SUPPORTING INFORMATION

Copper-Catalyzed Amidation of Allylic and Benzylic C–H Bonds

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**Experimental procedures, characterization data and NMR spectra
(59 pages)**

General Experimental:

All reactions were run under a nitrogen atmosphere with exclusion of moisture from reagents and glassware using standard techniques¹. Analytical thin-layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel (Merck 60 F₂₅₄). Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, ninhydrin or aqueous potassium permanganate. For purification, column chromatography was performed using 230-400 mesh ultra pure silica gel (Silicycle or EMD Chemicals). Celite 545® powder was purchased from Fisher Scientific.

¹H and ¹³C NMR spectra are recorded using a Bruker Advance 400 MHz and signals are represented in parts per million from tetramethylsilane with the solvent resonance used as the internal standard [CD₃OD: ¹H NMR δ = 4.88 ppm (singlet) and 3.31 ppm (quintet); ¹³C NMR δ = 48.0 ppm (heptet); CDCl₃: ¹H NMR δ = 7.26 ppm (singlet); ¹³C NMR δ = 77.0 ppm (triplet); (CD₃)₂SO: ¹H NMR δ = 2.50 ppm (quintet); ¹³C NMR δ = 40.0 ppm (heptet)]. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sx = sextet, h = heptet, m = multiplet and br = broad), coupling constant (in Hz) and integration. All ¹³C NMR spectra were obtained with complete proton decoupling. High-resolution mass spectra were performed by the McGill University's Chemistry Department using a Kratos MS25RFA high-resolution mass spectrometer equipped with a gas chromatograph. Optical rotations were determined with a Perkin-Elmer 241 polarimeter at 589 nm. Data are reported as follows: $[\alpha]_D^{23}$ (observed rotation/[length (dm) x mass (g)/volume (mL)]), concentration (*c* in g/100 mL), and solvent. Infrared spectra were obtained on a Nexus 470 FT-IR on NaCl plates (film) or as a KBr plate. Melting points were obtained by using a Mettler FP61 melting point apparatus and are uncorrected.

¹ Shriver, D. F.; Drezzdon, M. A. *The Manipulation of Air-sensitive Compounds*, 2nd Edition, Wiley: New York, 1986.

² Reetz, T. M.; Westermann, J.; Kyung, S.-H. *Chem. Ber.* **1985**, *118*, 1050-1057.

³ Inazu, T.; Yoshino, T. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 647-652.

Reagents:

Molecular sieves (4 Å beads) were obtained from Aldrich Chemical Company and were pre-dried in an oven at 140 °C for 3 days before proceeding to the experiments described below. Anhydrous 1,2-dichloroethane was purchased from Aldrich in sure-seal containers and was used without further purification. The indane and the copper (II) triflate were purchased from Aldrich. The indane was distilled under a reduced pressure of 0.80 mbar before use (bp 92 °C) and stored at 0 °C. The copper (II) triflate was pre-dried to a white free-flowing solid before use. Commercial copper (II) triflate was placed into a round-bottom flask and the contents placed under reduced pressure (1.0 mbar). The flask was heated with the aid of a heating mantle to 100° C under reduced pressure (1.0 mbar) for 3-4 h, then cooled to room temperature and transferred to vials which were stored in a desiccator. 1,1-Dimethylindane was prepared according to a literature procedure.² Ethyl 4-benzylbenzoate was prepared according to the literature.³ The following chemicals were purchased and used as received: *tert*-Butylperacetate 75% wt in aliphatic hydrocarbons (Aldrich), 1,10-Phenanthroline (Aldrich), Benzenesulfonamide (Aldrich), *N*-Methylbenzenesulfonamide (TCI-America), 2-Carbomethoxybenzenesulfonamide (Lancaster Synthesis), 4-Chlorobenzenesulfonamide (Aldrich), 4-Fluorobenzenesulfonamide (OmegaChem), 4-Methoxybenzenesulfonamide (Lancaster Synthesis), 3-(Trifluoromethyl)benzenesulfonamide (OmegaChem), 2-Thiophenesulfonamide (OmegaChem), (1*R*)-(+)-2,10-Camphor-sultam (Aldrich), 1,2,3,4-Tetrahydronaphtalene (Anachemia), Cyclohexene (Aldrich), Diphenylmethane (Aldrich), Adamantane (Aldrich), Ethylbenzene (Aldrich), 1-Bromo-4-ethylbenzene (Lancaster Synthesis), 4-Ethylaniline (Lancaster Synthesis), Benzoyl chloride (Aldrich), Potassium carbonate (Aldrich) and Diphenylmethane-4-carboxylic acid (Matrix Scientific).

