Electronic Supplementary Material (ESI) for ChemComm.

Regioselective differentiation of vicinal methylene C-H bonds enabled by silver-catalysed nitrene transfer

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I. General Information

All glassware was either oven-dried overnight at 130 °C or flame-dried under a stream of dry nitrogen prior to use. Unless otherwise specified, reagents were used as obtained from the vendor without further purification. Tetrahydrofuran and diethyl ether were freshly distilled from purple Na/benzophenone ketyl. Dichloromethane, acetonitrile and toluene were dried over CaH_2 and freshly distilled prior to use. All other solvents were purified in accordance with "Purification of Laboratory Chemicals".[1] Air- and moisture- sensitive reactions were performed using standard Schlenk techniques under an atmosphere of nitrogen. Analytical thin layer chromatography (TLC) was performed utilizing pre-coated silica gel 60 F_{254} plates containing a fluorescent indicator, while preparative chromatography was performed via Still's method using SilicaFlash P60 silica gel (230-400 mesh) or aluminum oxide (activated, neutral, Brockman I).[2] Unless otherwise stated, the mobile phases for column chromatography were mixtures of hexanes/ethyl acetate. Columns were typically run using a gradient method, beginning with 100% hexanes and gradually increasing the polarity using ethyl acetate. Various stains were used to visualize reaction products, including *p*-anisaldehyde, $KMnO_4$, ceric ammonium molybdate (CAM stain) and iodine powder.

^1H NMR and ^{13}C NMR spectra were obtained using Bruker-300, Varian-300, Bruker Avance-400, or Bruker Avance-500 spectrometers. For ^1H NMR, chemical shifts are reported relative to residual protiated solvent peaks (δ 7.26, 2.49, 7.15 and 7.09 ppm for $CDCl_3$, $(CD_3)_2SO$, C_6D_6 and $CD_3C_6D_5$ respectively). ^{13}C NMR spectra were measured at either 125 MHz or 75 MHz on the same instruments noted above for recording ^1H NMR spectra. Chemical shifts were again reported in accordance to residual solvent peaks (δ 77.2, 39.5, 128.0 and 137.9 ppm for $CDCl_3$, $(CD_3)_2SO$, C_6D_6, and $CD_3C_6D_5$, respectively). Accurate mass measurements were acquired at the

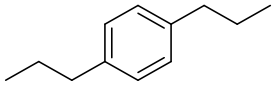
University of Wisconsin, Madison using a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact methods), a Q Exactive Plus, or a Waters Micromass Autospec (electron impact, high sector, direct probe). The NMR and Mass Spectrometry facilities are funded by the NSF (CHE-9974839, CHE-9304546, CHE-9208463, CHE-9629688) and the University of Wisconsin, as well as the NIH (RR08389-01 and 1S10OD020022-1).

II. Synthesis of Novel Arene Precursors to Benzenesulphonamides

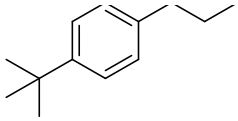
General Procedure A: This procedure was generalized to the synthesis of all arenes unless otherwise noted. Ethyltriphenylphosphonium bromide (11.5 g, 27.5 mmol, 1.1 equiv) was suspended in 45 mL THF under N_2. KO^{t}Bu (3.65 g, 32.5 mmol, 1.3 equiv) was added portionwise and the resulting red mixture was stirred 30 min. 4-*tert*-butylbenzaldehyde (4.2 mL, 25 mmol, 1 equiv) in 5 mL THF was added dropwise and the mixture was allowed to stir 4 hours. The reaction was quenched with 50 mL saturated NH_4Cl (aq) and the aqueous layer was extracted with 2x25 mL diethyl ether. The organic layers were combined and dried over $MgSO_4$, then filtered and concentrated to give the product adsorbed onto the solid byproduct. Filtration through a plug of silica with hexanes and concentration of the filtrate gave the resulting styrene (3.33 g, 19.1 mmol, 75%) as a mix of E and Z isomers. The intermediate was carried on to the next step without further purification.

The styrene mixture (3.3 g, 19 mmol, 1 equiv) in 5 mL ethyl acetate was added to a suspension of 5% Pd/C (1.2 g, 0.57 mmol, 0.03 equiv) in 10 mL ethyl acetate. The dark mixture was stirred vigorously overnight under a balloon of H_2. The mixture was subsequently filtered through a silica plug rinsed with ethyl acetate and concentrated to give *p-tert*-butylethylbenzene (3.4 g, 19 mmol, quantitative yield).

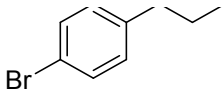
General Procedure B: Analogous to general procedure A except that the initial Wittig reaction occurred between a benzylphosphonium ylide and an α-disubstituted aldehyde. The resulting styrene mixture was subsequently reduced in a Parr reactor (600-800 psi H_2, 6% catalyst loading with respect to Pd).



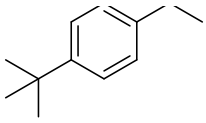
Arene 1-P. Synthesized according to General Procedure A. Isolated in 75% yield from the starting aldehyde as a clear oil. Characterization data was consistent with reported literature values.[3]



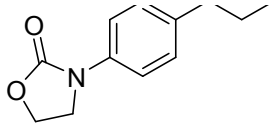
Arene 2-P. Synthesized according to General Procedure A. Isolated in 75% yield from the starting aldehyde as a clear oil. Characterization data was consistent with reported literature values.[4]



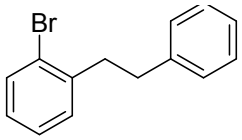
Arene 3-P. Obtained and used as received from Sigma Aldrich (item no. 319880).



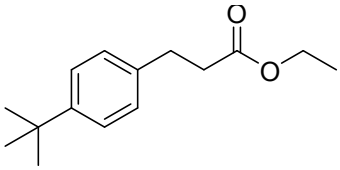
Arene 4-P. Synthesized according to General Procedure A. Characterization data was consistent with reported literature values.[5]



Arene 5-P. Synthesized from **3-P** according to literature procedure.[6] The product was isolated with gradient column chromatography (0-30% ethyl acetate/hexane) in 50% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 4.56 – 4.41 (m, 2H), 4.11 – 3.95 (m, 2H), 2.63 – 2.50 (m, 2H), 1.62 (h, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.36, 138.66, 135.93, 129.07, 129.02, 118.37, 118.35, 61.28, 45.37, 37.32, 24.57, 13.74. HRMS (ASAP-MS) *m*/*z* calculated for $C_{12}H_{16}NO_2$ $[M+H]^+$ 206.1176, found 206.1174.

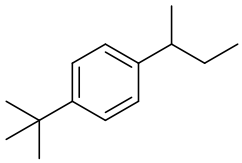


Arene 6-P. Synthesized according to General Procedure A in 72% yield as a clear oil. Characterization data was consistent with reported literature values.[7]

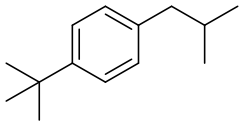


Arene 7-P. Synthesized according to General Procedure A in 61% yield from 4-*tert*-butylbenzaldehyde. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 2H), 7.20 – 7.11 (m, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.99 – 2.86 (m, 2H), 2.68 – 2.53 (m, 2H), 1.30 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.06, 149.03, 137.49, 127.93, 125.35, 60.38, 35.94,

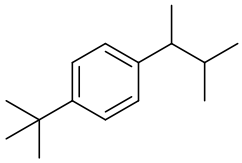
34.37, 31.37, 30.44, 14.21. HRMS (ESI) calculated for $C_{15}H_{23}O_2$ $[M+H]^+$ 252.1958, found 252.1955.



Arene 8-P. Synthesized according to General Procedure A from ethyl 4'-*tert*-butylbenzophenone. The overall yield of clear oil was 70%. Characterization data was consistent with reported literature values.[8]

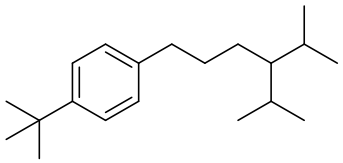


Arene 9-P. Synthesized according to General Procedure A from 4-*tert*-butylbenzaldehyde in 22% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 2.44 (d, J = 7.2 Hz, 2H), 1.90 – 1.79 (m, 1H), 1.31 (d, J = 0.6 Hz, 9H), 0.90 (d, J = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.30, 138.59, 128.73, 124.91, 44.92, 34.32, 31.43, 31.35, 30.19, 22.46. HRMS (ASAP-MS) calculated for $C_{14}H_{21}$ $[M-H]^+$ 189.1638, found 189.1638.

