Catalytic Synthesis of γ-Lactams via Direct Annulations of Enals and N-Sulfonylimines

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Supporting Information

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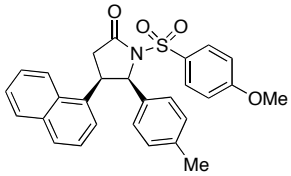
General Methods. All reactions utilizing air- or moisture-sensitive reagents were performed in dried glassware under an atmosphere of dry Ar. ^{i}PrOH, and *tert*-BuOH were distilled from Na. CH_2Cl_2 was distilled over CaH_2. THF, CH_3CN and EtOAc were dried by passage over activated alumina under Ar atmosphere. Imidazolium salts were prepared according to a reported protocol.[1] All aldehydes were purified by distillation prior to use. DBU was distilled from KOH. Other reagents were used without further purification. Chemical yields of the lactam products were reported for the combined yields of the diastereomers. Thin layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F_{254}, Art 5715, 0.25 mm) and were visualized by fluorescence quenching under UV light or by staining with phosphomolybdic acid. Silica-gel preparative thin-layer chromatography (PTLC) was performed using plates prepared from Merck Kieselgel 60 PF_{254} (Art 7747). Column chromatography was performed on E. Merck Silica Gel 60 (230–400 Mesh) using a forced flow of 0.5–1.0 bar. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a Varian Unity 400 spectrometer. The peaks with * indicate peaks of the minor diastereomer (*trans*-). Chemical shifts are expressed in parts per million (PPM) downfield from residual solvent peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared (IR) spectra were recorded on a JASCO FT/IR-430 spectrophotometer and are reported as wavenumber (cm^{-1}). Compounds that are not numbered in the manuscript are labelled as **S1**, **S2**, etc.

General Procedure for Catalytic Annulations of Enals and Imines.

The reaction of enal **2** and imine **7** is representative. Into an oven dried 20 mL vial was weighed the enal **2** (0.018 g, 0.10 mmol, 1.0 equiv), imine **7** (0.029 g, 0.10 mmol, 1.0 equiv) and IMes-Cl (5.2mg, 0.015 mmol, 0.15 equiv). The vial was closed with crimp seal, evacuated, and back-filled with argon. To this mixture was added 1.0 mL *tert*-BuOH , followed by DBU (1.5 μL, 0.01 mmol, 0.10 equiv). The resulting solution was stirred 14 h at 60 °C. The reaction mixture was concentrated under reduced pressure, and

(1) (a) Arduengo, A. J., III U.S. Patent 5 077 414, 1991. (b) We are grateful to Prof. Steven Nolan (U. New Orleans) for suggested improvements to this protocol.

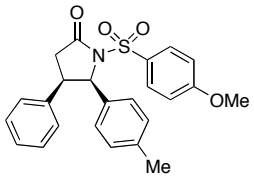
then the residue was purified by flash chromatography (4:1 hexane/EtOAc) to afford the lactam products as a white solid (0.036 g, 75% yield).



***cis*-1-(4-methoxyphenylsulfonyl)-4-(naphthalen-1-yl)-5-p-tolylpyrrolidin-2-one (S1)**

Prepared according to the general procedure in 75% as a 10:1 mixture of lactam diastereomers. (0.10 mmol scale)

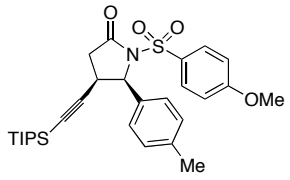
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, 1H, *J* = 8.6), 7.85 (d, 1H, *J* = 7.1), 7.74 (d, 2H, *J* = 9.1), 7.68—7.75 (m, 1H), 7.55—7.63 (m, 2H), 7.04—7.08 (m, 1H), 6.87—6.89 (m, 2H), 6.61—6.65 (m, 3H), 6.24 (d, 2H, *J* = 8.0), 5.97 (d, 1H, *J* = 7.7), 4.82—4.89 (m, 1H), 3.89 (s, 3H), 3.31 (dd, 1H, *J* = 13.5, 7.4), 2.72 (dd, 1H, *J* = 17.0, 7.4), 2.13 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 164.2, 137.6, 133.8, 132.1, 131.9, 131.4, 131.0, 129.8, 129.4, 128.7, 128.2, 127.0, 126.3, 126.0, 124.9, 124.3, 122.9, 113.8, 66.2, 55.9, 41.0, 34.6, 21.1
IR (thin film) *v* 3055, 2987, 2306, 1736, 1596, 1422, 1266, 1166, 896, 740 cm^{-1}
ESI—MS: 471.0 (M^+)
MP: 200—202°C



***cis*-1-(4-methoxyphenylsulfonyl)-4-phenyl-5-p-tolylpyrrolidin-2-one (8)**

Prepared according to the general procedure in 70% as a 4:1 mixture of lactam diastereomers. (0.10 mmol scale)

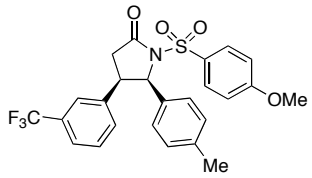
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, 2H, *J* = 9.0), 7.06—7.17 (m, 4H), 6.81—6.88 (m, 3H), 6.76—6.78 (m, 2H), 6.53 (d, 2H, *J* = 8.1), 5.57 (d, 1H, *J* = 8.0), 5.26* (d, 1H, *J* = 2.3), 4.06 (m, 1H), 3.34* (m, 1H), 3.87(s, 3H), 3.88* (s, 3H), 3.03 ((dd, 1H, *J* = 17.2, 13.7), 3.10* (dd, 1H, *J* = 17.8, 8.8), 2.68 (dd, 1H, *J* = 17.2, 7.8), 2.60* (dd, 1H, *J* = 17.8, 3.6), 2.23 (s, 3H), 2.37* (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 164.1, 142.6, 138.2, 137.8, 135.6, 132.3, 131.3, 131.1, 129.9, 129.8, 129.4, 128.9, 128.4, 128.2, 127.8, 127.6, 127.2, 126.4, 125.9, 113.9, 113.8, 71.1, 67.5, 60.6, 55.9, 47.0, 45.0, 37.9, 35.3, 21.2, 14.4.
IR (thin film) *v* 3059, 2982, 2304, 1735, 1596, 1497, 1363, 1266, 1165, 1092, 722, 703 cm^{-1}
ESI-MS: 421.0 (M^+)
MP: 158-161°C



***cis*-1-(4-methoxyphenylsulfonyl)-5-*p*-tolyl-4-(2-(triisopropylsilyl)ethynyl)pyrrolidin-2-one (24)**

Into an oven dried 20 mL vial was weighed the imine (98 mg, 0.11 mmol, 1.0 equiv), IMes-Cl (5.2 mg, 0.015 mmol, 0.15 equiv), DBU (1.7 μL, 0.011 mmol, 0.10 equiv) and 0.50 ml *tert*-BuOH. The vial was closed with crimp seal, evacuated, and back-filled with argon. To this mixture was slowly injected 0.80 mL *tert*-BuOH solution of the enal (27 mg, 0.11 mmol, 1.0 equiv.) over 3 h at 40°C. The resulting mixture was stirred 12 h at 40 °C. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (5:1 hexane/EtOAc) to afford the lactam products in 51% as a 10:1 mixture of diastereomers.

