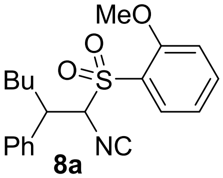
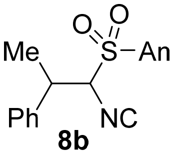
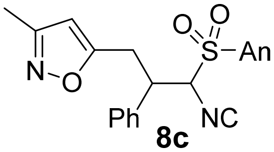
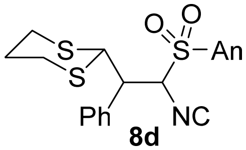
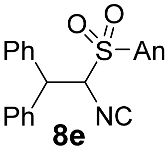
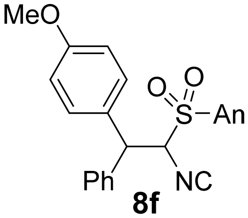
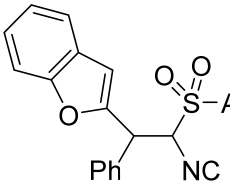
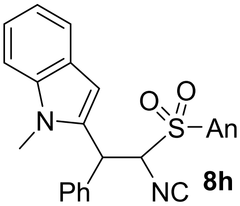
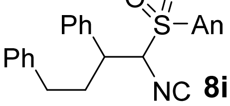
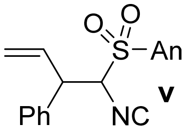
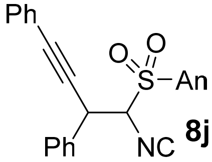
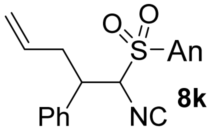
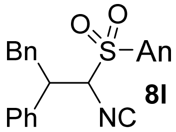
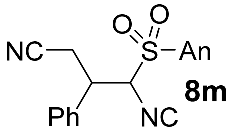
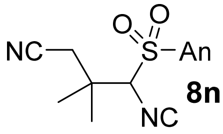
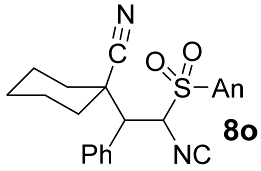
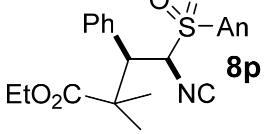
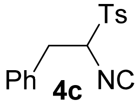
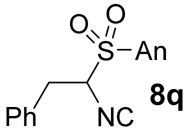
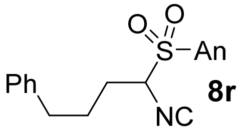
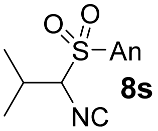
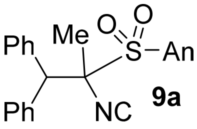
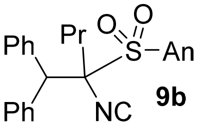
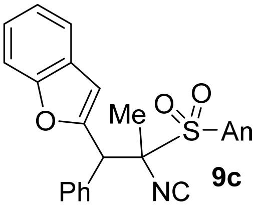
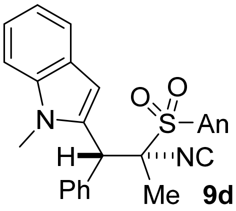
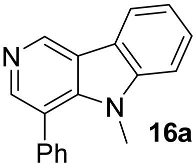
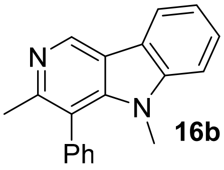
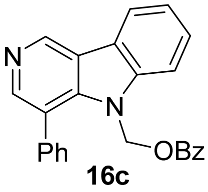
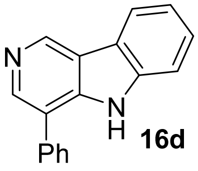
 **8a**	S19	S66	S66
 **8b**	S20	S67−S68	S67−S68
 **8c**	S21	S69−S70	S69−S70
 **8d**	S22	S71	S71
 **8e**	S23	S72	S72
 **8f**	S23	S73−S74	S73−S74
 **8g**	S24	S75−S76	S75−S76
 **8h**	S25	S77−S78	S77−S78
 **8i**	S27	S79	S79

 **v**	S28	S80	S80
 **8j**	S28	S81−S82	S81−S82
 **8k**	S29	S83−S84	S83−S84
 **8l**	S30	S85−S86	S85−S86
 **8m**	S31	S89	S89
 **8n**	S32	S88	S88
 **8o**	S33	S89	S89
 **8p**	S34	S90	S90
General isocyanide $NaBH_4$ reduction procedure	S34		
 **4c**	S35	S91	S91
 **8q**	S35	S92	S92
 **8r**	S36	S93	S93

 **8s**	S36	S94	S94
 **9a**	S36	S95	S95
 **9b**	S37	S96	S96
 **9c**	S38	S97	S97
 **9d**	S39	S98	S98
 **16a**	S40	S99	S99
 **16b**	S41	S100	S100
 **16c**	S41	S101	S101
 **16d**	S42	S102	S102

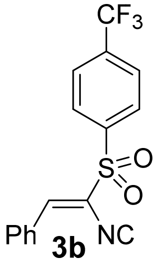
General Methods.

All nonaqueous reactions were performed in oven- or flame-dried glassware under a nitrogen atmosphere. All chemicals were purchased from commercial vendors and used as received unless otherwise specified. Anhydrous tetrahydrofuran (THF) and diethyl ether were distilled from benzophenone-sodium under N_2 before use, dichloromethane, dimethylsulfoxide (DMSO) and diisopropylamine were obtained from a solvent purification system (Innovative Technology Inc., model PS-MD7). Benzaldehyde was distilled under reduced pressure before use. Chlorotrimethylsilane, 3,5-dimethylisoxazole, DMPU and HMPA were dried over CaH_2 and distilled before use. MeLi, BuLi, *t*BuLi, PhLi and Bu_2Mg were used as solutions in Et_2O (1.6 M), hexanes (1.6 M), heptane (2 M), Bu_2O (1.45 M) and heptane (0.5 M) respectively. Arylsulfonylmethylisocyanides **2b-e**[1,2] and 1-isocyano-2-phenyl-1-tosylethene **3a**[3] were prepared by known methods. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 250 μm precoated silica gel plates. Preparative radial chromatography was performed on 1 or 2 mm plates prepared in-house that were coated with silica (PGF-Prep TLC w/Gypsum UV/254, 5-50 *μ*m). ^1H NMR and ^{13}C NMR high resolution nuclear magnetic resonance spectra were recorded on a Varian Inova 300 (300 MHz/75 MHz), Varian Inova 500 (500 MHz/126 MHz), Bruker Avance 400 (400 MHz/106 MHz), and Bruker Avance 500 (500 MHz/126 MHz) spectrometers at 25 °C. Chemical shifts are reported relative to TMS (δ 0.00), MeCN-D_3 (δ 1.94), CD_3OD (δ 3.31), DMSO-d_6 (δ 2.50) for ^1H NMR and chloroform (δ 77.16), acetonitrile (δ 1.32 and 118.26), methanol (δ 49.00) or DMSO (δ 39.52) for ^{13}C NMR. IR spectra were recorded as thin films (PerkinElmer Spectrum 100 FT-IR Spectrometer). High-resolution mass spectra were obtained on a Bruker 12.0 Tesla APEX

– Qe FTICR-MS with and Apollo II ion source (positive electrospray ionization) and Thermo-Finnigan LTQ-FT 7T FT-ICR spectrometer with an atmospheric pressure chemical ionization (APCI) source with direct infusion run in positive ion mode at 5 kV.

General isocyanide olefination procedure.

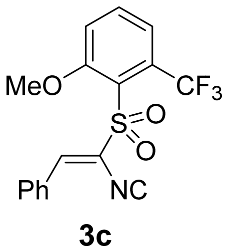
A hexanes solution (2.6 mL) of BuLi (1.6 M, 2.1 eq.) was added dropwise to a -78 °C, THF solution (15 mL) of the isocyanide (2 mmol, 1 eq.). After 10 min, a THF solution (2.5 mL) of TMSCl (2 mmol, 1 eq.) was added dropwise over 10 min. After 15 min, a THF solution (2.5 mL) of the aldehyde (2 mmol, 1 eq.) was added dropwise. After 1-3 h the reaction was allowed to warm to -30 °C (isocyanides **3b, e**) or to 10 °C (isocyanides **3c, d**) and then the mixture was added to a -5 °C H_2O-MeOH (5:1) solution of NH_4Cl (5%). After 15-30 min, methyl *tert*-butyl ether (MTBE) or CH_2Cl_2 (20 mL) was added, the phases were separated and aqueous phase was extracted with MTBE or CH_2Cl_2 (2 x 20 mL). The combined organic phase was washed with brine (2 x 10 mL), dried (Na_2SO_4), concentrated and purified by radial chromatography or crystallization to give the pure isocyanide.



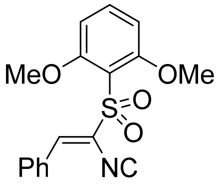
3b

(*E*)-1-((1-Isocyano-2-phenylvinyl)sulfonyl)-4-(trifluoromethyl)-benzene (3b) was prepared from isocyanide **2b**[4] (500 mg, 2 mmol) according to the general method. Crystallization (CH_2Cl_2/hexanes, 1:3) afforded 398 mg (59%) of isocyanide **3b** as pale-orange needles: mp 63-65 °C(dec); IR 2099, 1615, 1319, 1160 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.3 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 7.86-7.78 (m, 2H), 7.74 (s, 1H), 7.60-7.44 (m, 3H); ^{13}C NMR (101 MHz,

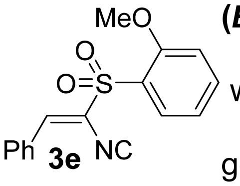
$CDCl_3$) δ 179.67, 140.19, 136.59, 136.42 (q, *J* = 33.4 Hz), 133.23, 131.12, 129.86, 129.59, 129.53, 126.90 (q, *J* = 3.5), 124.43, 123.24, 121.71, 119.00; HRMS (ESI) calcd for $C_{16}H_{10}F_3NO_2SNa$ [M+Na]$^+$: 360.0277, found: 360.0276.


3c

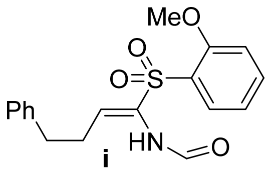
(*E*)-2-((1-Isocyano-2-phenylvinyl)sulfonyl)-1-methoxy-3-(trifluoromethyl)-benzene (3c) was prepared from isocyanide **2c**^{4} (560 mg, 2 mmol) according to the general method. Purification (2 mm plate, hexanes/Et_2O/CH_2Cl_2, 4:1:1) afforded 375 mg (51%) of isocyanide **3c** as a white crystalline solid. Crystallization (MeOH) afforded analytical sample of isocyanide **3c** as pale-yellow crystals: mp 96-98 °C(dec.); IR 2101, 1619, 1356, 1162 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0 and 1.8 Hz, 2H), 7.74 (t, *J* = 8.2 Hz, 1H), 7.63 (s, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.56-7.46 (m, 3H), 7.32 (d, *J* = 8.5 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.93, 159.20, 135.69, 135.60, 132.59, 132.18 (q, *J* = 33.5 Hz), 130.75, 130.05, 129.48, 126.37, 125.54, 124.46, 123.64, 120.87 (q, *J* = 7.5 Hz), 117.33, 57.14; HRMS (ESI) calcd for $C_{17}H_{12}F_3NO_3SNa$ [M+Na]$^+$: 390.0382, found: 390.0382.

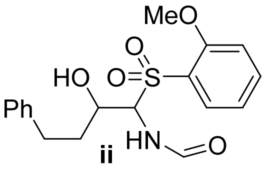

3d

(*E*)-2-((1-Isocyano-2-phenylvinyl)sulfonyl)-1,3-dimethoxybenzene (3d) was prepared from isocyanide **2d**^{4} (485 mg, 2 mmol) according to the general method. Purification (2 mm plate, hexanes/Et_2O/CH_2Cl_2, from 6:1:1 to 4:1:1) afforded 425 mg (64%) of isocyanide **3d** as a pale-pink solid. Crystallization (MeOH) afforded pure isocyanide **3d** as yellow leaves: mp 103-105 °C(dec); IR 2100, 1619, 1327, 1154 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.75 (m, 2H), 7.60 (s, 1H), 7.56-7.43 (m, 4H), 6.65 (d, *J* = 8.5 Hz, 2H), 3.89 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.74, 160.14, 136.24, 133.93, 132.03, 130.49, 130.34, 129.28, 126.42, 113.32, 105.18, 100.00, 56.76; HRMS (+APCI) calcd for $C_{17}H_{16}NO_4S$ [M+H]$^+$: 330.0795, found: 330.0794.

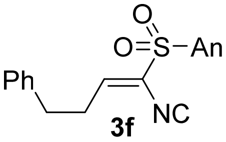

3e

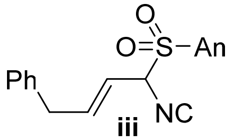
(*E*)-1-((1-Isocyano-2-phenylvinyl)sulfonyl)-2-methoxybenzene (3e) was prepared from isocyanide **2e**[4] (423 mg, 2 mmol) according to the general method. Purification (2 mm plate, hexanes/Et_2O/CH_2Cl_2, 6:1:1) afforded 401 mg (67%) of isocyanide **3e** as a white crystalline solid. Crystallization (MeOH) afforded an analytical sample of isocyanide **3e** as pale-yellow crystals: mp 116-118 (dec.); IR 2101, 1618, 1331, 1157 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 7.9 and 1.6 Hz, 1H), 7.90-7.78 (m, 2H), 7.73 (s, 1H), 7.70-7.62 (m, 1H), 7.57-7.44 (m, 3H), 7.17 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 8.1 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.23, 157.72, 136.96, 136.72, 132.47, 132.26, 130.73, 130.26, 129.38, 123.71, 120.97, 112.63, 56.33; HRMS (ESI) calcd for $C_{16}H_{13}NO_3SNa$ [M+Na]$^+$: 322.0508, found: 322.0508.


i


ii

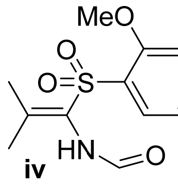
(*E*)-*N*-(1-((2-Methoxyphenyl)sulfonyl)-4-phenylbut-1-en-1-yl)-formamide (i) and *N*-(2-hydroxy-1-((2-methoxyphenyl)-sulfonyl)-4-phenylbutyl)formamide (ii). A THF solution (10 mL) of isocyanide **2e**[4] (2.053 g, 9.7 mmol) was added dropwise to a -70 °C, THF (45 mL) suspension of *t*-BuOK (1.450 g, 12.9 mmol). After 15 min a yellow-orange solution was formed, and then a THF solution (10 mL) of 3-phenyl-propionaldehyde (1.304 g, 9.7 mmol, 1.28 mL) was added dropwise. After 1 h the reaction was allowed to warm to -30 °C and then the mixture was poured into ice-cold water (75 mL) containing acetic acid (2 mL). After 5 min, CH_2Cl_2 (50 mL) was added, the phases were separated, and then the aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic phase was washed with brine (30 mL), cold water (30 mL), dried (Na_2SO_4), concentrated and purified by column chromatography (PhMe/EtOAc, 90:10 to 75:25 and then triturating with cold Et_2O) to afford 1.29 g (38%) of formamide **i** as a white solid: mp 101-103 °C; IR 3290, 1704, 1299, 1145 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{19}NO_4SNa$ $[M+Na]^+$: 368.0927, found: 368.0926. The ^1H NMR indicated a 1.6:1 ratio of rotamers. For rotamer 1: ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.87 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.56-7.51 (m, 1H), 7.37 (br. s, 1H), 7.32-6.92 (m, 8H), 3.82 (s, 3H), 2.82 (q, *J* = 7.2 Hz, 2H), 2.48 (q, *J* = 7.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.71, 158.34, 140.64, 139.88, 136.08, 131.61, 130.85, 128.61, 128.50, 126.34, 125.39, 120.41, 112.86, 56.19, 33.78, 30.87. For rotamer 2: ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.9 and 1.6 Hz, 1H), 7.67-7.56 (m, 1H), 7.46 (d, *J* = 11.0 Hz, 1H), 7.32-6.92 (m, 8H), 6.88 (d, *J* = 11.0 Hz, 1H), 3.82 (s, 3H), 2.82 (q, *J* = 7.2 Hz, 2H), 2.62 (q, *J* = 7.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.90, 157.44, 139.68, 139.00, 136.35, 135.24, 131.45, 128.76, 128.46, 126.71, 125.02, 121.07, 112.55, 56.26, 34.47, 29.61. Further elution (PhMe/EtOAc, 75:25 to 40:60) from the silica gel column afforded 0.29 g (8%) of the formamide **ii**, a pale-yellow solid, as a 9.2:1 ratio of diastereomers. Crystallization (CH_2Cl_2/hexanes, 1:2) afforded pure formamide **ii** as a white crystalline solid: mp 141-143 °C; IR 3323, 1670, 1312, 1146 cm^{-1}. For the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.86 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.66-7.56 (m, 1H), 7.40-7.27 (m, 2H), 7.24-7.12 (m, 3H), 7.12-6.96 (m, 2H), 6.66 (d, *J* = 10.2 Hz, 1H), 5.69 (d, *J* = 10.2 Hz, 1H), 4.83-4.72 (m, 1H), 4.01 (s, 3H), 3.03-2.93 (m, 1H), 2.89-2.66 (m, 2H), 1.98-1.82 (m, 1H), 1.81-1.67 (m, 1H). For the minor diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.71-7.66 (m, 1H), 7.40-7.27 (m, 3H), 7.24-7.12 (m, 3H), 7.12-6.96 (m, 2H), 6.66 (d, *J* = 10.2 Hz, 1H), 5.69 (d, *J* = 10.2 Hz, 1H), 4.67-4.58 (m, 1H), 3.97 (s, 3H), 3.11-3.03 (m, 1H), 2.89-2.66 (m, 2H), 1.98-1.82 (m, 1H), 1.81-1.67 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 160.27, 158.37, 140.94, 136.74, 131.60, 128.68, 128.58, 126.32, 123.67, 120.44, 112.77, 67.79, 66.53, 56.62, 35.56, 31.62; HRMS (ESI) calcd for $C_{18}H_{21}NO_5SNa$ [M+Na]$^+$: 386.1033, found: 386.1031.


3f


iii

(*E*)-1-((1-Isocyano-4-phenylbut-1-en-1-yl)sulfonyl)-2-methoxybenzene (3f) and (*E*)-1-((1-isocyano-4-phenylbut-2-en-1-yl)sulfonyl)-2-methoxybenzene (iii). A CH_2Cl_2 solution (5 mL) of Et_3N (1.31 g, 13 mmol, 1.8 mL) and a CH_2Cl_2 solution of $POCl_3$ (461 mg, 3 mmol, 0.28 mL) were added sequentially to a -25 °C, CH_2Cl_2 solution (25 mL) of formamide **i** (730 mg, 2.1 mmol). After 1 h the reaction was allowed to warm to -10 °C and then the mixture was poured into ice-cold water (30 mL). The phases were separated and the aqueous phase was then extracted with CH_2Cl_2 (20 mL). The combined organic phase was washed with cold, saturated, aqueous $NaHCO_3$ (15 mL), cold water (15 mL), dried (Na_2SO_4), and concentrated to afford 705 mg of a mixture of isocyanides **3f**:**iii (**2.0:1, determined by ^{1}H NMR integration of the MeO signals at 3.78 and 3.98 ppm, respectively). Separation by column chromatography (hexanes/Et_2O/ CH_2Cl_2, 7:1:1 to 6:1:1) afforded 220 mg (32%) of isocyanide **3f** as a colorless crystalline solid and 181 mg (26%) of a mixture of **3f** and **iii** (1:5.9 by ^{1}H NMR integration). Repeated purification (2 mm plate, hexanes/Et_2O/CH_2Cl_2, 6:1:1) afforded 132 mg (19%) of pure isocyanide **iii** as a thick, colorless oil. For **3f**: mp 93-94 °C; IR 2110, 1592, 1333, 1155 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.01 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.73-7.57 (m, 1H), 7.35-7.26 (m, 2H), 7.25-7.20 (m, 1H), 7.20-7.04 (m, 4H), 7.00 (d, *J* = 8.4 Hz, 1H), 3.78 (s, 3H), 2.93-2.80 (m, 2H), 2.80-

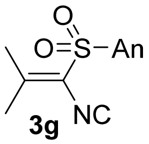
2.70 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.86, 157.75, 143.12, 139.37, 136.93, 132.09, 128.87, 128.35, 126.81, 123.87, 120.95, 112.54, 56.08, 33.65, 30.54; HRMS (ESI) calcd for $C_{18}H_{17}NO_3SNa$ $[M+Na]^+$: 350.0821, found: 350.0820. For **iii**: IR 2134, 1330, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.76-7.60 (m, 1H), 7.36-7.28 (m, 2H), 7.25-7.20 (m, 1H), 7.20-7.10 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.32 (dtd, *J* = 14.8, 6.8 and 1.0 Hz, 1H), 5.69 (ddt, *J* = 14.8, 6.3 and 1.5 Hz, 1H), 5.62 (dd, *J* = 6.3 and 1.0 Hz, 1H), 3.98 (s, 3H), 3.52 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.50, 157.72, 141.56, 138.05, 137.07, 132.65, 128.82, 128.78, 126.78, 123.08, 121.34, 115.65, 112.63, 72.59, 56.65, 38.70; HRMS (+APCI) calcd for $C_{18}H_{18}NO_3S$ $[M+H]^+$: 328.1002, found: 328.1008.



iv

***N*-(1-((2-Methoxyphenyl)sulfonyl)-2-methylprop-1-en-1-yl)formamide (iv)**. A THF solution (5 mL) of isocyanide **2e**[4] (1.290 g, 6.1 mmol) was added dropwise to a THF (25 mL) suspension of *t*-BuOK (0.959 g, 8.5 mmol) at -70 °C. After 15 min a yellow-orange solution was formed and then acetone (0.355 g, 6.1 mmol, 0.5 mL) was added dropwise. After 1.5 h the reaction was allowed to warm to -30 °C and then the mixture was poured into ice-cold water (50 mL) containing acetic acid (1 mL). The mixture was kept at -5 °C for 40 min and then filtered through a glass frit. The filtrate was extracted with CH_2Cl_2 (3 x 50 mL) and then the phases were separated. The combined organic phase was washed with brine (2 x 30 mL), dried (Na_2SO_4), concentrated and purified by triturating with Et_2O (3 x 5 mL) to afford 705 mg (43%) of formamide **iv** as a pale-orange solid. Crystallization (CH_2Cl_2/hexanes, 1:3) afforded a pure sample of formamide **iv**, a colorless solid, as a 1.8:1 ratio of rotamers: mp 165-166 °C; IR 3309, 1695, 1297, 1145 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{15}NO_4SNa$ $[M+Na]^+$:

292.0614, found: 292.0613. For the major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 1.1 Hz, 1H), 7.97 (dd, J = 7.6, 1.2 Hz, 1H), 7.62-7.50 (m, 2H), 7.09-7.04 (m, 1H), 7.00 (d, J = 8.4, 1H), 3.90 (s, 3H), 2.16 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.73, 157.84, 148.11, 135.60, 130.10, 127.83, 126.78, 120.33, 112.59, 56.39, 24.19, 20.55. For the minor rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, J = 7.6, 1,2 Hz, 1H), 7.84 (d, J = 11.2 Hz, 1H), 7.62-7.50 (m, 1H), 7.15 (br. s, 1H), 7.13-7.09 (m, 1H), 7.01 (d, J = 8.4, 1H), 3.91 (s, 3H), 2.17 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.17, 157.36, 148.27, 135.85, 130.39, 129.91, 127.72, 120.93, 112.59, 56.53, 23.43, 20.59.

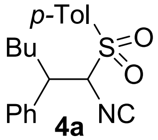


3g

1-((1-Isocyano-2-methylprop-1-en-1-yl)sulfonyl)-2-methoxybenzene (3g). A CH_2Cl_2 solution (5 mL) of Et_3N (1.31 g, 13 mmol, 1.8 mL) and a CH_2Cl_2 solution (5 mL) of $POCl_3$ (461 mg, 3 mmol, 0.28 mL) were sequentially added to a -25 °C, CH_2Cl_2 solution (25 mL) of formamide **iv** (667 mg, 2.5 mmol). After 1 h the reaction was allowed to warm to -10 °C and then the mixture was poured into ice-cold water (30 mL). The phases were separated and then the aqueous phase was extracted with CH_2Cl_2 (20 mL). The combined organic phase was washed with cold, saturated, aqueous $NaHCO_3$ (15 mL), cold water (15 mL), dried (Na_2SO_4), and then concentrated to afford 573 mg of crude isocyanide as yellow oil (solidified upon cooling). Purification by column chromatography (EtOAc/hexanes, 15:85 to 40:60) afforded 523 mg (84%) of isocyanide **3g** as a white crystalline solid: mp 106-107 °C; IR 2106, 1618, 1323, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.9, 1.7 Hz, 1H), 7.72-7.54 (m, 1H), 7.20-7.09 (m, 1H), 7.06 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 2.20 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.92, 157.76, 152.39, 136.37, 130.67, 126.59, 120.64, 112.57, 56.27, 24.79, 19.83; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_3SNa$ $[M+Na]^+$: 274.0508, found: 274.0508.

General alkeneisocyanide conjugate addition procedure.

A solution of the organo-metallic reagent (0.35-0.5 mmol) was added dropwise over 1 min to a cold (-78, -100, or -105 °C), THF solution (0.07 M) of the alkeneisocyanide **3a-g** (0.35 mmol). After 5-20 min, brine (3 mL) was added, the organic layer was separated, and then the aqueous phase was extracted with Et_2O, CH_2Cl_2, MTBE, or EtOAc (10-15 mL). The combined organic phase was washed with brine (2 x 5 mL) and dried (Na_2SO_4). Concentration of the solution and purification of the residue (dr ratio was determined from the crude ^{1}H NMR in $CDCl_3$ by integration of the $ArSO_2C\mathit{H}$ signals) by radial chromatography afforded the pure isocyanide, typically as a mixture of diastereomers.[5] Solutions of Bu_3MgLi were prepared by adding a hexanes solution of BuLi (1 eq.) to a -78 °C, THF solution (3 mL) of Bu_2Mg (1 eq.) and used after 10 min. Solutions of $BnBu_2MgLi$ and $AllylBu_2MgLi$[6] were prepared by adding a hexanes solution of BuLi (2 eq.) to a -30 °C, THF solution of BnMgBr (1 eq.) or AllylMgCl (1 eq.), respectively, and then the solutions were allowed to warm to 0 °C for 30 min.

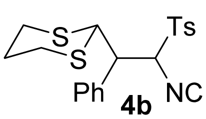


4a

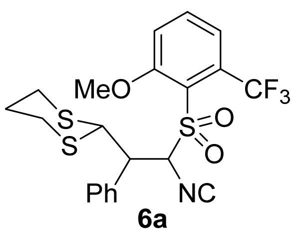
1-(((1*R, 2*S**)-1-Isocyano-2-phenylhexyl)sulfonyl)-4-methylbenzene and 1-(((1*S**, 2*S**)-1-isocyano-2-phenylhexyl)sulfonyl)-4-methylbenzene (4f).**

Following the general procedure with Bu_3MgLi (0.18 mmol) and isocyanide **3a** (51 mg, 0.18 mmol) at -100 °C then warming to -95 °C over 15 min (extraction with CH_2Cl_2) afforded a mixture of the diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:1.6 ratio) that were purified (1 mm plate, 5 °C hexanes/Et_2O/CH_2Cl_2, 6:1:1 to 4:1:1, under N_2) to afford 42 mg (69%)

of a mixture of diastereomers from which an enriched sample of (1*R**, 2*S**)-**4a** was obtained by repeated purification (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1, under N_2) as a pale-yellow oil: IR 2133, 1335, 1154 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NO_2SNa$ $[M+Na]^+$: 364.1342, found: 364.1343. For (1*R**, 2*S**)-**4a***:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.37-7.27 (m, 5H), 4.52 (d, *J* = 2.4, 1H), 3.65 (dt, *J* = 12.0 and 2.8 Hz, 1H), 2.46 (s, 3H), 2.21-2.05 (m, 1H), 2.04-1.90 (m, 1H), 1.40-1.24 (m, 2H), 1.24-1.05 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{1}H NMR (400 MHz, CD_3CN) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.40-7.22 (m, 5H), 5.03 (d, *J* = 4.1, 1H), 3.48 (dt, *J* = 11.6, 3.6 Hz, 1H), 2.46 (s, 3H), 2.071.96 (m, 1H), 1.93-1.82 (m, 1H), 1.40-1.21 (m, 2H), 1.21-0.97 (m, 2H), 0.80 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.70, 146.58, 139.52, 132.72, 130.29, 129.84, 129.22, 128.14, 127.97, 77.36, 42.94, 29.07, 22.53, 21.93, 14.00; ^{13}C NMR (101 MHz, CD_3CN) δ 166.99, 147.81, 139.87, 133.60, 131.09, 130.56, 129.74, 129.17, 128.76, 77.69, 44.10, 30.36, 29.45, 22.93, 21.75, 14.10. For (1*S**, 2*S**)-**4a**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.69 (d, *J* = 8.4, 2H), 7.43-7.28 (m, 7H), 4.70 (d, *J* = 5.3 Hz, 1H), 3.58-3.50 (m, 1H), 2.43 (s, 3H), 2.21-2.05 (m, 1H), 2.04-1.90 (m, 1H), 1.40-1.24 (m, 2H), 1.24-1.05 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{1}H NMR (400 MHz, CD_3CN) δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.40-7.22 (m, 5H), 5.13 (d, *J* = 5.6 Hz, 1H), 3.40 (dt, *J* = 11.6 and 4.0, 1H), 2.46 (s, 3H), 2.08-1.96 (m, 1H), 1.93-1.82 (m, 1H), 1.40-1.21 (m, 2H), 1.21-0.97 (m, 2H), 0.74 (t, *J* = 7.2 Hz, 3H). Reaction of isocyanide **3a** (52 mg, 0.18 mmol) with BuLi (0.18 mmol, 0.12 mL) at -95 °C (11 min) following the general procedure afforded, after purification (1 mm plate, 5 °C hexanes/Et_2O/CH_2Cl_2, 6:1:1, under N_2), 15 mg (24%) of a mixture of (1*S**, 2*S**)- and (1*R**, 2*S**)-**4a** (1:1.2 ratio) spectrally identical to material previously characterized.

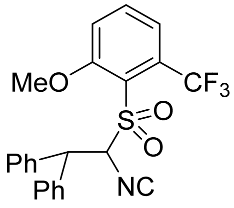


4b **2-((1*S**, 2*R**)-2-Isocyano-1-phenyl-2-tosylethyl)-1,3-dithiane and 2-((1*S**, 2*S**)-2-isocyano-1-phenyl-2-tosylethyl)-1,3-dithiane (4b)**. Following the general procedure with 2-lithio-1,3-dithiane[7] and isocyanide **3a** (0.46 mmol, 129 mg) at -78 °C for 18 min (extraction with MTBE) afforded crude **4b** as a mixture of diastereomers (1*S**, 2*S**:1*S**, 2*R**, 1:5.0 ratio) that was purified (2 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1) to afford 123 mg (67%) of a diastereomeric mixture of isocyanide **4b** (1*S**, 2*S**:1*S**, 2*R**, 1:8.3 ratio) as a pale-yellow oil: IR 2133, 1336, 1152 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}NO_2S_3Na$ $[M+Na]^+$: 426.0627, found: 426.0624. For (1*S**, 2*R**)-**4b***:* ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.50-7.20 (m, 7H), 5.56 (d, *J* = 3.7 Hz, 1H), 4.34 (d, *J* = 10.5 Hz, 1H), 4.08 (dd, *J* = 10.5 and 3.7 Hz, 1H), 3.10-2.92 (m, 1H), 2.92-2.77 (m, 2H), 2.77-2.61 (m, 1H), 2.42 (s, 3H), 2.18-2.01 (m, 1H), 2.011.85 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.99, 146.25, 133.35, 132.34, 129.95, 129.77, 129.75, 128.97, 128.45, 73.93, 47.44, 47.05, 28.51, 28.31, 25.27, 21.81. For (1*S**, 2*S**)-**4b**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.50-7.20 (m, 7H), 5.30 (d, *J* = 9.1 Hz, 1H), 4.74 (d, *J* = 5.2 Hz, 1H), 3.73 (dd, *J* = 9.1, 5.2 Hz, 1H), 3.10-2.92 (m, 1H), 2.92-2.77 (m, 2H), 2.77-2.61 (m, 1H), 2.44 (s, 3H), 2.18-2.01 (m, 1H), 2.01-1.85 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.15, 146.41, 133.35, 132.46, 130.07, 129.75, 129.66, 128.99, 128.32, 73.93, 51.30, 50.33, 30.85, 30.79, 25.43, 21.85.



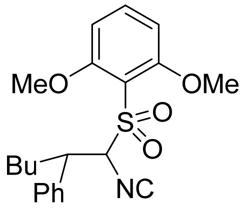
6a

2-((1*S, 2*R**)-2-Isocyano-2-((2-methoxy-6-(trifluoromethyl)phenyl)-sulfonyl)-1-phenylethyl)-1,3-dithiane and 2-((1*S**, 2*S**)-2-isocyano-2-((2-methoxy-6-(trifluoromethyl)phenyl)sulfonyl)-1-phenylethyl)-1,3-dithiane (6a)**. Following the general procedure with 2-lithio-1,3-dithiane[7] (from 20 mg, 0.17 mmol of 1,3-dithiane and 0.11 mL, 0.18 mmol of BuLi) and isocyanide **3c** (50 mg, 0.14 mmol) at -78 °C for 17 min (extraction with MTBE) afforded crude **6a** as a mixture of diastereomers (1*S**, 2*S**:1*S**, 2*R**, 1:4.9 ratio). Purification (1 mm plate, hexanes/ CH_2Cl_2/Et_2O, 6:1:1 to 3:1:1) afforded 48 mg (72%) of isocyanide **6a** as a mixture of diastereomers from which pure (1*S**, 2*R**)-**6a** was obtained by repeated purification (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 4:1:1) as a white solid. For (1*S**, 2*R**)-**6a**: mp 98-100 °C (dec.); IR 2134, 1305, 1154 cm^{-1}; NMR ^1H (500 MHz, $CDCl_3$) δ 7.74 (t, *J* = 8.2 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.47-7.41 (m, 2H), 7.41-7.37 (m, 3H), 7.36 (d, *J* = 7.9 Hz, 1H), 6.34 (d, *J* = 4.4 Hz, 1H), 4.51 (d, *J* = 9.8 Hz, 1H), 4.16 (dd, *J* = 9.8, 4.4 Hz, 1H), 4.09 (s, 3H), 3.04-2.94 (m, 1H), 2.94-2.81 (m, 2H), 2.81-2.70 (m, 1H), 2.16-2.05 (m, 1H), 1.99-1.86 (m, 1H); NMR ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.00, 159.74, 135.92, 133.50, 132.48 (q, *J* = 33.4 Hz), 129.87, 129.11, 128.53, 124.89, 123.02, 121.07 (q, *J* = 7.5 Hz), 117.70, 72.72, 57.82, 48.54, 47.06, 29.35, 29.18, 25.51; HRMS (ESI) calcd for $C_{21}H_{20}F_3NO_3S_3Na$ $[M+Na]^+$: 510.0449, found: 510.0447. For (1*S**, 2*S**)-**6a**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (t, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.37-7.32 (m, 2H), 7.32-7.28 (m, 3H), 7.25 (d, *J* = 7.6 Hz, 1H), 5.98 (d, *J* = 10.5 Hz, 1H), 4.73 (d, *J* = 4.2 Hz, 1H), 4.06 (s, 3H), 4.02 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.06-2.95 (m, 1H), 2.95-2.82 (m, 2H), 2.81-2.69 (m, 1H), 2.15-1.99 (m, 1H), 1.84-1.68 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.75, 159.29, 135.55, 132.35 (q, *J* = 33.4 Hz), 132.04, 129.63, 129.04, 128.16, 124.72, 120.93 (q, *J* = 7.7 Hz), 120.39, 117.46, 74.66, 57.84, 52.48, 49.05, 31.33, 31.26, 25.49.



6b

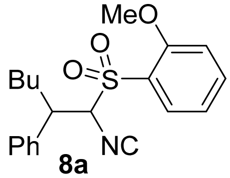
(2-Isocyano-2-((2-methoxy-6-(trifluoromethyl)phenyl)sulfonyl)ethane-1,1-diyl)dibenzene (**6b**). Following the general procedure with PhLi (0.17 mmol) and isocyanide **3c** (52 mg, 0.14 mmol) at -100 °C then warming to -79 °C over 30 min (extraction with MTBE) and purification (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 5:1:1 to 3.5:1:1) afforded 55 mg (87%) of isocyanide **6b** as a white solid: mp 92-93 °C (dec.); IR 2144, 1343, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (t, *J* = 8.3 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.45-7.14 (m, 11H), 6.03 (d, *J* = 8.6 Hz, 1H), 4.93 (d, *J* = 8.6 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.64, 159.54, 138.37, 138.06, 135.80, 131.73 (q, *J* = 33.4 Hz), 128.98, 128.94, 128.81, 128.22, 128.00, 127.94, 125.15, 123.40, 121.17 (q, *J* = 7.3 Hz), 120.67, 117.87, 76.03, 57.99, 50.50; HRMS (ESI) calcd for $C_{23}H_{18}F_3NO_3SNa$ $[M+Na]^+$: 468.0852, found: 468.0849.



7a

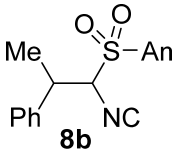
2-(((1*R, 2*S**)-1-Isocyano-2-phenylhexyl)sulfonyl)-1,3-dimethoxybenzene and 2-(((1*S**, 2*S**)-1-isocyano-2-phenylhexyl)sulfonyl)-1,3-dimethoxybenzene (7a)**. Following the general procedure with Bu_3MgLi (0.52 mmol) and isocyanide **3d** (172 mg, 0.52 mmol) at -95 °C then warming to -78 °C over 15 min (extraction with CH_2Cl_2) afforded a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1.4:1 ratio) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 5:1:1 to 4:1:1) to afford 107 mg (53%) of isocyanide **7a** as a colorless oil: IR 2135, 1334, 1105 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{25}NO_4SNa$ $[M+Na]^+$: 410.1397, found: 410.1399. For (1*S**, 2*S**)-**7a**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 8.5 Hz, 1H), 7.40-7.23 (m, 5H), 6.65 (d, *J* = 8.5 Hz, 2H), 5.19 (d, *J* = 7.6 Hz, 1H), 3.92 (s, 6H), 3.65-3.50 (m, 1H), 2.03-1.77 (m, 2H), 1.39-1.22 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C

NMR (101 MHz, CDCl₃) δ 164.69, 160.47, 137.92, 136.32, 128.85, 128.60, 127.99, 113.48, 105.35, 56.90, 46.53, 44.45, 25.70, 23.22, 11.77, 11.46. For (1*R**, 2*S**)-**7a**: ^{1}H NMR (400 MHz, CDCl₃) δ 7.47 (t, *J* = 8.5 Hz, 1H), 7.40-7.23 (m, 5H), 6.60 (d, *J* = 8.5 Hz, 2H), 5.14 (d, *J* = 3.5 Hz, 1H), 3.88 (s, 6H), 3.65-3.50 (m, 1H), 2.33-2.17 (m, 2H), 1.22-1.05 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, CDCl₃) δ 165.45, 160.52, 139.31, 136.37, 128.84, 127.79, 127.71, 112.86, 105.31, 56.88, 46.53, 44.45, 25.70, 23.22, 11.77, 11.46.



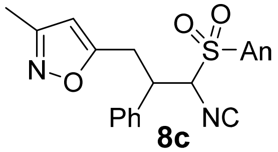
8a

1-(((1*R, 2*S**)-1-Isocyano-2-phenylhexyl)sulfonyl)-2-methoxybenzene and 1-(((1*S**, 2*S**)-1-isocyano-2-phenylhexyl)sulfonyl)-2-methoxybenzene (8a)**. Following the general procedure with Bu_3MgLi (0.23 mmol) and isocyanide **3e** (70 mg, 0.23 mmol) at -105 °C and, after 13 min, allowing the reaction to warm to -95 °C (extraction with EtOAc) afforded a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:1.8 ratio) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 5:1:1) to afford 52 mg (62%) of isocyanide **8a** as a colorless oil: IR 2134, 1331, 1154 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NO_3SNa$ [M+Na]$^+$: 380.1291, found: 380.1298; For (1*S**, 2*S**)-**8a**: ^{1}H NMR (400 MHz, CDCl₃) δ 7.92 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.67-7.60 (m, 1H), 7.38-7.26 (m, 5H), 7.19-7.09 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 5.24 (d, *J* = 5.9 Hz, 1H), 4.02 (s, 3H), 3.71-3.55 (m, 1H), 2.40-2.18 (m, 2H), 1.40-1.08 (m, 4H), 0.86 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (101 MHz, CDCl₃) δ 165.70, 157.32, 137.41, 136.75, 132.12, 128.99, 128.53, 127.95, 124.16, 121.18, 112.46, 74.65, 56.50, 43.86, 31.59, 28.92, 22.25, 14.13. For (1*R**, 2*S**)-**8a**: ^{1}H NMR (400 MHz, CDCl₃) δ 7.98 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.68-7.60 (m, 1H), 7.38-7.26 (m, 5H), 7.19-7.09 (m, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 5.14 (d, *J* = 3.1 Hz, 1H), 3.91 (s, 3H), 3.71-3.55 (m, 1H), 2.18-1.87 (m, 2H), 1.40-1.08 (m, 4H), 0.85 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 166.12, 157.32, 139.39, 136.82, 132.34, 128.99, 127.95, 127.89, 123.66, 121.18, 112.46, 75.81, 56.50, 42.59, 32.55, 29.19, 22.38, 13.87. Reaction of isocyanide **3e** (54 mg, 0.18 mmol) with BuLi (0.18 mmol, 0.11 mL) at -102 °C to -89 °C (12 min) afforded **8a** as a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:1.8 ratio) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 5:1:1) to afford 34 mg (53%) of **8a** as a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:2.0) spectrally identical to material previously characterized.



8b

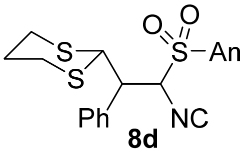
1-(((1*R, 2*S**)-1-Isocyano-2-phenylpropyl)sulfonyl)-2-methoxybenzene and 1-(((1*S**, 2*S**)-1-isocyano-2-phenylpropyl)sulfonyl)-2-methoxybenzene (8b)**. An Et_2O solution of MeLi·LiBr (0.69 mmol, 0.40 mL) was added to a -110 °C, THF solution (10 mL) of isocyanide **3e** (148 mg, 0.49 mmol). After 10 min the reaction was allowed to warm to -95 °C and then DMPU (532 mg, 4.15 mmol, 0.5 mL) was added. After 30 min, the mixture was allowed to warm to -78 °C and then brine (5 mL) was added. Extraction with MTBE afforded a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:1.3 ratio) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 7:1:1 to 6:1:1) to afford 112 mg (72%) of a mixture of diastereomers. Pure samples of each diastereomer were identified by ^{1}H NMR analysis of separate fractions obtained during chromatography. For (1*S**, 2*S**)-**8b**: mp 105-106 °C (dec.); IR 2135, 1329, 1151 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.97 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.70-7.60 (m, 1H), 7.447.30 (m, 5H), 7.18-7.10 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 5.13 (d, *J* = 7.6 Hz, 1H), 4.01 (s, 3H), 3.76 (dq, *J* = 7.6 and 7.0 Hz, 1H), 1.65 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 165.57, 157.57, 139.72, 136.94, 131.99, 128.83, 128.29, 128.15, 124.19, 121.27, 112.58, 75.90, 56.72, 39.64, 19.27; HRMS (ESI) calcd for $C_{17}H_{17}NO_3SNa$ $[M+Na]^+$: 338.0821, found: 338.0820. For (1*R**, 2*S**)-**8b**: mp 101-102 °C(dec.); IR 2133, 1328, 1151 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) *δ* 7.99 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.70-7.57 (m, 1H), 7.46-7.21 (m, 5H), 7.18-7.10 (m, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 5.21 (d, *J* = 2.7 Hz, 1H), 3.93 (s, 3H), 3.91-3.83 (m, 1H), 1.65 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 166.12, 157.34, 141.12, 137.02, 132.31, 129.06, 127.90, 127.30, 123.41, 121.22, 112.60, 75.96, 56.61, 37.05, 15.30; HRMS (ESI) calcd for C$_{17}$H$_{17}$NO$_3$SNa [M+Na]$^+$: 338.0821, found: 338.0820. Reaction of isocyanide **3e** (327 mg, 1.1 mmol) with MeLi (1.31 mmol, 0.82 mL) at -105 °C to -80 °C (20 min) afforded **8b** as a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:3.0 ratio) that were purified (2 mm plate, hexanes/CH$_2$Cl$_2$/Et$_2$O, 7:1:1 to 6:1:1) to afford 214 mg (62%) of isocyanide **8b** spectrally identical to material previously characterized.



8c

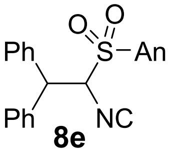
5-((2*S, 3*R**)-3-Isocyano-3-((2-methoxyphenyl)sulfonyl)-2-phenylpropyl)-3-methylisoxazole and 5-((2*S**, 3*S**)-3-isocyano-3-((2-methoxyphenyl)sulfonyl)-2-phenylpropyl)-3-methylisoxazole (8c)**. Following the general procedure with isocyanide **3e** (203 mg, 0.68 mmol) and ((3-methylisoxazol-5-yl)methyl)lithium[8] at -78 °C for 30 min (extraction with MTBE) afforded a mixture of diastereomers (2*S**, 3*S**:2*S**, 3*R**, 1:1.4 ratio) that were purified by column chromatography (hexanes/CH$_2$Cl$_2$/Et$_2$O, 6:1:1 to 3:1:1) to afford 197 mg (73%) of a mixture of diastereomers. Pure samples of each diastereomer were identified by ^{1}H NMR analysis of separate fractions obtained during chromatography. For (2*S**, 3*S**)-**8c**: mp 130-131 °C (dec.); IR 2135, 1332, 1153 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.88 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.71-7.60 (m, 1H), 7.48-7.30 (m, 5H), 7.17-7.08 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.89 (s, 1H), 5.41 (d, *J* = 4.6 Hz, 1H), 4.20-4.05 (m, 1H), 3.95 (s, 3H), 3.53 (dd, *J* = 16.0, 8.0 Hz, 1H), 3.30 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (101 MHz,

$CDCl_3$) δ 168.78, 166.93, 159.98, 157.42, 137.13, 135.82, 132.33, 128.95, 128.81, 128.77, 123.67, 121.26, 112.62, 103.89, 72.71, 56.55, 41.93, 30.45, 11.53; HRMS (ESI) calcd for $C_{21}H_{20}N_2O_4SNa$ $[M+Na]^+$: 419.1036, found: 419.1034. For (2*S**, 3*R**)-**8c**: mp 97-99 °C (dec.); IR 2133, 1328, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.75-7.61 (m, 1H), 7.40-7.26 (m, 5H), 7.23-7.12 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.62 (s, 1H), 5.24 (d, *J* = 2.6 Hz, 1H), 4.13 (dt, *J* = 12.0, 2.6 Hz, 1H), 3.94 (s, 3H), 3.77 (dd, *J* = 15.2, 3.2 Hz, 1H), 3.48 (dd, *J* = 15.2, 12.0 Hz, 1H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.01, 167.45, 159.72, 157.54, 137.66, 137.36, 132.60, 129.29, 128.61, 127.82, 123.07, 121.47, 112.71, 103.38, 74.89, 56.75, 41.02, 27.29, 11.49; HRMS (ESI) calcd for $C_{21}H_{20}N_2O_4SNa$ $[M+Na]^+$: 419.1036, found: 419.1035.

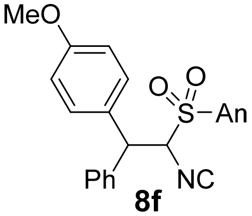


8d

2-((1*S, 2*R**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)-1,3-dithiane** and **2-((1*S**, 2*S**)-2-isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)-1,3-dithiane** (**8d**). Following the general procedure with isocyanide **3e** (225 mg, 0.75 mmol) and 2-lithio-1,3-dithiane[7] (1.05 mmol) at -102 °C and, after 17 min, allowing the reaction to warm to -78 °C (extraction with MTBE) afforded a mixture of diastereomers (1*S**, 2*S**:1*S**, 2*R**, 1:9.1 ratio) that were purified by triturating with hot MeOH (5 mL) to afford 480 mg (83%) of a diastereomeric mixture of isocyanide **8d** as a white solid that was recrystallized (MeOH) to afford a mixture of diastereomers (1*S**, 2*S**:1*S**, 2*R**, 1:24.5) of isocyanide **8d**: mp 141-142 °C (dec.); IR 2134, 1334, 1154 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}NO_3S_3Na$ $[M+Na]^+$: 442.0576, found: 442.0574. Repeated crystallization (MeOH) gave a pure material whose structure was secured by X-ray diffraction[9]. For (1*S**, 2*S**)-**8d**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.53-7.49 (m, 1H), 7.24-7.16 (m, 5H), 6.92 (d, *J* = 8.6 Hz, 1H), 6.93-6.85 (m, 1H), 5.82 (d, *J* = 9.9 Hz, 1H), 4.79 (d, *J* = 4.7 Hz, 1H), 3.98 (s, 3H), 3.89 (dd, *J* = 9.9, 4.7 Hz, 1H), 3.16-2.96 (m, 1H), 2.96-2.66 (m, 3H), 2.18-2.04 (m, 1H), 2.04-1.90 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 167.21, 157.37, 136.56, 133.34, 132.35, 131.35, 129.70, 128.12, 124.67, 121.16, 112.33, 70.78, 56.73, 52.07, 50.12, 30.03, 26.68, 25.59. For (1*S**, 2*R**)-**8d**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.87 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.75-7.57 (m, 1H), 7.50-7.38 (m, 5H), 7.16-7.09 (m, 1H), 7.08 (d, *J* = 8.5 Hz, 1H), 6.28 (d, *J* = 3.3 Hz, 1H), 4.41 (d, *J* = 10.8 Hz, 1H), 4.19 (dd, *J* = 10.8, 3.3 Hz, 1H), 4.02 (s, 3H), 3.16-2.99 (m, 1H), 2.96-2.66 (m, 3H), 2.18-2.04 (m, 1H), 2.04-1.90 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 167.21, 157.37, 137.04, 133.64, 132.48, 129.80, 129.07, 128.47, 123.81, 121.24, 112.61, 71.19, 56.61, 47.52, 46.04, 28.60, 28.33, 25.42.

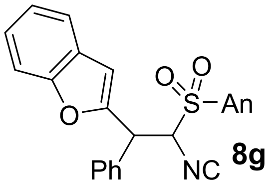

8e

(2-Isocyano-2-((2-methoxyphenyl)sulfonyl)ethane-1,1-diyl)dibenzene (**8e**). Following the general procedure with PhLi (0.45 mmol, 0.33 mL) and isocyanide **3e** (128 mg, 0.43 mmol) at -100 °C for 12 min, and then allowing the reaction to warm to -80 °C (extraction with MTBE) and purification (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 4:1:1), afforded 98 mg (61%) of isocyanide **8e** as a white solid: mp 110-112 °C (dec.); IR 2134, 1328, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.79 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.62-7.50 (m, 1H), 7.48-7.38 (m, 2H), 7.38-7.12 (m, 8H), 7.09-6.99 (m, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 5.84 (d, *J* = 6.8 Hz, 1H), 4.95 (d, *J* = 6.8 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.20, 157.30, 138.73, 138.01, 136.82, 131.98, 129.20, 128.90, 128.75, 128.03, 127.98, 127.78, 124.13, 121.23, 112.59, 74.03, 56.73, 49.72; HRMS (ESI) calcd for $C_{22}H_{19}NO_3SNa$ $[M+Na]^+$: 400.0978, found: 400.0976.


8f

1-(((1*R, 2*R**)-1-Isocyano-2-(4-methoxyphenyl)-2-phenylethyl)-sulfonyl)-2-methoxybenzene and 1-(((1*S**, 2*R**)-1-isocyano-2-(4-methoxyphenyl)-2-phenylethyl)sulfonyl)-2-methoxybenzene (8f)**.

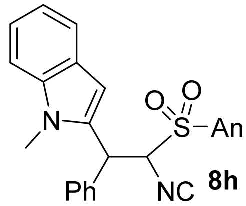
Following the general procedure with isocyanide **3e** (170 mg, 0.57 mmol) and (4-methoxyphenyl)lithium[10] at -78 °C for 15 min and then allowing the reaction to warm to -60 °C (extraction with MTBE) afforded a mixture of diastereomers (1*S**, 2*R**:1*R**, 2*R**, 1:1 ratio) that were purified (2 mm plate, hexanes/CH_2Cl_2/ Et_2O, 6:1:1 to 3:1:1) to afford 176 mg (76%) of isocyanide **8f** from which a pure sample of (1*R**, 2*R**)-**8f** and an enriched sample of (1*S**, 2*R**)-**8f** were obtained. For (1*R**, 2*R**)-**8f**: mp 101-103 °C (dec.); IR 2134, 1328, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.66-7.52 (m, 1H), 7.44-7.15 (m, 7H), 7.12-7.03 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.79 (d, *J* = 6.1 Hz, 1H), 4.95 (d, *J* = 6.1 Hz, 1H), 3.97 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.16, 159.22, 157.36, 139.33, 136.84, 132.18, 130.52, 129.86, 128.94, 127.92, 127.68, 124.14, 121.29, 114.09, 112.61, 74.13, 56.75, 55.29, 48.54; HRMS (ESI) calcd for $C_{23}H_{21}NO_4SNa$ [M+Na]$^+$: 430.1084, found: 430.1082. For (1*S**, 2*R**)-**8f**: mp 65-67 °C (dec.); IR 2134, 1328, 1151 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.62-7.51 (m, 1H), 7.46-7.37 (m, 2H), 7.37-7.30 (m, 2H), 7.30-7.25 (m, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.09-7.01 (m, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 5.79 (d, *J* = 7.3 Hz, 1H), 4.88 (d, *J* = 7.3 Hz, 1H), 3.98 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.09, 159.01, 157.28, 138.44, 136.65, 131.91, 130.57, 129.23, 128.97, 128.79, 127.89, 124.43, 121.21, 114.26, 112.57, 74.34, 56.78, 55.32, 49.35; HRMS (ESI) calcd for $C_{23}H_{21}NO_4SNa$ [M+Na]$^+$: 430.1083, found: 430.1082.



8g

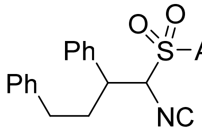
2-((1*R**, 2*R**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)benzofuran and 2-((1*R**, 2*S**)-2-isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)benzofuran (8g).

Following the general procedure with isocyanide **3e** (155 mg, 0.52 mmol) and benzofuran-2-yllithium[11] at -78 °C and, after 1 h, allowing the reaction to warm to -40 °C (extraction with MTBE) afforded a mixture of diastereomers (1*R**, 2*S**:1*R**, 2*R**, 1.3:1 ratio) that was purified by column chromatography (CH_2Cl_2/EtOAc/hexanes, 1:1:6 to 1:1:4) to afford 169 mg (78%) of isocyanide **8g** from which a pure sample of (1*R**, 2*R**)-**8g** and an enriched sample of (1*R**, 2*S**)-**8g** were obtained. For (1*R**, 2*S**)-**8g**: IR 2132, 1332, 1153 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, J = 7.9, 1.7 Hz, 1H), 7.63-7.54 (m, 2H), 7.43-7.31 (m, 5H), 7.29 (d, J = 7.9 Hz, 1H), 7.23-7.18 (m, 1H), 7.18-7.11 (m, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.87-6.80 (m, 1H), 6.58 (s, 1H), 6.01 (d, J = 7.5 Hz, 1H), 5.06 (d, J = 7.5 Hz, 1H), 4.05 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.37, 157.42, 154.80, 152.83, 136.54, 135.00, 131.90, 129.39, 129.01, 128.81, 128.05, 124.43, 123.61, 123.16, 121.23, 120.93, 112.45, 111.14, 106.24, 72.52, 56.83, 45.12; HRMS (+APCI) calcd for $C_{24}H_{20}NO_4S$ $[M+H]^+$: 418.1108, found: 418.1116. For (1*R**, 2*R**)-**8g**: IR 2133, 1336, 1155 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 7.9, 1.7 Hz, 1H), 7.61-7.55 (m, 1H), 7.55-7.49 (m, 1H), 7.49-7.39 (m, 3H), 7.33-7.27 (m, 2H), 7.25-7.21 (m, 2H), 7.21-7.16 (m, 1H), 7.08-7.00 (m, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.88 (s, 1H), 5.73 (d, J = 7.1 Hz, 1H), 5.08 (d, J = 7.1 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.54, 157.43, 155.13, 152.73, 136.89, 135.57, 132.01, 129.07, 128.69, 128.59, 128.09, 124.55, 124.21, 123.09, 121.40, 121.29, 112.55, 111.37, 106.53, 73.74, 56.80, 45.37; HRMS (+APCI) calcd for $C_{24}H_{20}NO_4S$ $[M+H]^+$: 418.1108, found: 418.1115.


8h

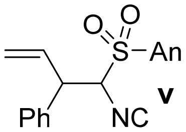
2-((1*R, 2*R**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)-1-methyl-1H-indole and 2-((1*R**, 2*S**)-2-isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)-1-methyl-1H-indole (8h)**. Following the general procedure with isocyanide **3e** (155 mg, 0.52 mmol) and (1-methyl-1H-indol-2-yl)lithium[12] at -78 °C and, after 1.5 h, allowing the reaction to warm to -40 °C (extraction with MTBE) afforded a mixture of diastereomers (1*R**, 2*S**:1*R**, 2*R**, 1:1.6 ratio) that was purified by column chromatography (EtOAc/hexanes, 1:4 to 1:2.5) to afford 170 mg (76%) of a mixture of diastereomers. Pure samples of each diastereomer were identified by ^{1}H NMR analysis of separate fractions obtained during chromatography. For (1*R**, 2*R**)-**8h**: mp 168-169 °C (dec.); IR 2134, 1332, 1152 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.63-7.50 (m, 2H), 7.48-7.39 (m, 2H), 7.39-7.27 (m, 3H), 7.23-7.15 (m, 2H), 7.13-7.06 (m, 1H), 7.06-6.97 (m, 2H), 6.66 (s, 1H), 5.93 (d, *J* = 4.1 Hz, 1H), 5.31 (d, *J* = 4.1 Hz, 1H), 3.99 (s, 3H), 3.50 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.90, 157.47, 137.44, 137.43, 137.04, 134.82, 132.36, 130.23, 128.72, 128.65, 127.19, 123.58, 122.12, 121.22, 120.56, 119.95, 112.75, 109.27, 100.13, 73.62, 56.80, 41.53, 29.95; HRMS (+APCI) calcd for $C_{25}H_{23}N_2O_3S$ [M+H]$^+$: 431.1424, found: 431.1420. For (1*R**, 2*S**)-**8h**: light-yellow oil; IR 2134, 1331, 1153 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.82 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.58-7.49 (m, 1H), 7.39-7.29 (m, 2H), 7.29-7.13 (m, 5H), 7.12-7.06 (m, 1H), 7.05-6.98 (m, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.88 (s, 1H), 5.72 (d, *J* = 6.7 Hz, 1H), 5.17 (d, *J* = 6.7 Hz, 1H), 4.00 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 167.83, 157.34, 137.33, 136.83, 136.36, 135.08, 131.94, 129.15, 128.89, 128.44, 127.54, 124.37, 121.95, 121.26, 120.87, 119.80, 112.58, 109.27, 101.98, 74.77, 56.77, 43.00, 29.99; HRMS (+APCI) calcd for $C_{25}H_{23}N_2O_3S$

$[M+H]^+$: 431.1424, found: 431.1423. *Equilibration*: a THF solution (5 mL) of *t*-BuOK (31 mg, 0.28 mmol) was added to a -78 °C, THF solution (5 mL) of (1*R**, 2*R**)-**8h** (108 mg, 0.25 mmol). After 30 min, a THF solution (2 mL) of *t*-BuOH (1.6 mmol, 0.15 mL) was added. After 10 min, brine (5 mL) and MTBE (20 mL) were added sequentially. Organic phase was separated, aqueous phase was extracted with MTBE (10 mL), and then combined organic solution was washed with brine (2 x 5 mL), dried (Na_2SO_4) and concentrated. The crude (1*R**, 2*S**:1*R**, 2*R**, 1:2 ratio) was purified by column chromatography (EtOAc/hexanes, 1:4 to 1:2.5) to afford 27 mg (25%) of (1*R**, 2*S**)-**8h** and 58 mg (54%) of (1*R**, 2*R**)-**8h** spectrally identical to materials previously characterized.



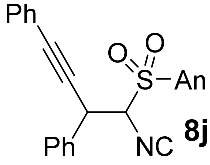
8i

((3*S, 4*R**)-4-Isocyano-4-((2-methoxyphenyl)sulfonyl)butane-1,3-diyl)dibenzene and ((3*S**, 4*S**)-4-isocyano-4-((2-methoxyphenyl)-sulfonyl)butane-1,3-diyl)dibenzene** (**8i**). Following the general procedure with PhLi (0.20 mmol, 0.15 mL) and isocyanide **3f** (48 mg, 0.15 mmol) at -100 °C for 18 min and then allowing the reaction to warm to -78 °C (extraction with MTBE) afforded a mixture of diastereomers (3*S**, 4*S**:3*S**, 4*R**, 1:2.1 ratio) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 7:1:1 to 6:1:1) to afford 45 mg (76%) of a diastereomeric mixture of isocyanide **8i** as a colorless oil: IR 2133, 1329, 1151 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{23}NO_3SNa$ $[M+Na]^+$: 428.1291, found: 428.1289. For (3*S**, 4*R**)-**8i**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.66-7.59 (m, 1H), 7.42-7.23 (m, 7H), 7.23-7.15 (m, 1H), 7.15-7.07 (m, 3H), 6.99 (d, *J* = 8.4 Hz, 1H), 5.14 (d, *J* = 3.0 Hz, 1H), 3.88 (s, 3H), 3.60 (dt, *J* = 11.6, 3.1 Hz, 1H), 2.80-2.59 (m, 1H), 2.59-2.39 (m, 2H), 2.39-2.20 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.52, 157.40, 140.95, 139.01, 136.96, 132.44, 129.29, 128.57, 128.52, 128.25, 128.15, 126.18, 123.57, 121.32, 112.55, 75.75, 56.62, 42.30, 32.85, 31.03. For (3*S**, 4*S**)-**8i**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.66-7.55 (m, 1H), 7.42-7.23 (m, 7H), 7.23-7.15 (m, 1H), 7.15-7.07 (m, 3H), 7.05 (d, *J* = 8.4 Hz, 1H), 5.25 (d, *J* = 6.0 Hz, 1H), 3.99 (s, 3H), 3.73-3.63 (m, 1H), 2.59-2.39 (m, 3H), 2.39-2.20 (m, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.01, 157.49, 140.78, 139.01, 136.93, 132.23, 129.20, 128.82, 128.61, 128.36, 128.15, 126.32, 124.15, 121.30, 112.63, 74.84, 56.69, 43.70, 34.64, 33.23.



v **1-(((1*S**, 2*S**)-1-Isocyano-2-phenylbut-3-en-1-yl)sulfonyl)-2-methoxybenzene and 1-(((1*R**, 2*S**)-1-isocyano-2-phenylbut-3-en-1-yl)sulfonyl)-2-methoxybenzene (v)**. Following the general procedure with vinyllithium[13] and isocyanide **3e** (273 mg, 0.91 mmol) at -78 °C for 13 min (extraction with MTBE) afforded a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:2.5 ratio) that were purified by column chromatography (hexanes/CH$_2$Cl$_2$/Et$_2$O, 6:1:1 to 4:1:1) to afford 128 mg (43%) of isocyanide **v** that was approximately 90% pure. Repeated purification (1 mm plate, hexanes/CH$_2$Cl$_2$/Et$_2$O, 7:1:1 to 5:1:1) afforded 51 mg (17%) of isocyanide **v** as an oily mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:1): IR 2134, 1332, 1151 cm^{-1}; HRMS (-APCI) calcd for $C_{18}H_{16}NO_3S$ [M-H]$^-$: 326.0851, found: 326.0856. For (1*S**, 2*S**)- and (1*R**, 2*S**)-**v**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96 (dd, *J* = 7.6 and 2.0 Hz, 1H), 7.95 (dd, *J* = 7.6 and 2.0 Hz, 1H), 7.69-7.60 (m, 2H), 7.42-7.28 (m, 10H), 7.17-7.10 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.36 (ddd, *J* = 16.8, 10.4, 8.0 and 2.4 Hz, 1H), 6.20 (ddd, *J* = 16.8, 10.4, 8.0 and 2.4 Hz, 1H), 5.41 (dt, *J* = 10.4 and 1.2 Hz, 1H), 5.36 (d, *J* = 7.2 Hz, 1H), 5.32 (dt, *J* = 8.0 and 1.2, 1H), 5.30-5.22 (m, 3H), 4.39 (dd, *J* = 8.0 and 3.6 Hz, 1H), 4.33 (t, *J* = 7.6 Hz, 1H), 4.02 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ

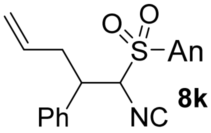
166.71 (166.22), 157.57 (157.43), 138.73 (137.04), 137.03 (136.99), 134.87 (133.27), 132.48 (132.17), 129.18 (128.96), 128.92 (128.31), 128.11 (128.08), 124.13 (123.75), 121.35 (121.31), 120.70 (119.03), 112.63 (112.61), 74.88 (74.06), 56.73 (56.69), 48.62 (46.89).