General procedure for the copper-catalyzed amidation of hydrocarbons with sulfonamides:

NOTE: Appropriate care should be exercised when heating the tert-butylperacetate oxidant in the presence of a transition metal; proper ventilation and safety shielding should be utilized for all reactions. However, we experienced no corresponding safety concerns for this reaction during our investigations. Approximately 25 beads of pre-dried 4 Å molecular sieves were placed into a flame-dried round bottom-flask equipped with a magnetic stirbar. 1,10-phenanthroline (27 mg, 0.15 mmol, 5 mol %) and anhydrous Cu(OTf)₂ (54 mg, 0.15 mmol, 5 mol %) were added to the flask followed by the addition of 1,2-dichloroethane (2.25 mL). The resulting mixture was stirred for 15 minutes to complex the copper with the 1,10-phenanthroline, affording a blue-green suspension. The sulfonamide (3.00 mmol, 1 equiv) and the hydrocarbon (9.00 mmol, 3 equiv) were then added to the reaction mixture. The mixture was heated an oil bath at 60 °C or 80 °C depending on the hydrocarbon species employed. The tert-butylperacetate (75 wt % in aliphatic hydrocarbons, 4.50 mmol, 896 µL, 1.5 equiv) was added dropwise to the mixture via a syringe pump over 6 hours. After 3 hours of stirring, a second addition of Cu(OTf)₂ (54 mg, 0.15 mmol, 5 mol %) was added to the flask. The reaction was stopped after all of the oxidant was added. The resulting mixture was poured onto a pad of Celite on a sintered glass funnel and washed with Et₂O. The filtrate was then concentrated under reduced pressure. The crude residue was purified by column chromatography through silica gel to afford the desired products.

***N*-(2,3-Dihydro-1*H*-inden-1-yl)benzenesulfonamide (Table 2, entry 1).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 15% ethyl acetate in hexanes afforded the desired aminoindan derivative as a pale yellow solid (597 mg, 73%). mp 118-119 °C; R_f = 0.26 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.97 (d, J = 8.0 Hz, 2H), 7.69-7.59 (m, 3H), 7.18-7.05 (m, 4H), 4.79 (t, J = 8.0 Hz, 1H), 2.89 (ddd, J = 16.0, 8.0, 3.5 Hz, 1H), 2.71 (dt, J = 16.0, 8.0 Hz, 1H), 2.21-2.13 (m, 1H), 1.69 (dq, J = 13.0, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 142.6, 142.4, 142.1, 132.2, 128.9, 127.6, 126.6, 126.2, 124.2, 123.8, 58.4, 33.7, 29.4; FTIR (KBr) ν 3309, 2939, 1685, 1446, 1333, 1158, cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{NH}_4]^+$: 291.1162, found: 291.1161.

***N*-(2,3-Dihydro-1*H*-inden-1-yl)-*N*-methylbenzenesulfonamide (Table 2, entry 2).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes, afforded the desired aminoindan derivative as a pale yellow oil (672 mg, 78%); R_f = 0.42 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.96-7.95 (m, 2H), 7.73-7.62 (m, 3H), 7.22 (d, J = 4.0 Hz, 2H), 7.19-7.11 (m, 1H), 6.90 (d, J = 7.5 Hz, 1H), 5.58 (t, J = 7.5 Hz, 1H), 2.92-2.76 (m, 2H), 2.53 (s, 3H), 2.12-2.04 (m, 1H), 1.73-1.64 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 143.2, 139.8, 139.7, 132.6, 129.1, 128.0, 127.0, 126.4, 124.6, 124.0, 62.8, 29.8, 27.9, 27.0; FTIR (NaCl) ν 2951, 1585, 1446, 1332, 1152, 960 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$ $[\text{M}+\text{NH}_4]^+$: 305.1318, found 305.1319.

***N*-(2,3-Dihydro-1*H*-inden-1-yl)-4-methoxybenzenesulfonamide (Table 2, entry 3).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% toluene to 4% ethyl acetate in toluene afforded the desired aminoindan derivative as a yellow solid (547 mg, 60%). mp 139-140 °C; R_f = 0.28 (10% ethyl acetate in toluene); ^1H NMR (400 MHz, CD_3OD) δ 7.89 (d, J = 8.5 Hz, 2H), 7.17-7.10 (m, 6H), 4.74 (t, J = 7.5 Hz, 1H), 3.90 (s, 3H), 2.88 (ddd, J = 16.0, 8.0, 3.5 Hz, 1H), 2.70 (dt, J = 16.0, 8.0 Hz, 1H), 2.20-2.12 (m, 1H), 1.74-1.64 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 163.0, 142.5, 133.5, 128.8, 127.5, 126.2, 124.2, 123.9, 113.9, 58.3, 54.8, 33.8, 29.4 (1 aromatic C not observed); FTIR (KBr) ν 3248, 3072, 2938, 1595, 1438, 1324, 1260, 1162, 1030 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_3\text{S}$ $[\text{M}+\text{NH}_4]^+$: 321.1267, found 321.1267