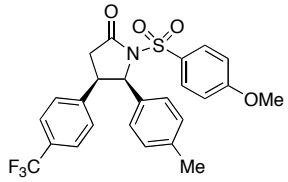
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, 2H, *J* = 8.9), 7.81* (d, 2H, *J* = 8.9), 7.01(d, 2H, *J* = 8.0), 6.89(d, 2H, *J* = 8.0), 6.79(d, 2H, *J* = 8.9), 5.45 (d, 1H, *J* = 8.1), 5.35* (d, 1H, *J* = 2.6), 3.84 (s, 3H), 3.86* (s, 3H), 3.70 (m, 1H), 3.01* (m, 1H), 2.83 (dd, 1H, *J* = 17.7, 9.1), 2.91* (dd, 1H, *J* = 17.2, 8.4), 2.76 (dd, 1H, *J* = 17.7, 12.1), 2.52* (dd, 1H, *J* = 17.1, 3.4), 2.30 (s, 3H), 2.36* (s, 3H), 0.81—0.84 (m 21H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 164.1, 138.4, 133.1, 131.2, 131.1, 129.8, 129.6, 129.2, 127.6, 125.8, 114.0, 113.8, 103.1, 87.5, 65.3, 55.9, 37.8, 34.9, 32.0, 21.3, 18.8, 18.5, 11.2, 11.1
IR (thin film) *v* 3054, 2986, 2305, 1734, 1641, 1596, 1497, 1421, 1364, 1262, 1166, 1092, 896, 836, 701 cm^{-1}
ESI-MS: 526.2 (M+H)
MP: 113-115°C



***cis*-1-(4-methoxyphenylsulfonyl)-5-*p*-tolyl-4-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (18)**

Prepared according to the general procedure in 70% as a 3:2 mixture of lactam diastereomers. (0.10 mmol scale)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, 2H, *J* = 8.9), 7.31—7.42(m, 1H), 7.16—7.24(m, 2H), 6.99(d, 1H, *J* = 7.7), 6.84—6.90(m, 4H), 6.49(d, 2H, *J* = 8.9), 5.58 (d, 1H, *J* = 7.8), 5.25* (d, 1H, *J* = 2.5), 4.14 (m, 1H), 3.41* (m, 1H), 3.87 (s, 3H), 3.00 (dd, 1H, *J* = 17.2, 13.5), 3.15* (dd, 1H, *J* = 17.8, 8.9), 2.72 (dd, 1H, *J* = 17.2, 8.0), 2.59* (dd, 1H, *J*=17.8, 3.2), 2.23 (s, 3H), 2.38* (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 172.1, 164.3, 164.2, 143.4, 138.5, 137.0, 136.9, 131.8, 131.4, 131.0, 129.9, 129.8, 129.6, 129.1, 128.9, 127.0, 125.9, 125.0, 124.8, 124.4, 123.5, 114.0, 113.9, 70.6, 67.2, 55.9, 46.9, 44.7, 37.8, 35.5, 21.3, 21.1
IR (thin film) *v* 3055, 2987, 2305, 1738, 1596, 1498, 1330, 1266, 1164, 1128, 896, 835, 805, 744 cm^{-1}
ESI-MS: 490.1 (M+H)
MP: 119-125°C

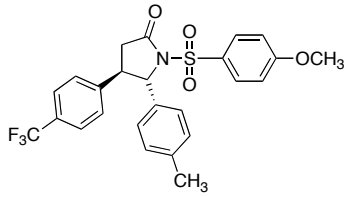


***cis*-1-(4-methoxyphenylsulfonyl)-5-*p*-tolyl-4-(4-(trifluoromethyl)phenyl)pyrrolidin-2-one (20)**

Prepared according to the general procedure in 70% combined yield (cis : trans = 3.5:1).

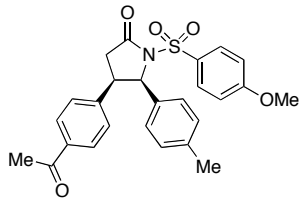
The diastereomers were separated by PTLC (4:1 hexane/EtOAc). (0.10 mmol scale)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, 2H, *J* = 8.5), 7.31(d, 2H, *J* = 8.3), 6.80—6.86(m, 6H), 6.49(d, 2H, *J* = 8.5), 5.57(d, 1H, *J* = 7.8), 4.07—4.11(m, 1H), 3.83(s, 3H), 2.99(dd, 1H, *J* = 17.2, 13.5), 2.68(dd, 1H, *J* = 17.2, 8.0), 2.21(s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 164.2, 139.9, 138.3, 131.9, 131.3, 129.8, 129.2, 128.7, 127.1, 125.3, 125.2, 113.9, 67.1, 55.9, 44.7, 44.7, 35.4, 21.3
IR (thin film) *v* 3055, 2987, 2305, 1738, 1596, 1498, 1362, 1328, 1261, 1162, 1124, 896, 836, 749, 674 cm^{-1}
ESI-MS: 490.1 (M+H)
MP: 164-166°C



***trans*-1-(4-methoxyphenylsulfonyl)-5-*p*-tolyl-4-(4-(trifluoromethyl)phenyl)pyrrolidin-2-one (S2)**

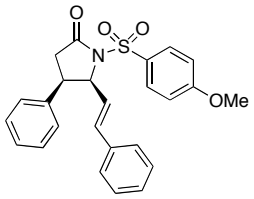
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J* = 9.1), 7.55(d, 2H, *J* = 8.0), 7.16—7.21(m, 4H), 7.10(d, 2H, *J* = 8.0), 6.87(d, 2H, *J* = 9.0), 5.57(d, 1H, *J* = 7.8), 4.07—4.11(m, 1H), 3.83(s, 3H), 2.99(dd, 1H, *J* = 17.2, 13.5), 2.68(dd, 1H, *J* = 17.2, 8.0), 2.21(s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 164.3, 138.6, 136.9, 131.0, 129.9, 129.7, 129.1, 127.3, 126.9, 126.4, 126.3, 125.9, 113.9, 70.6, 58.1, 46.8, 37.7, 21.3
IR (thin film) *v* 3054, 2987, 2395, 1735, 1596, 1497, 1421, 1364, 1266, 1165, 896, 739, 705 cm^{-1}
ESI-MS: 490.1 (M+H)
MP: 182-183°



***cis*-4-(4-acetylphenyl)-1-(4-methoxyphenylsulfonyl)-5-p-tolylpyrrolidin-2-one (22)**

Prepared according to the general procedure in 65% as a 3.5:1 mixture of lactam diastereomers. (0.10 mmol scale)

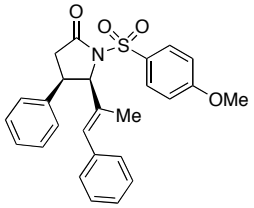
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89—7.65 (m, 4H), 7.19—6.97(m, 2H), 6.89—6.81(m, 4H), 6.53(d, 2H, *J* = 7.8), 5.61 (d, 1H, *J* = 7.8), 5.23* (d, 1H, *J* = 2.5), 4.12 (m, 1H), 3.40* (m, 1H), 3.86 (s, 3H), 3.89* (s, 3H), 3.06 (dd, 1H, *J* = 17.2, 13.5), 3.12* (dd, 1H, *J* = 17.8, 8.8), 2.72 (dd, 1H, *J* = 17.2, 7.8), 2.61* (dd, 1H, *J* = 17.8, 4.2), 2.51 (s, 3H), 2.61* (s, 3H), 2.22 (s, 3H), 2.37* (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 172.2, 164.1, 141.9, 138.2, 136.2, 131.9, 131.3, 131.0, 129.9, 129.7, 129.5, 129.1, 128.8, 128.5, 128.4, 127.2, 126.8, 125.9, 114.4, 113.9, 113.9, 70.6, 67.2, 55.9, 47.0, 44.8, 37.7, 35.3, 26.8, 21.3
IR (thin film) *v* 3054, 2986, 2305, 1734, 1641, 1596, 1497, 1421, 1364, 1262, 1166, 1092, 896, 836, 701 cm^{-1}
ESI-MS: 464.1 (M+H)
MP: 172-176°C