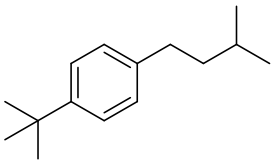


Arene 10-P. Synthesized according to General Procedure A from 4-(*tert*-butylphenyl)isopropyl ketone in 90% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.10 – 7.06 (m, 2H), 2.41 (p, J = 7.2 Hz, 1H), 1.75 (h, J = 6.8 Hz, 1H), 1.31 (s, 9H), 1.22 (d, J = 7.0 Hz, 3H), 0.91 (d, J = 6.7 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.30, 143.88,

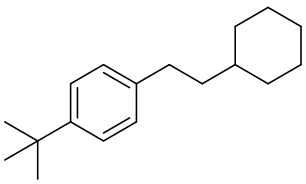
127.22, 124.79, 46.17, 34.43, 31.44, 21.23, 20.07, 18.48. HRMS (ASAP-MS) *m*/*z* calculated for $C_{15}H_{24}$ $[M]^+$ 204 .1873, found 204.1870.



Arene 11-P. Synthesized according to General Procedure A in 37% yield as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.15 – 7.09 (m, 2H), 2.60 – 2.51 (m, 2H), 1.78 – 1.67 (m, 2H), 1.66 – 1.56 (m, 2H), 1.31 (s, 9H), 1.29 – 1.21 (m, 2H), 0.90 – 0.84 (overlapped m, 1H and d, *J* = 6.8 Hz, 6H), 0.83 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.30, 139.88, 127.96, 125.09, 50.18, 36.17, 34.34, 32.66, 31.45, 29.33, 27.72, 21.51, 19.37. HRMS (ASAP-MS) *m*/*z* calculated for $C_{20}H_{34}$ $[M]^+$ 274.2655, found 274.2651. HRMS (ASAP-MS) *m*/*z* calculated for $C_{20}H_{34}$ $[M]^+$ 274.2655, found 274.2651.

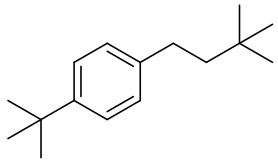


Arene 12-P. Synthesized according to General Procedure B as a clear oil in 50% yield. Characterization data was consistent with reported literature values.[9]

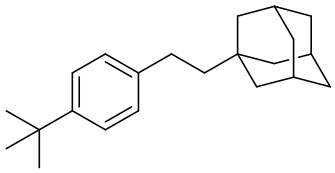


Arene 13-P. Synthesized according to General Procedure B as a clear oil in 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.13 – 7.09 (m, 2H), 2.63 – 2.55 (m, 2H), 1.83 – 1.74

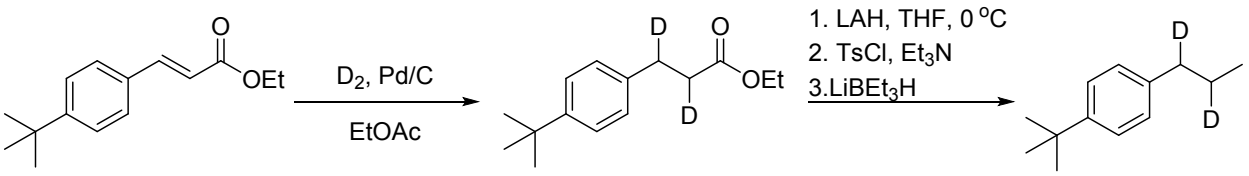
(m, 2H), 1.74 – 1.60 (m, 3H), 1.55 – 1.45 (m, 2H), 1.31 (s, 9H), 1.28 – 1.13 (m, 4H), 0.93 (dtd, *J* = 13.0, 11.3, 3.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.22, 140.18, 127.94, 125.11, 39.41, 37.45, 34.32, 33.33, 32.69, 31.42, 26.72, 26.35. HRMS (ASAP-MS) *m*/*z* calculated for $C_{18}H_{27}$ $[M]^+$ 244.2186, found 244.2184.



Arene 14-P. Synthesized according to General Procedure B in 46% yield as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.14 – 7.10 (m, 2H), 2.57 – 2.51 (m, 2H), 1.52 – 1.46 (m, 2H), 1.31 (s, 9H), 0.95 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.23, 140.47, 127.90, 125.16, 46.36, 34.31, 31.42, 30.59, 30.52, 29.34. HRMS (ASAP-MS) *m*/*z* calculated for $C_{15}H_{23}$ $[M\text{-}CH_3]^+$ 203.1794, found 203.1729.



Arene 15-P. Synthesized according to General Procedure B in 57% yield as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.13 – 7.10 (m, 2H), 2.55 – 2.50 (m, 2H), 2.01 – 1.94 (m, 3H), 1.75 – 1.70 (m, 3H), 1.69 – 1.62 (m, 3H), 1.55 (d, *J* = 2.8 Hz, 6H), 1.40 – 1.34 (m, 2H), 1.30 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.17, 140.70, 127.94, 125.15, 46.85, 42.43, 37.28, 34.31, 32.47, 31.43, 28.79, 28.47. HRMS (ASAP-MS) *m*/*z* calculated for $C_{18}H_{23}$ $[M\text{-}^tBu]^+$ 239.1794, found 239.1788.



Arene 16-P. Synthesized analogously to **Arene 7-P** through the Wittig olefination step. The styrene (4.23 g, 20.8 mmol, 1 equiv.) was stirred with Pd/C (10% w/w, 0.89 g) in 10mL ethyl acetate overnight under a balloon of D_2. The reaction mixture was filtered through a silica plug and the eluent concentrated to get the dideuterated ester (4.15 g, 17.6 mmol, 85%), which was used immediately.

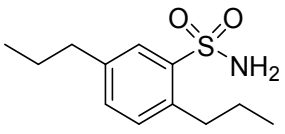
The ester intermediate (3.30 g, 17.0 mmol) was diluted with 40 mL CH_2Cl_2 under N_2 and triethylamine (7.1 mL, 51 mmol, 3 equiv) was added at 0 °C. Tosyl chloride (3.41 g, 17.9 mmol, 1.05 equiv) was added portionwise and the mixture stirred overnight. The mixture was concentrated and the residue stirred in 80 mL 1:1 ethyl acetate/aqueous saturated $NaHCO_3$ for 1 hr. The organic layer was separated and washed with 15 mL 0.1 N HCl, then 15 mL brine. After drying over Na_2SO_4, filtration, and concentration, the crude tosylate was isolated as a white solid (4.03 g, 11.6 mmol, 68%) and carried on without further purification.

The tosylate (11.6 mmol) was dissolved in 30 mL THF under N_2 and cooled to 0 °C. $LiEt_3BH$ (1 M THF solution, 34.8 mL, 3 equiv) was added dropwise and stirred for 10 hrs. The reaction was quenched with 30 mL H_2O and extracted with 300 mL ethyl acetate. The organic layer was washed with 2x100mL H_2O and 2x100 mL brine, then dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography (hexane eluent) to afford the pure arene **16-P** as a clear oil (1.69 g, 9.49 mmol, 82%). ^{13}C NMR indicated a single product with monodeuteration at the indicated positions. ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m,

2H), 7.13 – 7.10 (m, 2H), 2.58 – 2.50 (m, 1H), 1.67 – 1.57 (m, 1H), 1.31 (s, 9H), 0.94 (d, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.31, 139.59, 128.06, 125.06, 37.07 (1:1:1 t, CDH), 34.32, 31.43, 24.07 (1:1:1 t, CDH), 13.84. HRMS (ASAP-MS) m/z calculated for $C_{13}H_{18}D_2$ $[M]^+$ 176.1544, found 176.1544.