***N*-(2,3-Dihydro-1*H*-inden-1-yl)-4-chlorobenzenesulfonamide (Table 2, entry 4).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 15% ethyl acetate in hexanes afforded the desired aminoindan derivative as a yellow solid (654 mg, 71%). mp 147-148 °C; R_f = 0.17 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.95-7.91 (m, 2H), 7.63-7.60 (m, 2H), 7.18-7.10 (m, 4H), 4.80 (t, J = 7.5 Hz, 1H), 2.89 (ddd, J = 16.0, 8.5, 4.0 Hz, 1H), 2.72 (dt, J = 16.0, 8.5 Hz, 1H), 2.24-2.14 (m, 1H), 1.74 (dq, J = 13.0, 8.5 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 142.6, 142.3, 141.0, 138.3, 129.1, 128.4, 127.7, 126.2, 124.2, 123.8, 58.4, 33.7, 29.4; FTIR (KBr) ν 3266, 3085, 2966, 1584, 1438, 1328, 1163, 1095, 830, 754 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{15}\text{H}_{18}\text{ClN}_2\text{O}_2\text{S}$ $[\text{M}+\text{NH}_4]^+$: 325.0772, found 325.0772.

***N*-(2,3-Dihydro-1*H*-inden-1-yl)-4-fluorobenzenesulfonamide (Table 2, entry 5).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 15% ethyl acetate in hexanes afforded the desired aminoindan derivative as a yellow solid (605 mg, 69%). mp 146-147 °C; R_f = 0.20 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 8.03-7.98 (m, 2H), 7.36-7.31 (m, 2H), 7.21-7.09 (m, 4H), 4.79 (t, J = 7.5 Hz, 1H), 2.89 (ddd, J = 16.0, 8.5, 3.5 Hz, 1H), 2.72 (dt, J = 16.0, 8.5 Hz, 1H), 2.19 (ddt, J = 13.0, 8.5, 3.5 Hz, 1H), 1.70 (dq, J = 13.0, 8.5 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 165.0 (d, J = 252 Hz, $J_{\text{C-F}}$), 142.4 (d, J = 23 Hz, $J_{\text{C-F}}$), 138.4 (d, J = 4 Hz, $J_{\text{C-F}}$), 129.5 (d, J = 9 Hz, $J_{\text{C-F}}$), 127.6, 126.2, 124.2, 123.8, 116.0, 115.7, 58.4, 33.7, 29.4; FTIR (KBr) ν 3258, 3069, 2969, 1593, 1498, 1323, 1038 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{15}\text{H}_{18}\text{FN}_2\text{O}_2\text{S}[\text{M}+\text{NH}_4]^+$: 309.1068, found 309.1067.

***N*-(2,3-Dihydro-1*H*-inden-1-yl)-3-(trifluoromethyl)benzenesulfonamide (Table 2, entry 6).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminoindan derivative as a yellow oil (716 mg, 69%). R_f = 0.19 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 8.22-8.20 (m, 2H), 7.98 (d, J = 8.0 Hz, 1H), 7.82 (t, J = 8.0 Hz, 1H), 7.19-7.05 (m, 4H), 4.83 (t, J = 7.5 Hz, 1H), 2.90 (ddd, J = 16.0, 8.0, 4.0 Hz, 1H), 2.73 (dt, J = 16.0, 8.0 Hz, 1H), 2.19 (ddt, J = 13.0, 8.0, 4.0 Hz, 1H), 1.71 (dq, J = 13.0, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 143.7, 142.6, 142.1, 131.2 (q, J = 33 Hz, $J_{\text{C-F}}$),

130.3, 130.2, 128.6 (q, $J = 4$ Hz, $J_{\text{C-F}}$), 127.7, 126.2, 124.9 (q, $J = 272$ Hz, $J_{\text{C-F}}$), 124.3, 123.8, 123.4 (q, $J = 4$ Hz, $J_{\text{C-F}}$), 58.5, 33.7, 29.4; FTIR (KBr) ν 3282, 1065, 2985, 2948, 1610, 1402, 1140, 982 cm^{-1} ; HRMS (ESI-) m/z calcd for $\text{C}_{16}\text{H}_{13}\text{F}_3\text{NO}_2\text{S} [\text{M-H}]^-$: 340.0625, found: 340.0620.

Methyl-2-[(2,3-dihydro-1H-inden-1-yl)sulfonyl]benzoate (Table 2, entry 7).

