** and **39**), providing evidence that alcohol dehydrogenation is reversible (Scheme 3A).[21] Furthermore, replacing *p*-tolualdehyde **39** with *N*-sulfonyl imine **40** produced **4** in 85% NMR yield, indicating that **40** is a plausible reaction intermediate (Scheme 3B). In line with these observations, and previous related investigations,[14] a plausible reaction mechanism initiates with activation of precatalyst **3** with K_2CO_3 in a dehydrobromination reaction to form the active manganese complex (Scheme 4). Alcohol coordination forms an alkoxo-type complex, with subsequent dehydrogenation forming an aldehyde and a manganese hydride species. Condensation with *p*-toluenesulfonamide **2** forms an *N*-sulfonylimine, which is reduced by the manganese hydride species to give the *N*-alkylated product **4** with regeneration of the catalytically active species.

In conclusion, we have developed an efficient Mn-catalyzed *N*-alkylation of sulfonamides using benzylic and simple primary aliphatic alcohols as alkylating agents. A diverse array of aryl and alkyl sulfonamides undergoes mono-*N*-alkylation in excellent isolated yields (32 examples, 85% average yield).

Scheme 3. Mechanistic Control Experiments[a]



[a]Yield after 24 h as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

EXPERIMENTAL SECTION

General Information. Unless stated otherwise, all reactions were performed using oven-dried 10 mL microwave vials sealed with aluminum crimp caps and were stirred with Teflon-coated magnetic stirrer bars. Dry tetrahydrofuran (THF), toluene, hexanes, and diethyl

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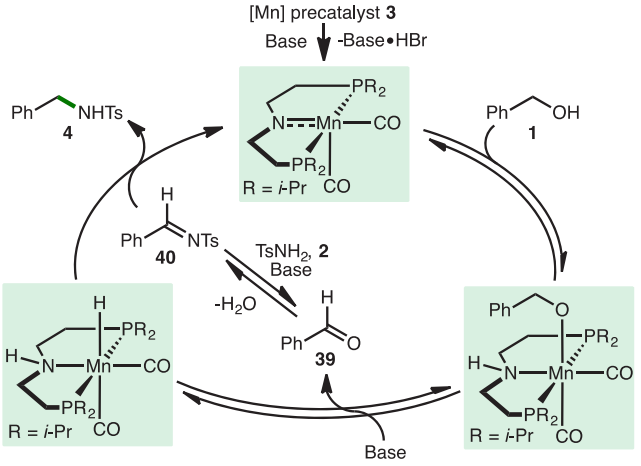
Scheme 4. Plausible Catalytic Cycle



ether were obtained after these previously degassed solvents were passed through activated alumina columns (Mbraun, SPS-800). All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise. Manganese precatalysts **3**[14b] and **5**[14d] were prepared according to literature procedures. Benzaldehyde was vacuum distilled at 75 °C prior to use. Room temperature (rt) refers to 20–25 °C. Ice/water baths were used to obtain temperatures of 0 °C. All reactions involving heating were carried out using DrySyn blocks and a contact thermometer. In vacuo refers to reduced pressure through the use of a rotary evaporator. Analytical thin-layer chromatography was carried out using aluminum plates coated with silica (Kieselgel 60 F254 silica), and visualization was achieved using ultraviolet light (254 nm) followed by staining with a 1% aqueous $KMnO_4$ solution. Flash chromatography used Kieselgel 60 silica in the solvent system stated. Melting points were recorded on a Gallenkamp melting point apparatus and corrected by linear interpolation of melting point standards benzophenone (47–49 °C) and benzoic acid (121–123 °C). Infrared spectra were recorded on a Shimadzu IRAffinity-1 Fourier Transform ATIR spectrometer as thin films using a Pike MIRacle ATR accessory. Characteristic peaks are quoted (ν_{max}/cm^{-1}). ^{1}H, ^{13}C, and ^{19}F NMR spectra were obtained on either a Bruker Avance 400 (400 MHz ^{1}H, 101 MHz ^{13}C, 376 MHz ^{19}F) or a Bruker Avance 500 (500 MHz ^{1}H, 126 MHz ^{13}C, 471 MHz ^{19}F) spectrometer at rt in the solvent stated. Chemical shifts are reported in parts per million (ppm) relative to the residual solvent signal. All coupling constants, *J*, are quoted in hertz. Multiplicities are reported with the following symbols: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and multiples thereof. The abbreviation Ph is used to denote phenyl, br to denote broad. High-resolution mass spectrometry (HRMS, *m*/*z*) data was acquired either at Cardiff University on a Micromass LCT spectrometer or at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