***cis*-1-(4-methoxyphenylsulfonyl)-4-phenyl-5-(2-p-tolylethylidene)pyrrolidin-2-one (14)**

Into an oven dried flask was weighed enal **6** (0.90 g, 6.8 mmol, 1.0 equiv), imine **13** (2.05 g, 6.8 mmol, 1.0 equiv) and IMes-Cl (0.35 g, 1.0 mmol, 0.15 equiv). The flask was evacuated, and back-filled with argon. To this mixture was added 68 mL *tert*-BuOH , followed by the addition of DBU (0.10 mL, 0.68 mmol, 0.10 equiv). The resulting solution was stirred 14 h at room temperature. The reaction mixture was concentrated under reduced pressure, and then residue purified by flash chromatography (4:1 hexane/EtOAc) to afford the products as an 8:1 mixture of lactam diastereomers (1.8 g, 4.2 mmol, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, 2H, *J* = 8.9), 7.28—7.21 (m, 3H), 7.15—7.04 (m, 2H), 6.86 (d, 2H, *J* = 8.1), 6.39 (d, 1H, *J* = 15.7), 5.58 (dd, 1H, *J* = 15.7, 8.2), 5.31 (m, 1H), 4.93* (m, 1H), 3.99 (m, 1H), 3.34* (m, 1H), 3.83 (s, 3H), 3.86* (s, 3H), 2.98 (dd, 1H, *J* = 17.2, 13.2), 3.15* (dd, 1H, *J* = 17.6, 8.4), 2.72 (dd, 1H, *J* = 17.2, 7.2), 2.61* (dd, 1H, *J* = 17.6, 3.2), 2.51 (s, 3H), 2.61* (s, 3H), 2.22 (s, 3H), 2.37* (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ172.1, 164.1, 135.8, 135.7, 134.7, 131.3, 131.1, 130.3, 129.4, 128.9, 128.7, 128.1, 127.9, 126.9, 126.7, 126.6, 123.2, 114.1, 65.8, 55.8, 43.5, 35.2
IR (thin film) *v* 3054, 2987, 2305, 1735, 1654, 1596, 1498, 1421, 1265, 1166, 1092, 898, 835, 739 cm^{-1}
ESI-MS: 434.1 (M+H)
MP: 135-136°C

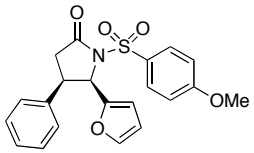


***cis*-1-(4-methoxyphenylsulfonyl)-4-phenyl-5-(2-p-tolylprop-1-enyl)pyrrolidin-2-one (16)**

Prepared according to the general procedure in 62% as a 5:1 mixture of lactam diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.93* (m, 2H), 7.35—7.20 (m, 8H), 6.93—6.85 (m, 4H), 6.25 (s, 1H), 6.45* (s, 1H), 5.19 (d, 1H, *J* = 9.3), 4.78* (d, 1H, *J*= 1.1),

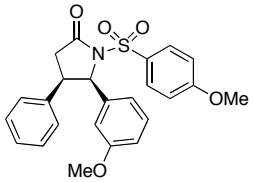
4.05 (m, 1H), 3.36* (m, 1H), 3.84 (s, 3H), 3.87* (s, 3H), 3.07 (dd, 1H, *J* = 17.4, 13.5), 3.27* (dd, 1H, *J* = 18.0, 8.6), 2.74 (dd, 1H, *J* = 17.4, 8.3), 2.59* (dd, 1H, *J* = 18.0, 2.6), 1.09 (d, 3H, *J* = 1.4), 1.86* (d, 3H, *J* = 1.2),
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 172.6, 164.1, 143.1, 136.5, 135.7, 135.0, 133.4, 131.2, 131.1,130.1, 130.0, 129.4, 129.3, 129.1, 128.7, 128.4, 128.3, 128.3, 127.9, 127.8, 127.7, 127.2, 127.1, 126.3, 114.1, 74.6, 70.1, 55.9, 43.0, 42.8, 38.4, 35.4, 16.7, 15.0
IR (thin film) *v* 3067, 3024, 2957, 2253, 1731, 1596, 1498, 1364, 1264, 1165, 1092, 1029, 834, 741, 650 cm^{-1}
ESI-MS: 448.1 (M+H)
MP: 148-151°C



***cis*-5-(furan-2-yl)-1-(4-methoxyphenylsulfonyl)-4-phenylpyrrolidin-2-one (12)**

Prepared according to the general procedure with 2.0 equiv enal **6** and 1.0 equiv imine **11** at 75°C for 63 h in 73% as a 1.7:1 mixture of lactam diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60—7.52 (m, 2H), 7.35—7.05 (m, 3H), 7.15—7.04 (m, 4H), 6.95—6.92 (m, 1H), 6.88—6.81 (m, 3H), 6.14—6.09 (m, 1H), 6.44—6.39* (m, 1H), 5.59 (d, 1H, *J* = 7.7), 5.33* (d, 1H, *J* = 1.7), 4.03 (m, 1H), 3.85* (m, 1H), 3.84 (s, 3H), 3.86* (s, 3H), 3.25 (dd, 1H, *J* = 17.0, 13.4), 3.27* (dd, 1H, *J* = 17.5, 9.0), 2.76 (dd, 1H, *J* = 17.0, 8.2), 2.63* (dd, 1H, *J* = 17.5, 2.2)
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 163.9, 149.3, 143.0, 142.5, 135.6, 134.7, 131.3, 130.8, 129.5, 129.4, 128.9, 128.7, 128.6, 128.4, 128.1, 127.9, 127.8, 127.6, 126.8, 126.4, 123.2, 114.1, 114.0, 113.9, 111.3, 110.7, 110.5, 94.6, 63.6, 61.1, 55.8, 43.8, 43.6, 43.1, 38.7, 36.1
IR (thin film) *v* 3054, 2987, 2305, 1735, 1596, 1498, 1421, 1267, 1166, 896, 739 cm^{-1}
ESI-MS: 398.1 (M+H)
MP: 118-121°C



***cis*-5-(3-methoxyphenyl)-1-(4-methoxyphenylsulfonyl)-4-phenylpyrrolidin-2-one (10)**

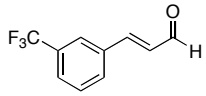
Prepared according to the general procedure in 69% as a 3:1 mixture of lactam diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.69 (m, 2H,), 7.32—7.24 (m, 2H), 7.14—7.05(m, 3H), 6.96—6.84 (m, 3H), 6.82—6.75 (m, 1H), 6.23 (m, 1H), 6.65* (m, 1H), 6.05 (m, 1H), 6.23* (m, 1H), 5.56 (d, 1H, *J* = 7.8), 5.26* (d, 1H, *J* = 2.3), 4.10 (m, 1H), 3.36* (m,

1H), 3.87 (s, 3H), 3.88* (s, 3H), 3.48 (s, 3H), 3.75* (s, 3H), 3.04 (dd, 1H, *J* = 17.2, 14.0), 3.10* (dd, 1H, *J* = 18.0, 9.2), 2.71 (dd, 1H, *J* = 17.2, 7.6), 2.60* (dd, 1H, *J* = 18.0, 3.2)
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 172.7, 164.2, 160.2, 159.4, 142.6, 141.9, 136.7, 135.5, 131.3, 131.1, 130.3, 129.9, 129.4, 129.2, 128.4, 128.2, 127.8, 127.7, 126.4, 119.5, 118.2, 114.2, 113.9, 112.5, 111.5, 67.6, 55.9, 55.4, 55.1, 46.8, 45.0, 38.0, 35.2
IR (thin film) *v* 3054, 2987, 2305, 1735, 1685, 1422, 1266, 1165, 896, 742 cm^{-1}
ESI-MS: 438.1 (M+H)
MP: 198-202°C