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 20% ethyl acetate in hexanes afforded the desired aminoindan derivative as a yellow oil (755 mg, 76%). $R_f = 0.84$ (50% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 8.13-8.08 (m, 1H), 7.79-7.67 (m, 3H), 7.18-7.09 (m, 4H), 4.87-4.84 (m, 1H), 3.93 (s, 3H), 2.87 (ddd, $J = 16.0, 8.0, 3.5$ Hz, 1H), 2.70 (dt, $J = 16.0, 8.0$ Hz, 1H), 2.24-2.16 (m, 1H), 1.76 (dq, $J = 13.0, 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.5, 142.7, 142.1, 139.7, 132.4, 131.4, 131.2, 129.7, 128.9, 127.8, 126.3, 124.4, 123.7, 58.8, 52.5, 33.7, 29.5; FTIR (NaCl) ν 3311, 3020, 2956, 1722, 1215, 1168 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_4\text{S} [\text{M}+\text{NH}_4]^+$: 349.1217, found 349.1217.

N-(2,3-Dihydro-1H-inden-1-yl)thiophen-2-sulfonamide (Table 2, entry 8).

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminoindan derivative as a white solid (561 mg, 67%). mp 102-103 $^{\circ}\text{C}$; $R_f = 0.40$ (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.82 (dd, $J = 5.0, 1.5$ Hz, 1H), 7.70 (dd, $J = 4.0, 1.5$ Hz, 1H), 7.21-7.09 (m, 5H), 4.85 (t, $J = 7.5$ Hz, 1H), 2.93 (ddd, $J = 16.0, 8.0, 4.0$ Hz, 1H), 2.76 (dt, $J = 16.0, 8.0$ Hz, 1H), 2.28 (ddt, $J = 13.0, 8.0, 4.0$ Hz, 1H),

1.78 (dq, $J = 13.0, 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 143.1, 142.6, 142.3, 131.6, 131.4, 127.6, 127.2, 126.2, 124.2, 123.9, 58.7, 33.6, 29.4; FTIR (KBr) ν 3250, 3087, 2998, 1443, 1336, 1155, 1016, 589 cm^{-1} ; HRMS (ESI-) m/z calcd for $\text{C}_{13}\text{H}_{12}\text{NO}_2\text{S}_2$ $[\text{M}-\text{H}]^-$: 278.0315, found 278.0313.

2,3-Dihydro-1*H*-inden-1-yl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-3,3-dioxide
(Table 2, entry 9).

The general procedure for the copper-catalyzed amidation was followed, using (1*R*)-(+)-2,10-camphorsultam as the starting material. ^1H NMR analysis of the crude reaction mixture revealed a 1:1 mixture of diastereomers as determined by the height of the peaks at 5.19 and 5.24 ppm. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the two camphorsultam diastereoisomers **B** and **C** as white solids (271 mg for **B**, 312 mg for **C** and 272 mg of mixed fractions **B**+**C**, 86% combined yield). The stereochemistries of these compounds were assigned based on the X-ray crystal structure of the more polar diastereomer **C**.

(1*R*,5*S*,7*S*)-4-[(1*S*)-2,3-Dihydro-1*H*-inden-1-yl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-3,3-dioxide (B**, less polar diastereomer).**

mp 130-131 $^{\circ}\text{C}$; $R_f = 0.28$ (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, $J = 7.5$ Hz, 1H), 7.31-7.23 (m, 3H), 5.19 (dd, $J = 8.5, 3.5$ Hz, 1H), 3.22-3.02 (m, 4H), 2.89 (ddd, $J = 16.0, 9.0, 3.5$ Hz, 1H), 2.51-2.41 (m, 1H), 2.36-2.28 (m, 1H), 1.88-1.70 (m, 4H), 1.37 (dt, $J = 10.5, 2.5$ Hz, 1H), 1.19 (s, 3H), 1.16-1.08 (m, 1H), 0.95-0.92 (m, 1H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 144.9, 138.6, 128.5, 127.2, 126.4, 124.9, 64.4, 58.0, 49.4(5), 49.4(0), 47.8, 44.8, 36.2, 32.5, 31.8, 30.7, 26.6, 20.4, 20.1; $[\alpha]_{\text{D}}^{23} +1.6^{\circ}$ ($c = 0.75$, CHCl_3); FTIR (KBr) ν 3020, 2926, 1732, 1455, 1303, 1218, 1126, 753 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_2\text{SNa}$ $[\text{M}+\text{Na}]^+$: 354.1498, found 354.1496.

(1*R*,5*S*,7*S*)-4-[(1*R*)-2,3-Dihydro-1*H*-inden-1-yl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-3,3-dioxide (C, more polar diastereomer).

