Supporting Information

Complementary regioselectivity in the synthesis of iminohydantoins: Remarkable effect of amide substitution on the cyclization

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General Information

Isocyanocarboxamides were prepared according to literature[1] Chloramine hydrates were dried in a vacuum oven over P_2O_5 at 35-40 °C until constant weight. Dry chloroform was used in all of the preparations.

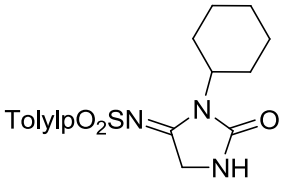
Melting points are not corrected. Infrared spectra were registered in potassium bromide tablets. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$with instruments operating at 300 and 75 MHz, respectively, or at 400 and 100 MHz, respectively. Chemical shifts are reported in ppm with respect to residual solvent protons, coupling constants ($J_{X\text{-}X'}$) are reported in Hz. Low resolution mass spectra and HRMS were recorded in the positive ion mode by electronic impact at 70 eV. All solvents were previously dried according to standard procedures. Analytical TLC was performed on silica gel 60 F254 plates. Flash column chromatography was carried out on silica gel (0.040–0.063 mm).

[1] (a) Bossio, R.; Marcaccini, S.; Pepino, R. *Liebigs Ann. Chem.* **1990**, 935. (b) Matsumoto, K.; Suzuki, M.; Yoneda, N.; Miyoshi, M. *Synthesis* **1977**, 249.

General experimental procedure for the synthesis of iminohydantoin derivatives 3 and 4. A small amount of TEBA (30-35 mg) was added to a stirred suspension of isocyanoamide **1a-k** (2.5 mmol) and dry chloramine (B or T) (2.5 mmol) in 10 ml of dry chloroform. After 4 days water was added to the reaction mixture. The organic layer was separated, dried over Na_2SO_4 or $MgSO_4$ and evaporated to dryness. The residue was recrystallized from the proper solvent.

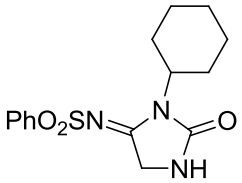
Regioisomer mixtures were separated by column chromatography (SiO_2, Hexane/Dichloromethane) to provide the pure regioisomers. The Rf for 2-iminohydantoin derivatives is higher than the Rf for 4-iminohydantoin derivatives.

1-Cyclohexyl-5-[(4-tolylsulfonyl)imino]imidazolidin-2-one (3a).



White solid (0.57 g, 68% yield), m.p. 227-228 ºC (EtOH). IR (KBr): 3240 (NH), 1746 (CO), 1144 (SO_2) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.12-1.34 (m, 3H), 1.63-1.82 (m, 5H), 2.11-2.19 (m, 2H), 2.43 (s, 3H, CH_{3tolyl}), 4.06 (tt, *J* = 12.2, 3.7 Hz, 1H, CH_{cycl}), 4.61 (s, 2H, H-4), 5.96 (br s, 1H, NH), 7.31 (d, *J* = 8.1 Hz, 2H, H_{ar}), 7.81 (d, *J* = 8.1 Hz, 2H, H_{ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.8 (CH_{3tolyl}), 25.0 (CH_2), 25.1 (CH_2), 28.6 (CH_2), 45.4 (CH_2-4), 53.7 (CH_{cycl}), 126.8 (CH_{ar}), 129.8 (CH_{ar}), 138.5 (C_{ar}), 143.7 (C_{ar}), 156.9 (C=O), 166.2 (C=N). MS (EI) *m/z* (relative intensity) 335 (M^+, 0.6), 254 (100), 155 (16), 91 (24). HRMS (EI) calcd for $C_{16}H_{21}N_3O_3S$ 335.1304, found 335.1293.

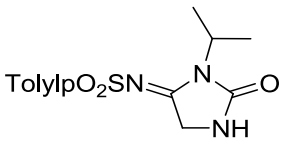
1-Cyclohexyl-5-phenylsulfonyliminoimidazolidin-2-one (3b).



White solid. (0.49 g, 61% yield), m.p. 208-210 ºC (EtOH). IR (KBr): 3128 (NH), 1745 (CO), 1152 (SO_2) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ 1.12-1.35 (m, 3H), 1.63-1.82 (m, 5H), 2.12-2.23 (m, 2H), 4.07 (tt, *J* = 12.1, 4.1 Hz, 1H, CH_{cycl}), 4.63 (s, 2H, H-4), 5.78 (br s, 1H, NH), 7.50-7.56 (m, 3H, H_{ar}), 7.94 (d, *J* = 8.1 Hz, 2H, H_{ar}). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0 (CH_2), 24.8 (CH_2), 27.5 (CH_2), 44.2 (CH_2-4), 52.7 (CH_{cycl}), 125.6

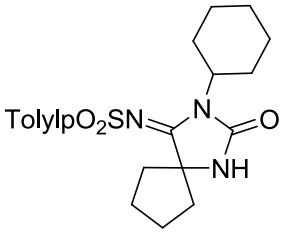
(CH_{ar}), 128.0 (CH_{ar}), 131.8 (CH_{ar}), 140.4 (C_{ar}), 155.3 (C=O), 165.1 (C=N). MS (EI) *m/z* (relative intensity) 322 (M^++1, 0.5), 240 (100), 77 (18). HRMS (EI) *m/z* calcd for $C_{15}H_{20}N_3O_3S$ [M+H] 322.1225, found 322.1227.

1-Isopropyl-5-[(4-tolylsulfonyl)imino]imidazolidin-2-one (3c).



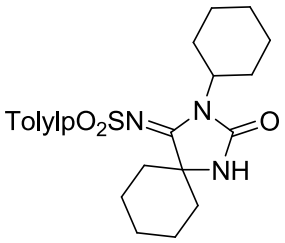
White solid. (0.52 g, 70% yield), m.p. 249-250 ºC (EtOH). IR (KBr): 3126 (NH), 1747 (CO), 1149 (SO_2) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (d, *J* = 7.0 Hz, 6H, 2xCH_{3iPr}), 2.43 (s, 3H, CH_{3tolyl}), 4.47 (quint, *J* = 7.0 Hz, 1H, CH_{iPr}), 4.63 (s, 2H, H-4), 5.58 (br s, 1H, NH), 7.31 (d, *J* = 8.1 Hz, 2H, H_{ar}), 7.82 (d, *J* = 8.1 Hz, 2H, H_{ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.2 (CH_{3iPr}), 21.8 (CH_{3tolyl}), 45.4 (CH_2-4), 45.9 (CH_{iPr}), 126.8 (CH_{ar}), 129.7 (CH_{ar}), 138.5 (C_{ar}), 143.7 (C_{ar}), 156.4 (C=O), 165.7 (C=N). MS (EI) *m/z* (relative intensity) 295 (M^+, 49), 254 (100), 155 (41), 140 (51), 91 (76). HRMS (EI) calcd for $C_{13}H_{17}N_3O_3S$ 295.0991, found 295.0989.

3-Cyclohexyl-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.4]nonan-2-one (3d).



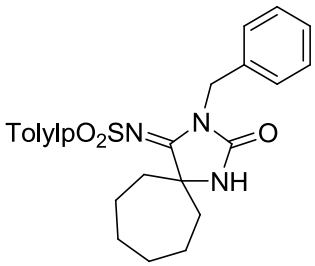
White solid. (0.65 g, 67% yield), m.p. 262-263 ºC (EtOH). IR (KBr): 3207 (NH), 1747 (CO), 1148 (SO_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.07-1.30 (m, 2H), 1.54-1.67 (m, 4H), 1.70-1.87 (m, 6H), 2.02-2.21 (m, 4H), 2.44 (s, 3H, CH_{3tolyl}), 2.99-3.11 (m, 2H), 4.03 (tt, *J* = 12.3, 3.7 Hz, 1H, CH_{cycl}), 6.04 (br s, 1H, NH), 7.30 (d, *J* = 8.3 Hz, 2H, H_{ar}), 7.85 (d, *J* = 8.3 Hz, 2H, H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5 (CH_{3tolyl}), 25.1 (CH_2), 25.2 (CH_2), 25.8 (CH_2), 28.4 (CH_2), 38.6 (CH_2), 53.5 (CH_{cycl}), 69.4 (C-5), 126.3 (CH_{ar}), 129.3 (CH_{ar}), 140.0 (C_{ar}), 142.8 (C_{ar}), 154.6 (C=O), 168.5 (C=N). MS (EI) *m/z* (relative intensity) 389 (M^+, 57), 308 (100), 91 (92). Anal. Calcd for $C_{20}H_{27}N_3O_3S$: C, 61.67; H, 6.99; N, 10.79. Found: C, 61.72; H 6.80; N 10.88.

3-Cyclohexyl-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-2-one (3e).



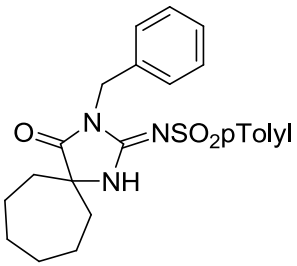
White solid. (0.65 g, 61% yield), m.p. 282-284 ºC. IR (KBr): 3218 (NH), 1745 (CO), 1152 (SO_2) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.99-2.15 (m, 18H), 2.43 (s, 3H, CH_{3tolyl}), 2.81-2.90 (m, 2H), 3.96-4.04 (m, 1H, CH_{cycl}), 7.10 (s, 1H, NH), 7.30 (d, *J* = 8.0 Hz, 2H, H_{ar}), 7.85 (d, *J* = 8.0 Hz, 2H, H_{ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7 (CH_{3tolyl}), 22.2 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 26.1 (CH_2), 28.6 (CH_2), 32.6 (CH_2), 53.6 (CH_{cycl}), 63.8 (C_q-5), 126.5 (CH_{ar}), 129.5 (CH_{ar}), 140.4 (C_{ar}), 143.0 (C_{ar}), 155.5 (C=O), 168.9 (C=N). MS (EI) *m/z* (relative intensity) 403 (M^+, 1.1), 322 (100), 169 (28), 91 (33). HRMS (EI) calcd for $C_{21}H_{29}N_3O_3S$ 403.1930, found 403.1947.

3-Benzyl-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.6]undecan-2-one (3f).



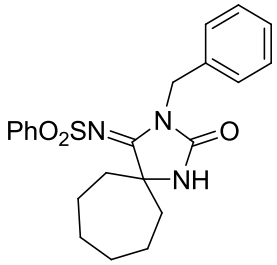
White solid. (0.65 g, 61% yield), m.p. 228-230ºC. IR (KBr): 3316 (NH), 1745 (CO), 1145 (SO_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.46-1.88 (m, 10H), 2.42 (s, 3H, CH_{3tolyl}), 2.87 (ddd, *J* = 2.9, 11.7, 14.3 Hz, 2H), 4.64 (s, 2H, $CH_{2benzyl}$), 7.13-7.26 (m, 8H, H_{ar}, NH), 7.72 (d, *J* = 8.2 Hz, 2H, H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (CH_{3tolyl}), 23.3 (CH_2), 26.7 (CH_2), 36.1 (CH_2), 43.9 ($CH_{2benzyl}$), 67.5 (C_q-5), 126.6 (CH_{ar}), 128.0 (CH_{ar}), 128.6 (CH_{ar}), 128.7 (CH_{ar}), 129.4 (CH_{ar}), 135.5 (C_{ar}), 140.0 (C_{ar}), 143.0 (C_{ar}), 155.5 (C=O), 169.3 (C=N). MS (EI) *m/z* (relative intensity) 425 (M^+, 7.8), 426 (M^++1, 3.1), 271 (24), 270 (57), 91 (100). HRMS (EI) calcd for $C_{23}H_{27}N_3O_3S$ 425.1773, found 425.1783. Anal. Calcd for $C_{23}H_{27}N_3O_3S$: C, 64.92; H, 6.40; N, 9.88. Found: C, 64.88; H, 6.35; N, 10.02.

3-Benzyl-2-[(4-tolylsulfonyl)imino]-1,3-diaza-spiro[4.6]undecan-4-one (4f).



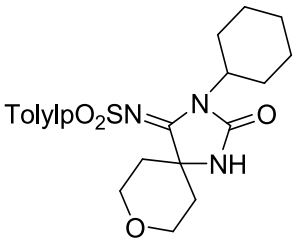
White solid. (0.04 g, 4% yield), m.p. 157-158ºC. IR KBr): 3304 (NH), 1749 (CO), 1145 (SO_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.42-1.80 (m, 10H), 1.94-2.00 (m, 2H), 2.40 (s, 3H, CH_{3tolyl}), 4.64 (s, 2H, $CH_{2benzyl}$), 7.16-7.25 (m, 7H, H_{ar}), 7.68 (d, *J* = 7.9 Hz, 2H, H_{ar}), 7.82 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.7 (CH_{3tolyl}), 23.0 (CH_2), 29.3 (CH_2), 37.1 (CH_2), 42.9 ($CH_{2benzyl}$), 65.8 (C_q-5), 126.3 (CH_{ar}), 128.1 (CH_{ar}), 128.6 (CH_{ar}), 128.8 (CH_{ar}), 129.5 (CH_{ar}), 135.6 (C_{ar}), 139.5 (C_{ar}), 143.1 (C_{ar}), 155.2 (C=N), 176.6 (C=O). MS (EI) *m/z* (relative intensity) 425 (M^+, 100), 426 (M^++1, 31), 270 (95), 242 (68), 91 (52). HRMS (EI) calcd for $C_{23}H_{27}N_3O_3S$ 425.1773, found 425.1767. Anal. Calcd for $C_{23}H_{27}N_3O_3S$: C, 64.92; H, 6.40; N, 9.88. Found: C, 64.90; H, 6.34; N, 10.00.