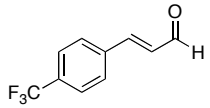
Preparation of Enals

The enals **17, 19** and **21** were prepared according to the procedure of Battistuzzi et. al. [2] To a stirred solution of the aryl halide (1.0 equiv) in DMF was added acrolein diethyl acetal (3.0 equiv), n-Bu_4NOAc (2.0 equiv), K_2CO_3 (1.5 equiv), KCl (1.0 equiv), and $Pd(OAc)_2$ (3.0 mol %). The mixture was stirred for 1.5 h at 90 °C. After cooling, 2 N HCl was slowly added and the reaction mixture was stirred at room temperature for 10 min. Then, it was diluted with ether and washed with water. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography to give the products. The spectral data were compared to previous reports.[2]



(*E*)-3-(3-(trifluoromethyl)phenyl)acrylaldehyde (17)

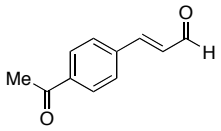
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, 1H, *J* = 7.5), 7.81—7.57 (m, 4H), 7.51 (d, 1H, *J* = 16.1), 6.78 (dd, 1H, *J* = 16.1, 7.5)
^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 150.6, 134.9, 131.4, 130.2, 129.9, 127.8, 127.7, 125.4, 125.3



(*E*)-3-(4-(trifluoromethyl)phenyl)acrylaldehyde (19)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, 1H, *J* = 7.5), 7.69 (s, 4H), 7.51 (d, 1H, *J* = 16.1), 6.77 (dd, 1H, *J* = 16.1, 7.5)
^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 150.5, 130.7, 128.8, 126.3, 126.2,

(2) Battistuzzi, G.; Cacchi, S.; Fabrizi, G.; *Org. Lett.* **2003**, *5*, 777—780



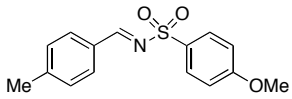
(*E*)-3-(4-acetylphenyl)acrylaldehyde (21)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (d, 1H, *J* = 7.5), 8.00 (d, 2H, *J* = 8.3), 7.66 (d, 1H, *J* = 8.3), 7.51 (d, 1H, *J* = 16.1), 6.77 (dd, 1H, *J* = 16.1, 7.5)
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 193.6, 151.0, 138.8, 138.3, 130.6, 129.2, 128.8, 26.9

Preparation of Imines

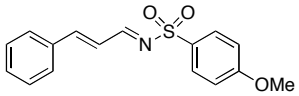
The imines **7, 9, 13** and **15** were prepared according to the following procedure.

The corresponding dimethyl acetal (1.0 eqiv) and the arylsulfonamide (1.0 eqiv) were mixed in a flask equipped with a Dean-Stark condenser. The neat mixture was heated to 180 °C for 30 min. The resulting melt was cooled to room temperature and the solid was crystallized from toluene to yield the product.



(*E*)-4-methoxy-N-((E)-p-toylethylidene)benzenesulfonamide (7)

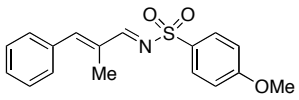
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.93 (d, 2H, *J* = 8.7), 7.81 (d, 2H, *J* = 8.0), 7.29 (d, 2H, *J* = 8.0), 7.01 (d, 2H, *J* = 8.7), 3.88 (s, 3H), 2.43 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 163.8, 146.5, 131.6, 130.4, 130.1, 130.0, 129.9, 114.6, 55.9, 22.2
IR (thin film) *v* 3054, 2987, 2305, 1597, 1421, 1265, 1154, 1092, 896, 809, 740 cm^{-1}
ESI-MS: 290.1 (M+H)
MP: 106-108°C



(*E*)-4-methoxy-N-((E)-3-phenylallylidene)benzenesulfonamide (13)

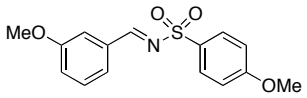
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, 1H, *J* = 9.5), 7.89 (d, 2H, *J* = 8.9), 7.54—7.40 (m, 6H), 7.00—6.93 (m, 3H,), 3.85 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 163.7, 153.8, 134.2, 131.7, 130.2, 129.7, 129.3, 128.7, 124.7, 114.5, 55.8
IR (thin film) *v* 3054, 2987, 2305, 1581, 1499, 1421, 1266, 1153, 1092, 896, 857, 807, 743, 705 cm^{-1}

ESI-MS: 302.1 (M+H)
MP: 125-190°C



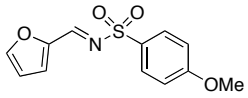
(*E*)-4-methoxy-*N*-((*E*)-2-methyl-3-phenylallylidene)benzenesulfonamide (15)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, 1H, *J* = 0.5), 7.93 (d, 2H, *J* = 8.9), 7.51—7.40 (m, 5H), 7.27 (m, 1H), 7.01 (d, 2H, *J* = 8.9), 3.85 (s, 3H), 2.17 (d, 3H, *J* = 3.2)
^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 163.7, 151.2, 135.3, 135.1, 130.5, 130.3, 130.2, 130.1, 128.9, 114.5, 55.9, 13.1
IR (thin film) *v* 3054, 2987, 2305, 1566, 1499, 1321, 1265, 1153, 1092, 833, 807, 739, 700 cm^{-1}
ESI-MS: 316.1 (M+H)
MP: 88-90°C



(*E*)-N-(3-methoxybenzylidene)-4-methoxybenzenesulfonamide (9)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H,), 7.92 (d, 2H, *J* = 8.7), 7.46—7.36 (m, 3H), 7.15—7.13 (m, 1H), 7.00 (d, 2H, *J* = 8.7), 3.86 (s, 3H), 3.82 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 163.9, 160.2, 133.8,130.5, 130.2, 129.5, 125.4, 122.2, 114.6, 55.8, 55.7
IR (thin film) *v* 3054, 2987, 2305, 1597, 1577, 1266, 1155, 896, 811, 736 cm^{-1}
ESI-MS: 306.1 (M+H)
MP: 198-201°C



(*E*)-N-(furan-2-ylmethylene)-4-methoxybenzenesulfonamide (11)

Imine **11** was prepared according to the procedure of Harris J. M. et al[3].

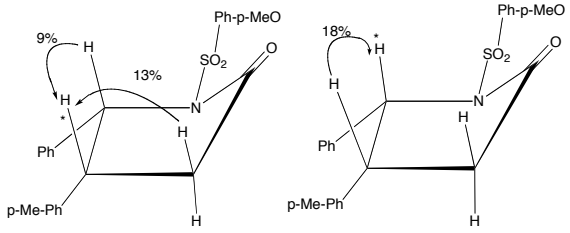
A sample of 2-furaldehyde (0.24 g, 2.5 mmol, 1.3 equiv), 4-methoxybenzenesulphonamide (0.37 g, 2.0 mmol, 1.0 equiv), 5 ml toluene, and p-toluenesulfonic acid (7.6 mg, 0.040mmol, 2.0 mol%) was placed in a round-bottom flask with a Dean Stark trap and heated at reflux for 10 h. The reaction turned a deep brown color. After 10 h, charcoal was added to the hot solution and the mixture was stirred for 1 h and filtered.