The solid could be further purified by recrystallization in EtOAc/Et₂O. mp 220-221 °C; *R*_f = 0.22 (20% ethyl acetate in hexanes); ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 7.5 Hz, 1H), 7.29-7.20 (m, 3H), 5.24 (dd, *J* = 8.5, 4.0 Hz, 1H), 3.34 (t, *J* = 6.5 Hz, 1H), 3.20-3.12 (m, 2H), 3.09-2.91 (m, 2H), 2.53-2.45 (m, 1H), 2.38-2.28 (m, 1H), 1.90-1.77 (m, 2H), 1.62-1.60 (m, 1H), 1.51-1.46 (m, 1H), 1.23-1.16 (m, 1H), 1.13-1.11 (m, 2H), 1.08 (s, 3H), 0.89 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 143.5, 141.4, 128.4, 126.7, 125.4, 124.8, 62.9, 57.5, 49.6, 48.8, 47.7, 44.7, 35.3, 32.7, 31.3, 26.7, 26.1, 20.2, 20.1; [α]_D²³ -13.0° (*c* = 0.50, CHCl₃); FTIR (KBr) ν 3020, 2926, 1732, 1455, 1303, 1218, 1126, 753 cm⁻¹; HRMS (ESI+) *m/z* calcd for C₁₉H₂₅NO₂SNa [M+Na]⁺: 354.1498, found 354.1496. CCDC 622779 contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. A perspective view of the X-ray crystal structure is found at the end of the supporting information.

***N*-(3,3-Dimethyl-2,3-dihydro-1*H*-inden-1-yl)-*N*-methylbenzenesulfonamide (Table 3, entry 1).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminoindan derivative as a yellow solid (595 mg, 63%). mp

100-101 °C; R_f = 0.50 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.96-7.94 (m, 2H), 7.74-7.63 (m, 3H), 7.27-7.12 (m, 3H), 6.81 (d, J = 7.5 Hz, 1H), 5.63 (t, J = 8.5 Hz, 1H), 2.57 (s, 3H), 1.89 (dd, J = 13.0, 8.5 Hz, 1H), 1.66 (dd, J = 13.0, 8.5 Hz, 1H), 1.31 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 151.5, 139.7, 138.4, 132.6, 129.1, 128.3, 126.9, 126.6, 123.6, 122.2, 60.8, 42.9, 41.4, 29.2, 27.9, 27.6; FTIR (KBr) ν 962, 2867, 1479, 1446, 1337, 1151 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{SNa}$ $[\text{M}+\text{Na}]^+$: 338.1185, found 338.1183.

N-Methyl-(1,2,3,4-tetrahydronaphthalen-1-yl)benzenesulfonamide (Table 3, entry 2).

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminonaphthalen derivative as a white solid (488 mg, 54%). mp 99-100 °C; R_f = 0.45 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.94 (d, J = 8.0 Hz, 2H), 7.72-7.62 (m, 3H), 7.13-7.08 (m, 4H), 5.19 (t, J = 7.5 Hz, 1H), 2.78-2.68 (m, 2H), 2.60 (s, 3H), 1.93-1.87 (m, 1H), 1.77-1.65 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 140.4, 138.5, 134.2, 132.5, 129.1, 128.9, 127.0, 126.9, 126.7, 125.8, 56.9, 28.8, 28.6, 26.6, 21.5; FTIR (KBr) ν 3057-2868, 1447, 1332, 1154, 1088, 977 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_2\text{SNa}$ $[\text{M}+\text{Na}]^+$: 324.1029, found 324.1025.

N-Cyclohex-2-en-1-ylbenzenesulfonamide (Table 3, entry 3).

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminocyclohexene derivative as a beige solid (538 mg, 75%).

mp 62-64 °C; R_f = 0.18 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.90 (d, J = 7.5 Hz, 2H), 7.58-7.47 (m, 3H), 5.69-5.64 (m, 1H), 5.26-5.22 (m, 1H), 3.74 (br, 1H), 1.94-1.80 (m, 2H), 1.66-1.56 (m, 2H), 1.49-1.41 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 142.1, 132.1, 130.2, 128.8, 127.3, 126.5, 48.9, 29.9, 24.1, 19.3; FTIR (NaCl) ν 3382, 3278, 3020, 2929, 1611, 1447, 1328, 1215, 1161 cm^{-1} ; HRMS (ESI-) m/z calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_2\text{S}$ $[\text{M}-\text{H}]^-$: 236.0751, found 236.0748.

***N*-Cyclohex-2-en-1-yl-*N*-methylbenzenesulfonamide (Table 3, entry 4).**

The general procedure for the copper-catalyzed amidation was followed. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminocyclohexene derivative as a colorless oil (456 mg, 61%). R_f = 0.47 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.85 (d, J = 7.5 Hz, 2H), 7.67-7.57 (m, 3H), 5.81 (dd, J = 10.5, 3.5 Hz, 1H), 5.07 (d, J = 10.5 Hz, 1H), 4.56-4.53 (br, 1H), 2.72 (s, 3H), 1.99-1.88 (m, 2H), 1.74-1.48 (m, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 140.0, 132.5, 132.4, 129.1, 126.8, 126.6, 54.3, 28.5, 26.4, 24.0, 21.1; FTIR (NaCl) ν 3020, 2943, 1586, 1447, 1331, 1216, 1167 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2\text{SK}$ $[\text{M}+\text{K}]^+$: 290.0612, found 290.0613.