3-Benzyl-4-phenylsulfonylimino-1,3-diazaspiro[4.6]undecan-4-one (3g).



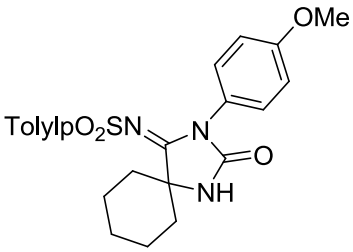
White solid. (0.70 g, 68% yield), m.p. 238-241 ºC (EtOH). IR (KBr): 3217 (NH), 1750 (CO), 1157 (SO_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.48-1.91 (m, 10H), 2.89 (ddd, *J* = 14.44 11.69, 3.04 Hz, 2H), 4.66 (s, 2H, $CH_{2benzyl}$), 6.69 (br s, 1H, NH), 7.11-7.22 (m, 5H, H_{ar}), 7.45-7.49 (m, 2H, H_{ar}), 7.58-7.54 (m, 1H, H_{ar}), 7.83-7.86 (m, 2H, H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4 (CH_2), 26.7 (CH_2), 36.0 (CH_2), 44.0 ($CH_{2benzyl}$), 67.4 (C_q-5), 126.6 (CH_{ar}), 128.1 (CH_{ar}), 128.6 (CH_{ar}), 128.7 (CH_{ar}), 128.9 (CH_{ar}), 132.4 (C_{ar}), 135.4 (C_{ar}), 142.7 (C_{ar}), 155.2 (C=O), 169.5 (C=N). MS (EI) *m/z* (relative intensity) 411 (M^+, 6.8), 270 (100), 91 (32). HRMS (EI) calcd for $C_{22}H_{25}N_3O_3S$ 411.1617, found 411.1603. Anal. Calcd for $C_{22}H_{25}N_3O_3S$: C, 64.21; H, 6.13; N, 10.21. Found: C, 64.50; H, 6.17; N, 10.03.

3-Cyclohexyl-4-[(4-tolylsulfonyl)imino]-1,3-diaza-8-oxaspiro[4.5]decan-2-one (3h).



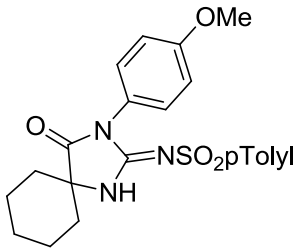
White solid. (0.62 g, 61% yield), m.p. 273-275 ºC (^{i}PrOH). IR (KBr): 3114 (NH), 1746 (CO), 1149 (SO_2) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.03-1.28 (m, 3H), 1.48-1.80 (m, 7H), 2.04-2.15 (m, 2H), 2.44 (s, 3H, CH_{3tolyl}), 3.20 (td, *J* = 13.2, 5.3 Hz, 2H), 3.55 (td, *J* = 12.3, 1.4 Hz, 2H), 4.06-4.12 (m, 3H), 7.31 (d, *J* = 8.2 Hz, 2H, H_{ar}), 7.44 (br s, 1H, NH), 7.85 (d, *J* = 8.2 Hz, 2H, H_{ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.8 (CH_{3tolyl}), 25.2 (CH_2), 26.0 (CH_2), 33.1 (CH_2), 54.1 (CH_{cycl}), 61.3 (C_q-5), 63.8 (2xCH_2O), 126.6 (CH_{ar}), 129.6 (CH_{ar}), 140.0 (C_{ar}), 143.2 (C_{ar}), 155.6 (C=O), 166.7 (C=N). MS (EI) *m/z* (relative intensity) 405 (M^+, 0.5), 324 (100), 250 (30), 168 (25), 91 (25). HRMS (EI) calcd for $C_{20}H_{27}N_3O_4S$ 405.1722, found 405.1717.

3-(4-Methoxyphenyl)-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-2-one (3i).



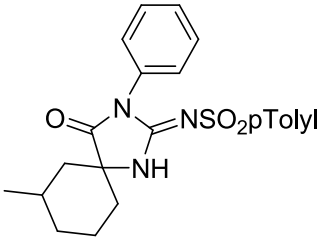
White solid. (0.24 g, 23% yield), m.p. 261-262 ºC (DMF). IR (KBr): 3297 (NH), 1754 (CO), 1148 (SO_2) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.93 (m, 8H), 2.37 (s, 3H, CH_{3tolyl}), 2.76 (td, *J* = 13.2, 4.0 Hz, 2H), 3.82 (s, 3H, $CH_{3methoxy}$), 6.43 (s, 1H, NH), 6.90-6.94 (m, 2H, H_{ar}), 7.18-7.20 (m, 4H, H_{ar}), 7.66-7.64 (m, 2H, H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (CH_{3tolyl}), 22.3 (CH_2), 24.1 (CH_2), 33.2 (CH_2), 55.7 ($CH_{3methoxy}$), 64.1 (C_q-5), 114.2 (CH_{ar}), 124.9 (C_{ar}), 126.5 (CH_{ar}), 129.1 (CH_{ar}), 129.4 (CH_{ar}), 140.0 (C_{ar}), 142.9 (C_{ar}), 154.8 (C=O), 159.9 (C_{ar}), 167.8 (C=N). MS (EI) *m/z* (relative intensity) 427 (M^+, 14), 428 (M^++1, 4.3), 272 (100). HRMS (EI) calcd for $C_{22}H_{25}N_3O_4S$ 427.1566, found 427.1568. Anal. Calcd for $C_{22}H_{25}N_3O_4S$: C, 61.81; H, 5.90; N, 9.83. Found: C, 61.97; H, 5.90; N, 9.52.

3-(4-Methoxyphenyl)-2-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-4-one (4i).



White solid. (0.42 g, 39% yield) m.p. 237-238 ºC. IR (KBr): 3287 (NH), 1756 (CO), 1148 (SO_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.43-1.96 (m, 10H, CH_{2cycl}), 2.39 (s, 3H, CH_{3tolyl}), 3.80 (s, 3H, $CH_{3methoxy}$), 6.92-6.98 (m, 2H, H_{ar}), 7.10-7.14 (m, 2H, H_{ar}), 7.24 -7.26 (m, 2H, H_{ar}), 7.73-7.76 (m, 2H, H_{ar}), 8.15 (s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (CH_{3tolyl}), 21.8 (CH_2), 24.5 (CH_2), 33.7 (CH_2), 55.7 ($CH_{3methoxy}$), 62.8 (C_q-5), 114.5 (CH_{ar}), 123.5 (C_{ar}), 126.4 (CH_{ar}), 128.5 (CH_{ar}), 129.6 (CH_{ar}), 139.5 (C_{ar}), 143.2 (C_{ar}), 155.5 (C=N), 159.8 (C_{ar}), 175.0 (C=O). MS (EI) *m/z* (relative intensity) 427 (M^+, 100), 428 (M^++1, 25), 302 (34), 147 (45), 91 (41). HRMS (EI) calcd for $C_{22}H_{25}N_3O_4S$ 427.1566, found 427.1577. Anal. Calcd for $C_{22}H_{25}N_3O_4S$: C, 61.81; H, 5.90; N, 9.83. Found: C, 61.89; H, 5.88; N, 9.62.

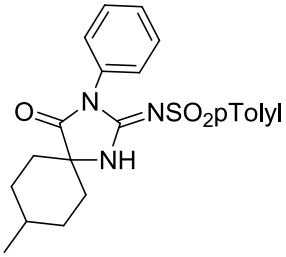
7-Methyl-3-phenyl-2-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-4-one (4j).



White solid. (0.63 g, 61% yield), m.p. 258-261 ºC (DMF/EtOH). IR (KBr): 3284 (NH), 1756 (CO), 1145 (SO_2) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.82-0.92 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H, CH_{3cycl}), 1.31-1.39 (m, 1H), 1.59-1.79 (m, 3H), 1.94-2.19 (m, 4H), 2.41 (s, 3H, CH_{3tolyl}), 7.21-7.28 (m, 4H, H_{ar}) 7.32-7.44 (m, 3H, H_{ar}), 7.75 (d, *J* = 8.2 Hz, 2H, H_{ar}), 7.81 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9 (CH_2), 21.8 (CH_3), 22.2 (CH_3), 27.5 (CH_{cycl}), 33.2 (CH_2), 34.6 (CH_2), 42.8 (CH_2), 62.0 (C_q-5), 126.4 (CH_{ar}), 127.5 (CH_{ar}), 128.9 (CH_{ar}), 129.1 (CH_{ar}), 129.1 (CH_{ar}), 129.6 (CH_{ar}), 130.9 (C_{ar}), 139.5 (C_{ar}), 143.2 (C_{ar}), 154.8 (C=N). MS (EI) *m/z* (relative intensity) 411 (M^+, 100), 342 (73), 91 (52). HRMS (EI) calcd for $C_{22}H_{25}N_3O_3S$ 411.1617, found 411.1622. Anal.

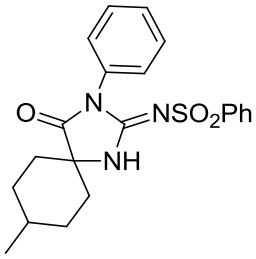
Calcd for $C_{22}H_{25}N_3O_3S$: C, 64.21; H, 6.13; N, 10.21. Found: C, 64.46; H, 6.05; N, 10.09.

8-Methyl-3-phenyl-2-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-4-one (4k).



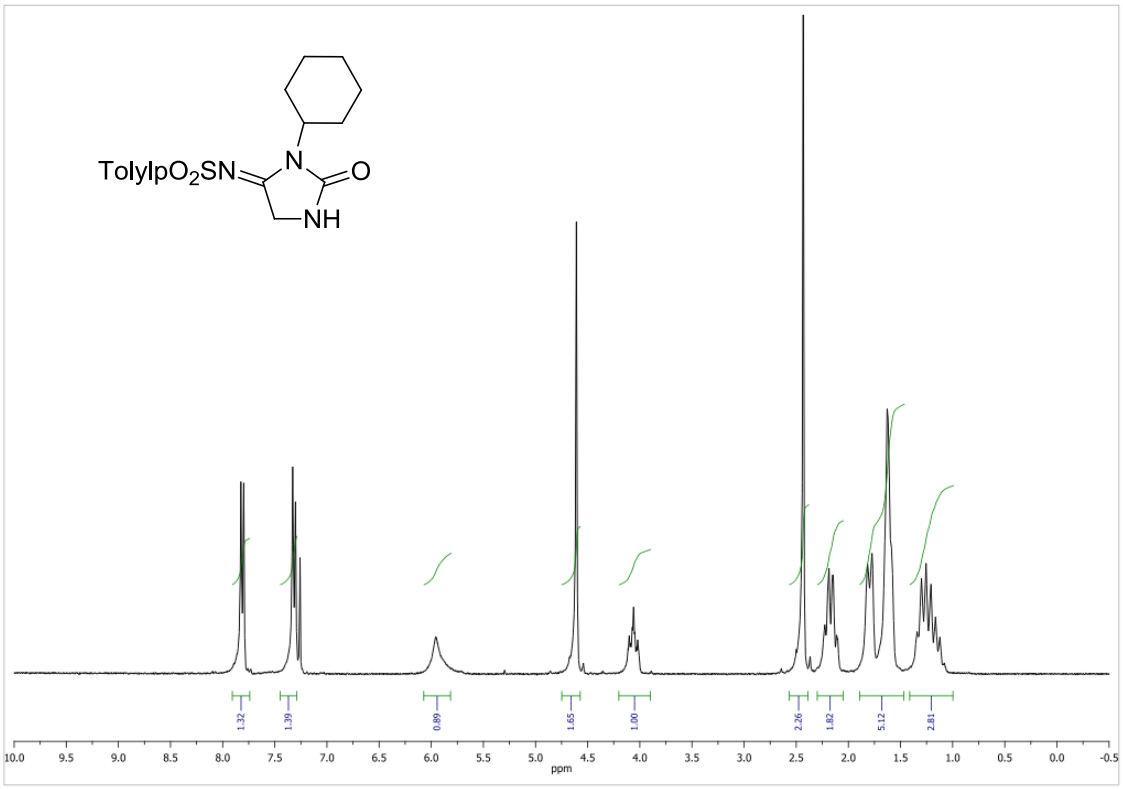
White solid. (0.73 g, 71% yield), m.p. 210-212 ºC (DMF/EtOH). IR (KBr): 3266 (NH), 1754, 1635, 1148 (SO_2) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.01 (d, *J* = 6.6 Hz, 3H, CH_{3cycl}), 1.54-1.77 (m, 7H), 2.05-2.10 (m, 2H), 2.40 (s, 3H, CH_{3tolyl}), 7.19-7.45 (m, 7H, H_{ar}), 7.75 (d, *J* = 8.4 Hz, 2H, H_{ar}), 7.84 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.7 (CH_3), 21.5 (CH_3), 28.8 (CH_2), 29.9 (CH_{cycl}), 33.4 (CH_2), 61.3 (C_q-5), 126.1 (CH_{ar}), 127.1 (CH_{ar}), 128.7 (CH_{ar}), 128.9 (CH_{ar}), 129.3 (CH_{ar}), 130.6 (C_{ar}), 139.2 (C_{ar}), 143.0 (C_{ar}), 154.6 (C=N), 174.1 (C=O). MS (EI) *m/z* (relative intensity) 411 (M^+, 100), 256 (50), 140 (69), 91 (72). HRMS (EI) calcd for $C_{22}H_{25}N_3O_3S$: 411.1617, found 411.1641.