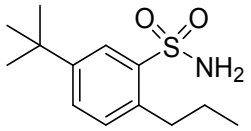
III. Synthesis of Benzenesulphonamides

General Procedure C: This procedure was generalized to synthesize all substrates unless otherwise noted. Chlorosulphonic acid (8.8 mL, 130 mmol, 4.5 equiv) was added dropwise at 0 °C under N_2 atmosphere to a solution of 1,4-dipropylbenzene (4.95 g, 29.8 mmol, 1 equiv) in CH_2Cl_2 (60 mL). The mixture was stirred warming to room temperature 4 h. The dark solution was poured onto 250 g crushed ice and stirred until the ice completely melted. The resulting colloidal suspension was extracted with 3x50 mL CH_2Cl_2. The organic layers were combined and dried over $MgSO_4$, followed by filtration. The filtrate was cooled to 0 °C and 30% NH_4OH (aq) (8.0 mL, 150 mmol, 5 equiv) was added. The mixture was stirred vigorously overnight. 50 mL H_2O was added and the phases separated. Extraction of the aqueous layer with 2x50 mL ethyl acetate, followed by drying of the combined organic layers over $MgSO_4$, filtration and concentration, gave a crude solid residue. Purification by silica column chromatography (hexanes/ethyl acetate) gave the pure benzenesulphonamide (6.14 g, 25.4 mmol, 85%).

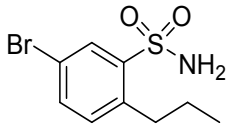


Compound 1. Purified with gradient column chromatography (0-20% ethyl acetate/hexanes) and isolated in 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 1.8 Hz, 1H), 7.30 (dd, J = 7.9, 1.8 Hz, 1H), 7.27 (d, J = 7.0 Hz, 1H), 4.88 (d, J = 7.2 Hz, 2H), 3.01 – 2.86 (m, 2H), 2.59 (dd, J =

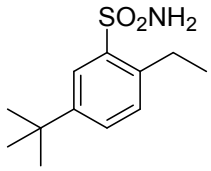
8.5, 6.8 Hz, 2H), 1.79 – 1.68 (h, 2H), 1.68 – 1.58 (h, 2H), 1.02 (t, J = 7.3 Hz, 3H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.84, 139.29, 138.53, 132.84, 131.20, 128.08, 128.07, 37.34, 34.63, 24.35, 14.26, 13.74. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{23}N_2O_2S$ $[M+NH_4]^+$ 259.1475 found 259.1473.



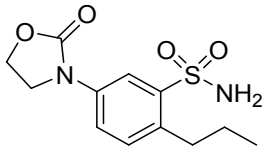
Compound 2. Purified with gradient column chromatography (0-25% ethyl acetate/hexanes) and isolated in 62% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 2.1 Hz, 1H), 7.51 (dd, J = 8.1, 2.2 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 4.83 (s, 2H), 3.00 – 2.90 (m, 2H), 1.73 (h, J = 8.0, 7.3 Hz, 2H), 1.32 (s, 9H), 1.03 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.38, 139.09, 138.28, 131.07, 129.81, 125.14, 34.56, 31.16, 24.28, 14.30. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{20}NO_2S$ $[M-H]^+$ 254.1220, found 254.1224. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{25}N_2O_2S$ $[M+NH_4]^+$ 273.1631, found 273.1628.



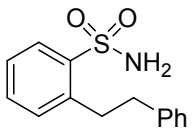
Compound 3. Recrystallized from CH_2Cl_2/hexane and isolated in 19% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, J = 2.1 Hz, 1H), 7.61 (dd, J = 8.2, 2.1 Hz, 1H), 7.25 (d, J = 8.3 Hz, 1H), 4.87 (s, 2H), 3.01 – 2.86 (m, 2H), 1.79 – 1.68 (m, 2H), 1.03 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.29, 140.38, 135.62, 132.92, 130.99, 119.41, 34.53, 24.14, 14.16. HRMS (ESI) *m*/*z* calculated for $C_9H_{12}BrN_2O_4SNa$ $[M+Na]^+$ 299.9664, found 299.9662.



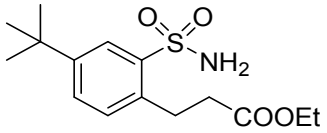
Compound 4. Isolated by gradient column chromatography (0-30% ethyl acetate/hexane) as a white solid in 48% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 2.1 Hz, 1H), 7.54 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 4.78 (s, 2H), 3.04 (q, *J* = 7.5 Hz, 2H), 1.39 – 1.25 (m; overlapped s, 9H and t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.40, 139.62, 138.87, 130.39, 130.06, 125.16, 34.69, 31.16, 25.50, 15.12. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{23}N_2O_2S$ $[M+NH_4]^+$ 259.1475, found 259.1473.



Compound 5. Isolated with gradient column chromatography (0-75% ethyl acetate/hexane) as a white solid in 5% yield. ^{1}H NMR (400 MHz, CD_3CN) δ 7.82 (d, *J* = 2.5 Hz, 1H), 7.27 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.63 (s, 2H), 4.08 (dd, *J* = 9.1, 6.9 Hz, 2H), 3.69 (dd, *J* = 9.1, 7.0 Hz, 2H), 2.65 – 2.46 (m, 2H), 1.32 (h, *J* = 7.3 Hz, 2H), 0.64 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CD_3CN) δ 156.52, 142.47, 137.78, 136.77, 132.97, 122.40, 118.02, 62.78, 45.88, 34.91, 25.21, 14.44, 1.32. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{20}N_3O_2S$ $[M+NH_4]^+$ 302.1169, found 302.1164.

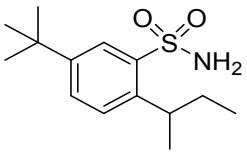


Compound 6. Arene **6-P** (7.93 g, 30.4 mmol, 1 equiv) in 5 mL THF was added with stirring to Mg turnings (0.739 g, 30.4 mmol, 1 equiv) in 20 mL THF. A pellet of iodine dissolved in 5 mL THF was then added and the mixture was refluxed 3 hours. The resulting solution was added dropwise via cannula to sulfuryl chloride (12.3 mL, 152 mmol, 5 equiv) at 0 ^{o}C. After stirring overnight, the mixture was poured onto 50 g crushed ice and stirred until melted. The aqueous mixture was extracted twice with 50 mL CH_2Cl_2 and the organic layer was concentrated without drying. The residue was diluted with 100 mL chloroform, followed by dropwise addition of 30% aqueous NH_4OH (8.02 mL, 152 mmol, 5 equiv). . The mixture was stirred vigorously overnight. 50 mL H_2O was added and the phases separated. Extraction of the aqueous layer with 2x50 mL ethyl acetate, followed by drying of the combined organic layers over $MgSO_4$, filtration and concentration, gave a crude solid residue. Purification by gradient column chromatography (0-30% hexanes/ethyl acetate) gave the white solid benzenesulphonamide (1.47 g, 5.62 mmol, 18%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 – 7.97 (m, 1H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 8.7 Hz, 1H), 7.34 – 7.23 (m, 2H; extra integration from CDCl3 overlap), 7.20 (d, *J* = 7.1 Hz, 3H), 4.64 (d, *J* = 17.2 Hz, 2H), 3.32 (t, *J* = 8.0 Hz, 2H), 3.02 (t, *J* = 8.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.40, 140.48, 139.85, 132.79, 131.72, 128.64, 128.53, 128.40, 126.46, 126.25, 37.59, 35.20. HRMS (ESI) *m/z* calculated for $C_{14}H_{16}NO_2S$ $[M+H]^+$ 279.1162, found 279.1157.