8j

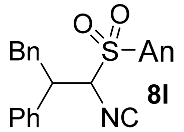
((3*R, 4*R**)-4-Isocyano-4-((2-methoxyphenyl)sulfonyl)but-1-yne-1,3-diyl)dibenzene and ((3*R**, 4*S**)-4-isocyano-4-((2-methoxyphenyl)-sulfonyl)but-1-yne-1,3-diyl)dibenzene (8j).** Following the general procedure with isocyanide **3e** (173 mg, 0.58 mmol) and (phenylethynyl)lithium[14] at -78 °C for 2 h, and then allowing the reaction to warm to 4 °C (extraction with MTBE) afforded a mixture of diastereomers (3*R**, 4*S**:3*R**, 4*R**, 1:3.2 ratio) that were purified by column chromatography (hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 4:1:1) to afford 156 mg (67%) of diastereomeric isocyanides (3*R**, 4*R**)- and (3*R**, 4*S**)-**8j** as an orange oil. Although not fully separable, enriched fractions of the two diastereomers were obtained which allowed a complete spectral assignment. For (3*R**, 4*S**)-**8j**: IR 2135, 1335, 1153 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.72-7.59 (m, 3H), 7.477.27 (m, 8H), 7.13-7.08 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.42 (d, *J* = 6.6 Hz, 1H), 4.81 (d, *J* = 6.6 Hz, 1H), 4.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.13, 157.62, 137.07, 134.55, 132.18, 131.95, 129.52, 128.98, 128.84, 128.81, 128.35, 124.16, 122.33, 121.35, 112.65, 86.63, 84.96, 74.58, 56.80, 38.26. Pure (3*R**, 4*R**)-**8j** was isolated by fractional crystallization (cyclohexane/CH_2Cl_2/pentane, 10:1:10) as a white crystalline solid: mp 98-100 °C (dec.); IR 2135, 1336, 1153 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.72-7.59 (m, 1H), 7.59-7.46 (m, 4H), 7.46-7.27 (m, 6H), 7.20-7.09 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.17 (d, *J* = 2.7 Hz, 1H), 4.98 (d, *J* = 2.7 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (101

MHz, $CDCl_3$) δ 166.89, 157.70, 137.23, 136.23, 132.82, 132.09, 129.31, 128.74, 128.69, 128.32, 128.13, 123.38, 122.55, 121.33, 112.65, 88.10, 82.90, 75.86, 56.67, 37.79; HRMS (ESI) calcd for $C_{24}H_{19}NO_3SNa$ [M+Na]$^+$: 424.0978, found: 424.0977.



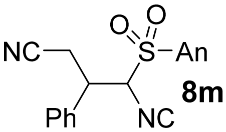
8k

1-(((1*R, 2*S**)-1-Isocyano-2-phenylpent-4-en-1-yl)sulfonyl)-2-methoxybenzene and 1-(((1*S**, 2*S**)-1-isocyano-2-phenylpent-4-en-1-yl)sulfonyl)-2-methoxybenzene (8k).** Following the general procedure with isocyanide **3e** (165 mg, 0.55 mmol) and allylMgBu$_2$Li^6 (0.58 mmol) at -105 °C and, after 20 min, allowing the reaction to warm to -78 °C (extraction with MTBE) afforded a mixture of diastereomers (1*S**, 2*S**:1*R**, 2*S**, 1:1.4 ratio) that were purified (2 mm plate, hexanes/ CH_2Cl_2/Et_2O, 6:1:1 to 5:1:1) to afford 130 mg (69%) of isocyanide **8k** from which enriched samples of both diastereomers were obtained. For (1*R**, 2*S**)-**8k**: mp 106-108 °C (dec.); IR 2133, 1330, 1152 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.72-7.55 (m, 1H), 7.53-7.26 (m, 5H), 7.19-7.08 (m, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 5.91-5.52 (m, 1H), 5.42 (d, *J* = 4.4 Hz, 1H), 5.27-4.92 (m, 2H), 3.99 (s, 3H), 3.85-3.70 (m, 1H), 2.99-2.73 (m, 1H), 2.73-2.60 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.14, 157.37, 136.97, 136.91, 134.44, 132.39, 129.19, 128.55, 128.31, 124.13, 121.29, 118.86, 112.58, 73.14, 56.52, 42.59, 37.38; HRMS (ESI) calcd for $C_{19}H_{19}NO_3SNa$ [M+Na]$^+$: 364.0978, found: 364.0976. For (1*S**, 2*S**)-**8k**: IR 2134, 1330, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.747.53 (m, 1H), 7.50-7.26 (m, 5H), 7.20-7.11 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 5.65-5.50 (m, 1H), 5.31-5.10 (m, 1H), 5.10-4.90 (m, 2H), 3.91 (s, 3H), 3.86-3.68 (m, 1H), 3.152.99 (m, 1H), 2.94-2.73 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.56, 157.41, 138.61, 137.06, 134.15, 132.41, 129.06, 128.22, 128.10, 123.52, 121.29, 118.00, 112.60, 75.39, 56.64, 42.59, 33.96.

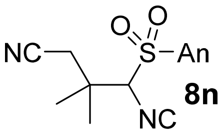


8l **((2*S**, 3*R**)-3-Isocyano-3-((2-methoxyphenyl)sulfonyl)propane-1,2-diyl)dibenzene and ((2*S**, 3*S**)-3-isocyano-3-((2-methoxyphenyl)sulfonyl)propane-1,2-diyl)dibenzene (8l)**. Following the general procedure with $Bu_2BnMgLi$ (0.65 mmol) and isocyanide **3e** (185 mg, 0.62 mmol) at -110 °C for 15 min, allowing the reaction to warm to -85 °C (extraction with MTBE), triturating of the residue (Et_2O/CH_2Cl_2, 6:1), filtration (filtrate **F**), and washing with cold Et_2O (3 x 2 mL) afforded 69 mg (29%) of isocyanide (2*S**, 3*S**)-**8l** as a white solid. An analytically pure sample of (2*S**, 3*S**)-**8l** was obtained by radial chromatography (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 4:1:1 to 1:1:1). Evaporation of the filtrate **F** afforded a mixture of diastereomers (2*S**, 3*S**: 2*S**, 3*R**, 1:1.2) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 5.5:1:1) to afford 104 mg (43%) of a diastereomeric mixture of isocyanide **8l** (2*S**, 3*S**:2*S**, 3*R**, 1:1.3) from which pure (2*S**, 3*R**)-**8l** was identified by ^1H NMR analysis of separate fractions obtained during chromatography. For (2*S**, 3*S**)-**8l**: mp 129-131 °C (dec.); IR 2134, 1334, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.69-7.55 (m, 1H), 7.55-7.45 (m, 2H), 7.45-7.25 (m, 8H), 7.11-7.01 (m, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 5.20 (d, *J* = 3.5 Hz, 1H), 4.08-3.93 (m, 1H), 3.52 (s, 3H), 3.29 (dd, *J* = 14.0, 11.2 Hz, 1H), 3.19 (dd, *J* = 14.0, 5.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.36, 157.10, 137.88, 136.96, 136.81, 132.25, 129.30, 129.17, 129.03, 128.54, 128.45, 127.23, 123.86, 121.11, 112.33, 71.99, 56.00, 44.55, 39.37; HRMS (ESI) calcd for $C_{23}H_{21}NO_3SNa$ $[M+Na]^+$: 414.1134, found: 414.1132. For (2*S**, 3*R**)-**8l**: IR 2132, 1327, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.74-7.59 (m, 1H), 7.26-7.06 (m, 9H), 7.06-6.96 (m, 3H), 5.26 (d, *J* = 2.8 Hz, 1H), 3.98-3.85 (m, 1H), 3.92 (s, 3H), 3.73 (dd, *J* = 13.8, 3.1 Hz, 1H), 3.19 (dd, *J* = 13.8, 11.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

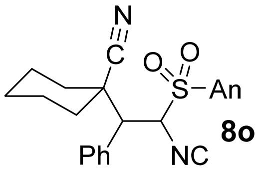
166.76, 157.49, 138.67, 138.13, 137.11, 132.49, 129.35, 128.93, 128.30, 128.27, 128.06, 126.41, 123.56, 121.36, 112.63, 75.28, 56.67, 44.67, 36.54; HRMS (ESI) calcd for $C_{23}H_{21}NO_3SNa$ [M+Na]$^+$: 414.1134, found: 414.1133.



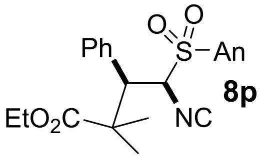
8m **(3*S***, **4*R***)-4-Isocyano-4-((2-methoxyphenyl)sulfonyl)-3-phenylbutanenitrile and (3*S***, 4*S***)-4-isocyano-4-((2-methoxyphenyl)sulfonyl)-3-phenylbutanenitrile (8m).** Following the general procedure with isocyanide **3e** (76 mg, 0.25 mmol) and lithiated acetonitrile (from 0.30 mmol, 0.02 mL of MeCN and 0.30 mmol, 0.19 mL of BuLi in 5 mL of THF, -78 °C, 30 min) at -78 °C for 15 min (extraction with MTBE) afforded a mixture of diastereomers (3*S**, 4*S**:3*S**, 4*R**, 1:1.4 ratio) that were purified (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 6:1:1 to 3:1:1) to afford 76 mg (88%) of a diastereomeric mixture of isocyanide **8m** (3*S**, 4*S**:3*S**, 4*R**, 1:2.1) as a white solid: mp 118-122 °C (dec.); IR 2251, 2134, 1330, 1153 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{16}N_2O_3SNa$ [M+Na]$^+$: 363.0774, found: 363.0773. For (3*S**, 4*R**)-**8m**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 8.0, 1.6 Hz, 1H), 7.77-7.62 (m, 1H), 7.45-7.38 (m, 5H), 7.23-7.15 (m, 1H), 7.06 (d, J = 8.4 Hz, 1H), 5.25 (d, J = 2.7 Hz, 1H), 4.14-3.98 (m, 1H), 3.95 (s, 3H), 3.46 (dd, J = 17.0, 4.0 Hz, 1H), 3.10 (dd, J = 16.9, 11.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.46, 157.45, 137.56, 135.94, 132.45, 129.60, 129.31, 127.49, 121.41, 121.23, 116.80, 112.70, 73.42, 56.72, 39.11, 19.31. For (3*S**, 4*S**)-**8m**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.0, 1.6 Hz, 1H), 7.77-7.62 (m, 1H), 7.45-7.38 (m, 5H), 7.19-7.14 (m, 1H), 7.12 (d, J = 8.4 Hz, 1H), 5.61 (d, J = 7.6 Hz, 1H), 4.14-3.98 (m, 1H), 4.08 (s, 3H), 3.19 (dd, J = 17.1, 6.9 Hz, 1H), 3.10 (dd, J = 11.2, 6.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.30, 157.59, 137.41, 135.12, 132.04, 129.31, 129.25, 128.18, 123.03, 122.24, 116.77, 112.70, 71.86, 56.70, 40.40, 22.32.



4-Isocyano-4-((2-methoxyphenyl)sulfonyl)-3,3-dimethylbutanenitrile 8n (8n). Following the general procedure with lithiated acetonitrile (from 0.32 mmol, 0.02 mL of MeCN and 0.30 mmol, 0.19 mL of BuLi) and isocyanide **3g** (54 mg, 0.21 mmol) at -78 °C for 30 min (extraction with MTBE) and purification (1 mm plate, hexanes/CH_2Cl_2/Et_2O, 5:1:1 to 4.5:1:1) afforded 57 mg (91%) of pure isocyanide **8n** as a white solid: mp 107-108 °C; IR 2246, 2133, 1331, 1152 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.78-7.63 (m, 1H), 7.23-7.15 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 5.22 (s, 1H), 4.06 (s, 3H), 3.30 (d, *J* = 16.9 Hz, 1H), 2.61 (d, *J* = 16.9 Hz, 1H), 1.52 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.66, 157.58, 137.39, 132.07, 124.08, 121.18, 117.02, 112.82, 75.05, 56.70, 38.67, 28.38, 26.55, 23.54; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_3SNa$ $[M+Na]^+$: 315.0774, found: 315.0773.



8o **1-((1*R**, 2*R**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)cyclohexane-1-carbonitrile and 1-((1*R**, 2*S**)-2-isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylethyl)cyclohexane-1-carbonitrile (8o).** Following the general procedure with lithiated cyclohexanecarbonitrile (from 0.34 mmol of LDA and 0.34 mmol, 0.04 mL of cyclohexanecarbonitrile in 2 mL of THF, -78 °C, 1 h) and isocyanide **3e** (93 mg, 0.31 mmol) at -78 °C for 35 min (extraction with MTBE) afforded a mixture of diastereomers (1*R**, 2*S**:1*R**, 2*R**, 1:10.6 ratio) that was purified by column chromatography (hexanes/ CH_2Cl_2/Et_2O, 6:1:1 to 4:1:1) to afford 106 mg (84%) of a diastereomeric mixture of isocyanide **8o** as a colorless oil: IR 2253, 2135, 1335, 1153 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{24}N_2O_3SNa$ $[M+Na]^+$: 431.1400, found: 431.1398. For (1*R**, 2*R**)-**8o**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.77-7.51 (m, 3H), 7.51-7.29 (m, 3H), 7.18-7.04 (m, 2H), 5.79 (d, *J* = 1.5 Hz, 1H), 4.00 (s, 3H), 3.72 (d, *J* = 1.5 Hz, 1H), 2.33-2.06 (m, 1H), 1.99-1.32 (m, 7H), 1.32-1.03 (m, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 169.47, 157.19, 137.25, 132.63, 132.49, 130.69, 129.03, 128.57, 122.57, 121.49, 121.27, 112.74, 70.00, 56.71, 48.71, 42.25, 35.62, 34.02, 24.71, 22.82, 22.63. For (1*R**, 2*S**)-**8o**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.77-7.51 (m, 1H), 7.51-7.29 (m, 2H), 7.25-7.18 (m, 3H), 7.04-6.96 (m, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 5.77 (d, *J* = 6.9 Hz, 1H), 3.73 (s, 3H), 3.49 (d, *J* = 6.9 Hz, 1H), 3.00-2.62 (m, 1H), 1.99-1.32 (m, 7H), 1.32-1.03 (m, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 169.53, 156.90, 136.78, 136.07, 131.36, 130.69, 128.79, 128.57, 123.72, 121.49, 121.27, 112.42, 73.95, 56.36, 48.71, 41.68, 36.10, 35.58, 24.64, 22.82, 22.63.

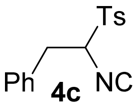


8p

Ethyl (3*R, 4*R**)-4-isocyano-4-((2-methoxyphenyl)sulfonyl)-2,2-dimethyl-3-phenylbutanoate (8p)**. Following the general procedure with isocyanide **3e** (156 mg, 0.52 mmol) and lithium 1-ethoxy-2-methylprop-1-en-1-olate (prepared from 0.74 mmol, 0.10 mL of ethyl isobutyrate and 0.79 mmol of LDA in 5 mL of THF, -78 °C, 30 min) at -78 °C for 35 min (extraction with MTBE) afforded a mixture of diastereomers (3*R**, 4*S**:3*R**, 4*R**, 1:3.6 ratio). Purification by column chromatography (hexanes/CH$_2$Cl$_2$/Et$_2$O, 6:1:1) afforded 165 mg (76%) of pure isocyanide (3*R**, 4*R**)-**8p** as a white solid. The (3*R**, 4*S**)-diastereomer was not eluted from the column. For (3*R**, 4*R**)-**8p**: mp 127-128 °C (dec.); IR 2136, 1719, 1331, 1152 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.70-7.58 (m, 1H), 7.47-7.38 (m, 2H), 7.38-7.29 (m, 3H), 7.16-7.08 (m, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.86 (d, *J* = 1.5 Hz, 1H), 4.26-4.12 (m, 2H), 4.00 (s, 3H), 3.95 (d, *J* = 1.5 Hz, 1H), 1.32 (s, 3H), 1.30 (s, 3H), 1.28 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 175.86, 167.22, 157.23, 136.85, 134.32, 132.60, 130.80, 128.31, 128.11, 122.96, 121.11, 112.53, 70.74, 61.32, 56.42, 48.75, 46.23, 25.52, 23.39, 13.97; HRMS (ESI) calcd for $C_{22}H_{25}NO_5SNa$ [M+Na]$^+$: 438.1346, found: 438.1343.

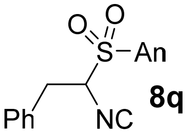
General isocyanide $NaBH_4$ reduction procedure.

Solid sodium borohydride (19 mg, 0.5 mmol) was added to a 0 °C, THF-MeOH-H_2O (7:7:1) solution (5 mL) of the alkeneisocyanide (0.25 mmol). After stirring overnight, the reaction was allowed to warm to room temperature, evaporated and partitioned between CH_2Cl_2 and H_2O (5:3). The phases were separated and then the aqueous phase was extracted with CH_2Cl_2 (5 mL). The combined organic phase was washed with cold water (2 x 5 mL), dried (Na_2SO_4), concentrated and then the crude isocyanide was purified by chromatography to give the pure isocyanide.



4c

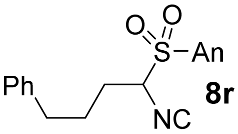
1-((1-Isocyano-2-phenylethyl)sulfonyl)-4-methylbenzene (4c). Isocyanide **2a** (150 mg, 0.53 mmol) was reduced with $NaBH_4$ according to the general method and then purified by crystallization (ethyl acetate/cyclohexane/hexanes, 1:10:15) to afford 128 mg (85%) of isocyanide **4c** as a pale-orange solid: mp 96-98 °C (Lit.[15], 93.5-94.5 °C); IR 2132, 1332, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.39-7.12 (m, 5H), 4.61 (dd, J = 11.5, 2.9 Hz, 1H), 3.60 (dd, J = 13.8, 2.9 Hz, 1H), 2.99 (dd, J = 13.8, 11.5 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.73, 146.90, 133.31, 131.05, 130.34, 130.21, 129.41, 129.15, 128.14, 74.27, 34.77, 21.95; HRMS (ESI) calcd for $C_{16}H_{15}NO_2SNa$ [M+Na]$^+$: 308.0716, found: 308.0716.



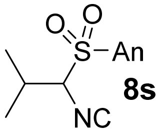
8q

1-((1-Isocyano-2-phenylethyl)sulfonyl)-2-methoxybenzene (8q).

Isocyanide **3e** (75 mg, 0.25 mmol) was reduced with $NaBH_4$ according to the general method. Purification by radial chromatography (1 mm plate, hexanes/ Et_2O/CH_2Cl_2, 6:1:1 to 5:1:1) afforded 63 mg (84%) of isocyanide **8q** as a white crystalline solid: mp 118 °C; IR 2134, 1329, 1151 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.74-7.63 (m, 1H), 7.48-7.27 (m, 5H), 7.23-7.13 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 5.16 (dd, *J* = 11.3, 3.0 Hz, 1H), 3.99 (s, 3H), 3.58 (dd, *J* = 13.9, 3.0 Hz, 1H), 3.24 (dd, *J* = 11.3, 13.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.40, 157.72, 137.22, 133.73, 132.52, 129.57, 129.15, 128.08, 122.62, 121.35, 112.63, 72.36, 56.70, 33.32; HRMS (ESI) calcd for $C_{16}H_{15}NO_3SNa$ [M+Na]$^+$: 324.0665, found: 324.0664.

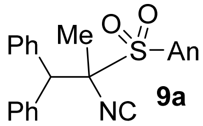


8r **1-((1-Isocyano-4-phenylbutyl)sulfonyl)-2-methoxybenzene (8r)**. Isocyanide **3f** (82 mg, 0.25 mmol) was reduced with $NaBH_4$ according to the general method with purification by filtration through a short SiO_2 plug (CH_2Cl_2) to afford 74 mg (90%) of isocyanide **8r** as a colorless oil which solidified upon cooling: mp 88-90 °C (dec.); IR 2135, 1328, 1150 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.75-7.57 (m, 1H), 7.40-7.25 (m, 2H), 7.25-7.11 (m, 4H), 7.07 (d, *J* = 8.1 Hz, 1H), 5.02 (dd, *J* = 10.1, 3.9 Hz, 1H), 3.96 (s, 3H), 2.72 (t, *J* = 7.5 Hz, 2H), 2.39-1.97 (m, 3H), 1.97-1.73 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.61, 157.64, 140.70, 137.06, 132.43, 128.63, 128.43, 126.33, 122.76, 121.23, 112.62, 70.83, 56.60, 35.00, 27.19, 26.53; HRMS (ESI) calcd for $C_{18}H_{19}NO_3SNa$ [M+Na]$^+$: 352.0978, found: 352.0977.



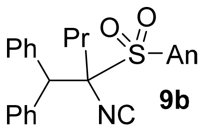
8s **1-((1-Isocyano-2-methylpropyl)sulfonyl)-2-methoxybenzene (8s)**. Isocyanide **3g** (63 mg, 0.25 mmol) was reduced with $NaBH_4$ according to the general method with purification by filtration through a short SiO_2 plug (CH_2Cl_2) to afford 58 mg (91%) of isocyanide **8s** as a colorless oil: IR 2135, 1328, 1152 cm^{-1}; ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.01 (dd, J = 7.9, 1.7 Hz, 1H), 7.77-7.58 (m, 1H), 7.24-7.13 (m, 1H), 7.10 (d, J = 8.4 Hz, 1H), 4.93 (d, J = 3.5 Hz, 1H), 4.00 (s, 3H), 2.90-2.59 (m, 1H), 1.28 (d, J = 6.7 Hz, 3H), 1.21 (d, J = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.89, 157.45, 136.95, 132.30, 123.78, 121.21, 112.65, 75.89, 56.63, 27.45, 20.96, 17.32; HRMS (ESI) calcd for $C_{12}H_{15}NO_3SNa$ $[M+Na]^+$: 276.0665, found: 276.0664.

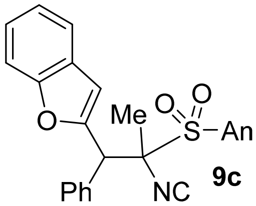


9a

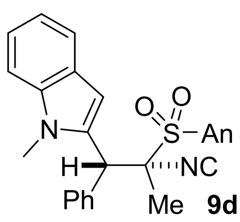
(2-Isocyano-2-((2-methoxyphenyl)sulfonyl)propane-1,1-diyl)dibenzene (9a). Phenyllithium (0.58 mmol, 0.4 mL) was added dropwise to a THF solution (5 mL) of isocyanide **3e** (112 mg, 0.37 mmol) at -78 °C. After 15 min, neat DMPU (1.55 mmol, 0.2 mL) was added and after 2 min neat iodomethane (1.61 mmol, 228 mg, 0.1 mL) was added dropwise. The reaction was allowed to slowly warm to rt over 12 h, and then brine (5 mL) was added. The organic layer was separated and then the aqueous phase was extracted with MTBE (15 mL). The combined organic phase was washed with brine (2 x 5 mL) and dried (Na_2SO_4). Concentration of the solution and purification of the residue by radial chromatography (1 mm plate, hexanes/Et_2O/CH_2Cl_2, 7:1:1 to 4:1:1) afforded 116 mg (79%) of pure isocyanide **9a** as a colorless oil: IR 2123, 1324, 1148 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68-7.52 (m, 5H), 7.52-7.43 (m, 1H), 7.39-7.27 (m, 2H), 7.27-7.21 (m, 1H), 7.21-7.06 (m, 3H), 6.90 (d, J = 8.2 Hz, 1H), 6.88-6.80 (m, 1H), 4.63 (s, 1H), 3.89 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.58, 158.58, 138.87, 137.97, 136.65, 133.88, 129.50, 129.27, 129.01, 128.31, 127.88, 127.66, 123.63, 120.44, 112.44, 81.92, 55.87, 54.70, 24.72; HRMS (ESI) calcd for $C_{23}H_{21}NO_3SNa$ $[M+Na]^+$: 414.1134, found: 414.1132. Repeating the reaction with HMPA instead of DMPU gave 110 mg (75%) of isocyanide **9a**. Performing the methylation without DMPU gave 78 mg (53%) of isocyanide **9a** and unreacted **3e** (15%), as calculated by comparative integration from the crude ^{1}H NMR.


9b

(2-Isocyano-2-((2-methoxyphenyl)sulfonyl)pentane-1,1-diyl)-dibenzene (9b). Phenyllithium (0.54 mmol, 0.4 mL) was added dropwise to a THF solution (5 mL) of isocyanide **3e** (116 mg, 0.39 mmol) at -78 °C. After 15 min, neat DMPU (1.55 mmol, 0.2 mL) was added, and after 2 min, neat 1-iodopropane (1 mmol, 174 mg, 0.1 mL) was added dropwise. The reaction was allowed to slowly warm to rt over 12 h and then brine (5 mL) was added. The phases were separated and aqueous phase was extracted with MTBE (15 mL). The combined organic extract was dried (Na_2SO_4), concentrated and purified (2 mm plate, hexanes/Et_2O/CH_2Cl_2, 8:1:1 to 6:1:1) to afford 134 mg (82%) of isocyanide **9b** as a colorless oil: IR 2122, 1322, 1148 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.53 (m, 4H), 7.49-7.39 (m, 1H), 7.36 (dd, J = 8.0, 1.6 Hz, 1H), 7.33-7.25 (m, 2H), 7.25-7.18 (m, 1H), 7.13-7.03 (m, 3H), 6.88 (d, J = 8.3 Hz, 1H), 6.81-6.66 (m, 1H), 4.68 (s, 1H), 3.90 (s, 3H), 2.24-2.08 (m, 1H), 2.08-1.91 (m, 1H), 1.59-1.40 (m, 2H), 0.65 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.84, 158.58, 139.23, 138.11, 136.30, 133.06, 129.92, 129.00, 128.94, 128.27, 127.74, 127.58, 124.84, 120.27, 112.16, 85.54, 55.77, 53.68, 38.60, 17.34, 13.88; HRMS (ESI) calcd for $C_{25}H_{25}NO_3SNa$ [M+Na]$^+$: 442.1447, found: 442.1445.

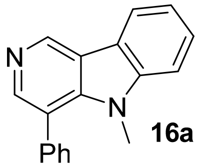

9c

2-((1*R, 2*R**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylpropyl)benzofuran and 2-((1*R**, 2*S**)-2-isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylpropyl)benzofuran (9c).** A THF solution (5.5 mL) of isocyanide **3e** (200 mg, 0.7 mmol) was added to a -78 °C, THF solution (10 mL) of benzofuran-2-yllithium[11] (1.3 mmol) at -78 °C. After 1 h, the reaction was allowed to warm to -40 °C, and then DMPU (1 mL) and MeI (332 mg, 2.3 mmol, 0.15 mL) were added sequentially. The resulting mixture was allowed to warm to rt over 22 h, and then brine (5 mL) was added. The organic phase was separated and the aqueous phase was extracted with MTBE (20 mL). The combined organic extract was washed with brine (2 x 5 mL), dried (Na_2SO_4) and concentrated to afford a mixture of diastereomers (1*R**, 2*S**:1*R**, 2*R**, 3.1:1 ratio) that were purified by column chromatography (CH_2Cl_2/Et_2O/hexanes, 1:1:6 to 1:1:4) to afford 236 mg (82%) of a diastereomeric mixture of isocyanide **9c** (1*R**, 2*S**:1*R**, 2*R**, 4.7:1) as a pale-pink oil: IR 2125, 1592, 1481, 1326, 1150 cm^{-1}; HRMS (+APCI) calcd for $C_{25}H_{22}NO_4S$ $[M+H]^+$: 432.1264, found: 432.1267. For (1*R**, 2*S**)-**9c**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.64-7.57 (m, 2H), 7.43-7.22 (m, 6H), 7.22-7.15 (m, 1H), 7.15-7.08 (m, 1H), 6.78 (s, 1H), 6.75 (d, *J* = 8.4, 1H), 6.72-6.63 (m, 1H), 4.90 (s, 1H), 3.88 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.25, 158.66, 154.11, 153.04, 136.37, 135.39, 133.68, 129.70, 128.87, 128.49, 127.94, 124.10, 122.97, 122.74, 120.95, 119.96, 112.15, 111.09, 105.86, 81.31, 55.85, 49.05, 23.35; For (1*R**, 2*R**)-**9c**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.70-7.67 (m, 1H), 7.57-7.53 (m, 1H), 7.53-7.50 (m, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.43-7.22 (m, 5H), 7.22-7.15 (m, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.98-6.90 (m, 1H), 6.77 (s, 1H), 5.05 (s, 1H), 3.93 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.41, 158.89, 154.95, 153.01, 136.87, 136.40, 134.81, 134.28, 130.36, 128.40, 128.36, 127.86, 124.38, 123.00, 121.15, 120.43, 112.72, 111.29, 107.07, 81.70, 55.97, 49.15, 22.59.



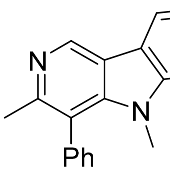
9d

2-((1*R, 2*S**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-phenylpropyl)-1-methyl-1H-indole (9d)**. A THF solution (6 mL) of isocyanide **3e** (200 mg, 0.7 mmol) was added to a -78 °C, THF solution (10 mL) of (1-methyl-1H-indol-2-yl)lithium[12] (1.3 mmol). After 1 h, the reaction was allowed to warm to -40 °C, and then DMPU (1 mL) and MeI (342 mg, 2.4 mmol, 0.15 mL) were added sequentially. The resulting mixture was allowed to warm to rt over 23 h, and then brine (5 mL) was added. The organic phase was separated and the aqueous phase was extracted with MTBE (25 mL). The combined organic extract was washed with brine (2 x 5 mL), dried (Na_2SO_4) and concentrated to afford a mixture of diastereomers (1*R**, 2*S**:1*R**, 2*R**, 3.8:1 ratio) that was purified by column chromatography (EtOAc/hexanes, 1:6 to 1:2) to afford 187 mg (63%) of isocyanide (1*R**, 2*S**)-**9d** as a white solid whose configuration was secured by crystallographic analysis.[16] Isocyanide (1*R**, 2*R**)-**9d** was not isolated because of partial adsorption and decomposition on silica gel. For (1*R**, 2*S**)-**9d**: mp 140-142 °C (dec.); IR 2124, 1319, 1148 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57-7.46 (m, 2H), 7.40-7.30 (m, 3H), 7.30-7.25 (m, 2H), 7.19-7.12 (m, 1H), 7.12-7.05 (m, 2H), 7.02-6.91 (m, 1H), 6.86 (s, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 6.43 (t, *J* = 7.6 Hz, 1H), 4.79 (s, 1H), 3.86 (s, 3H), 3.61 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.05, 158.44, 136.23, 136.13, 135.97, 134.66, 132.35, 130.09, 129.05, 128.43, 127.45, 123.88, 121.76, 120.74, 119.67, 119.46, 112.05, 108.96, 101.67, 82.51, 55.93, 46.62, 29.44, 24.41; HRMS (+APCI) calcd for $C_{26}H_{25}N_2O_3S$ [M+H]$^+$: 445.1580, found: 445.1575.



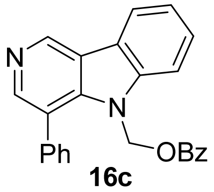
16a

5-Methyl-4-phenyl-5H-pyrido[4,3-b]indole (16a). A CH_2Cl_2 solution (12 mL) of TFA (19 mg, 0.17 mmol, 0.012 mL) was added to a rt, CH_2Cl_2 solution (10 mL) of isocyanide (1*R**, 2*S**)-**8h** (357 mg, 0.83 mmol). After 5 days, the ^{1}H NMR showed complete consumption of isocyanide (1*R**, 2*S**)-**8h**. The reaction was concentrated and then the residue was dissolved in CH_2Cl_2 (15 mL). The resulting solution was washed with saturated, aqueous $NaHCO_3$ (2 x 5 mL), dried (Na_2SO_4), and concentrated to afford the crude *γ*-carboline **16a** that was purified by radial chromatography (2 mm plate, EtOAc/hexanes, 1:4 to 1:1) to afford 186 mg (87%) of *γ*-carboline **16a**. Repeated purification by column chromatography (CH_2Cl_2/*i*-PrOH, 100:0 to 50:1) afforded **16a** as a pale-pink solid: mp 107-109 °C; IR 3053, 1580 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 9.31 (s, 1H), 8.38 (s, 1H), 8.20 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.58-7.52 (m, 1H), 7.52-7.43 (m, 5H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.37-7.32 (m, 1H), 3.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 146.55, 142.35, 141.98, 141.88, 137.00, 130.42, 128.36, 128.08, 126.99, 121.36, 120.85, 120.56, 120.09, 109.32, 32.41; HRMS (+APCI) calcd for $C_{18}H_{15}N_2$ $[M+H]^+$: 259.1230, found: 259.1231.

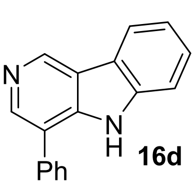


16b

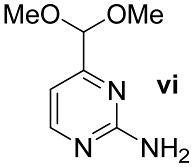
3,5-Dimethyl-4-phenyl-5H-pyrido[4,3-b]indole (**16b**). A CH_2Cl_2 solution (7 mL) of TFA (11 mg, 0.1 mmol) was added to a rt, CH_2Cl_2 solution (7 mL) of isocyanide **9d** (223 mg, 0.50 mmol). After 5 days the reaction was concentrated and then the residue was dissolved in CH_2Cl_2 (15 mL). The resulting solution was washed with saturated, aqueous $NaHCO_3$ (2 x 5 mL), dried (Na_2SO_4), and concentrated to afford the crude *γ*-carboline **16b**. Purification by radial chromatography (1 mm plate, EtOAc/hexanes, 1:3 to 1.5:1) afforded 119 mg (87%) of pure *γ*-carboline **16b**[17] as a thick, yellow oil: IR 2159, 1700, 1199 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 9.21 (s, 1H), 8.15 (d, *J* = 7.3 Hz, 1H), 7.58-7.42 (m, 4H), 7.42-7.34 (m, 2H), 7.34-7.27 (m, 2H), 3.18 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 152.33, 143.35, 141.95, 140.93, 137.41, 130.65, 128.68, 128.07, 126.53, 121.26, 120.64, 120.29, 119.50, 118.57, 109.13, 31.62, 23.20; HRMS (+APCI) calcd for $C_{19}H_{17}N_2$ $[M+H]^+$: 273.1386, found: 273.1383.


16c

(4-Phenyl-5H-pyrido[4,3-b]indol-5-yl)methyl benzoate (16c). A CCl_4 solution (8 mL) of γ-carboline **16a** (71 mg, 0.27 mmol) and 70% dibenzoyl peroxide (160 mg, 0.46 mmol) was heated to reflux. After 12 h the solution was allowed to cool to rt.[18] The reaction was concentrated and then the residue was dissolved in CH_2Cl_2 (20 mL). The resulting solution was washed with saturated, aqueous $NaHCO_3$ (2 x 5 mL), the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (10 mL). The combined organic phase was washed with water (5 mL), dried (Na_2SO_4) and concentrated. The resulting residue was purified by radial chromatography (1 mm plate, CH_2Cl_2/*i*-PrOH, 100:0 to 30:1) to afford 69 mg (67%) of pure γ-carboline **16c** as an oil: IR 3057, 1717 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.43 (s, 1H), 8.20 (dd, *J* = 7.8, 0.4 Hz, 1H), 7.96-7.82 (m, 2H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.59-7.49 (m, 4H), 7.48-7.33 (m, 6H), 6.09 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.61, 147.16, 142.16, 141.91, 140.77, 135.88, 133.53, 129.88, 129.76, 129.22, 128.63, 128.54, 127.66, 122.30, 122.02, 121.09, 120.69, 110.14, 67.81; HRMS (+APCI) calcd for $C_{25}H_{19}N_2O_2$ $[M+H]^+$: 379.1441, found: 379.1443.

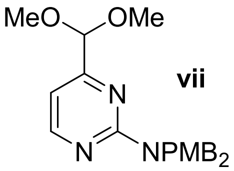

16d

4-Phenyl-5H-pyrido[4,3-b]indole (16d). A MeOH solution (4 mL) of NaOH (7 mg, 0.18 mmol) was added to a rt MeOH solution (3 mL) of γ-carboline **16c** (50 mg, 0.13 mmol)[18]. The reaction was stirred overnight, concentrated *in vacuo* and the residue was dissolved in $CHCl_3$ (40 mL). The resulting solution was washed with saturated, aqueous $NaHCO_3$ (10 mL). Aqueous phase was extracted with $CHCl_3$ (15 mL) and combined organic phase was washed with brine (2 x 5 mL), dried (Na_2SO_4) and evaporated *in vacuo* to afford 32 mg (100%) of pure γ-carboline **16d** as almost colorless solid: IR 3450, 2799, 1595 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.64 (s, 1H), 8.55 (s, 1H), 8.25-8.11 (m, 1H), 7.73-7.64 (m, 2H), 7.64-7.53 (m, 2H), 7.53-7.43 (m, 3H), 7.39-7.31 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.25, 142.06, 141.92, 139.42, 135.97, 129.67, 128.49, 128.39, 127.20, 122.00, 121.22, 121.04, 111.26; HRMS (+APCI) calcd for $C_{17}H_{13}N_2$ [M+H]$^+$: 245.1073, found: 245.1071.



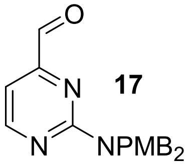
vi

4-(Dimethoxymethyl)pyrimidin-2-amine (**vi**)[19]. Guanidine hydrochloride (7.55 g, 79 mmol) was added in portions to a 0 °C, methanolic solution (200 mL) of MeONa (4.77 g, 88 mmol). After 5 min, a methanolic solution (65 mL) of (*E*)-4-(dimethylamino)-1,1-dimethoxybut-3-en-2-one[20] was added dropwise. After 20 min, the solution was heated to reflux and, after 20 h, the reaction was allowed to cool to rt. The solution was concentrated and then the solid residue was extracted with hot *i*-PrOH (3 x 200 mL) and then the combined extracts were filtered through a glass frit. The resulting filtrate was concentrated to 250 mL and then cooled to 0 °C. After 20 h, the crystalline product was filtered, washed sequentially with cold *i*-PrOH (2 x 15 mL) and hexanes (2 x 30 mL), and then dried under vacuum to afford 10.30 g (81%) of pure amine **vi** as a colorless crystalline solid:[21] IR 3314, 1659, 1569, 1342, 1197 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 5.0 Hz, 1H), 6.84 (d, *J* = 5.0 Hz, 1H), 5.34 (br. s, 2H), 5.14 (s, 1H), 3.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.22, 163.11, 159.10, 108.68, 102.29, 53.40; ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 8.26 (d, *J* = 5.0 Hz, 1H), 6.70 (br. s, 2H), 6.62 (d, *J* = 5.0 Hz, 1H), 5.01 (s, 1H), 3.29 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d$_6$) δ 166.00, 163.93, 159.26, 107.04, 103.27, 53.78; HRMS (+APCI) calcd for $C_7H_{12}N_3O_2$ [M+H]$^+$: 170.0924, found: 170.0924.



vii

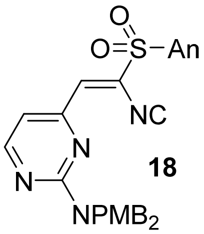
4-(Dimethoxymethyl)-N,N-bis(4-methoxybenzyl)pyrimidin-2-amine (vii). Amine **vi** (1.27 g, 7.5 mmol) was added to a 0 °C, DMF suspension (35 mL) of sodium hydride (0.73 g, 30.3 mmol). After 30 min, a DMF solution (5 mL) of PMBCl (2.41 g, 15.4 mmol) was added dropwise. The reaction was allowed to warm to rt over 18 h, and then the DMF was removed by vacuum distillation. The resulting solid was partitioned between 0 °C CH_2Cl_2 (150 mL) and water (20 mL). After 5 min, the mixture was filtered through a celite plug that was subsequently washed with CH_2Cl_2 (3 x 15 mL). The organic phase was washed with brine (20 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (EtOAc/hexanes, 10:90 to 15:85) to afford 2.86 g (93%) of amine **vii** as a thick, colorless oil: IR 2833, 1577, 1242 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 4.9 Hz, 1H), 7.18 (d, J = 8.6 Hz, 4H), 6.83 (d, J = 8.6 Hz, 4H), 6.74 (d, J = 4.9 Hz, 1H), 5.07 (s, 1H), 4.78 (s, 4H), 3.78 (s, 6H), 3.41 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.77, 162.11, 158.70, 130.46, 129.10, 113.79, 106.42, 103.89, 55.26, 54.05, 48.09; HRMS (+APCI) calcd for $C_{23}H_{28}N_3O_4$ $[M+H]^+$: 410.2074, found: 410.2073.



17

2-(bis(4-Methoxybenzyl)amino)pyrimidine-4-carbaldehyde (17). An emulsion of acetal **vii** (9.62 g, 23.5 mmol) in aqueous hydrochloric acid (25 mL, 3M, 75.2 mmol) was heated to 60 °C. After 8 h, the heating was discontinued and then the reaction was allowed to cool to rt overnight. The reaction mixture was extracted with CH_2Cl_2 (150 mL), the phases were separated, and then the organic phase was washed with saturated aqueous $NaHCO_3$ (2 x 20 mL), water (20 mL), dried (Na_2SO_4) and then concentrated. The crude aldehyde was purified by column chromatography (EtOAc/hexanes, 5:95 to 10:90) to afford 8.02 g (94%) of pure aldehyde

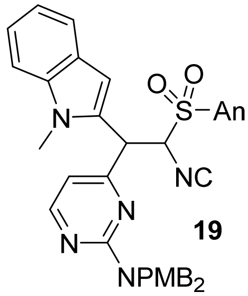
17 as a yellow solid: mp 73-75 °C; IR 2836, 1718, 1245 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 9.84 (d, *J* = 0.8 Hz, 1H), 8.56 (d, *J* = 4.7 Hz, 1H), 7.20 (d, *J* = 8.5 Hz, 4H), 7.01 (d, *J* = 4.7 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 4H), 4.84 (s, 4H), 3.79 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 194.18, 163.00, 160.12, 158.89, 129.85, 129.05, 113.95, 105.05, 55.28, 48.31; HRMS (+APCI) calcd for $C_{21}H_{22}N_3O_3$ $[M+H]^+$: 364.1656, found: 364.1657.



18

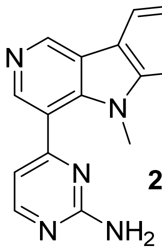
(*E*)-4-(2-Isocyano-2-((2-methoxyphenyl)sulfonyl)vinyl)-N,N-bis-(4-methoxybenzyl)pyrimidin-2-amine (18). A hexanes solution of BuLi (2.2 mL, 3.4 mmol) was added dropwise to a -78 °C, THF solution (35 mL) of isocyanide **2e** (690 mg, 3.3 mmol). After 10 min, a THF solution (5 mL) of TMSCl (365 mg, 3.4 mmol, 0.45 mL) was added, and then after 10 min a hexanes solution of BuLi (2.2 mL, 3.4 mmol) was added dropwise. After 10 min, a THF solution (15 mL) of aldehyde **17** (1.22 g, 3.4 mmol) was added dropwise. After 2.5 h the reaction was allowed to warm to -28 °C and then poured into a -5 °C, methanol-water solution (100 mL of water and 15 mL of MeOH) of NH_4Cl (3 g). MTBE (100 mL) was added and, after 10 min, the organic phase was separated. The aqueous phase was extracted with MTBE (50 mL), the organic phase was combined, washed with brine (2 x 20 mL), dried (Na_2SO_4) and then concentrated. The resulting solid was recrystallized from CH_2Cl_2:cyclohexane:hexanes (1:2:6) to afford 1.31 g (72%) of pure isocyanide **18** as yellow powder: mp 86-90 °C (dec.); IR: 2104, 1566, 1350, 1158 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.51 (d, *J* = 4.8 Hz, 1H), 8.07 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.70-7.61 (m, 1H), 7.55 (s, 1H), 7.22-7.11 (m, 1H), 7.16 (d, *J* = 8.6 Hz, 4H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.88-6.79 (m, 1H), 6.83 (d, *J* = 8.6 Hz, 4H), 4.80 (s, 4H), 3.84 (s, 3H), 3.78 (s, 6H); ^{13}C NMR (126 MHz,

$CDCl_3$) δ 162.38, 159.98, 158.80, 157.78, 156.65, 137.15, 134.69, 132.27, 129.92, 129.01, 123.08, 120.98, 113.89, 112.61, 110.69, 109.99, 56.21, 55.28, 48.20; HRMS (+APCI) calcd for $C_{30}H_{29}N_4O_5S$ $[M+H]^+$: 557.1853, found: 557.1852.



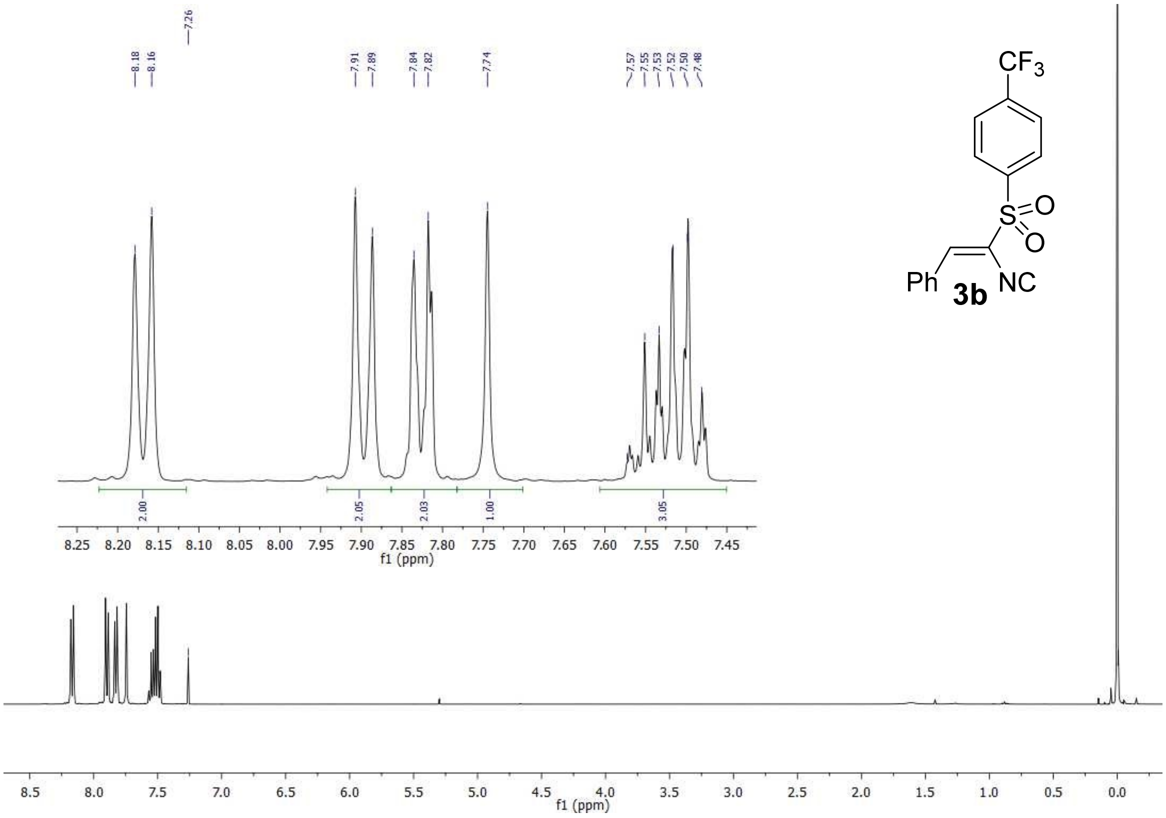
19

4-((1*S, 2*R**)-2-Isocyano-2-((2-methoxyphenyl)sulfonyl)-1-(1-methyl-1H-indol-2-yl)ethyl)-N,N-bis(4-methoxybenzyl)pyrimidin-2-amine and 4-((1*S**, 2*S**)-2-isocyano-2-((2-methoxyphenyl)-sulfonyl)-1-(1-methyl-1H-indol-2-yl)ethyl)-N,N-bis(4-methoxybenzyl)pyrimidin-2-amine (19)**. A THF solution (5 mL) of isocyanide **18** (157 mg, 0.28 mmol) was added to a -78 °C, THF solution (10 mL) of (1-methyl-1H-indol-2-yl)lithium[12] (0.51 mmol). After 40 min the reaction was allowed to warm to -30 °C, brine (5 mL) and MTBE (15 mL) were added sequentially, and then the mixture was allowed to warm to 0 °C. After 5 min, the organic phase was separated, the aqueous phase was extracted with MTBE (10 mL), and then the organic phases were combined and washed with brine (2 x 5 mL), dried (Na_2SO_4) and concentrated. The crude isocyanide diastereomers (1*S**, 2*S**:1*S**, 2*R**, 1:1 ratio) were purified by column chromatography (EtOAc/hexanes, 1:3) to afford 122 mg (63%) of isocyanide **19** as a thick, yellow-orange oil. For (1*S**, 2*R**)-**19**: IR: 2132, 1350, 1155 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 4.9 Hz, 1H), 7.35 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 4H), 7.14-7.05 (m, 4H), 6.94-6.89 (m, 1H), 6.85 (d, *J* = 8.6 Hz, 4H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.50 (d, *J* = 4.9 Hz, 1H), 6.49-6.44 (m, 1H), 6.16 (d, *J* = 10.1 Hz, 1H), 6.07 (s, 1H), 4.90 (d, *J* = 15.4 Hz, 2H), 4.78 (d, *J* = 10.1 Hz, 1H), 4.77 (br. s, 2H), 3.80 (s, 6H), 3.76 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.53, 165.23, 162.38, 159.23, 158.85, 156.63, 136.96, 135.66, 132.34, 130.08, 129.41, 128.90, 126.94, 124.09, 121.94, 120.35, 119.99, 119.54, 114.01, 111.78, 109.33, 108.96, 102.41, 73.98, 56.20, 55.31, 48.80, 45.11, 29.81; HRMS (+APCI) calcd for $C_{39}H_{38}O_5N_5S$ $[M+H]^+$: 688.2588, found: 688.2591. For (1*S**, 2*S**)-**19**: IR 2130, 1349, 1156 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, *J* = 5.0 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.59-7.51 (m, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.36-7.30 (m, 1H), 7.25-7.10 (m, 1H), 7.19 (d, *J* = 8.2 Hz, 4H), 7.10-7.06 (m, 1H), 7.06-7.00 (m, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 4H), 6.44 (s, 1H), 6.42 (d, *J* = 6.6 Hz, 1H), 6.38 (d, *J* = 5.0 Hz, 1H), 5.15 (d, *J* = 6.6 Hz, 1H), 5.01 (d, *J* = 14.9 Hz, 2H), 4.56 (d, *J* = 15.3 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 6H), 3.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.57, 165.02, 161.76, 159.04, 158.94, 157.61, 137.43, 136.85, 133.15, 132.06, 130.08, 128.95, 127.48, 123.67, 122.02, 121.03, 120.80, 119.77, 114.03, 112.52, 109.53, 109.20, 103.51, 72.34, 56.37, 55.31, 48.53, 42.52, 30.21; HRMS (+APCI) calcd for $C_{39}H_{38}O_5N_5S$ $[M+H]^+$: 688.2588, found: 688.2586. *Equilibration*: a THF solution (4 mL) of *t*-BuOK (25 mg, 0.22 mmol) was added to a -78 °C, THF solution (5 mL) of (1*S**, 2*R**)-**19** (138 mg, 0.20 mmol). After 30 min, a THF solution (1.5 mL) of *t*-BuOH (1.1 mmol, 0.1 mL) was added. After 10 min, brine (5 mL) and MTBE (25 mL) were added sequentially. Organic phase was separated, aqueous phase was extracted with MTBE (15 mL), and then combined organic solution was washed with brine (2 x 5 mL), dried (Na_2SO_4) and concentrated. The crude (1*S**, 2*R**:1*S**, 2*S**, 1:1 ratio) was purified by chromatography (12g-SiO_2, Reveleris X2, EtOAc/hexanes, 5:95 to 25:75) to afford 51 mg (37%) of (1*S**, 2*S**)-**19**, 21 mg (15%) of a 1:1 mixture of 1*S**, 2*R**:1*S**, 2*S** and 48 mg (35%) of (1*S**, 2*R**)-**19** spectrally identical to materials previously characterized.

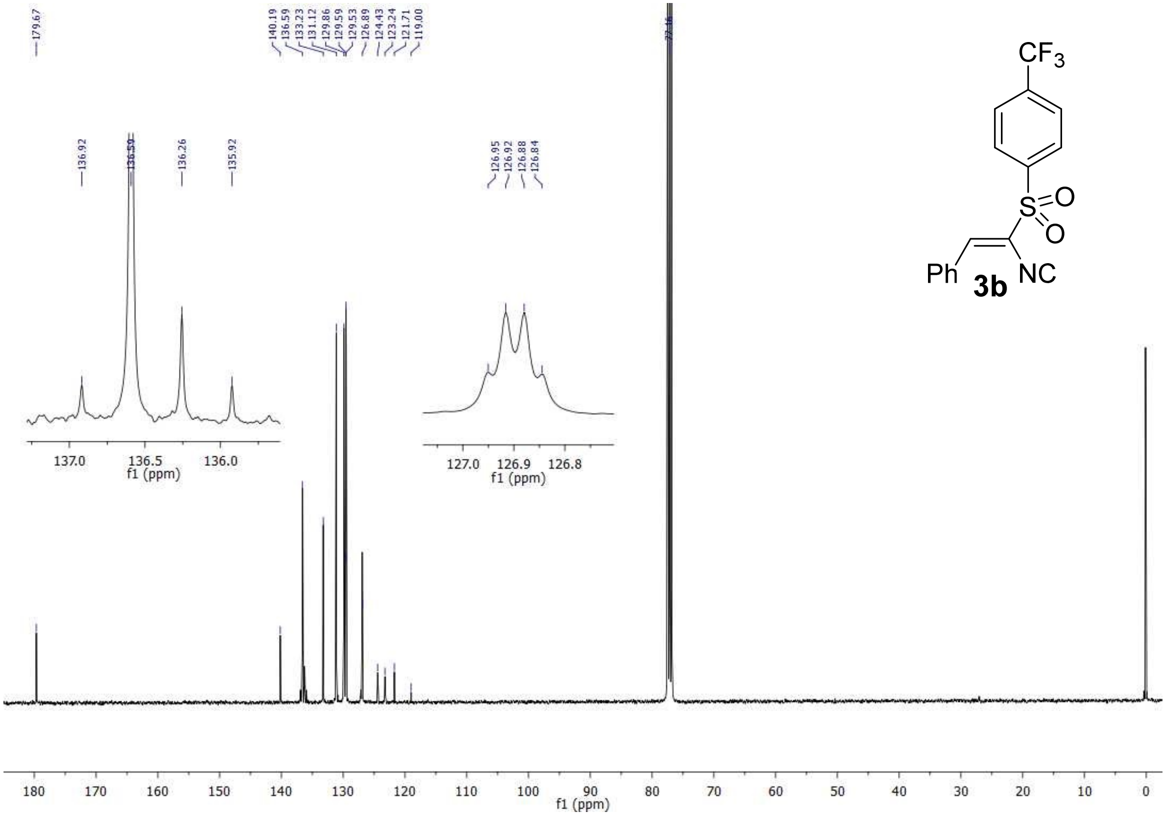


20

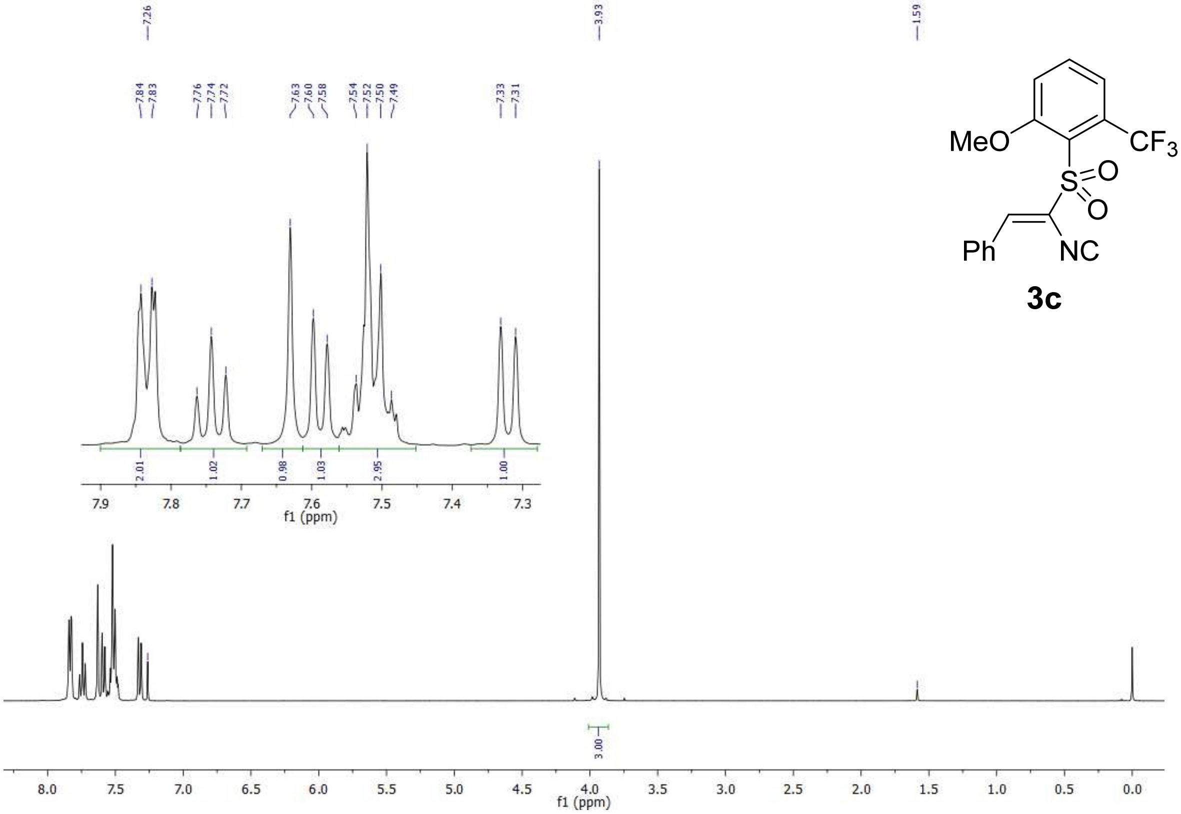
4-(5-Methyl-5H-pyrido[4,3-b]indol-4-yl)pyrimidin-2-amine (20). A CH_2Cl_2 solution (1.5 mL) of TFA (2.3 mg, 0.02 mmol) was added to a rt, CH_2Cl_2 solution (4 mL) of isocyanide (1*S**, 2*S**)-**19** (34 mg, 0.05 mmol). After 6 days, the solution was concentrated, the resulting material (HRMS (+APCI) calcd for $C_{32}H_{30}O_2N_5$ $[M+H]^+$: 516.2394, found: 516.2395) was dissolved in TFA (4 mL) and the solution was heated to reflux. After 20 h, the solution was allowed to cool to rt and then the solvent was removed under vacuum to afford a residue that was partitioned between CH_2Cl_2 (15 mL) and saturated aqueous $NaHCO_3$ (5 mL). The organic phase was separated, the aqueous phase was extracted with CH_2Cl_2 (10 mL), and then the organic phases were combined and washed with saturated, aqueous $NaHCO_3$ (5 mL), dried (Na_2SO_4) and concentrated. The crude carboline was purified by column chromatography (CH_2Cl_2/*i*-PrOH, 13:1 to 5:1) and then crystallized from CCl_4 to afford 11 mg (82%) of *γ*-carboline **20** as an almost colorless solid: mp > 200 °C (dec.); IR 3307, 1630, 1571, 1232 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.54 (s, 1H), 8.47 (d, *J* = 5.0 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.63-7.54 (m, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.43-7.33 (m, 1H), 6.98 (d, *J* = 5.0 Hz, 1H), 5.25 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.97, 162.47, 158.92, 145.60, 142.86, 142.00, 127.36, 121.18, 121.08, 120.52, 112.21, 109.51, 33.18; ^1H NMR (300 MHz, CD_3OD) δ 9.34 (s, 1H), 8.45 (d, *J* = 5.1 Hz, 1H), 8.44 (s, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 7.69-7.59 (m, 2H), 7.47-7.36 (m, 1H), 7.03 (d, *J* = 5.1 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 165.75, 164.34, 160.05, 145.06, 143.63, 143.49, 142.59, 129.01, 122.65, 122.02, 121.63, 112.30, 111.05, 33.58; HRMS (+APCI) calcd for $C_{16}H_{14}N_5$ $[M+H]^+$: 276.1244, found: 276.1243.