8-Methyl-3-phenyl-2-phenylsulfonylimino-1,3-diazaspiro[4.5]decan-4-one (4l).

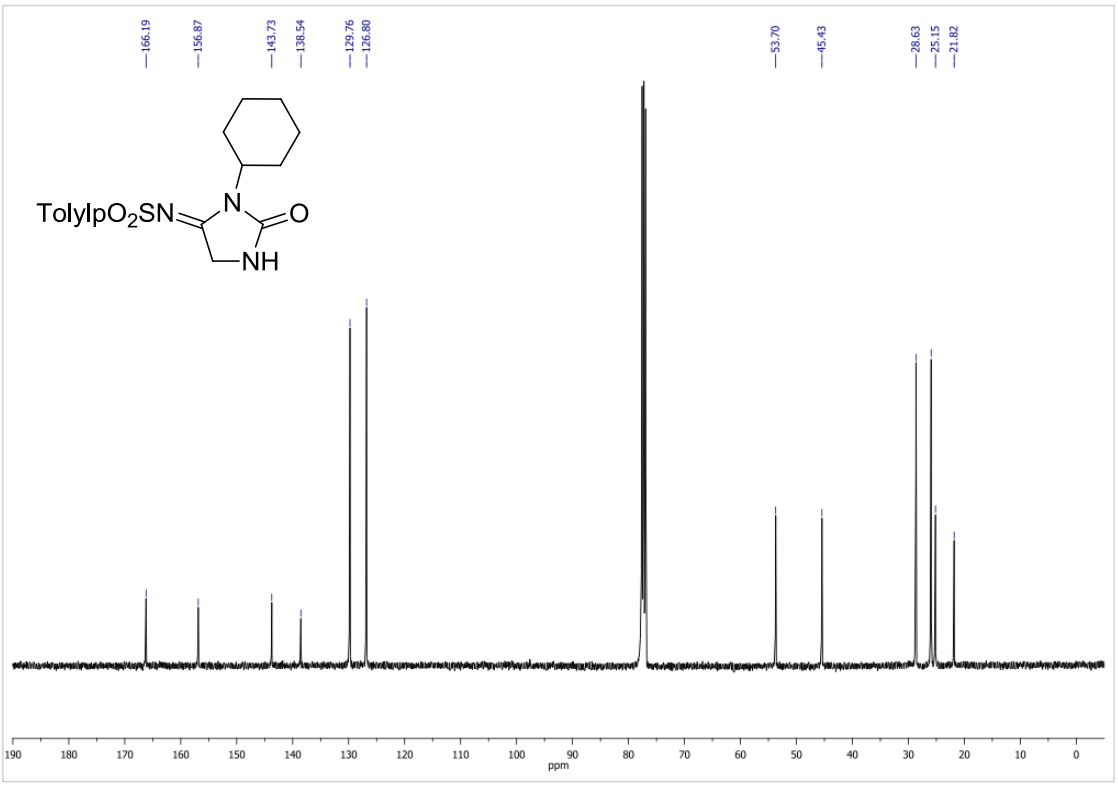


White solid. (0.64 g, 65% yield), m.p. 221-223 ºC (DMF/EtOH). IR (KBr): 3328 (NH), 1751, 1633, 1138 (SO_2) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.97 (d, *J* = 6.6 Hz, 3H, CH_{3cycl}), 1.49-1.74 (m, 7H), 2.02-2.08 (m, 2H), 7.18-7.20 (m, 2H, H_{ar}), 7.27-7.52 (m, 6H, H_{ar}), 7.79 (br s, 0.85H, NH), 7.81-7.84 (m, 2H, H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9 (CH_{3cycl}), 29.0 (CH_2), 30.1 (CH_{cycl}), 33.7 (CH_2), 61.6 (C_q-5), 126.3 (CH_{ar}), 127.4 (CH_{ar}), 128.9 (CH_{ar}), 129.0 (CH_{ar}), 129.2 (CH_{ar}), 130.8 (C_{ar}), 132.5 (CH_{ar}), 142.3 (C_{ar}), 155.0 (C=N), 174.3 (C=O). MS (EI) *m/z* (relative intensity) 397 (M^+, 100), 228 (21), 77 (28). HRMS (EI) calcd for $C_{21}H_{23}N_3O_3S$ 397.1460, found 397.1451.

1-Cyclohexyl-5-[(4-tolylsulfonyl)imino]imidazolidin-2-one (3a).

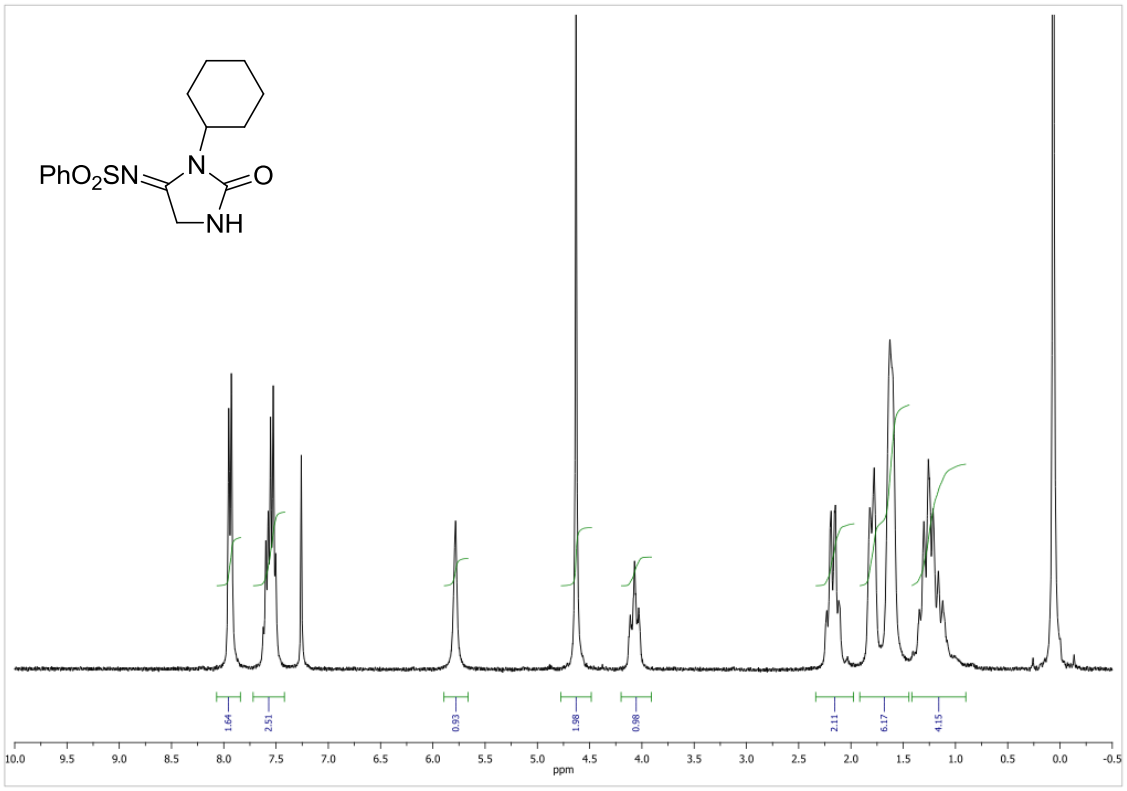


^{1}H NMR (300 MHz, $CDCl_3$)

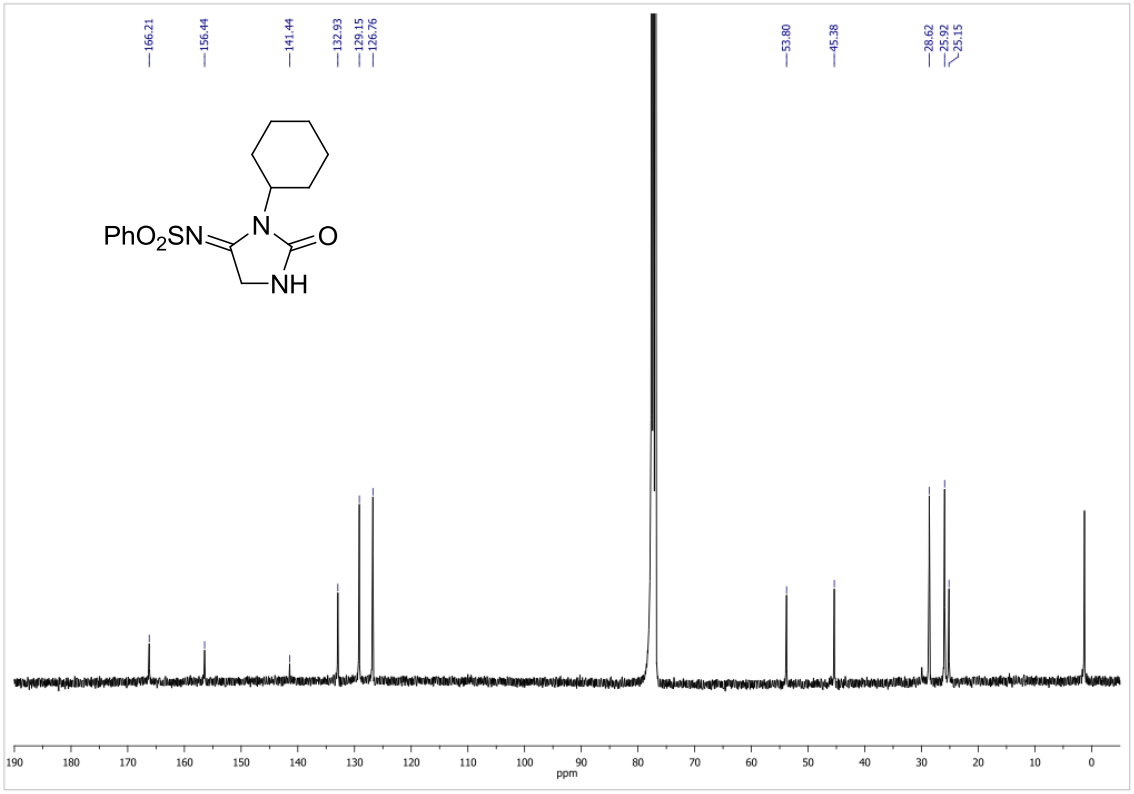


^{13}C NMR (75 MHz, $CDCl_3$)

1-Cyclohexyl-5-phenylsulfonyliminoimidazolidin-2-one (3b).