(3) Harris, J. M.; Padwa, A., *J. Org. Chem.* **2003**, *68*, 4371—4381

The solvent was removed and the product crystallized from benzene to give the desired product (424 mg, 80% yield) as brown crystals.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H,), 7.91 (dd, 2H, *J* = 6.9, 2.0), 7.74 (d, 1H, *J* = 0.8), 7.33 (d, 1H, *J* = 3.7), 6.99 (dd, 2H, *J* = 6.9, 2.0), 6.64 (dd, 1H, *J* = 3.7, 1.7), 3.86 (s, 3H)
^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 155.4, 149.8, 149.2, 130.5, 129.7, 124.7, 114.6, 113.9, 55.9
IR (thin film) *v* 3054, 2985, 2305, 1598, 1546, 1265, 1160, 896, 821, 738, 705 cm^{-1}
ESI-MS: 266.0 (M+H)
MP: 97-99°C

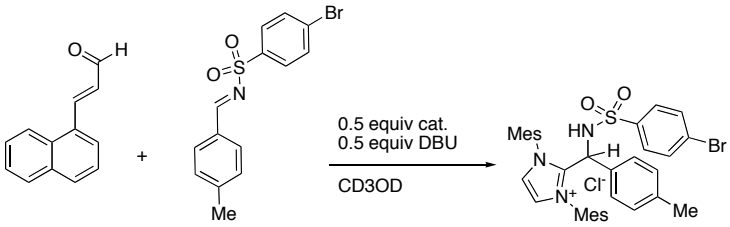
NOE Experiment of Product 10



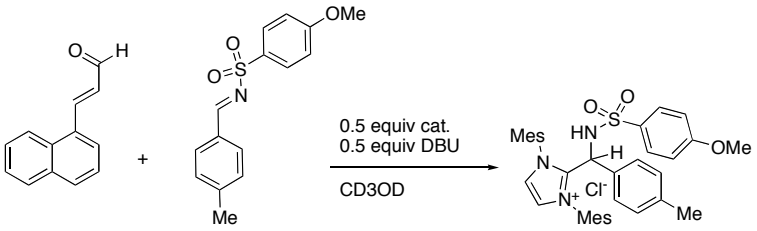
NMR Studies of Catalyst Inhibition

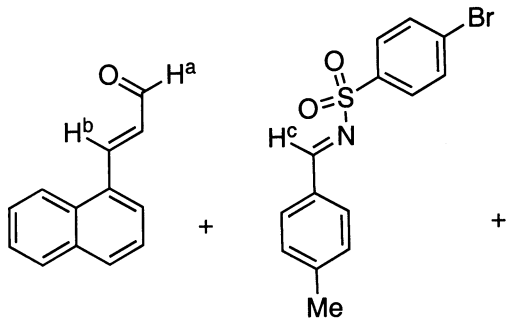
In a NMR tube was dissolved the enal (1.0 equiv), imine (1.0 equiv) and IMes-Cl (0.5 equiv) in CD_3OD, and the ^{1}H-NMR spectrum was measured. After addition of 0.5 equiv DBU to the mixture the reaction was followed by the ^{1}H-NMR was.

1) See Page 15 for ^{1}H-NMR spectrum.



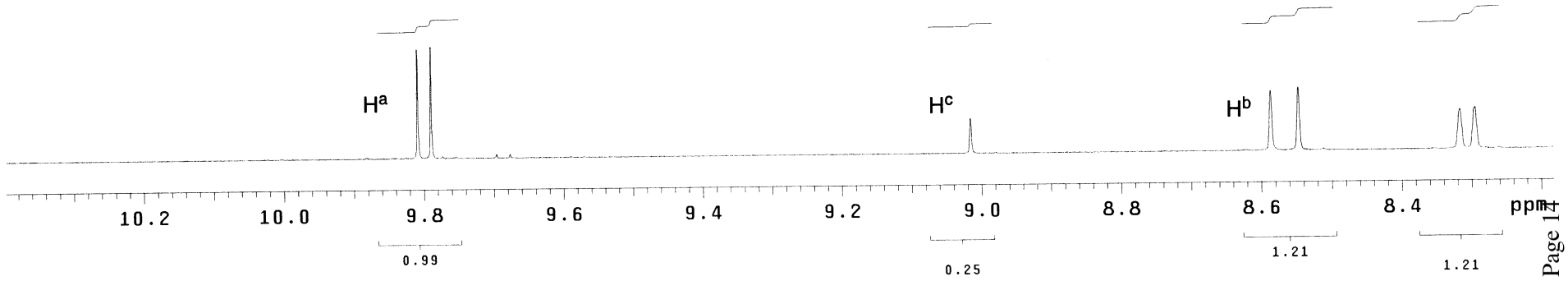
2) See Page 16 for ^{1}H-NMR spectrum.