***N*-(Diphenylmethyl)-*N*-methylbenzenesulfonamide (Table 3, entry 5).**

The general procedure for the copper-catalyzed amidation was followed, except the reaction was conducted at 80 °C. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes, afforded the desired aminodiphenylmethane derivative as a yellow oil (502 mg, 50%); R_f = 0.43 (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.79 (d, J = 7.5 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.52

(t, $J = 7.5$ Hz, 2H), 7.31-7.25 (m, 6H), 7.11-7.04 (m, 4H), 6.42 (s, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 139.7, 138.4, 132.4, 128.8, 128.5, 128.1, 127.4, 126.9, 64.3, 30.7; FTIR (NaCl) ν 3065, 3020, 1447, 1341, 1216, 1163, 959 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{SNa}$ $[\text{M}+\text{Na}]^+$: 360.1029, found 360.1025.

Ethyl 4-[(methyl(phenylsulfonyl)amino)phenylmethyl]benzoate (Table 3, entry 6).

The general procedure for the copper-catalyzed amidation was followed, except the reaction was conducted at 80 °C. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminodiphenylmethane derivative as a white solid (571 mg, 47%). mp 120-121 °C; $R_f = 0.26$ (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.96-7.94 (m, 2H), 7.82-7.80 (m, 2H), 7.66-7.62 (m, 1H), 7.56-7.52 (m, 2H), 7.31-7.21 (m, 5H), 7.03-7.01 (m, 2H), 6.48 (s, 1H), 4.38 (q, $J = 7.0$ Hz, 2H), 2.73 (s, 3H), 1.40 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 166.2, 144.1, 139.6, 137.7, 132.5, 129.6, 129.1, 128.9, 128.7, 128.3, 128.2, 127.7, 126.9, 64.1, 60.8, 30.7, 13.2; FTIR (KBr) ν 3061, 2939, 1709, 1610, 1343, 1288, 1164, 1104, 963 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{23}\text{H}_{23}\text{NO}_4\text{SNa}$ $[\text{M}+\text{Na}]^+$: 432.1240, found 432.1238.

N-(1-Phenylethyl)benzenesulfonamide (Table 3, entry 7).

The general procedure for the copper-catalyzed amidation was followed, except the reaction was conducted at 80 °C. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminoethylbenzene derivative as a yellow solid (467 mg, 60%). mp 103-104 °C; $R_f = 0.31$ (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.70 (d, $J = 7.5$ Hz, 2H), 7.50 (t, $J = 7.5$

Hz, 1H), 7.40 (t, $J = 7.5$ Hz, 2H), 7.18-7.10 (m, 5H), 4.44 (q, $J = 6.5$ Hz, 1H), 1.35 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 142.8, 141.4, 131.7, 128.4, 127.9, 126.7, 126.5, 125.8, 53.4, 22.6; FTIR (KBr) ν 3274, 3067, 2978, 2928, 1447, 1324, 1212, 1162, 1079, 954 cm^{-1} ; HRMS (ESI-) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{NO}_2\text{S}$ $[\text{M}-\text{H}]^-$: 260.0751, found 260.0747.

***N*-[1-(4-Bromophenyl)ethyl]-*N*-methylbenzenesulfonamide (Table 2, entry 8).**

The general procedure for the copper-catalyzed amidation was followed, except the reaction was conducted at 80 °C. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminoethylbenzene derivative as a yellow solid (517 mg, 49%). mp 78-80 °C; $R_f = 0.37$ (20% ethyl acetate in hexanes); ^1H NMR (400 MHz, CD_3OD) δ 7.88 (d, $J = 7.5$ Hz, 2H), 7.72-7.59 (m, 3H), 7.50-7.46 (m, 2H), 7.28-7.23 (m, 2H), 5.23 (q, $J = 7.0$ Hz, 1H), 2.62 (s, 3H), 1.26 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 139.9, 139.4, 132.5, 131.1, 129.1, 129.0, 126.8, 121.1, 54.5, 27.6, 14.1; FTIR (KBr) ν 3055-2882, 1489, 1355, 1172, 1146, 925, 617, 578 cm^{-1} ; HRMS (ESI+) m/z calcd for $\text{C}_{15}\text{H}_{16}\text{NO}_2\text{SKBr}$ $[\text{M}+\text{K}]^+$: 391.9717, found 391.9716 (for ^{35}Br).