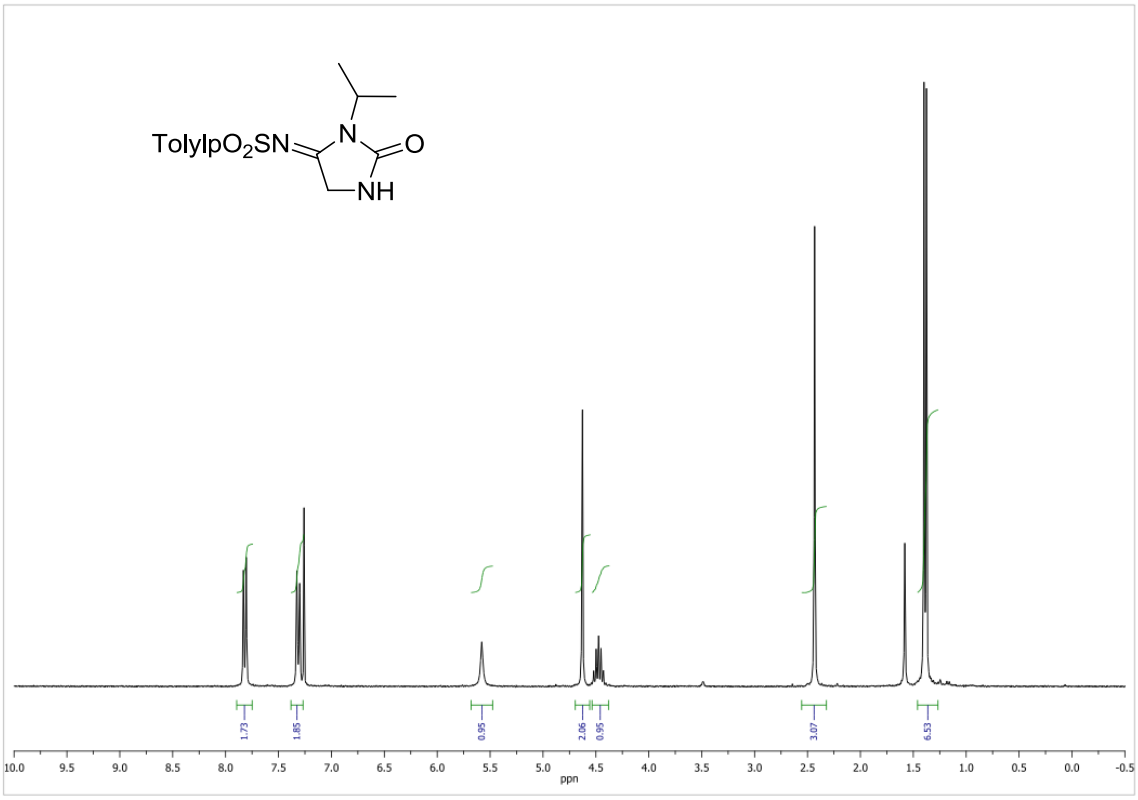


^{1}H NMR (300 MHz, $CDCl_3$)

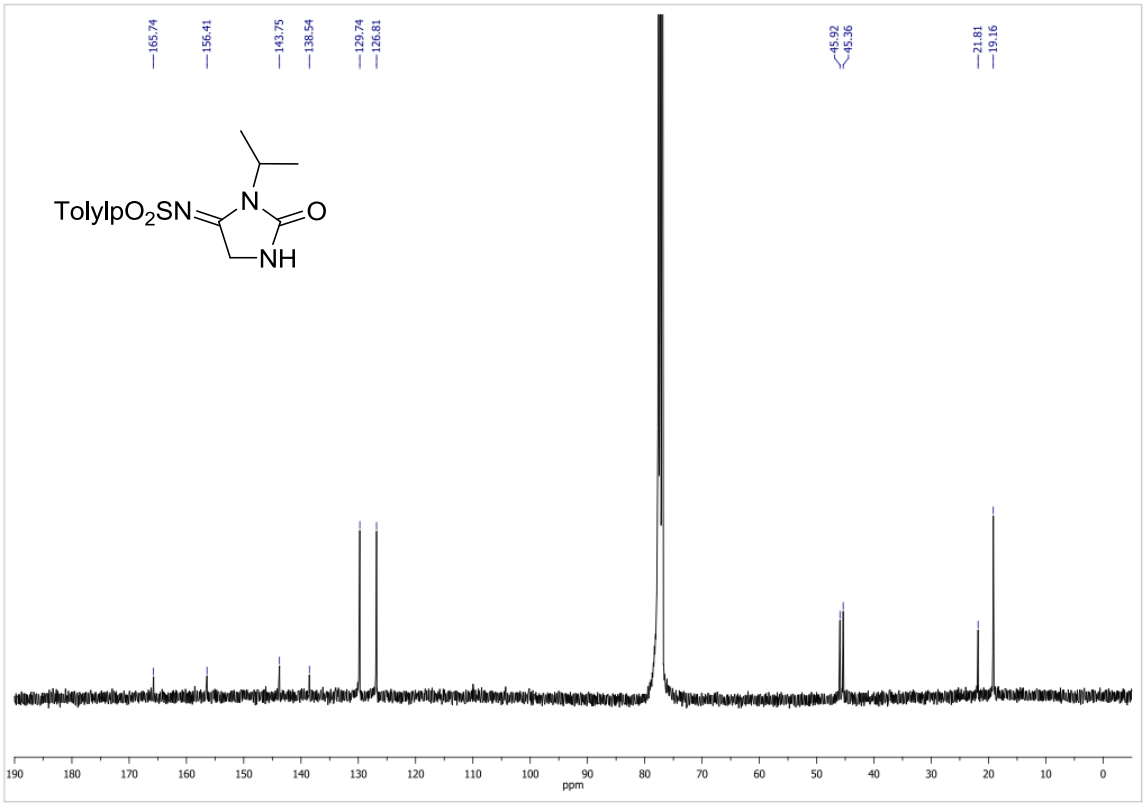


^{13}C NMR (75 MHz, $CDCl_3$)

1-Isopropyl-5-[(4-tolylsulfonyl)imino]imidazolidin-2-one (3c).

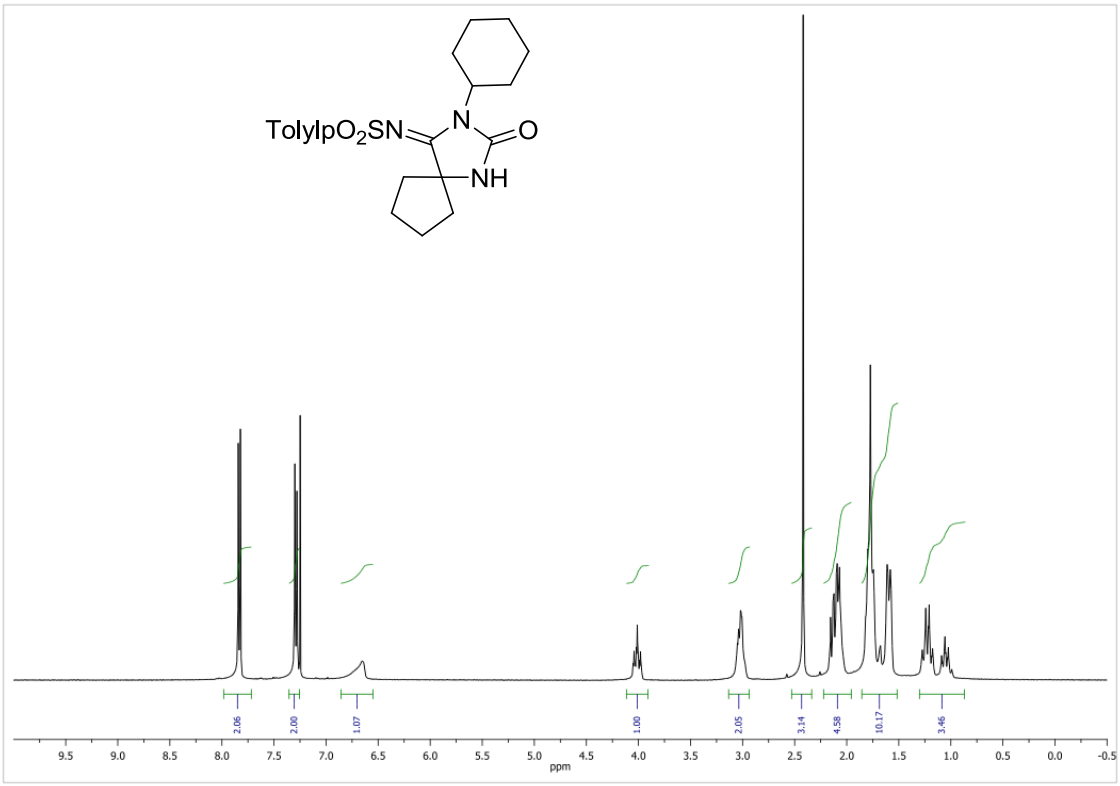


^{1}H NMR (300 MHz, $CDCl_3$)

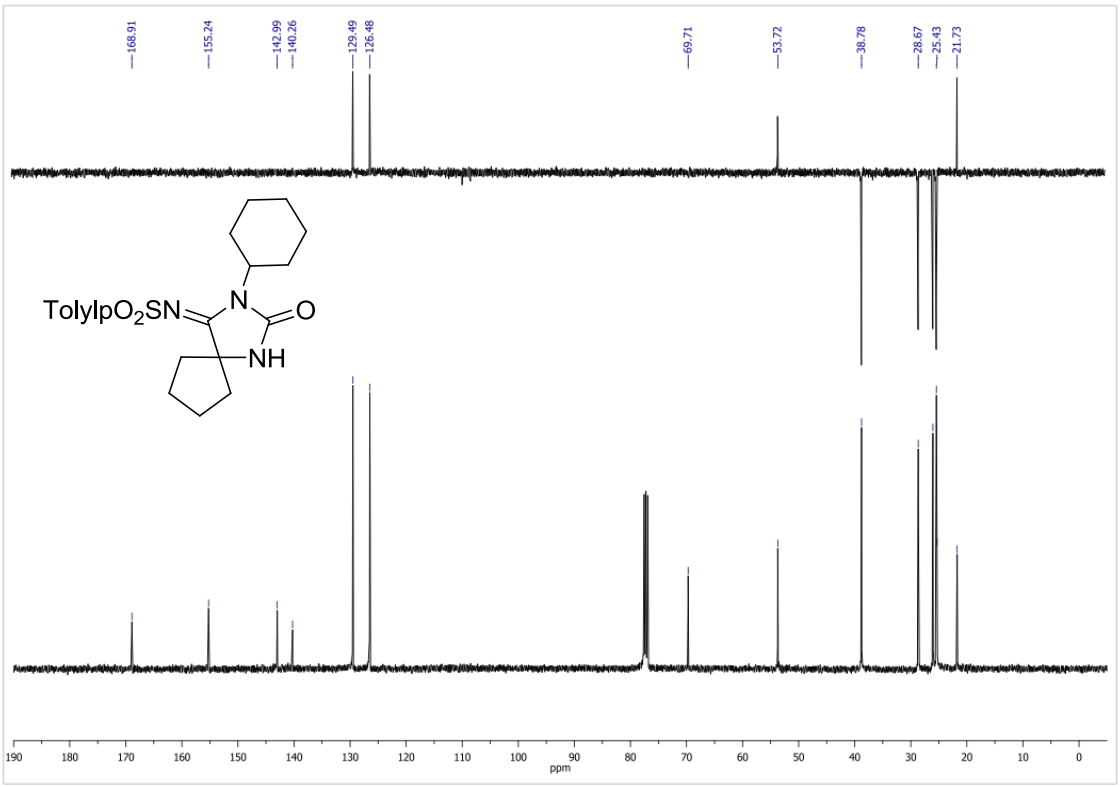


^{13}C NMR (75 MHz, $CDCl_3$)

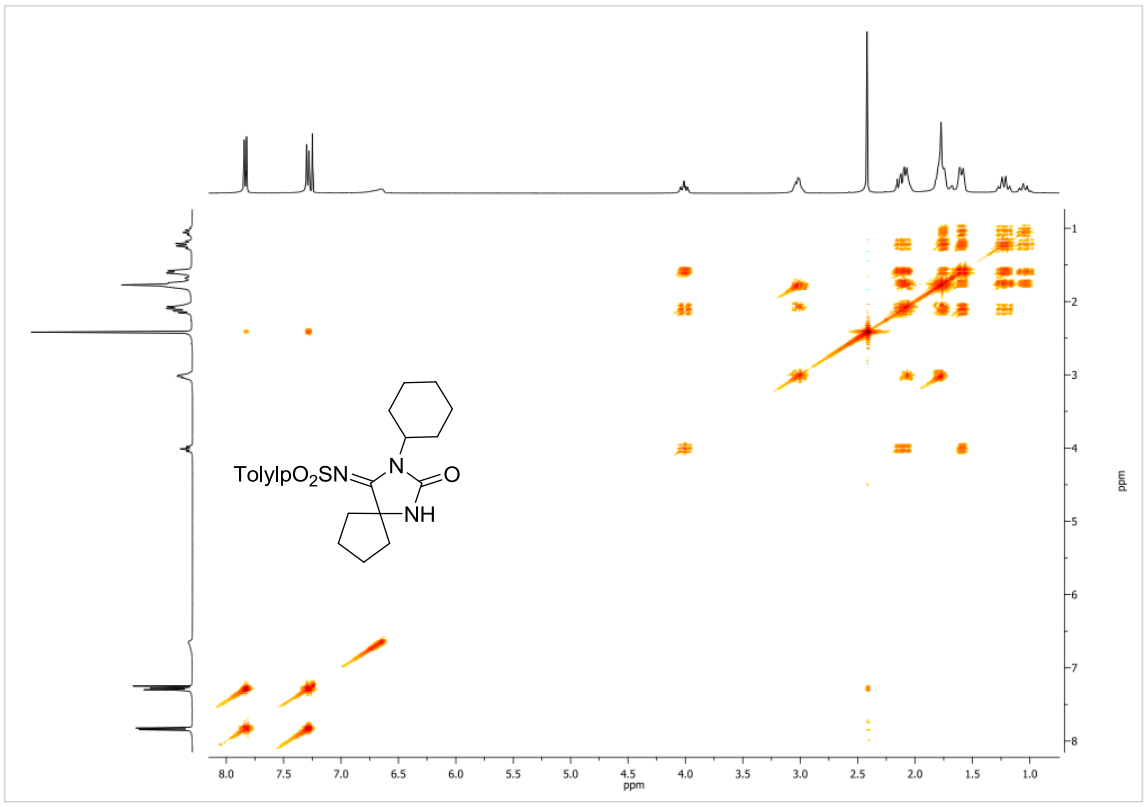
3-Cyclohexyl-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.4]nonan-2-one (3d).