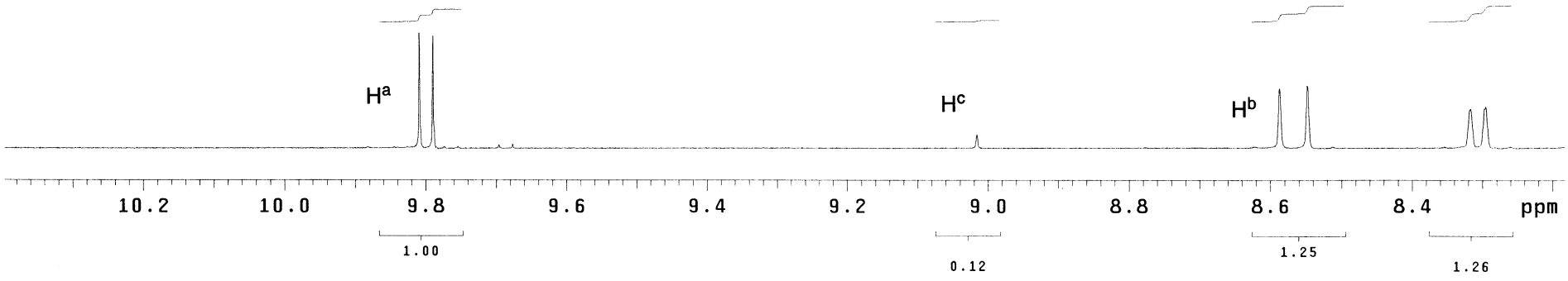


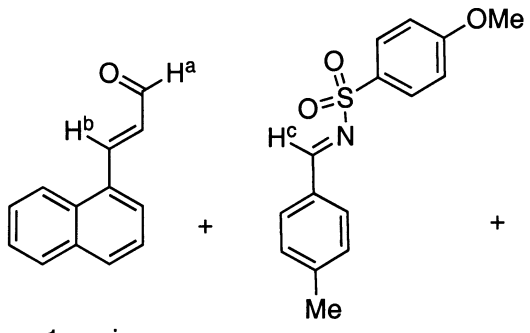
1 equiv + 1 equiv + IMes-Cl 0.5 equiv

0.02 M in CD_3OD

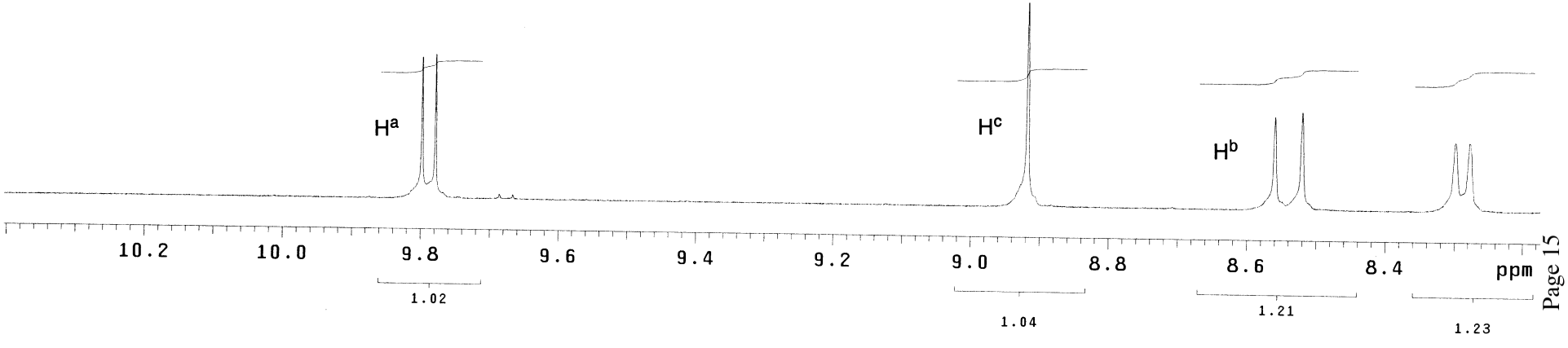


After addition of 0.5 equiv DBU

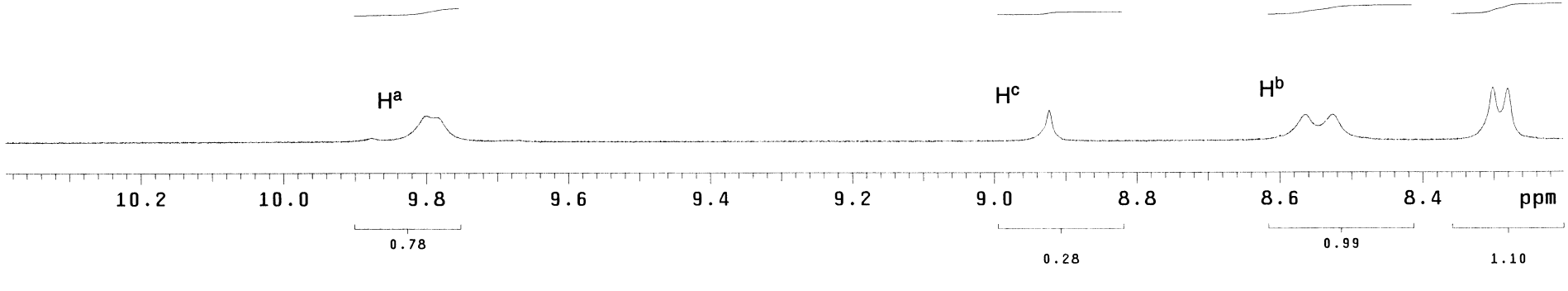




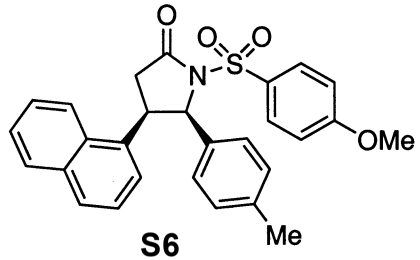
1 equiv + 1 equiv + IMes-Cl 0.5 equiv 0.05 M in CD_3OD



After addition of 0.5 equiv DBU



INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	3307.938	8.271	11.6	40	2645.052	6.613	12.7
2	3299.339	8.249	12.5	41	2501.020	6.253	26.3
3	3146.093	7.866	11.7	42	2492.882	6.233	25.0
4	3137.955	7.846	13.1	43	2390.002	5.976	14.8
5	3102.792	7.758	3.7	44	2382.325	5.957	15.5
6	3099.721	7.750	33.7	45	1957.292	4.894	3.0
7	3097.725	7.745	13.4	46	1949.768	4.875	6.0
8	3092.811	7.733	10.8	47	1942.858	4.858	5.3
9	3090.661	7.728	39.0	48	1936.102	4.841	6.4
10	3087.590	7.720	10.8	49	1928.424	4.822	3.1
11	3086.208	7.717	9.0	50	1557.442	3.894	7.4
12	3083.291	7.709	2.9	51	1552.682	3.882	152.2
13	3080.680	7.703	8.1	52	1338.783	3.347	7.7
14	3079.145	7.699	12.2	53	1325.117	3.313	7.3
15	3077.763	7.695	8.3	54	1321.739	3.305	9.1
16	3072.081	7.681	7.0	55	1308.073	3.271	8.1
17	3070.853	7.678	7.9	56	1100.931	2.753	9.4
18	3052.427	7.632	12.9	57	1093.407	2.734	9.8
19	3044.595	7.612	13.7	58	1084.040	2.710	8.6
20	3034.154	7.586	7.8	59	1076.516	2.692	8.1
21	3033.233	7.584	9.8	60	965.498	2.414	4.8
22	3026.169	7.566	13.2	61	852.944	2.133	86.9
23	3025.094	7.564	11.6	62	822.541	2.057	7.3
24	3019.106	7.549	5.8	63	634.286	1.586	33.3
25	3018.184	7.546	7.6	64	507.452	1.269	4.6
26	2907.627	7.270	68.4	65	504.227	1.261	4.2
27	2906.552	7.267	19.2				
28	2889.354	7.224	7.7				
29	2830.851	7.078	9.5				
30	2822.866	7.058	14.2				
31	2815.495	7.040	9.9				
32	2758.374	6.897	3.9				
33	2755.457	6.890	36.2				
34	2753.460	6.885	14.0				
35	2748.393	6.872	10.3				
36	2746.397	6.867	36.1				
37	2743.326	6.859	6.5				
38	2659.793	6.650	21.6				
39	2651.962	6.631	36.3				

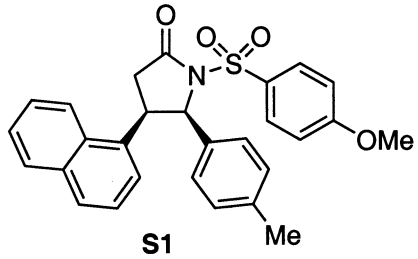


S6

$C_{28}H_{25}NO_4S$

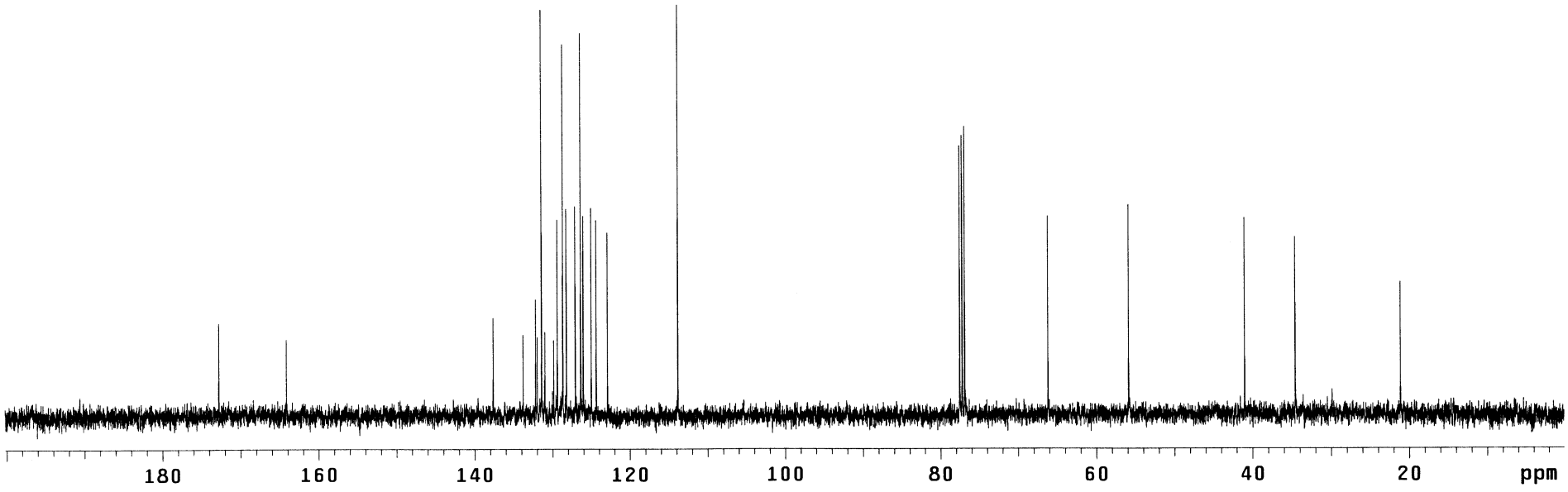
Exact Mass: 471.2

INDEX	FREQUENCY	PPM	HEIGHT
1	17374.791	172.768	15.1
2	16505.777	164.127	12.5
3	13839.985	137.619	15.9
4	13452.400	133.765	13.2
5	13290.652	132.157	18.8
6	13268.526	131.937	12.8
7	13212.829	131.383	64.6
8	13170.866	130.966	13.6
9	13057.185	129.835	12.3
10	13009.881	129.365	31.4
11	12938.163	128.652	59.1
12	12892.385	128.197	33.1
13	12775.652	127.036	33.5
14	12706.222	126.346	60.9
15	12672.652	126.012	32.0
16	12568.889	124.980	33.3
17	12504.800	124.343	31.3
18	12357.548	122.879	29.4
19	11448.097	113.835	65.3
20	7798.846	77.549	42.9
21	7766.801	77.230	44.5
22	7734.757	76.911	45.9
23	6655.165	66.176	31.8
24	5619.061	55.874	33.6
25	4123.654	41.004	31.5
26	3478.188	34.586	28.4
27	2125.455	21.135	21.3