***N*-(4-Ethylphenyl)benzamide (starting material for Table 3, entry 9).**

Dichloromethane (40 mL) was added to a 100 mL round-bottom flask equipped with a magnetic stirbar. The solvent was cooled to 0 °C in an ice bath and potassium carbonate (9.13 g, 66.1 mmol, 2.0 equiv) was added to the solvent in one portion. After the addition of the base, 4-ethylaniline (4.10 mL, 33.0 mmol, 1.0 equiv) was added to the flask and the suspension was stirred at 0 °C for 10 minutes. Benzoyl chloride (4.60 mL, 39.7 mmol, 1.2 equiv) was added dropwise into the reaction mixture, the ice bath was removed and the

mixture allowed to warm to room temperature. After 2 h of stirring at room temperature, the reaction was poured into a 250 mL separatory funnel containing 150 mL of water and was extracted with ethyl acetate (3 x 75 mL). The combined organic layers were washed with brine, dried over MgSO₄ and evaporated under reduced pressure. The resulting orange solid was recrystallized from EtOAc/hexanes to give the title compound as a white solid (6.77 g, 91%). mp 150-151 °C; *R_f* = 0.61 (35% ethyl acetate in hexanes); ¹H NMR (400 MHz, CD₃OD) δ 7.96-7.91 (m, 2H), 7.62-7.49 (m, 5H), 7.25-7.19 (m, 2H), 2.66 (q, *J* = 7.5 Hz, 2H), 1.25 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 167.4, 140.6, 136.0, 135.0, 131.4, 128.2, 127.7, 127.2, 121.1, 28.0, 14.9; FTIR (KBr) ν 3276, 3107-2874, 1653, 1507, 1412, 1313, 1271, 1026, 833 cm⁻¹; HRMS (ESI+) *m/z* calcd for C₁₅H₁₆NO [MH]⁺: 226.1226, found 226.1228.

***N*-(4-{1-[Methyl(phenylsulfonyl)amino]ethyl}phenyl)benzamide (Table 3, entry 9).**

The general procedure for the copper-catalyzed amidation was followed, except the reaction was conducted at 80 °C. Purification by column chromatography on silica gel using a gradient of 100% toluene to 10% ethyl acetate in toluene afforded the desired aminoethylbenzene derivative as a yellow solid (754 mg, 64%). mp 215-217 °C; *R_f* = 0.36 (15% ethyl acetate in toluene); ¹H NMR (400 MHz, (CD₃)₂SO) δ 10.27 (s, 1H, *NH*), 7.96 (d, *J* = 7.5 Hz, 2H), 7.87 (d, *J* = 7.5 Hz, 2H), 7.79-7.51 (m, 8H), 7.24 (d, *J* = 8.5 Hz, 2H), 5.16 (q, *J* = 7.0 Hz, 1H), 2.54 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, (CD₃)₂SO) δ 166.0, 140.0, 139.0, 135.4, 135.3, 133.3, 132.1, 130.0, 128.9, 128.1, 127.9, 127.3, 120.6, 54.8, 28.8, 15.7; FTIR (KBr) ν 3402, 3059, 2973, 1668, 1595, 1520, 1323, 1172, 937 cm⁻¹; HRMS (ESI+) *m/z* calcd for C₂₂H₂₃N₂O₃S [MH]⁺: 395.1424, found 395.1421.

N-1-Adamantylbenzenesulfonamide (Table 3, entry 10).

The general procedure for the copper-catalyzed amidation was followed, except the reaction was conducted at 80 °C. Purification by column chromatography on silica gel using a gradient of 100% hexanes to 10% ethyl acetate in hexanes afforded the desired aminoadamantane derivative as a white solid (491 mg, 56%). The regioselectivity in this reaction was determined by comparison of the NMR data with that of the *N*-1-adamantyl 4-nitrobenzenesulfonamide synthesized by Muller.² Less than 5% of the corresponding *N*-2-adamantylbenzenesulfonamide was observed based on ¹H NMR analysis. The solid could be further purified by recrystallization in Et₂O/hexanes. mp 129-131 °C; *R*_f = 0.22 (20% ethyl acetate in hexanes); ¹H NMR (400 MHz, CD₃OD) δ 7.91 (d, *J* = 7.5 Hz, 2H), 7.62-7.53 (m, 3H), 1.98 (s, 3H), 1.81-1.51 (m, 12H); ¹³C NMR (100 MHz, CD₃OD) δ 144.8, 131.7, 128.7, 126.5, 54.1, 42.7, 35.7, 29.6; FTIR (KBr) ν 3234, 2905, 2850, 1447, 1325, 1167, 1100, 854 cm⁻¹; HRMS (ESI-) *m/z* calcd for C₁₆H₂₀NO₂S [M-H]⁻: 290.1220, found 290.1217.