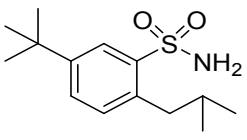


Compound 7. Isolated by gradient column chromatography (0-30% ethyl acetate/hexane) as a clear oil in 2% yield with an inseparable impurity consistent with fragmentation of the ester chain. This impurity was considered benign to the amination reaction. The compound was stored

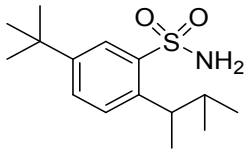
and used as a 0.15 M solution in CH_2Cl_2. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.1 Hz, 1H), 7.52 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.48 (dd, *J* = 8.0, 2.2 Hz, 0H), 7.29 (d, *J* = 8.1 Hz, 1H), 5.36 (s, 2H), 5.00 (s, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.33 (t, *J* = 7.4 Hz, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 2.64 (s, 1H), 1.32 (d, *J* = 1.1 Hz, 12H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.60, 150.17, 139.85, 135.98, 130.79, 129.89, 125.28, 60.85, 34.98, 34.75, 31.16, 31.11, 27.09, 14.14. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{27}N_2O_4S$ $[M+NH_4]^+$ 331.1686, found 331.1682. The molecule coeluted with an impurity identified as 5-*tert*-butyl-2-methylbenzenesulphonamide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.2 Hz, 1H), 7.48 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 5.00 (s, 2H), 2.64 (s, 3H), 1.32 (s, 9H; overlap with main product). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.60, 139.34, 133.52, 132.29, 129.78, 125.04, 31.16, 19.77. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{27}N_2O_4S$ $[M+NH_4]^+$ 245.1318, found 245.1315.



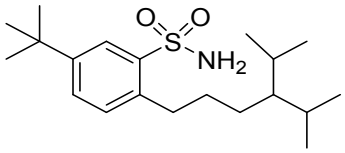
Compound 8. Purified by gradient column chromatography (0-20% ethyl acetate/hexanes). Isolated in 48% yield as a waxy white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.1 Hz, 1H), 7.55 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 4.92 (d, *J* = 6.9 Hz, 2H), 3.60 – 3.45 (m, 1H), 1.79 – 1.69 (m, 1H), 1.69 – 1.60 (m, 1H), 1.33 (s, 9H), 1.27 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.02, 143.84, 139.06, 130.13, 127.75, 124.82, 36.19, 34.68, 31.15, 30.90, 22.15, 12.33. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{27}N_2O_2S$ $[M+NH_4]^+$ 287.1788, found 287.1783.



Compound 9. Isolated by gradient column chromatography (0-20% ethyl acetate/hexane) as an off-white solid in 23% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.1 Hz, 1H), 7.50 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 4.90 (s, 2H), 2.86 (d, *J* = 7.2 Hz, 2H), 2.18 – 2.03 (nonet, *J* = 6.8 Hz, 1H), 1.33 (s, 9H), 0.96 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.45, 139.64, 137.20, 131.78, 129.46, 125.25, 41.30, 34.68, 31.16, 29.37, 22.56. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{27}N_2O_2S$ $[M+NH_4]^+$ 287.1788, found 287.1784.

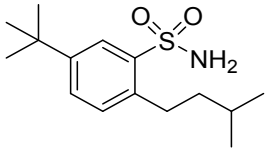


Compound 10. Isolated by gradient column chromatography (0-24% ethyl acetate/hexane) as a white solid in 31% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.1 Hz, 1H), 7.55 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 4.80 (s, 2H), 3.25 (dq, *J* = 9.4, 6.9 Hz, 1H), 1.92 (dsept, *J* = 9.3, 6.6 Hz, 1H), 1.33 (s, 9H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.94, 144.04, 139.09, 130.09, 128.07, 124.87, 41.72, 34.68, 34.35, 31.17, 31.14, 21.76, 20.56, 20.47. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{29}N_2O_4S$ $[M+NH_4]^+$ 301.1944, found 301.1941.

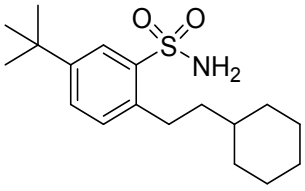


Compound 11. Purified by gradient column column chromatography (0-30% ethyl acetate/hexanes). Isolated as a white solid in 40% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 2.2 Hz, 1H), 7.52 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 4.75 (s, 2H), 3.05 – 2.87 (m, 2H), 1.79 – 1.64 (m, 4H), 1.37 – 1.30 (m, 11H), 0.89 (dd, *J* = 6.8, 4.9 Hz, 7H;

overlap d, J = 6.9 Hz, 6H and m, 1H), 0.85 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.37, 138.92, 138.52, 130.99, 129.88, 125.20, 50.24, 34.70, 33.30, 32.38, 31.60, 31.17, 29.34, 28.08, 22.67, 21.52, 19.34, 14.14. HRMS (ESI) *m*/*z* calculated for $C_{20}H_{39}N_2O_2S$ $[M+NH_4]^+$ 371.2727, found 371.2719.

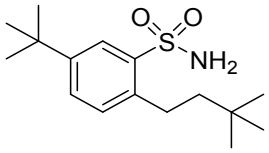


Compound 12. Purified by gradient column column chromatography (0-30% ethyl acetate/hexanes). Isolated as a white solid in 20% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.02 (d, J = 2.1 Hz, 1H), 7.51 (dd, J = 8.1, 2.1 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 4.81 (s, 2H), 3.03 – 2.92 (m, 2H), 1.70 (hept, J = 6.6 Hz, 1H), 1.63 – 1.53 (m, 2H), 1.32 (s, 9H), 0.97 (d, J = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.30, 138.94, 138.77, 131.14, 129.89, 125.17, 40.47, 34.68, 31.16, 30.55, 28.36, 22.55. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{29}N_2O_2S$ $[M+NH_4]^+$ 301.1944, found 301.1944.

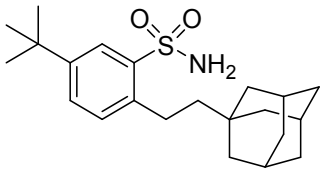


Compound 13. Purified by gradient column column chromatography (0-60% ethyl acetate/ hexanes). Isolated as a white solid in 32% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 2.1 Hz, 1H), 7.51 (dd, J = 8.1, 2.1 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 4.77 (s, 2H), 3.06 – 2.89 (m, 2H), 1.88 – 1.76 (m, 2H), 1.69 (m, 3H), 1.62 – 1.54 (m, 2H), 1.32 (s, 9H), 1.30 – 1.10 (m, 4H), 0.96 (qd, J = 11.9, 3.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.30, 138.94, 138.91, 131.13,

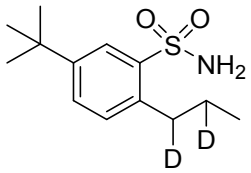
129.91, 125.19, 39.09, 38.00, 34.70, 33.32, 31.18, 30.08, 26.64, 26.33. HRMS (ESI) *m*/*z* calculated for $C_{18}H_{33}N_2O_2S$ $[M+NH_4]^+$ 341.2257, found 341.2255.



Compound 14. Purified by gradient column column chromatography (0-30% ethyl acetate/hexanes). Isolated as a white solid in 24% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 2.1 Hz, 1H), 7.51 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 4.78 (s, 2H), 3.08 – 2.83 (m, 2H), 1.62 – 1.52 (m, 2H), 1.32 (s, 9H), 0.99 (s, 9H). 13C NMR (101 MHz, CDCl3) δ 149.27, 139.19, 138.94, 131.51, 129.95, 125.17, 45.96, 34.69, 31.18, 30.73, 29.33, 28.02. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{31}N_2O_2S$ $[M+NH_4]^+$ 315.2101, found 315.2097.