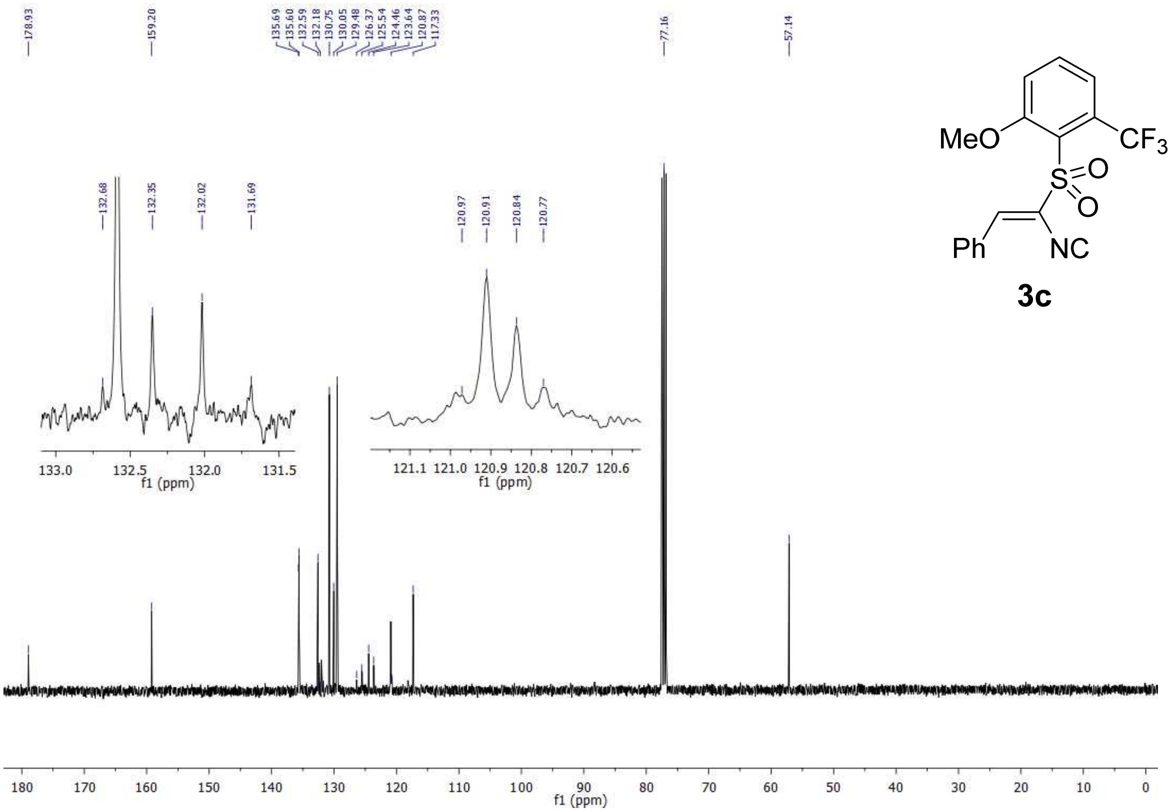
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **3b**.



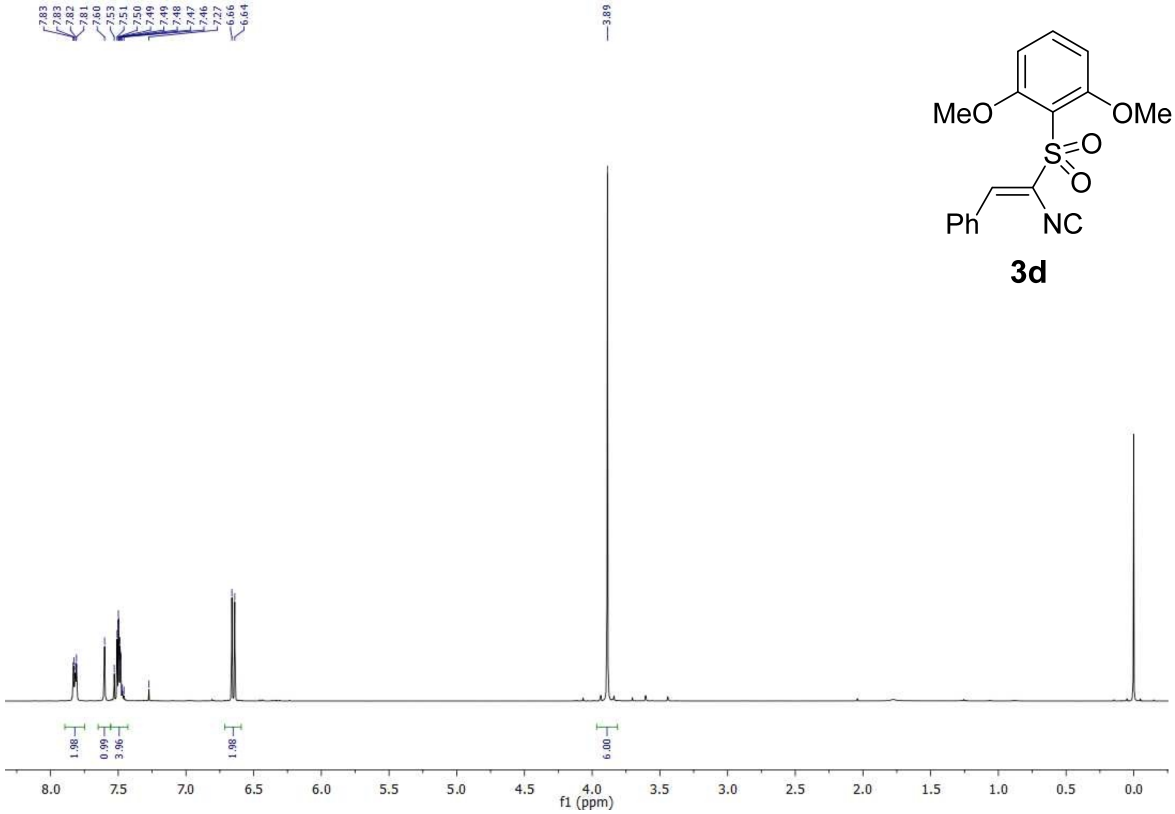
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **3b**.



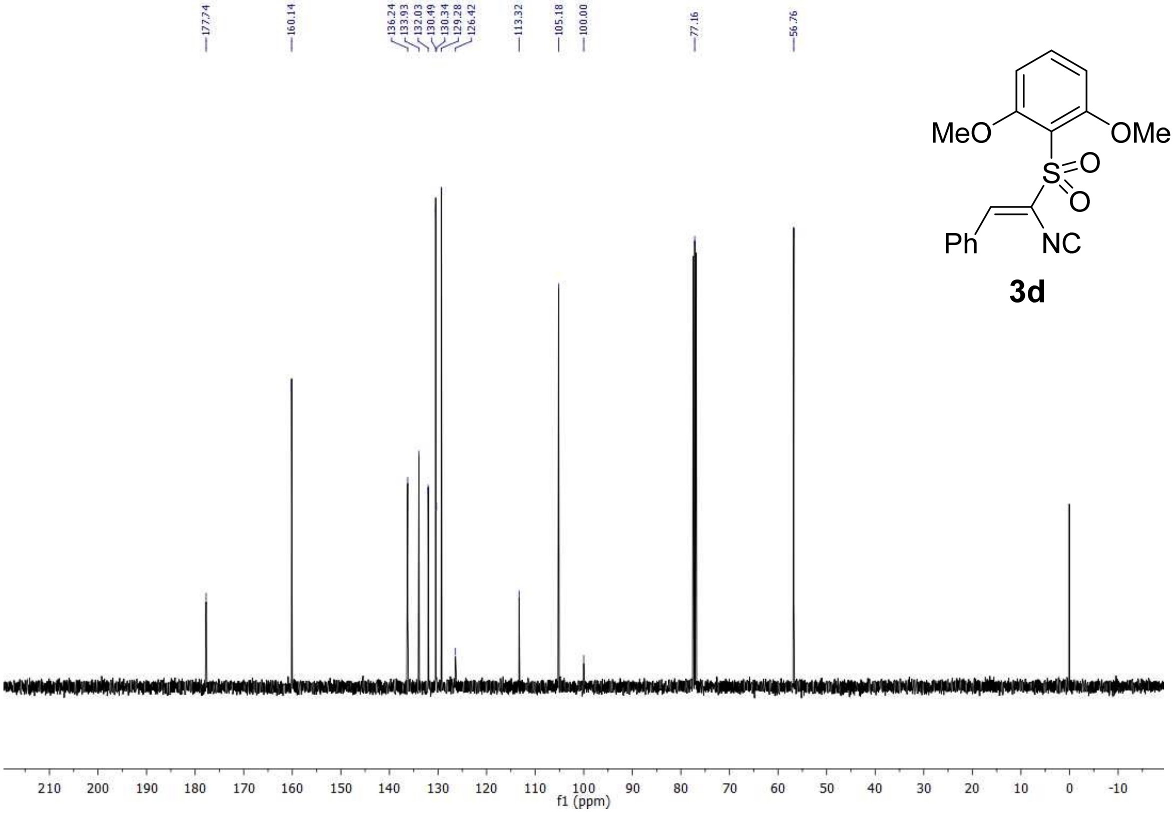
^1H NMR (400 MHz, $CDCl_3$) of isocyanide **3c**.



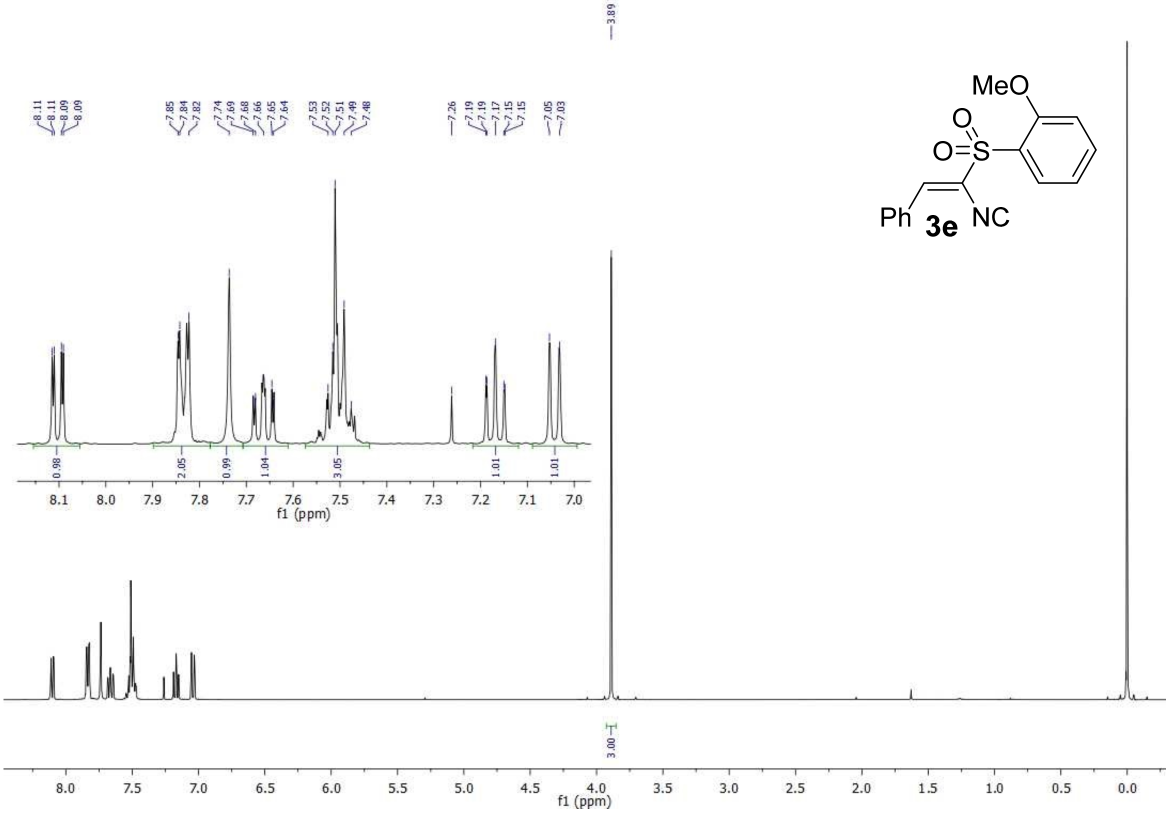
^{13}C NMR (101 MHz, $CDCl_3$) of isocyanide **3c**.



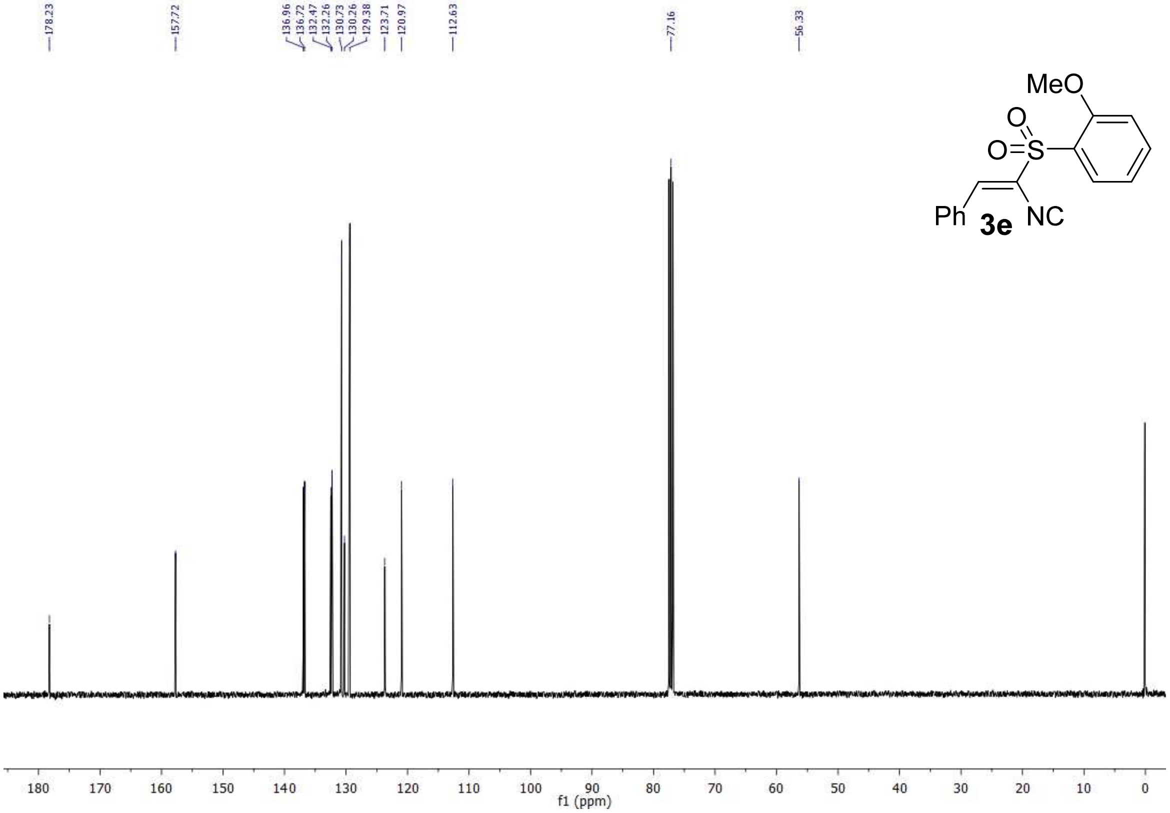
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **3d**.



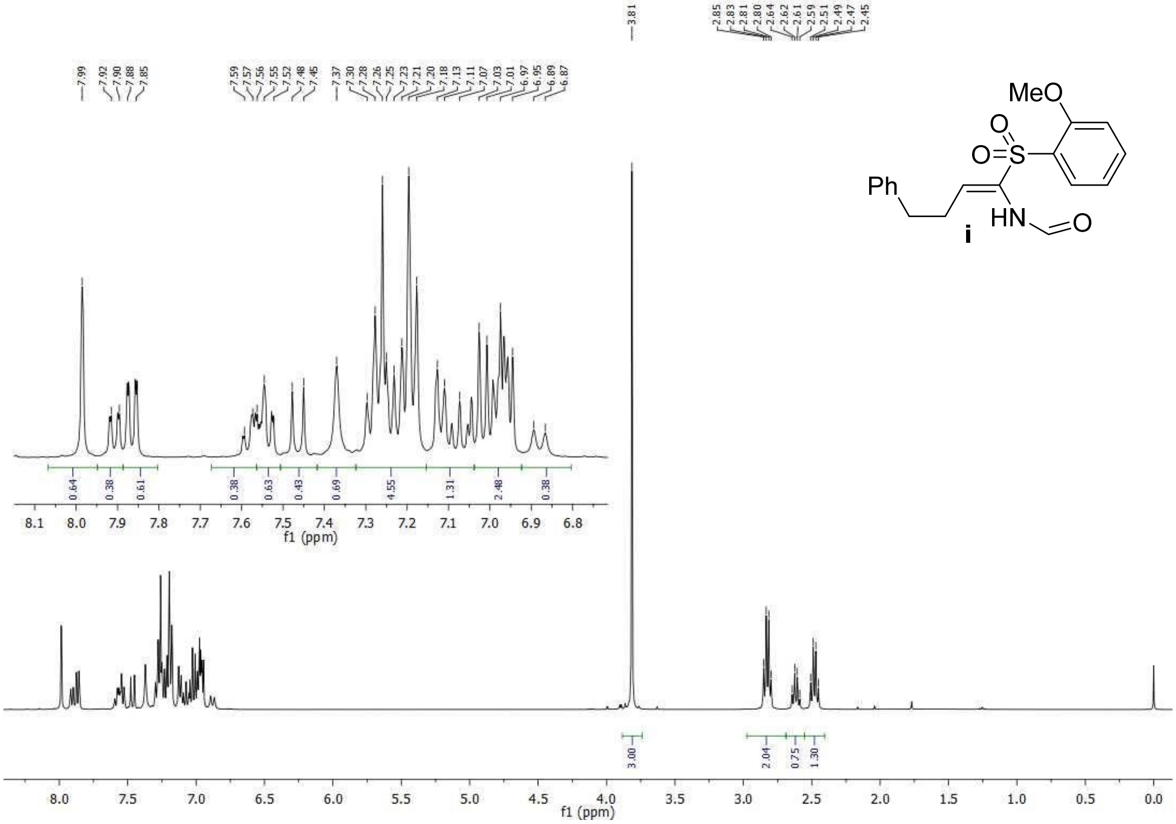
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **3d**.



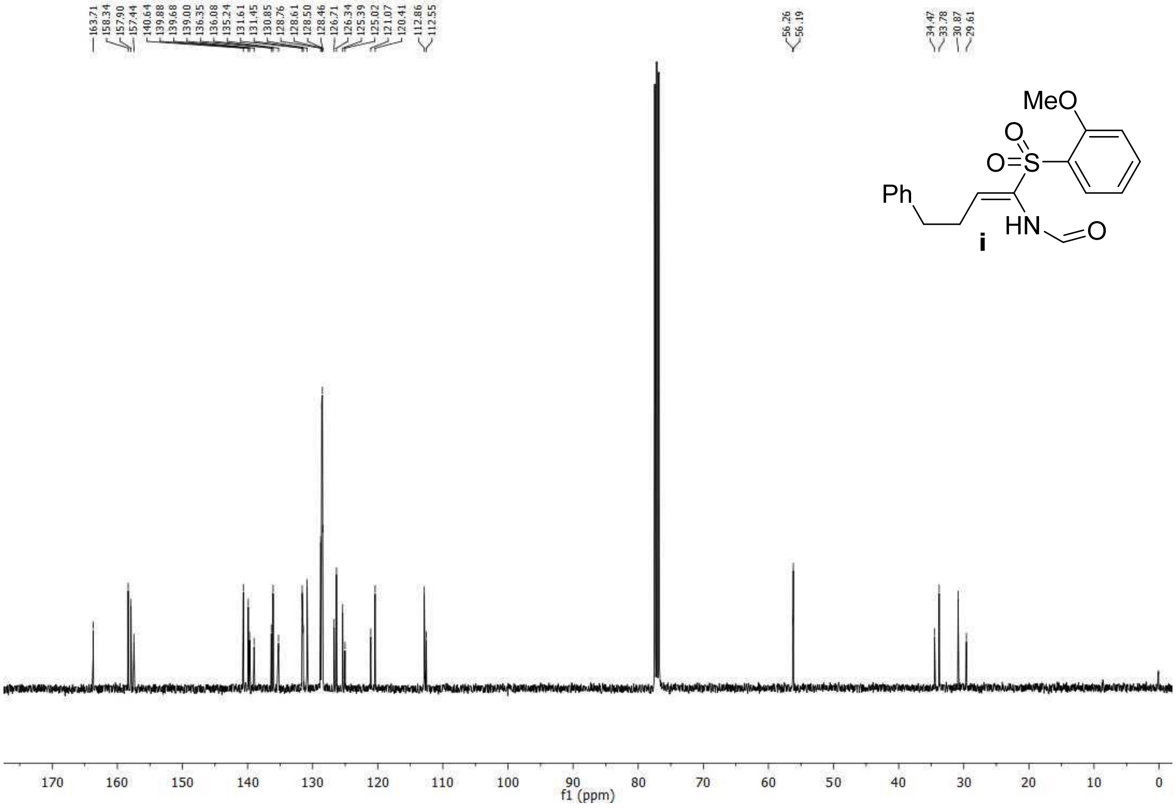
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **3e**.



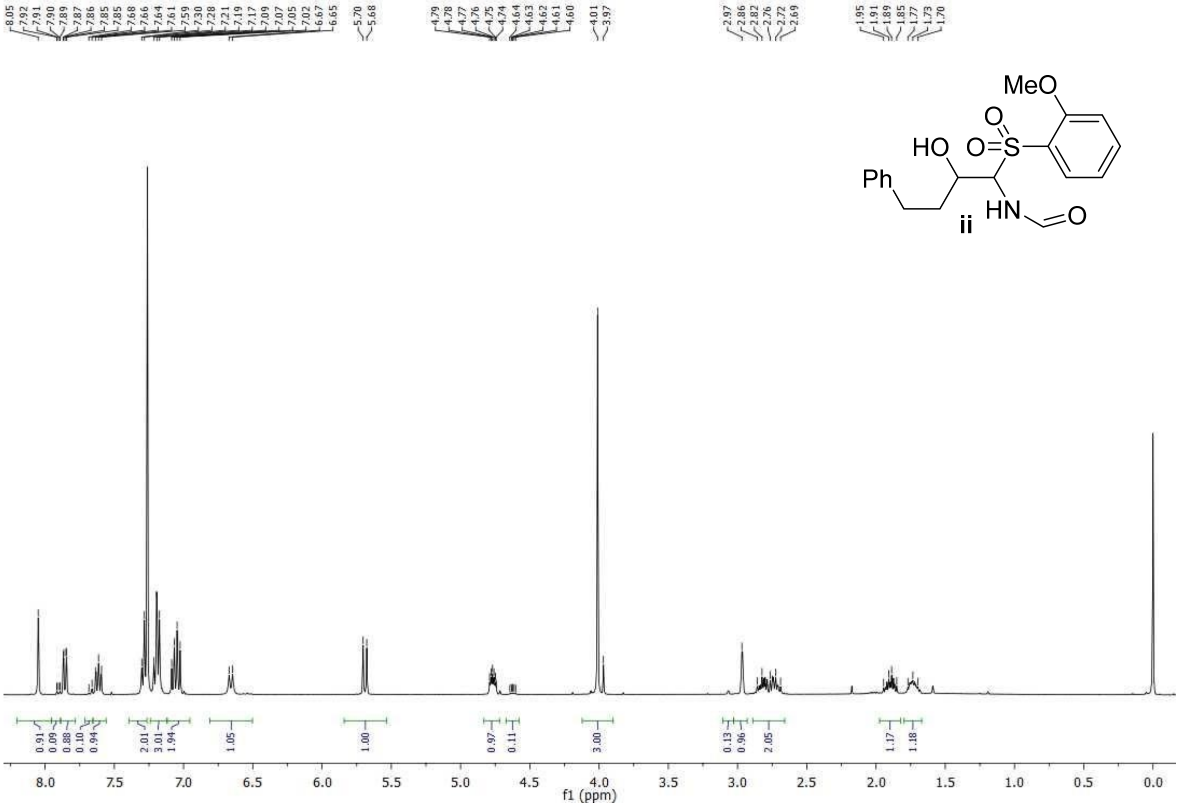
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **3e**.



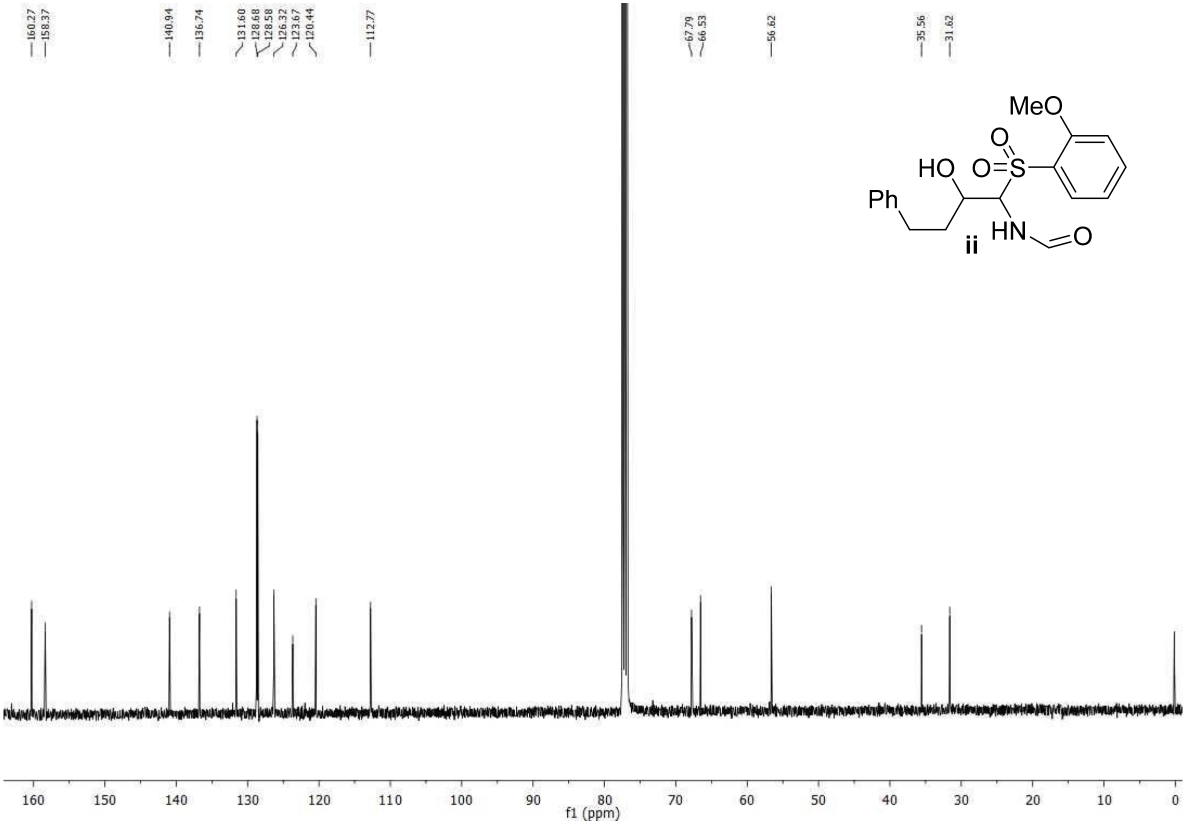
^{1}H NMR (400 MHz, CDCl$_3$) of formamide **i**.



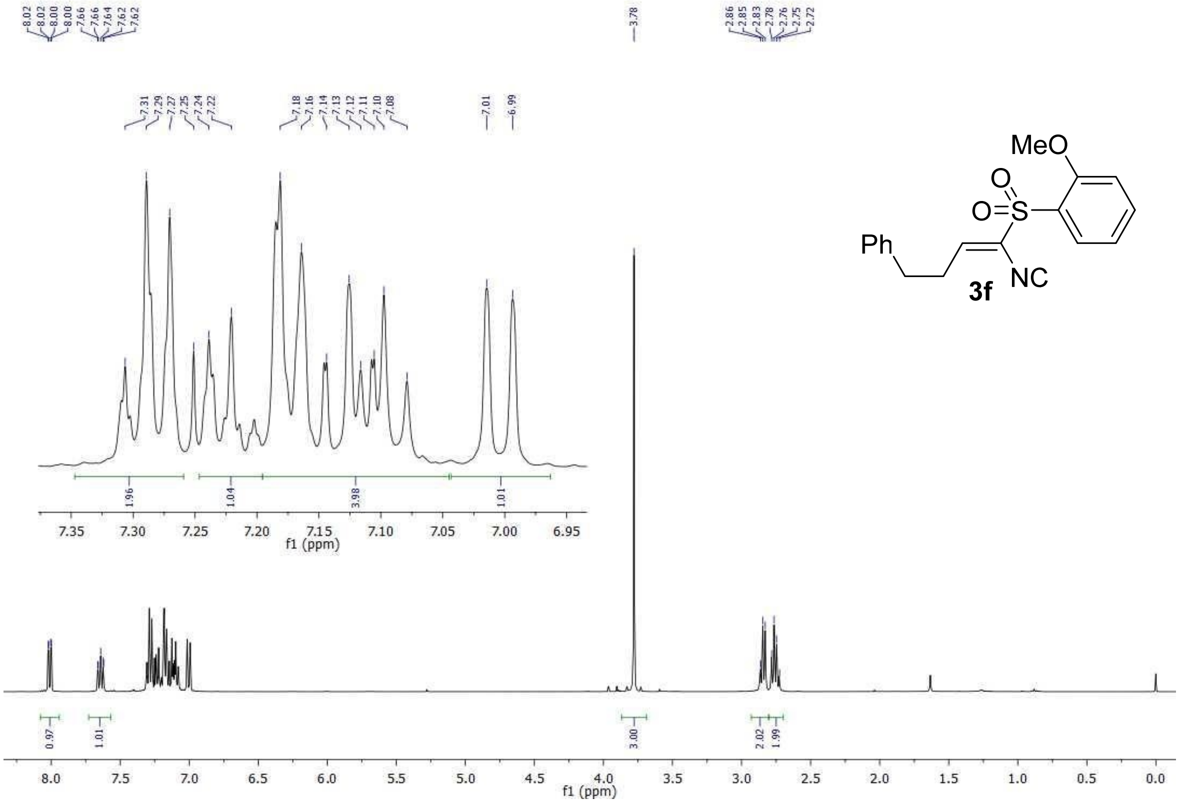
^{13}C NMR (101 MHz, CDCl$_3$) of formamide **i**.



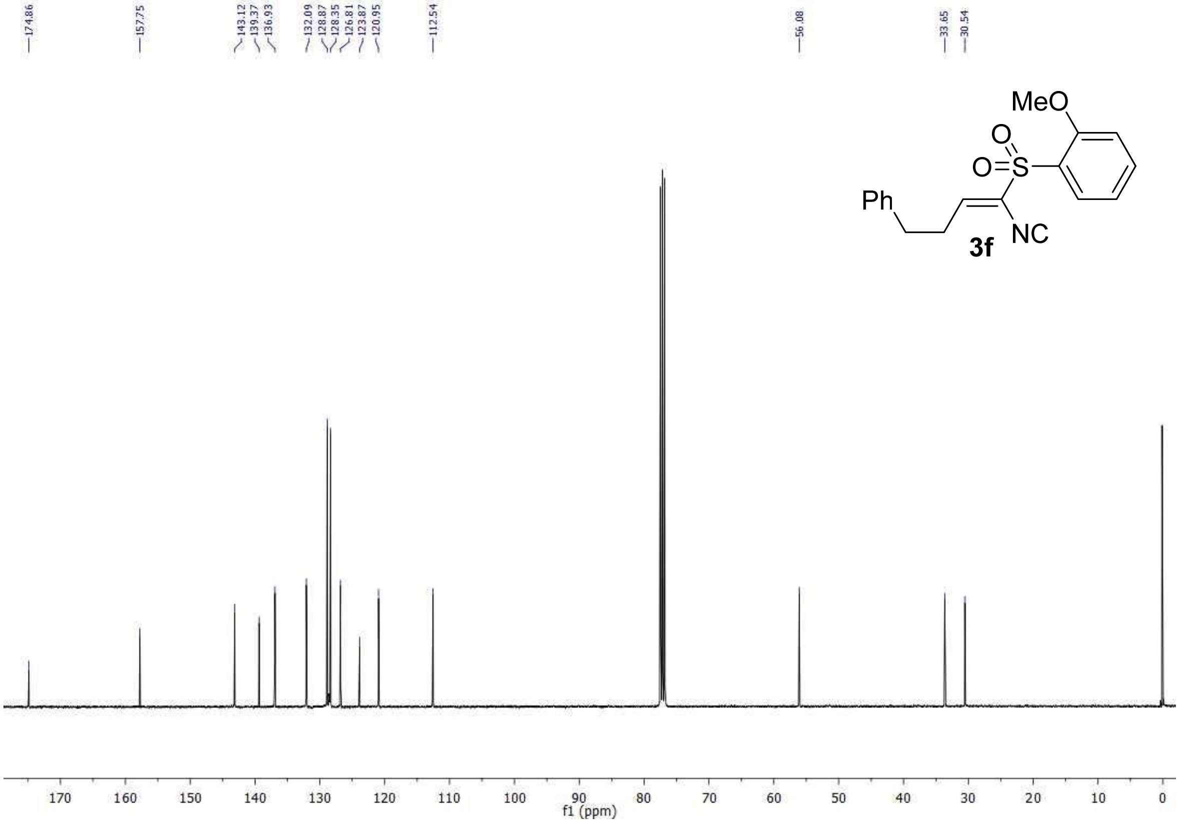
^{1}H NMR (400 MHz, CDCl$_3$) of formamide **ii**.



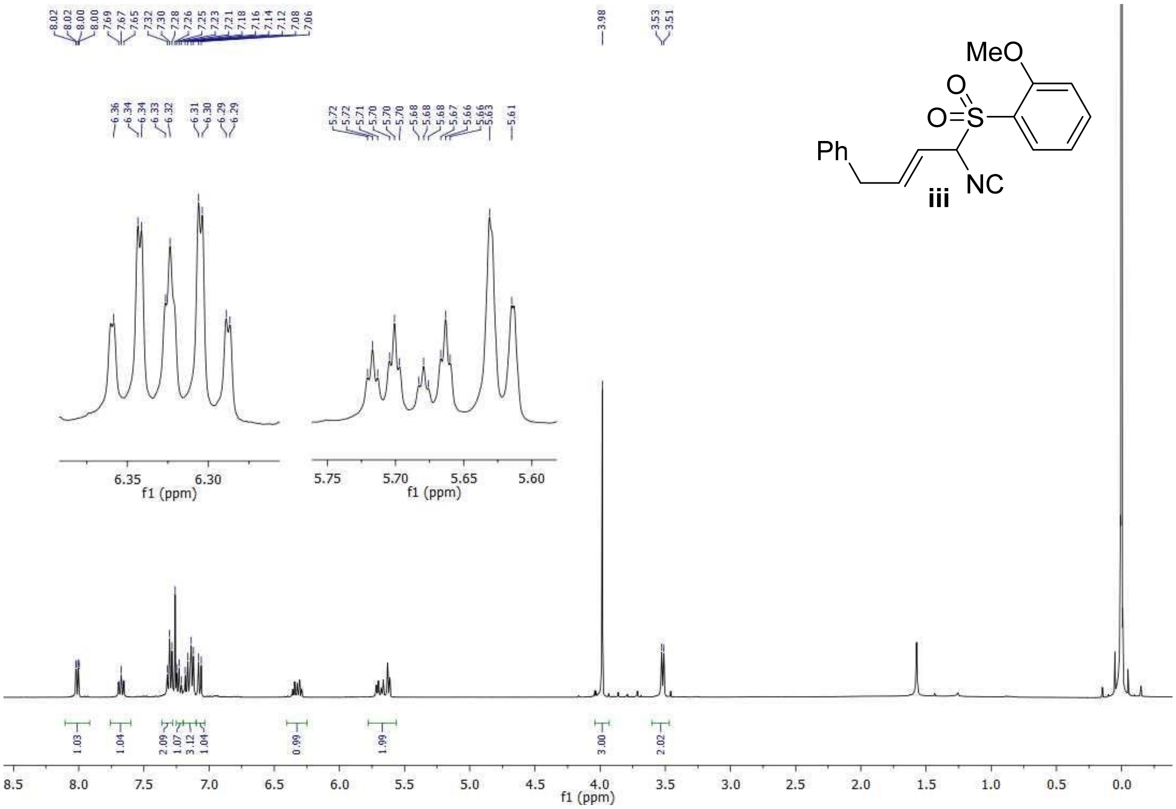
^{13}C NMR (101 MHz, CDCl$_3$) of formamide **ii**.



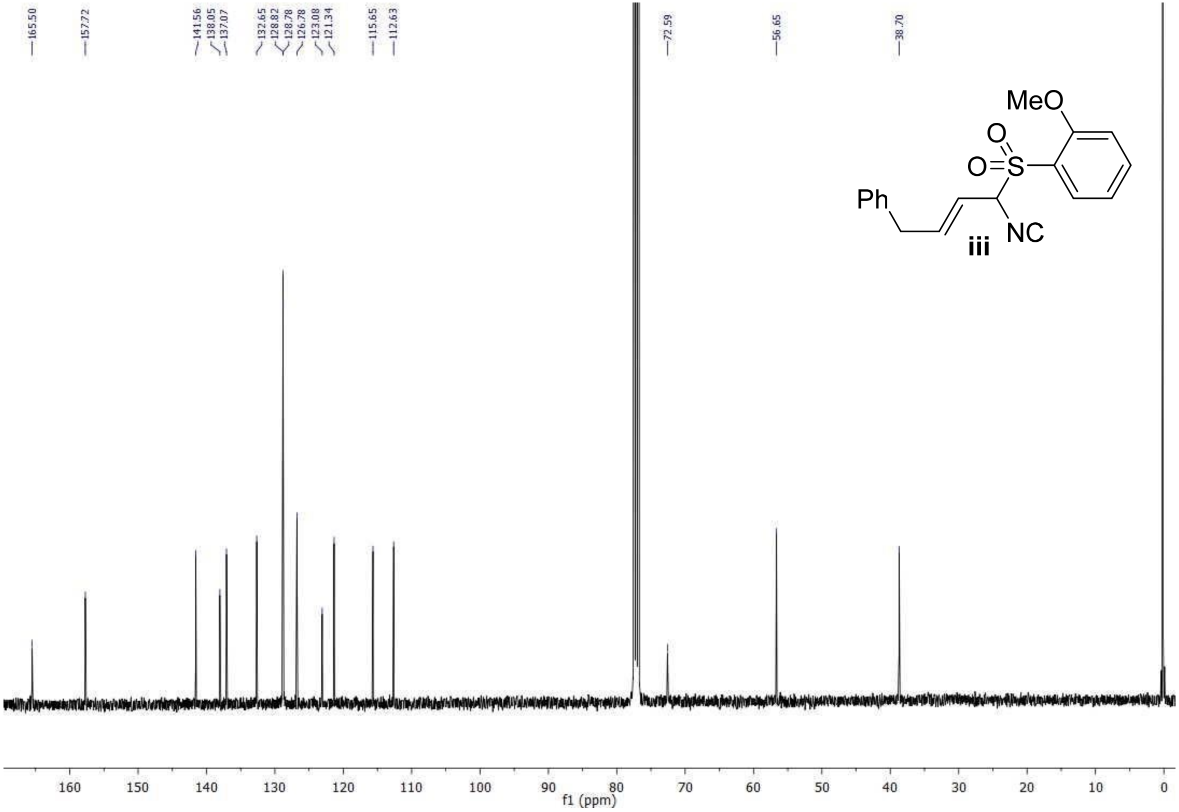
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **3f**.



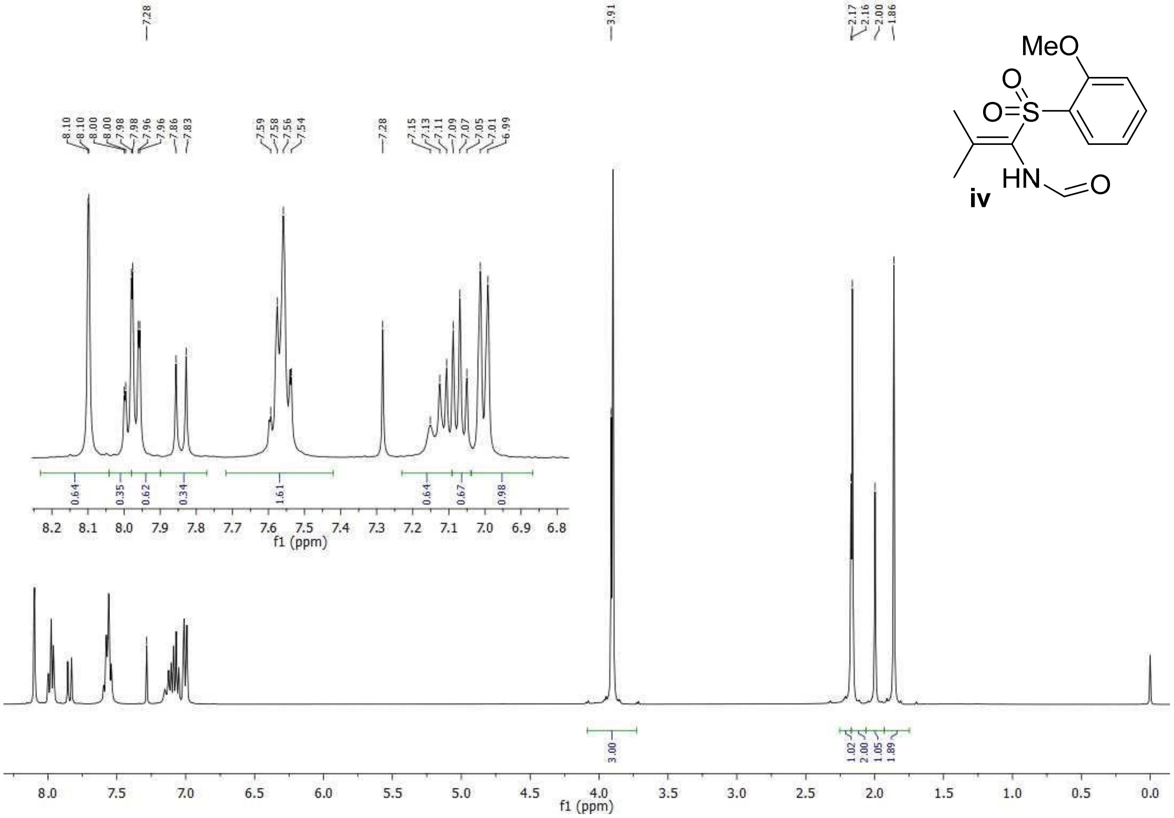
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **3f**.



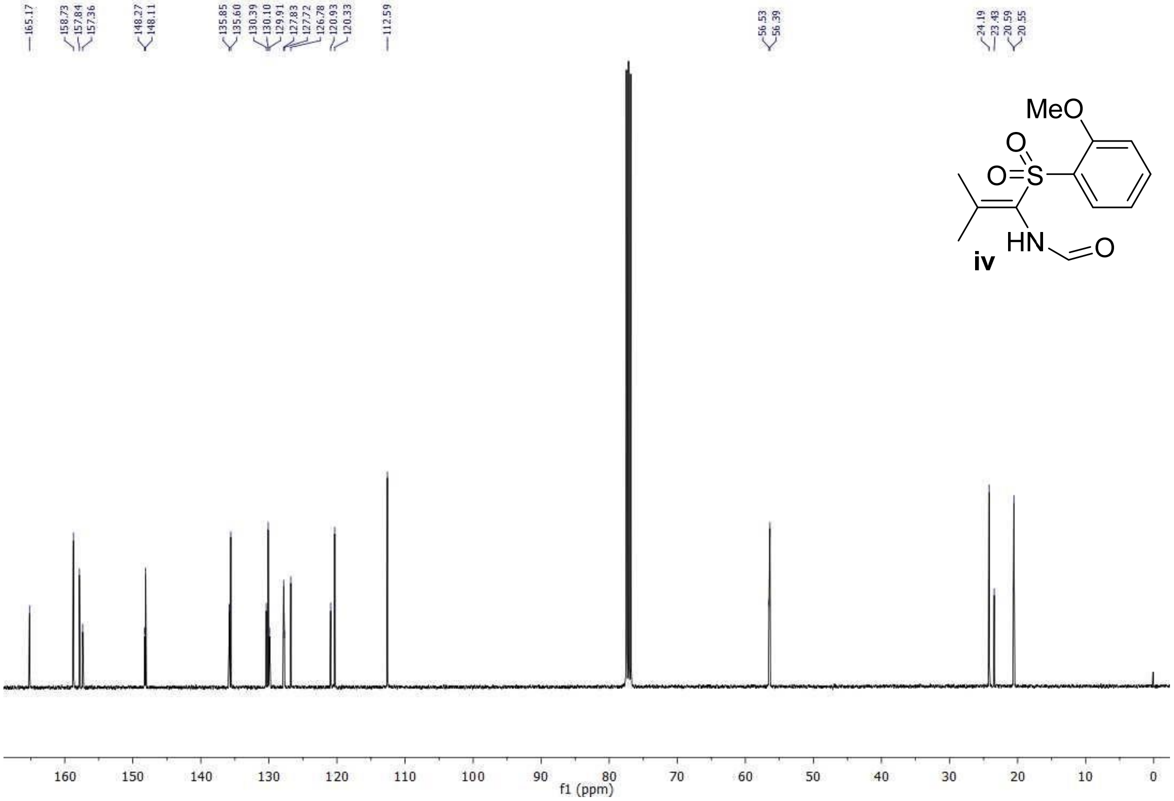
^{1}H NMR (400 MHz, $CDCl_3$) of isocyanide **iii**.



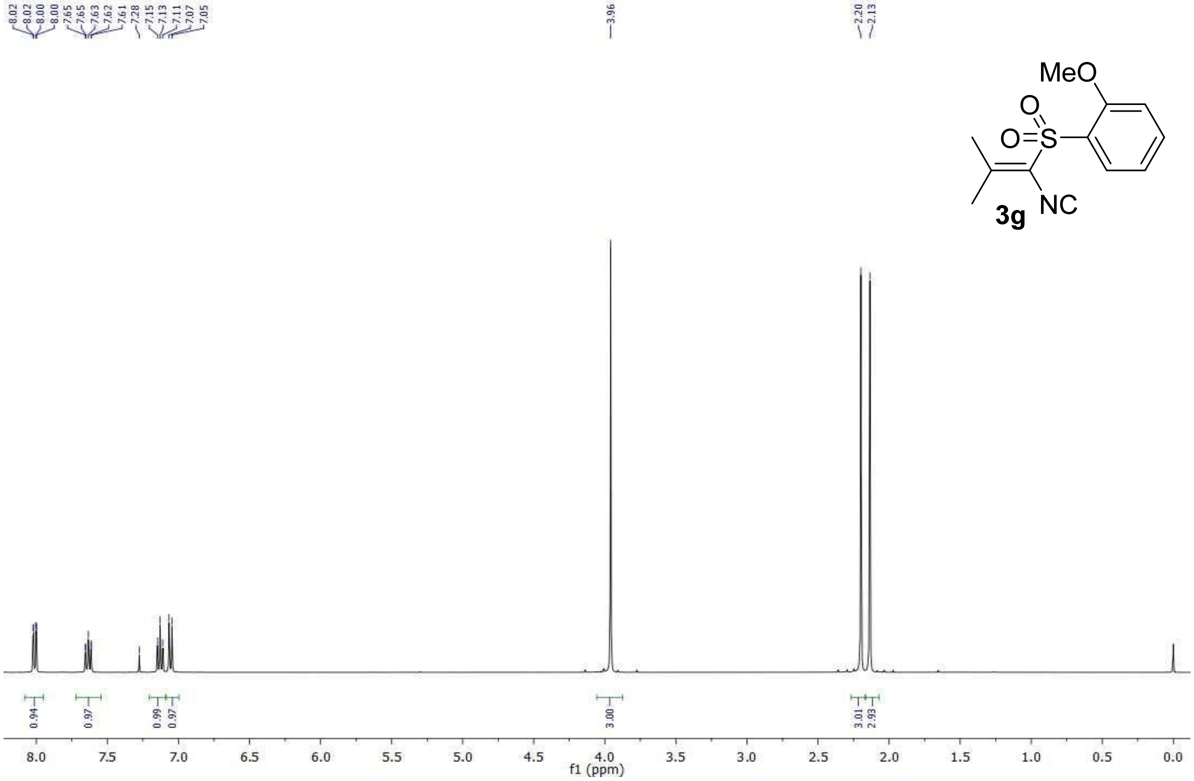
^{13}C NMR (101 MHz, $CDCl_3$) of isocyanide **iii**.



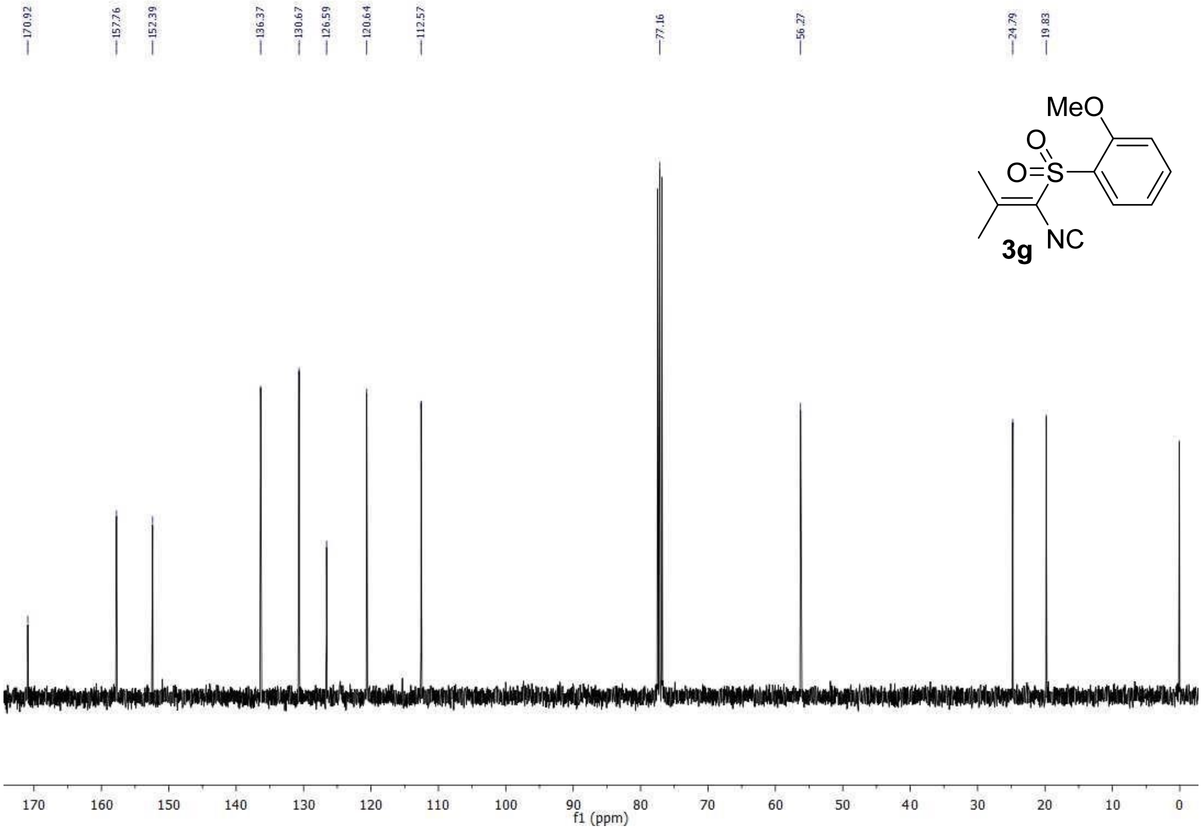
^{1}H NMR (400 MHz, CDCl$_3$) of formamide **iv**.



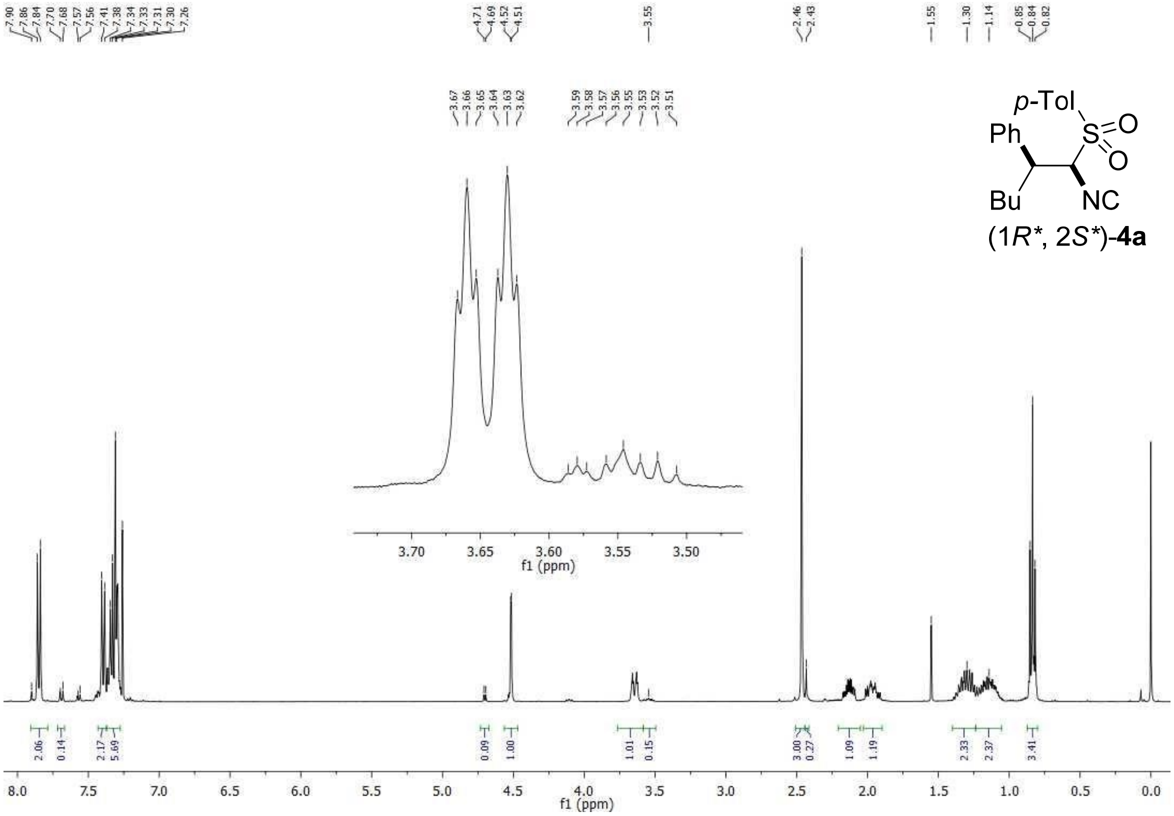
^{13}C NMR (101 MHz, CDCl$_3$) of formamide **iv**.



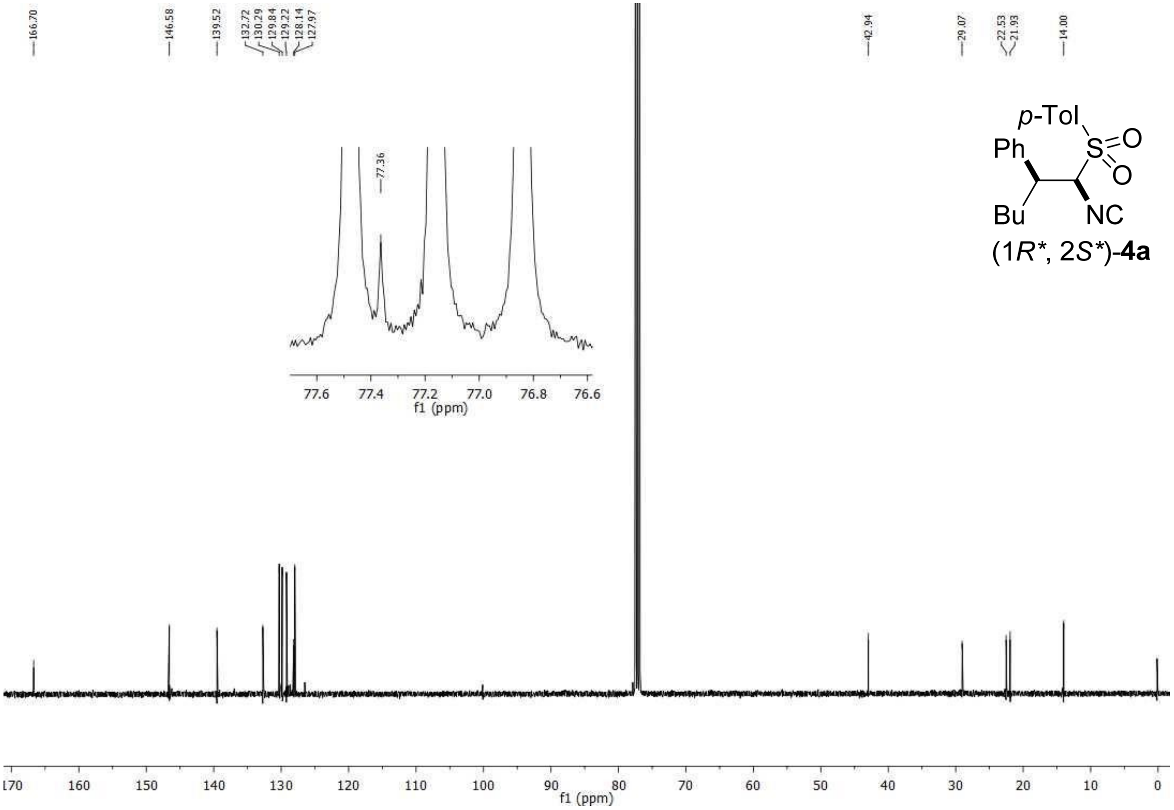
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **3g**.



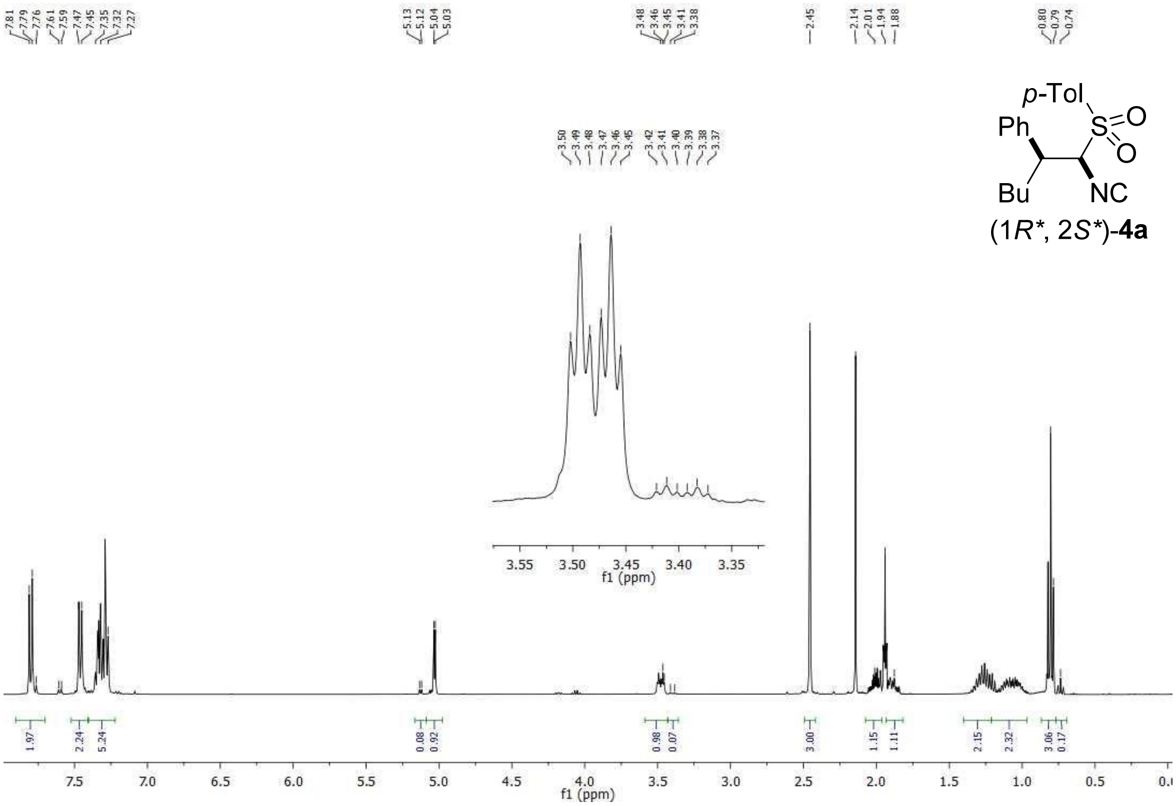
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **3g**.



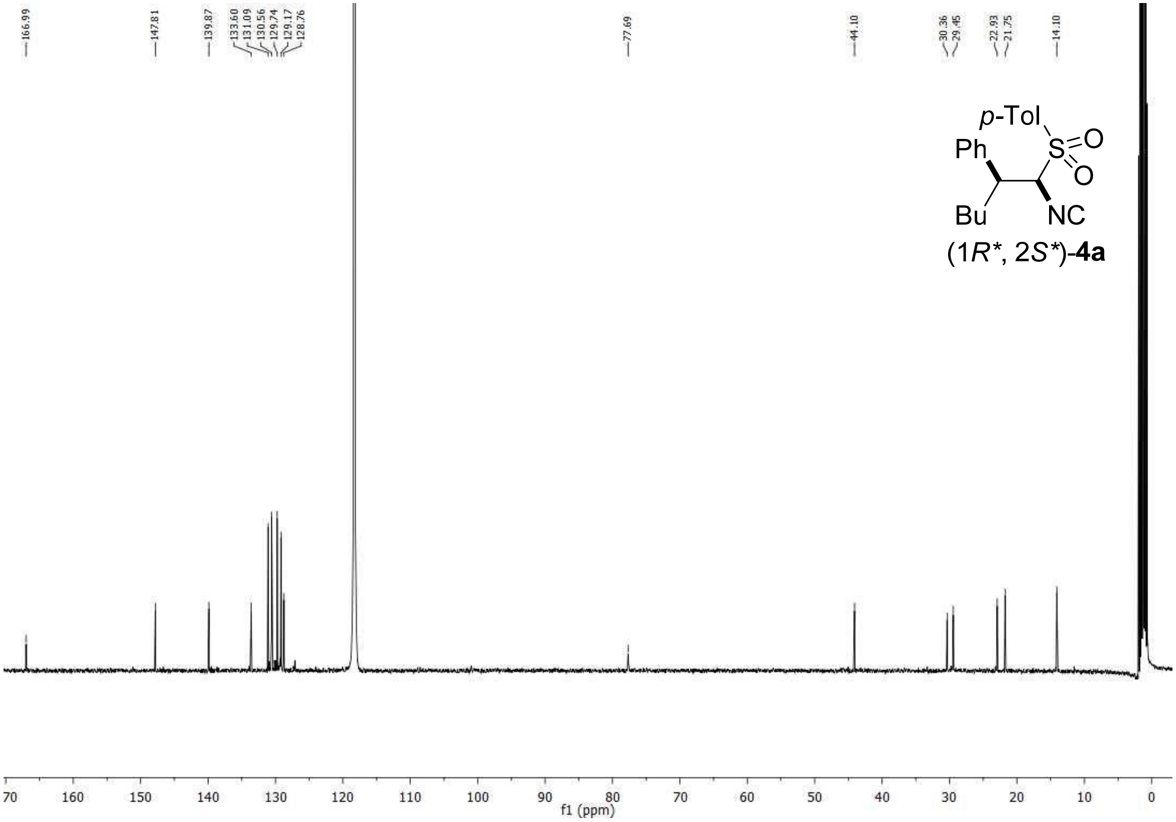
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**4a**.