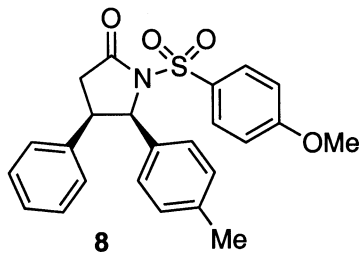


S1

$C_{28}H_{25}NO_4S$
Exact Mass: 471.2



INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	3091.468	7.730	3.5	40	2704.669	6.763	12.0
2	3088.397	7.722	34.3	41	2702.213	6.756	13.9
3	3086.400	7.717	10.1	42	2614.074	6.536	27.2
4	3081.487	7.705	10.7	43	2605.935	6.516	23.9
5	3079.337	7.699	38.0	44	2234.800	5.588	15.2
6	3076.266	7.692	5.3	45	2226.968	5.568	15.6
7	3071.199	7.679	2.1	46	2106.276	5.266	2.9
8	3069.049	7.674	6.8	47	2103.973	5.261	2.9
9	2917.646	7.295	4.3	48	1644.084	4.111	3.2
10	2915.650	7.290	2.8	49	1636.253	4.091	6.7
11	2913.961	7.286	5.8	50	1630.418	4.077	4.3
12	2911.197	7.279	7.0	51	1628.422	4.072	4.2
13	2905.055	7.264	33.8	52	1622.587	4.057	7.1
14	2867.896	7.171	2.4	53	1614.756	4.037	3.5
15	2859.757	7.150	5.6	54	1553.335	3.884	27.9
16	2847.320	7.119	8.7	55	1546.578	3.867	153.1
17	2845.323	7.114	7.5	56	1531.377	3.829	3.0
18	2844.709	7.113	7.0	57	1235.021	3.088	2.4
19	2842.252	7.107	33.8	58	1228.111	3.071	8.7
20	2840.563	7.102	32.5	59	1226.268	3.066	2.7
21	2837.799	7.095	13.7	60	1214.445	3.037	8.2
22	2836.878	7.093	13.2	61	1210.913	3.028	10.5
23	2835.189	7.089	18.9	62	1197.247	2.994	10.1
24	2831.964	7.081	6.6	63	1084.540	2.712	10.9
25	2830.429	7.077	6.6	64	1076.709	2.692	11.2
26	2828.586	7.072	4.3	65	1067.342	2.669	9.1
27	2825.976	7.066	4.0	66	1059.511	2.649	8.4
28	2822.444	7.057	2.8	67	949.107	2.373	15.2
29	2753.038	6.883	6.8	68	890.450	2.226	84.0
30	2750.889	6.878	3.0	69	638.470	1.596	7.9
31	2749.660	6.875	4.4	70	502.423	1.256	7.4
32	2746.743	6.868	37.3	71	29.636	0.074	2.2
33	2744.593	6.862	13.7				
34	2739.679	6.850	10.8				
35	2737.683	6.845	35.7				
36	2732.923	6.833	20.3				
37	2725.092	6.814	22.2				
38	2711.579	6.780	13.6				
39	2709.737	6.775	16.1				



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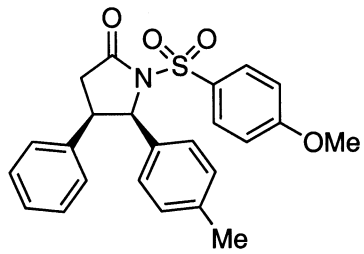
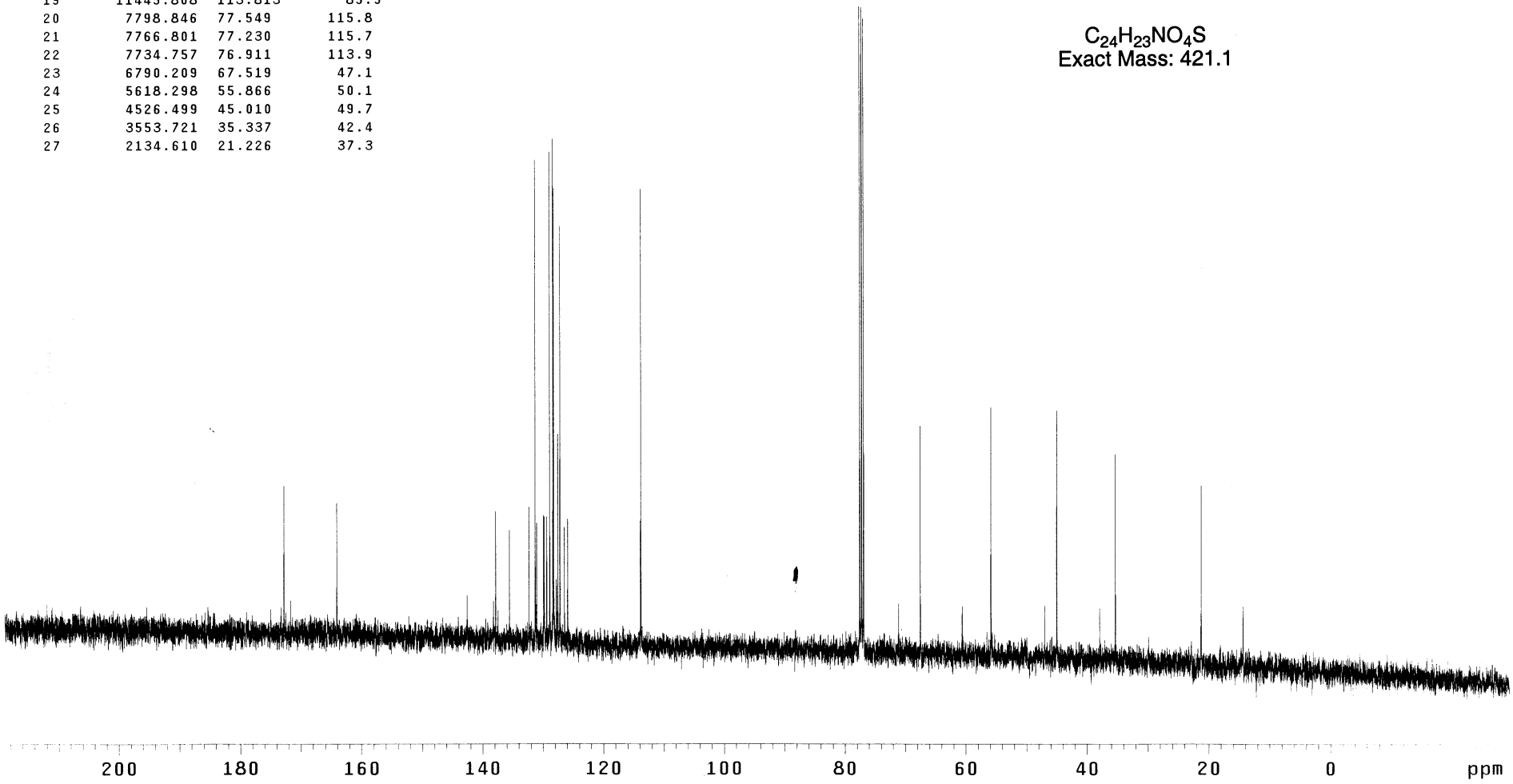
$C_{24}H_{23}NO_4S$
Exact Mass: 421.1