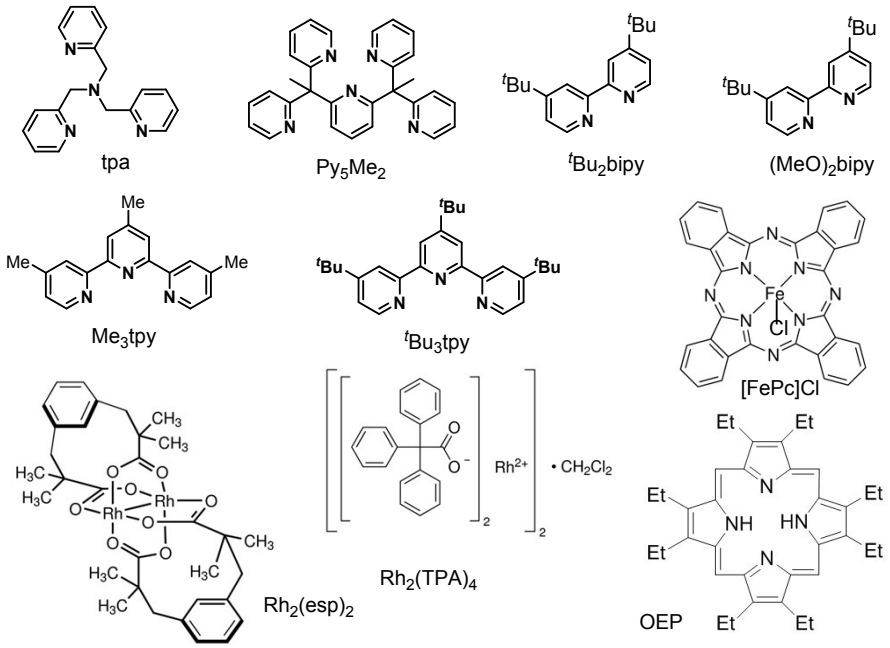
Compound 15. Purified by gradient column column chromatography (0-24% ethyl acetate/hexanes). Isolated as a white solid in 7% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 2.1 Hz, 1H), 7.51 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 4.74 (s, 2H), 2.97 – 2.90 (m, 2H), 1.99 (dt, *J* = 6.2, 3.0 Hz, 3H), 1.77 – 1.70 (m, 3H), 1.66 (dq, *J* = 12.3, 1.9 Hz, 3H), 1.58 (d, *J* = 2.8 Hz, 6H), 1.46 – 1.41 (m, 2H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.23, 139.38, 138.97, 131.53, 129.94, 125.19, 46.49, 42.39, 37.17, 34.69, 32.67, 31.17, 28.72, 25.94. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{37}N_2O_2S$ $[M+NH_4]^+$ 393.2570, found 393.2562.



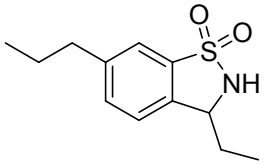
Compound 16. Isolated in 54% yield as an off-white solid from the corresponding arene by gradient column chromatography (0-24% ethyl acetate/hexanes). The substrate was deemed 50% deuterated (monosubstituted) at both positions as judged by ^{13}C NMR (1:1:1 triplets with no corresponding signals for undeuterated carbons). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 2.1 Hz, 1H), 7.52 (dd, J = 8.1, 2.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 4.76 (s, 2H), 2.99 – 2.88 (m, 1H), 1.72 (m, 1H), 1.33 (s, 9H), 1.03 (d, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 149.42, 139.04, 138.26, 131.07, 129.85, 125.20, 34.69, 34.31, 34.16, 34.00, 31.16, 23.99, 23.84, 23.68, 14.17. HRMS (ESI) *m/z* calculated for $C_{13}H_{18}D_2N_2O_2S$ $[M-H]^-$ 256.1346, found 256.1346.

IV. Synthesis of Benzosultam Products

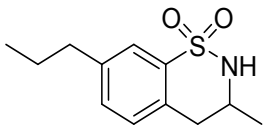
Table S1-1. Catalysts used in preliminary screening studies in Table 1 of the manuscript.



Experimental Procedure: AgOTf (6.4 mg, 0.025 mmol, 0.1 equiv) and the desired ligand (0.030 mmol, 0.12 equiv unless otherwise specified) were stirred in 2 mL dry CH_2Cl_2 in a foil-covered 25 mL round-bottom flask equipped with a stir bar for 30 min. 4 Å molecular sieves (0.25 g) and sulphonamide (0.25 mmol, 1 equiv) in 3 mL CH_2Cl_2 were added. Iodosobenzene (0.193 g, 0.875 mmol, 3.5 equiv) was added and the mixture was stirred another 30 min. The mixture was then filtered and the solvent evaporated. The crude residue was purified by column chromatography on silica, or alumina for more difficult separations.

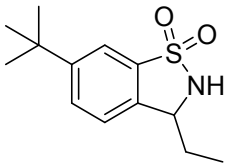


Compound 1a. Purified with gradient column chromatography (alumina, 0-3% ethyl acetate/CH_2Cl_2) and isolated in 13% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.54 (m, 1H), 7.43 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 4.70 (d, *J* = 5.1 Hz, 1H), 4.63 (dt, *J* = 8.6, 4.4 Hz, 1H), 2.68 (dd, *J* = 8.4, 6.9 Hz, 2H), 2.03 (dqd, *J* = 14.8, 7.4, 3.9 Hz, 1H), 1.85 – 1.75 (m, 1H), 1.67 (h, *J* = 7.4 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). 13C NMR (126 MHz, CDCl3) δ 144.63, 137.56, 135.73, 133.68, 123.77, 120.67, 77.27, 77.02, 76.76, 58.87, 37.58, 28.75, 24.25, 13.69, 9.91. HRMS (ESI) *m/z* calculated for $C_{12}H_{21}N_2O_2S$ $[M+NH_4]^+$ 257.1318, found 257.1315.

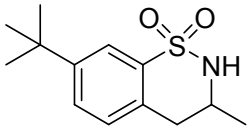


Compound 1b. Purified with gradient column chromatography (alumina, 0-3% ethyl acetate/CH_2Cl_2) and isolated as a white solid in 64% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63

(d, J = 1.8 Hz, 1H), 7.25 (dd, J = 7.9, 1.8 Hz, 1H), 7.11 (d, J = 7.9 Hz, 1H), 4.24 (d, J = 11.4 Hz, 1H), 4.08 – 3.98 (m, 1H), 2.93 (dd, J = 16.9, 3.8 Hz, 1H), 2.75 (dd, J = 17.0, 11.4 Hz, 1H), 2.63 – 2.58 (m, 2H), 1.64 (h, J = 7.4 Hz, 2H), 1.39 (d, J = 6.5 Hz, 3H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.68, 136.90, 132.40, 129.24, 123.61, 77.27, 77.02, 76.77, 49.57, 37.41, 36.06, 24.14, 21.82, 13.70. HRMS (ESI) m/z calculated for $C_{12}H_{21}N_2O_2S$ $[M+NH_4]^+$ 257.1318, found 257.1314.

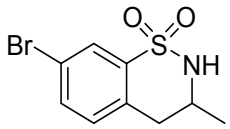


Compound 2a. Purified with gradient column chromatography (alumina, 0-3% ethyl acetate/CH_2Cl_2) and isolated as a white solid in 12% yield, inseparable from a small amount of **2b**. Reported values exclude **2b** (reported below). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 1.8 Hz, 1H), 7.58 (dd, J = 8.3, 1.8 Hz, 1H), 7.23 (d, J = 8.2 Hz, 1H), 4.73 (d, J = 5.1 Hz, 1H), 4.56 (dt, J = 8.5, 4.4 Hz, 1H), 1.96 (dqd, J = 14.8, 7.4, 3.9 Hz, 1H), 1.72 (dp, J = 14.7, 7.4 Hz, 1H), 1.28 (s, 9H), 0.96 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.28, 136.27, 134.51, 129.86, 122.63, 116.65, 57.77, 34.18, 30.16, 30.04, 27.71, 8.92. HRMS (ESI) m/z calculated for $C_{12}H_{17}NO_2SNa$ $[M+Na]^+$ 262.0872, found 262.0871.

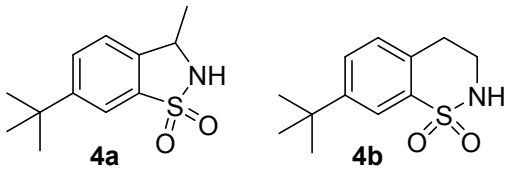


Compound 2b. Purified with gradient column chromatography (alumina, 0-3% ethyl acetate/CH_2Cl_2) and isolated as a white solid in 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 2.0 Hz, 1H), 7.48 (dd, J = 8.2, 2.1 Hz, 1H), 7.14 (d, J = 8.1 Hz, 1H), 4.19 (d, J = 11.5 Hz,

1H), 4.09 – 3.99 (m, 1H), 2.94 (dd, J = 17.0, 3.8 Hz, 1H), 2.74 (dd, J = 16.7, 11.0 Hz, 1H), 1.40 (d, J = 6.6 Hz, 3H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.30, 135.73, 130.98, 128.52, 128.13, 119.52, 76.25, 75.99, 75.74, 48.54, 35.01, 33.87, 30.05, 20.83. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{23}N_2O_2S$ $[M+NH_4]^+$ 271.1475, found 271.1473.