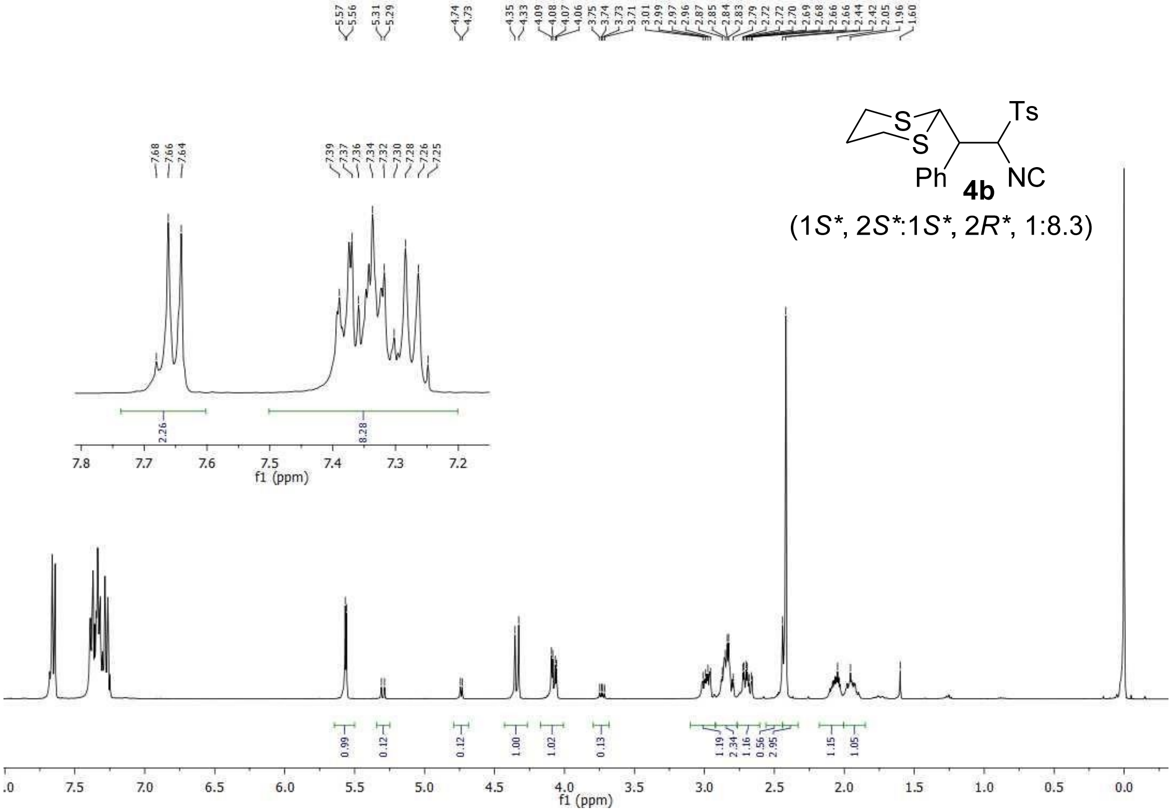
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**4a**.



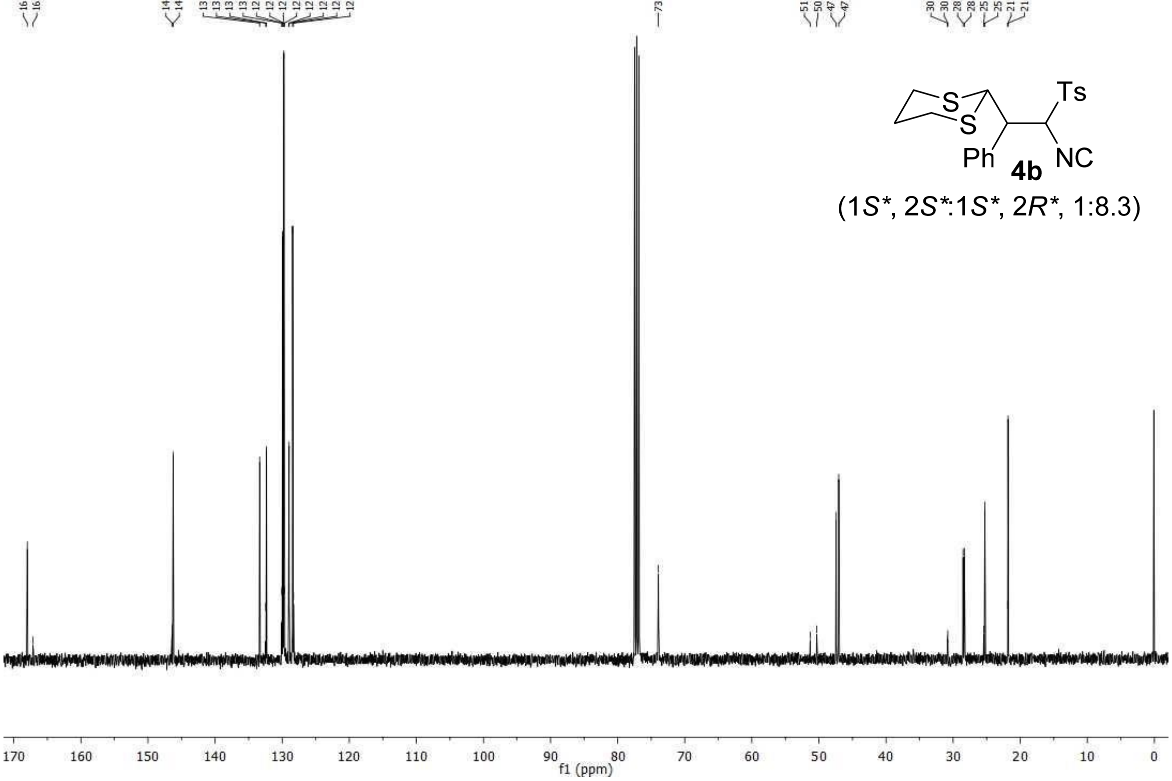
^{1}H NMR (400 MHz, CD$_3$CN) of isocyanide (1*R**, 2*S**)-**4a**.



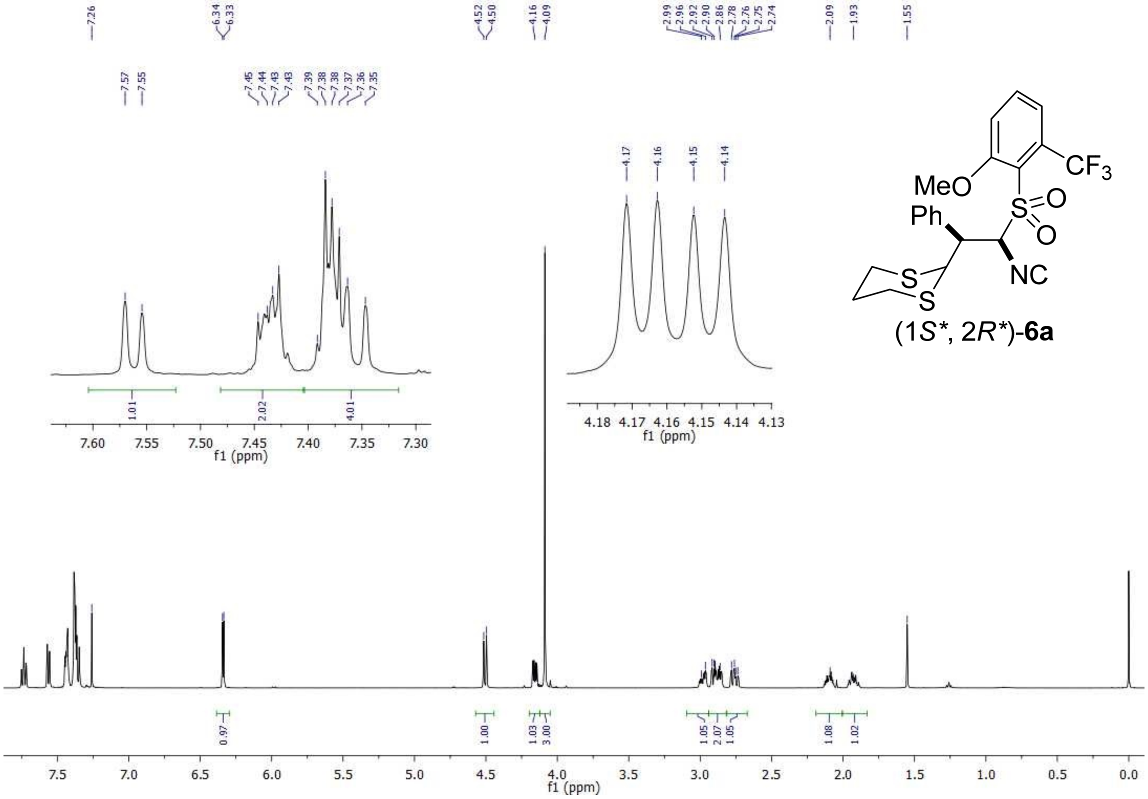
^{13}C NMR (101 MHz, CD$_3$CN) of isocyanide (1*R**, 2*S**)-**4a**.



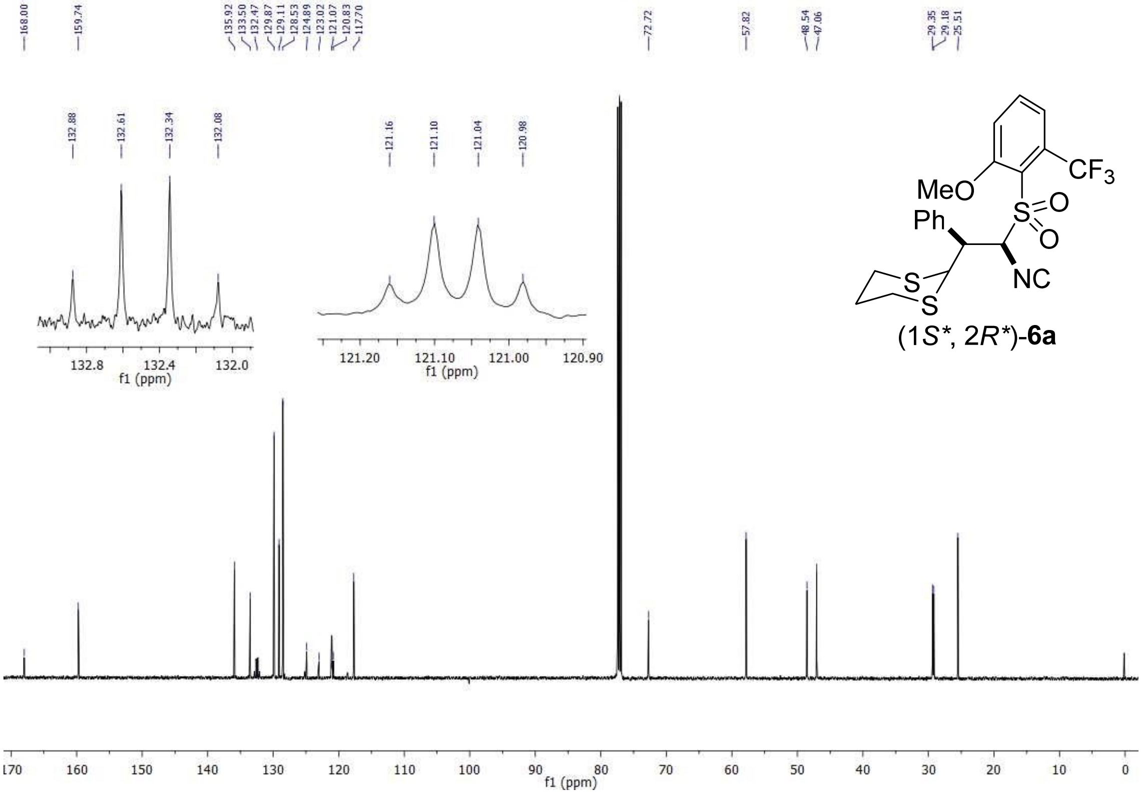
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **4b**.



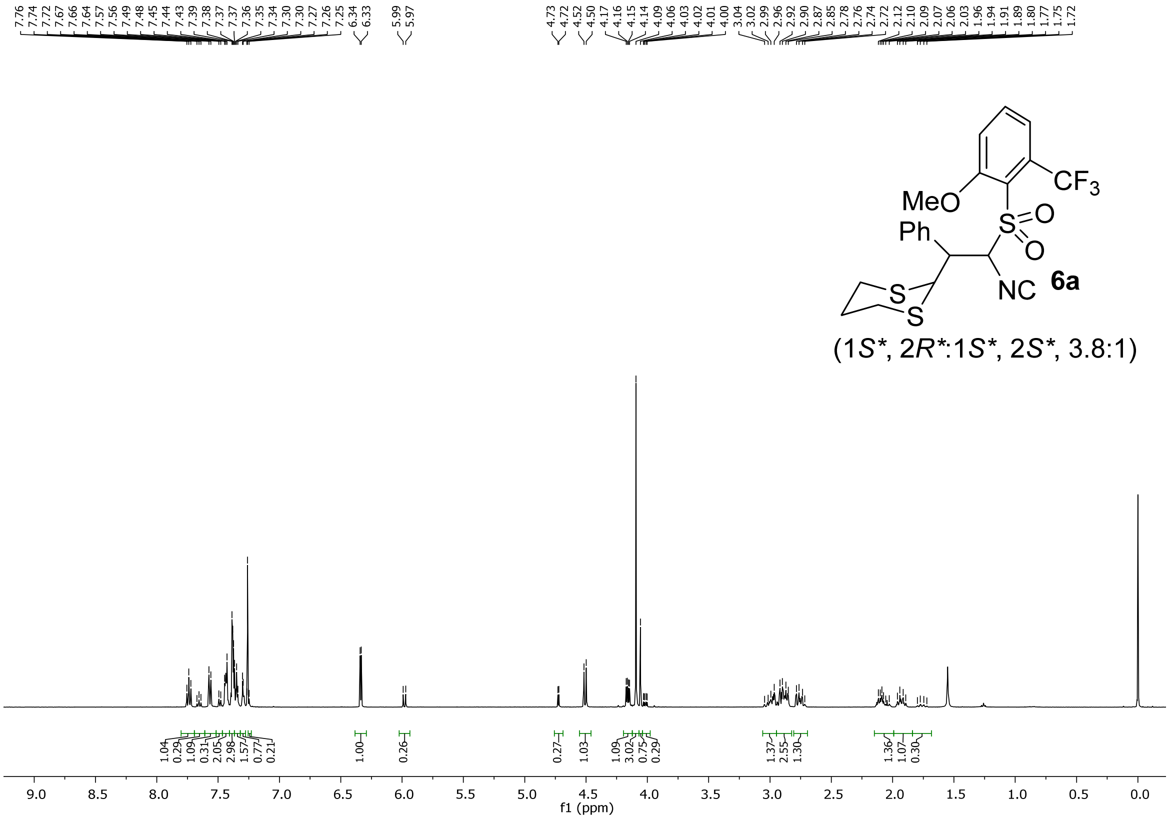
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **4b**.



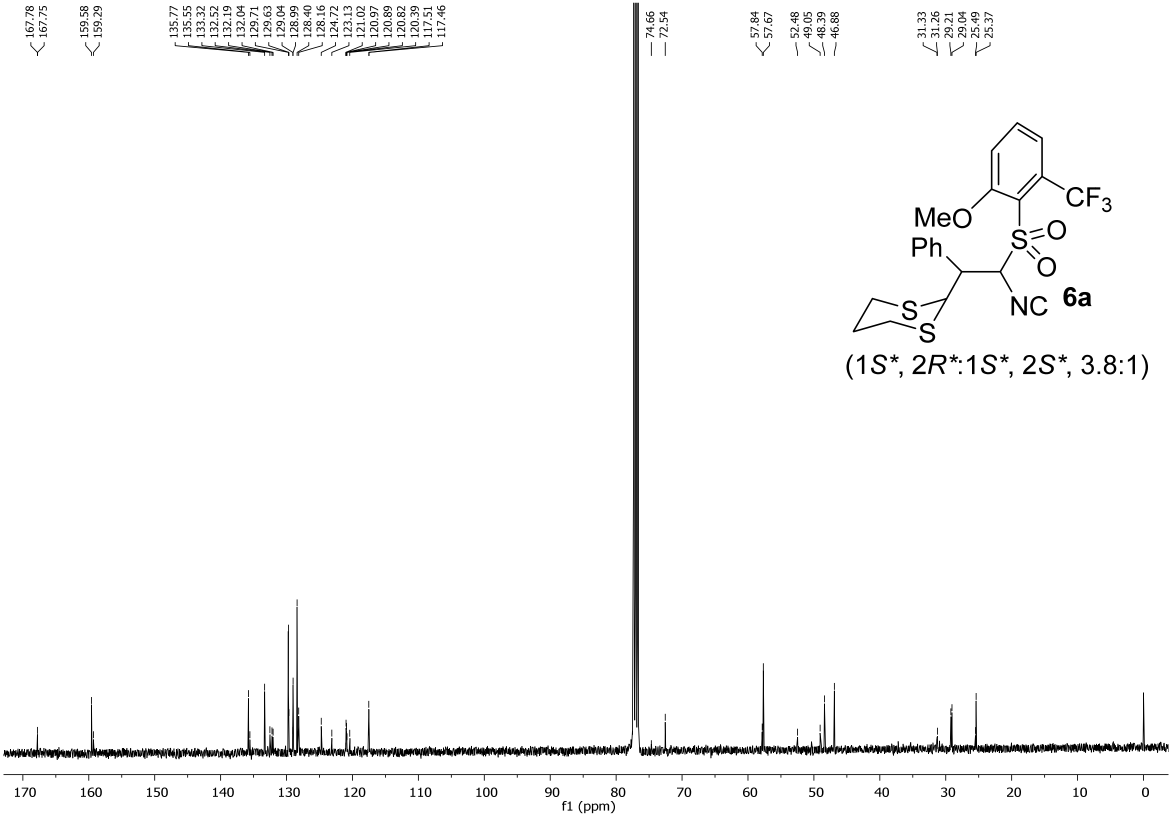
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*S**, 2*R**)-**6a**.



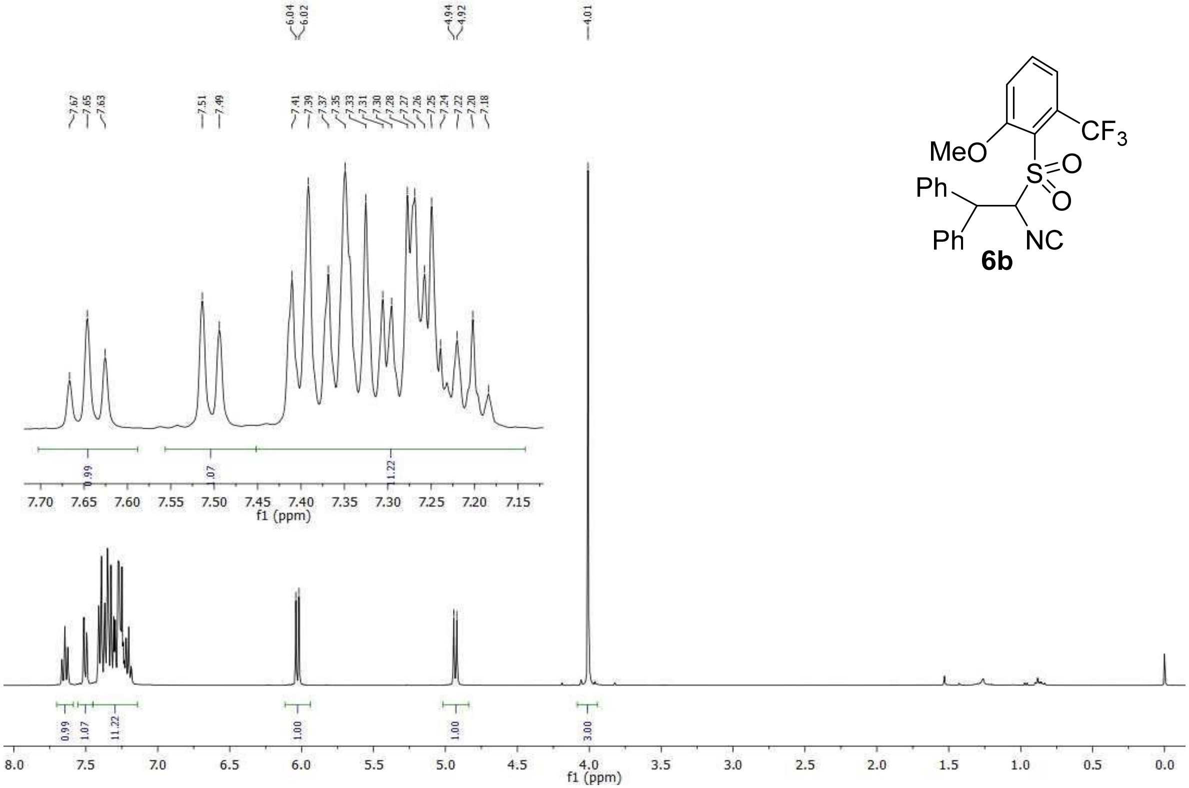
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide (1*S**, 2*R**)-**6a**.



^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide **6a**.

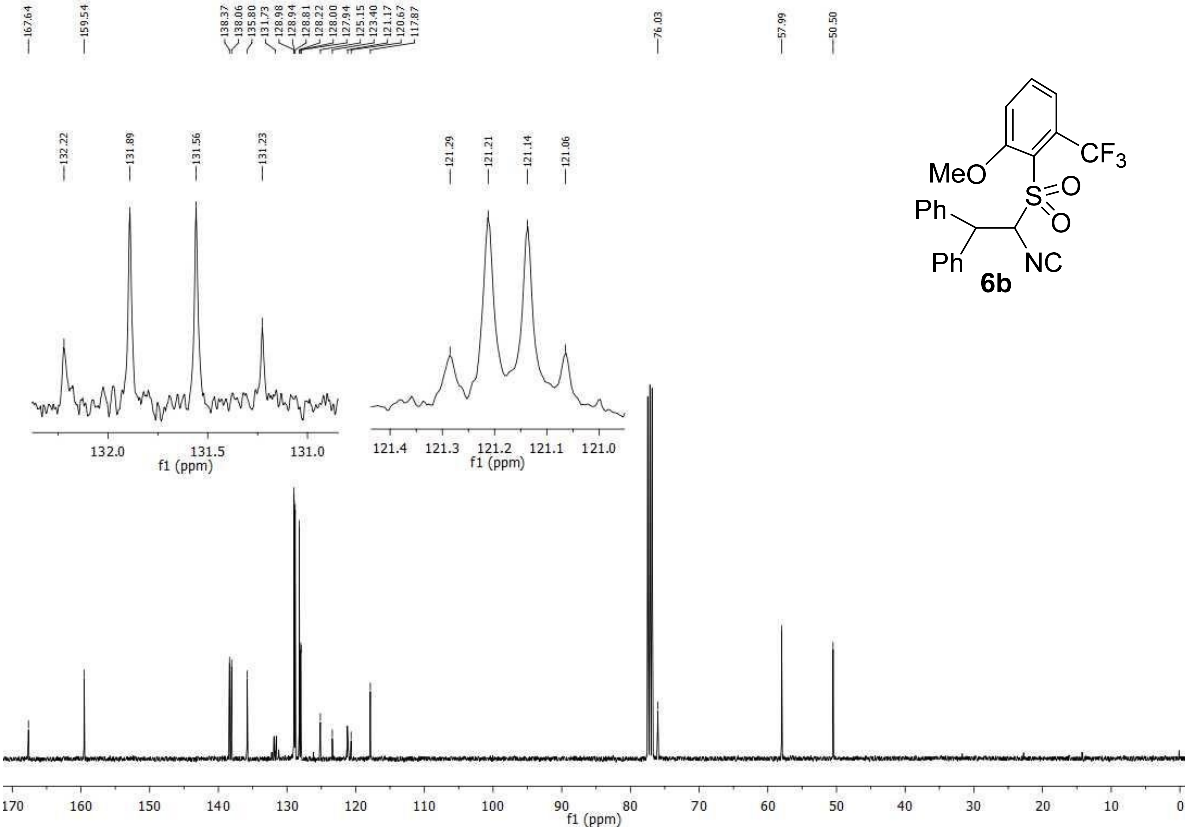


^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **6a**.



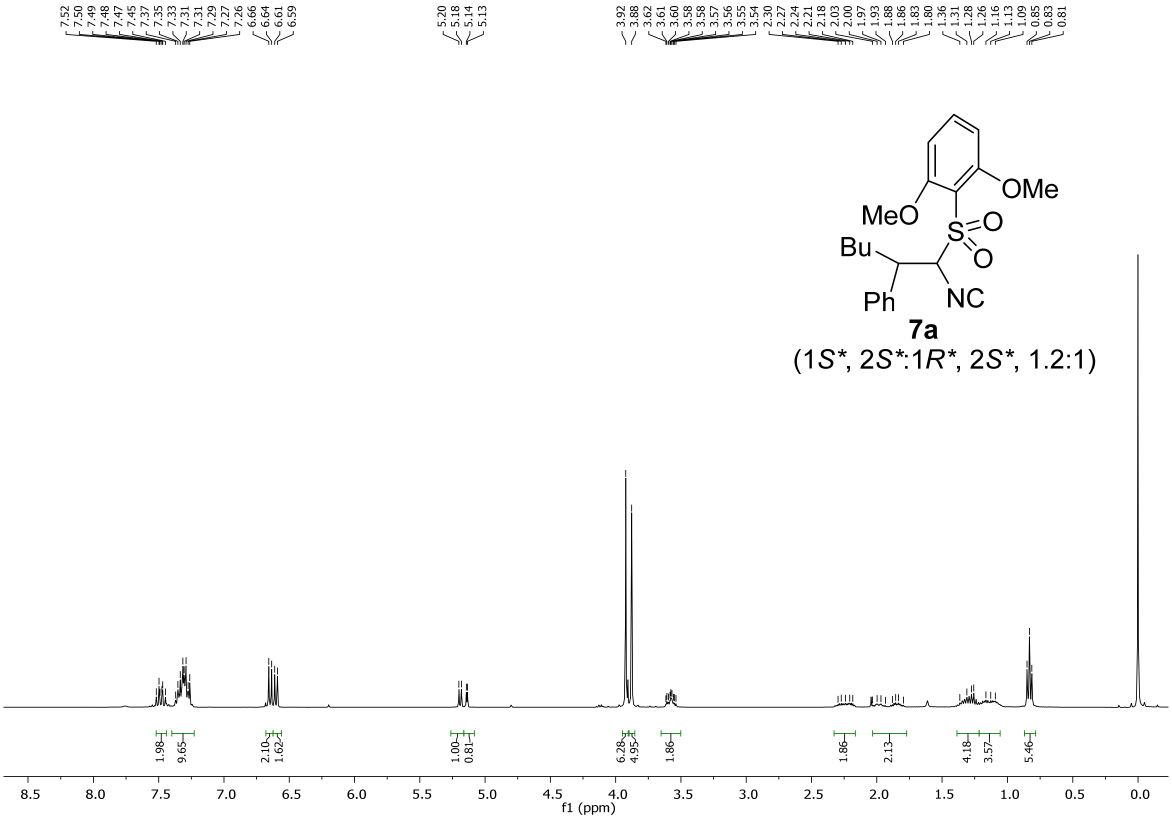
6b

^{1}H NMR (400 MHz, $CDCl_3$) of isocyanide **6b**.

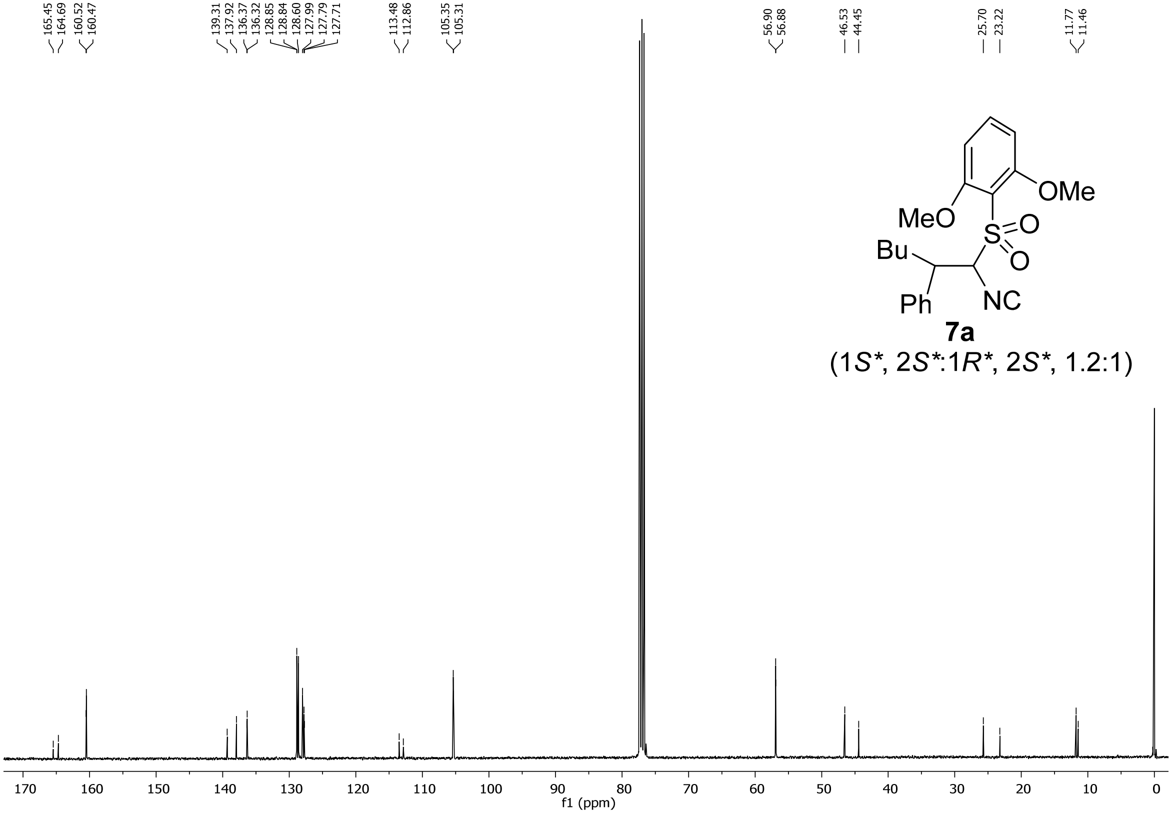


6b

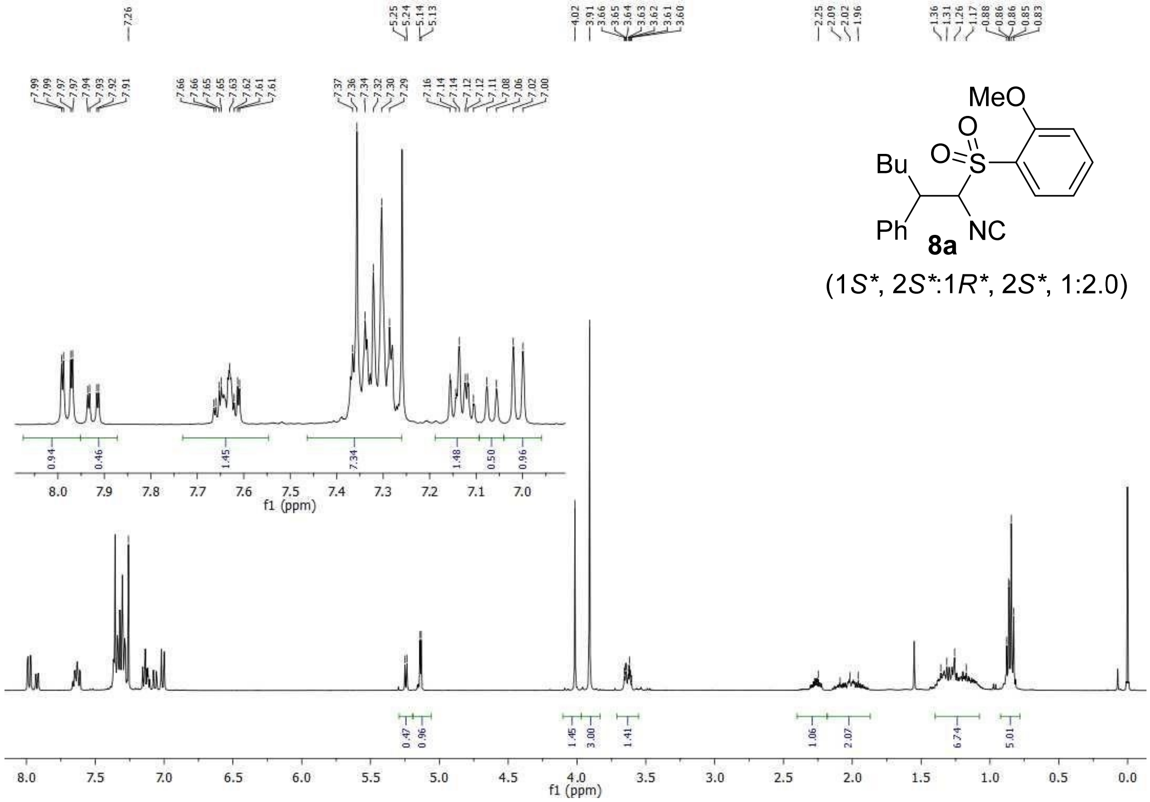
^{13}C NMR (101 MHz, $CDCl_3$) of isocyanide **6b**.



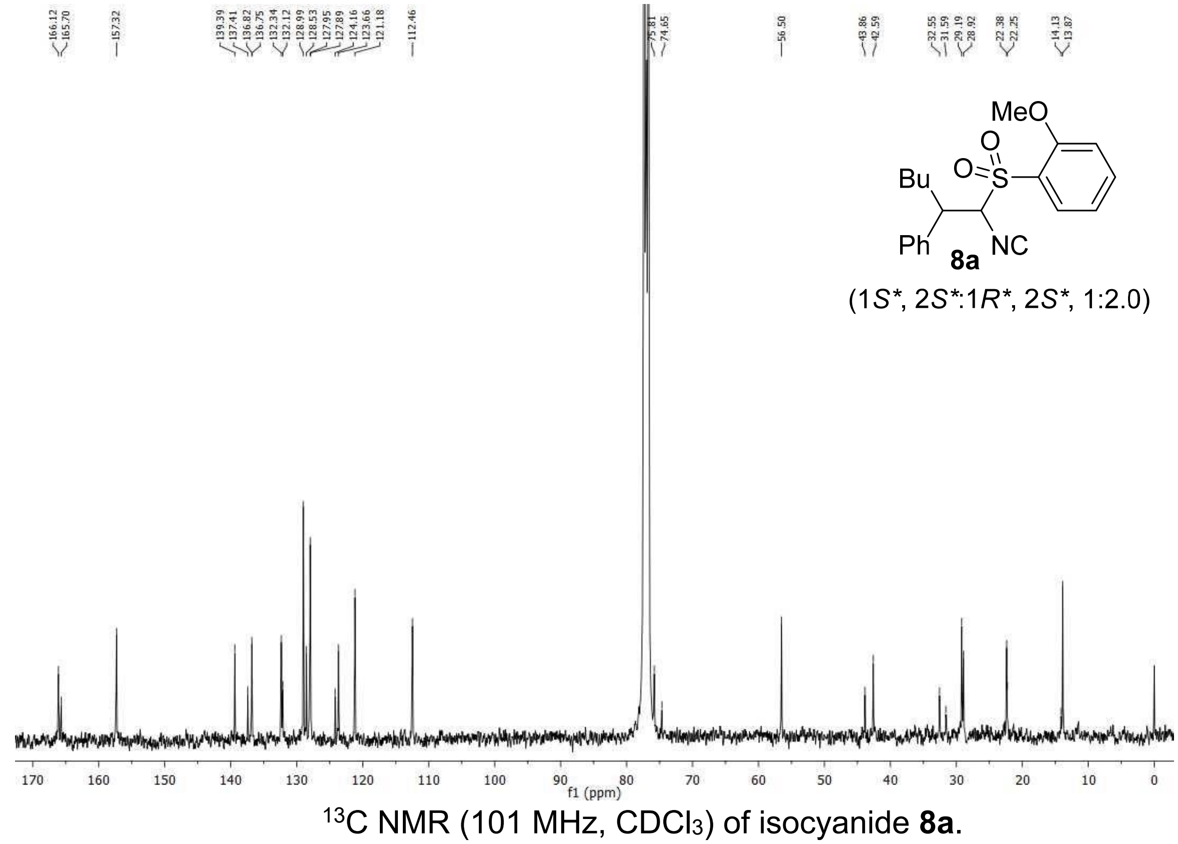
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **7a**.



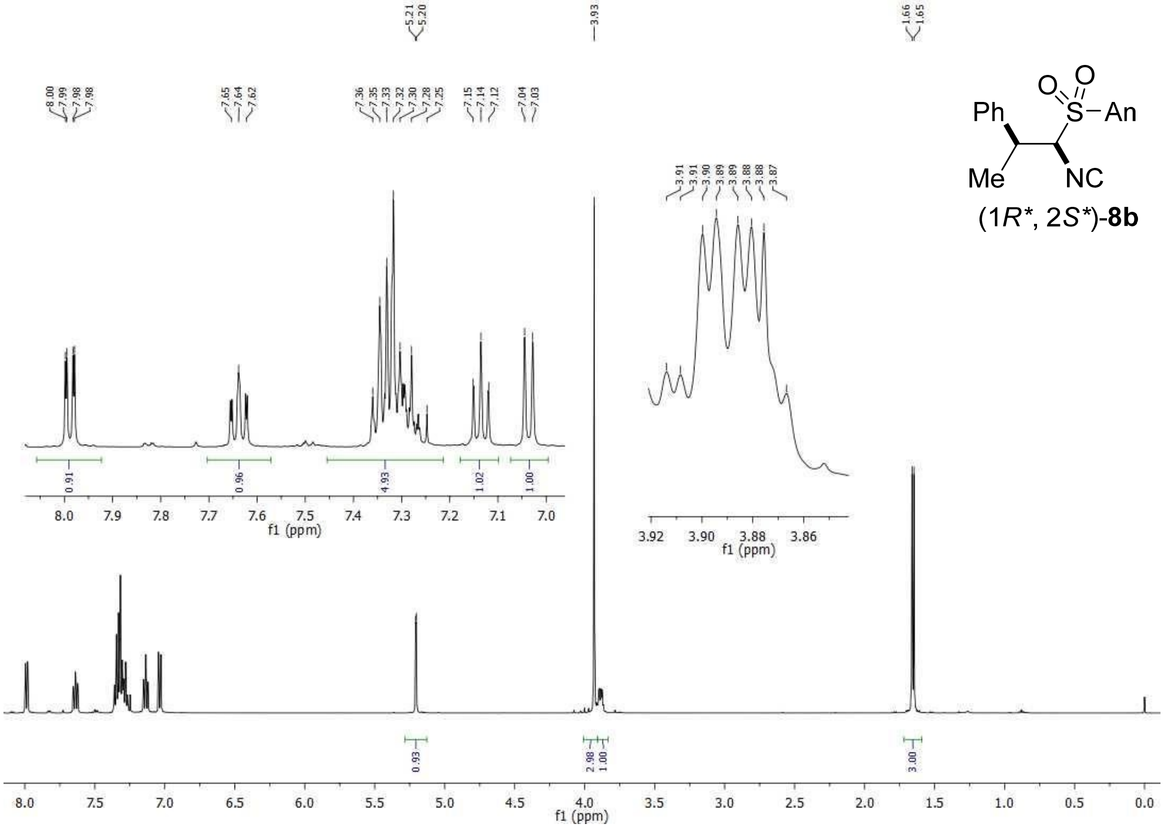
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **7a**.



^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8a**.

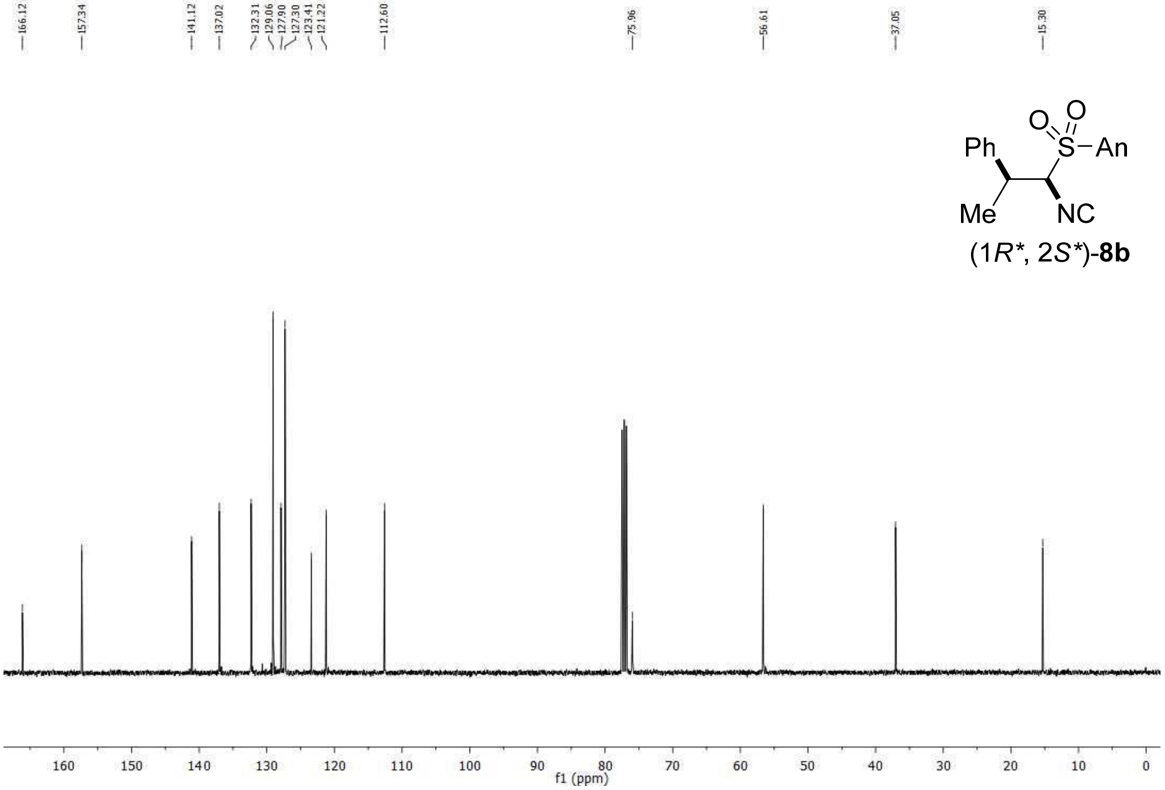


^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8a**.



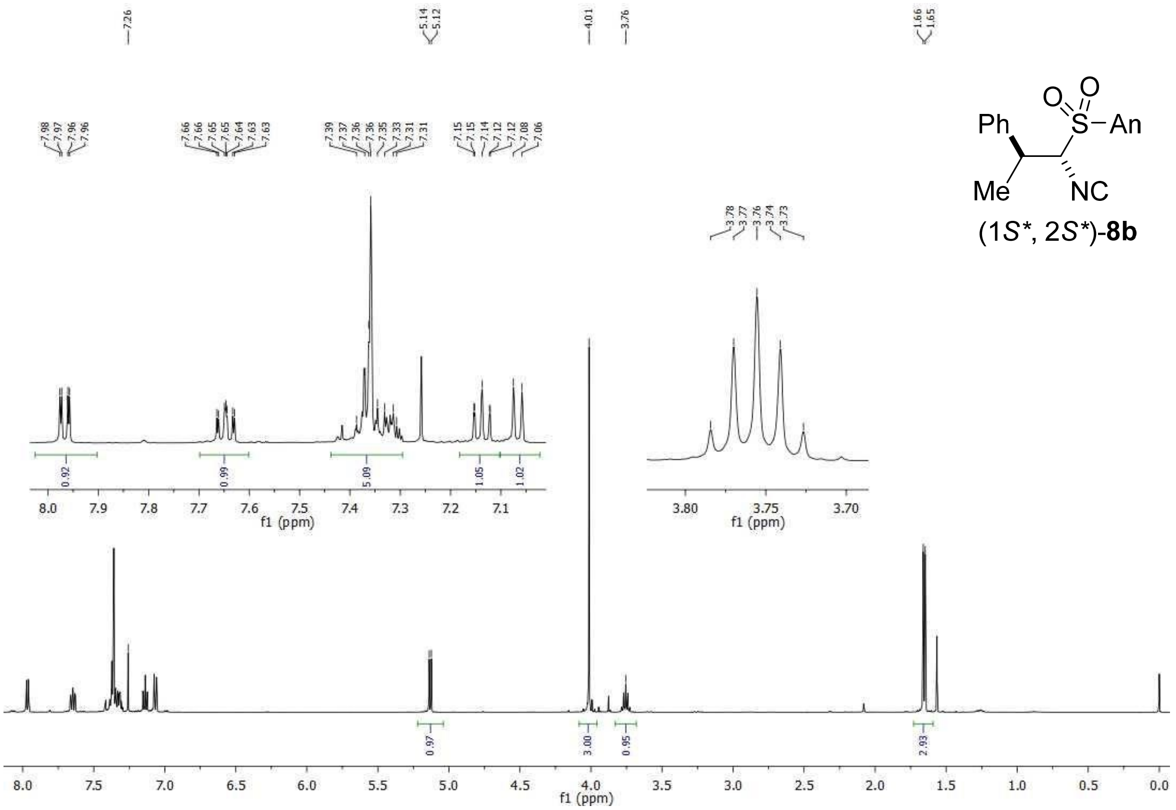
(1*R**, 2*S**)-**8b**

^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**8b**.



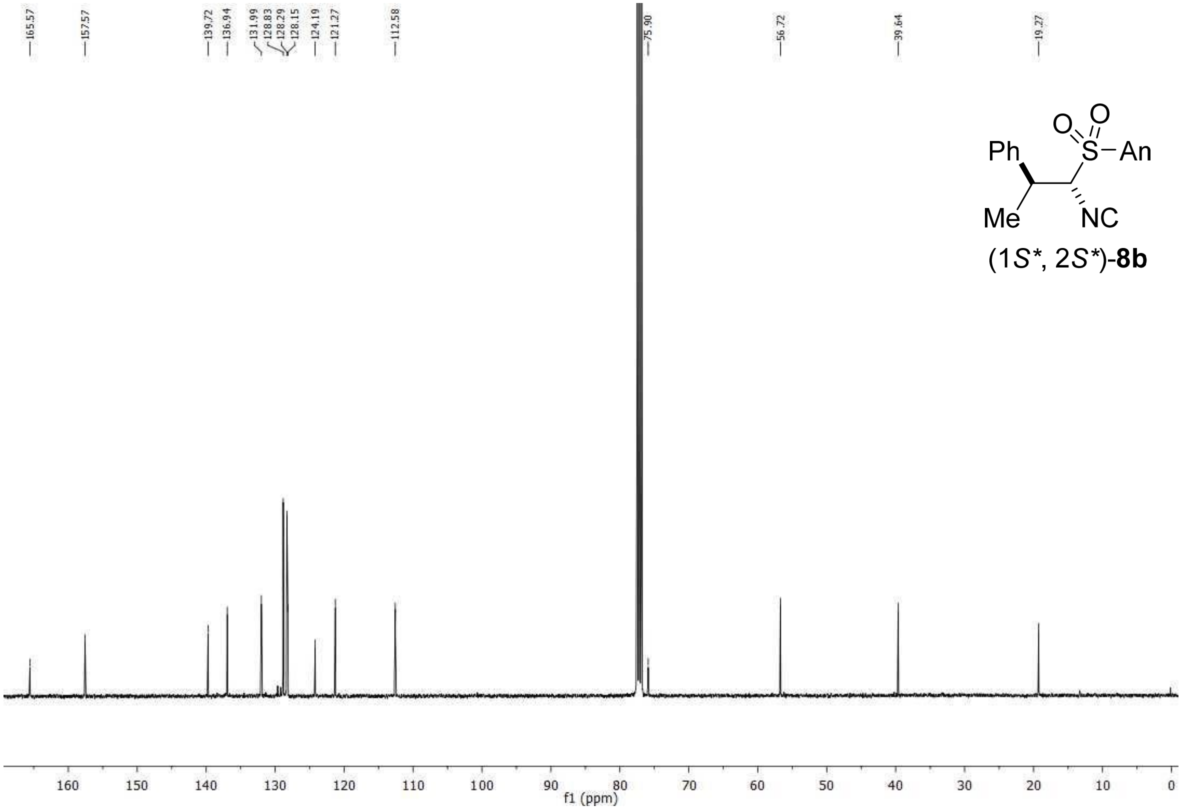
(1*R**, 2*S**)-**8b**

^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**8b**.



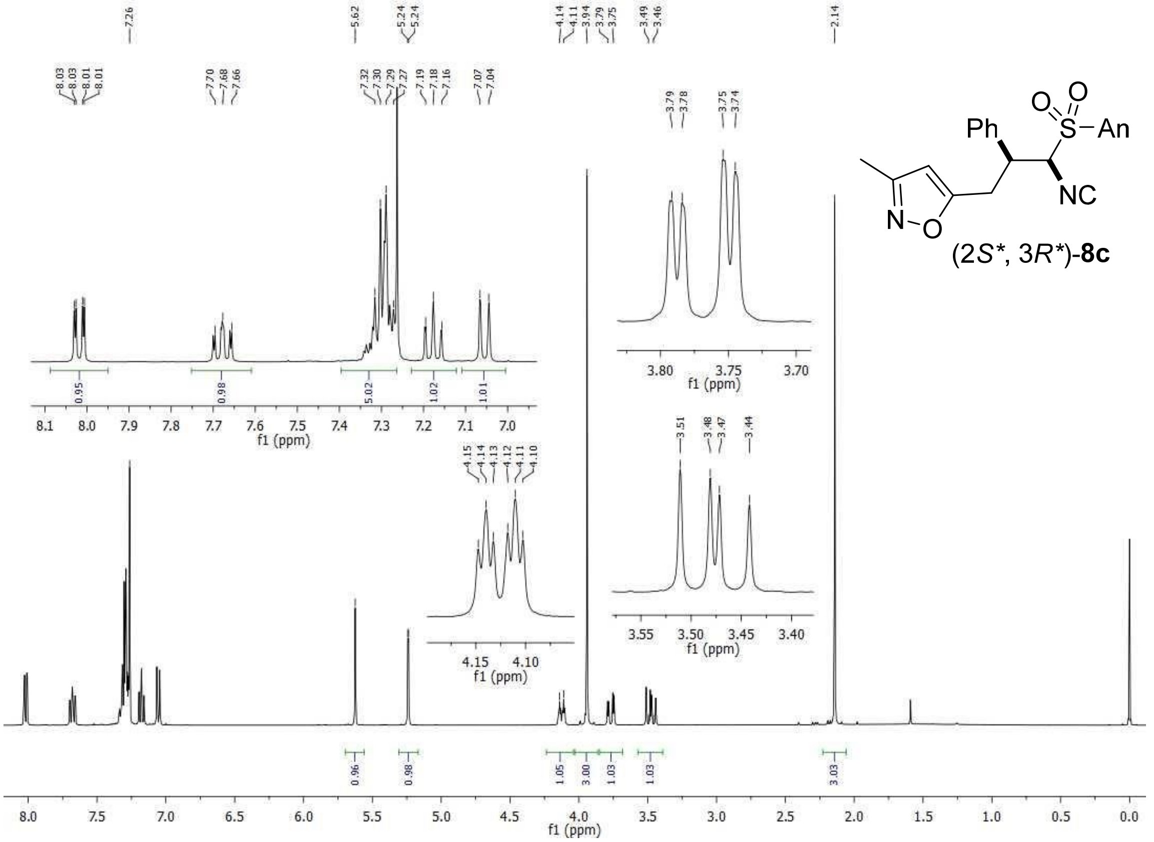
(1*S**, 2*S**)-**8b**

^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*S**, 2*S**)-**8b**.

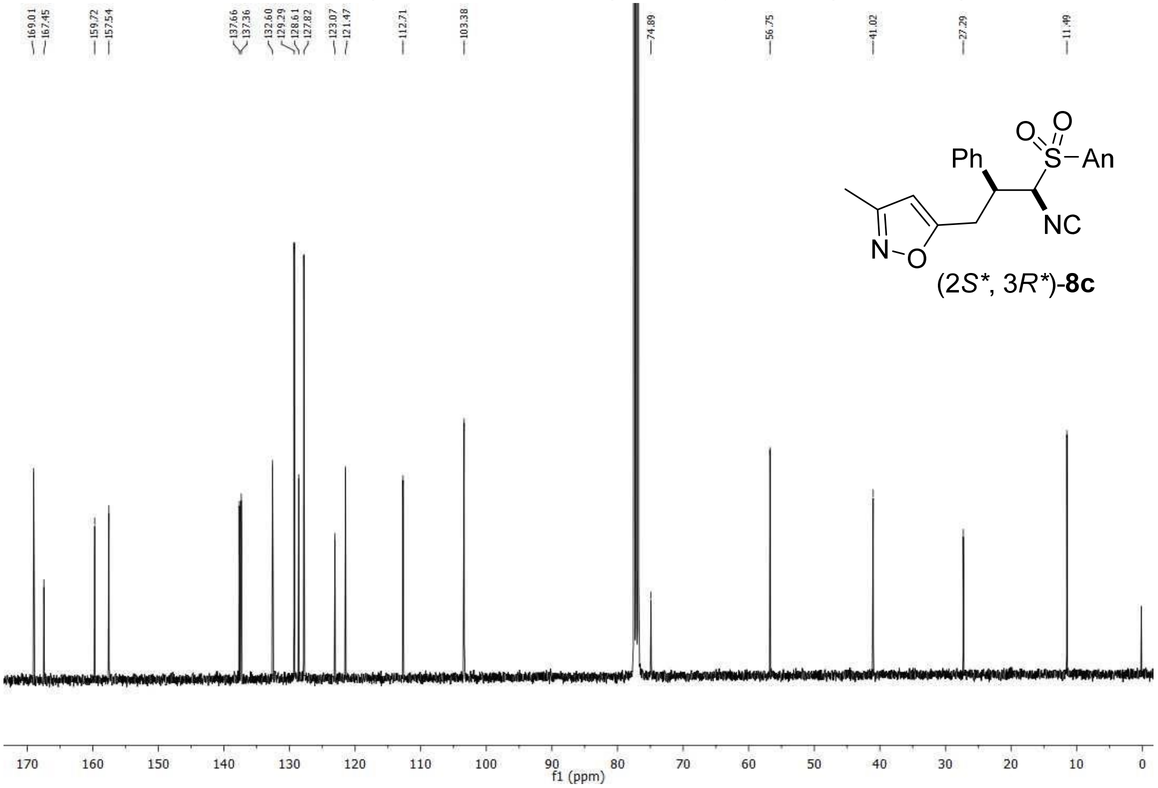


(1*S**, 2*S**)-**8b**

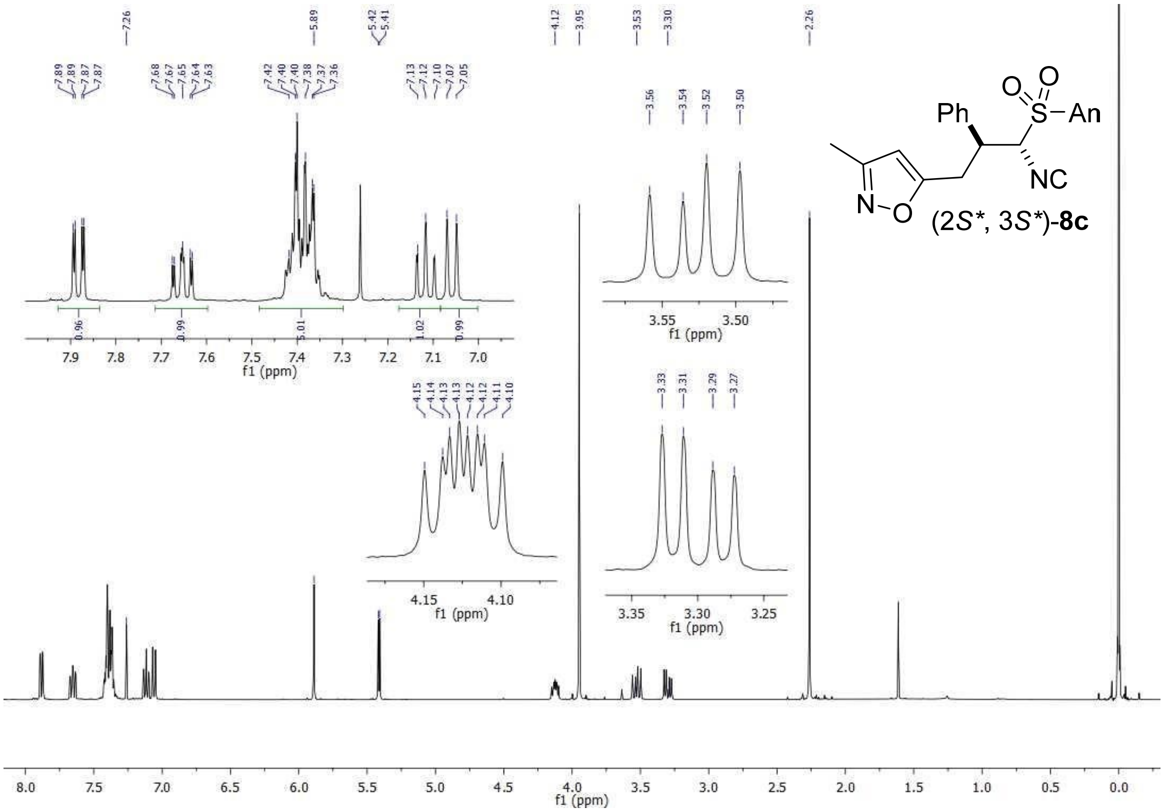
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (1*S**, 2*S**)-**8b**.



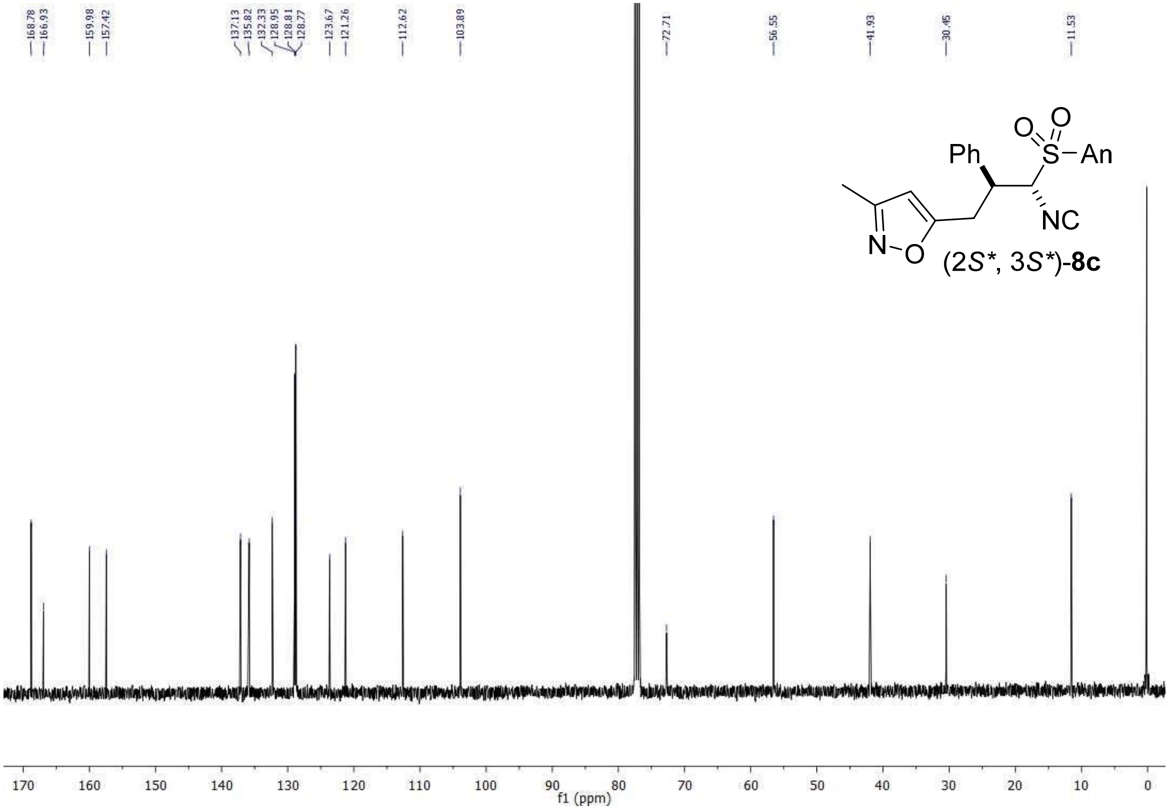
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (2*S**, 3*R**)-**8c**.



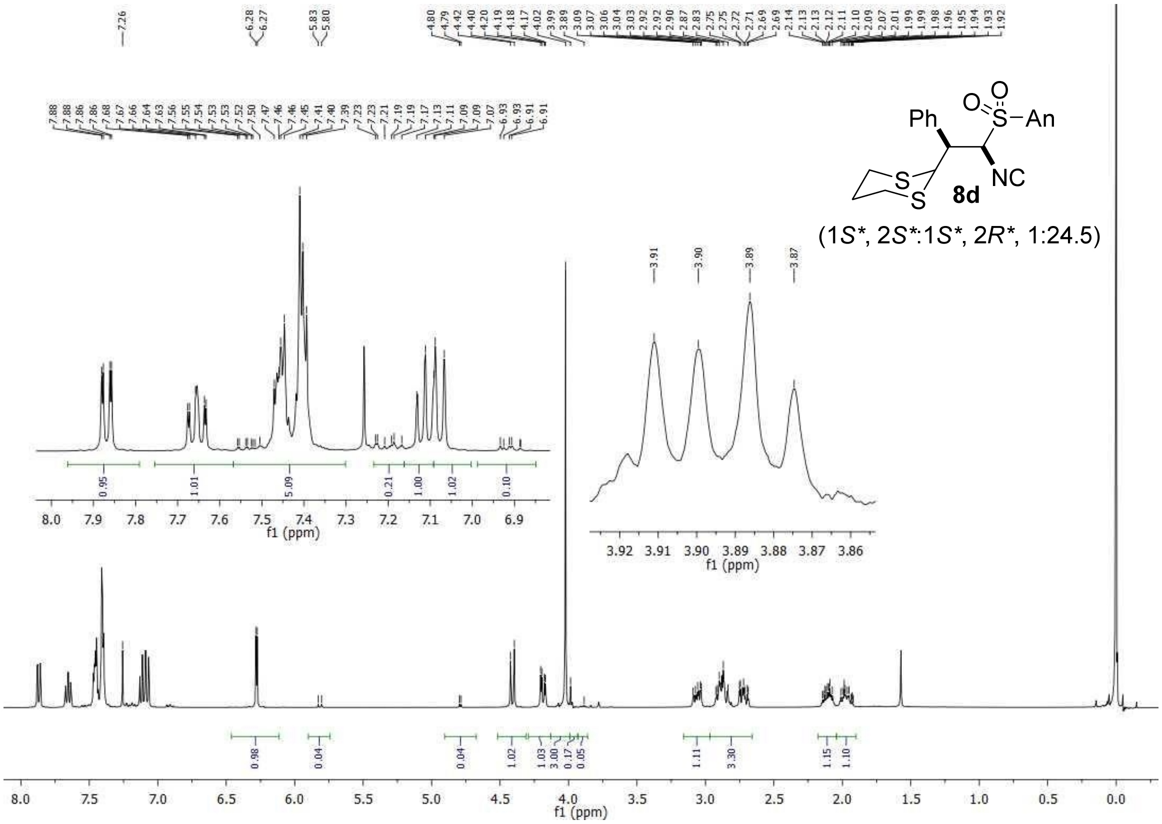
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (2*S**, 3*R**)-**8c**.