(4-Vinylphenyl)methanol. Following modified literature procedures,[22] a flame-dried round-bottomed flask was charged with a magnetic stirrer bar, magnesium turnings (262 mg, 11.5 mmol), a crystal of iodine, and dry THF (20 mL) under inert atmosphere. The resulting suspension was cooled to 0 °C under vigorous stirring. To the reaction mixture was added 4-bromostyrene dropwise (1.00 mL, 7.64 mmol) over 30 min, and the reaction was warmed to room temperature. After being stirred at this temperature for 4 h, a multinecked flame-dried round-bottomed flask was fitted with a drying column of anhydrous calcium sulfate, fitted with a suba seal. Through the side arm of the flask were added small quantities of CO_2(s), and the side arm was sealed with a suba seal. The resultant CO_2(g) was passed through the drying column and bubbled into the reaction solution at rt by use of a cannula. This process was continued with a low flow rate for 3 h, after which time the reaction mixture was quenched with 2 M H_2SO_4(10 mL) and extracted in Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo. The crude solid was recrystallized from boiling petroleum ether 40–60 to remove major impurities, yielding 4-vinylbenzoic acid that was used directly in the next step. Following a literature procedure,[23] a flame-dried round-bottomed flask was charged with a magnetic stirrer bar, lithium aluminum hydride (758 mg, 20.0 mmol), and THF (80 mL) under inert atmosphere. The resulting slurry was cooled to 0 °C under rapid stirring, and a solution of 4-vinylbenzoic acid (500 mg, 3.37 mmol) in Et_2O (25 mL) was added dropwise. The resulting reaction mixture was then warmed to room temperature, stirred for 1 h at this temperature, and then quenched with dropwise H_2O (256 μL), 10% w/w NaOH/H_2O (512 μL), and then H_2O (768 μL). The mixture was stirred vigorously until a white solid was formed and then was filtered. The filtrate was dried with $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude material was then purified by flash column chromatography (30 × 110 mm silica, 10–20% ethyl acetate/petroleum ether 40–60) to give the title compound (423 mg, 94%) as a colorless oil: R_f 0.20 (20% EtOAc/petroleum ether 40–60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.70 (1H, s, br), 4.68 (2H, s), 5.25 (1H, dd, *J* 10.9, 0.8), 5.75 (1H, dd, *J* 17.6, 0.8), 6.72 (1H, dd, *J* 17.6, 10.9), 7.33 (2H, d, *J* 8.2), 7.40–7.42 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 65.3, 114.1, 126.5, 127.3, 136.6, 137.2, 140.5. Spectroscopic data are in accordance with the literature.[24]

Benzyl 4-(Hydroxymethyl)benzoate. A 100 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with 4-(hydroxymethyl)benzyl alcohol (3.04 g, 20 mmol), K_2CO_3 (3.04 g, 22 mmol), *N*,*N*-dimethylformamide (23 mL), and benzyl bromide (2.40 mL, 3.42 g, 20 mmol) and the reaction heated at 30 °C for 24 h using a heating block. The resulting mixture was then cooled and H_2O added (30 mL). The mixture was then transferred to a separatory funnel filled with EtOAc (50 mL). The organic layer was collected, and the aqueous layer was washed with EtOAc (2 × 50 mL). The organics were then combined, washed with brine (7 × 100 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by recrystallization gave the title compound as a white solid (3.7 g, 76%): mp 56–58 °C (Et_2O/hexanes); R_f = 0.16 (20% EtOAc/petroleum ether 40–60); ν_{max}/cm^{-1} (film) 1719, 1611, 1454, 1416, 1366, 1263, 1171, 1115, 1098, 1080, 1040, 1015, 934, 914, 845, 822, 785, 746, 700, 598, 523, 465, 438, 415, 403; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 1.83 (1H, t, *J* 6.0), 4.77 (2H, d, *J* 6.0), 5.37 (2H, s), 7.30–7.50 (7H, m), 8.07 (2H, d, *J* 8.0); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C: 64.9, 66.9, 126.6, 128.3, 128.4, 128.7, 129.4, 130.1, 136.2, 146.2, 166.4; HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{15}O_3$ 243.1021, found 243.1002.

3-Methylbenzenesulfonamide. Following a modified literature procedure,[25] a round-bottomed flask was charged with a magnetic stirrer bar, 3-methylbenzene sulfonyl chloride (290 μL, 2.00 mmol), and acetone (3 mL). The resulting solution was stirred and cooled to 0 °C. Concentrated ammonium hydroxide solution (28–30% w/w, 8 mL, 118 mmol) was then added, and the resulting solution was allowed to warm to room temperature before being stirred at this temperature for 4 h. The reaction was then concentrated in vacuo until a precipitate was observed. The resulting slurry was then filtered and washed with water to yield the title compound (112 mg, 33%) as a white solid: mp 107–108 °C (lit.[26] mp 109–111 °C); R_f 0.20 (30% EtOAc/petroleum ether 40–60); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.43 (3H, s), 4.81 (2H, s, br), 7.38–7.43 (2H, m), 7.72–7.75 (2H, m); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 21.5, 123.7, 127.0, 129.2, 133.7, 139.6, 141.9. Spectroscopic data are in accordance with the literature.[26]

4-Vinylbenzenesulfonamide. Following a literature procedure,[27] a round-bottomed flask was charged with a magnetic stirrer bar and dimethylformamide (8.3 mL). Thionyl chloride (4.14 mL, 41.0 mmol) was then added dropwise over the course of 30 min. The reaction mixture was then stirred at 0 °C for 6 h before stirring was stopped, and the reaction vessel was sealed and left in the refrigerator overnight. The solution was then poured slowly over ice–water (15 mL), extracted in diethyl ether (3 × 7 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. To the resulting

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crude mixture was then added a magnetic stirrer bar, and concentrated ammonium hydroxide solution (28−30% w/w, 18 mL) was added slowly. This reaction mixture was then stirred for 2 h before dilution in water (5 mL) and subsequent extraction in diethyl ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to yield the title compound (400 mg, 43%) as a white solid: mp 138−140 °C (lit.[28] mp 141 °C); R_f 0.21 (30% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.81 (2H, s, br), 5.44 (1H, d, J 10.9), 5.88 (1H, d, J 17.6), 6.75 (1H, dd, J 10.9, 17.6), 7.53 (2H, d, J 8.1), 7.88 (2H, d, J 8.1); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 117.8, 127.0, 127.1, 135.5, 140.9, 142.3. Spectroscopic data are in accordance with the literature.[28]