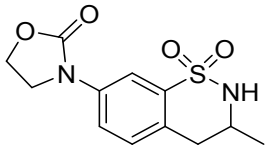


Compound 3a. Isolated by gradient column chromatography (silica, 0-20% ethyl acetate/hexane) as a white solid in 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 2.1 Hz, 1H), 7.54 (dd, J = 8.2, 2.1 Hz, 1H), 7.10 (d, J = 8.2 Hz, 1H), 4.41 (d, J = 11.4 Hz, 1H), 4.12 – 3.96 (m, 1H), 2.93 (dd, J = 17.2, 3.9 Hz, 1H), 2.72 (ddd, J = 17.0, 11.4, 1.1 Hz, 1H), 1.41 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.64, 135.16, 133.91, 131.02, 126.93, 121.08, 49.40, 35.71, 21.74. HRMS (ESI) *m*/*z* calculated for $C_9H_{11}NO_2S$ $[M+H]^+$ 275.9688, found 275.9688.

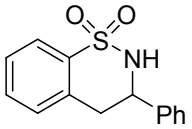


Compound 4a/b. Isolated by gradient column chromatography (alumina, 0-20% ethyl acetate/CH_2Cl_2) in 62% yield as an inseparable 11.9:1 mixture of (**4a + imine byproduct)** to **5a**. NMR characterization of the mixture was simplified by exposure of the mixture to 4 equiv $NaBH_4$ in 5 mL MeOH to reduce the byproduct to **4a**, followed by repurification with the described column conditions. NMR assignments were made with assistance of HSQC and HMBC data. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.75 (d, J = 2.1 Hz, 1H **4b**), 7.69 (d, J = 1.8

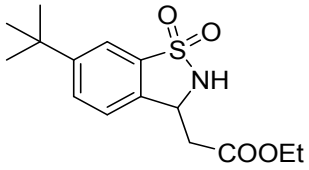
Hz, 1H **4a**), 7.59 (dd, *J* = 8.3, 1.8 Hz, overlapped 1H each **4a** and **4b**), 7.24 (d, *J* = 8.2 Hz, 1H **4a**), 7.09 (d, *J* = 8.2 Hz, 1H **4b**), 4.81 – 4.72 (m, 1H, overlapped NH peaks of isomers), 4.72 – 4.62 (m, 1H **4a**), 3.78 – 3.67 (m, 1H **4b**), 2.88 (t, *J* = 6.1 Hz, 1H **4b**), 1.52 (d, *J* = 6.6 Hz, 3H **4a**), 1.28 (s, overlapped 9H each of isomers). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.23 (**4a**), 150.23 (**4b**), 137.78 (**4a**), 136.53 (**4b**), 134.28 (**4a**), 131.27 (**4b**), 129.95 (**4a**), 128.50 (**4b**), 128.27 (**4b**), 122.40 (**4a**), 119.65 (**4b**), 116.54 (**4a**), 52.07 (**4a**), 41.10 (**4b**), 34.18 (**4a**), 33.86 (**4b**), 30.16 (**4a**), 30.04 (**4b**), 28.67 (**4b**), 20.48 (**4a**). HRMS (ESI) *m*/*z* calculated for $C_{12}H_{18}NO_2S$ $[M+H]^+$ 240.1053, found 240.1052.



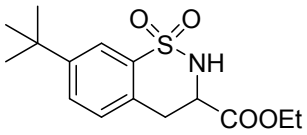
Compound 5a. Isolated by gradient column chromatography (silica, 0-75% ethyl acetate/hexane) in 45% yield as a white solid. ^{1}H NMR (500 MHz, CD_3CN) δ 7.92 (d, *J* = 2.4 Hz, 1H), 7.70 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 4.91 (d, *J* = 11.7 Hz, 1H), 4.49 (t, *J* = 8.0 Hz, 2H), 4.13 (td, *J* = 7.7, 2.2 Hz, 2H), 3.94 (dddd, *J* = 11.3, 8.8, 6.4, 3.9 Hz, 1H), 2.99 (dd, *J* = 17.2, 3.8 Hz, 1H), 2.79 (dd, *J* = 17.2, 11.3 Hz, 1H), 1.36 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, CD_3CN) δ 203.83, 151.45, 134.07, 133.31, 126.81, 126.34, 117.45, 108.22, 45.67, 40.71, 30.69, 16.28. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{14}N_2O_2SNa$ $[M+Na]^+$ 305.0567, found 305.0562.



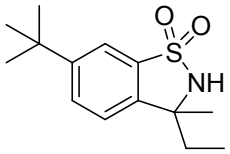
Compound 6a. Isolated by column chromatography (silica, 0-30% ethyl acetate/hexane) in 62% yield as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.48 (td, *J* = 7.6, 1.4 Hz, 1H), 7.46 – 7.33 (m, 6H), 7.28 (d, *J* = 7.7 Hz, 1H), 4.97 (td, *J* = 10.3, 5.7 Hz, 1H), 4.83 (d, *J* = 10.2 Hz, 1H), 3.32 – 3.20 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.55, 137.82, 134.94, 132.26, 129.43, 128.99, 128.38, 127.83, 126.17, 123.74, 56.78, 35.56. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{14}NO_2S$ $[M+H]^+$ 260.7040, found 260.7043.



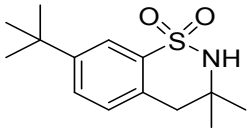
Compound 7a. Attempted to purify by gradient column chromatography (alumina, 0-30% ethyl acetate/hexane). The compound was found to decompose upon repeated column chromatography (silica or alumina) and was characterized as part of a crude oily mixture with **Xb** (**Xa** major component) and the catalyst. Signals were assigned based on data from other 5-membered benzosultams reported here. The crude yield from Py_5Me_2 ligand conditions was 20%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, *J* = 1.8 Hz, 1H), 8.70 (dd, *J* = 8.2, 1.8 Hz, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 6.45 (d, *J* = 4.4 Hz, 1H), 6.08 (dt, *J* = 10.1, 3.9 Hz, 1H), 5.24 (q, *J* = 7.1 Hz, 2H), 3.98 (dd, *J* = 17.0, 3.4 Hz, 1H), 3.79 (dd, *J* = 16.9, 10.1 Hz, 1H), 2.38 (s, 9H), 2.31 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.79, 153.94, 135.38, 135.07, 131.01, 123.45, 118.00, 60.04, 53.35, 40.37, 35.30, 31.16, 14.16. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{25}N_2O_2S$ $[M+H]^+$ 329.1530, found 359.1527.



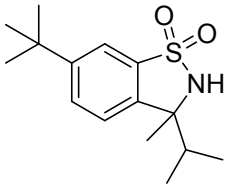
Compound 7b. Purified by gradient column chromatography (alumina, 0-30% ethyl acetate/hexane) as a clear oil. The yield from Py_5Me_2 ligand conditions was 20%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 2.0 Hz, 1H), 7.51 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 1H), 5.01 (d, *J* = 8.5 Hz, 1H), 4.63 (td, *J* = 8.8, 5.6 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.38 (dd, *J* = 16.5, 5.6 Hz, 1H), 3.14 (dd, *J* = 16.5, 9.1 Hz, 1H), 1.34 – 1.32 (m, 12H; overlapped s, 9H and t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.81, 151.77, 137.44, 129.80, 129.02, 120.32, 62.57, 54.66, 34.98, 31.07, 30.45, 14.14. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{25}N_2O_2S$ $[M+H]^+$ 329.1530, found 329.1527.



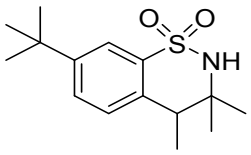
Compound 8a. Purified by gradient column chromatography (silica, 0-20% ethyl acetate/hexane) as a white solid. The yield was 81%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 1.8 Hz, 1H), 7.66 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 4.62 (s, 1H), 1.98 – 1.83 (m, 2H), 1.35 (s, 9H), 1.64 – 1.57 (m, 3H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.07, 141.70, 135.20, 131.08, 122.55, 117.57, 64.06, 35.16, 34.66, 31.17, 27.97, 8.54. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{25}N_2O_2S$ $[M+NH_4]^+$ 285.1631, found 285.1627.