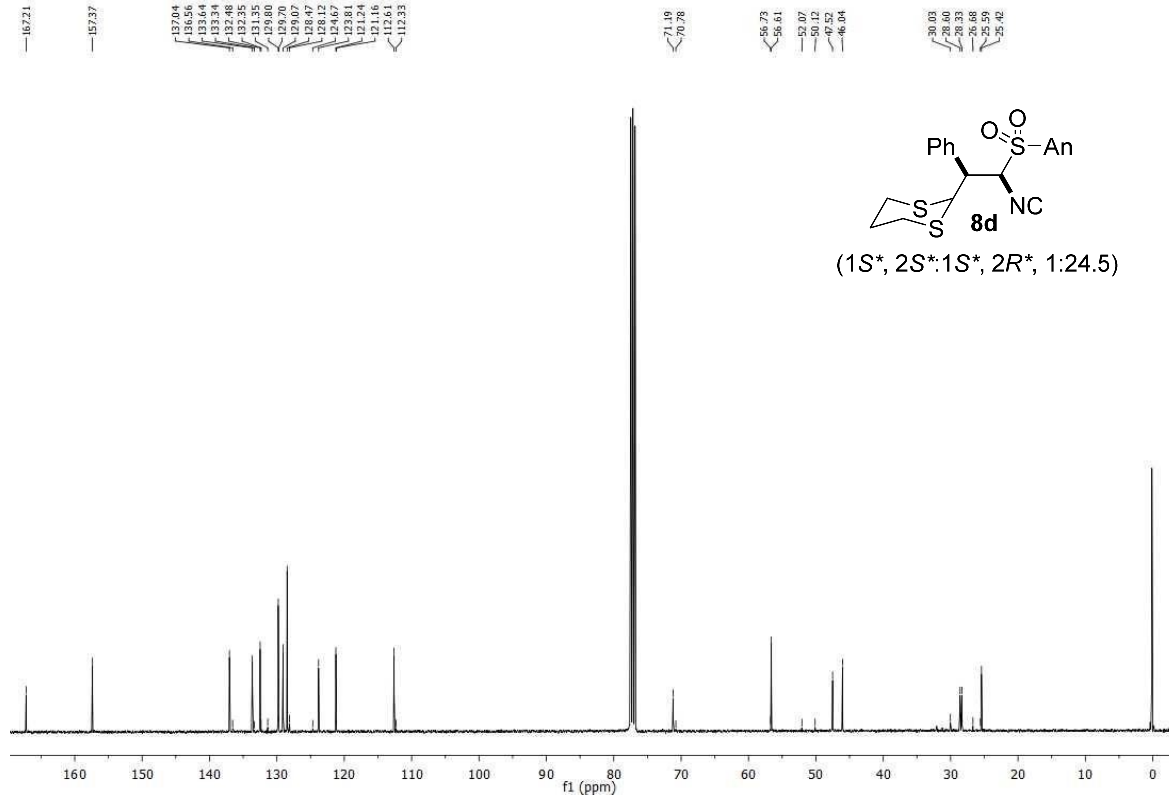
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (2*S**, 3*S**)-**8c**.



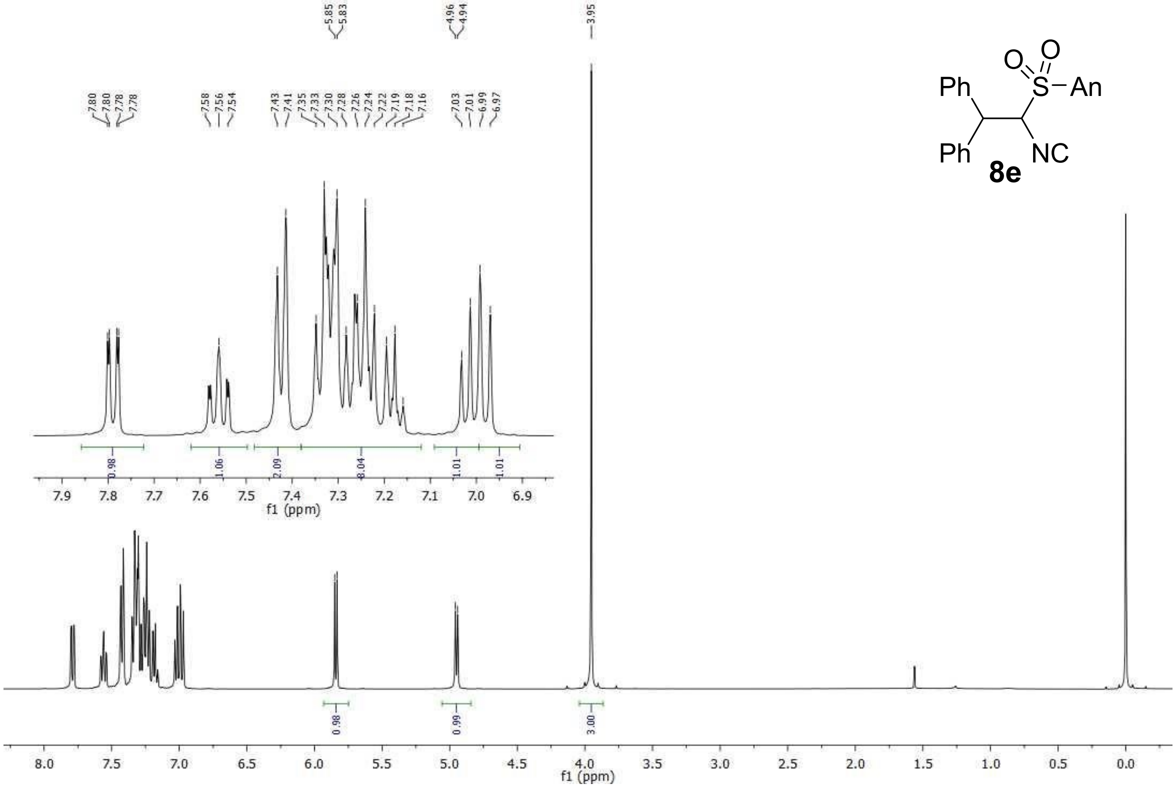
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (2*S**, 3*S**)-**8c**.



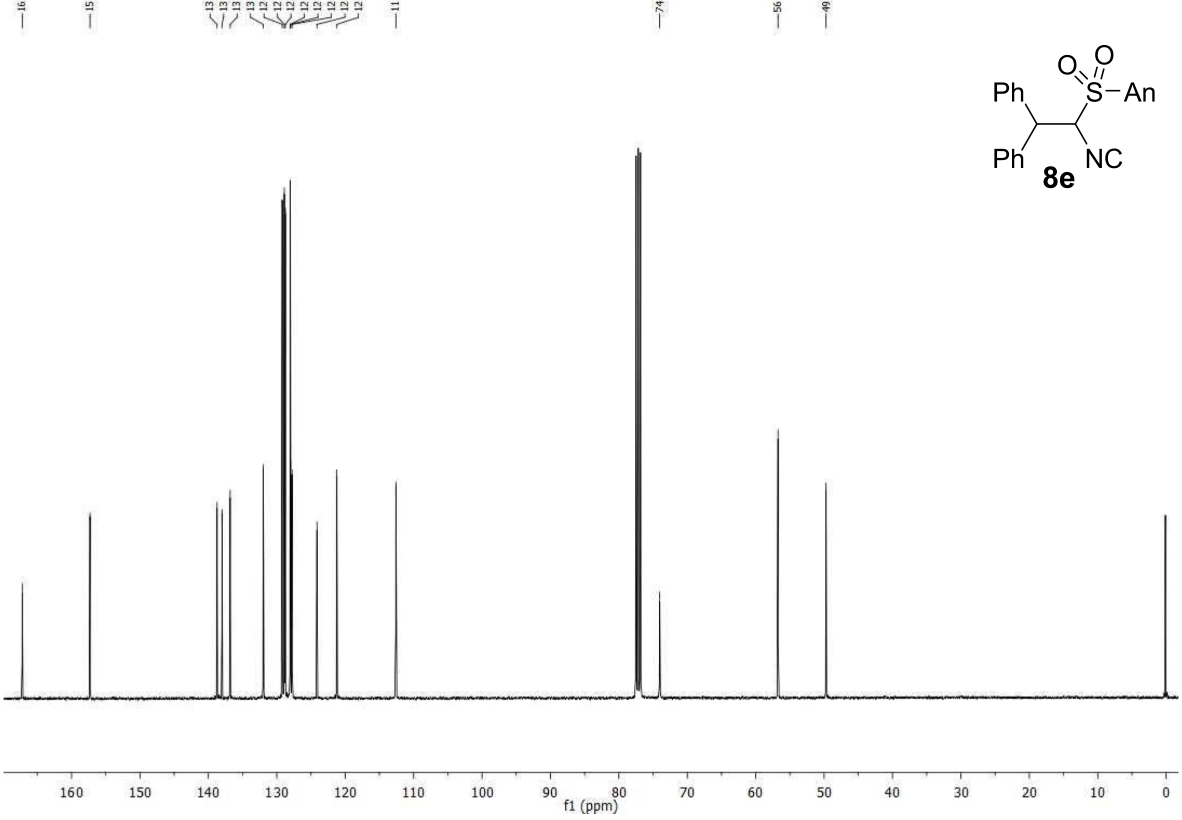
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8d**.



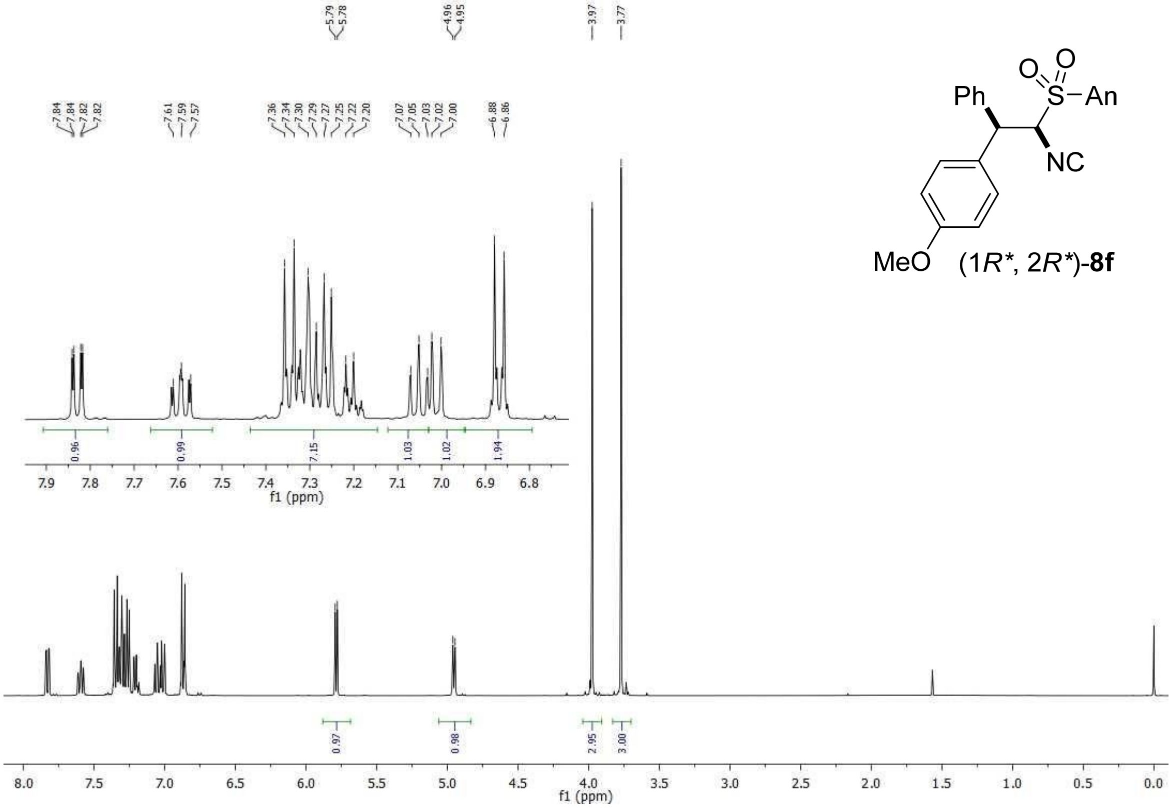
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8d**.



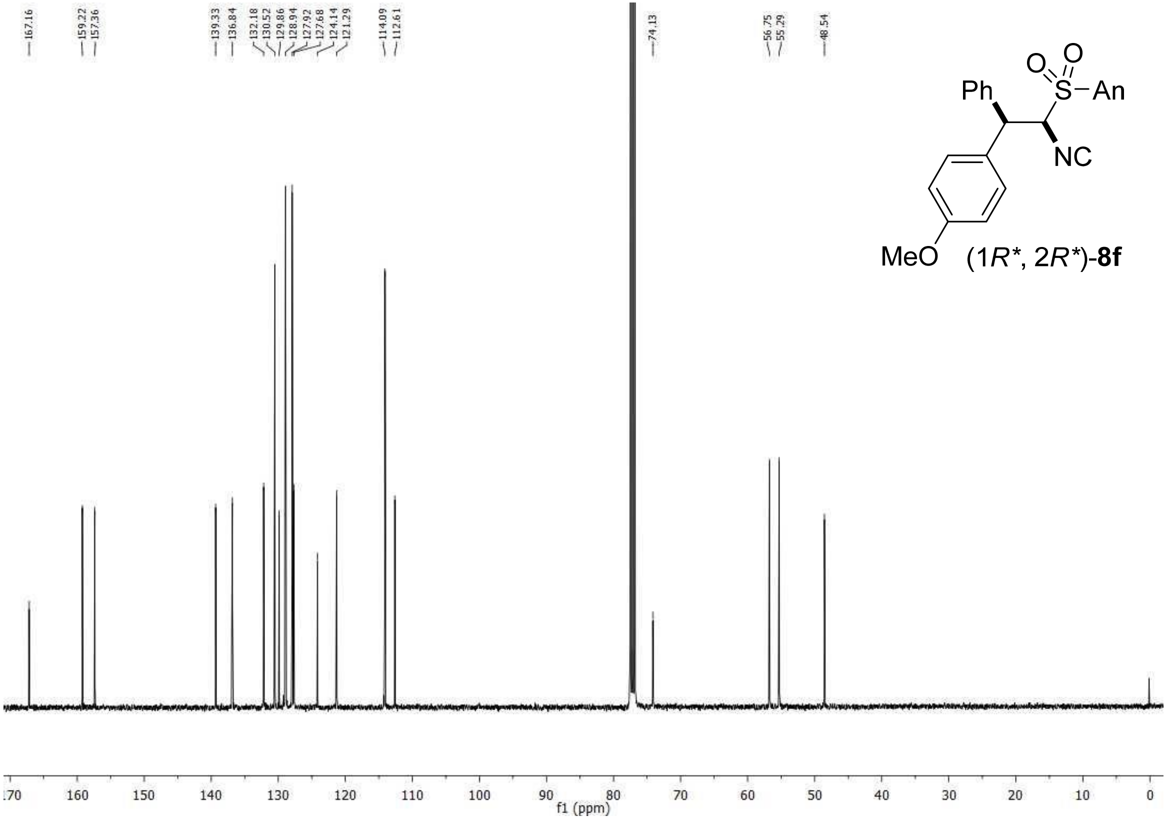
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8e**.



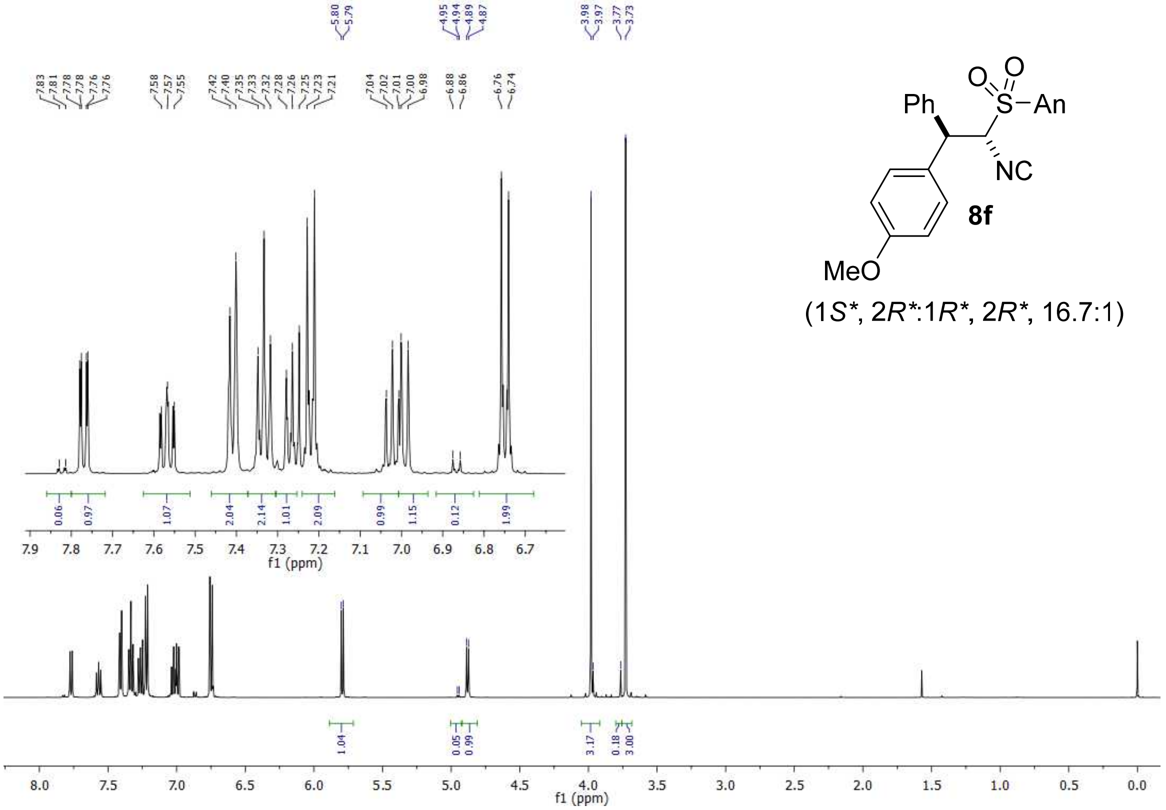
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8e**.



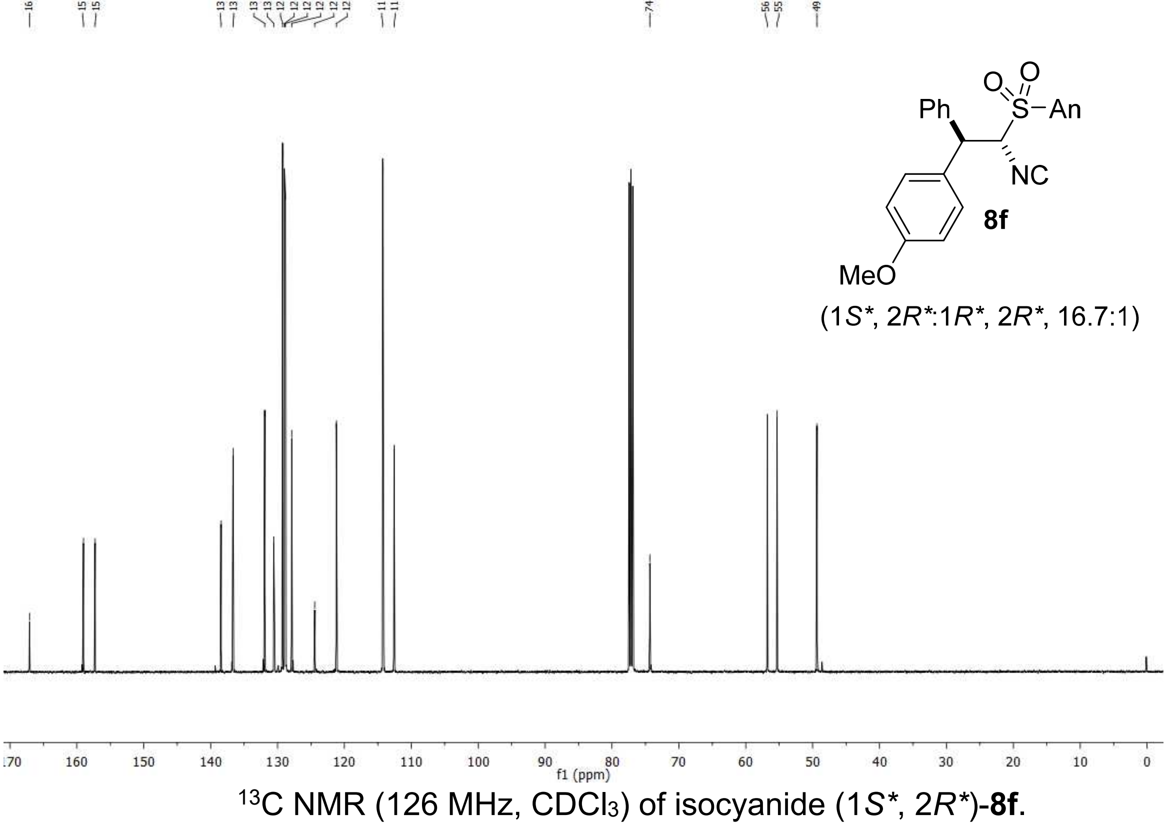
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (1*R**, 2*R**)-**8f**.



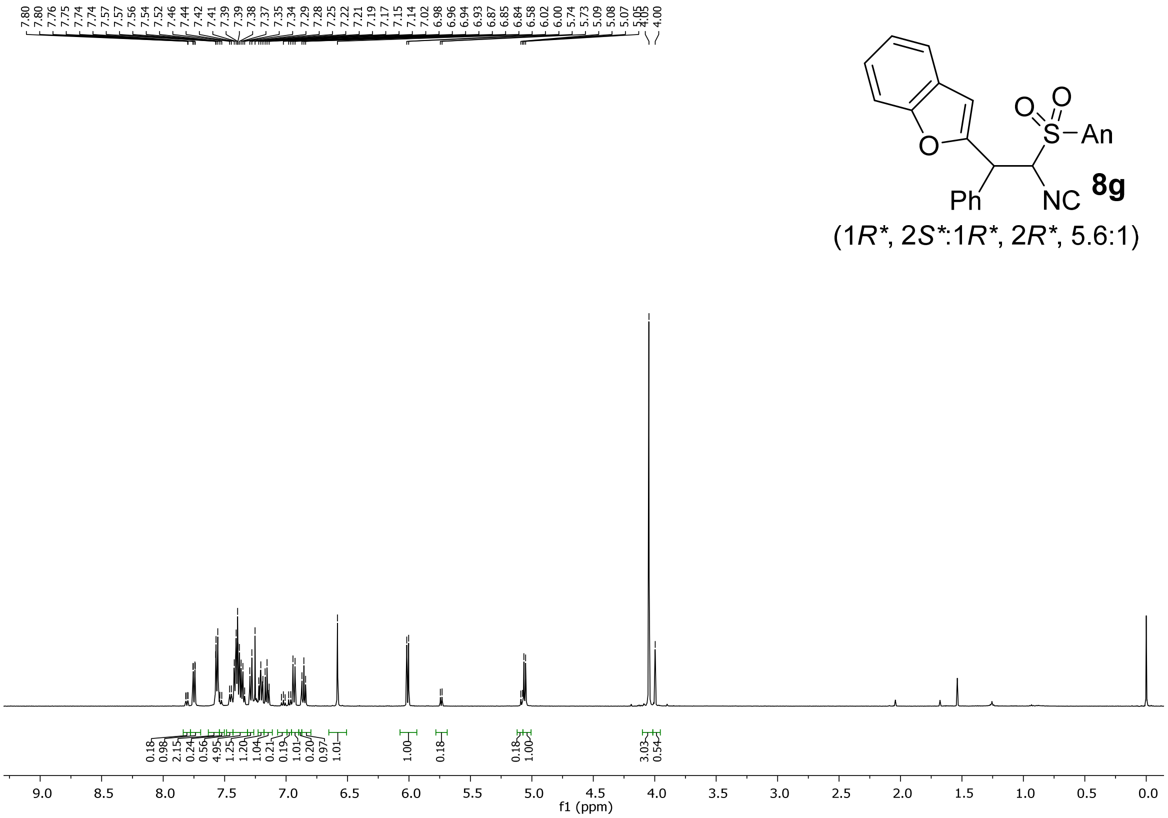
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (1*R**, 2*R**)-**8f**.



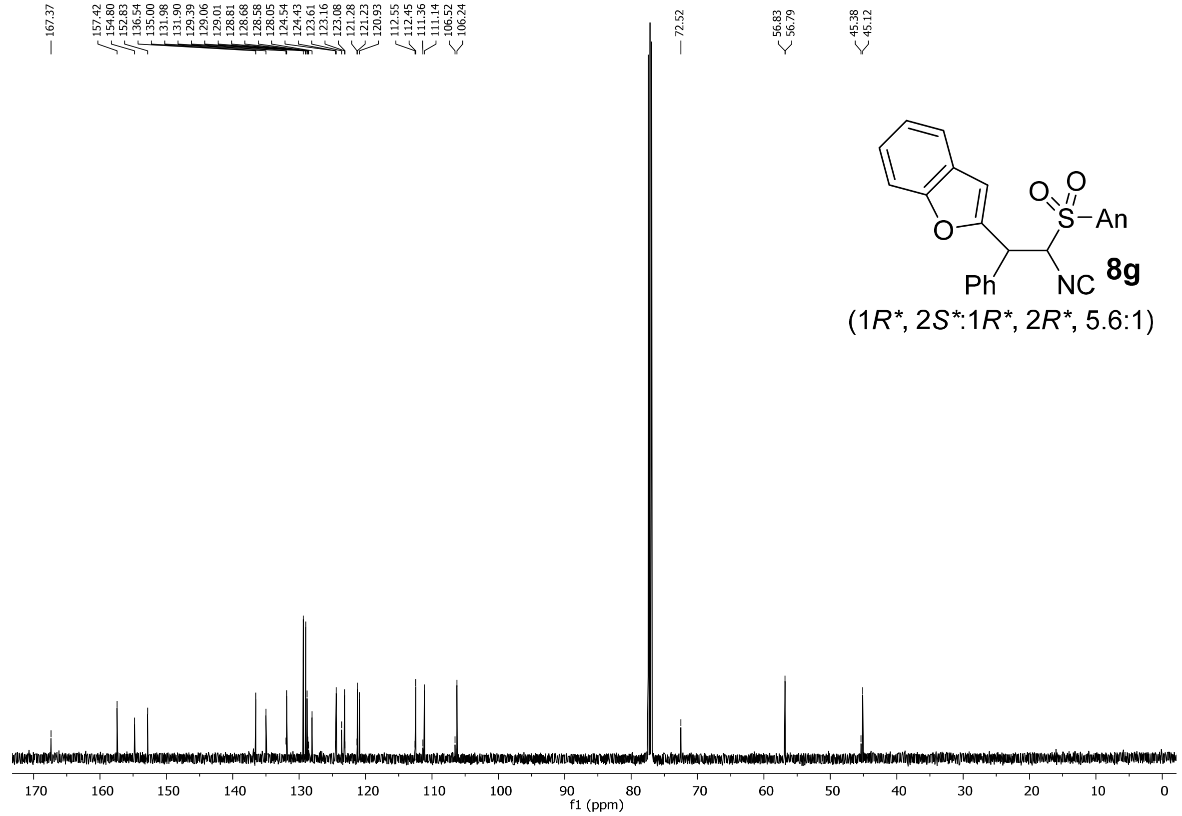
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*S**, 2*R**)-**8f**.



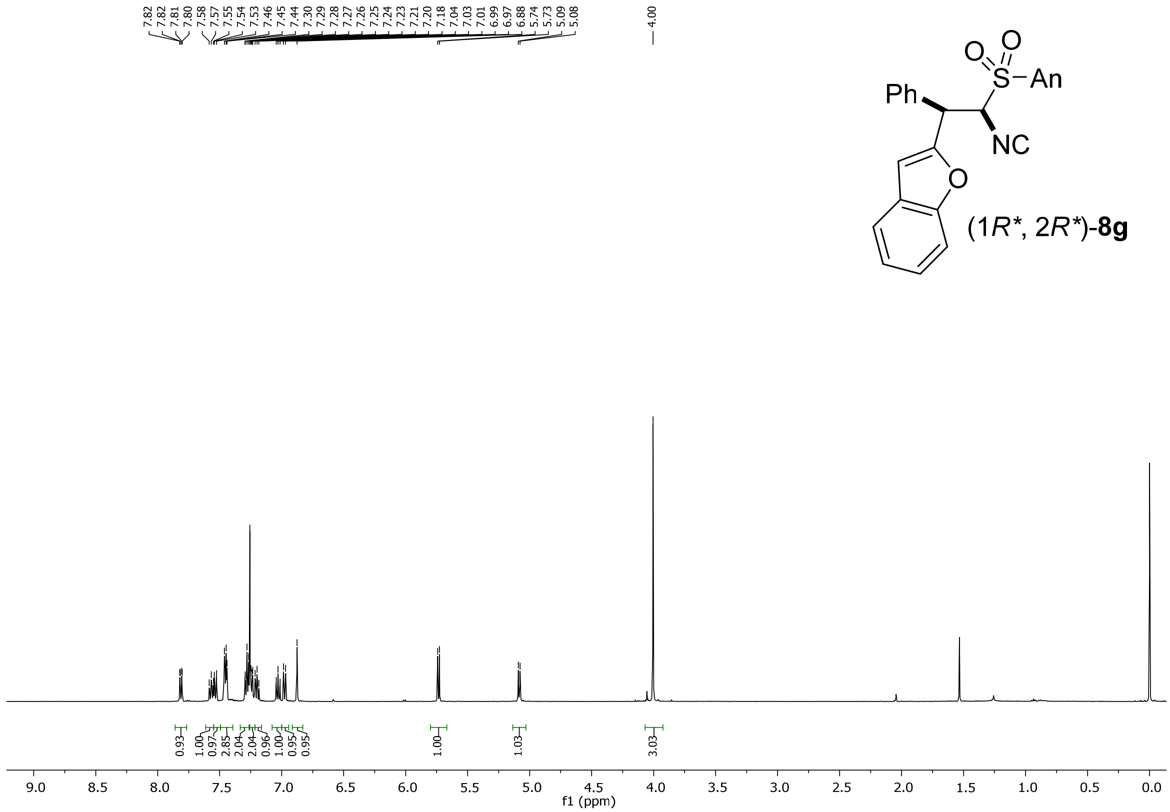
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide (1*S**, 2*R**)-**8f**.



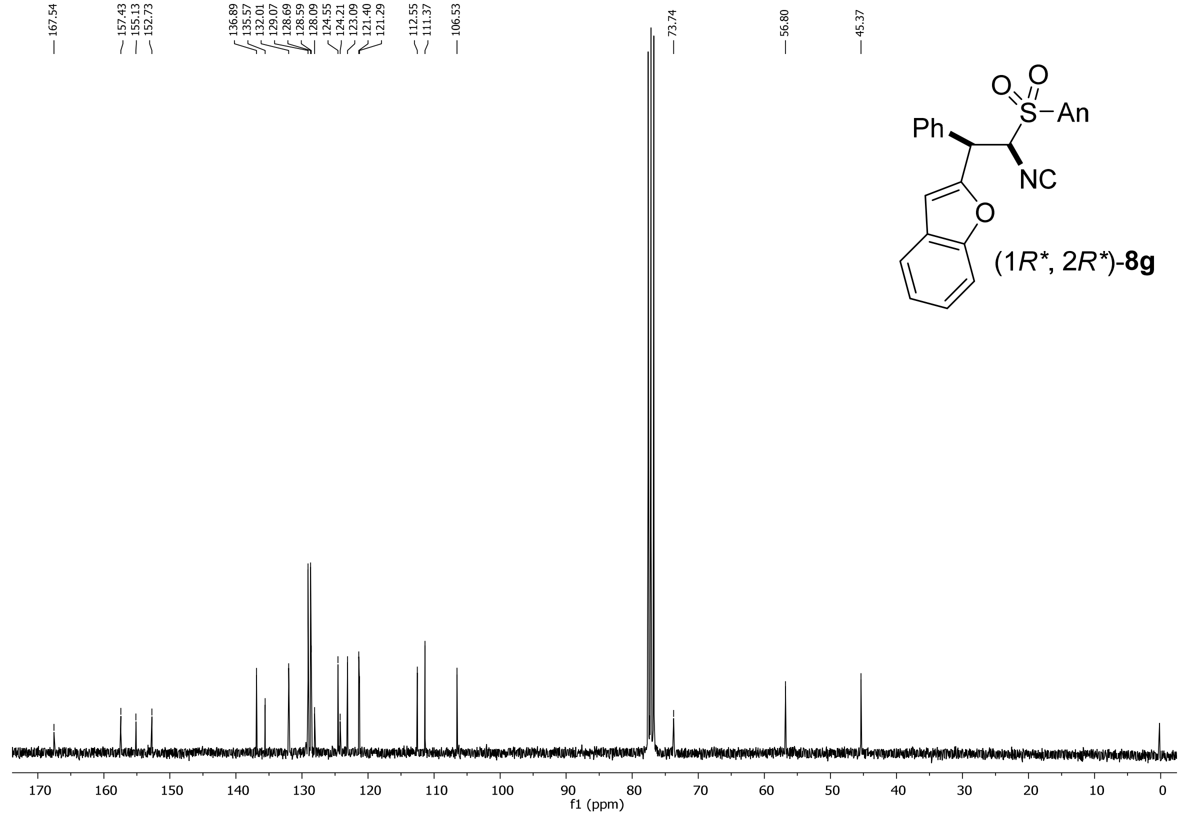
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide **8g**.



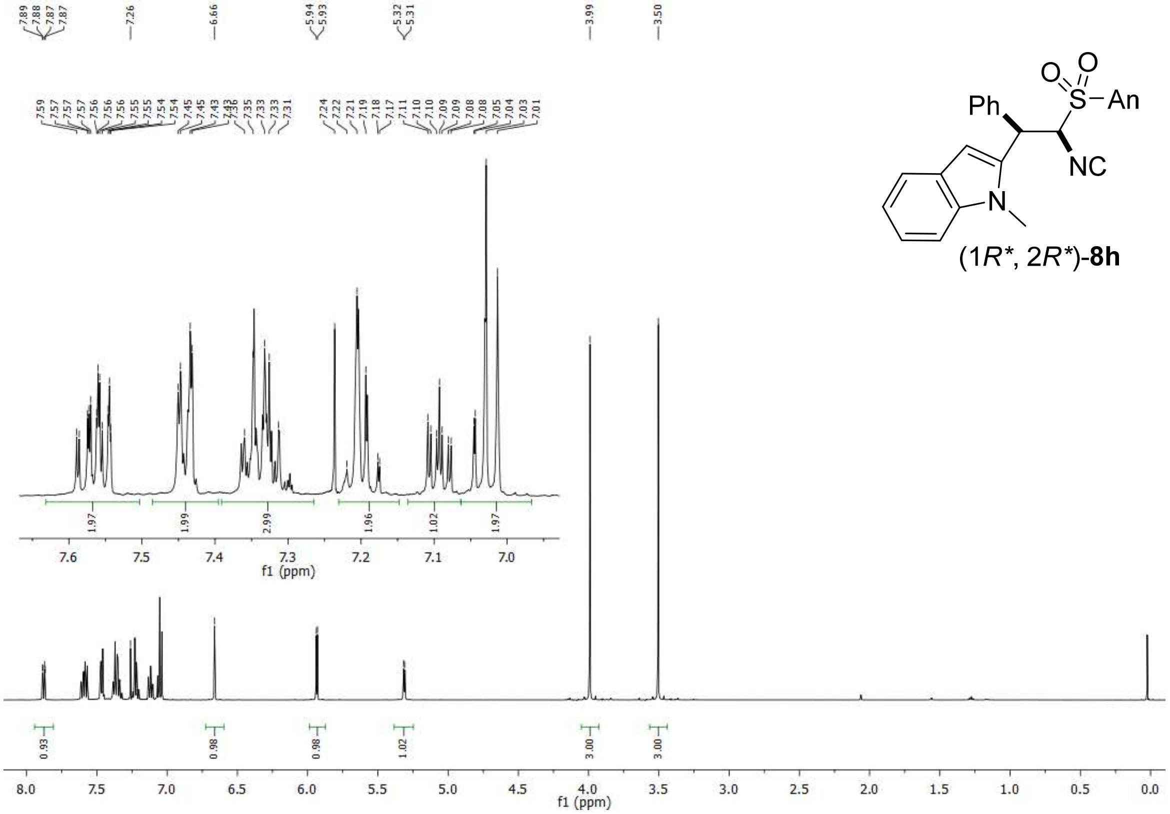
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide **8g**.



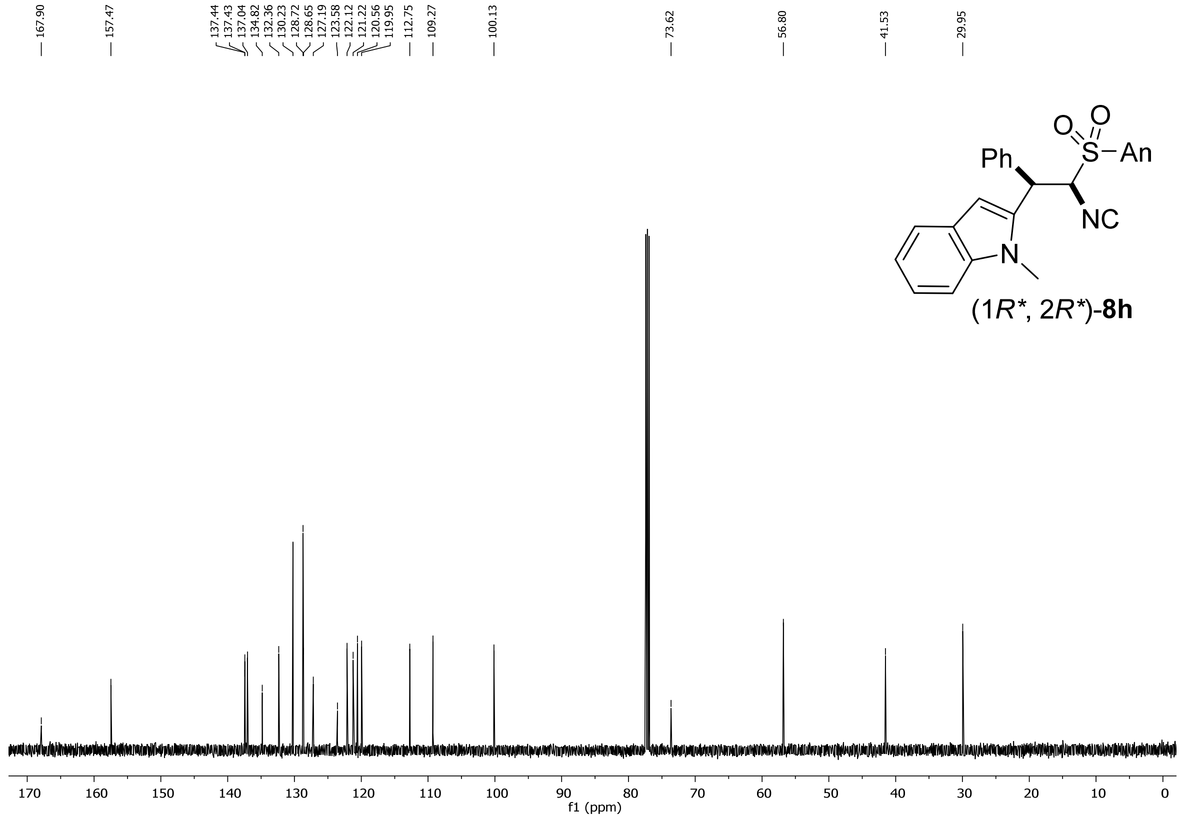
^{1}H NMR (500 MHz, $CDCl_3$) of isocyanide (1*R**, 2*R**)-**8g**.



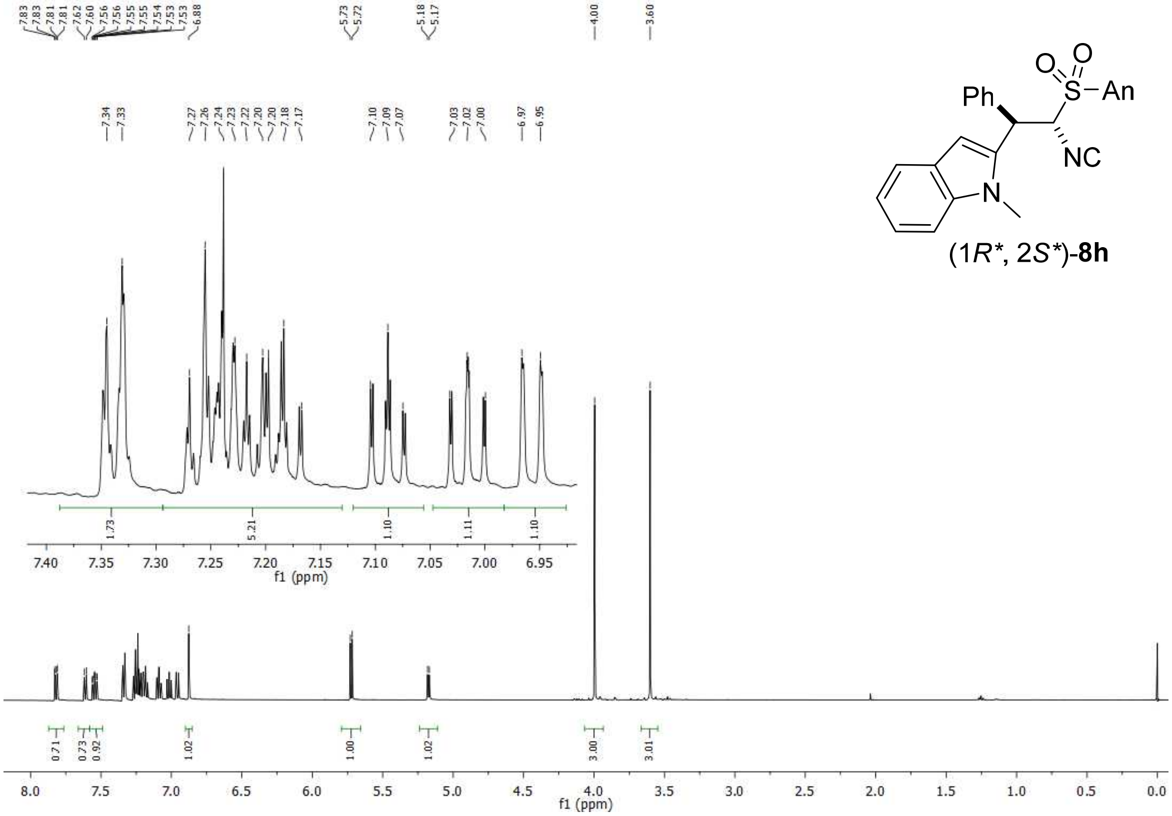
^{13}C NMR (75 MHz, $CDCl_3$) of isocyanide (1*R**, 2*R**)-**8g**.



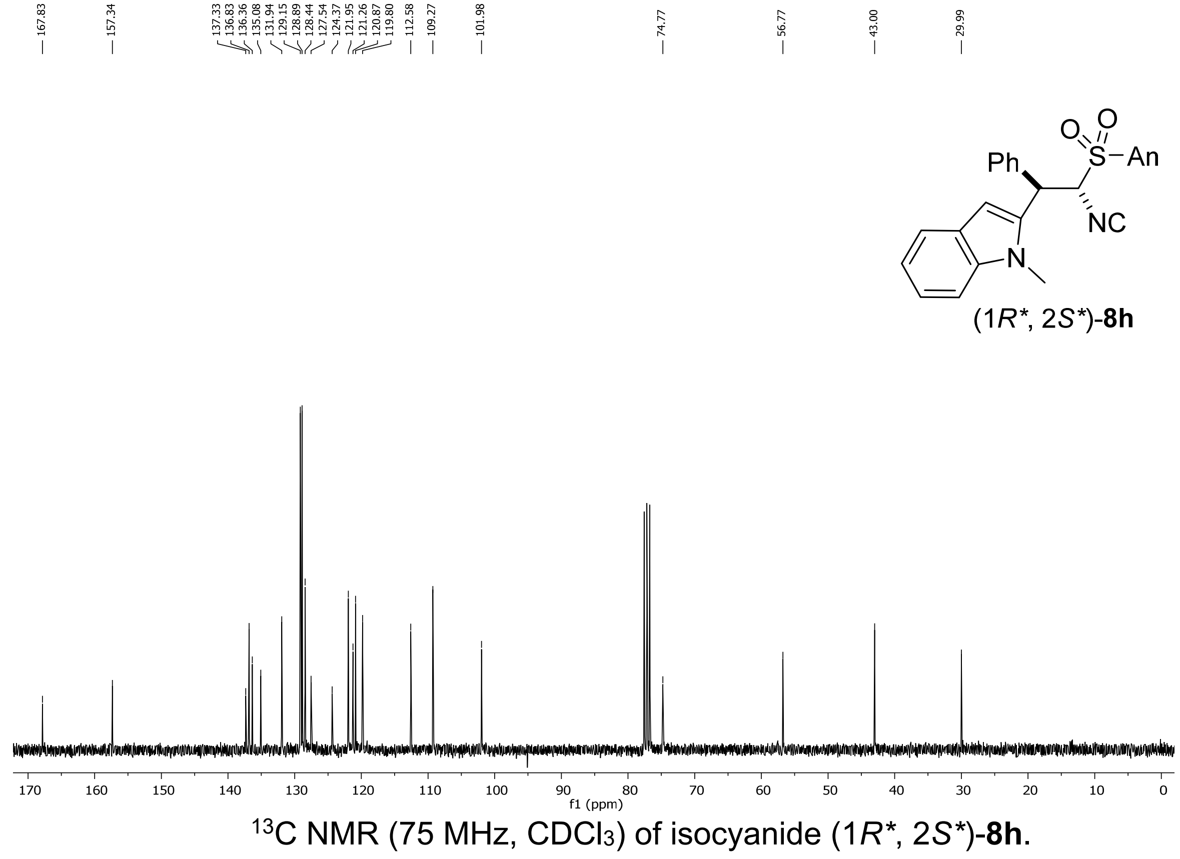
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*R**, 2*R**)-**8h**.



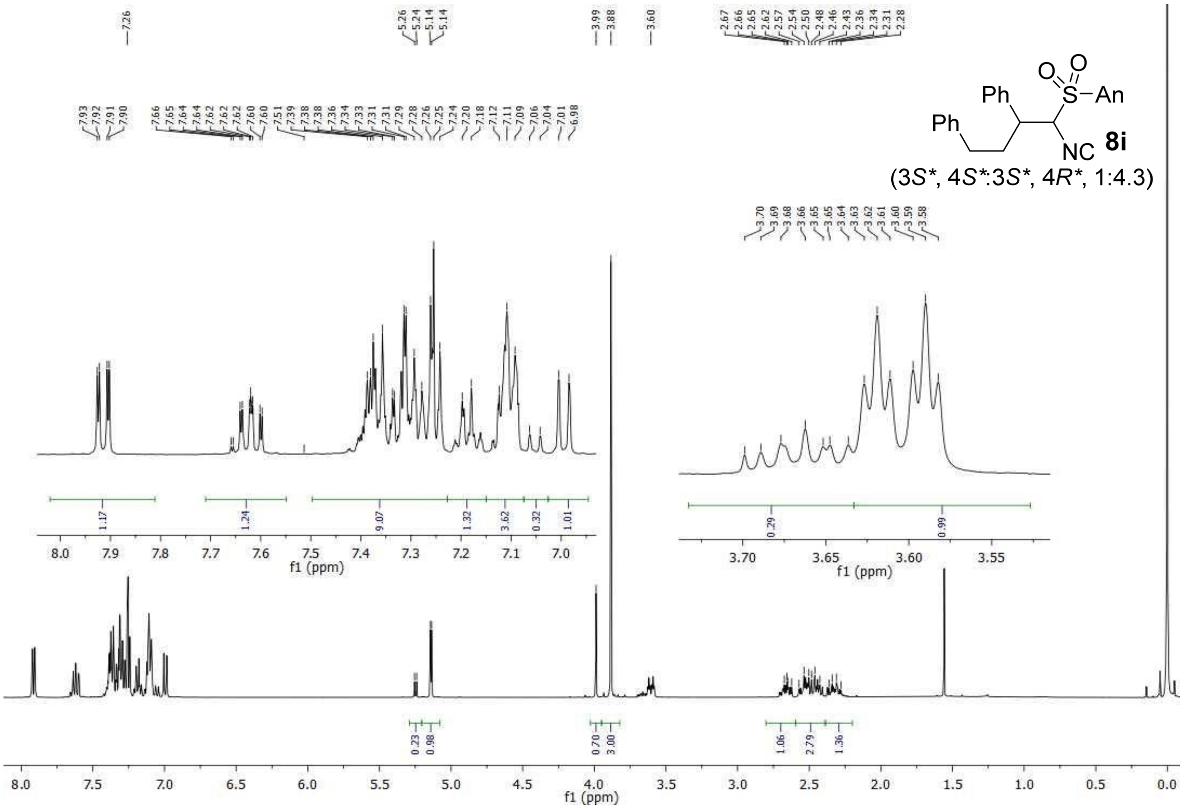
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide (1*R**, 2*R**)-**8h**.



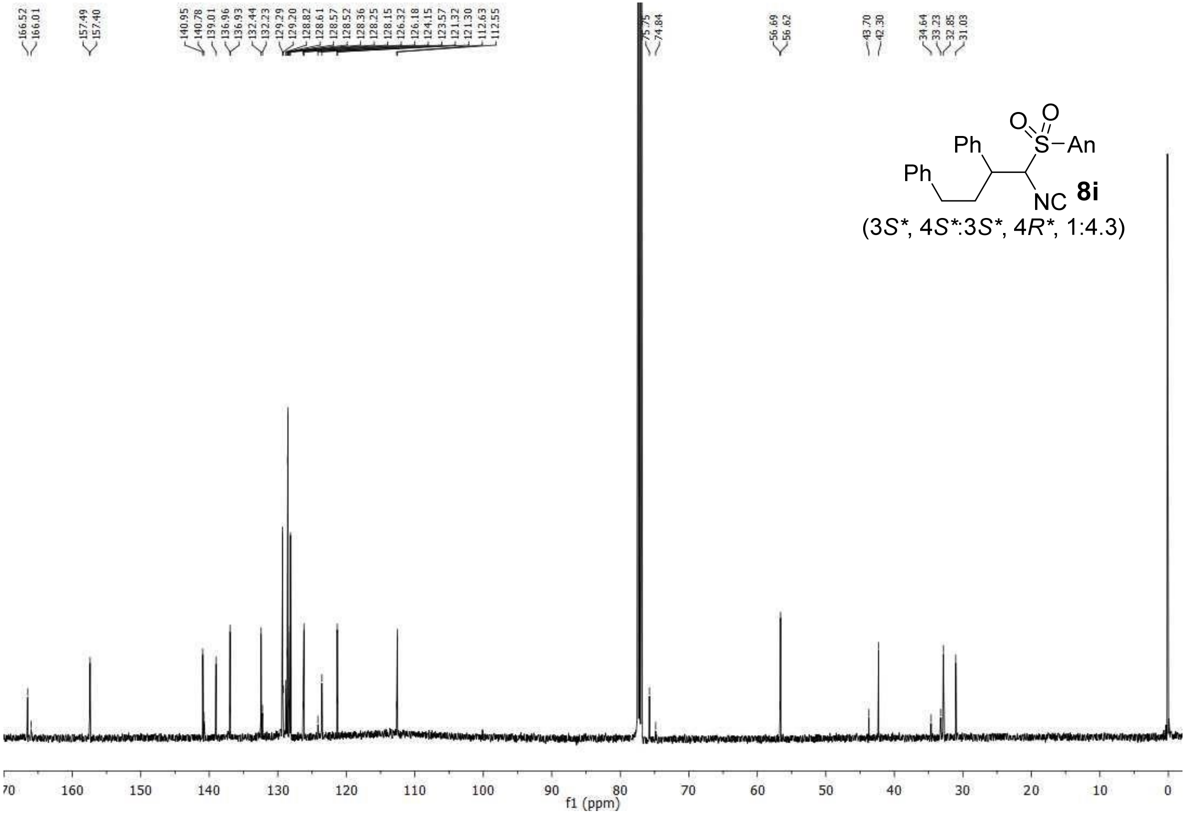
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**8h**.



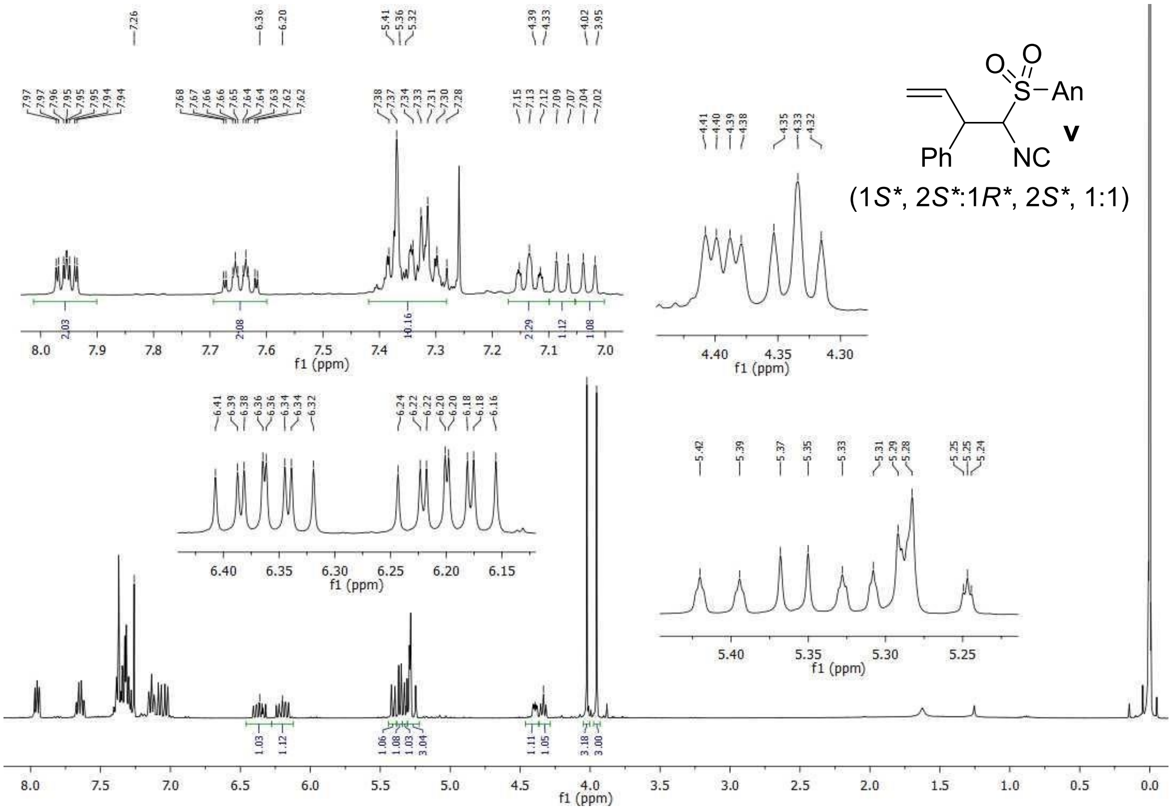
^{13}C NMR (75 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**8h**.



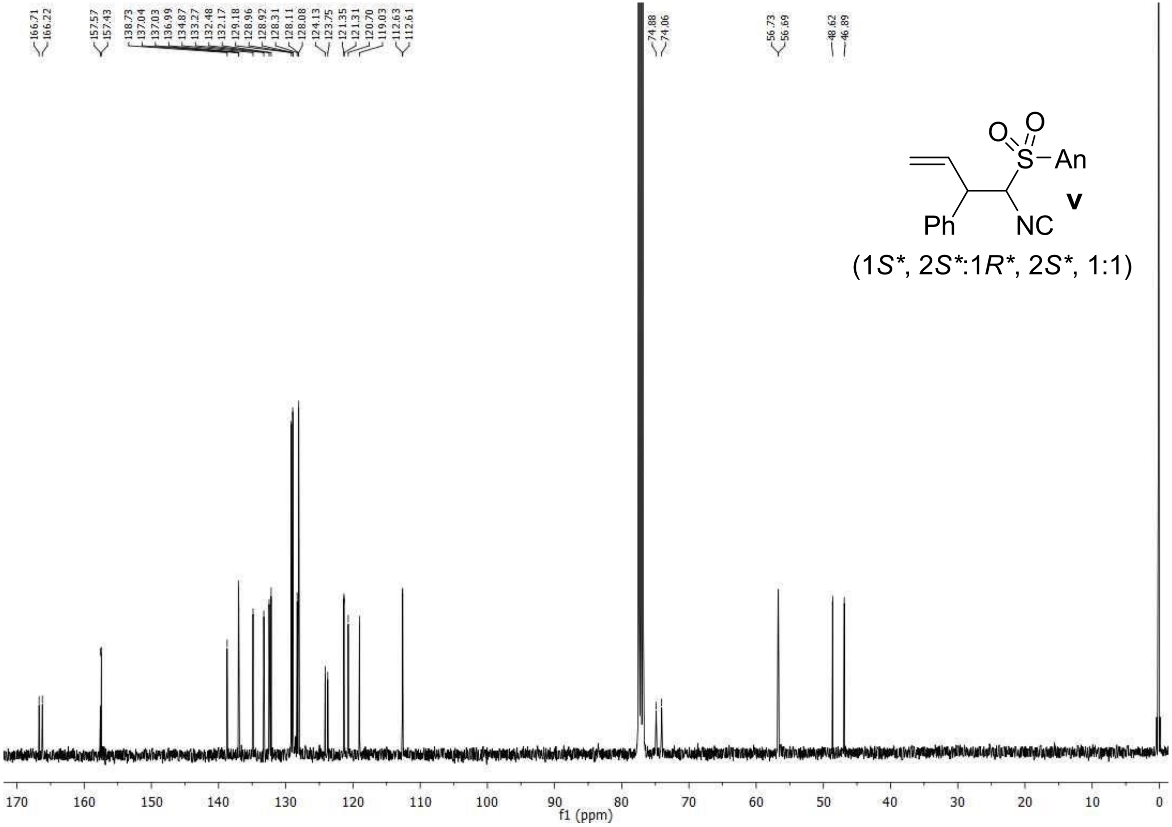
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8i**.



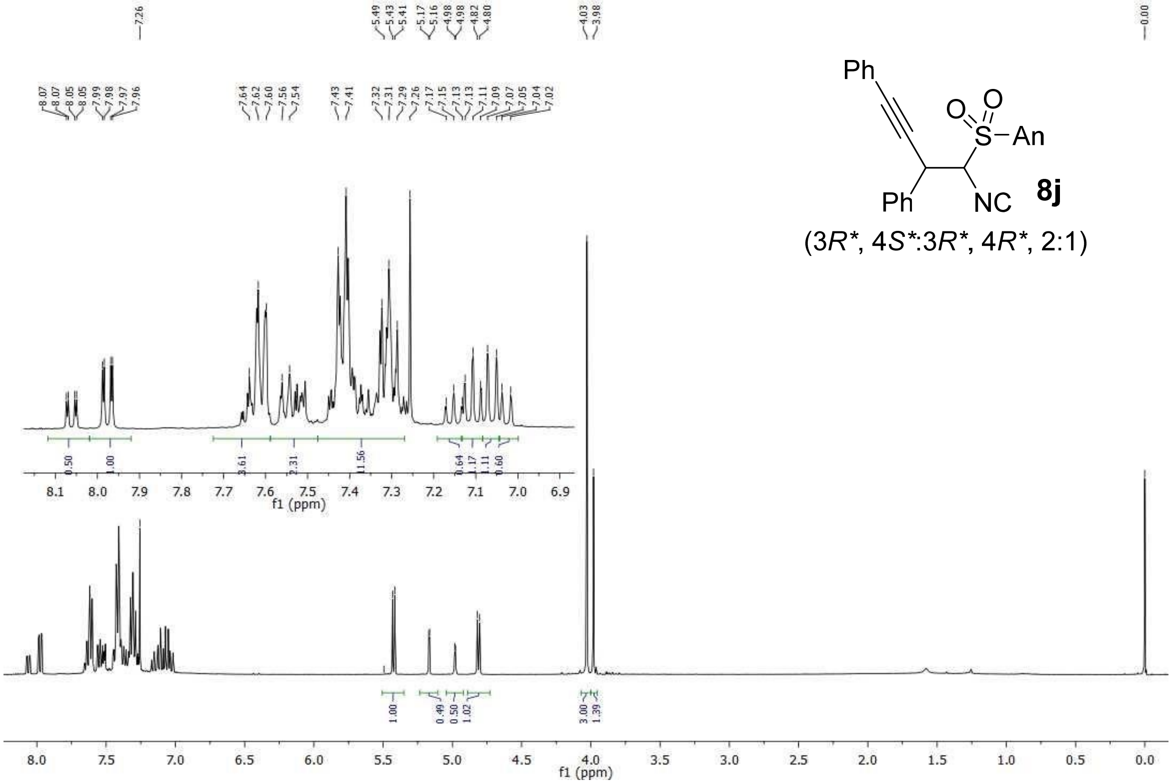
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide **8i**.