*N-Benzylidene-4-methylbenzenesulfonamide (**40**).* Following a literature procedure,[29] an oven-dried pressure tube was charged with a magnetic stirrer bar, *p*-toluenesulfonamide (1.03 g, 6.0 mmol), and DCM (18.8 mL). The solution was stirred vigorously, and benzaldehyde (704 μL, 7.2 mmol), molecular sieves (6.0 g, 1 g/mmol), and pyrrolidine (49.3 μL, 0.6 mmol) were added. The reaction vessel was then sealed and heated to 60 °C in an oil bath for 24 h. The reaction vessel was cooled to room temperature and filtered through a pad of Celite. The solvent was removed in vacuo to yield a crude oil. The residual benzaldehyde was removed under high vacuum with gentle heating (40 °C), to yield the title compound (1.38 g, 89%) as a yellow solid: mp 104−106 (lit.[30] 105 °C); R_f 0.30 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.44 (3H, s), 7.35 (2H, d, J 8.1), 7.49 (2H, t, J 7.7), 7.62 (1H, t, J 7.4) 7.89 (2H, d, J 8.2), 7.93 (2H, d, J 7.3), 9.04 (1H, s); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.8, 128.3, 129.3, 130.0, 131.5, 132.6, 135.1, 135.3, 144.8, 170.3. Spectroscopic data are in accordance with the literature.[30]

General Procedure A. A 10 mL microwave vial was charged with a magnetic stirrer bar, an amide (1.00 mmol), potassium carbonate (13.8 mg, 10 mol %), [Mn] precatalyst **3** (24.8 mg, 0.05 mol %), an alcohol (1.00 mmol), and xylenes (1 mL). The vial was then crimped shut and stirred vigorously at 150 °C for 24 h using a heating block. The reaction vessel was then cooled and decrimped, and to the reaction mixture were added mesitylene (69.6 μL, 0.5 mmol), water (1 mL), and ethyl acetate (1 mL). The reaction mixture was then stirred for an additional 5 min, sampled directly, and analyzed by proton NMR. The crude reaction mixture was then separated, washing the aqueous layer with ethyl acetate (3 × 5 mL). The organic layers were then combined, dried over $MgSO_4$, and filtered. The resulting solution was then concentrated under reduced pressure, loaded directly onto silica, and purified by flash column chromatography. Extra purification steps are listed as applicable.

General Procedure B. A 10 mL microwave vial was charged with a magnetic stirrer bar, an amide (1.00 mmol), potassium carbonate (138 mg, 1.00 mmol), [Mn] precatalyst **3** (24.8 mg, 5 mol %), and an alcohol (1 mL). The vial was then crimped shut and stirred vigorously at 150 °C for 24 h using a heating block. The reaction vessel was then cooled and decrimped, and to the reaction mixture were added mesitylene (69.6 μL, 0.5 mmol), water (1 mL), and ethyl acetate (1 mL). The reaction mixture was then stirred for an additional 5 min, then sampled directly, and analyzed by proton NMR. The crude reaction mixture was then separated, washing the aqueous layer with ethyl acetate (3 × 5 mL). The organic layers were then combined, dried over $MgSO_4$, and filtered. The resulting solution was then concentrated under reduced pressure, loaded directly onto silica, and purified by flash column chromatography. Extra purification steps are listed as applicable.

*N-Benzyl-4-methylbenzenesulfonamide (**4**).* Compound **4** was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and benzyl alcohol (101 μg, 1.00 mmol) and purified by flash column chromatography (30 × 150 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (225 mg, 86%) as a white crystalline powder: mp 163−165 °C (lit.[31] mp 166−168 °C); R_f 0.20 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.44 (3H, s), 4.13 (2H, d, J 6.2), 4.61 (1H, t, J 5.8), 7.19−7.21 (2H, m), 7.24−7.33 (5H, m), 7.75−7.78 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 47.5, 127.4, 128.0, 128.1, 128.9, 129.9, 136.4, 137.0, 143.7. Spectroscopic data are in accordance with the literature.[31]

*4-Methyl-N-(2-methylbenzyl)benzenesulfonamide (**6**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and 4- methylbenzyl alcohol (122 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% ethyl acetate/petroleum ether 40−60) to yield the title compound (263 mg, 96%) as a pale yellow solid: mp 93−94 °C (lit.[32] mp 95 °C {cyclohexane/ethyl acetate}); R_f 0.25 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.31 (3H, s), 2.44 (3H, s), 4.07 (2H, d, J 6.1), 4.56 (1H, t, J 5.9), 7.06−7.10 (4H, m), 7.30−7.32 (2H, d, J 8.0), 7.76 (2H, d, J 8.2); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.2, 21.7, 47.2, 127.4, 128.0, 129.5, 129.9, 133.3, 137.0, 137.9, 143.6. Spectroscopic data are in accordance with the literature.[32]

*3-Methyl-N-(2-methylbenzyl)benzenesulfonamide (**7**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and 3-methylbenzyl alcohol (122 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 110 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (264 mg, 96%), as an off-white solid: mp 65−66 °C (lit.[33] mp 64−66 °C); R_f 0.29 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.28 (3H, s), 2.44 (3H, s), 4.09 (2H, d, J 6.2), 4.68 (1H, t, J 5.9), 6.97−6.98 (2H, m), 7.05−7.08 (1H, m), 7.14−7.17 (1H, m), 7.31 (2H, d, J 7.9), 7.74−7.77 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.4, 21.7, 47.4, 125.0, 127.4, 128.7, 128.8, 128.8, 129.9, 136.3, 137.1, 138.6, 143.7. Spectroscopic data are in accordance with the literature.[33]