Compound 9a. Purified by gradient column chromatography (silica, 0-20% ethyl acetate/hexane) as a white solid. The yield was 89%. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 2.1 Hz, 1H), 7.49 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 4.41 (s, 1H), 2.94 (s, 2H), 1.34 (s, 6H), 1.33 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.99, 137.41, 132.13, 129.30, 119.79, 56.05, 39.93, 34.89, 31.14, 29.83. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{25}N_2O_2S$ $[M+NH_4]^+$ 285.1631, found 285.1625.

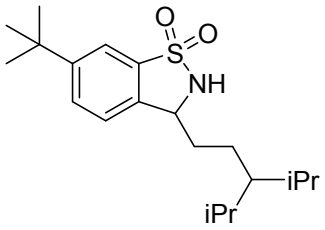


Compound 10a. Purified by gradient column chromatography (alumina, 0-24% ethyl acetate/hexane) as a white solid (mixture of **14a/b**). The yield was 47% with Py_5Me_2 as the ligand. Characterized with **10b** below.

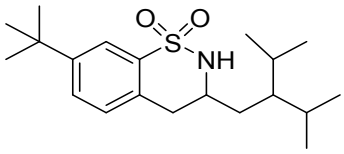


Compound 10b. Purified by gradient column chromatography (alumina, 0-24% ethyl acetate/hexane) as a white solid. The yield was 42% with Py_5Me_2 as the ligand. The isomeric mixture was analyzed using HSQC- and HMBC-NMR to identify signals for individual isomers. **10a:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 1.8 Hz, 1H), 7.55 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.15 (d (overlap with **10b**), *J* = 8.3 Hz, 1H), 4.50 (s, 1H), 2.02 (h, *J* = 6.5 Hz, 1H), 1.49 (s, 3H), 1.24 (s (overlap with **10b** CH_3), 9H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.65 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.05, 141.68, 134.71, 131.04, 122.67, 117.58, 66.82, 37.30, 35.15, 28.65,

17.62, 17.35. HRMS (ESI) *m/z* calculated for $C_{14}H_{25}N_2O_2S$ $[M+NH_4]^+$ 285.1631, found 285.1625. **10b:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 2.1 Hz, 1H), 7.42 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.13 (d (overlap with **10a**), *J* = 8.3 Hz, 1H), 4.53 (s, 1H), 2.93 (q, *J* = 7.1 Hz, 1H), 1.38 (s, 3H), 1.23 (d (overlap with **10a** ^{t}Bu), *J* = 7.1 Hz, 3H), 1.22 (s, 9H), 1.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.77, 137.01, 136.47, 129.59, 128.06, 120.25, 58.38, 40.81, 34.82, 26.91, 25.75, 15.95. HRMS (ESI) *m/z* calculated for $C_{15}H_{24}NO_2S$ $[M+H]^+$ 282.1522, found 282.1518.

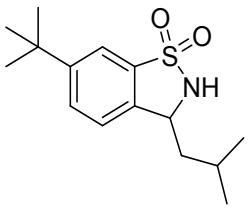


Compound 11a. Purified by gradient column chromatography (silica, 0-20% ethyl acetate/hexane) as a white solid. The yield was 20% with Py_5Me_2 as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 1.8 Hz, 1H), 7.65 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 4.66 (d, *J* = 5.2 Hz, 1H), 4.65 – 4.58 (m, 1H), 1.81 – 1.70 (m, 3H), 1.41 – 1.33 (m, 13H integrated as 17H-sample purity confirmed with ^{13}C data), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 2H), 0.84 (d, *J* = 6.8 Hz, 3H). HRMS (ESI) *m/z* calculated for $C_{20}H_{37}N_2O_2S$ $[M+NH_4]^+$ 369.2570, found 369.2563.

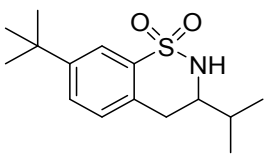


Compound 11b. Purified by gradient column chromatography (silica, 0-20% ethyl acetate/hexane) as a white solid. The yield was 53% with Py_5Me_2 as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 2.0 Hz, 1H), 7.46 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 1H),

4.10 (d, J = 11.8 Hz, 1H), 3.89 (tddd, J = 11.9, 8.5, 5.6, 3.7 Hz, 1H), 2.93 (dd, J = 16.9, 3.7 Hz, 1H), 2.69 (dd, J = 16.9, 11.6 Hz, 1H), 1.89 – 1.74 (m, 2H), 1.53 – 1.46 (m, 2H), 1.35 – 1.30 (m, 10H; overlapped s, 9H and m, 1H), 0.93 (d, J = 6.8 Hz, 6H), 0.90 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.27, 137.11, 132.12, 129.44, 129.23, 120.62, 53.89, 45.23, 35.13, 34.88, 34.33, 31.08, 31.05, 29.59, 28.81, 21.59, 21.26, 19.65, 18.82. HRMS (ESI) m/z calculated for $C_{20}H_{37}N_2O_2S$ $[M+NH_4]^+$ 369.2570, found 369.2566.

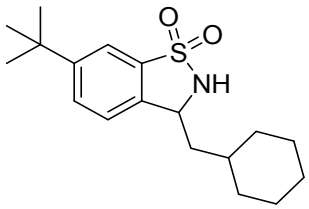


Compound 12a. Purified by gradient column chromatography (alumina, 0-20% ethyl acetate/hexane) as a white solid. The yield was 35% with Py_5Me_2 as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 1.7 Hz, 1H), 7.65 (dd, J = 8.2, 1.8 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H), 4.68 (dt, J = 9.7, 4.5 Hz, 1H), 4.60 (d, J = 5.2 Hz, 1H), 1.95 – 1.81 (m, 1H), 1.80 – 1.61 (m, 2H), 1.56 (s, 3H), 1.35 (s, 9H), 1.04 (d, J = 6.6 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.32, 138.32, 135.38, 130.84, 123.62, 117.72, 55.81, 45.29, 35.22, 31.19, 25.56, 23.41, 21.41. HRMS (ESI) m/z calculated for $C_{15}H_{27}N_2O_2S$ $[M+NH_4]^+$ 299.1788, found 299.1786.

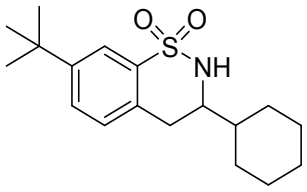


Compound 12b. Purified by gradient column chromatography (alumina, 0-20% ethyl acetate/hexane) as a white solid. The yield was 30% with Py_5Me_2 as the ligand. ^{1}H NMR (500

MHz, $CDCl_3$) δ 7.83 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 4.16 – 4.08 (m, 1H), 3.65 (tdd, *J* = 11.8, 6.4, 3.9 Hz, 1H), 2.92 (dd, *J* = 16.9, 4.0 Hz, 1H), 2.81 (dd, *J* = 16.9, 11.9 Hz, 1H), 1.94 – 1.79 (m, *J* = 6.8 Hz, 1H), 1.57 (s, 1H), 1.32 (s, 9H), 1.07 (dd, *J* = 11.1, 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.23, 137.13, 132.26, 129.40, 120.54,,58.98, 34.88, 32.90, 31.63, 31.08, 18.71, 18.28. HRMS (ESI) *m*/*z* calculated for $C_{15}H_{27}N_2O_2S$ $[M+NH_4]^+$ 299.1788, found 299.1787.

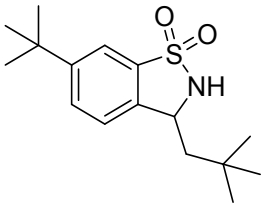


Compound 13a. Purified by gradient column chromatography (alumina, 0-5% ethyl acetate/CH_2Cl_2) as a white solid. The yield was 42% with Py_5Me_2 as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 1.8 Hz, 1H), 7.64 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.28 (d, *J* = 8.3 Hz, 1H), 4.78 – 4.68 (m, 1H), 4.61 (d, *J* = 5.2 Hz, 1H), 1.97 – 1.87 (m, 1H), 1.84 – 1.59 (m, 6H), 1.35 (s, 9H), 1.34 – 1.16 (m, 4H), 1.08 – 0.93 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.25, 138.48, 135.42, 130.82, 123.60, 117.70, 55.15, 43.92, 35.20, 34.89, 34.06, 32.19, 31.19, 26.37, 26.15, 25.97. HRMS (ESI) *m*/*z* calculated for $C_{18}H_{26}NO_2S$ $[M-H]^-$ 320.1690, found 320.1690.