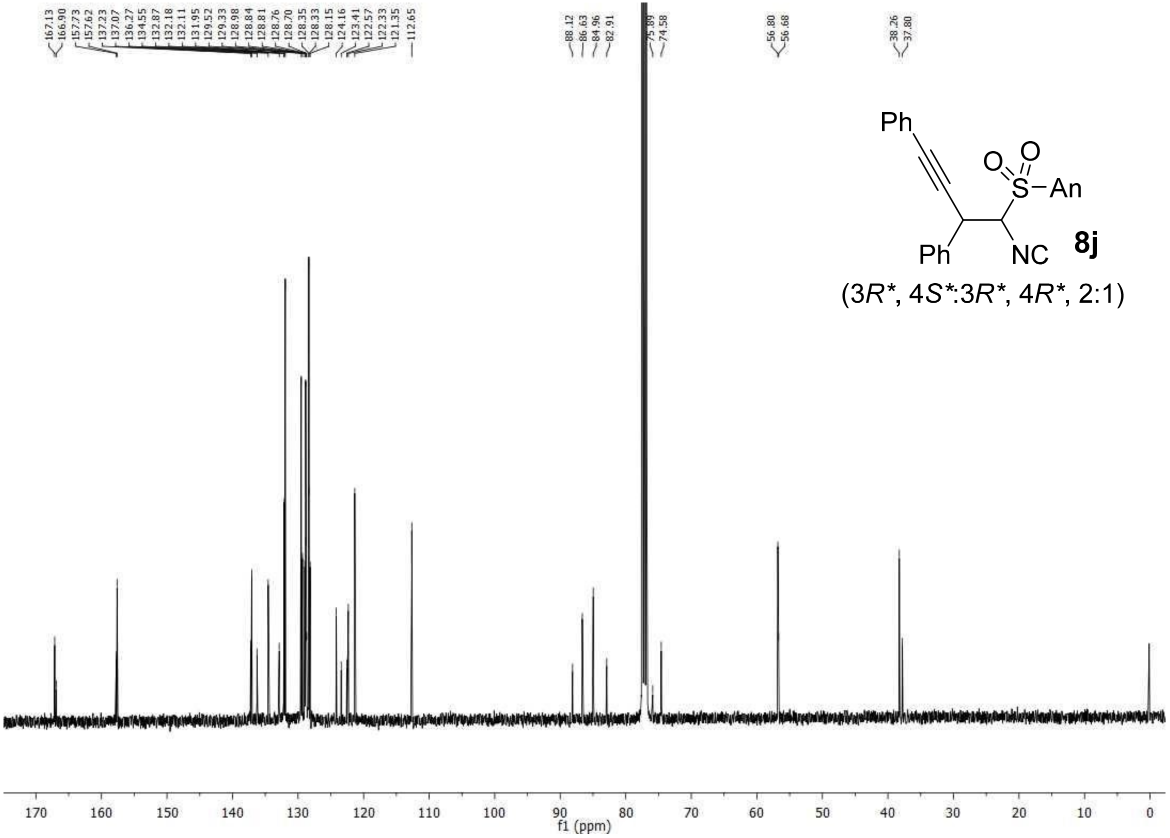
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **v**.



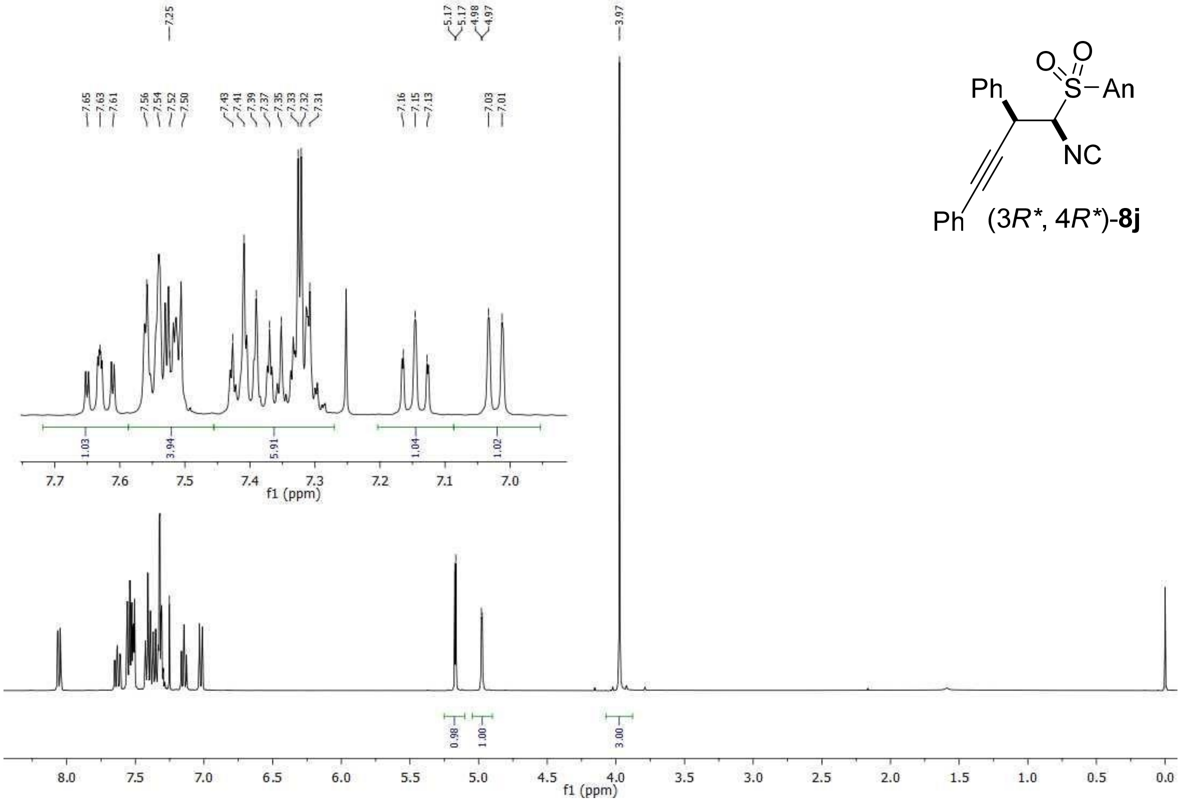
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **v**.



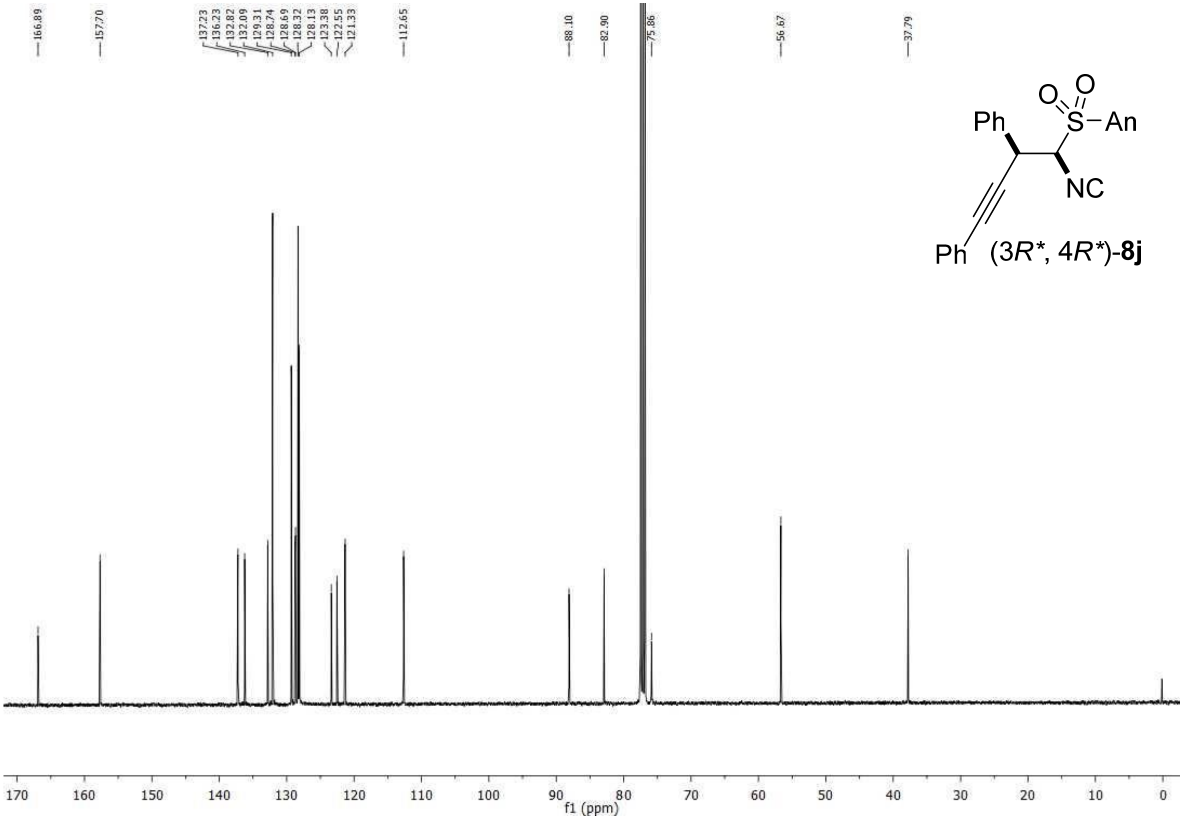
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8j**.



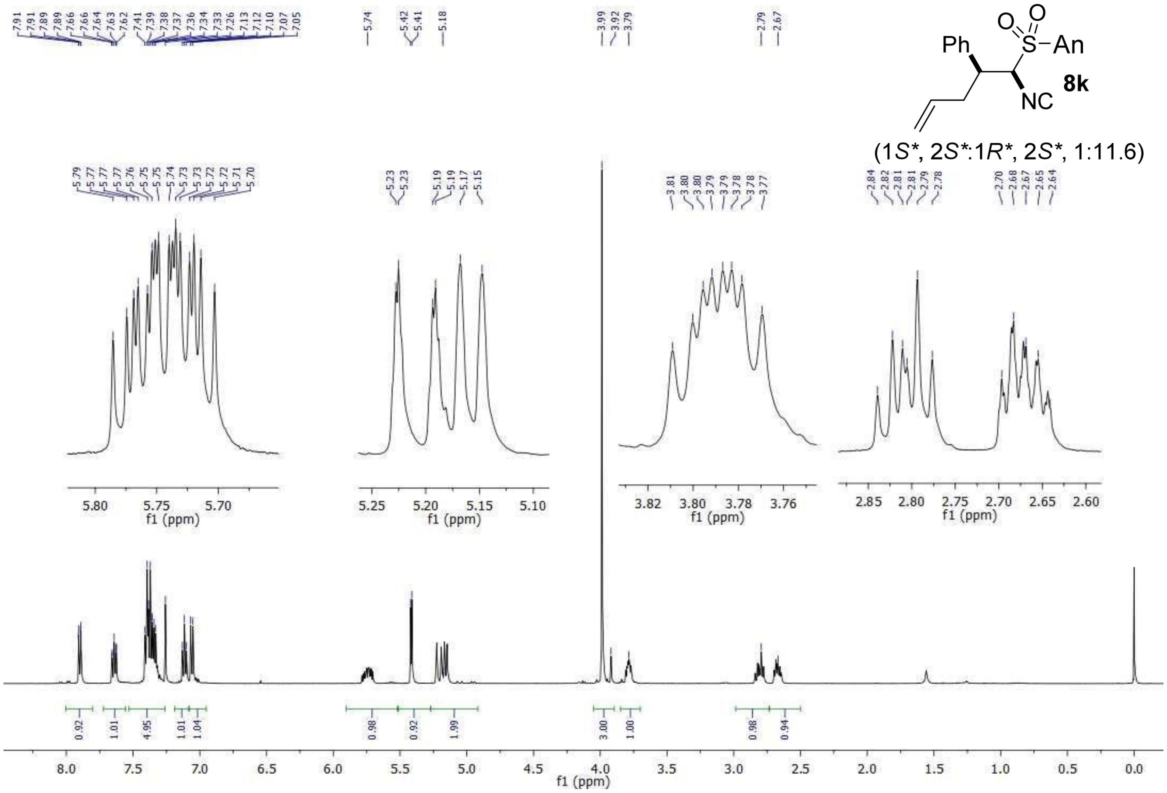
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8j**.



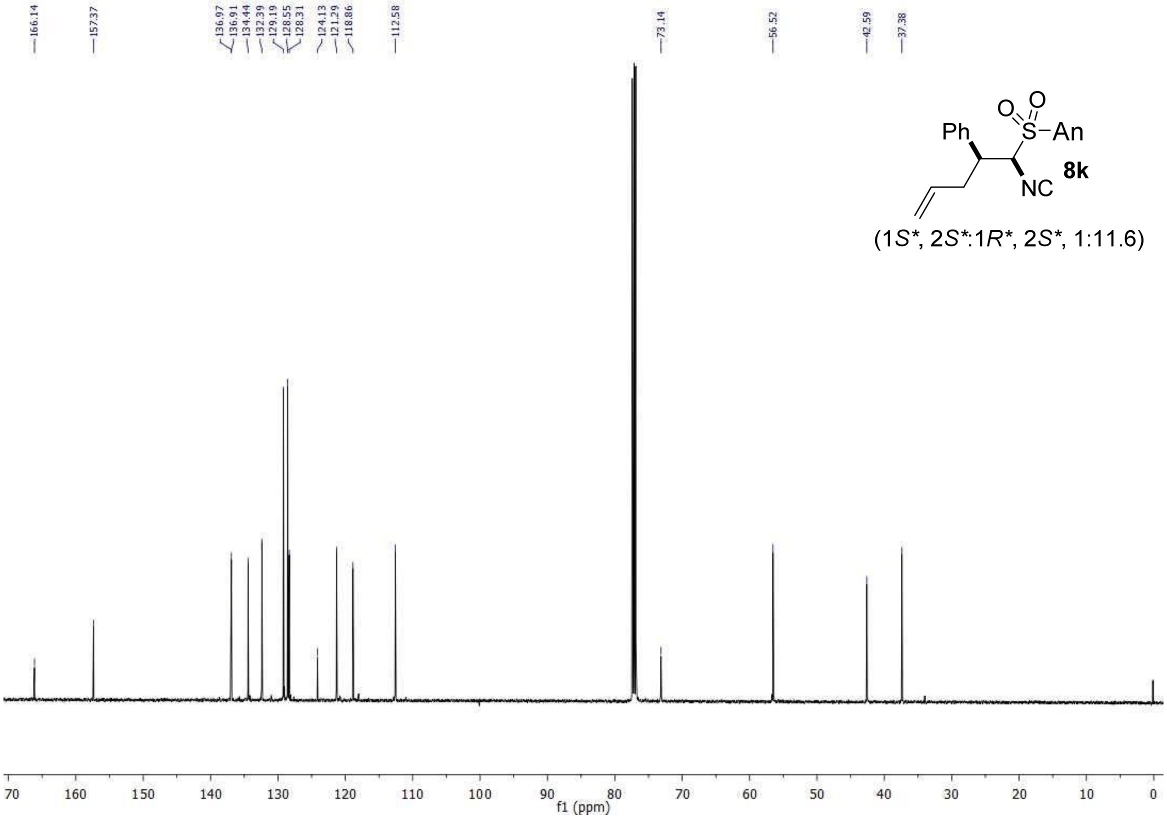
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (3*R**, 4*R**)-**8j**.



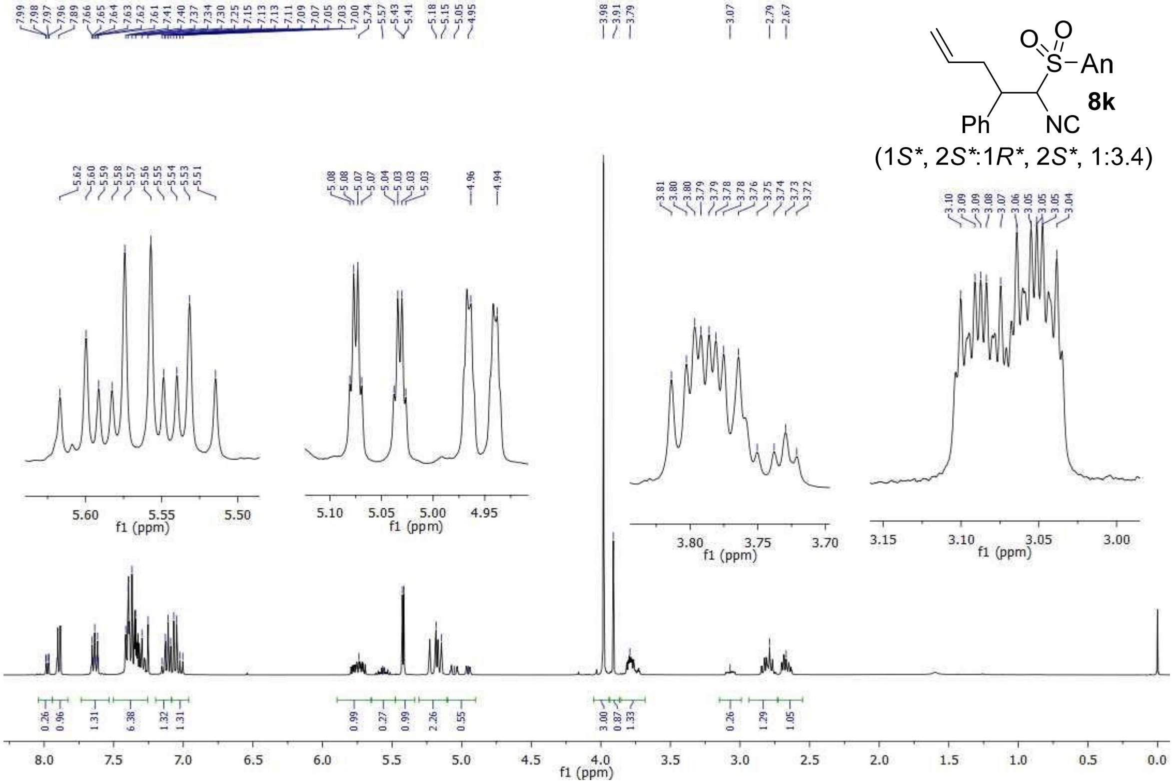
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (3*R**, 4*R**)-**8j**.



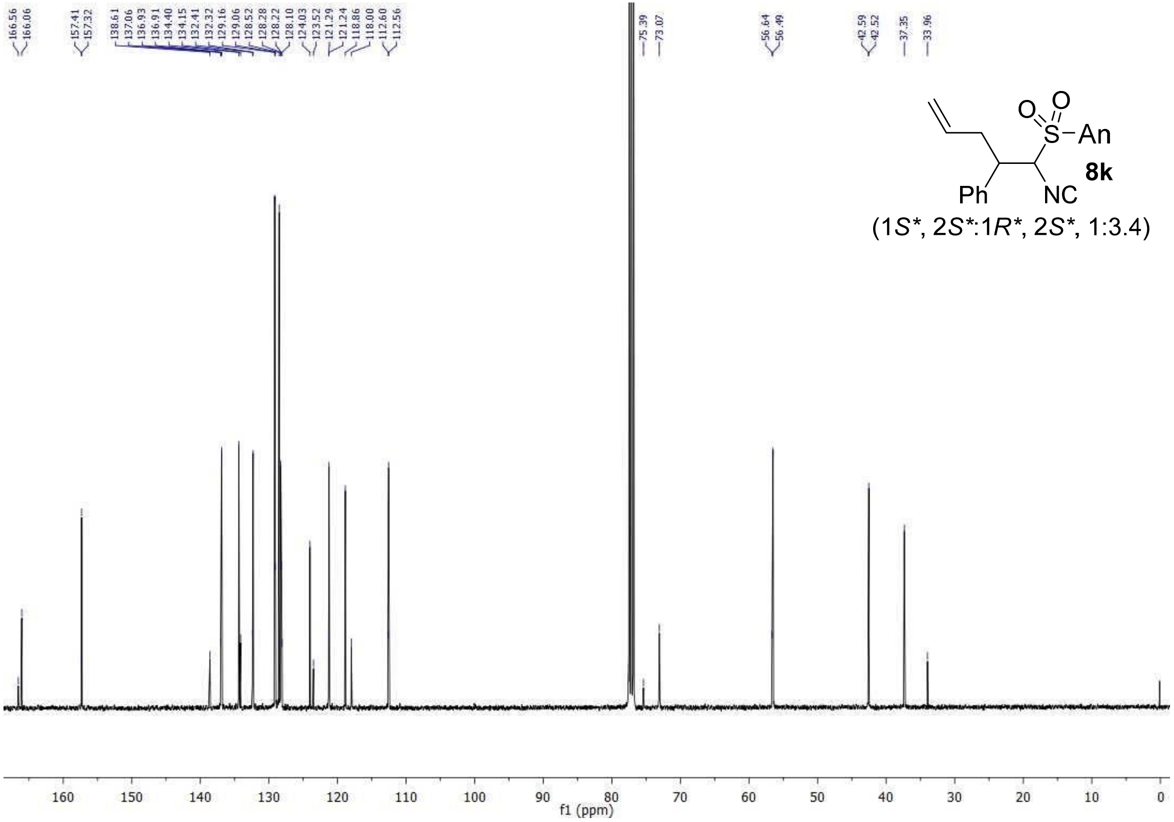
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**8k**.



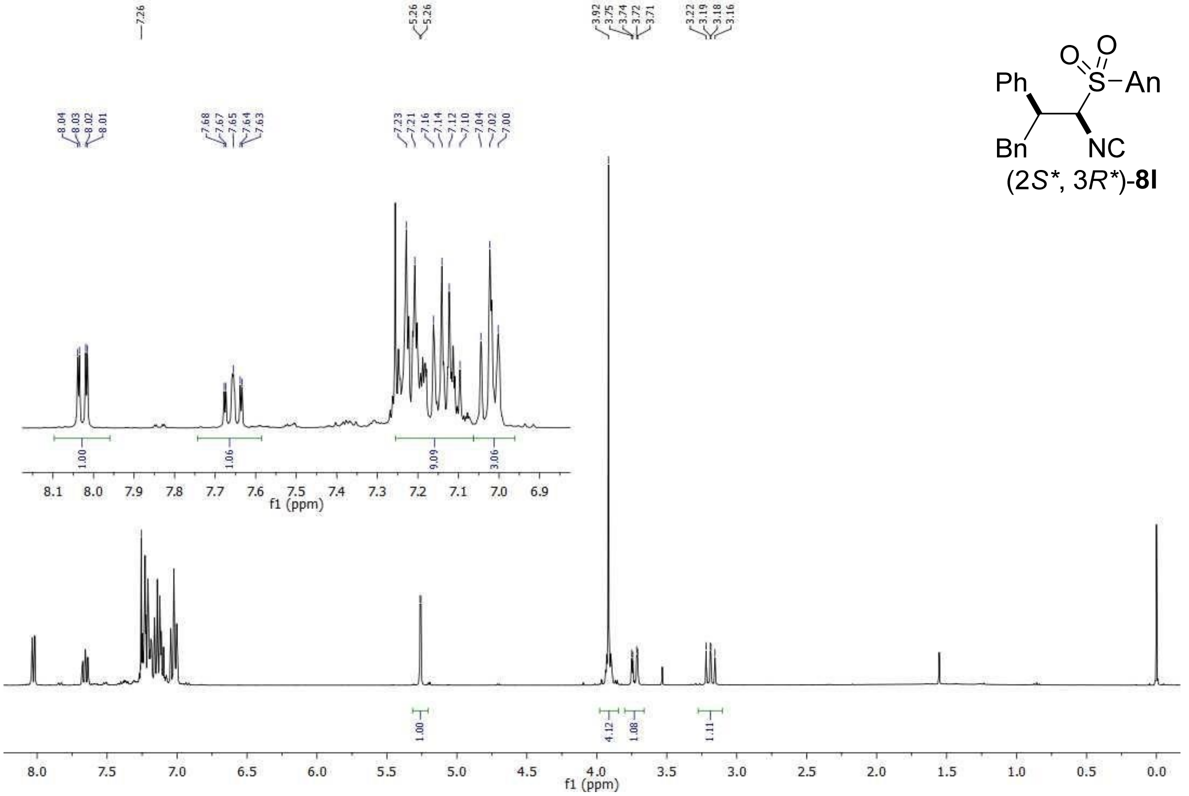
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**8k**.



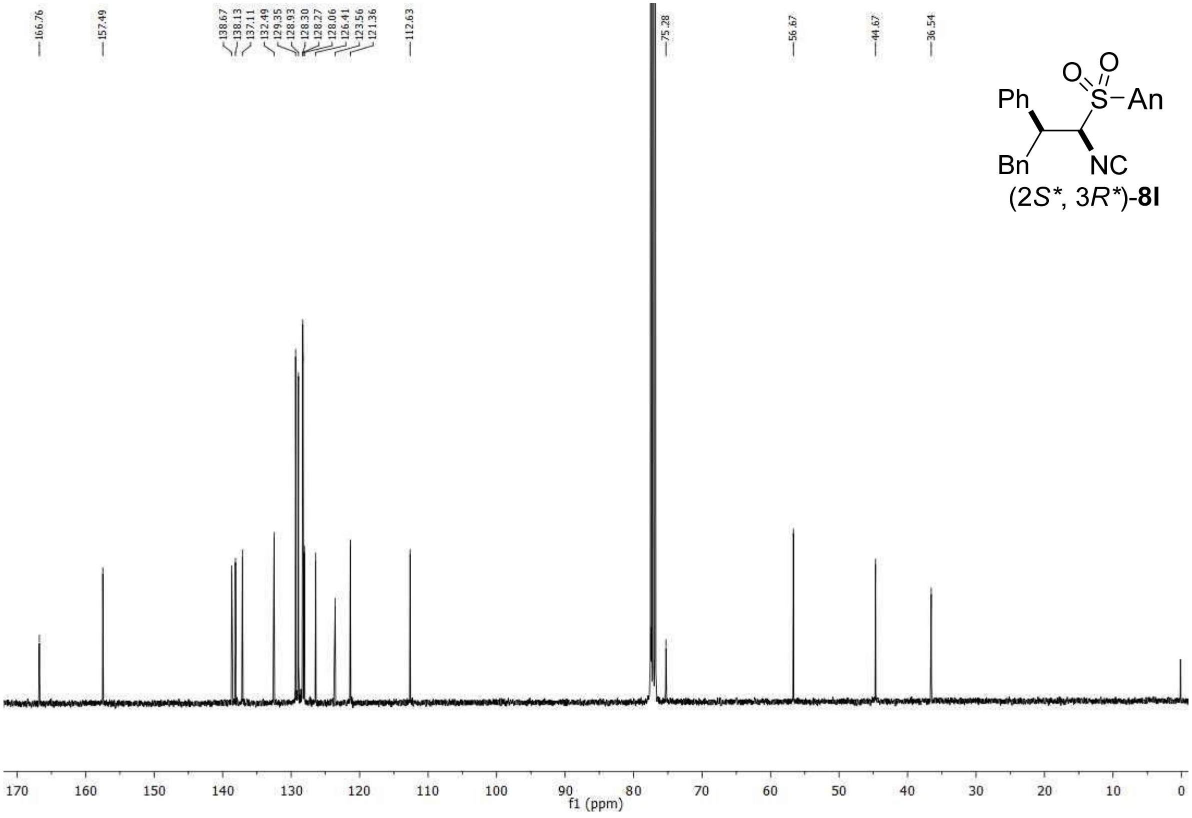
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8k**.



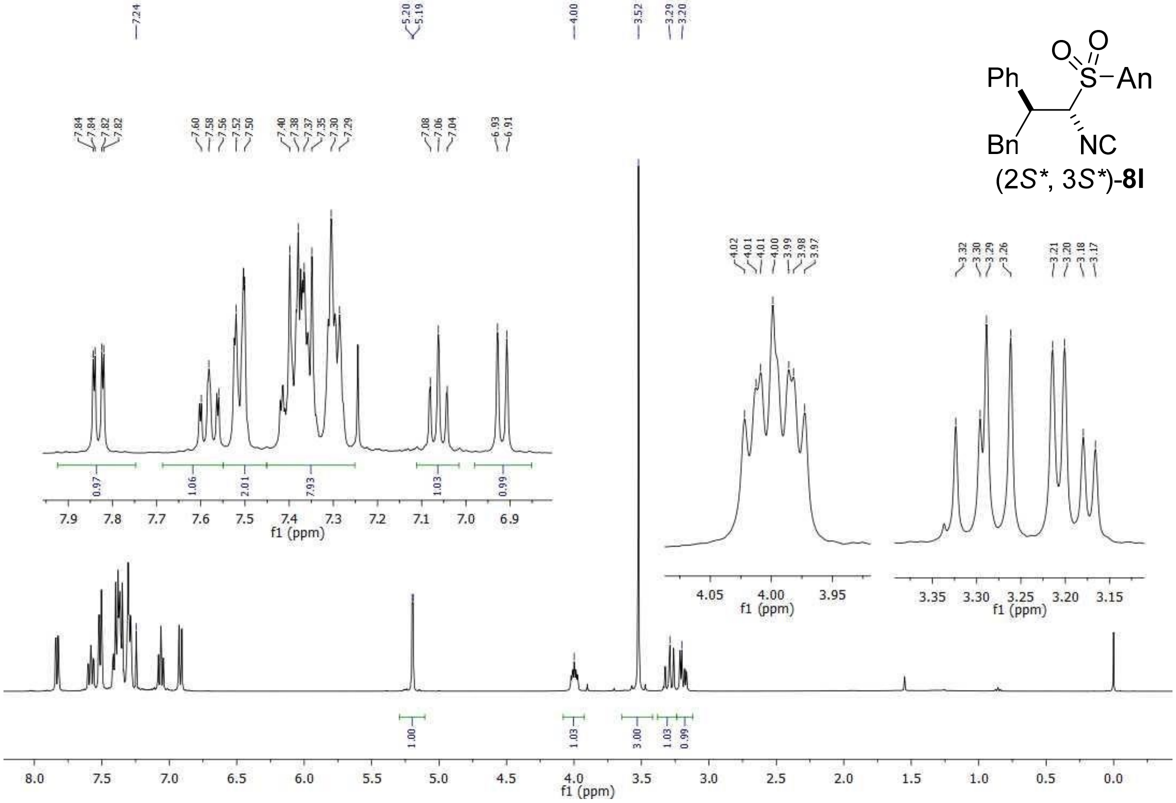
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8k**.



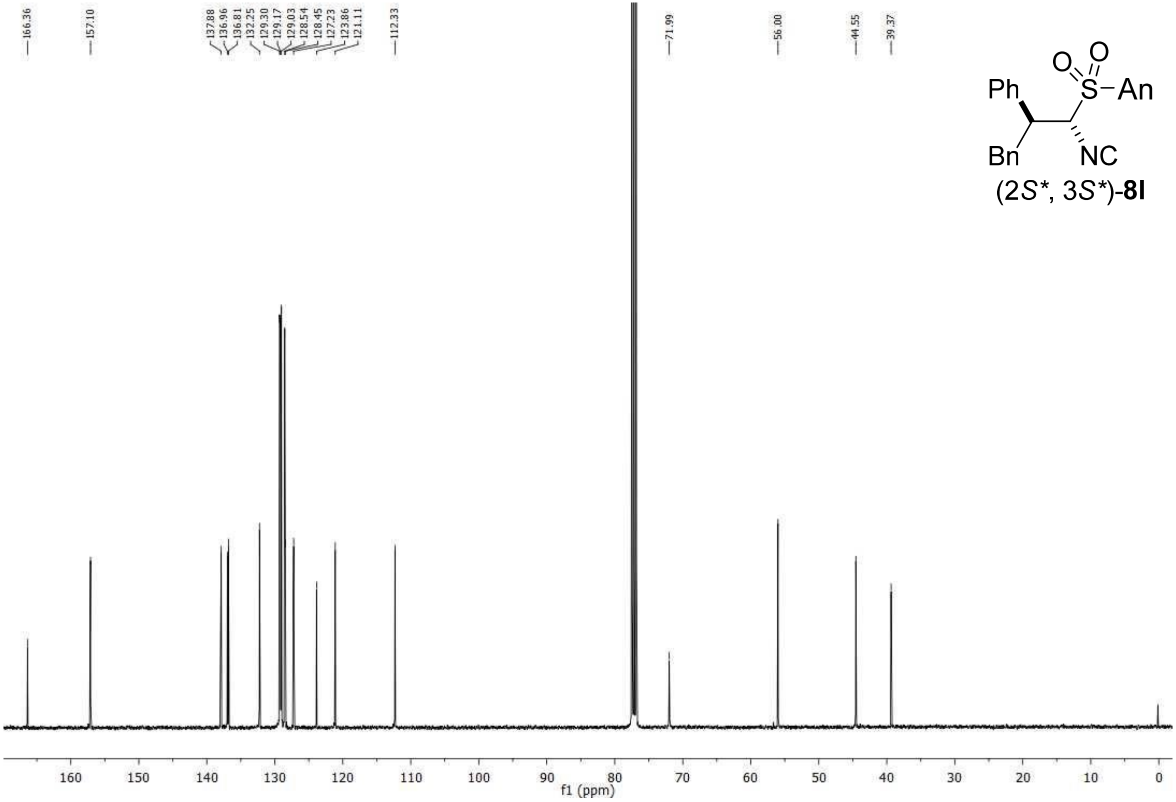
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (2*S**, 3*R**)-**8l**.



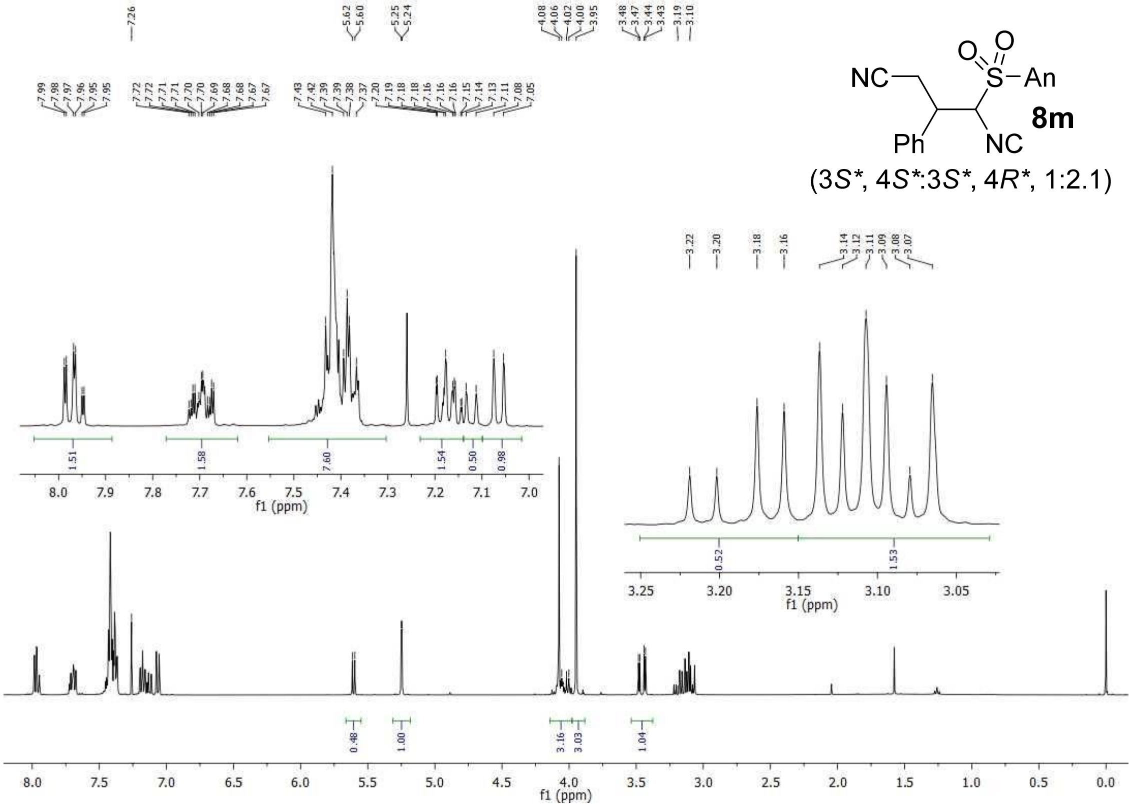
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (2*S**, 3*R**)-**8l**.



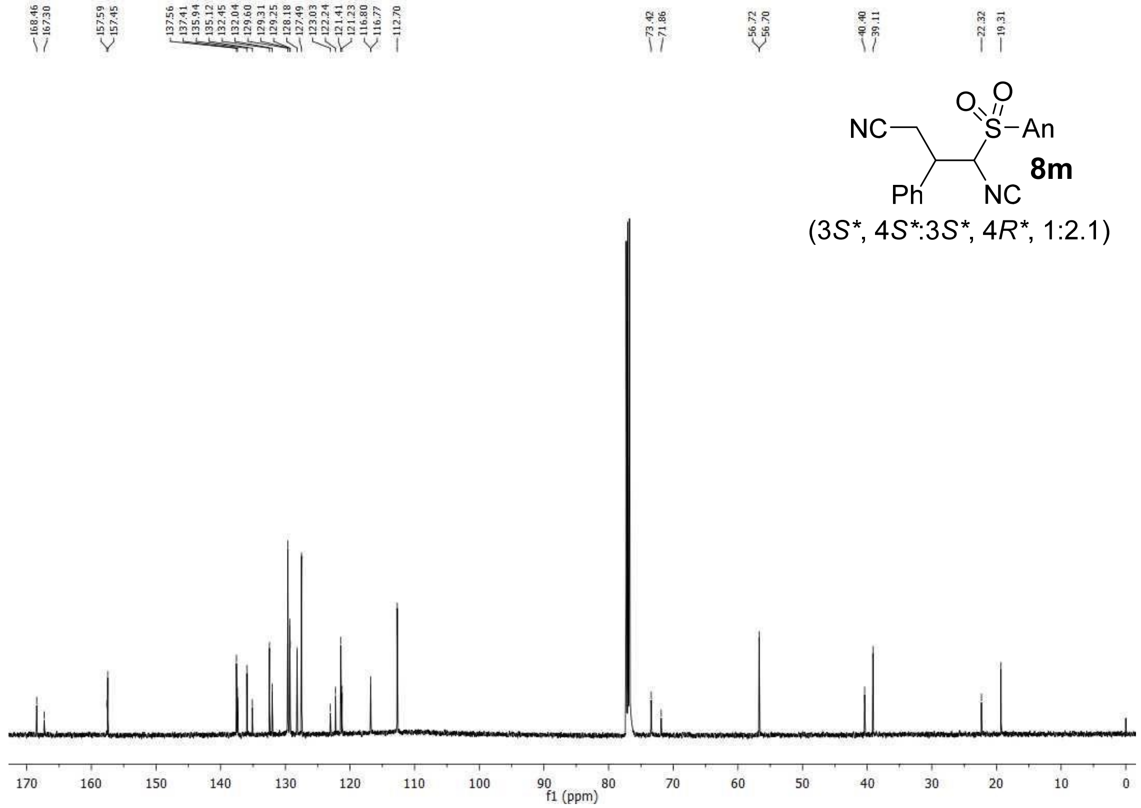
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (2*S**, 3*S**)-**8l**.



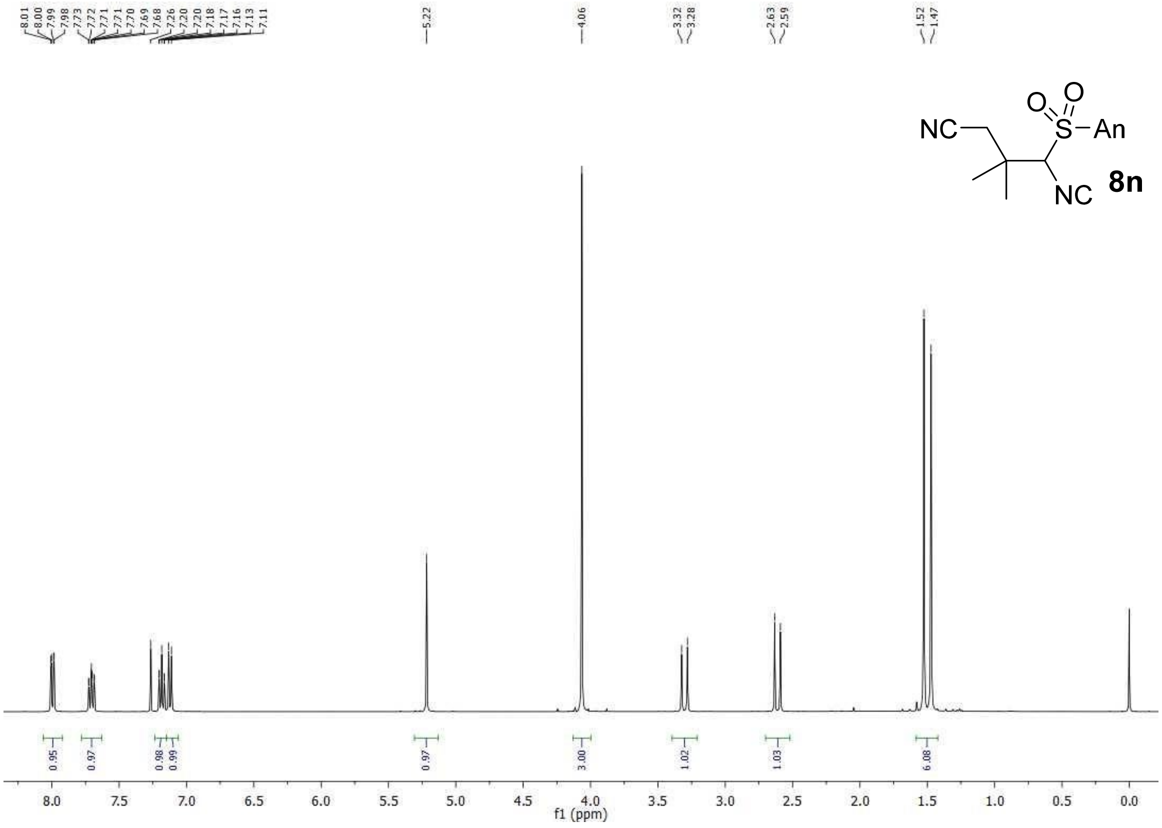
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (2*S**, 3*S**)-**8l**.



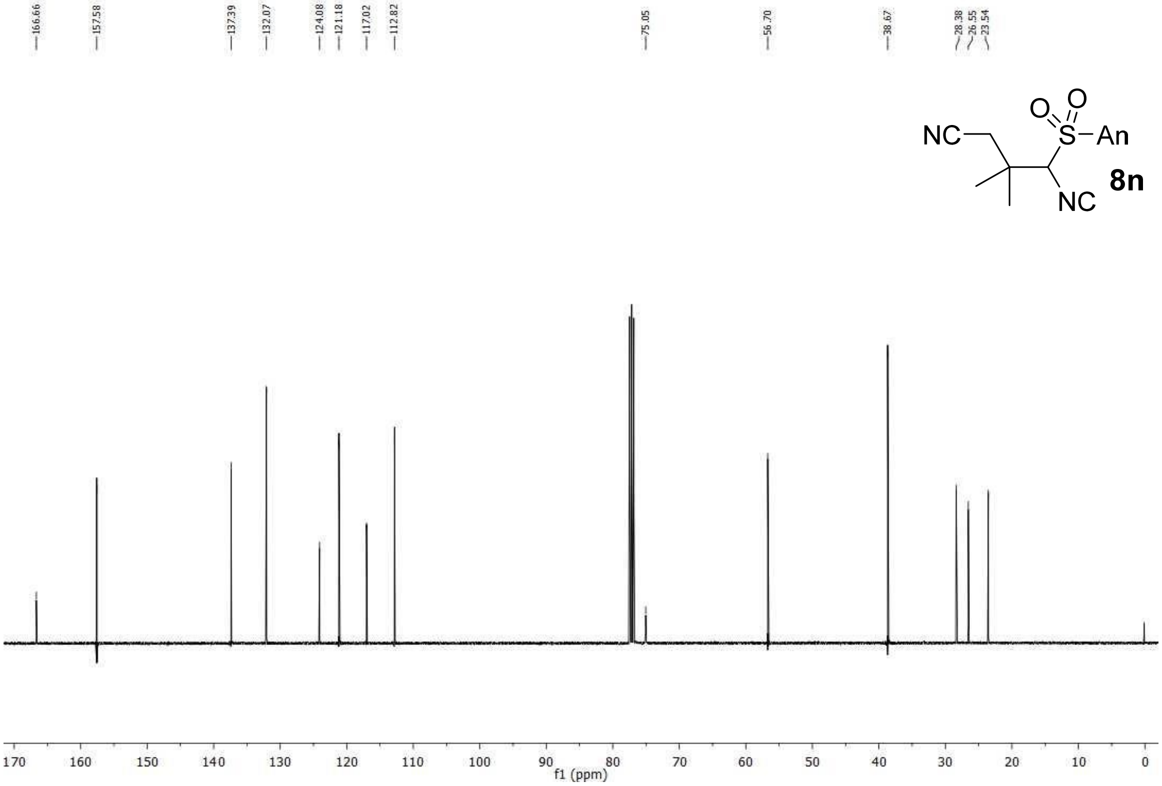
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8m**.



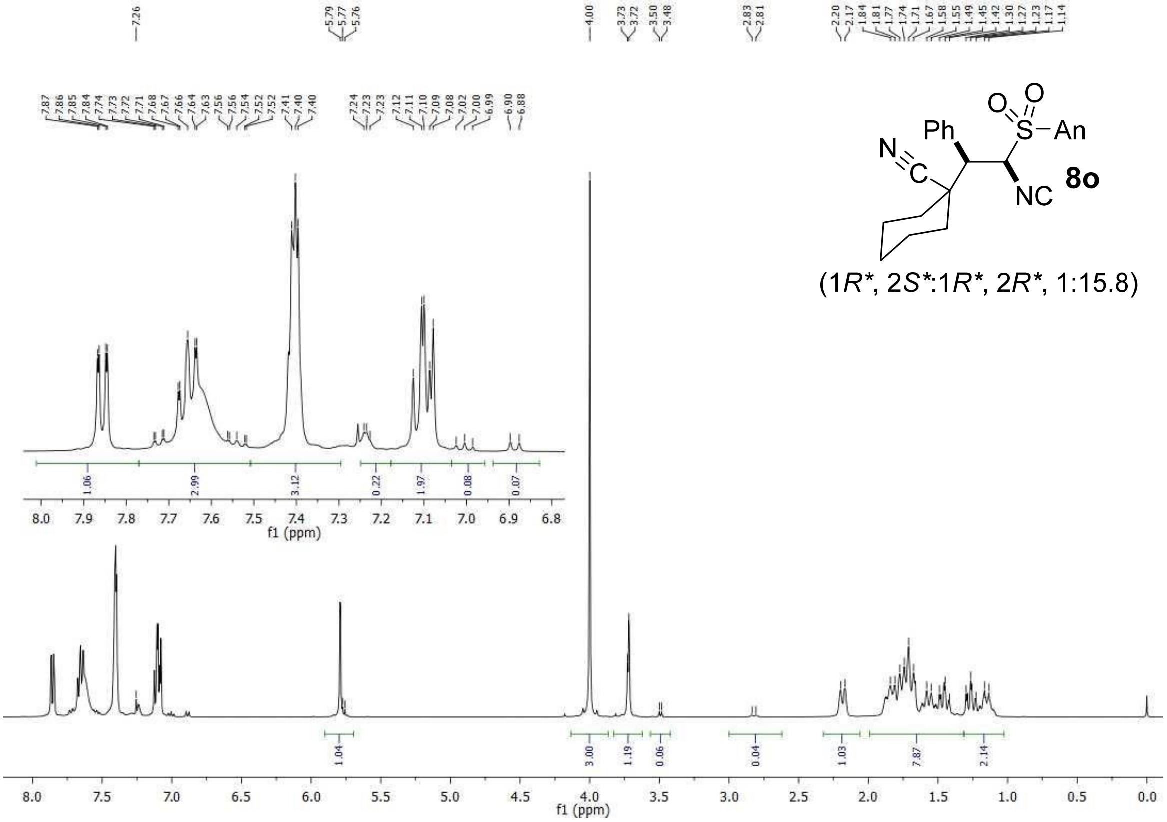
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide **8m**.



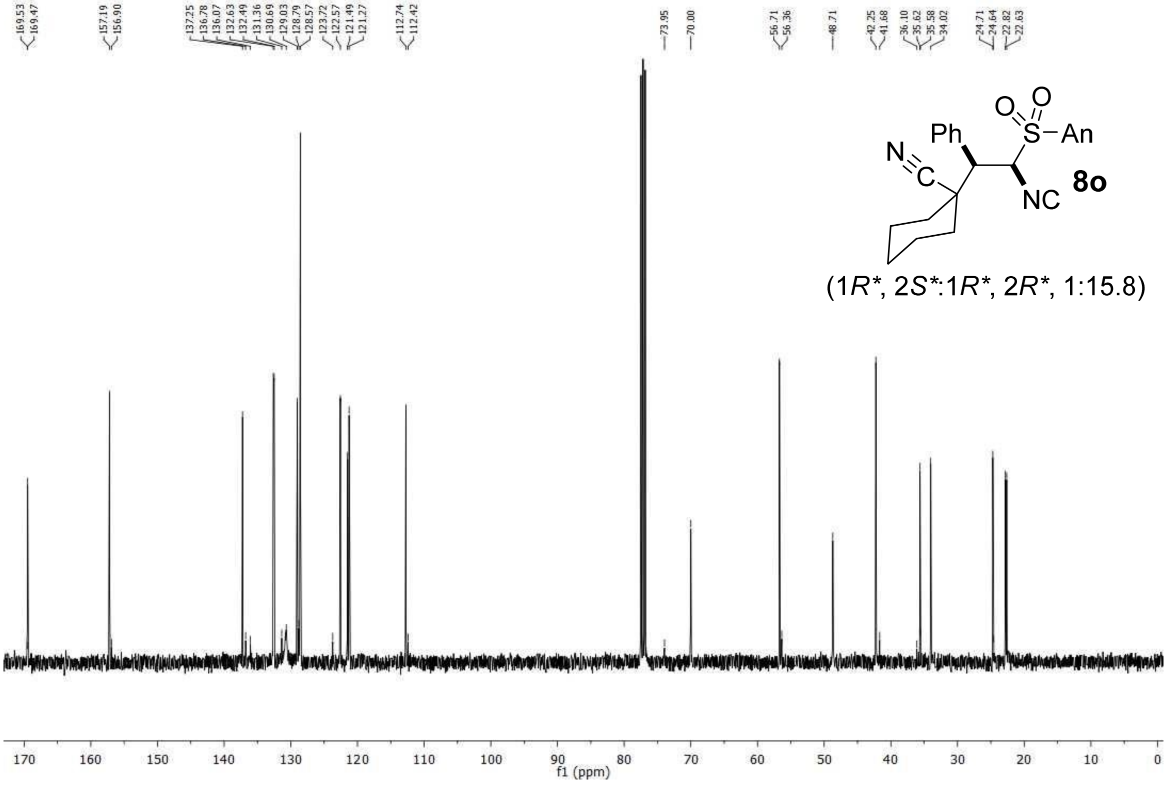
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8n**.



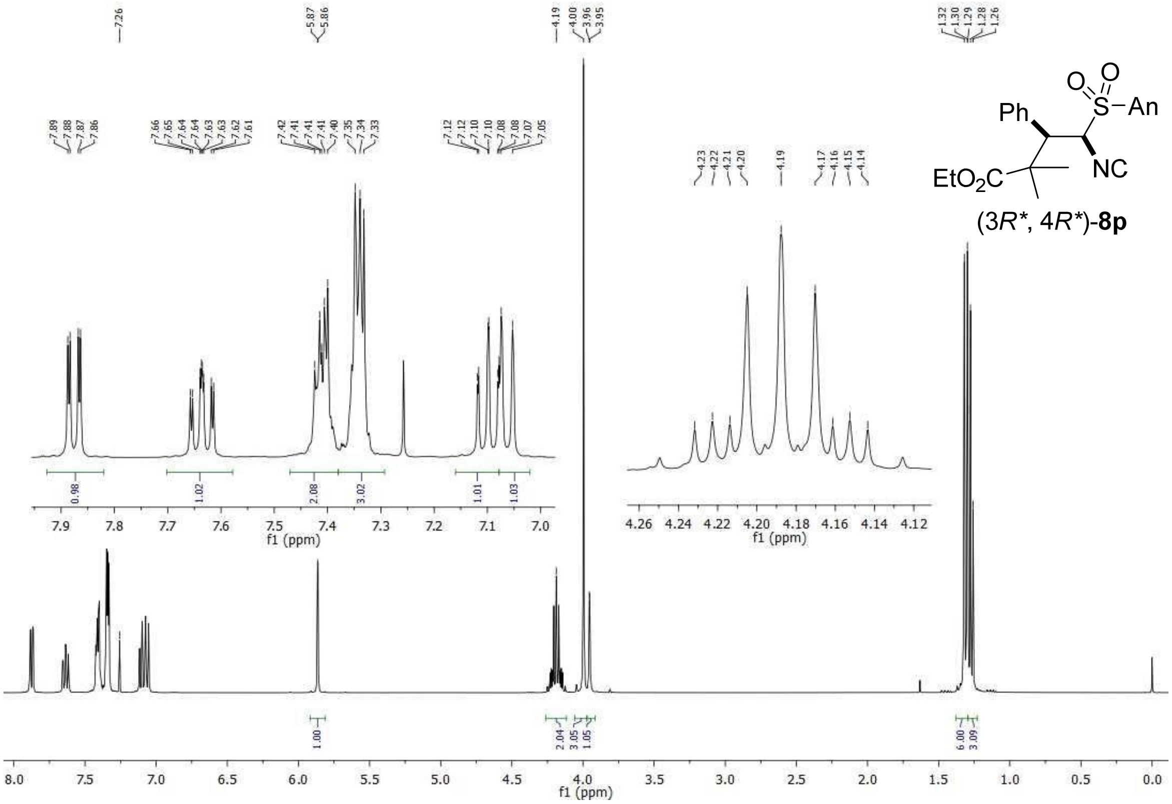
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8n**.



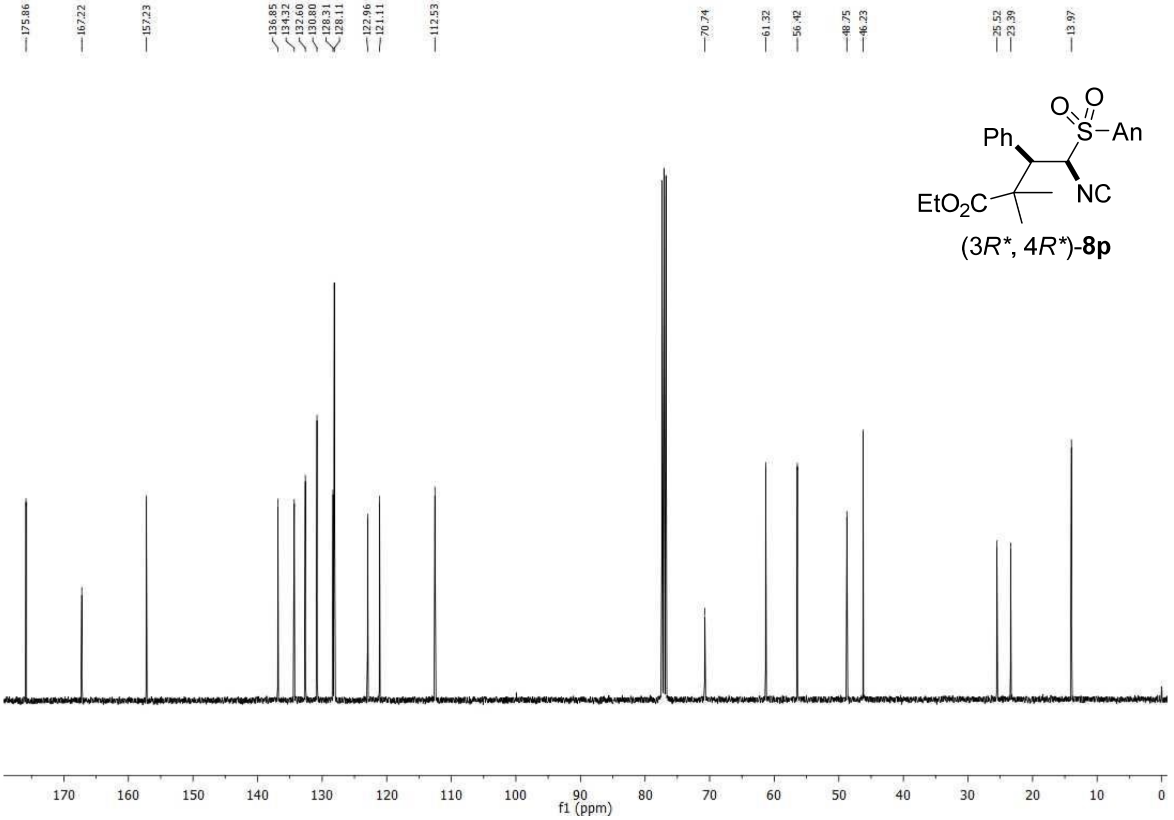
^{1}H NMR (400 MHz, $CDCl_3$) of isocyanide **8o**.



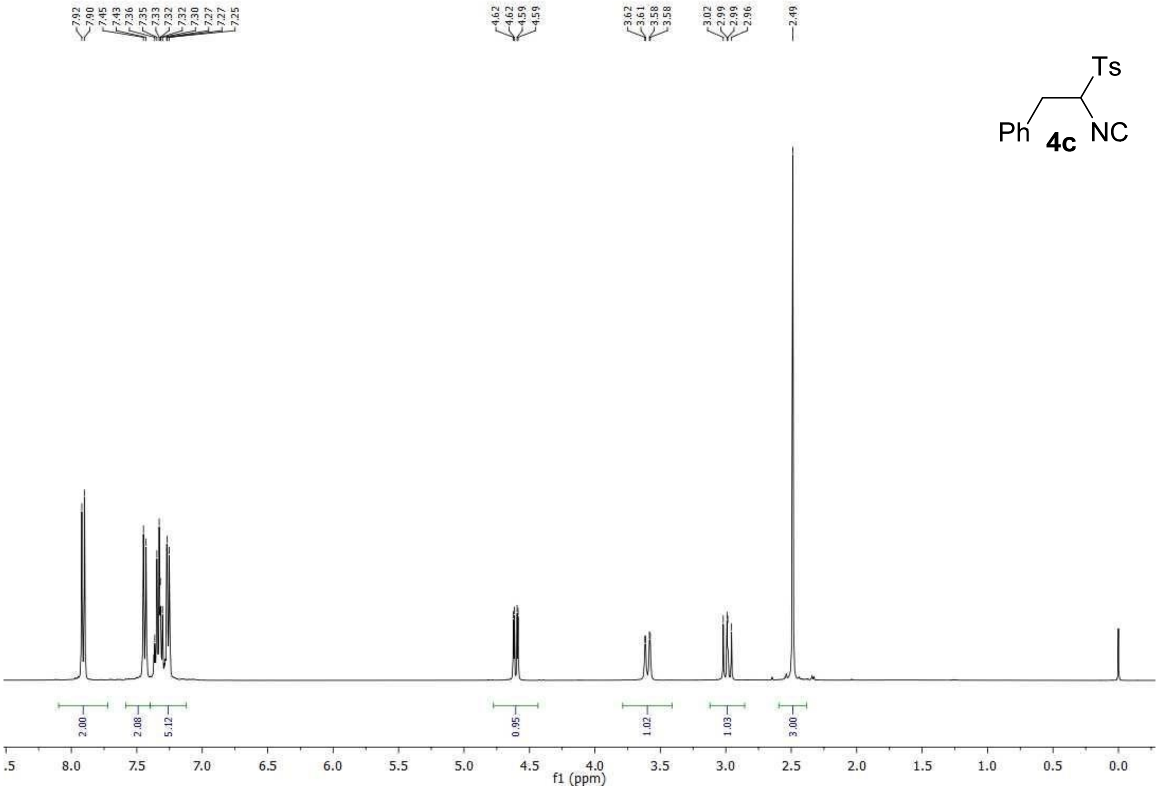
^{13}C NMR (101 MHz, $CDCl_3$) of isocyanide **8o**.



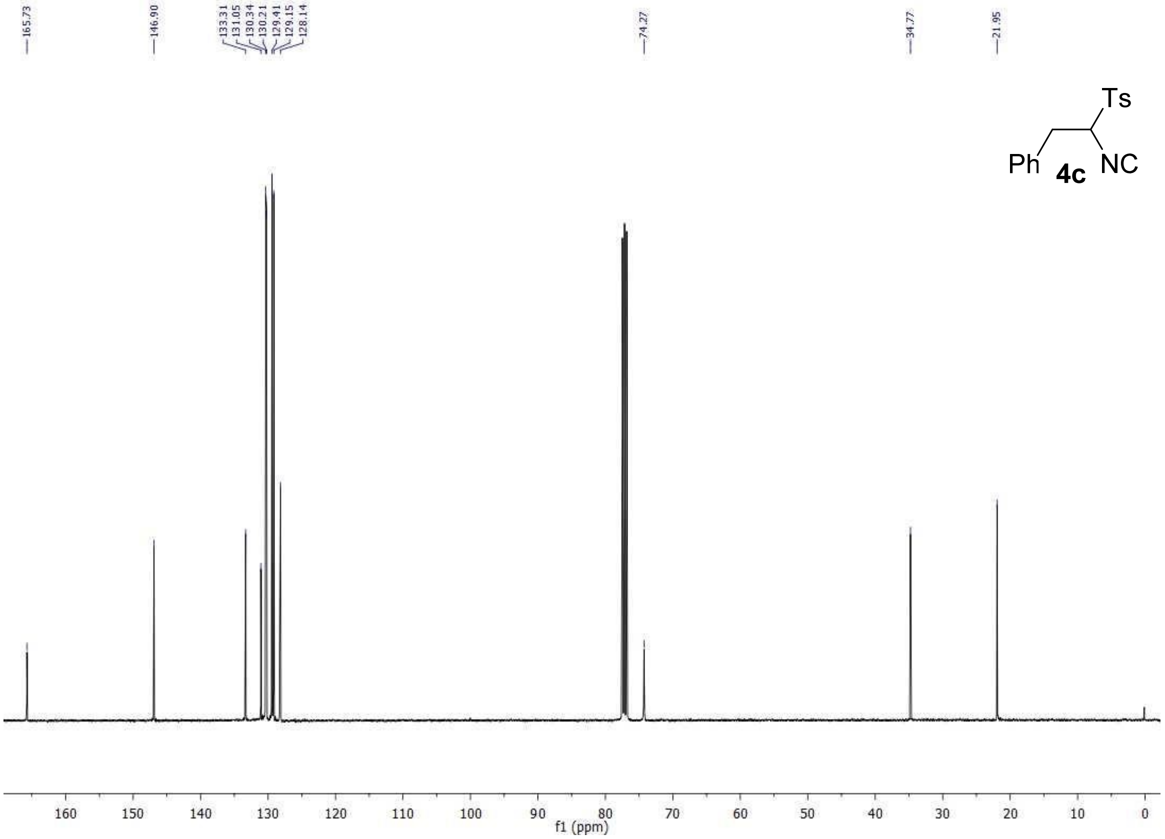
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide (3*R**, 4*R**)-**8p**.