*2-Methyl-N-(2-methylbenzyl)benzenesulfonamide (**8**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and 2-methylbenzyl alcohol (122 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (219 mg, 80%) as a pale yellow solid: mp 115−117 °C (lit.[33] mp 113−117 °C); R_f 0.24 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.25 (3H, s), 2.45 (3H, s), 4.09 (2H, d, J 6.0), 4.44 (1H, t, br, J 5.7), 7.10−7.13 (3H, m), 7.16−7.20 (1H, m), 7.32 (2H, d, J 8.0), 7.76−7.78 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 18.9, 21.7, 45.6, 126.4, 127.4, 128.4, 129.0, 129.9, 130.8, 134.0, 136.8, 136.9, 143.7. Spectroscopic data are in accordance with the literature.[33]

*N-(4-Methoxybenzyl)-4-methylbenzenesulfonamide (**9**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and 4-methoxybenzyl alcohol (138 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (269 mg, 91%) as an off-white solid: mp 120−123 °C (lit.[33] mp 119−121 °C); R_f 0.13 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.44 (3H, s), 3.78 (3H, s), 4.06 (2H, d, J 6.1), 4.51 (1H, t, J 5.7), 6.80 (2H, d, J 8.7), 7.11 (2H, d, J 8.6), 7.31 (2H, d, 8.0), 7.76 (2H, d, J 2.8); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 47.0, 55.4, 114.2, 127.4, 128.4, 129.4, 129.9, 137.0, 143.4, 159.5. Spectroscopic data are in accordance with the literature.[33]

*4-Methyl-N-(4-(trifluoromethyl)benzyl)benzenesulfonamide (**10**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and (4-(trifluoromethyl)phenyl)methanol (126 μL, 1.00 mmol) and was purified by flash column chromatography (30 × 110 mm silica, 20% EtOAc/petroleum ether 40−60) and trituration in petroleum ether 40−60 to give the title compound (235 mg, 70%) as an off-white solid: mp 134−137 °C; R_f 0.29 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3263, 2980, 1618, 1446, 1317, 1308, 1288, 1155, 1111, 1092, 1067, 1018, 878, 822, 812, 731, 706, 662, 631, 594, 561, 544, 490, 419; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.43 (3H, s), 4.20 (2H, d, J 6.4), 4.91 (1H, t, br, J 6.3), 7.28 (2H, d, J 8.0), 7.30 (2H, d, J 8.0), 7.51 (2H, d, J 8.1), 7.72 (2H, d, J 8.3); ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ_F:-62.65; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 46.8, 124.1 (q, J 272.5), 125.8 (q, J 3.8), 127.2, 128.2, 130.0,

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J. Org. Chem. 2019, 84, 3715−3724

130.1 (q, *J* 32.5), 136.8, 140.5, 143.9; HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{15}NO_2SF_3$ 330.0776, found 330.0774.

*N-(4-Iodobenzyl)-4-methylbenzenesulfonamide (**11**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and (4-iodophenyl)-methanol (234 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% EtOAc/petroleum ether 40−60) to give the product (326 mg, 84%) as an off-white solid: mp 135−137 °C (lit.[34] mp 135−137 °C); R_f 0.22 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.45 (3H, s), 4.08 (2H, d, *J* 6.3), 4.62 (1H, t, br, *J* 6.0), 6.95 (2H, d, *J* 8.4), 7.30 (2H, d, *J* 8.0), 7.60 (2H, d, *J* 8.3), 7.73 (2H, d, *J* 8.3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 46.9, 93.6, 127.3, 129.9, 129.9, 136.1, 137.0, 137.9, 143.9. Spectroscopic data are in accordance with the literature.[34]

*4-Methyl-N-(thiophene-3-ylmethyl)benzenesulfonamide (**12**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and thiophene-3-ylmethanol (94.3 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 150 mm silica, 20% EtOAc/petroleum ether) to give the title compound (234 mg, 87%) as a dark yellow solid: mp 108−110 °C; R_f 0.18 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3264, 1599, 1456, 1422, 1335, 1319, 1308, 1163, 1094, 1065, 874, 856, 812, 772, 706, 696, 656, 590, 552, 540, 509, 476; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.44 (3H, s), 4.16 (2H, d, *J* 6.1), 4.56 (1H, t, br, *J* 5.7), 6.89 (1H, dd, *J* 5.0, 1.1), 7.03−7.07 (1H, m), 7.24 (1H, dd, *J* 5.0, 3.0), 7.31 (2H, d, *J* 8.1), 7.75 (2H, d, *J* 8.3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 42.6, 123.1, 126.8, 127.2, 127.3, 129.9, 137.0, 137.2, 143.7; HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}NO_2S_2$ 268.0466, found 268.0470.

*N-(4-(Benzyloxy)benzyl)-4-methylbenzenesulfonamide (**13**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and (4-(benzyloxy)-phenyl)methanol (214 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 125 mm silica, 20% EtOAc/petroleum ether) to yield the title compound (342 mg, 92%) as a white solid: mp 123−126 °C; R_f 0.19 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3291, 3269, 1616, 1597, 1585, 1495, 1452, 141412, 1383, 1323, 1256, 1153, 1090, 1028, 862, 841, 812, 743, 723, 689, 565, 546, 532, 513, 492, 461; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.44 (3H, s), 4.06 (2H, d, *J* 6.1), 4.46 (1H, t, br, *J* 6.0), 5.04 (2H, s), 6.87−6.89 (2H, m), 7.09−7.12 (2H, m), 7.31−7.34 (3H, m), 7.36−7.42 (4H, m), 7.75−7.77 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 47.0, 70.2, 115.2, 127.4, 127.6, 128.2, 128.7, 128.8, 129.4, 129.9, 136.9, 137.1, 143.7, 158.7; HRMS (EI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{21}NO_3S$ 367.1242, found 367.1237.