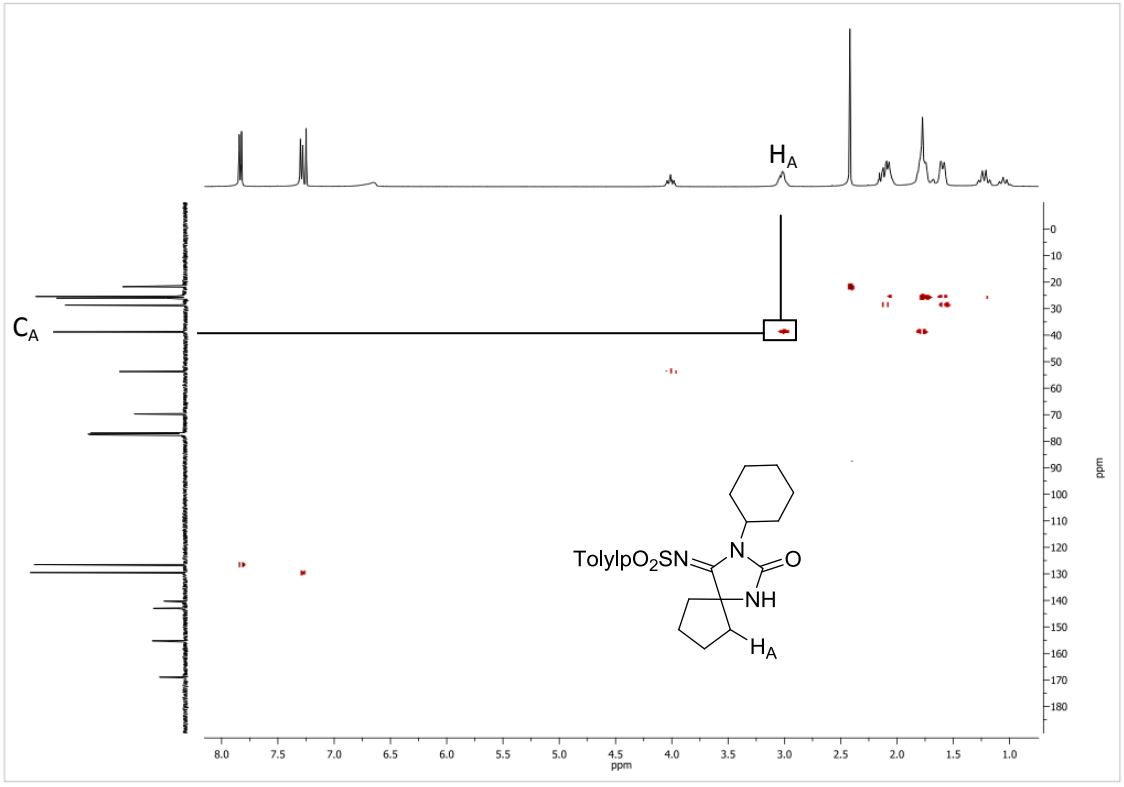
^{1}H NMR (400 MHz, $CDCl_3$)



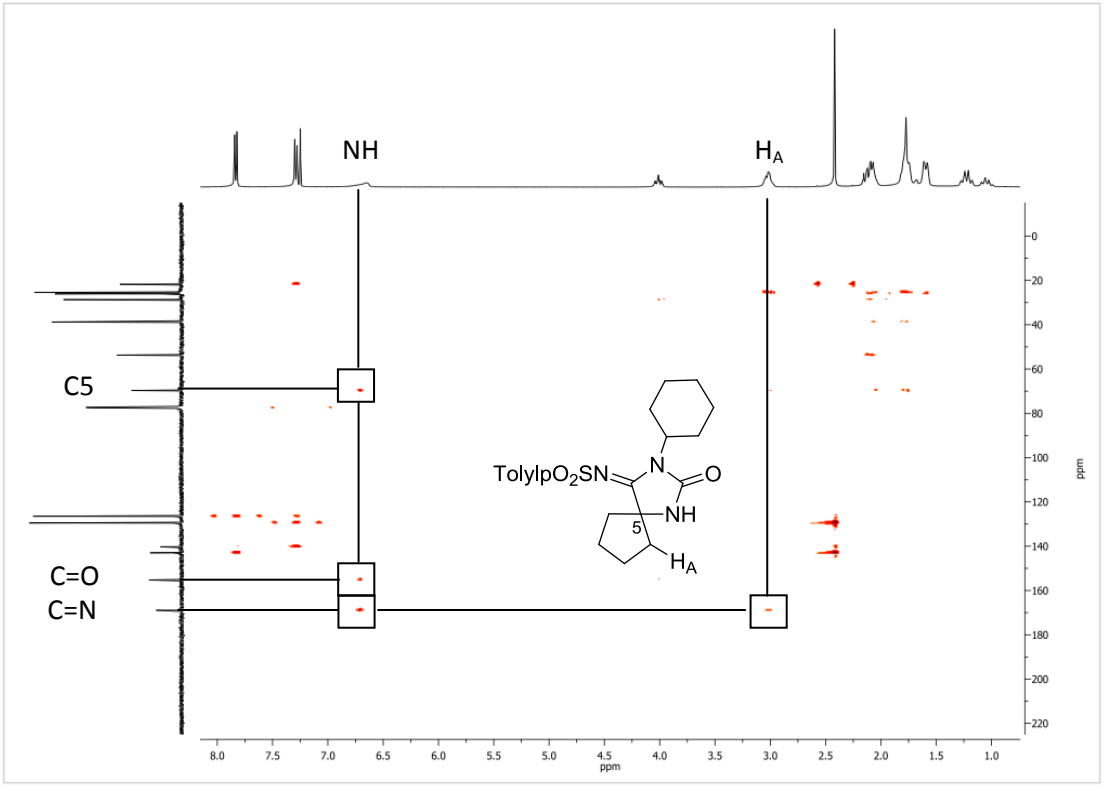
^{13}C NMR (100 MHz, $CDCl_3$)



COSY

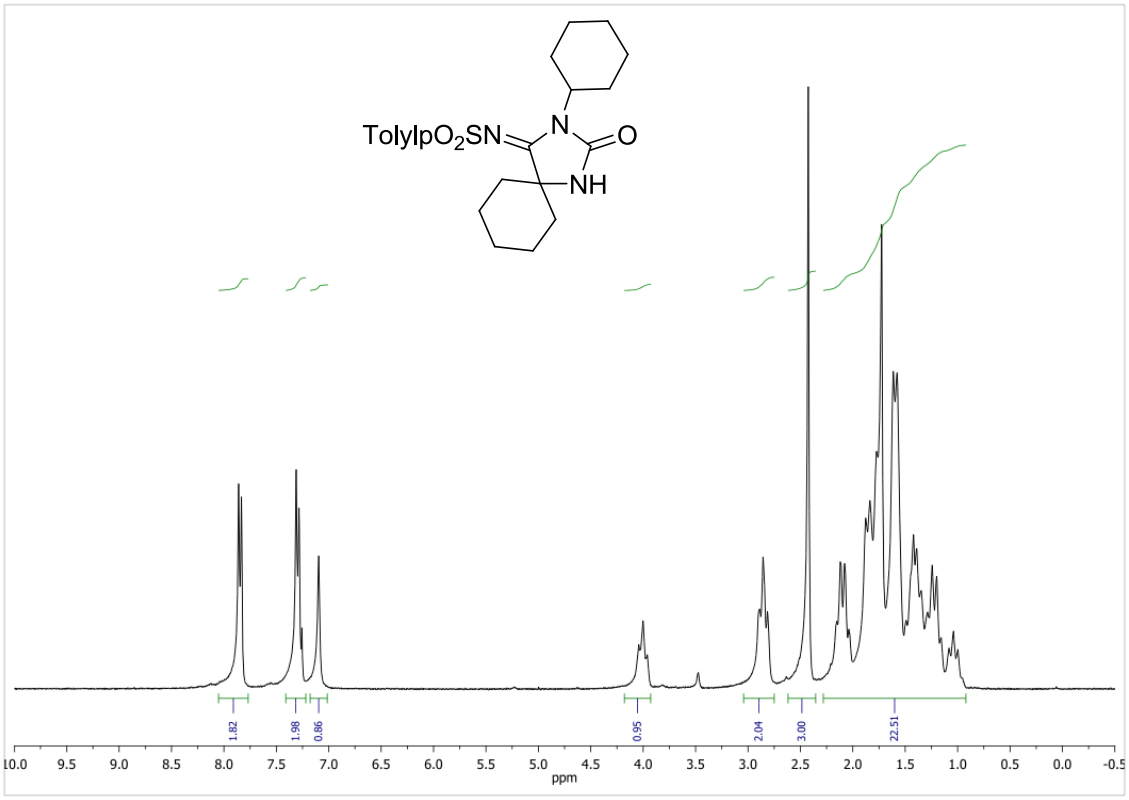


HMQC

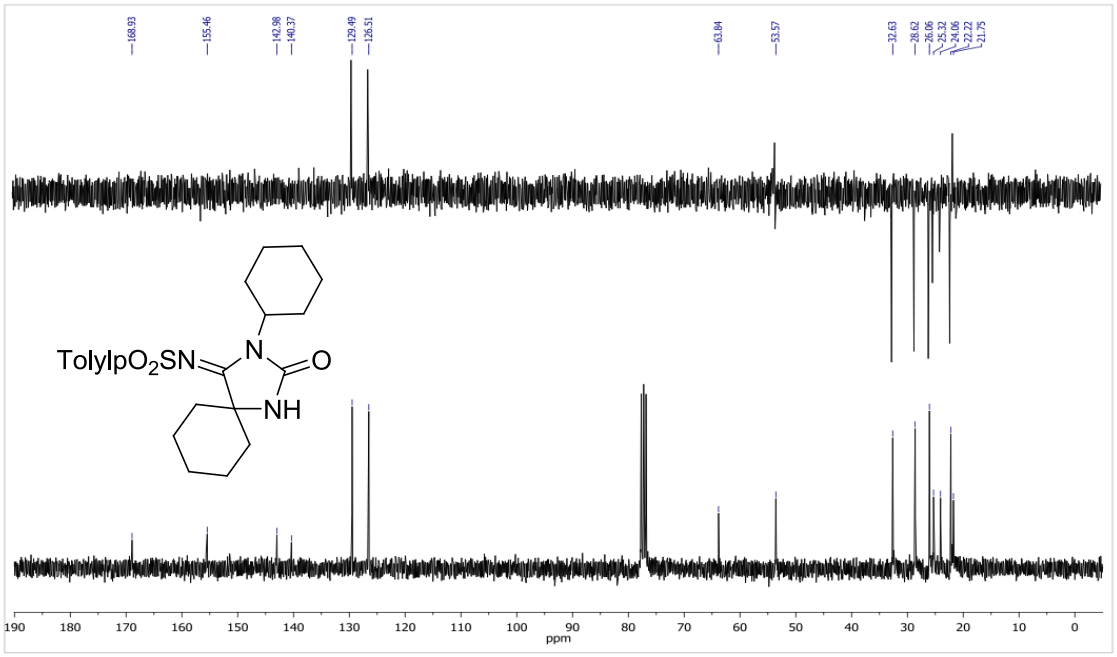


HMBC

3-Cyclohexyl-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-2-one (3e).