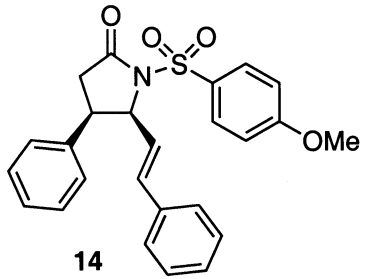
INDEX	FREQUENCY	PPM	HEIGHT
1	17378.606	172.806	37.4
2	16500.436	164.074	34.6
3	13861.348	137.832	33.1
4	13633.222	135.563	30.1
5	13305.148	132.301	33.9
6	13203.674	131.292	90.7
7	13180.022	131.057	31.3
8	13064.815	129.911	32.5
9	13051.844	129.782	32.3
10	13010.644	129.373	32.3
11	12961.815	128.887	92.0
12	12908.407	128.356	94.1
13	12894.674	128.220	86.1
14	12827.533	127.552	45.8
15	12790.911	127.188	79.9
16	12716.141	126.444	30.6
17	12663.496	125.921	31.9
18	11452.674	113.881	31.6
19	11445.808	113.813	85.9
20	7798.846	77.549	115.8
21	7766.801	77.230	115.7
22	7734.757	76.911	113.9
23	6790.209	67.519	47.1
24	5618.298	55.866	50.1
25	4526.499	45.010	49.7
26	3553.721	35.337	42.4
27	2134.610	21.226	37.3



$C_{24}H_{23}NO_4S$
Exact Mass: 421.1



INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	3188.052	7.971	36.2	40	2228.197	5.571	10.1
2	3186.056	7.966	11.1	41	2220.366	5.552	11.7
3	3181.142	7.954	11.2	42	2131.920	5.330	7.8
4	3179.146	7.949	38.6	43	2124.396	5.312	14.2
5	3176.075	7.941	4.3	44	2116.564	5.292	7.0
6	2938.990	7.348	6.4	45	1598.479	3.997	6.4
7	2927.627	7.320	10.2	46	1592.030	3.981	4.8
8	2926.092	7.316	4.8	47	1585.120	3.963	6.8
9	2920.717	7.303	26.8	48	1544.275	3.861	12.2
10	2919.336	7.299	16.1	49	1529.688	3.825	151.3
11	2915.957	7.291	5.9	50	1206.307	3.016	8.3
12	2913.040	7.284	21.0	51	1192.794	2.982	7.9
13	2904.595	7.262	13.3	52	1189.262	2.974	11.0
14	2902.905	7.258	6.1	53	1175.750	2.940	10.4
15	2900.909	7.253	9.9	54	1101.584	2.754	10.6
16	2899.527	7.250	14.2	55	1094.060	2.736	11.0
17	2897.992	7.246	23.7	56	1084.693	2.712	8.3
18	2894.153	7.236	15.8	57	1077.016	2.693	7.6
19	2891.850	7.231	41.8	58	819.355	2.049	5.6
20	2890.621	7.227	35.3	59	661.657	1.654	17.6
21	2886.782	7.218	8.8				
22	2885.093	7.214	8.1				
23	2859.911	7.151	23.7				
24	2852.694	7.133	20.3				
25	2823.672	7.060	19.7				
26	2821.369	7.054	16.1				
27	2819.219	7.049	9.7				
28	2818.452	7.047	9.4				
29	2815.995	7.041	17.3				
30	2814.306	7.037	14.1				
31	2751.042	6.878	6.7				
32	2748.125	6.871	38.4				
33	2746.129	6.866	11.6				
34	2741.215	6.854	11.1				
35	2739.065	6.849	36.8				
36	2562.327	6.407	13.5				
37	2546.664	6.367	14.8				
38	2244.013	5.611	11.2				
39	2236.182	5.591	12.9				



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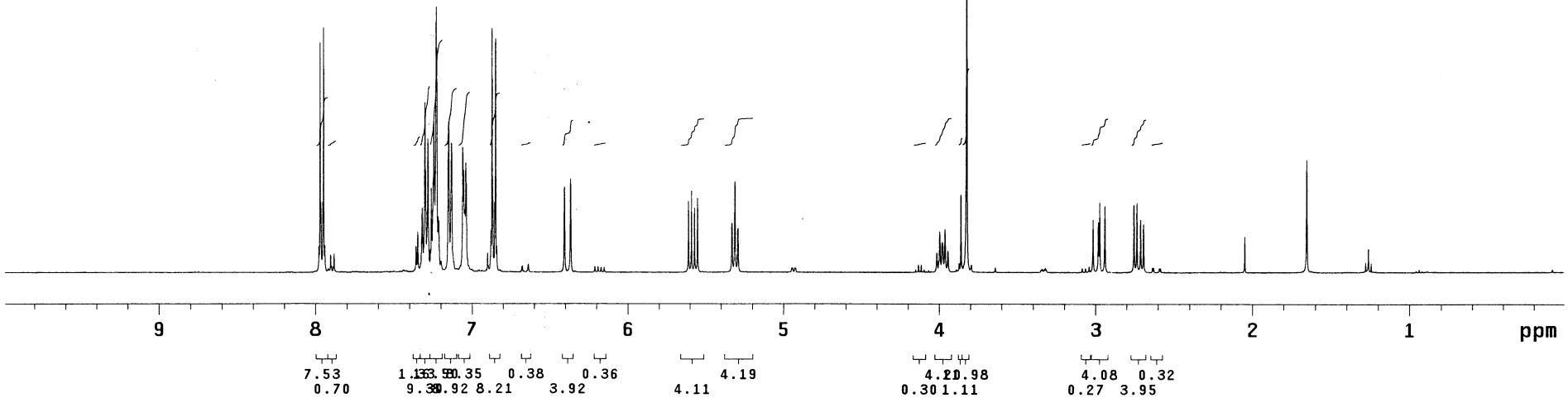
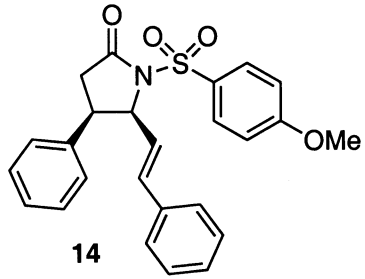
$C_{25}H_{23}NO_4S$
Exact Mass: 433.1



INDEX	FREQUENCY	PPM	HEIGHT
1	17312.991	172.154	12.0
2	16501.199	164.081	20.6
3	13657.637	135.806	13.8
4	13648.481	135.715	20.4
5	13544.718	134.683	52.1
6	13205.200	131.307	97.0
7	13183.074	131.087	11.1
8	13104.489	130.306	11.2
9	12958.763	128.857	104.9
10	12941.978	128.690	103.9
11	12904.593	128.318	48.5
12	12880.941	128.083	114.1
13	12861.104	127.886	53.1
14	12745.896	126.740	114.9
15	12731.400	126.596	12.5
16	12388.830	123.190	36.2
17	11473.274	114.086	110.5
18	7798.083	77.541	54.8
19	7766.039	77.222	57.5
20	7733.994	76.904	58.2
21	6612.439	65.751	50.6
22	5615.247	55.836	40.2
23	4377.721	43.530	42.4
24	3541.514	35.215	48.8



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$C_{25}H_{23}NO_4S$
Exact Mass: 433.1