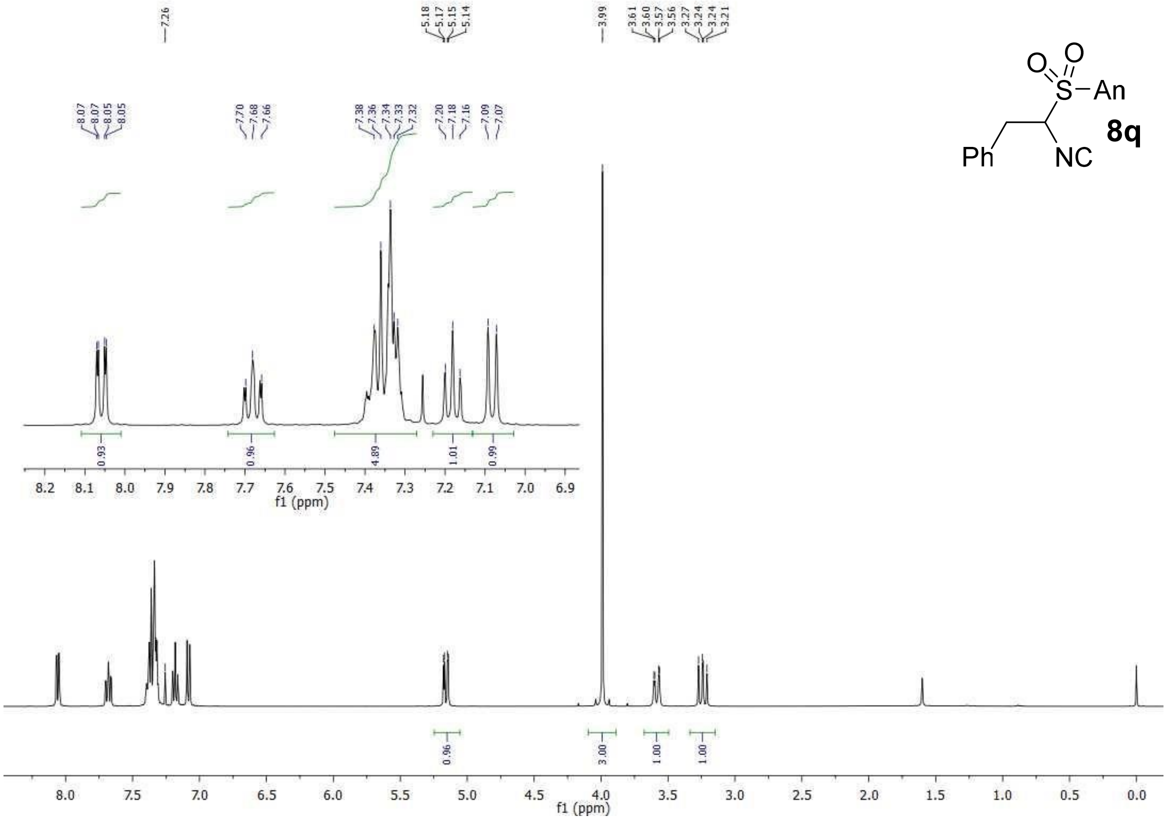
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide (3*R**, 4*R**)-**8p**.



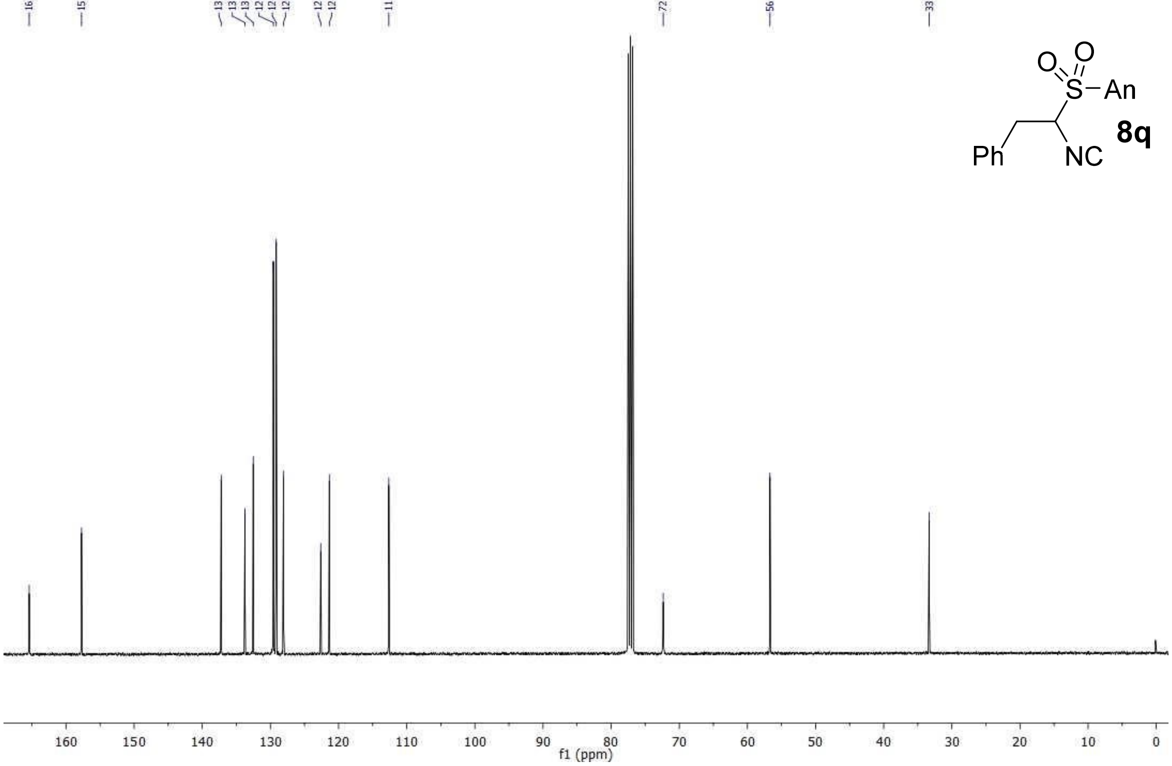
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **4c**.



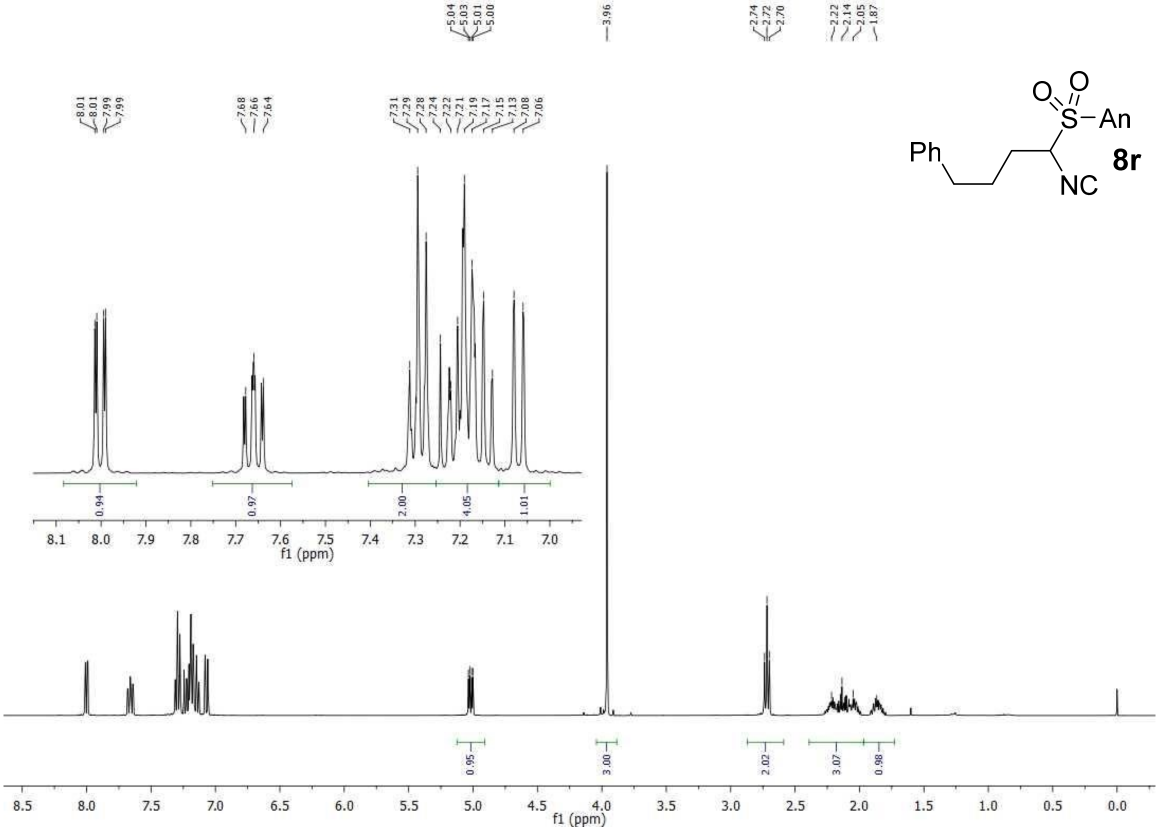
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **4c**.



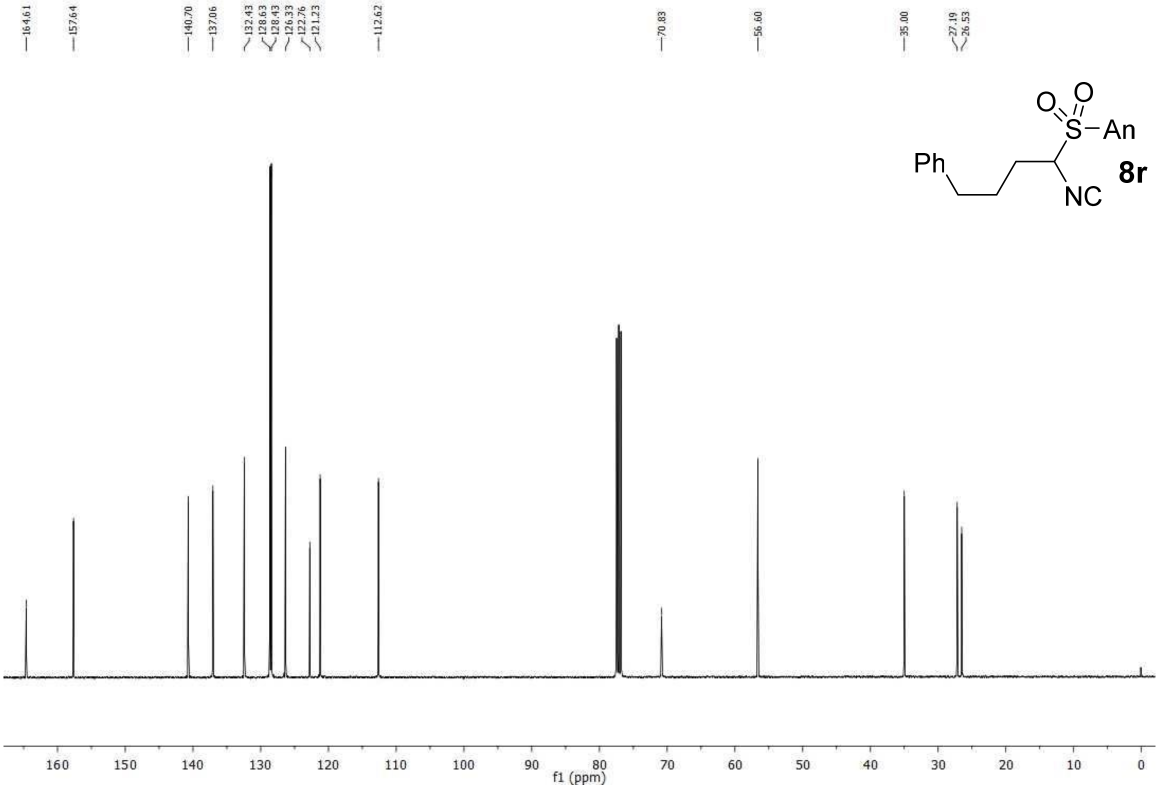
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8q**.



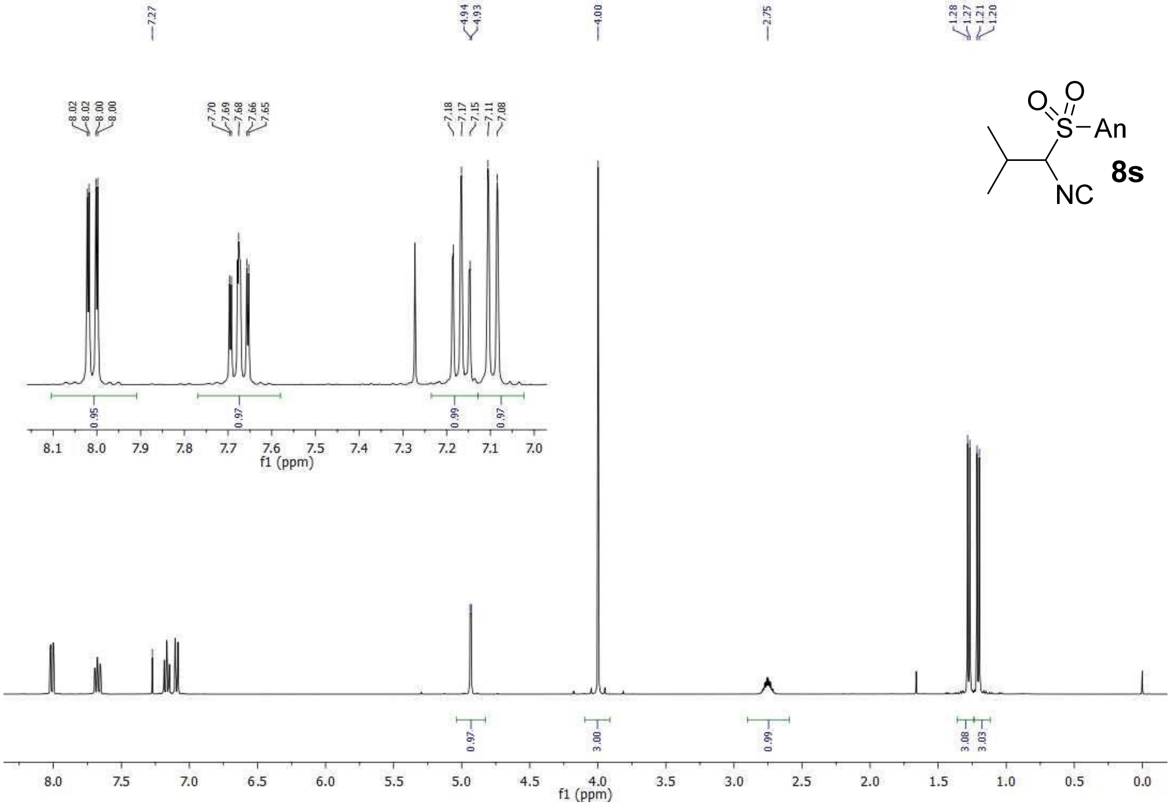
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8q**.



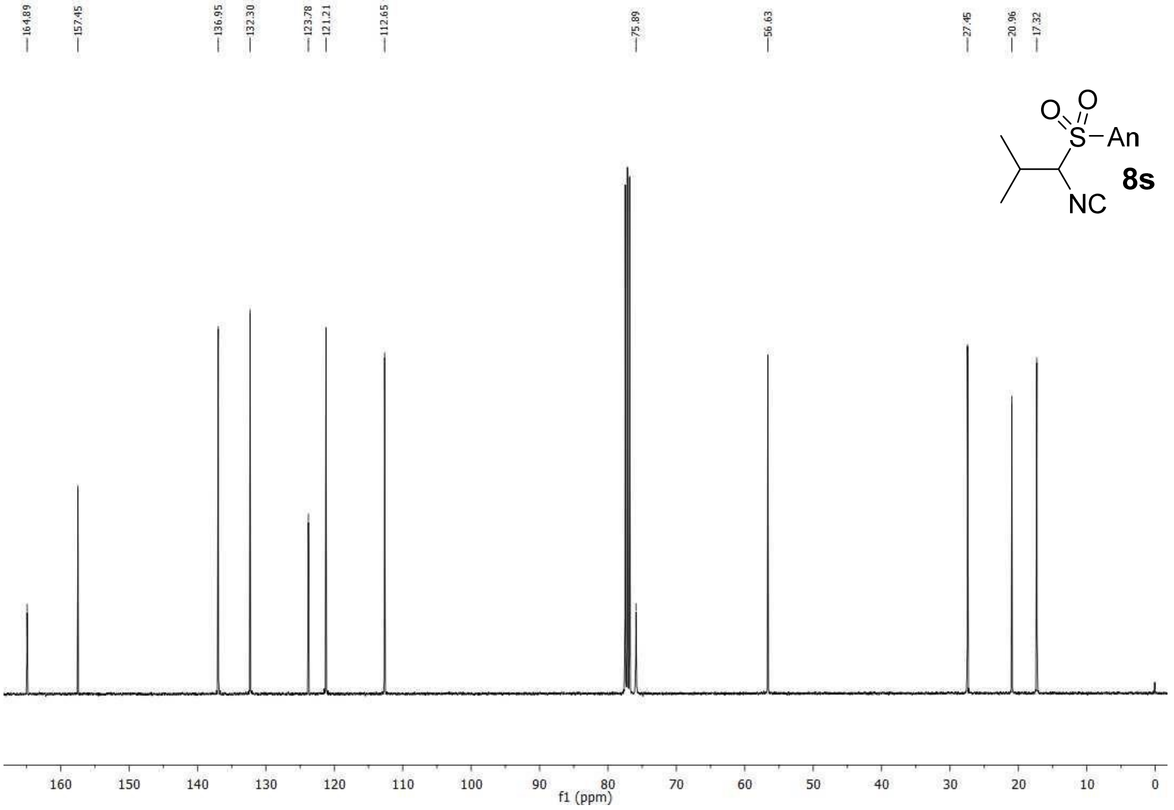
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8r**.



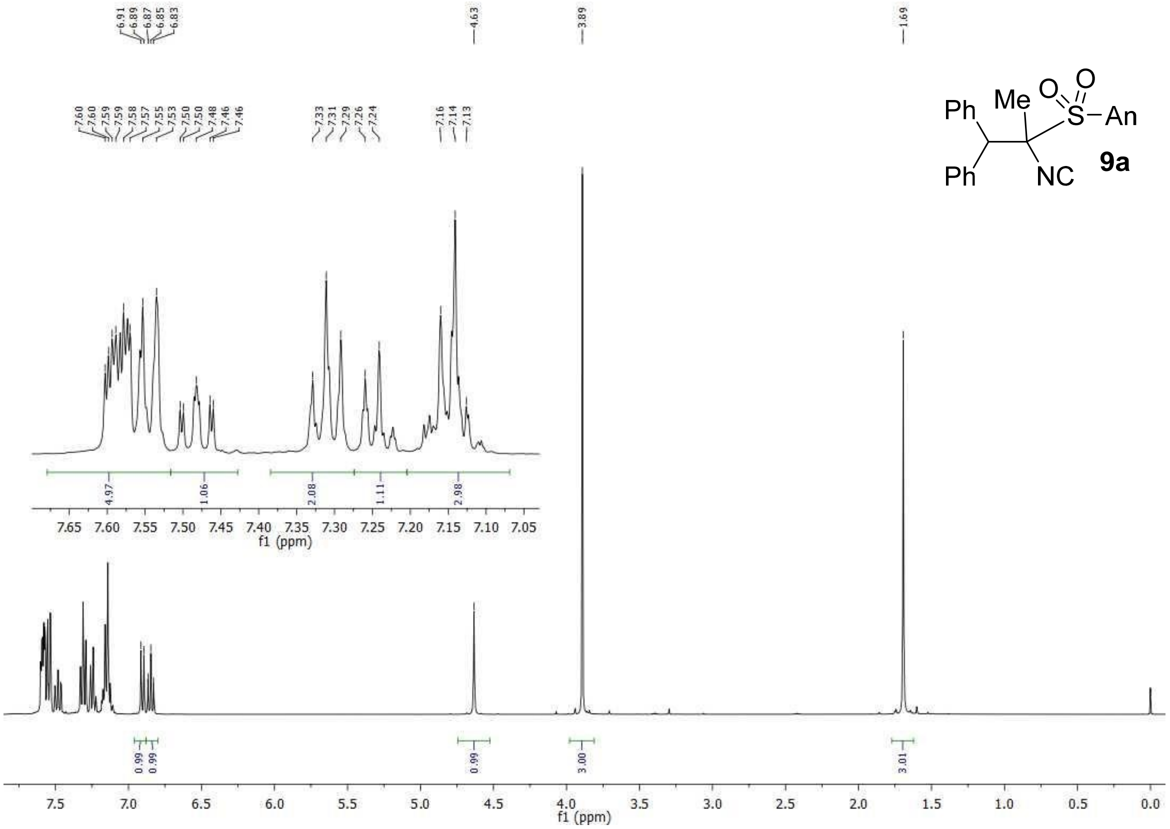
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8r**.



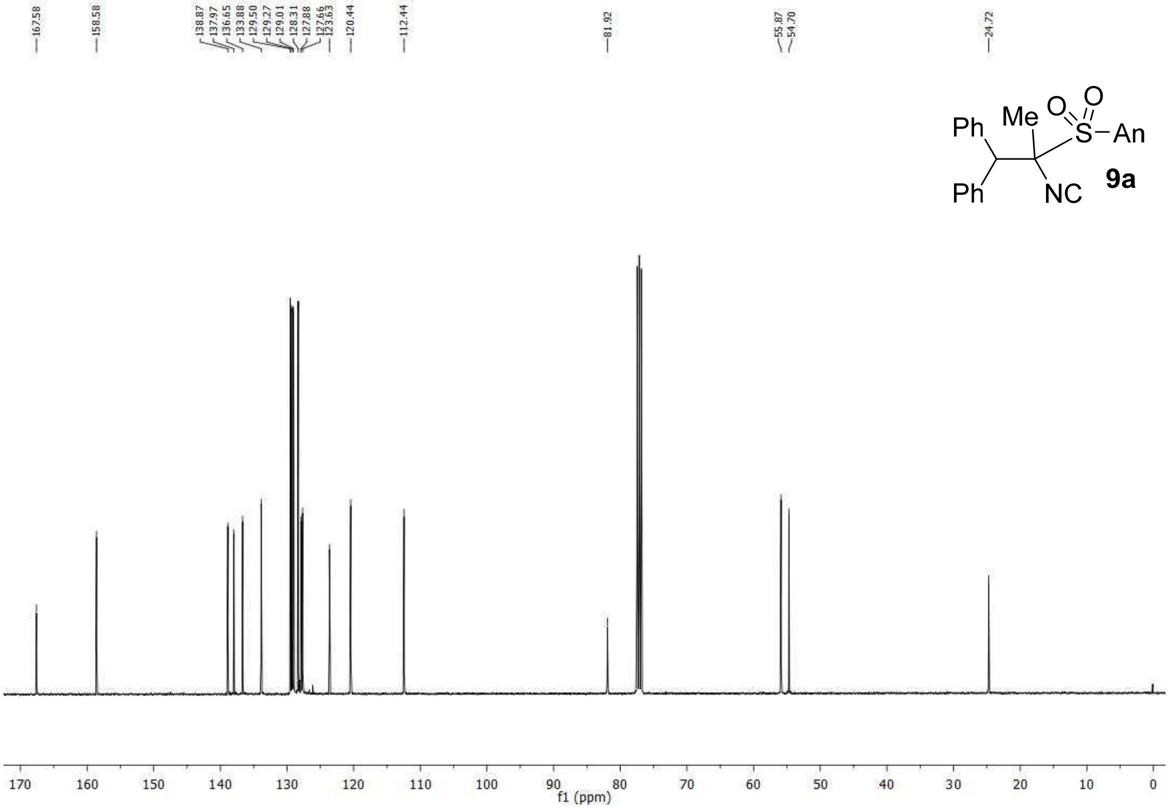
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **8s**.



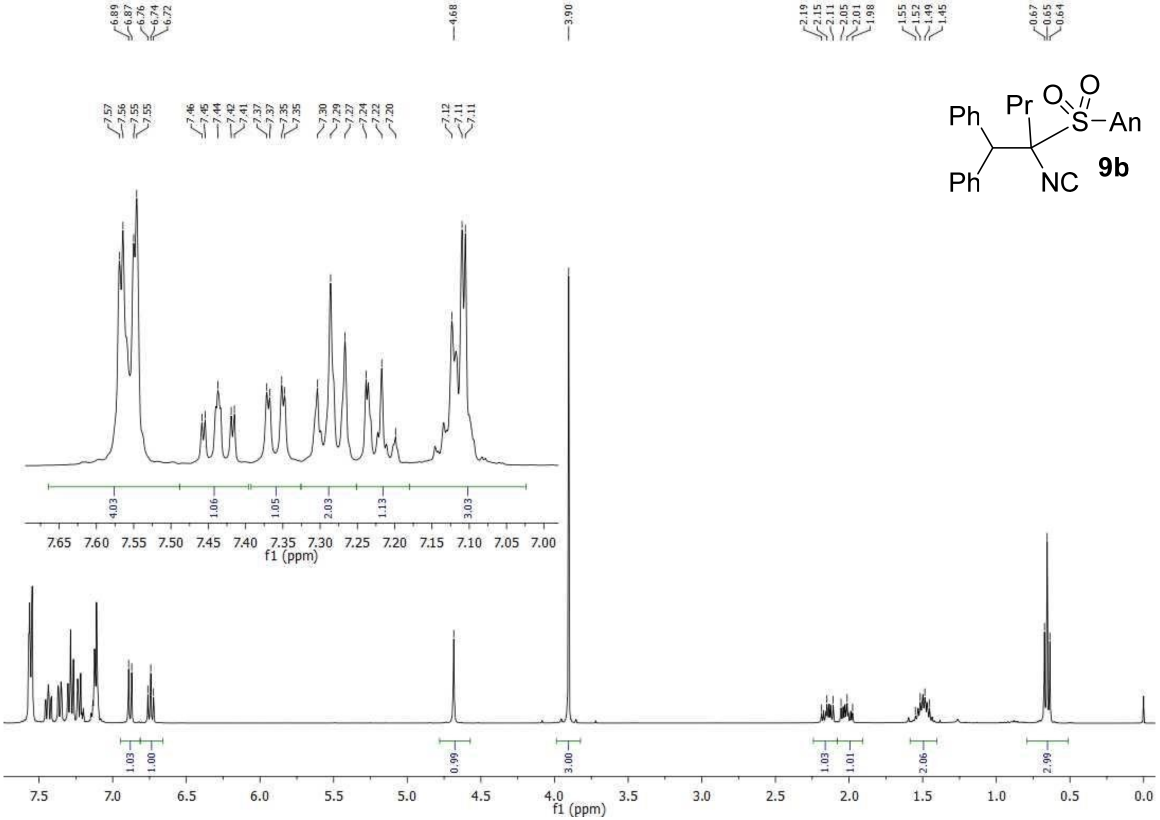
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **8s**.



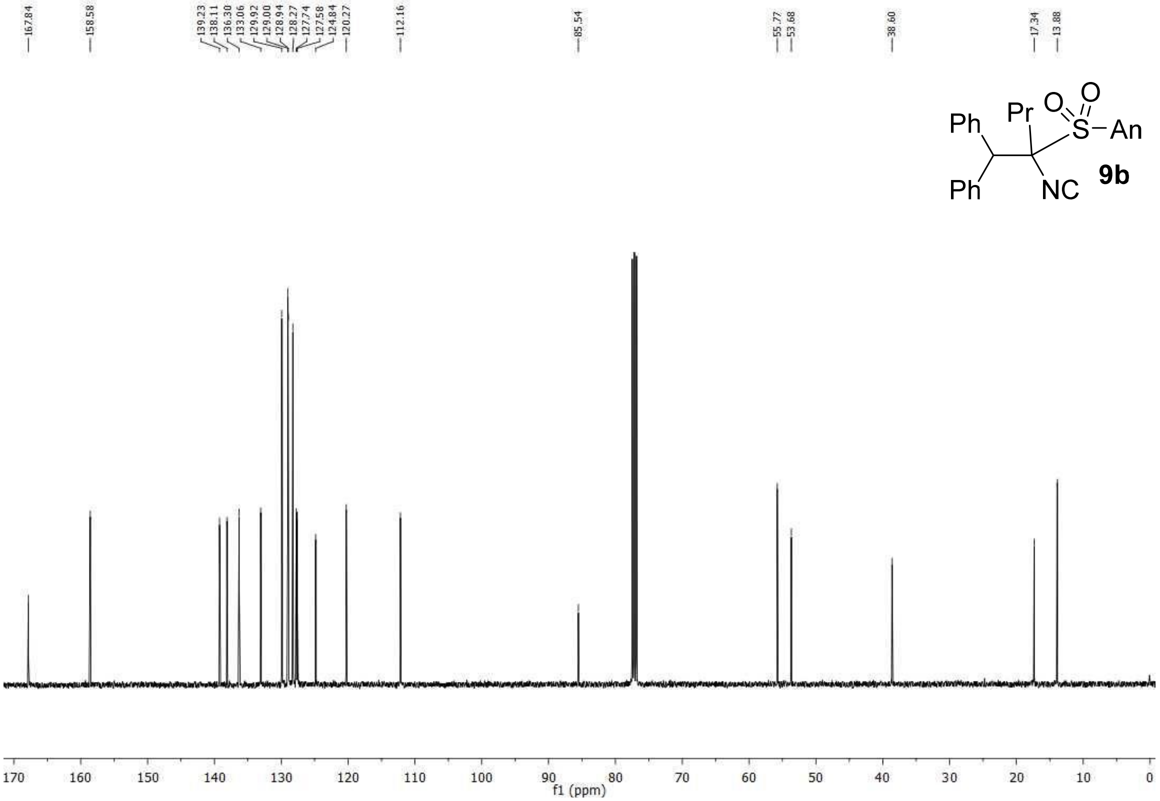
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **9a**.



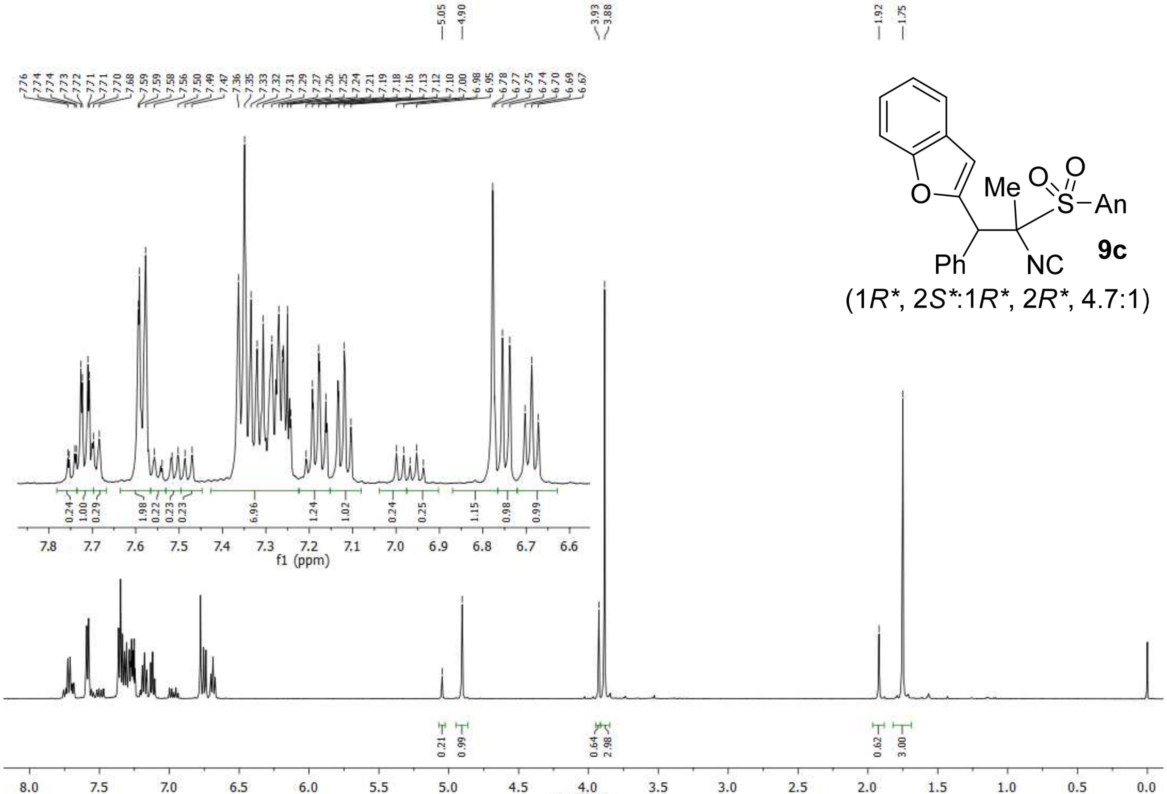
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **9a**.



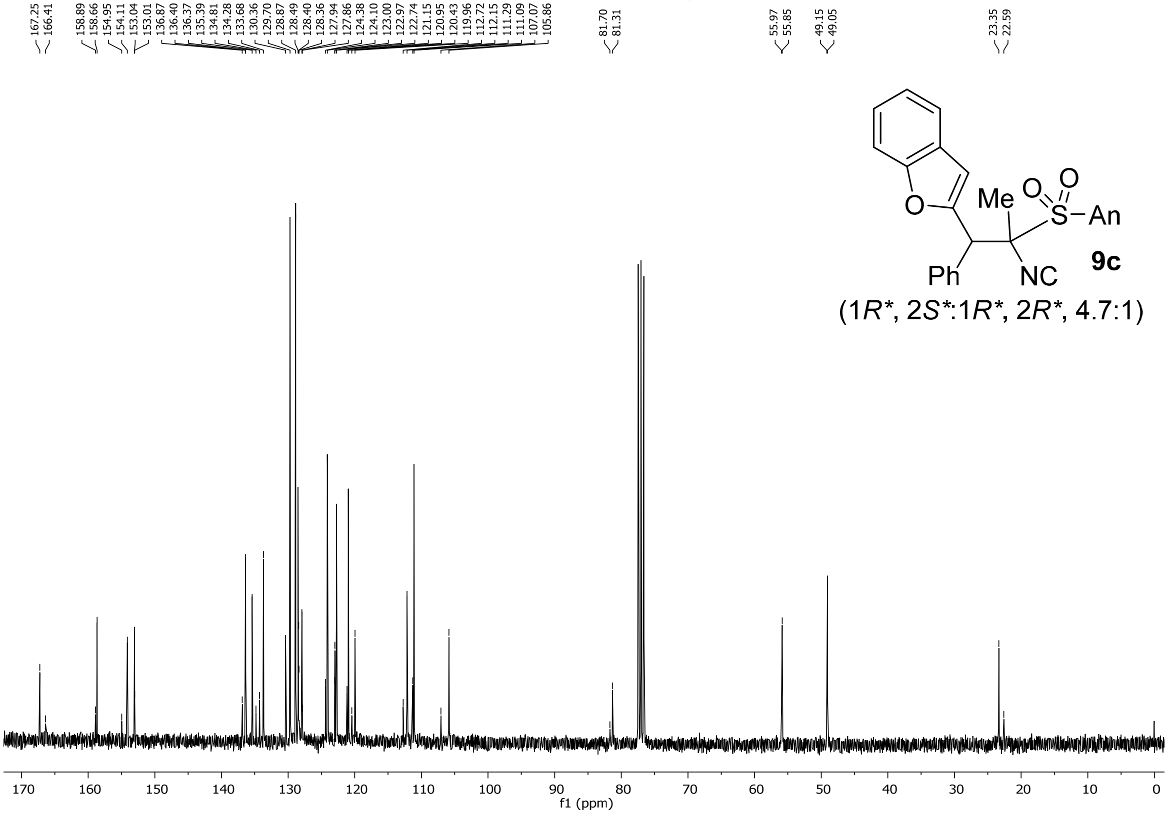
^{1}H NMR (400 MHz, CDCl$_3$) of isocyanide **9b**.



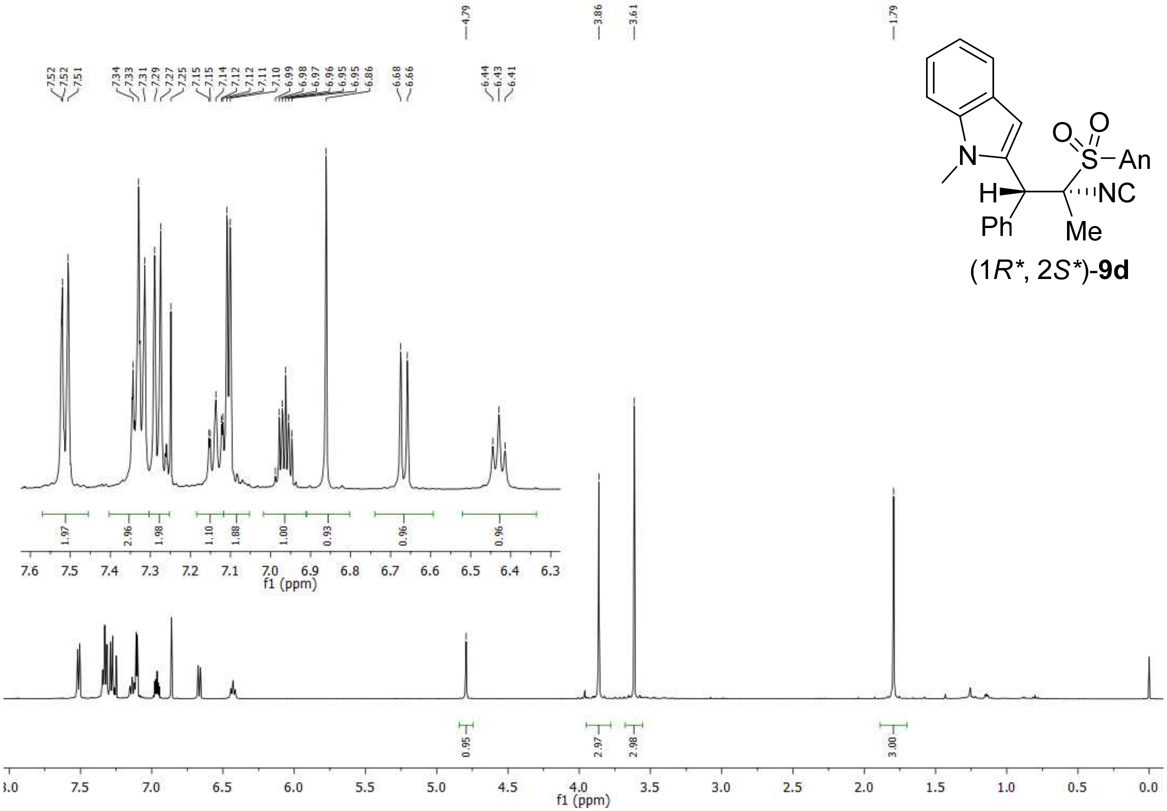
^{13}C NMR (101 MHz, CDCl$_3$) of isocyanide **9b**.



^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide **9c**.

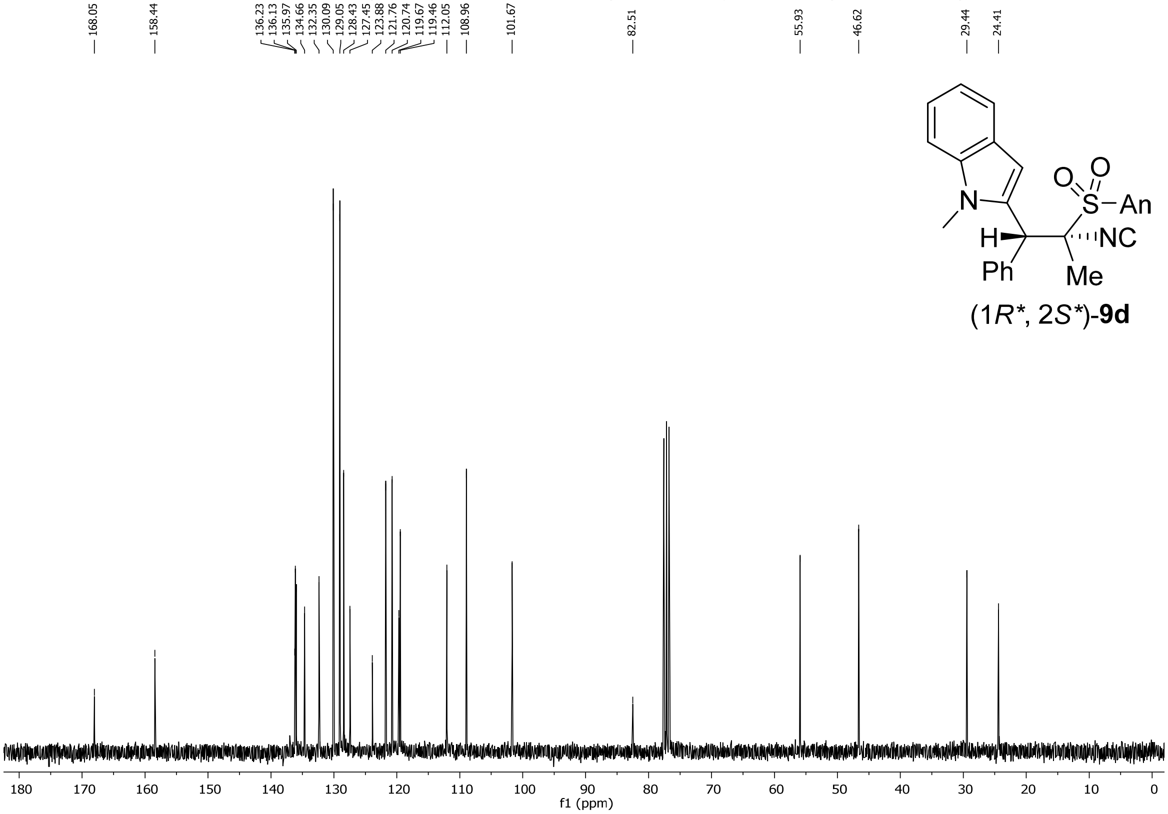


^{13}C NMR (75 MHz, CDCl$_3$) of isocyanide **9c**.



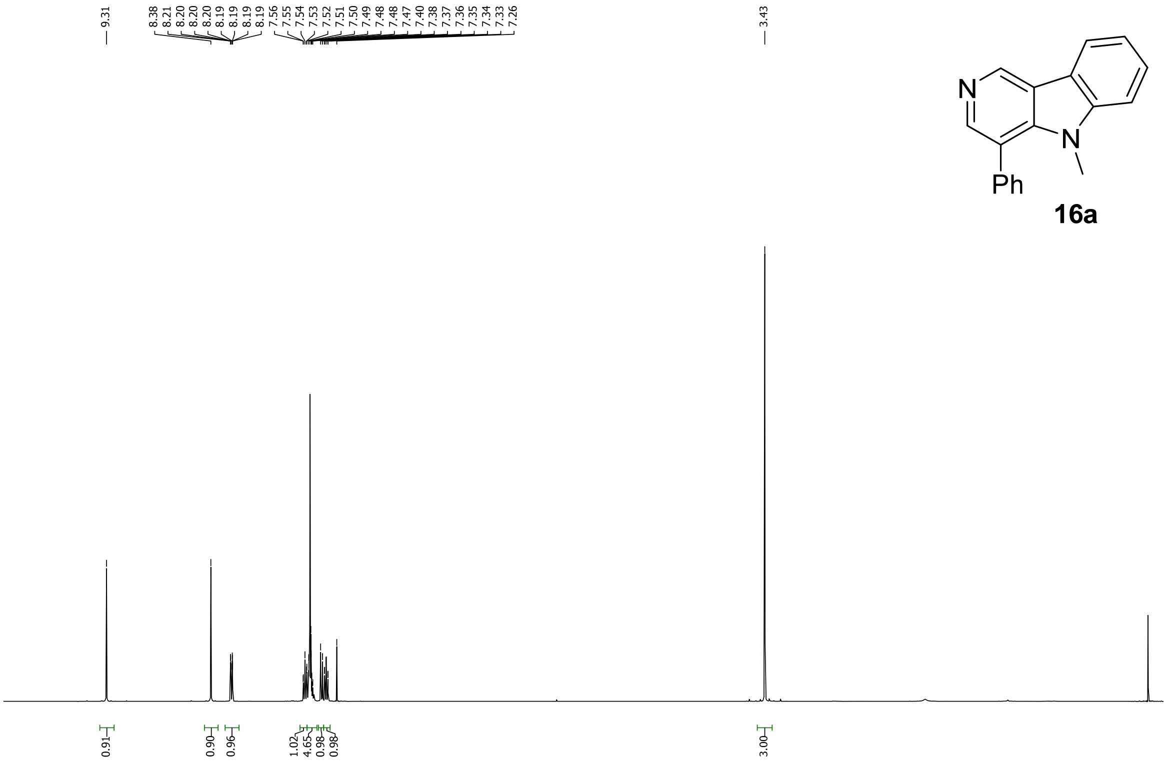
(1*R**, 2*S**)-**9d**

^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**9d**.



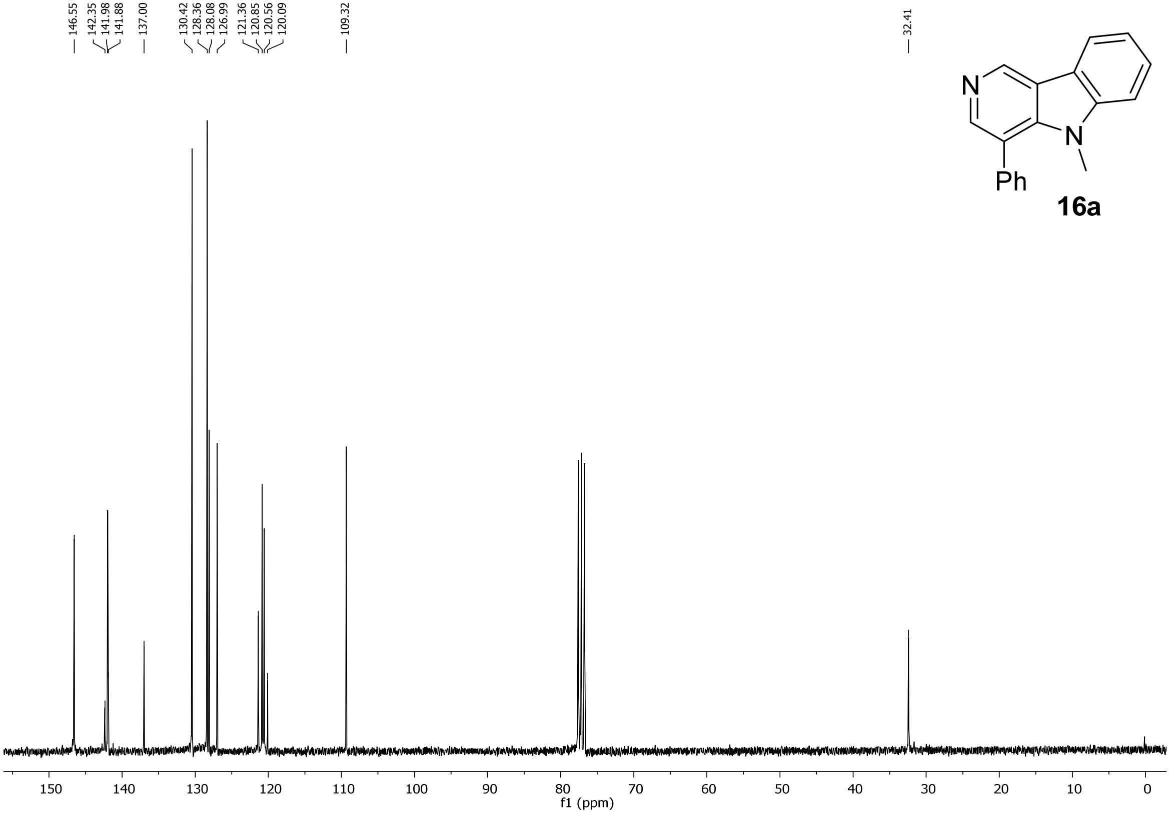
(1*R**, 2*S**)-**9d**

^{13}C NMR (75 MHz, CDCl$_3$) of isocyanide (1*R**, 2*S**)-**9d**.



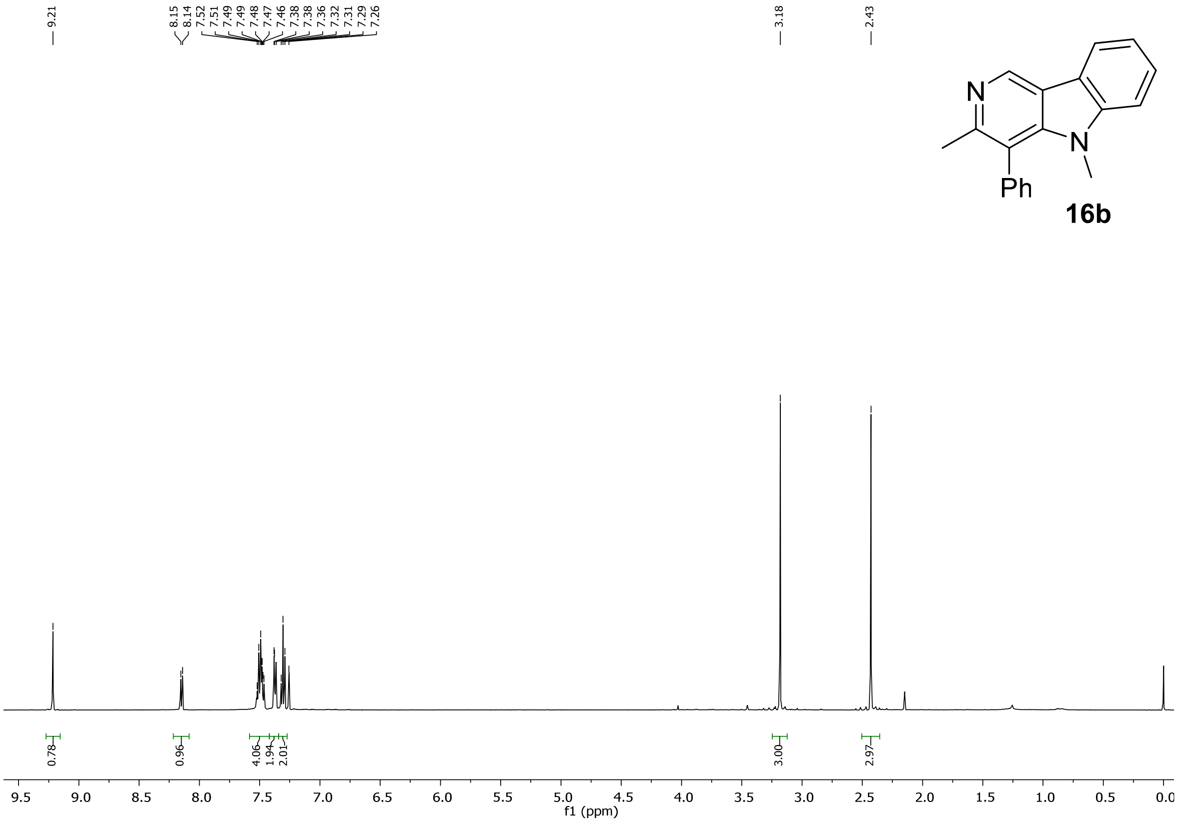
16a

^{1}H NMR (500 MHz, CDCl$_3$) of γ-carboline **16a**.

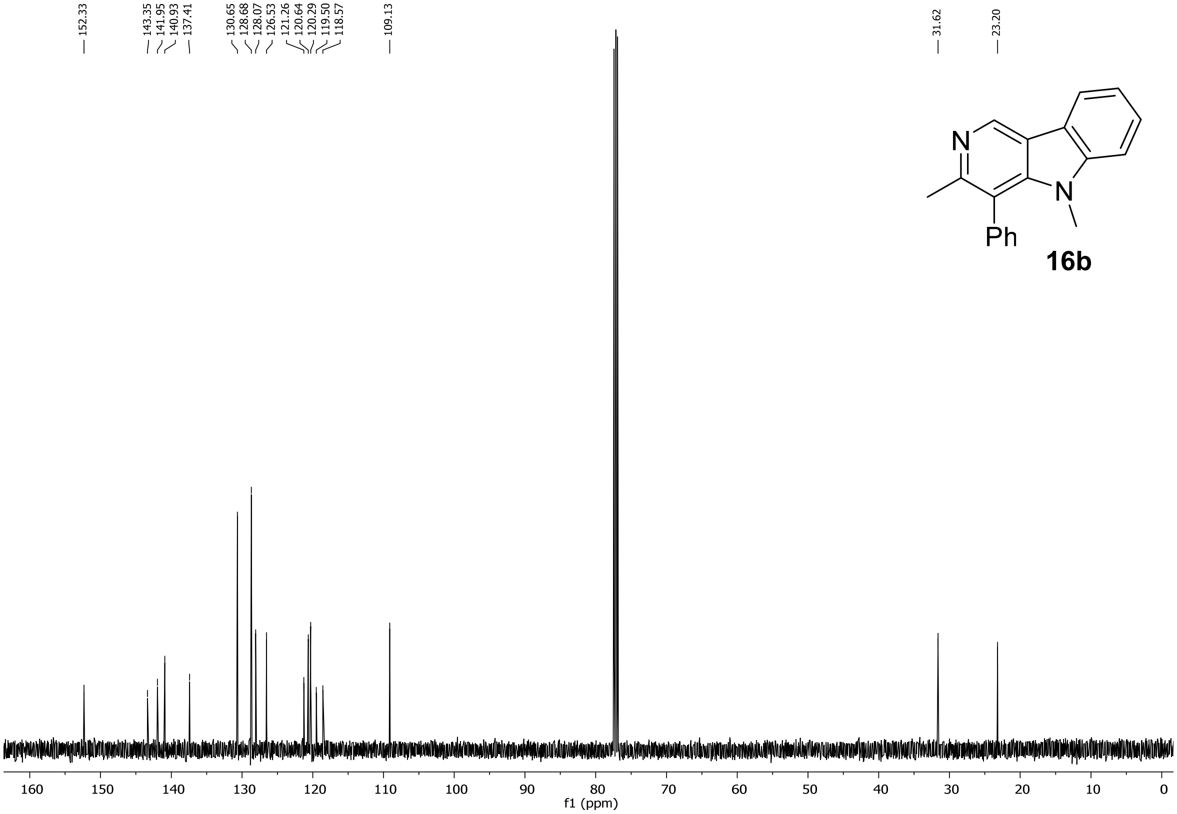


16a

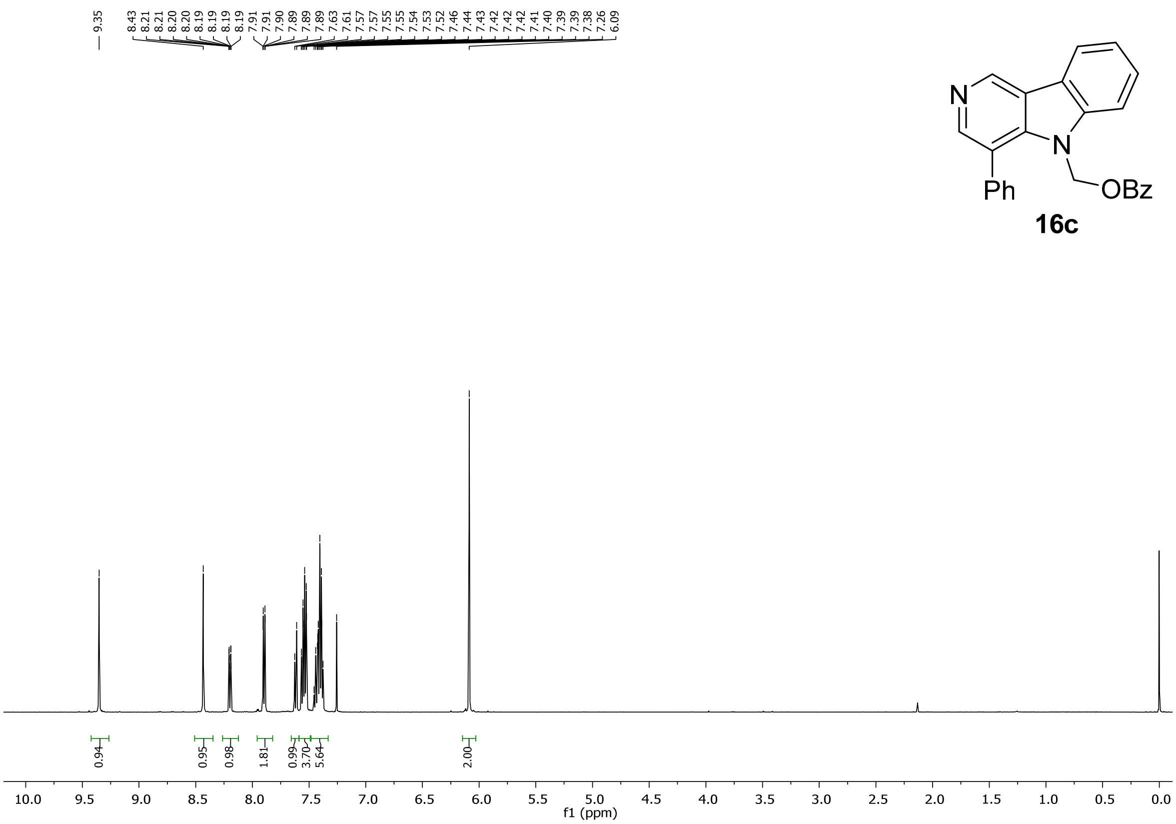
^{13}C NMR (75 MHz, CDCl$_3$) of γ-carboline **16a**.



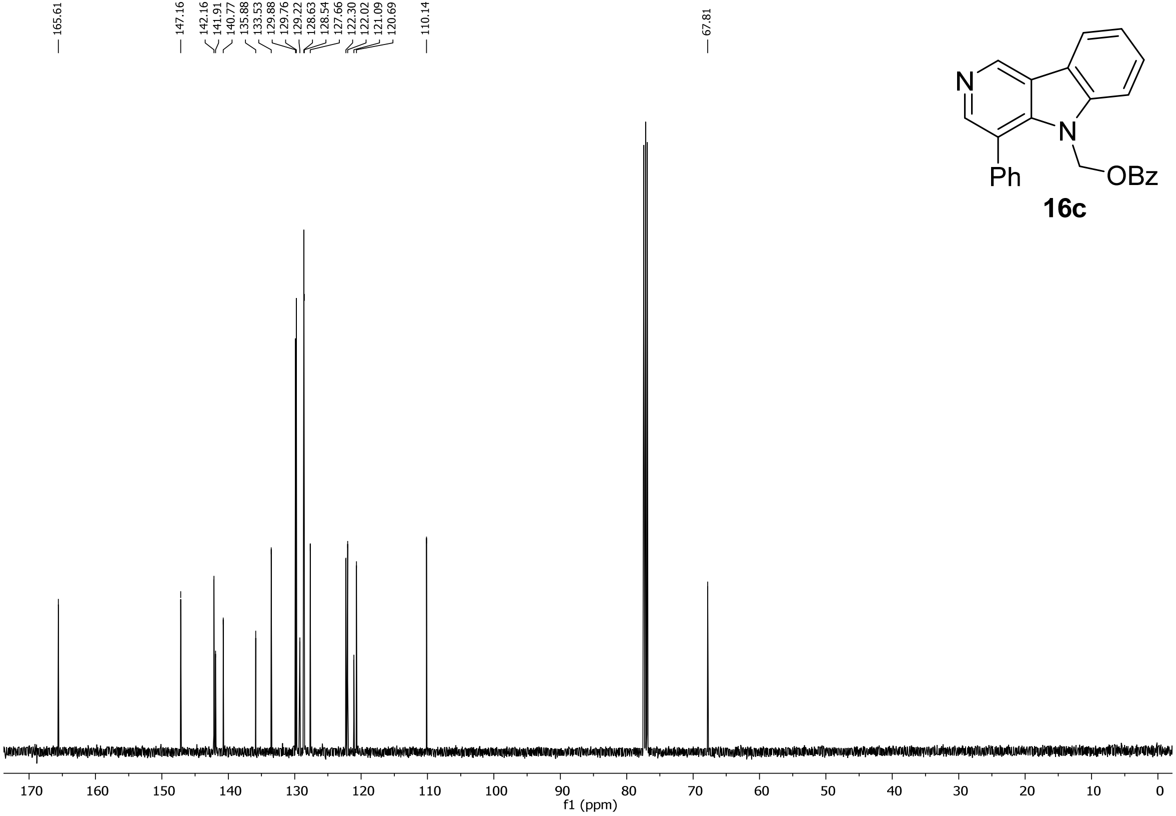
^{1}H NMR (500 MHz, CDCl$_3$) of γ-carboline **16b**.



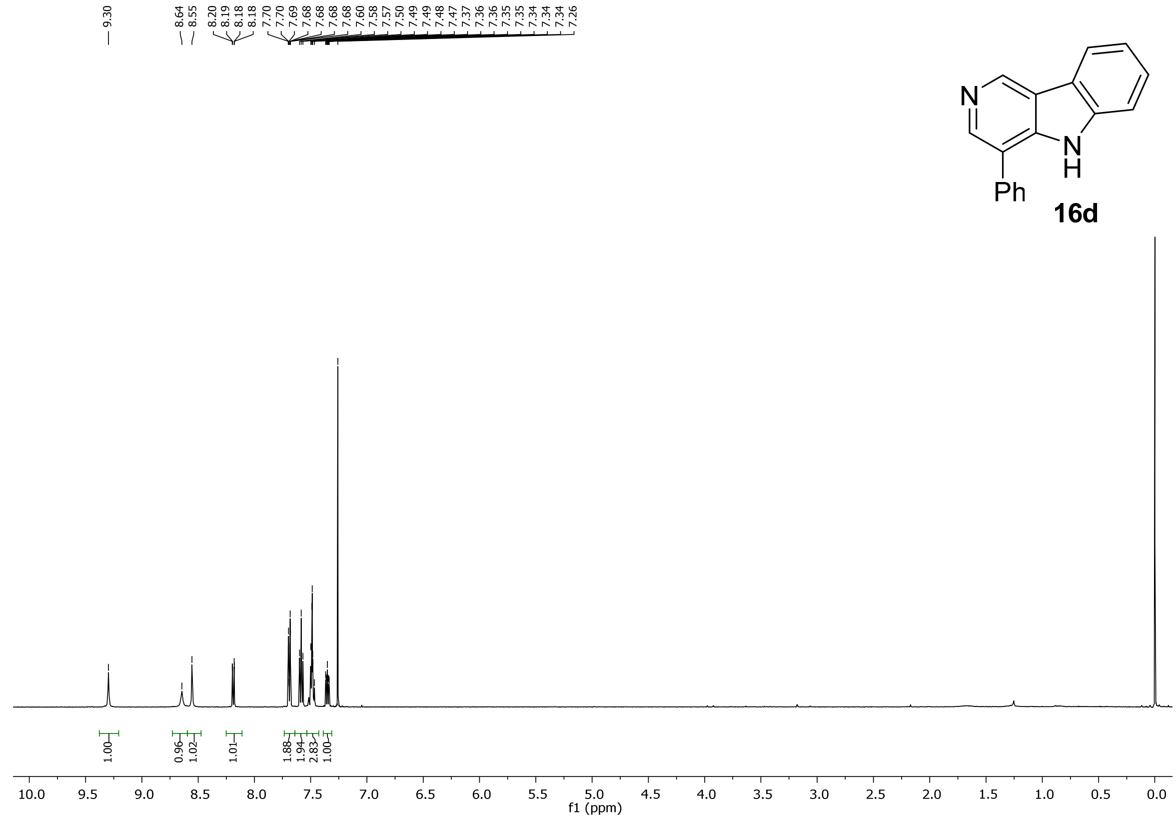
^{13}C NMR (126 MHz, CDCl$_3$) of γ-carboline **16b**.