*4-Methyl-N-(4-vinylbenzyl)benzenesulfonamide (**14**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and (4-vinylphenyl)-methanol (134 mg, 1.00 mmol) and was purified by flash column chromatography (30 × 95 mm silica, 20% EtOAc/petroleum ether 40−60) to give the title compound (240 mg, 84%) as a pale yellow solid: mp 108−110 °C (lit.[35] mp 111−113 °C); R_f 0.27 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.44 (3H, s), 4.11 (2H, d, *J* 6.2), 4.57 (1H, t, br, *J* 6.0), 5.24 (1H, dd, *J* 10.9, 0.5), 5.72 (1H, dd, *J* 17.6, 0.5), 6.67 (1H, dd, *J* 17.6, 10.9), 7.15 (2H, d, *J* 8.1), 7.30−7.33 (4H, m), 7.52−7.53 (2H, m), 7.76 (2H, d, *J* 8.3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 47.2, 114.4, 126.6, 127.3, 128.2, 129.9 135.8, 136.3, 137.0, 137.5, 143.8. Spectroscopic data are in accordance with the literature.[35]

*Benzyl 4-(((4-Methylphenyl)sulfonamido)methyl)benzoate (**15**).* The title compound was prepared according to general procedure A, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and benzyl 4-(hydroxymethyl)benzoate (242 mg, 1.00 mmol), and was purified by flash column chromatography (30 × 120 mm silica, 20% ethyl acetate/petroleum ether 40−60), followed by trituration in petroleum ether 40−60, to give the title compound (205 mg, 52%) as a white solid: mp 120−123 °C; R_f 0.11 (20% ethyl acetate/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3250, 1701, 1609, 1499, 1433, 1420, 1383, 1360, 1333, 1315, 1279, 1244, 1179, 1159, 1123, 1113, 1094, 1059, 1032, 1018, 982, 907, 883, 853, 814, 787, 762, 733, 719,708, 694, 656, 648, 583, 561, 546, 530, 519, 492,459, 419; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.42 (3H, s), 4.18 (2H, d, *J* 6.3), 4.79 (1H, t, br, *J* 6.0), 5.35 (2H, s), 7.28−7.44 (9H, m), 7.74 (2H, d, *J* 7.9), 7.97 (2H, d, *J* 8.0); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 47.0, 66.9, 127.3, 127.8, 128.3, 128.5, 129.8, 130.0, 130.2, 136.1, 136.9, 141.7, 143.9, 166.1; HRMS (AP-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{22}NO_4S$ 396.1270, found 396.1274.

*4-Methyl-N-phenethylbenzenesulfonamide (**16**).* The title compound was prepared according to general procedure B, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and 2-phenylethanol (1 mL), and was purified by flash column chromatography (45 × 115 mm silica, 5−20% EtOAc/petroleum ether 40−60), followed by trituration in petroleum ether 40−60 to give the title compound (198 mg, 72%) as a white solid: mp 59−60 °C (lit.[36] mp 62−64 °C); R_f 0.27 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.43 (3H, s), 2.76 (2H, t, *J* 6.9), 3.22 (2H, q, *J* 6.8), 4.36 (1H, t, br, *J* 5.9), 7.08 (2H, d, *J* 6.9), 7.20−7.23 (1H, m), 7.26−7.30 (4H, m), 7.39 (2H, d, *J* 8.3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.7, 35.9, 44.3, 127.0, 127.2, 128.9, 128.9, 129.9, 137.1, 137.8, 143.6. Spectroscopic data are in accordance with the literature.[37]

*4-Methyl-N-pentylbenzenesulfonamide (**17**).* The title compound was prepared according to general procedure B, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and *n*- pentanol (1 mL), and was purified by flash column chromatography (30 × 80 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (208 mg, 86%) as a yellow oil: R_f 0.31 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.83−0.85 (3H, m), 1.20−1.27 (4H, m), 1.42−1.48 (2H, m), 2.43 (3H, s), 2.93 (2H, q, *J* 7.1), 4.35 (1H, t, br, *J* 6.0), 7.31 (2H, d, *J* 8.0), 7.73−7.76 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 14.0, 21.7, 22.3, 28.8, 29.4, 43.4, 127.2, 129.8, 137.1, 143.5. Spectroscopic data are in accordance with the literature.[38]

*N-Ethyl-4-methylbenzenesulfonamide (**18**).* The title compound was prepared according to general procedure B, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and ethanol (1 mL), and was purified by flash column chromatography (30 × 150 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (68.3 mg, 34%) as a yellow oil: R_f 0.30 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.10 (3H, t, *J* 7.2), 2.43 (3H, s), 3.00 (2H, qd *J* 7.2, 6.2), 4.39 (1H, t, br, *J* 5.3), 7.31 (2H, d, *J* 7.9), 7.74−7.76 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 15.2, 21.7, 38.4, 127.3, 129.8, 137.1, 143.5. Spectroscopic data are in accordance with the literature.[39]

*N-Methyl-4-methylbenzenesulfonamide (**19**).* The title compound was prepared according to general procedure B, using *p*-toluenesulfonamide (171 mg, 1.00 mmol) and methanol (1 mL), and was purified by flash column chromatography (30 × 150 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (30.8 mg, 17%) as a white solid: mp 72−73 °C (lit.[40] mp 70−71 °C); R_f 0.28 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.43 (3H, s), 2.65 (3H, d, *J* 5.4), 4.37 (1H, d, br, *J* 3.8) 7.32 (2H, d, *J* 2.1), 7.75 (2H, d, *J* 2.1); ^{13}C{^{1}H} NMR 126 MHz, $CDCl_3$) δ_C 22.8, 29.5, 127.4, 129.9, 136.0, 143.7. Spectroscopic data are in accordance with the literature.[40]