Procedure for the copper-catalyzed amidation of 1-indenyl acetate with benzenesulfonamide (Scheme 2). Into a flame-dried 10 mL round-bottom flask, equipped with a magnetic stirbar, oven-dried 4 Å molecular sieves (≈ 25 beads) and under a N₂ atmosphere was added anhydrous Cu(OTf)₂ (108 mg, 0.30 mmol), 1,10-phenanthroline (54 mg, 0.30 mmol) and anhydrous 1,2-dichloroethane (2.25 mL). The resulting suspension was stirred at room temperature for 10 minutes, and then benzenesulfonamide (471 mg, 3.00 mmol) and 2,3-dihydro-1*H*-inden-1-yl acetate (792 mg, 4.50 mmol) was added to the flask. Finally, *tert*-butylperacetate (62 μL, 0.30 mmol, 75 wt% in aliphatic hydrocarbons) was added via syringe and the reaction mixture stirred at room temperature for 2 h, after which TLC analysis indicated complete consumption of starting material. The crude reaction mixture

² Nägeli, I.; Baud, C.; Bernardinelli, G.; Jacquier, Y.; Moran, M.; Müller, P. *Helv. Chim. Acta* **1997**, *80*, 1087-1105.

was poured onto a pad of Celite on a sintered glass funnel and washed with Et₂O. The filtrate was then concentrated under reduced pressure and the crude residue purified by column chromatography through silica gel, eluting with 10% ethyl acetate in hexanes to afford the desired product as an off-white solid (678 mg, 83%). TLC, ¹H and ¹³C NMR analysis revealed this compound to be identical to that of *N*-(2,3-dihydro-1*H*-inden-1-yl)benzenesulfonamide synthesized in table 2, entry 1.

^1H NMR and ^{13}C NMR spectra of selected compounds

Perspective view of X-ray crystal structure (Table 2, entry 9-C)

Table 2, entry 1

Table 2, entry 1

Table 2, entry 2

Table 2, entry 2

Table 2, entry 3

Table 2, entry 3

Table 2, entry 4

Table 2, entry 4

Table 2, entry 5

Table 2, entry 5

Table 2, entry 6

Table 2, entry 6

Table 2, entry 7

Table 2, entry 7

DU=/mt_bruker, USER=powdavid, NAME=10000-0099, EXPNO=3, PROCNO=1
F1=215.000ppm, F2=-5.000ppm, MI=0.85cm, MAXI=10000.00cm, PC=1.400

#	ADDRESS	FREQUENCY [Hz]	[PPM]	INTENSITY
1	6957.1	16964.574	168.5409	2.60
2	10514.9	14360.817	142.6729	4.15
3	10590.5	14305.518	142.1235	3.07
4	10927.7	14058.711	139.6715	2.79
5	11927.2	13327.278	132.4048	6.58
6	12062.6	13328.201	131.4205	2.76
7	12090.0	13308.097	131.2208	7.11
8	12306.1	13050.001	129.6501	6.88
9	12409.6	12874.237	128.8974	5.96
10	12562.2	12862.518	127.7875	6.43
11	12765.6	12713.678	126.3088	6.37
12	13032.9	12518.084	124.3656	7.05
13	13120.8	12453.738	123.7263	6.65
14	22046.9	5921.292	58.8273	6.66
15	22924.0	5279.401	52.4502	6.98
16	23491.0	4864.422	48.3274	1.81
17	23520.3	4843.039	48.1150	4.84
18	23549.7	4821.463	47.9006	9.68
19	23579.0	4800.082	47.6882	12.50
20	23608.1	4778.759	47.4764	10.63
21	23637.3	4757.345	47.2636	4.84
22	23666.8	4735.775	47.0493	1.78
23	25507.3	3388.848	33.6678	5.59
24	26086.6	2964.908	29.4560	5.85

Table 2, entry 8

Table 2, entry 8

Table 2, entry 9
less polar diastereomer

Table 2, entry 9
less polar diastereomer

Table 2, entry 9
more polar diastereomer

Table 2, entry 9
more polar diastereomer

Table 3, entry 1

Table 3, entry 1

Table 3, entry 2

Table 3, entry 2

Table 3, entry 3

Table 3, entry 3

Table 3, entry 4

Table 3, entry 4

Table 3, entry 5

Table 3, entry 5

Table 3, entry 6

Table 3, entry 6

Table 3, entry 7

Table 3, entry 7

Table 3, entry 8

Table 3, entry 8

Table 3, entry 9

Table 3, entry 10

Perspective view (ball and stick) generated from the X-ray crystal structure of Table 2, entry 9
(more polar diastereomer)

(1R,5S,7S)-4-[(1R)-2,3-dihydro-1H-inden-1-yl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-3,3-dioxide

The presence of the S-atom permits an unambiguous assignment of the absolute stereochemistry as R,S,S,R for C2,C4,C6,C11 respectively.