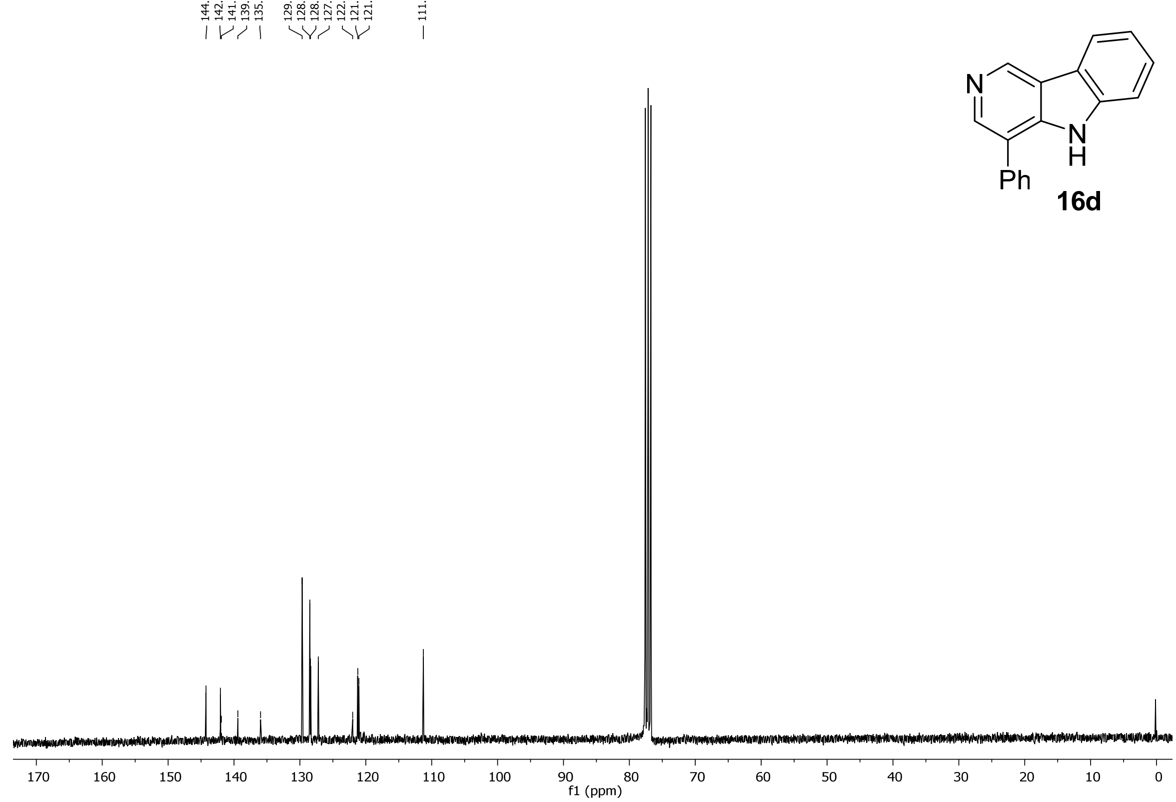
^{1}H NMR (500 MHz, CDCl$_3$) of γ-carboline **16c**.



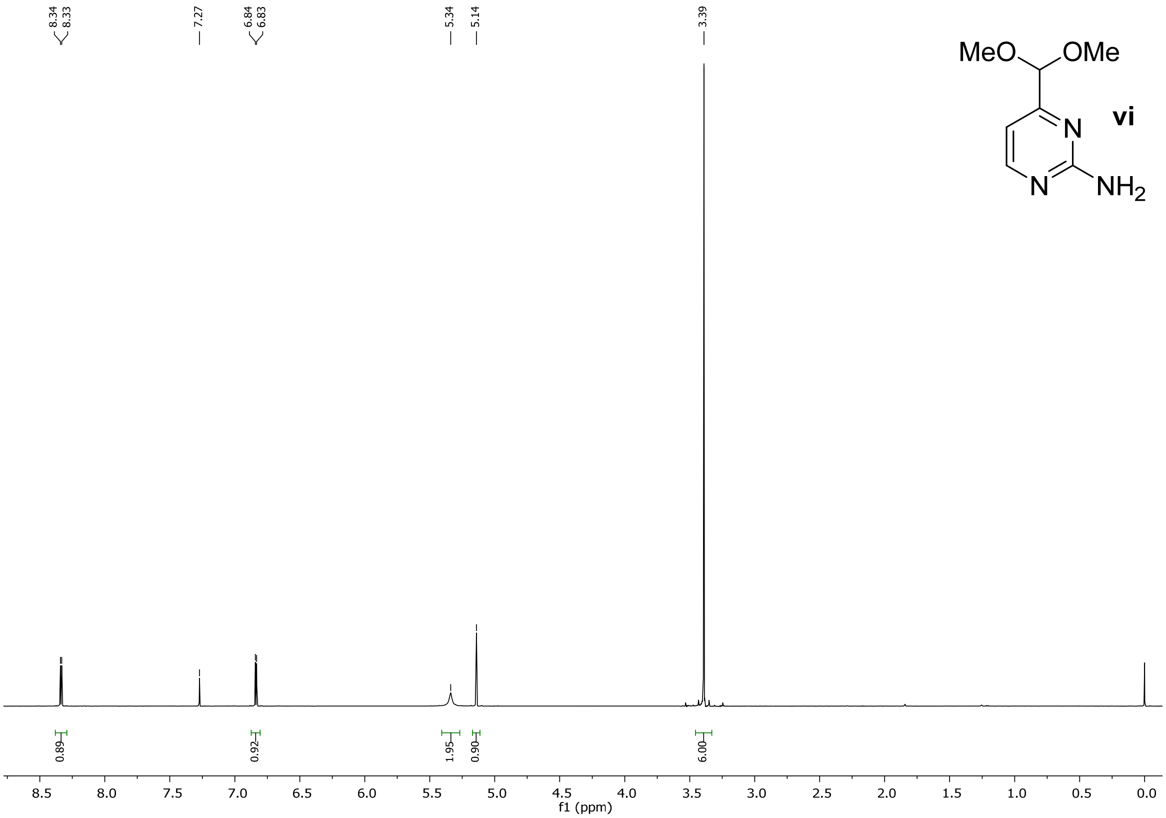
^{13}C NMR (126 MHz, CDCl$_3$) of γ-carboline **16c**.



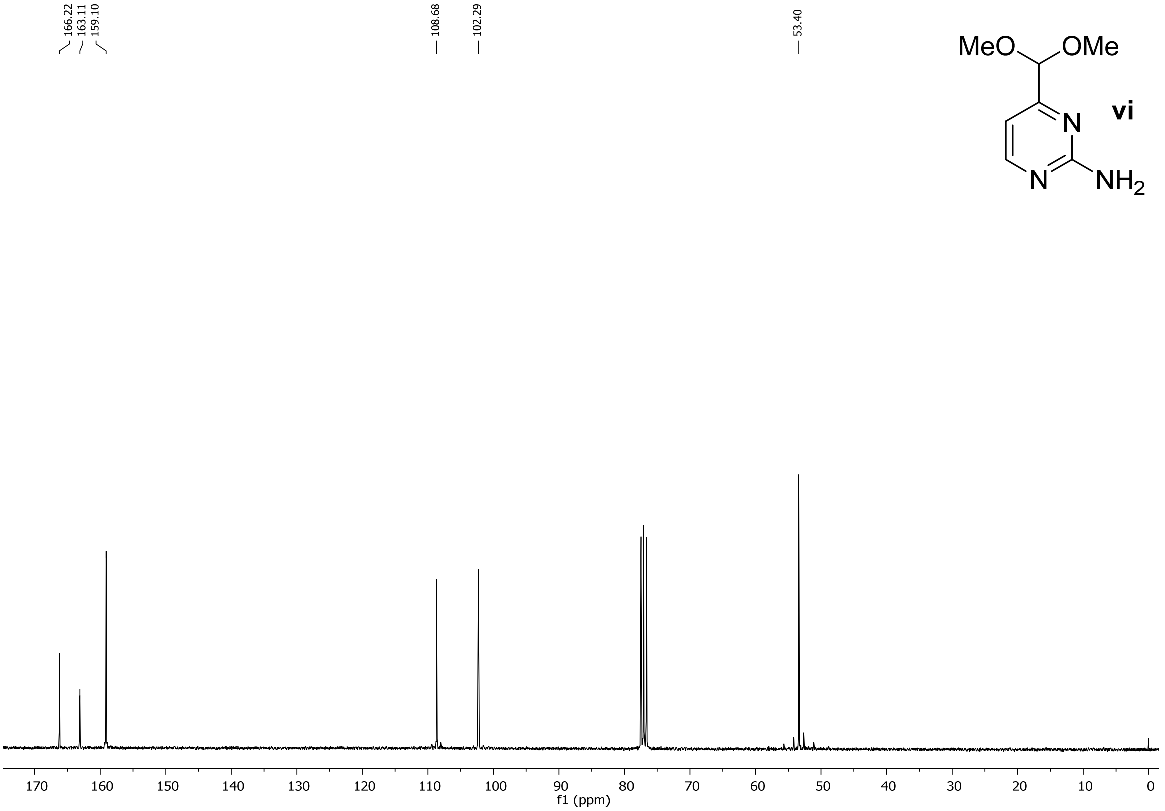
^{1}H NMR (500 MHz, CDCl$_3$) of γ-carboline **16d**.



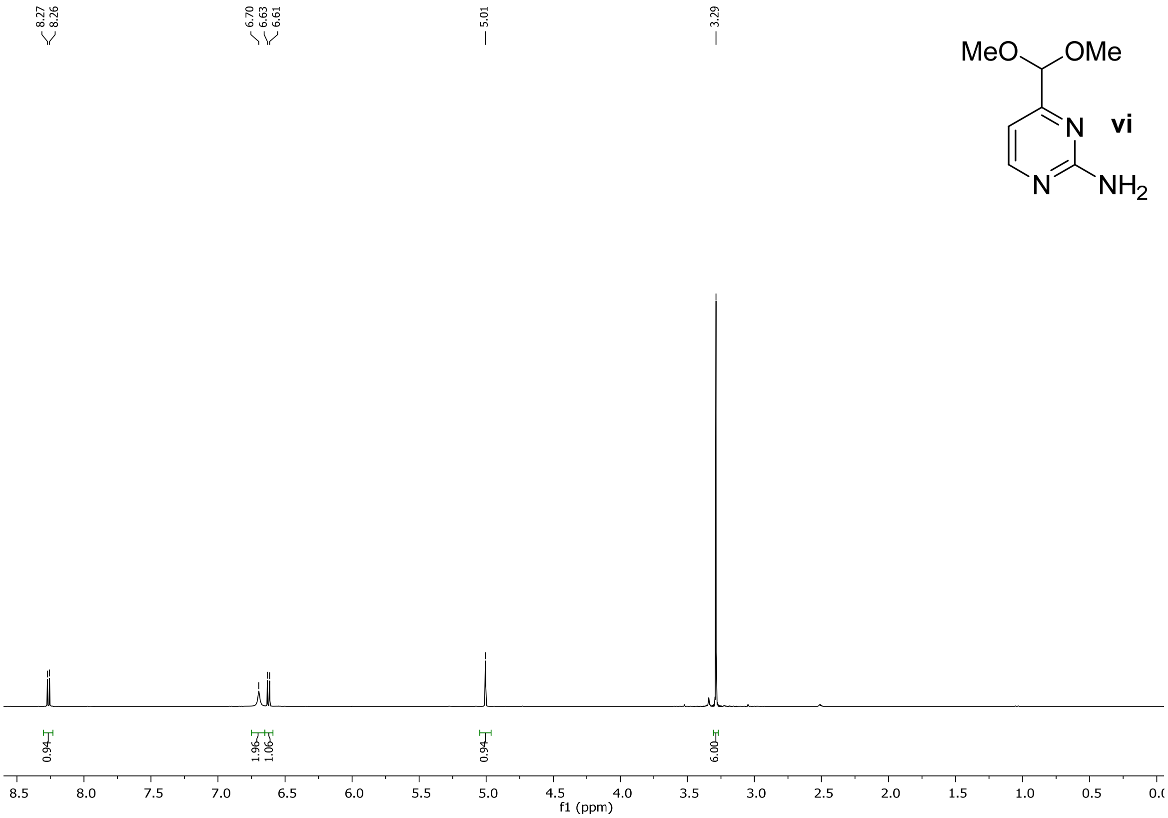
^{13}C NMR (75 MHz, CDCl$_3$) of γ-carboline **16d**.



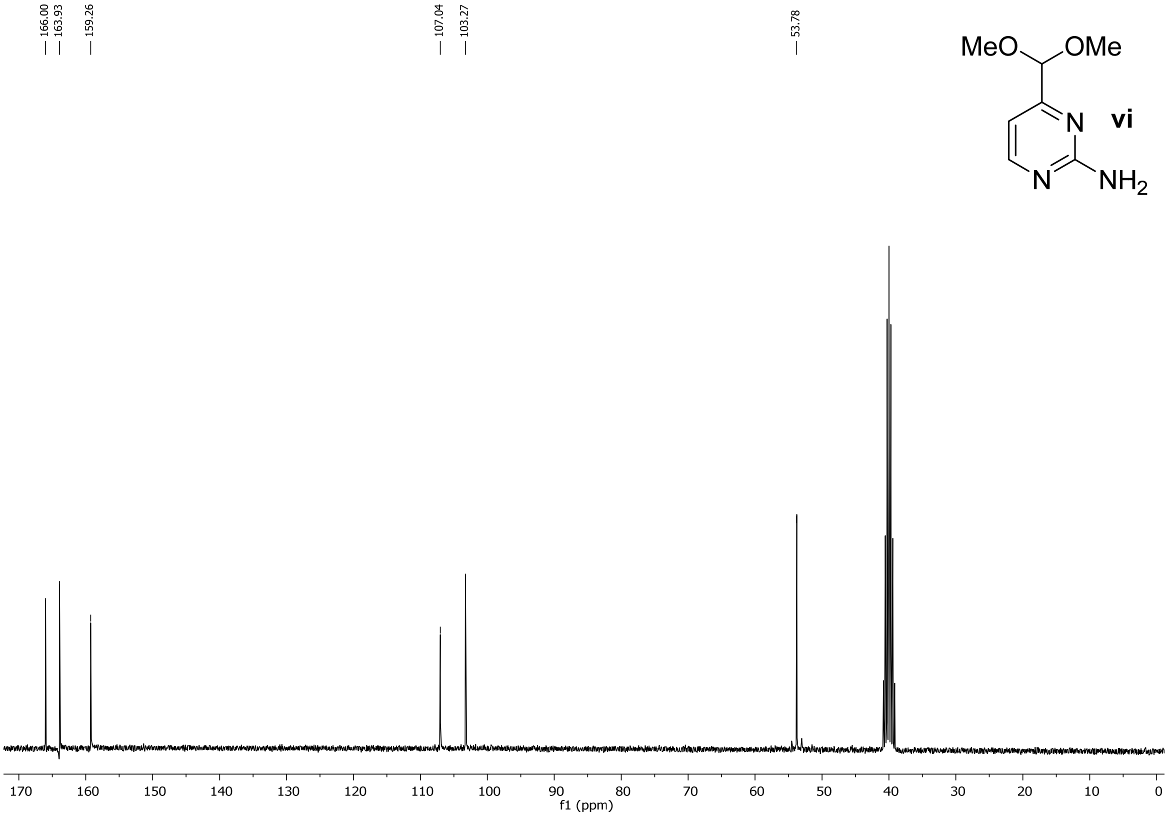
^{1}H NMR (500 MHz, CDCl$_3$) of pyrimidine **vi**.



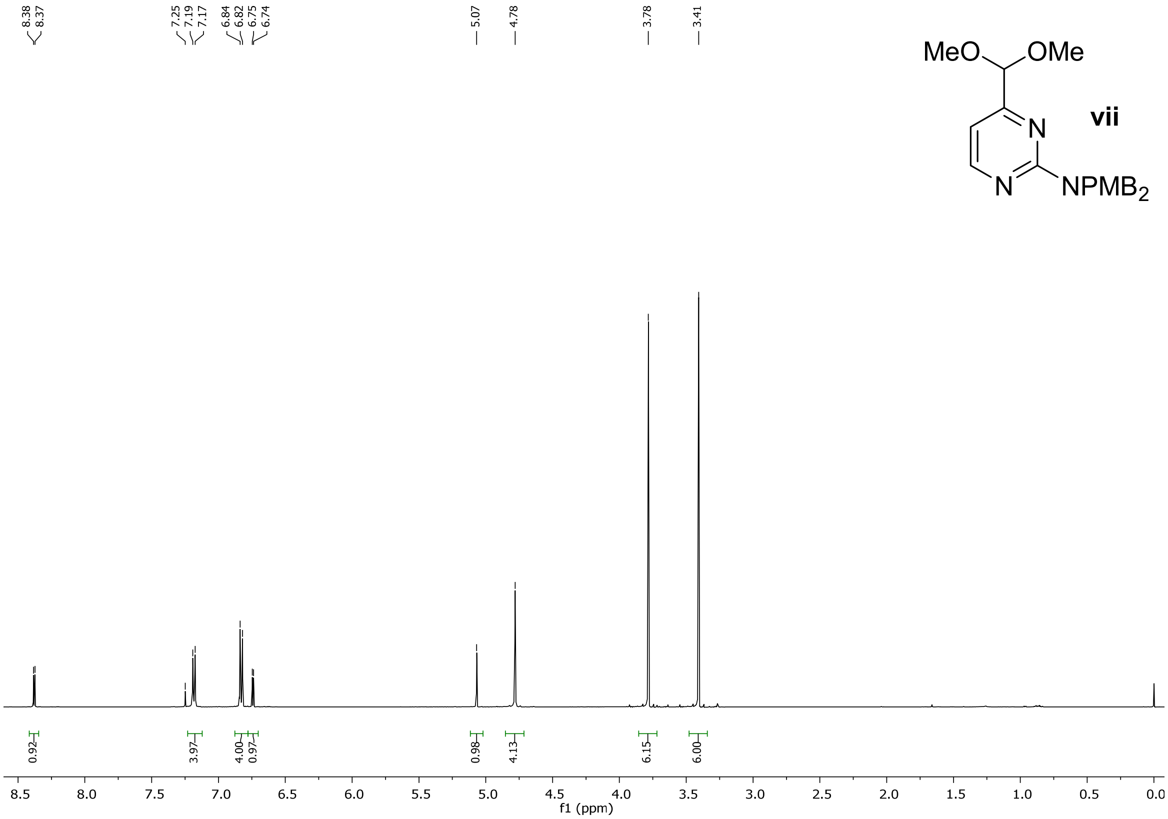
^{13}C NMR (75 MHz, CDCl$_3$) of pyrimidine **vi**.



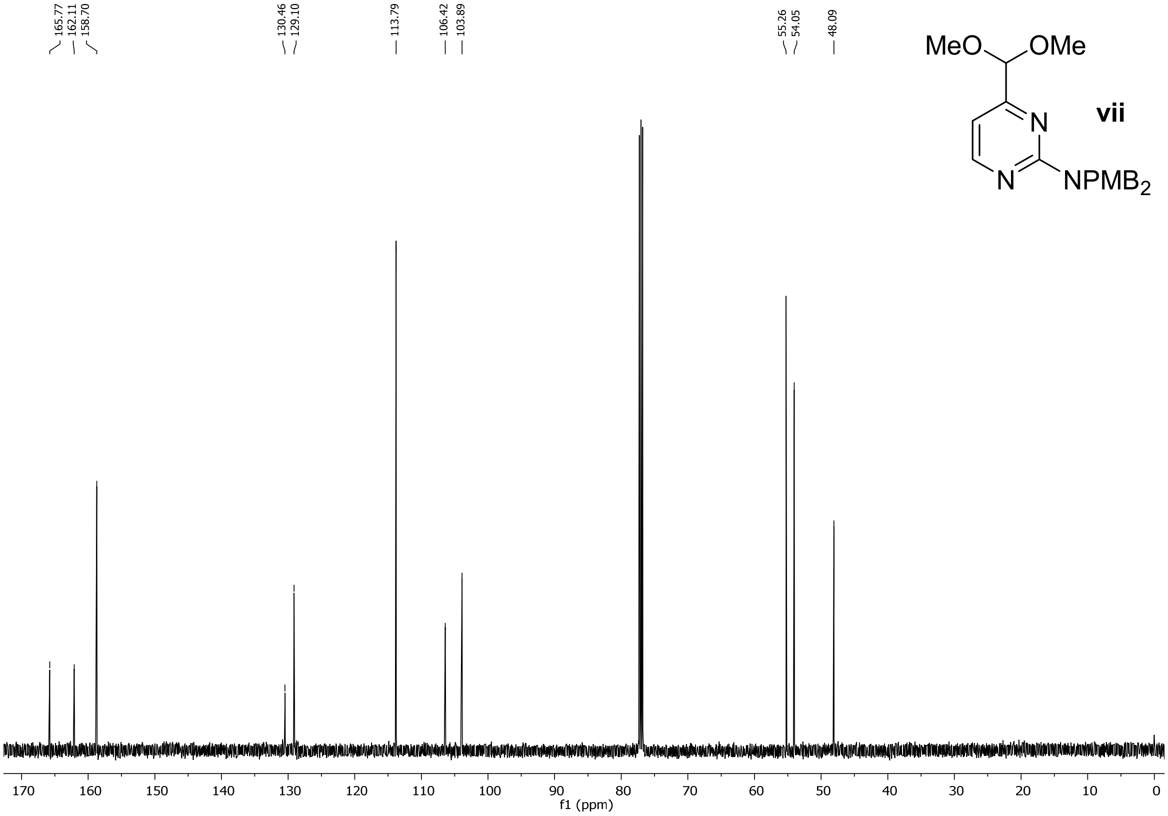
^{1}H NMR (300 MHz, DMSO-d$_6$) of pyrimidine **vi**.



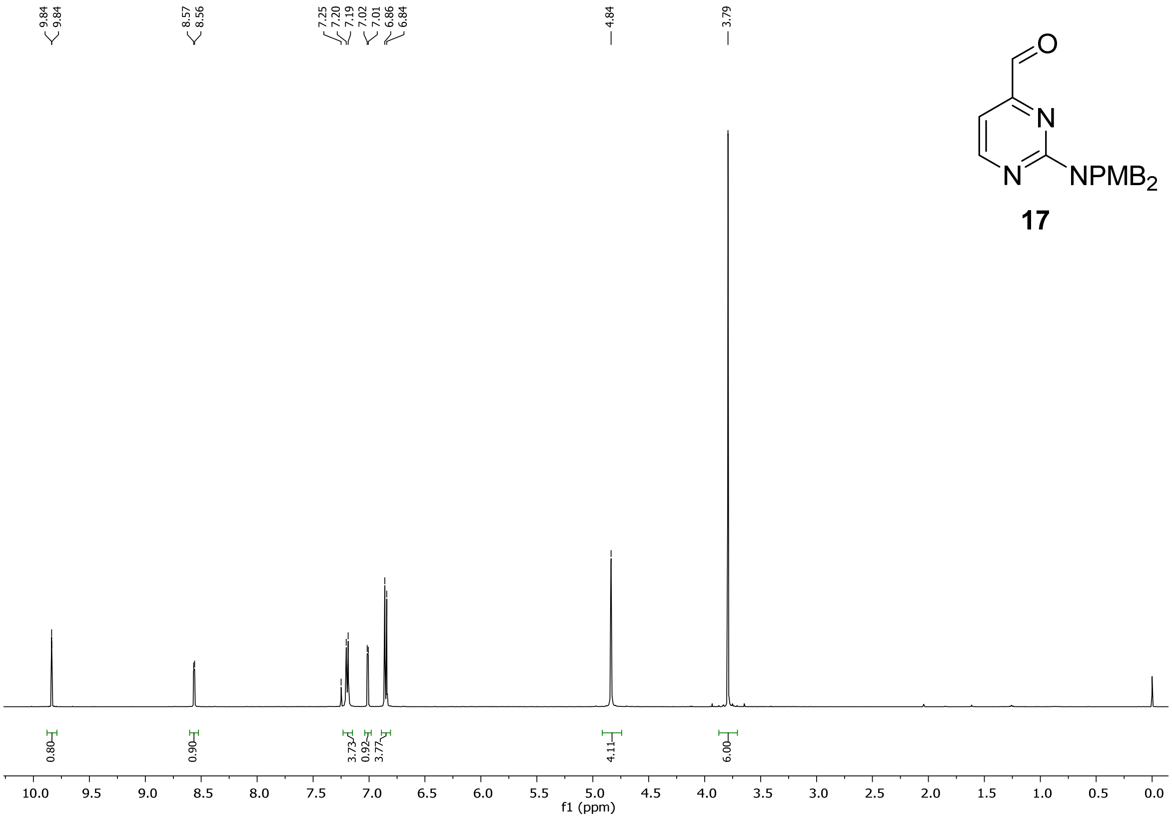
^{13}C NMR (75 MHz, DMSO-d$_6$) of pyrimidine **vi**.



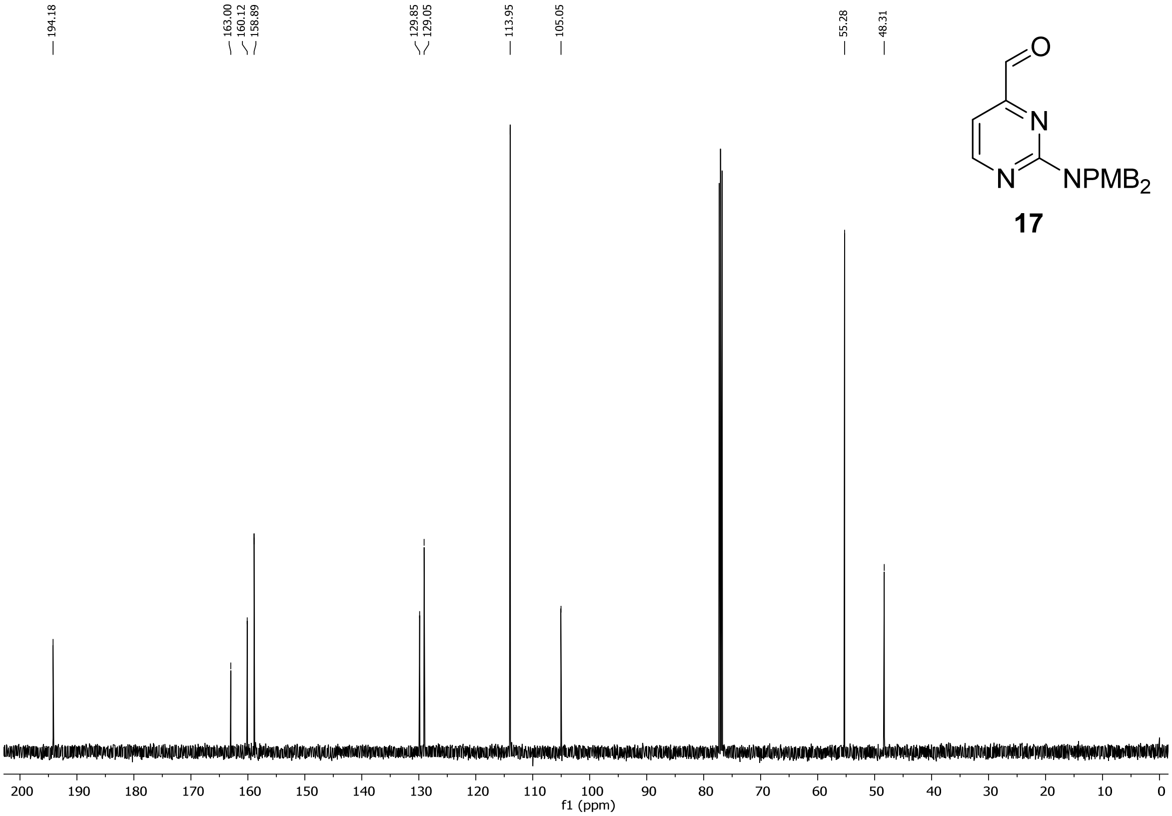
^{1}H NMR (500 MHz, CDCl$_3$) of pyrimidine **vii**.



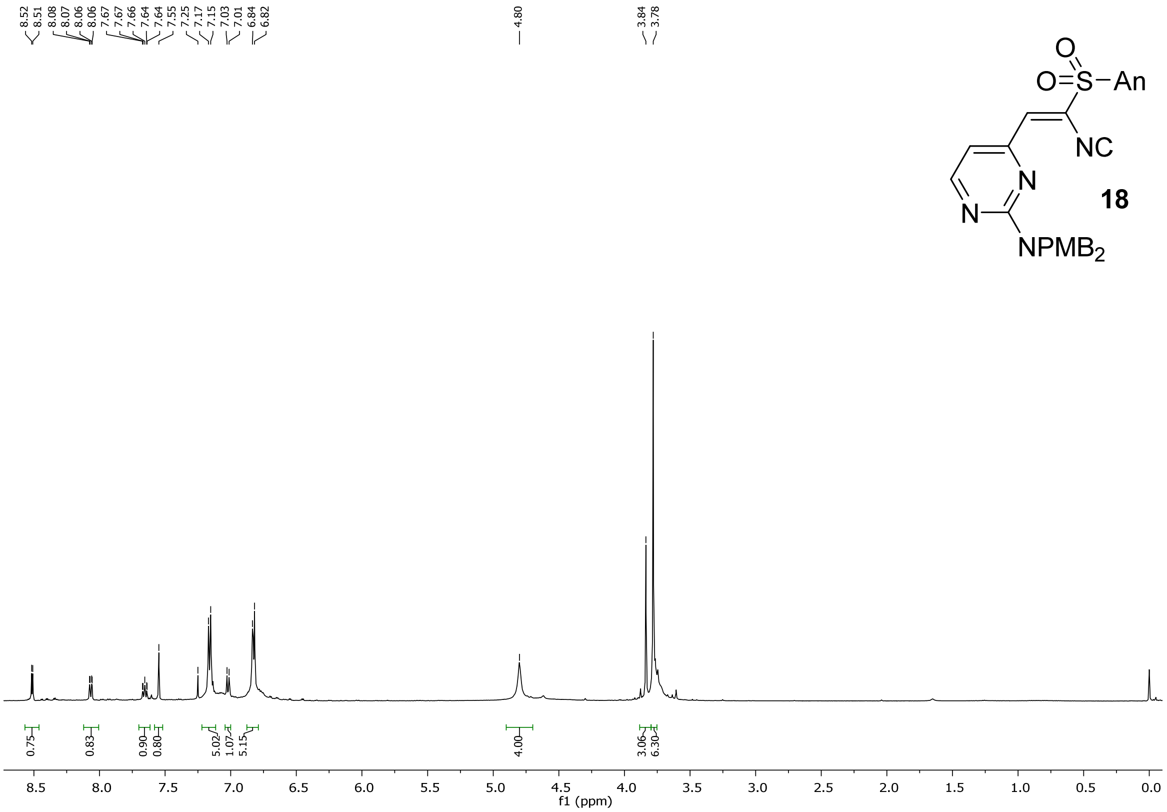
^{13}C NMR (126 MHz, CDCl$_3$) of pyrimidine **vii**.



^{1}H NMR (500 MHz, CDCl$_3$) of pyrimidine **17**.

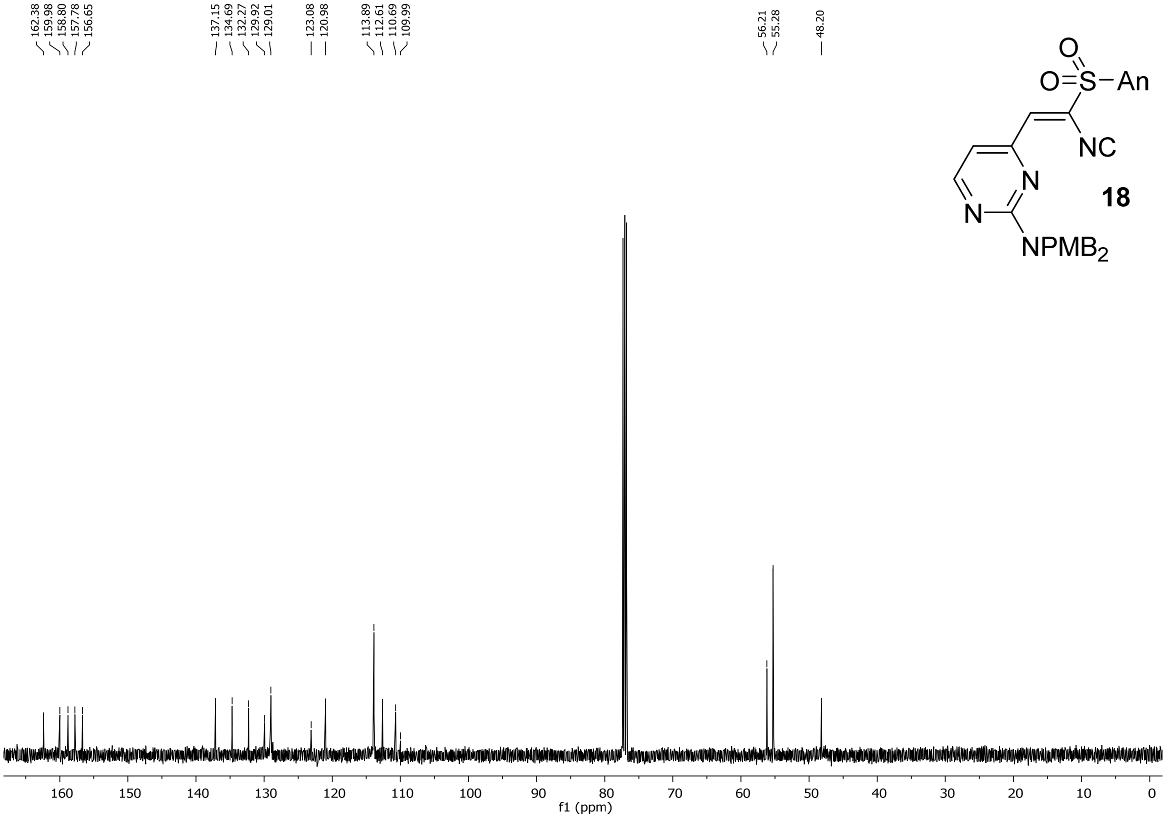


^{13}C NMR (126 MHz, CDCl$_3$) of pyrimidine **17**.



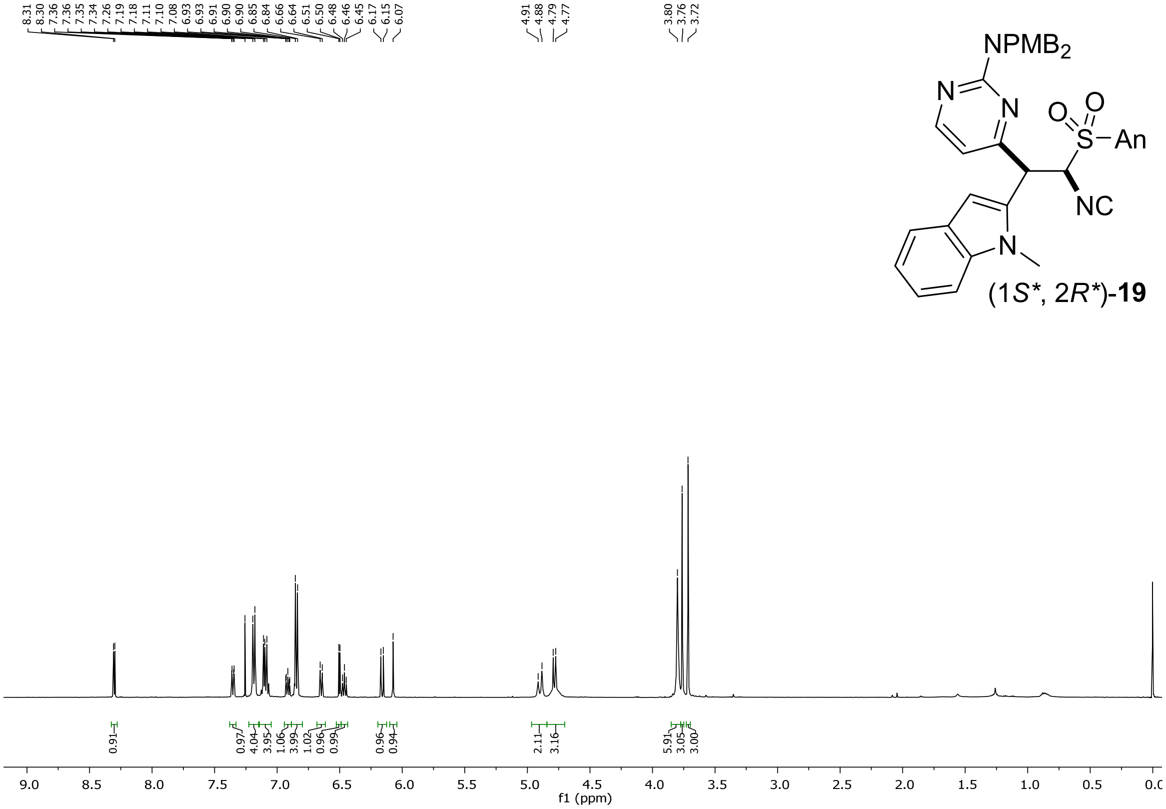
18

^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide **18**.

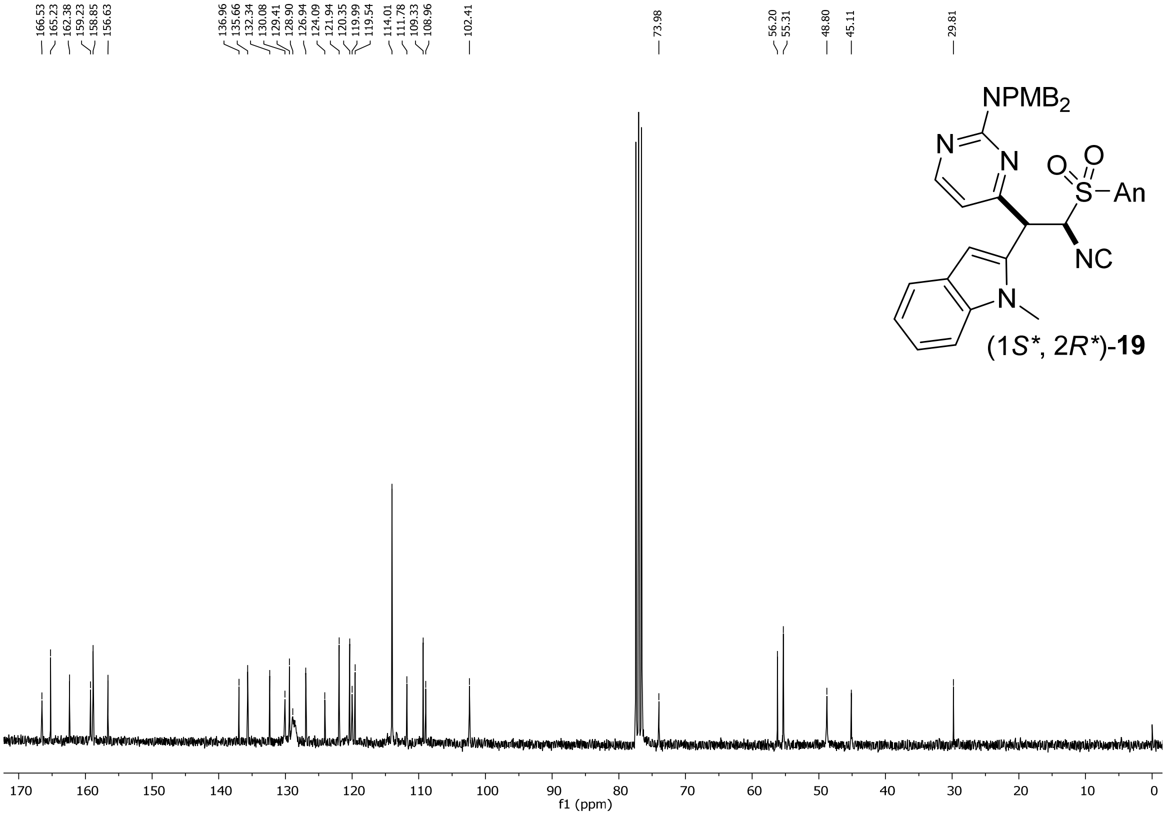


18

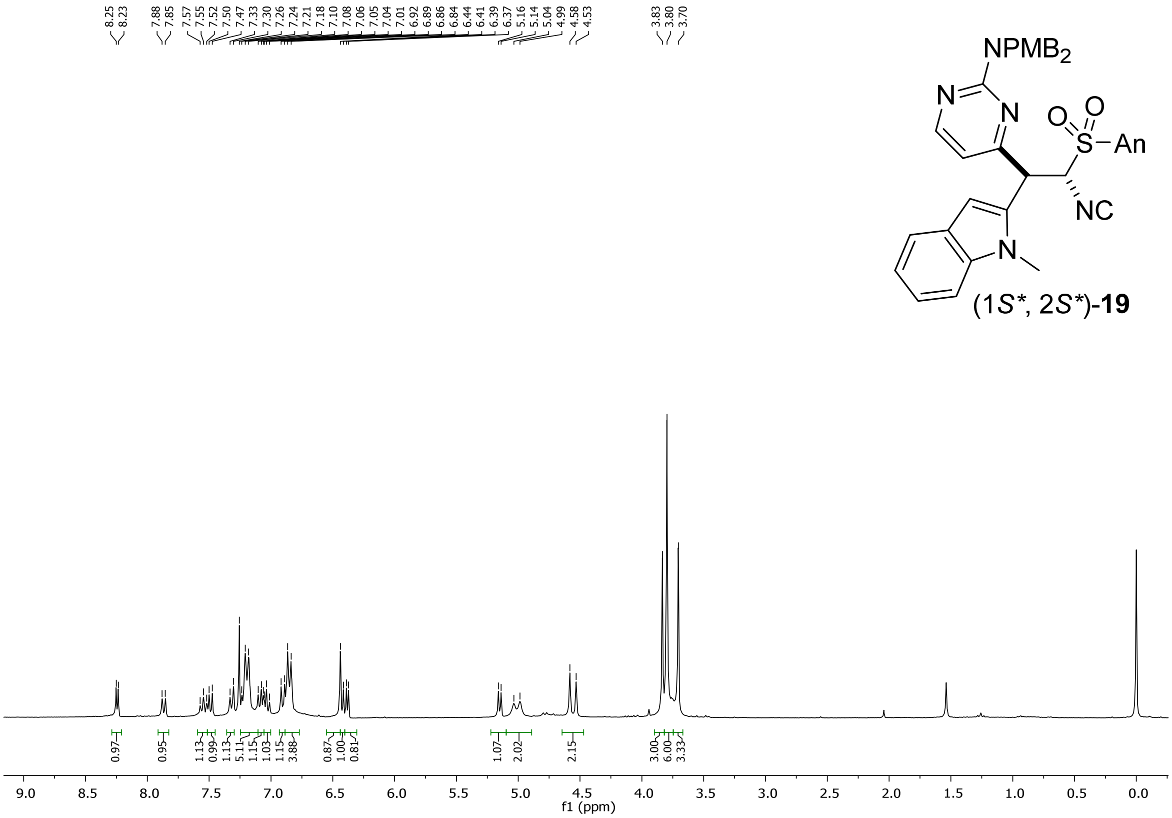
^{13}C NMR (126 MHz, CDCl$_3$) of isocyanide **18**.



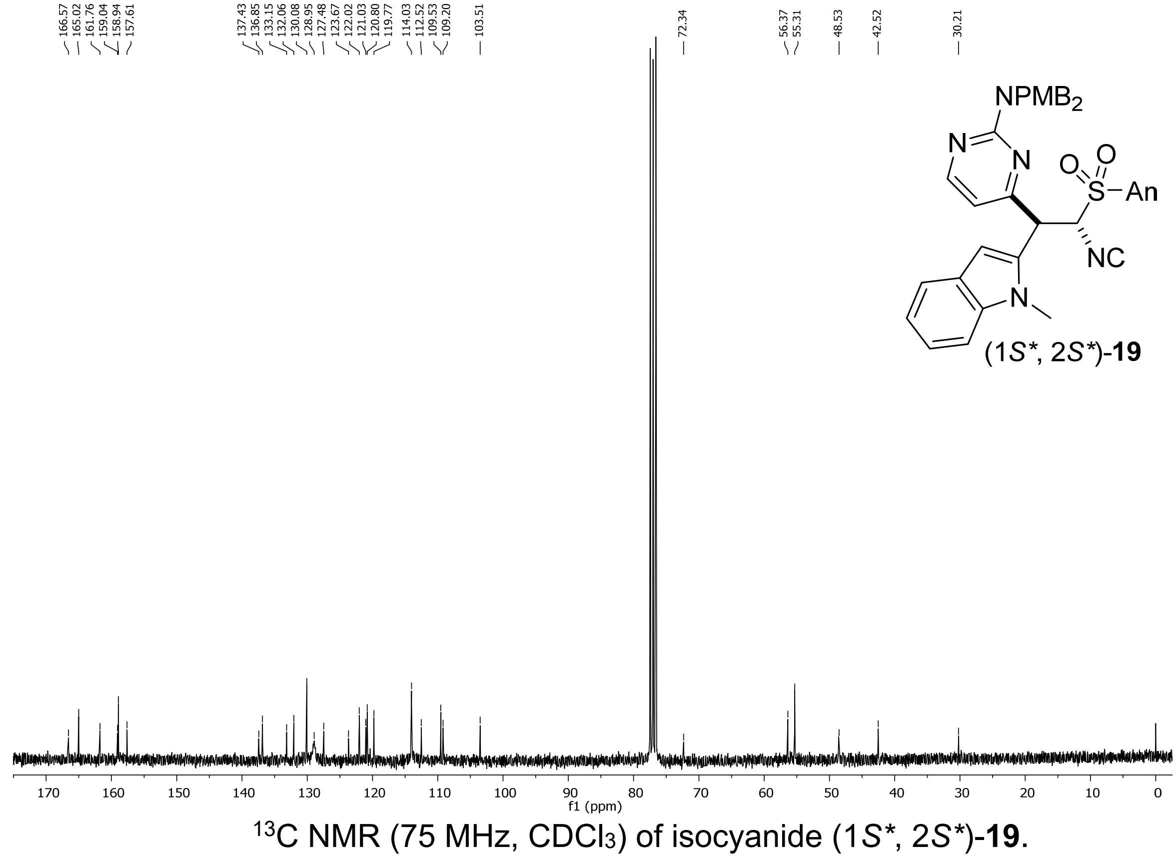
^{1}H NMR (500 MHz, CDCl$_3$) of isocyanide (1*S**, 2*R**)-**19**.



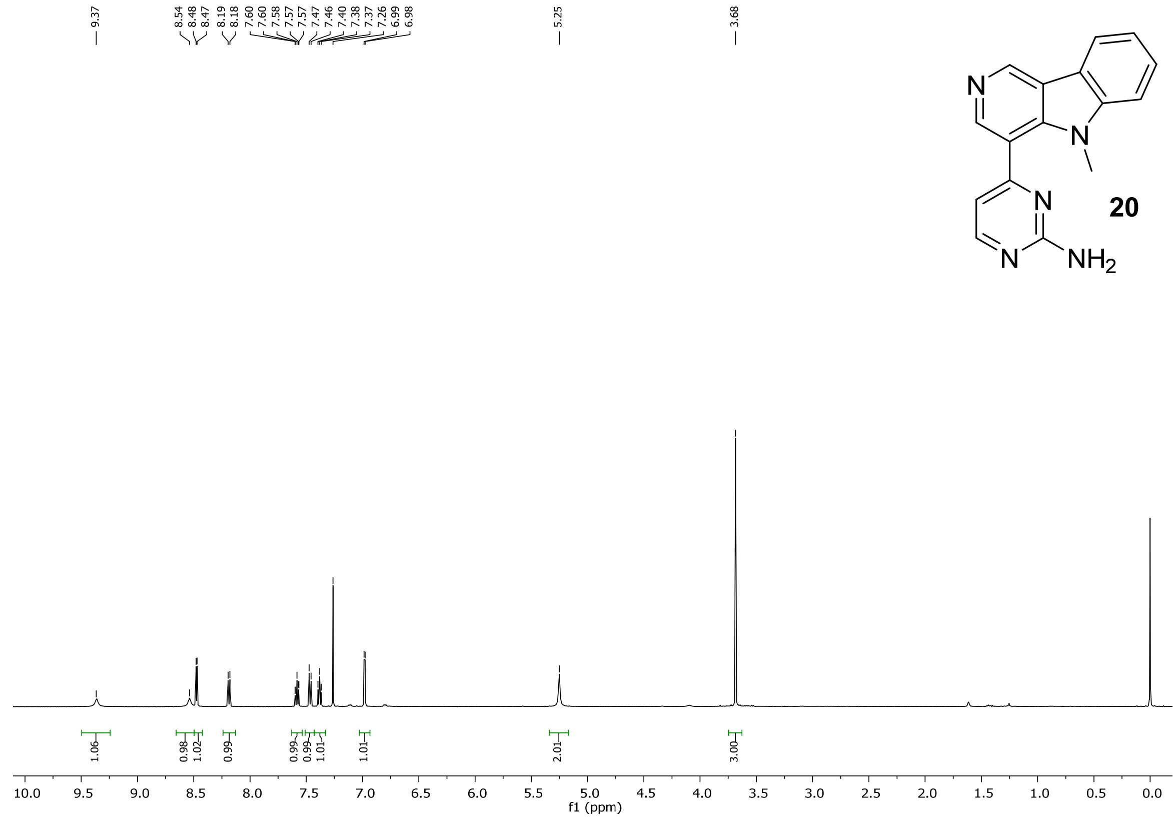
^{13}C NMR (75 MHz, CDCl$_3$) of isocyanide (1*S**, 2*R**)-**19**.



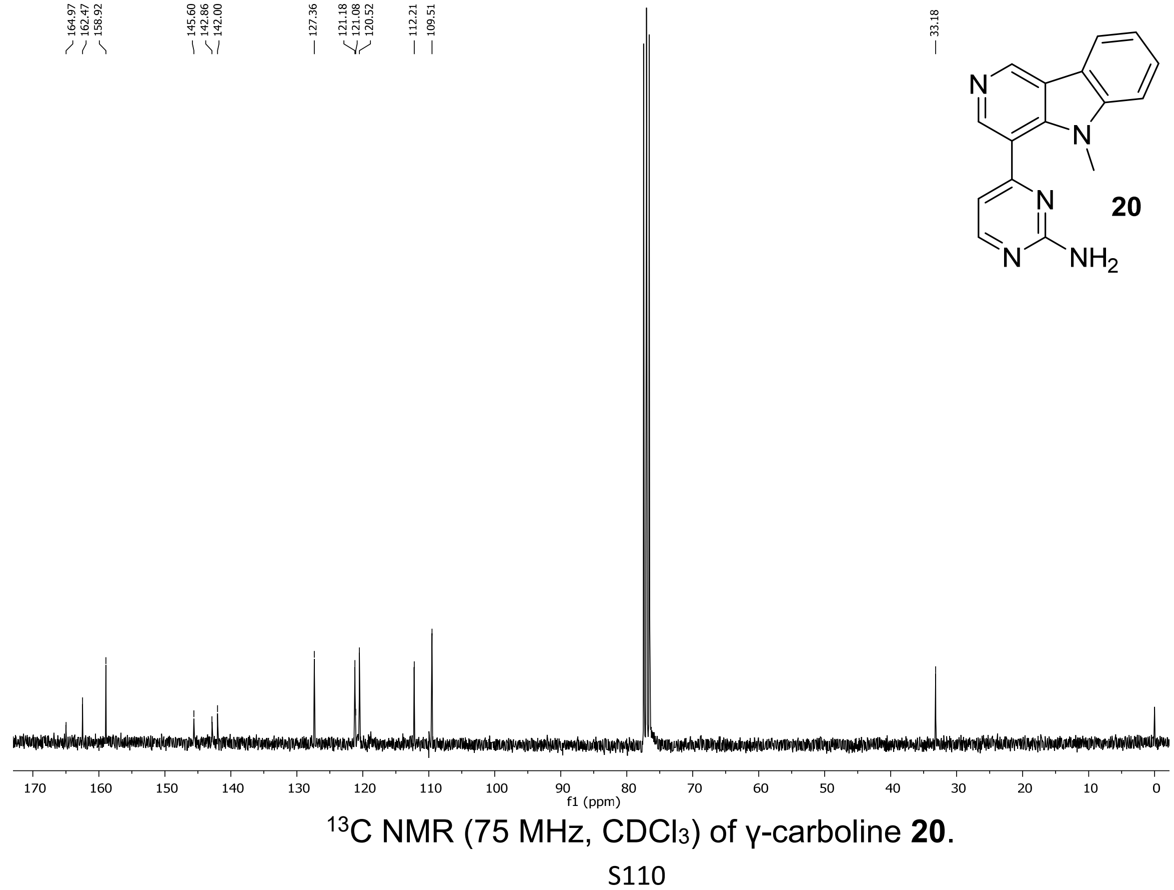
^{1}H NMR (300 MHz, CDCl$_3$) of isocyanide (1*S**, 2*S**)-**19**.



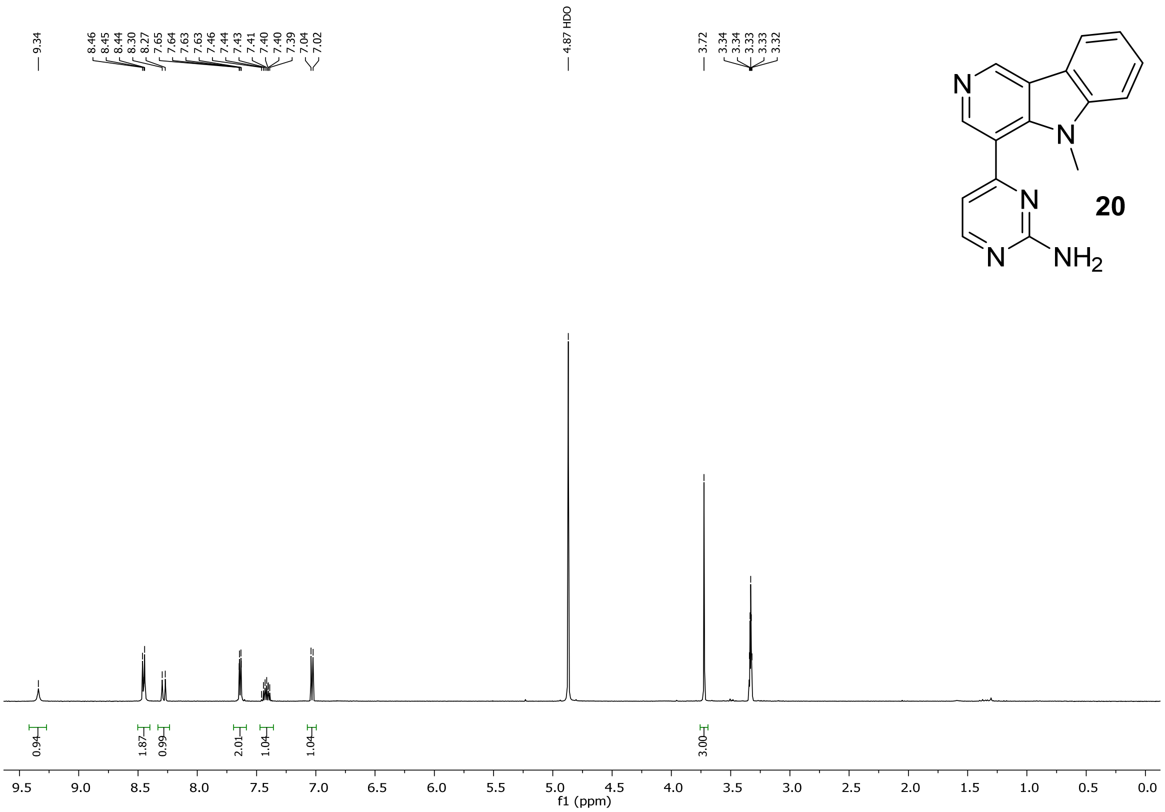
^{13}C NMR (75 MHz, CDCl$_3$) of isocyanide (1*S**, 2*S**)-**19**.



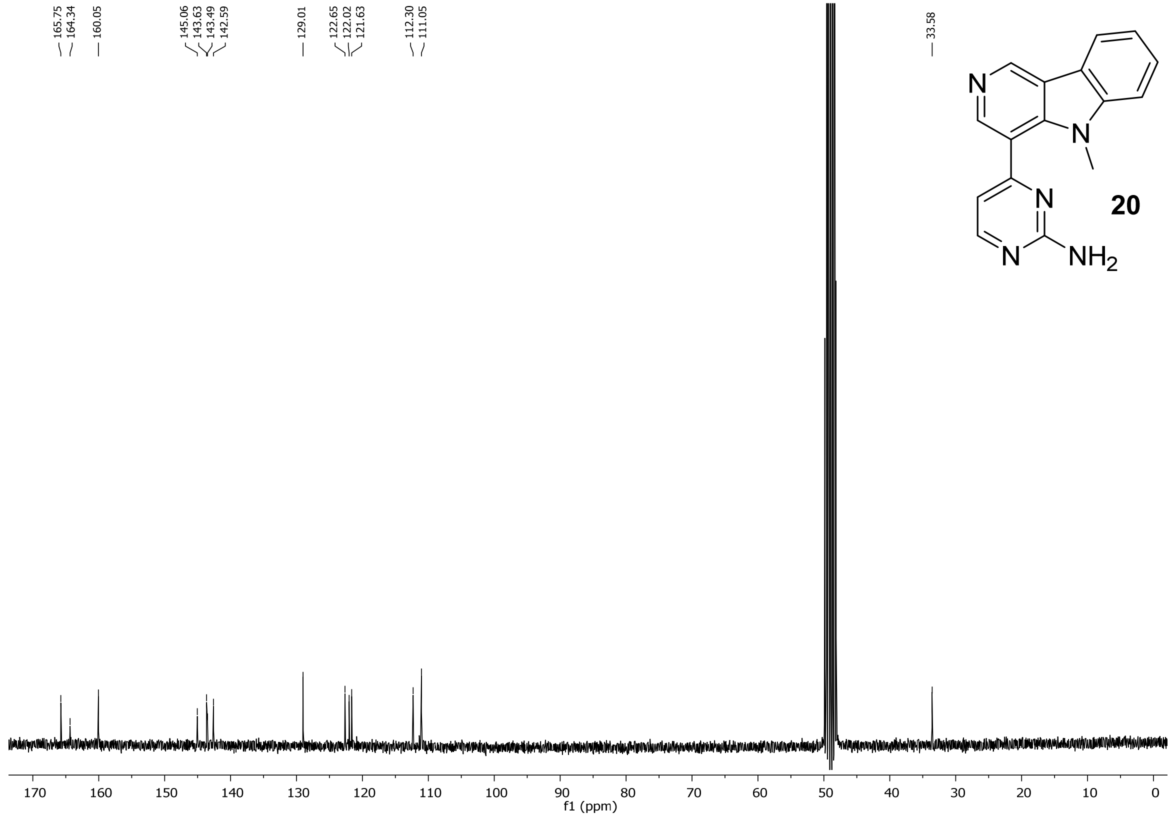
^{1}H NMR (500 MHz, CDCl$_3$) of γ-carboline **20**.



^{13}C NMR (75 MHz, CDCl$_3$) of γ-carboline **20**.



^{1}H NMR (300 MHz, CD$_3$OD) of γ-carboline **20**.



^{13}C NMR (75 MHz, CD$_3$OD) of γ-carboline **20**.

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[1] J. A. Lujan-Montelongo, A. O. Estevez, F. F. Fleming *Chem. Eur. J.* **2015**, *7*, 1602.

[2] F. J. A. Hundscheid, V. K. Tandon, P. H. F. M. Rouwette, A. M. van Leusen *Tetrahedron* **1987**, *43*, 5073.

[3] A. M. van Leusen, J. Wildeman *Rec. Trav. Chim. Pays-Bas* **1982**, *101*, 202.

[4] Prepared following the previously published synthesis except that CH_2Cl_2 and Et_3N were employed at -25 °C to -10 °C (1 h) in the dehydration rather than a $THF:CH_3CN$ solution with *i*-Pr_2NH.

[5] The configuration was assigned by comparing the coupling constants with those of structurally analogous diastereomers: P. R. Krishna, Y. L. Prapurna, *Synlett* **2009**, *16*, 2613.

[6] J. G. Sośnicki *Tetrahedron Lett.* **2006**, *47*, 6809.

[7] Prepared by addition of a hexanes solution (0.46 mmol, 0.28 mL) of BuLi to a -30 °C, THF solution (4 mL) of 1,3-dithiane (0.55 mmol, 66 mg): S. R. Wilson, J. Mathew *Synthesis* **1980**, 625.

[8] Prepared by addition of a hexanes solution (0.95 mmol, 0.60 mL) of BuLi to a -78 °C, THF solution (5 mL) of 3,5-dimethylisoxazole (99 mg, 1.02 mmol): J-C. Cherton, M. Lanson, D. Ladjama, N. Lefebvre, Z. Vossough, J-J. Basselier *Can. J. Chem.* **1991**, *69*, 625.

[9] The authors have deposited the crystallographic data for (1*S**, 2*R**)-**8d** with the Cambridge Crystallographic Data Center (CCDC# 1052082). The data can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK.

[10] Prepared by addition of a heptane solution of *t*-BuLi (1.58 mmol, 0.80 mL) to a -78 °C, THF solution (6 mL) of 1-iodo-4-methoxybenzene (0.83 mmol, 194 mg): M. H. Nguyen, A. B. Smith, III *Org. Lett.* **2014**, *16*, 2070.

[11] Prepared by addition of a hexanes solution (1.01 mmol, 0.63 mL) of BuLi to a THF solution (8 mL) of benzofuran (126 mg, 1.07 mmol) at -78 °C. After 1 h, the reaction was allowed to warm to 0 °C and then maintained at -5 °C for 1 h: J. Wu, X. Yang, Z. He, X. Mao, T. A. Hatton, T. F. Jamison *Angew. Chem. Int. Ed.*, **2014**, *53*, 8416; *Angew. Chem.* **2014**, *126*, 8556.

[12] Prepared by addition of a hexanes solution (1.01 mmol, 0.63 mL) of BuLi to a THF solution (8 mL) of 1-methyl-1H-indole (150 mg, 1.14 mmol) at -78 °C. After 1 h, the reaction was allowed to warm to 0 °C and then maintained at -5 °C for 1 h: J. Wu, X. Yang, Z. He, X. Mao, T. A. Hatton, T. F. Jamison *Angew. Chem. Int. Ed.*, **2014**, *53*, 8416; *Angew. Chem.* **2014**, *126*, 8556.

[13] Prepared by addition of BuLi (1.55 mmol, 0.97 mL) to a -78 °C, THF solution (5 mL) of tributyl(vinyl)stannane (0.45 mL, 1.55 mmol) and used after 15 min.

[14] Prepared by addition of BuLi (0.85 mmol, 0.53 mL) to a -78 °C, THF solution (5 mL) of phenylacetylene (102 mg, 1 mmol, 0.11 mL) and used after 15 min.

[15] Although a known compound, no spectral data was previously reported: A. M. van Leusen, R. J. Bouma, O. Possel *Tetrahedron Lett.* **1975**, *16*, 3487.

[16] The authors have deposited the crystallographic data for (1*R**, 2*S**)-**9d** with the Cambridge Crystallographic Data Center (CCDC# 1516436). The data can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK.

[17] The material exhibited a ^{1}H NMR spectrum identical to that previously reported: H. Zhang, R. C. Larock *J. Org. Chem.* **2002**, *67*, 9318.

[18] S. Nakatsuka, O. Asano, T. Goto *Heterocycles* **1986**, *24*, 2791.

[19] J.-P. K. Meigh, PhD thesis, University of Manchester (UK), **2000**.

[20] H. McNab *J. Chem. Soc. Perkin Trans. 1* **1987**, *3*, 653.

[21] Complete spectral data is provided because previous NMR characterization was performed in DMSO-d_6: N. H. Naik, A. K. Sikder, R. S. Kusurkar, *Tetrahedron Lett.* **2013**, *54*, 3715; M. Hoefener, F. Pachl, T. Take, G. Fischer von Mollard, B. Kuster, N. Sewald *J. Proteome Research* **2014**, *13*, 3628.