*N-Benzylbenzenesulfonamide (**20**).* The title compound was prepared according to general procedure A, using benzenesulfonamide (157 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (232 mg, 93%) as a yellow solid: mp 77−79 °C (lit.[41] mp 78−80 °C); R_f 0.27 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.15 (2H, d, *J* 6.2), 4.75 (1H, t, br), 7.18−7.20 (2H, m), 7.24−7.30 (3H, m), 7.50−7.54 (2H, m), 7.58−7.61 (1H, m), 7.87−7.89 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 47.5, 127.3, 128.0, 128.1, 128.9, 129.3, 132.9, 136.3, 140.0. Spectroscopic data are in accordance with the literature.[41]

*N-Benzyl-3-methylbenzenesulfonamide (**21**).* The title compound was prepared according to general procedure A, using 3-methylbenzenesulfonamide (171 mg, 1.00 mmol) and benzyl alcohol

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(109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% EtOAc/petroleum ether 40−60) to give the title compound (242 mg, 93%) as a white solid: mp 46−48 °C; R_f 0.20 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3265, 1599, 1454, 1427, 1360, 1319, 1256, 1209, 1150, 1099, 1055, 916, 889, 866, 810, 783, 746, 694, 658, 584,559, 527, 511, 484, 434, 407; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.42 (3H, s), 4.15 (2H, d, J 6.2), 4.61 (1H, t, br, J 5.4), 7.19−7.21 (2H, m), 7.24−7.30 (3H, m), 7.38−7.42 (2H, m), 7.67−7.69 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.5, 47.4, 124.4, 127.6, 128.0, 128.1, 128.8, 129.1, 133.6, 136.3, 139.5, 139.8; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{14}H_{16}NO_2S$ 262.0902, found 262.0901.

*N-Benzyl-2-methylbenzenesulfonamide (**22**).* The title compound was prepared according to general procedure A, using 2-methylbenzenesulfonamide (171 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (231 mg, 86%) as an off-white solid: mp 98−100 °C (lit.[11b] mp 101.2−102.5 °C); R_f 0.27 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.62 (3H, s), 4.12 (2H, d, J 6.1), 4.67 (1H, t, br, J 4.9), 7.16−717 (2H, m), 7.24−7.34 (m, 5H), 7.47 (1H, td, J 7.5, 1.0), 8.00 (1H, d, J 7.9); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 20.4, 47.3, 126.4, 128.1, 128.2, 128.9, 129.8, 132.7, 133.0, 136.4, 137.2, 137.9. Spectroscopic data are in accordance with the literature.[11b]

*N-Benzyl-2,4,6-trimethylbenzenesulfonamide (**23**).* The title compound was prepared according to general procedure A, using 2,4,6-trimethylbenzenesulfonamide (199 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 120 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (266 mg, 92%) as a white solid: mp 94−97 °C (lit.[42] mp 96−98 °C); R_f 0.41 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.31 (3H, s), 2.64 (6H, s), 4.08 (2H, d, J 6.2), 4.64 (1H, t, br, J 5.8), 6.96 (2H, s), 7.23−7.25 (1H, m), 7.27−7.29 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 21.1, 23.1, 46.9, 128.0, 128.0, 128.8, 132.1, 133.5, 136.4, 139.3, 142.5. Spectroscopic data are in accordance with the literature.[42]

*N-Benzyl-2,4,6-triisopropylbenzenesulfonamide (**24**).* The title compound was prepared according to general procedure A, using 2,4,6-triisopropylbenzenesulfonamide (283 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% EtOAc/petroleum ether 40−60) to yield the title compound (368 mg, 99%) as a white powder: mp 83−85 °C; R_f 0.60 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3316, 2959, 2866, 1763, 1599, 1454, 1425, 1383, 1362, 1319, 1298, 1256, 1196, 1152, 1105, 1057, 968, 941, 916, 889, 862, 810, 746, 694, 658, 627, 594, 559, 546, 529, 509, 436, 419; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.27 (18 H, t, J 6.9), 2.92 (1H, dt, J 13.9, 6.9), 4.15−4.21 (4H, m), 4.51 (1H, t, br, J 6.1), 7.18 (2H, s), 7.19−7.21 (2H, m), 7.27−7.30 (3H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 23.8, 25.0, 29.9, 34.3, 47.2, 124.0, 128.1, 128.2, 128.9, 132.4, 136.6, 150.5, 153.0; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{22}H_{32}NO_2S$ 374.2154, found 374.2153.

*N-Benzylnaphthalene-1-sulfonamide (**25**).* The title compound was prepared according to general procedure A, using naphthalene-1-sulfonamide (207 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 110 mm silica, 20% EtOAc/petroleum ether 40−60) to give the title compound (251 mg, 84%) as a white solid: mp 165−166 °C (lit.[31] mp 166−168 °C); R_f 0.30 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.08 (2H, d, J 6.1), 4.82 (1H, t, br, J 5.9), 7.05−7.07 (2H, m), 7.16−7.19 (3H, m), 7.53 (1H, dd, J 8.1, 7.5), 7.60−7.63 (1H, m), 7.65−7.69 (1H,m), 7.96 (1H, d, J 8.1), 8.07 (1H, d, J 8.2), 8.28 (1H, dd, J 7.3, 1.2), 8.65 (1H, d, J 8.6); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 47.5, 124.3, 124.4, 127.0, 127.9, 128.0, 128.3, 128.6, 128.7, 129.3, 130.1, 134.4, 134.5, 134.5, 136.2. Spectroscopic data are in accordance with the literature.[31]