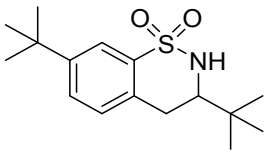


Compound 13b. Purified by gradient column chromatography (alumina, 0-5% ethyl acetate/CH_2Cl_2) as a white solid. The yield was 37% with Py_5Me_2 as the ligand. NMR integrals were reported as determined by the software; integration errors due to overlapping signals in

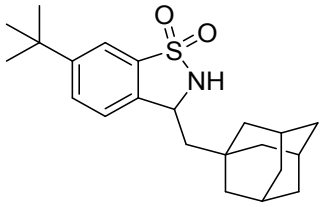
aliphatic region yielded 30H instead of 27H. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.0 Hz, 1H), 7.46 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 4.21 (d, *J* = 11.8 Hz, 1H), 3.66 (tdd, *J* = 11.6, 6.6, 3.9 Hz, 1H), 2.90 (dd, *J* = 16.9, 3.9 Hz, 1H), 2.79 (dd, *J* = 17.0, 11.8 Hz, 1H), 2.04 – 1.97 (m, 1H), 1.85 – 1.74 (m, 4H), 1.74 – 1.67 (m, 2H), 1.52 (dtd, *J* = 11.4, 7.5, 7.1, 3.3 Hz, 1H), 1.32 (s, 9H), 1.29 – 1.14 (m, 5H), 1.09 (qd, *J* = 12.2, 3.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.15, 137.19, 132.38, 129.43, 129.42, 120.49, 58.24, 42.46, 34.86, 31.61, 31.08, 31.05, 29.03, 28.70, 26.25, 25.93, 25.84. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{25}N_2O_2S$ $[M-H]^-$ 320.1690, found 320.1688.



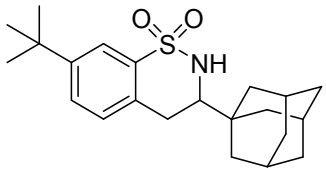
Compound 14a. Purified by gradient column chromatography (alumina, 0-100% CH_2Cl_2/hexane) as a white solid. The yield was 77% with Py_5Me_2 as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 1.7 Hz, 1H), 7.65 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 4.68 (ddt, *J* = 10.2, 5.4, 1.2 Hz, 1H), 4.60 (d, *J* = 5.4 Hz, 1H), 1.92 (dd, *J* = 15.0, 1.7 Hz, 1H), 1.68 (dd, *J* = 14.8, 10.3 Hz, 1H), 1.35 (s, 9H), 1.08 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.17, 139.19, 135.30, 130.90, 123.69, 117.54, 54.96, 50.63, 35.18, 31.18, 30.89, 29.88. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{29}N_2O_2S$ $[M+NH_4]^+$ 313.1944, found 313.1936.



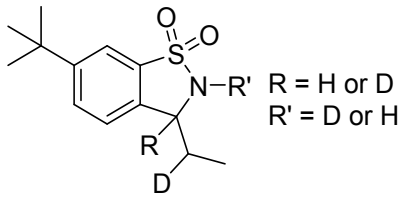
Compound 14b. Purified by gradient column chromatography (alumina, 0-100% CH_2Cl_2/hexane) as a white solid. The yield was 12% with Py_5Me_2 as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 1H), 4.15 (d, *J* = 12.1 Hz, 1H), 3.59 (td, *J* = 12.0, 4.0 Hz, 1H), 2.96 – 2.78 (m, 2H), 1.33 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.19, 137.11, 132.45, 129.47, 120.53, 62.17, 34.88, 33.89, 31.09, 29.09, 25.99. HRMS (ESI) *m*/*z* calculated for $C_{16}H_{29}N_2O_2S$ $[M+NH_4]^+$ 313.1944, found 313.1935.



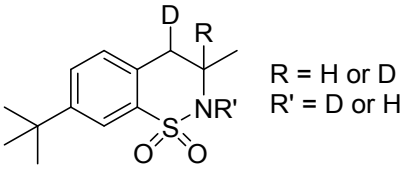
Compound 15a. Isolated in 46% yield with Py_5Me_2 as the ligand with an inseparable impurity of **16b**. Characterization of **16a** was performed with overlaps noted where appropriate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 1.7 Hz, 1H), 7.64 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 4.73 (ddd, *J* = 10.6, 5.3, 1.5 Hz, 1H), 4.54 (d, *J* = 5.1 Hz, 1H), 2.03 (m, 3H), 1.81 – 1.73 (m, 7H, mixture of isomers), 1.72 – 1.60 (m, 13H, mixture of isomers), 1.60 – 1.54 (m, 2H), 1.35 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.09, 139.35, 135.36, 130.87, 123.70, 117.51, 53.39, 51.60, 42.77, 36.79, 35.17, 32.74, 31.19, 28.50. HRMS (ESI) *m*/*z* calculated for $C_{22}H_{30}NO_2S$ $[M-H]^-$ 372.2003, found 372.2000.



Compound 15b. Purified with column chromatography (alumina, 0-5% ethyl acetate/CH_2Cl_2) Isolated in 59% yield with $^tBu_3$tpy as the ligand. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 2.2 Hz, 1H), 7.47 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 4.19 (d, *J* = 12.0 Hz, 1H), 3.43 (ddd, *J* = 12.0, 9.6, 6.4 Hz, 1H), 2.91 – 2.82 (m, 2H), 2.11 – 2.02 (m, 3H), 1.81 – 1.72 (m, 6H), 1.72 – 1.62 (m, 4H), 1.62 – 1.52 (m, 3H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.11, 137.28, 132.61, 129.63, 129.42, 120.50, 62.53, 38.30, 36.92, 35.48, 34.87, 31.09, 28.19, 27.68. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{32}N_2O_2S$ $[M+H]^+$ 374.2148, found 374.2140.



Compound 16a. Isolated in 8% yield with Py_5Me_2 as the ligand as part of a crude reaction mixture. A sample adequate for characterization (~2:1 CH/CD insertion ratio) was isolated with column chromatography (alumina, 0-20% ethyl acetate/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 1.8 Hz, 1H), 7.66 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 4.62 (d, *J* = 5.8 Hz, 1.3H, C<u>H</u>N + NH), 2.08 – 1.96 (m, 0.3H, homobenzylic CH of CD insertion product), 1.78 (q, *J* = 7.2 Hz, 0.8H, homobenzylic CH of CH insertion product), 1.35 (s, 9H), 1.03 (d, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.37, 137.26, 137.20, 135.61, 130.89, 123.65, 117.72, 58.80-58.20 (m, homobenzylic CHD), 35.22, 31.19, 29.70 (benzylic CH), 28.39-28.10 (m, benzylic CD), 9.82. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{17}D_2NO_2S$ $[M-H]^-$ 254.1189, found 254.1190.



Compound 16b. Isolated in 59% yield with Py_5Me_2 as the ligand as part of a crude reaction mixture. A sample adequate for characterization (~2:1 CH/CD insertion ratio) was isolated with column chromatography (alumina, 0-20% ethyl acetate/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 2.0 Hz, 1H), 7.48 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 4.21 (m, 1H, NH), 4.09 – 3.97 (m, 0.3H, $R_2C\underline{H}N$ of CD insertion product), 2.98 – 2.89 (m, 0.3 H benzylic CH after CD insertion), 2.72 (m, 0.9 H, benzylic CH after CH insertion), 1.41 – 1.38 (m, 3H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.31, 136.76, 131.98, 129.53, 129.18, 129.15, 129.13, 120.53, 49.56-48.98 (m, homobenzylic CH and CD), 49.50, 49.33, 49.15, 48.98, 36.02-35.21 (m, benzylic CHD), 34.89, 31.07, 21.71. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{17}D_2NO_2S$ $[M-H]^-$ 254.1189, found 254.1190.

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