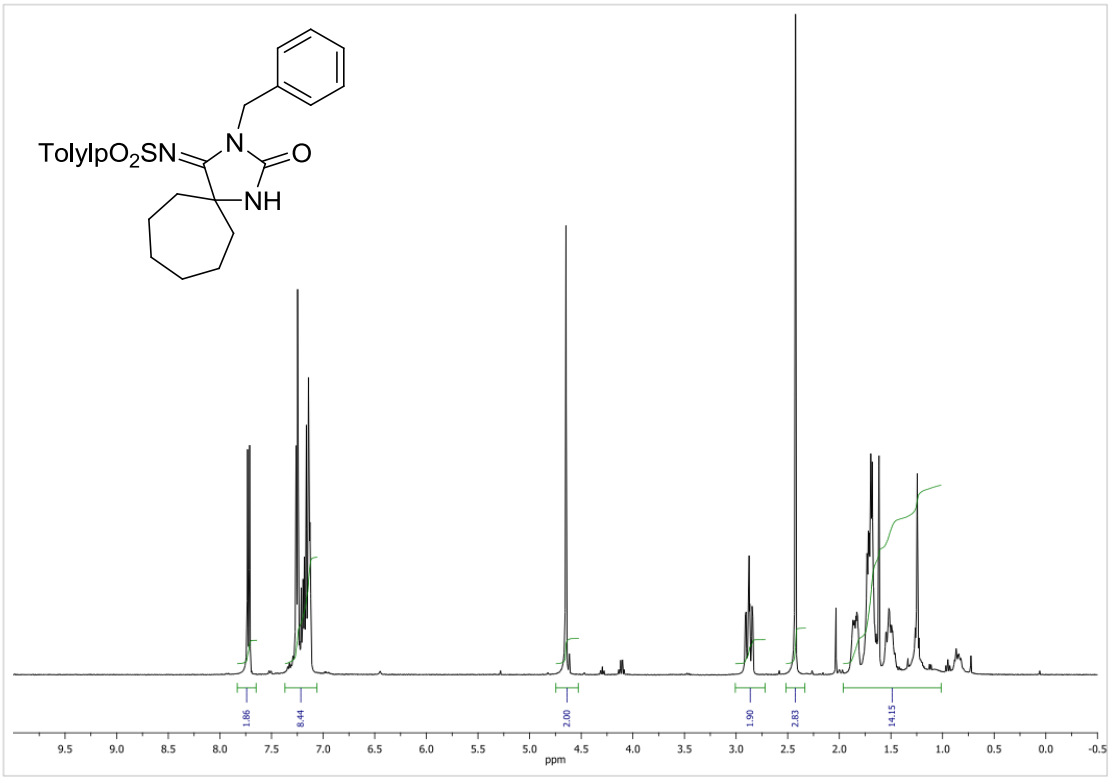


^{1}H NMR (300 MHz, $CDCl_3$)

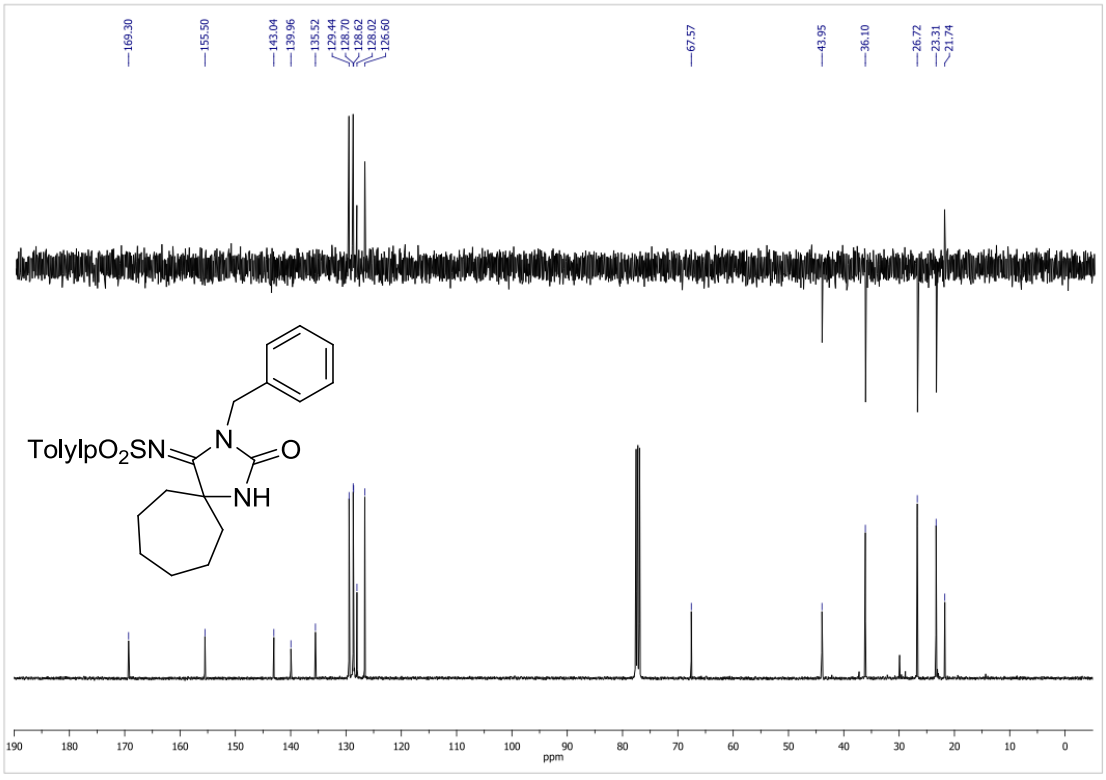


^{13}C NMR (75 MHz, $CDCl_3$)

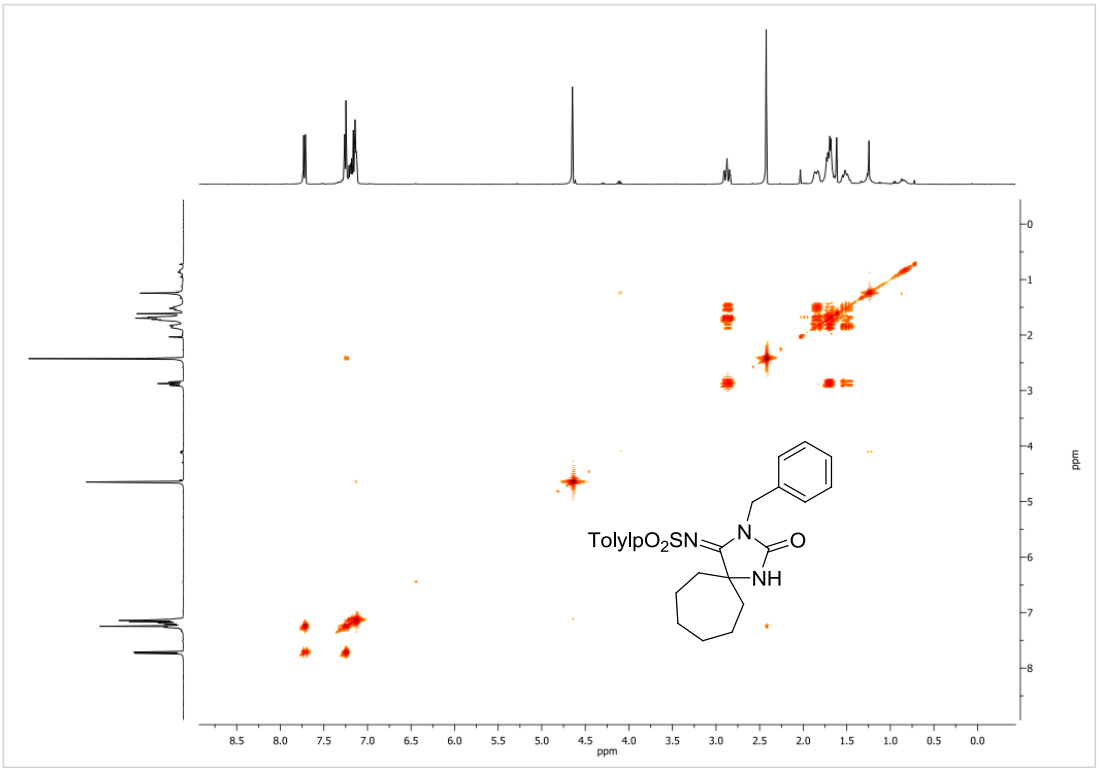
3-Benzyl-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.6]undecan-2-one (3f).



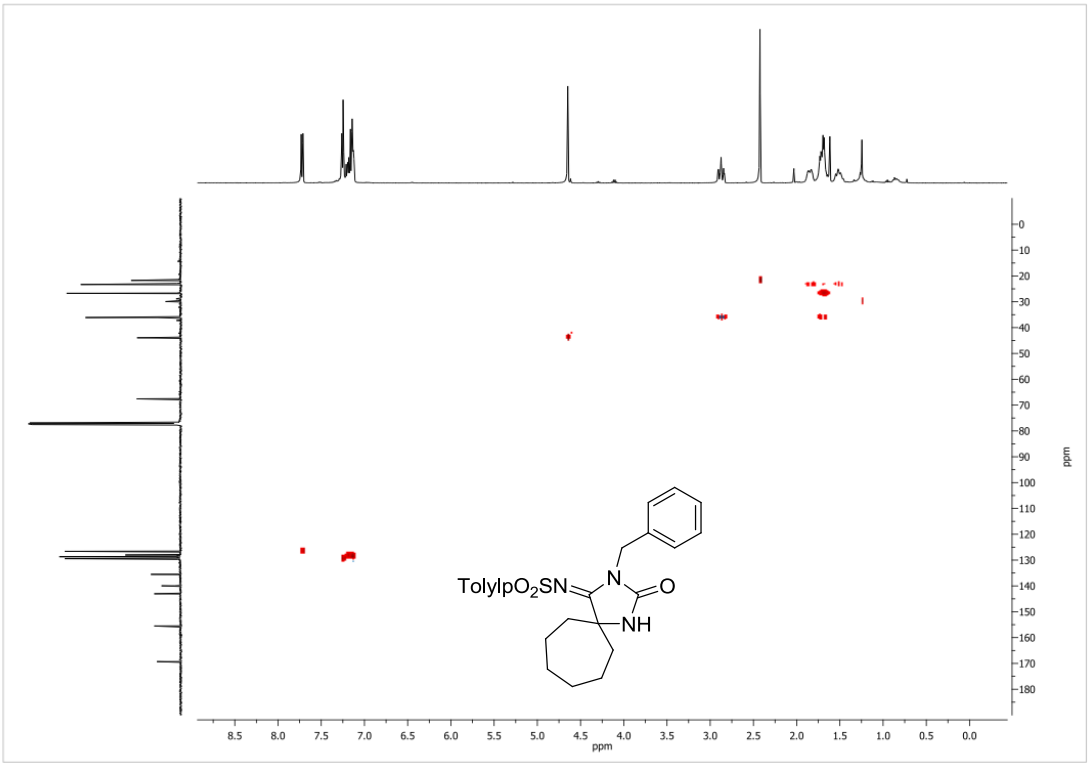
^{1}H NMR (400 MHz, $CDCl_3$)



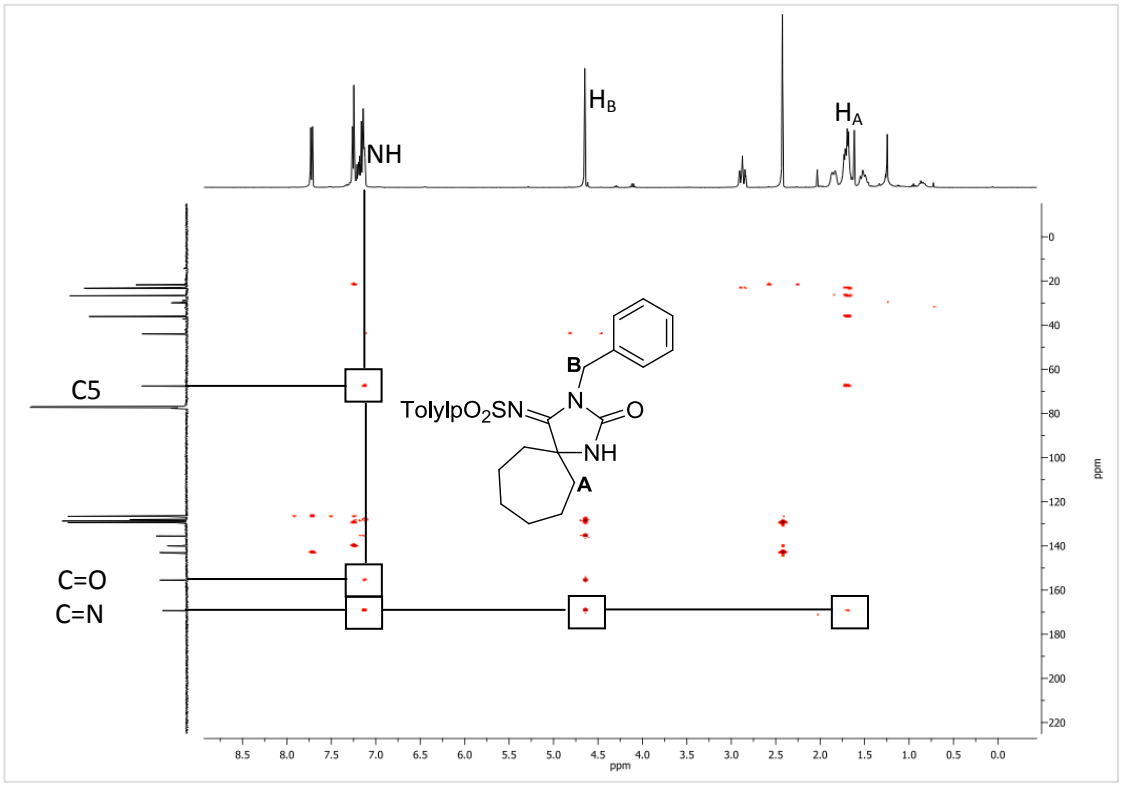
^{13}C NMR (100 MHz, $CDCl_3$)