*N-Benzylnaphthalene-2-sulfonamide (**26**).* The title compound was prepared according to general procedure A, using naphthalene-2-sulfonamide (207 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol) and was purified by flash column chromatography (30 × 105 mm silica, 20% EtOAc/petroleum ether 40−60) to give the title compound (270 mg, 91%) as an off-white solid: mp 121−122 °C (lit.[10a] mp 126.5 °C); R_f 0.28 (20% EtOAc/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.18 (2H, d, J 6.2), 4.77 (1H, t, br, 5.9), 7.18−7.25 (5H, m), 7.61−7.68 (2H, m), 7.84 (1H, dd, J 8.7, 1.9), 7.92 (1H, d, J 8.1), 7.96−7.98 (2H, m), 8.45 (2H, d, J 1.2); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 47.6, 122.4, 127.8, 128.0, 128.1, 128.2, 128.8, 128.9, 129.0, 129.4, 129.8, 132.3, 135.0, 136.2, 136.8. Spectroscopic data are in accordance with the literature.[10a]

*N-Benzyl-4-methoxybenzenesulfonamide (**27**).* The title compound was prepared according to general procedure A, using *p*-methoxybenzenesulfonamide (187 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol) and was purified by flash column chromatography (30 × 100 mm silica, 20−40% ethyl acetate/petroleum ether 40−60) to give the title compound (255 mg, 92%) as an off-white solid; mp 109−111 °C (lit.[9d] mp 112−113 °C); R_f 0.35 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 3.88 (3H, s), 4.12 (2H, d, J 6.2), 4.63 (1H, t, br, J 6.0), 6.96−6.99 (2H, m), 7.18−7.21 (2H, m), 7.24−7.30 (3H, m), 7.80−7.83 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 47.4, 55.8, 114.4, 128.0, 128.1, 128.9, 129.5, 131.6, 136.4, 163.1. Spectroscopic data are in accordance with the literature.[9d]

*N-Benzyl-4-(trifluoromethyl)benzenesulfonamide (**28**).* The title compound was prepared according to general procedure B, using 4-(trifluoromethyl)benzenesulfonamide (225 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and purified by flash column chromatography (45 × 150 mm silica, 10% EtOAc/petroleum ether 40−60), then triturated in petroleum ether 40−60 to yield the product (193 mg, 61%) as an off-white solid: mp 119−121 °C; R_f 0.21 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3271, 1404, 1323, 1157, 1130, 1111, 1094, 1061, 1028, 1013, 907,876, 841, 733, 712, 696, 613, 598, 532, 488, 453, 430; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.21 (2H, d, J 8.1), 4.76 (1H, t, br, J 5.8), 7.16−7.18 (2H, m), 7.27−7.30 (3H, m), 7.75 (2H, d, J 8.2), 7.96 (2H, d, J 8.2); ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ_F −63.16; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 475, 123.4 (q, J 273), 126.4 (q, J 3.7), 127.7, 128.0, 128.2, 128.9, 134.5 (q, J 33.1), 1235.8, 143.8; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{14}H_{13}NO_2SF_3$ 316.0619, found 316.0623.

*N-Benzyl-4-bromobenzenesulfonamide (**29**).* The title compound was prepared according to general procedure A, using 4-bromobenzenesulfonamide (236 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 150 mm silica, 20% EtOAc/petroleum ether 40−60) to give the title compound (288 mg, 88%) as a white solid: mp 117−118 °C (lit.[11b] mp 119−120 °C); R_f 0.32 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.13 (2H, d, J 6.1), 5.11 (1H, t, br, J 5.3), 7.16−7.17 (2H, m), 7.25−7.26 (3H, m), 7.60 (2H, d, J 8.2), 7.68 (2H, d, J 8.2); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 47.4, 127.7. 128.0, 128.1, 128.8, 128.8, 132.5, 132.5, 136.0, 139.1. Spectroscopic data are in accordance with the literature.[11b]

*N-Benzylthiophene-2-sulfonamide (**30**).* The title compound was prepared according to general procedure A, using 2-thiophenesulfonamide (163 mg, 1.00 mmol) and benzyl alcohol (104 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 100 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (186 mg, 73%) as a yellow solid: mp 69−71 °C (lit.[9e] mp 70−72 °C; R_f 0.20 (20% ethyl acetate/petroleum ether 40−60); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.22 (2H, d, J 5.8), 4.94 (1H, s, br), 7.08 (1H, s), 7.22−7.30 (5 H, m) 7.59−7.61 (2H, m); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 47.7, 127.6, 128.1, 128.3, 129.0, 132.2, 132.6, 136.0, 141.0. All spectroscopic data are in accordance with the literature.[9e]

*N-Benzyl-4-(benzyloxy)benzenesulfonamide (**31**).* The title compound was prepared according to general procedure A, using 4-(benzyloxy)benzenesulfonamide (263 mg) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 95 mm silica, 20% EtOAc/petroleum ether 40−60) to give the

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J. Org. Chem. 2019, 84, 3715−3724

title compound (315 mg, 99%) as an off-white solid: mp 131−132 °C; R_f 0.22 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3265, 1593, 1576, 1497, 1452, 1425, 1321, 1250, 1152, 1094, 1047, 993, 862, 840, 829, 810, 752, 656, 608, 590, 511, 455, 407; ^1H NMR (500 MHz, $CDCl_3$) δ_H 4.13 (2H, d, *J* 6.2), 4.60 (1H, t, br, *J* 6.1), 5.14 (2H, s), 7.05 (2H, d, *J* 8.7), 7.19−7.20 (2H, m), 7.19 (2H, d, *J* 6.6), 7.24−7.28 (2H, m), 7.35−7.43 (5H, m) 7.81 (2H, d, *J* 8.7); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 47.4, 70.4, 115.2, 127.6, 128.0, 128.0, 128.5, 128.8, 128.9, 129.4, 131.7, 135.9. 136.4, 162.1; HRMS (EI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{20}NO_3S$ 354.1164, found 354.1159.