COSY

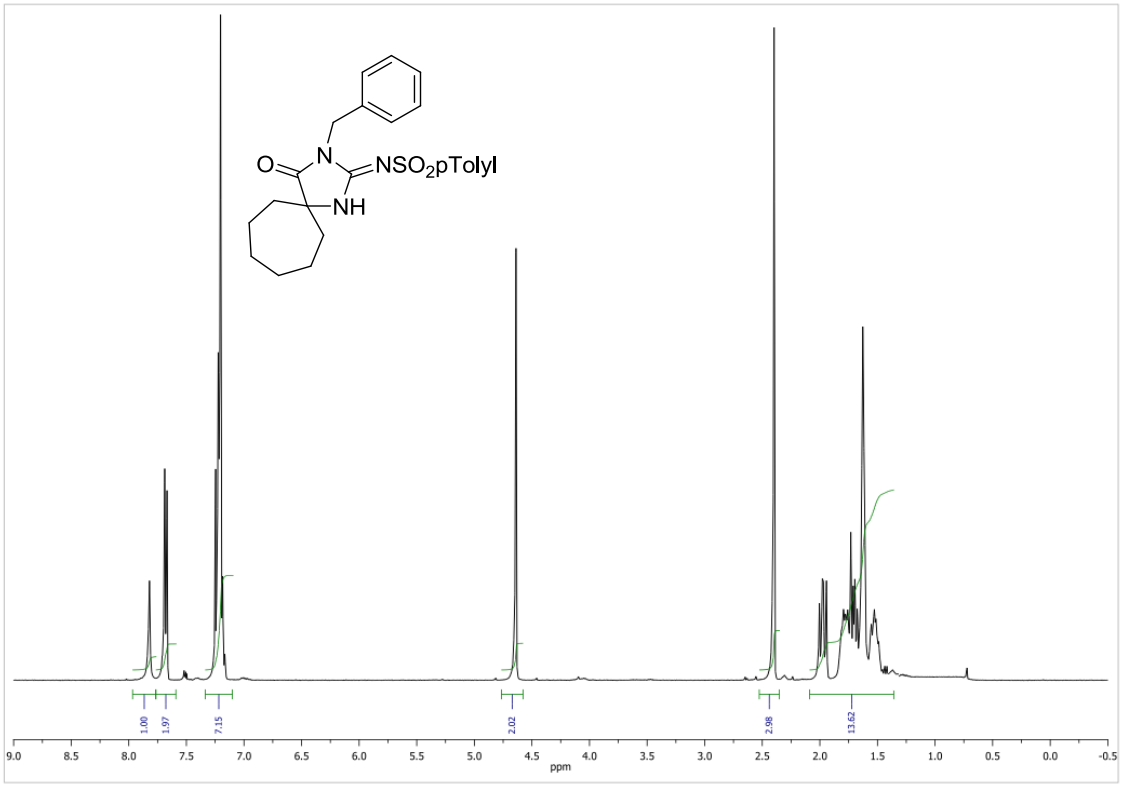


HMQC

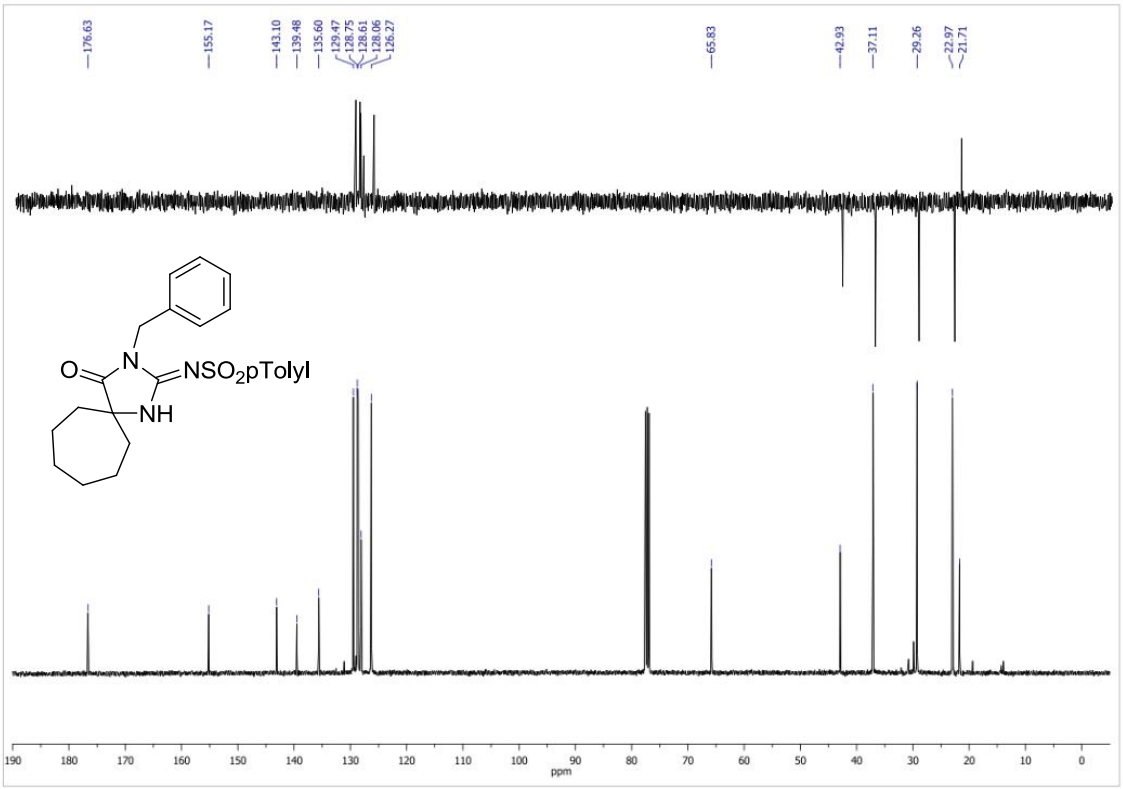


HMBC

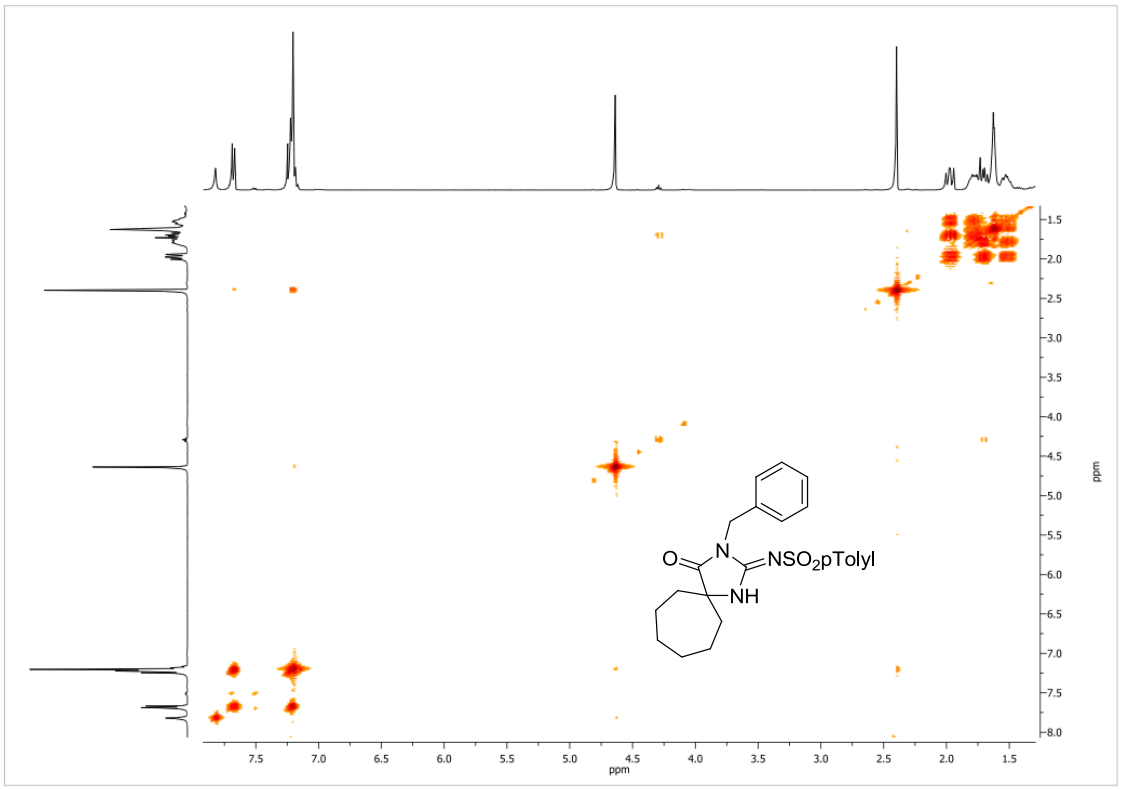
3-Benzyl-2-[(4-tolylsulfonyl)imino]-1,3-diaza-spiro[4.6]undecan-4-one (4f).



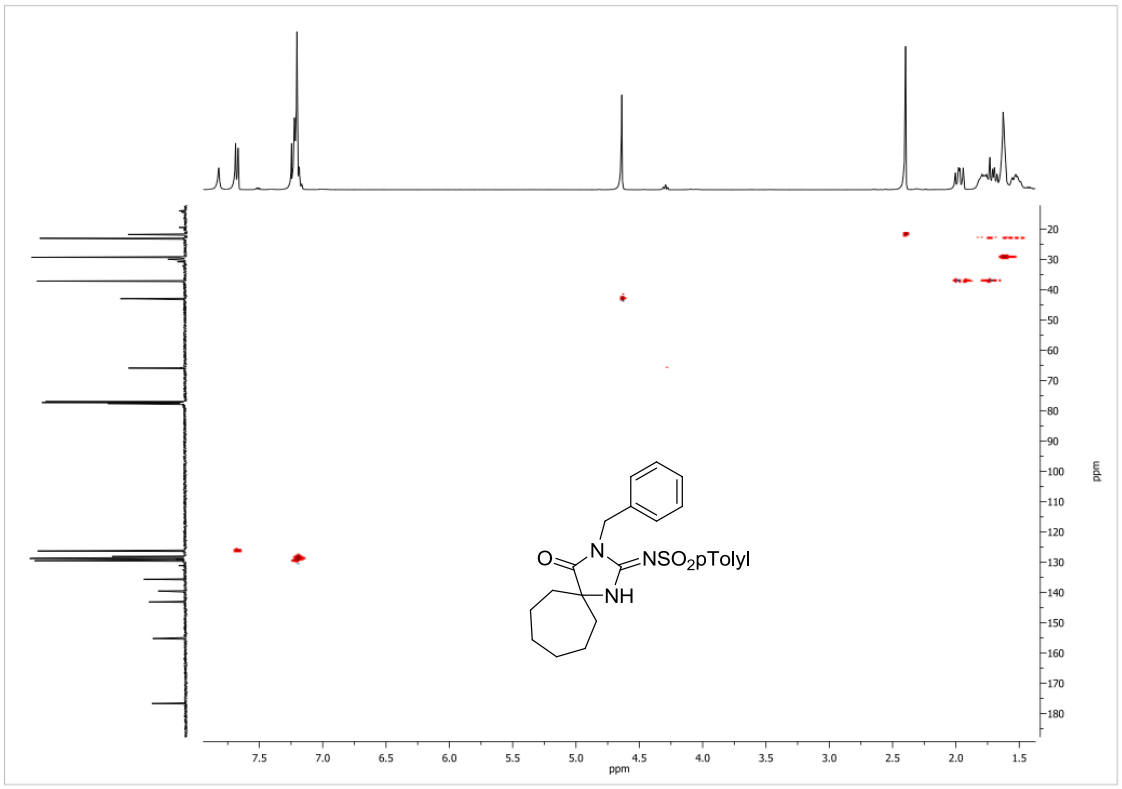
^{1}H NMR (400 MHz, $CDCl_3$)