*N-Benzyl-4-vinylbenzenesulfonamide (**32**).* The title compound was prepared according to general procedure A, using 4-vinylbenzenesulfonamide (183 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and purified by flash column chromatography (30 × 95 mm silica, 20% EtOAc/petroleum ether 40−60) to give the title compound (191 mg, 72%) as a white solid: mp 85−87 °C; R_f 0.30 (20% EtOAc/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3267, 1597, 1495, 1456, 1437, 1395, 1319, 1310, 1153, 1055, 1028, 986, 914, 868, 841, 731, 696, 654, 594, 563, 529, 484, 449, 411; ^1H NMR (500 MHz, $CDCl_3$) δ_H 4.14 (2H, d, *J* 6.2), 4.71 (1H, t, br, *J* 5.9), 5.44 (1H, d, *J* 10.9), 5.89 (1H, d, *J* 17.6), 6.76 (1H, dd, *J* 17.6, 10.9), 7.20 (2H, d, *J* 7.32), 7.19−7.30 (3H, m), 7.52 (2H, d, *J* 8.2), 7.82 (2H, d, *J* 8.3); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 47.5, 177.6, 126.9, 127.6, 128.0, 128.1, 128.9, 135.5, 136.3, 138.8, 142.1; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{16}NO_2S$ 274.0902, found 274.0903.

*N-Benzylmethanesulfonamide (**33**).* The title compound was prepared according to general procedure A, using methane sulfonamide (95.1 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 105 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (158 mg, 85%) as an off-white solid: mp 58−61 °C (lit.[43] mp 57−60 °C); R_f 0.29 (20% ethyl acetate/petroleum ether 40−60); ^1H NMR (500 MHz, $CDCl_3$) δ_H 2.88 (3H, s), 4.34 (2H, d, *J* 6.1), 4.58 (1H, s, br), 7.31−7.40 (5H, m); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 41.3, 47.4, 128.1, 128.3, 129.1, 136.8. Spectroscopic data are in accordance with the literature.[43]

*N-Benzylethanesulfonamide (**34**).* The title compound was prepared according to general procedure A, using ethane sulfonamide (109 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 105 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (165 mg, 83%) as a white solid: mp 58−59 °C; R_f 0.31 (20% ethyl acetate/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3287, 1456, 1429, 1314, 1283, 1227, 1130, 1055, 993, 854, 779, 758, 718, 704, 640, 584, 538, 517, 496, 444; ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.33 (3H, t, *J* 7.4), 2.97 (2H, q, *J* 7.4), 4.31 (2H, d, *J* 6.1), 4.46 (1H, s, br), 7.30−7.39 (5H, m); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 8.4, 47.4, 47.8, 128.0, 128.3, 129.0, 137.1; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_9H_{14}NO_2S$ 200.0745, found 200.0740.

*N-Benzylcyclopropanesulfonamide (**35**).* The title compound was prepared according to general procedure A, using cyclopropane sulfonamide (121 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 105 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (184 mg, 87%) as a white solid: mp 62−64 °C (lit.[10a] mp 62.3 °C); R_f 0.30 (20% ethyl acetate/petroleum ether 40−60); ^1H NMR (500 MHz, $CDCl_3$) δ_H 0.88−0.92 (2H, m), 1.10−1.14 (2H, m), 2.32 (1H, tt, *J* 8.0, 4.9), 4.32 (2H d, *J* 6.2), 4.89 (1H, t, br, *J* 5.6), 7.28−7.36 (5H, m); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 5.6, 30.7, 47.5, 127.9, 128.2, 129.0, 137.2. Spectroscopic data are in accordance with the literature.[10a]

*N-Benzyl-2-methylpropane-2-sulfonamide (**36**).* The title compound was prepared according to general procedure A, using *tert*-butyl sulfonamide (137 mg, 1.00 mmol) and benzyl alcohol (109 μL, 1.00 mmol), and was purified by flash column chromatography (30 × 110 mm silica, 20% ethyl acetate/petroleum ether 40−60) to give the title compound (215 mg, 95%) as a white solid: mp 125−126 °C; R_f 0.32 (20% ethyl acetate/petroleum ether 40−60); ν_{max}/cm^{-1} (film) 3283, 1497, 1474, 1447, 1296, 1202, 1119, 1092, 1070, 1026, 1007, 903, 868, 731, 693, 662, 615, 592, 521, 509, 459; ^1H NMR (500 MHz, $CDCl_3$) δ_H 1.44 (9H, s), 4.08 (1H, t, br, *J* 5.0), 4.37 (2H, d, *J* 6.0) 7.29−7.33 (1H, m), 7.34−7.38 (4H, m); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ_C 24.5, 48.8, 63.2, 127.9, 128.1, 129.0, 137.8; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{18}NO_2S$ 228.1058, found 228.1063.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b00203.

Optimization data and spectral data (PDF)

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Notes

The authors declare no competing financial interest.

Information about the data that underpins the results presented in this article, including how to access them, can be found in the Cardiff University data catalogue at http://doi.org/10.17035/d.2019.0069100566 (accessed February 21, 2019).

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