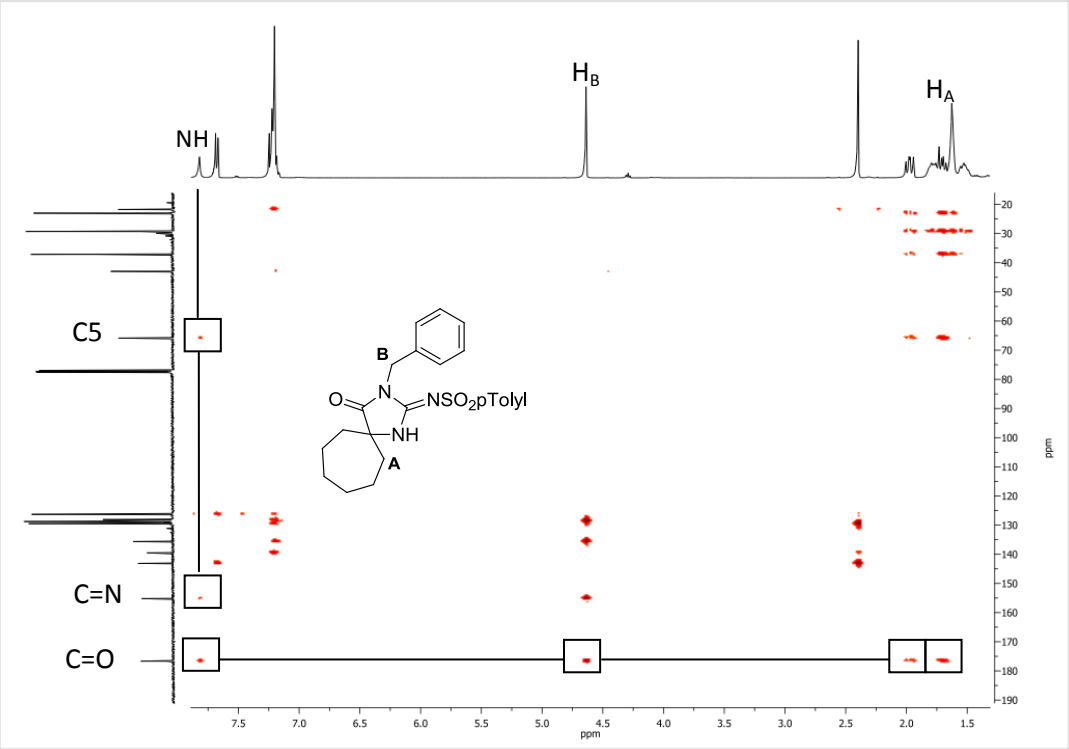
^{13}C NMR (400 MHz, $CDCl_3$)



COSY

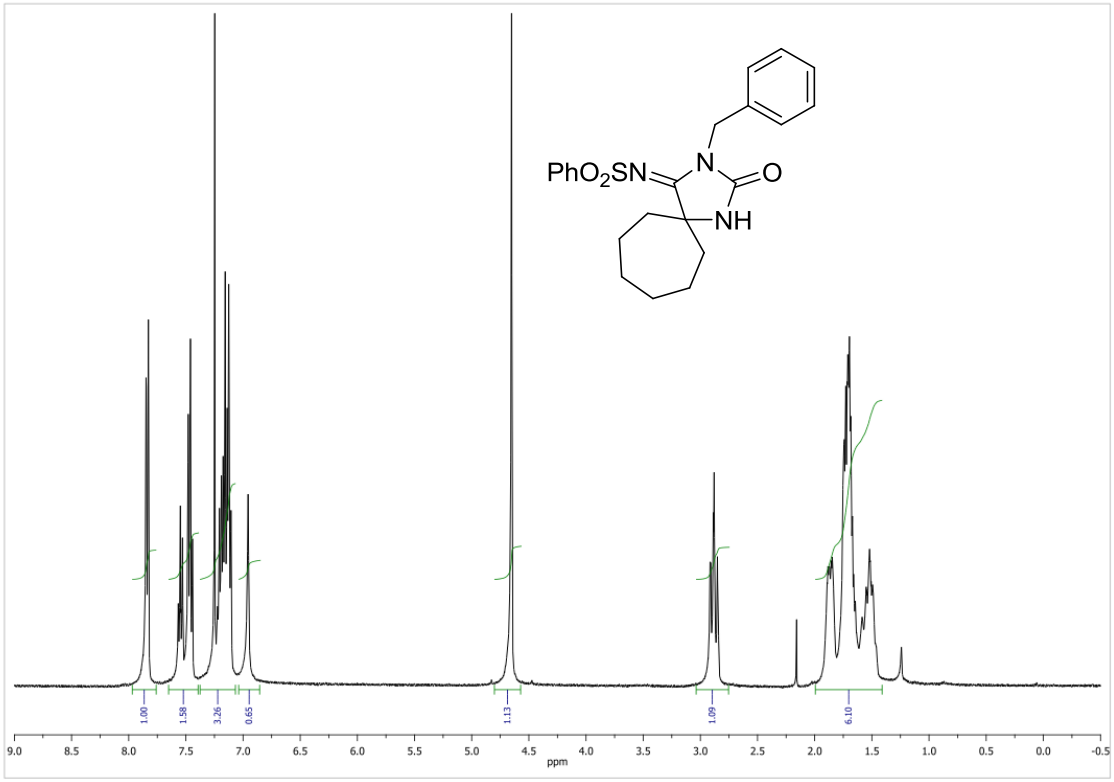


HMQC

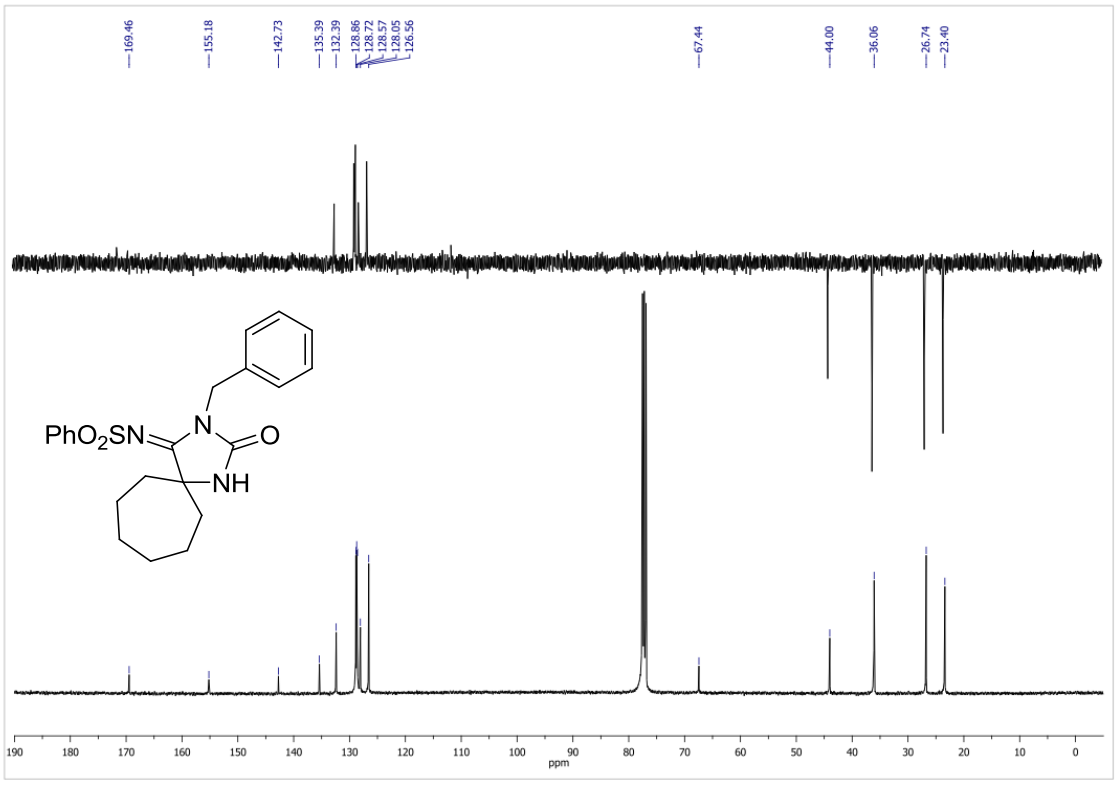


HMBC

3-Benzyl-4-phenylsulfonylimino-1,3-diazaspiro[4.6]undecan-4-one (3g).

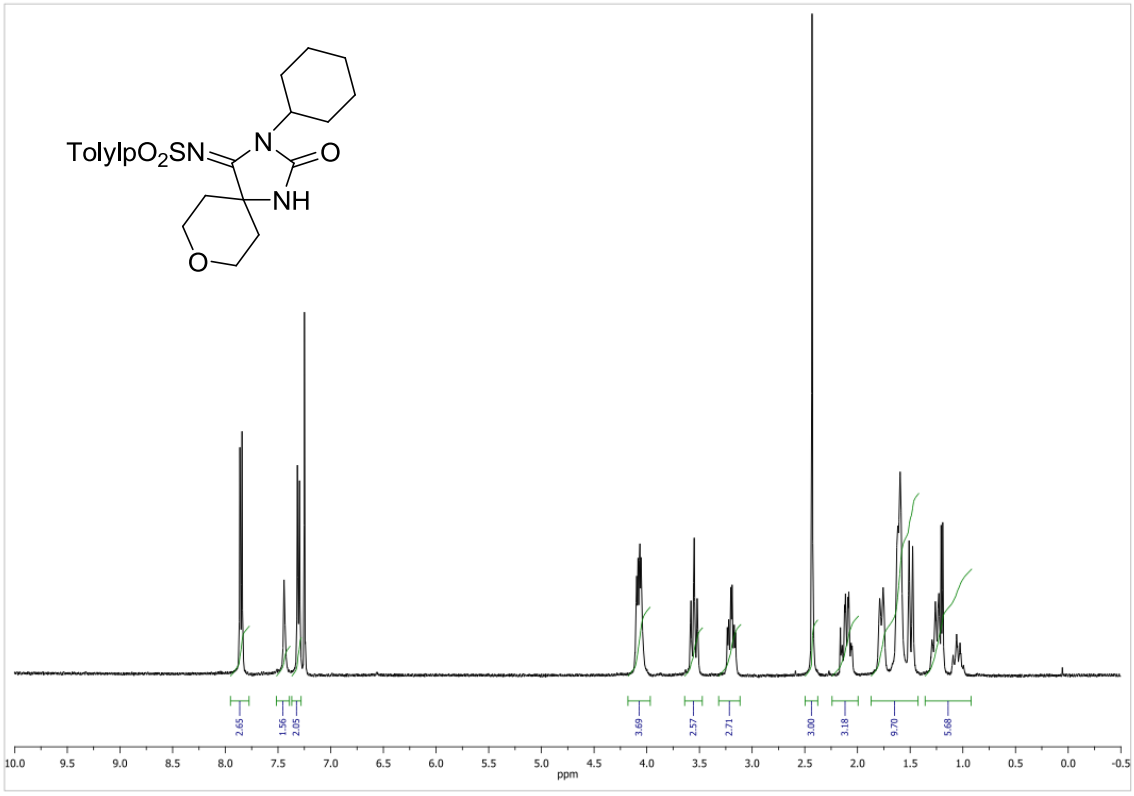


^{1}H NMR (400 MHz, $CDCl_3$)

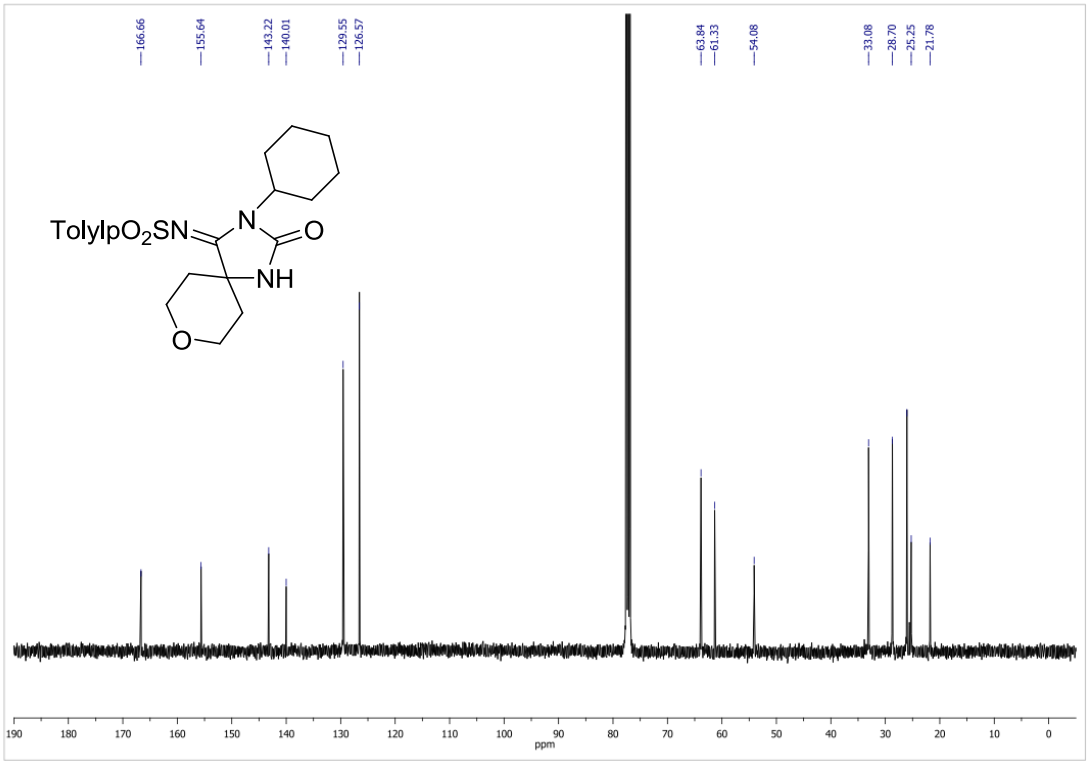


^{13}C NMR (100 MHz, $CDCl_3$)

3-Cyclohexyl-4-[(4-tolylsulfonyl)imino]-1,3-diaza-8-oxaspiro[4.5]decan-2-one (3h).

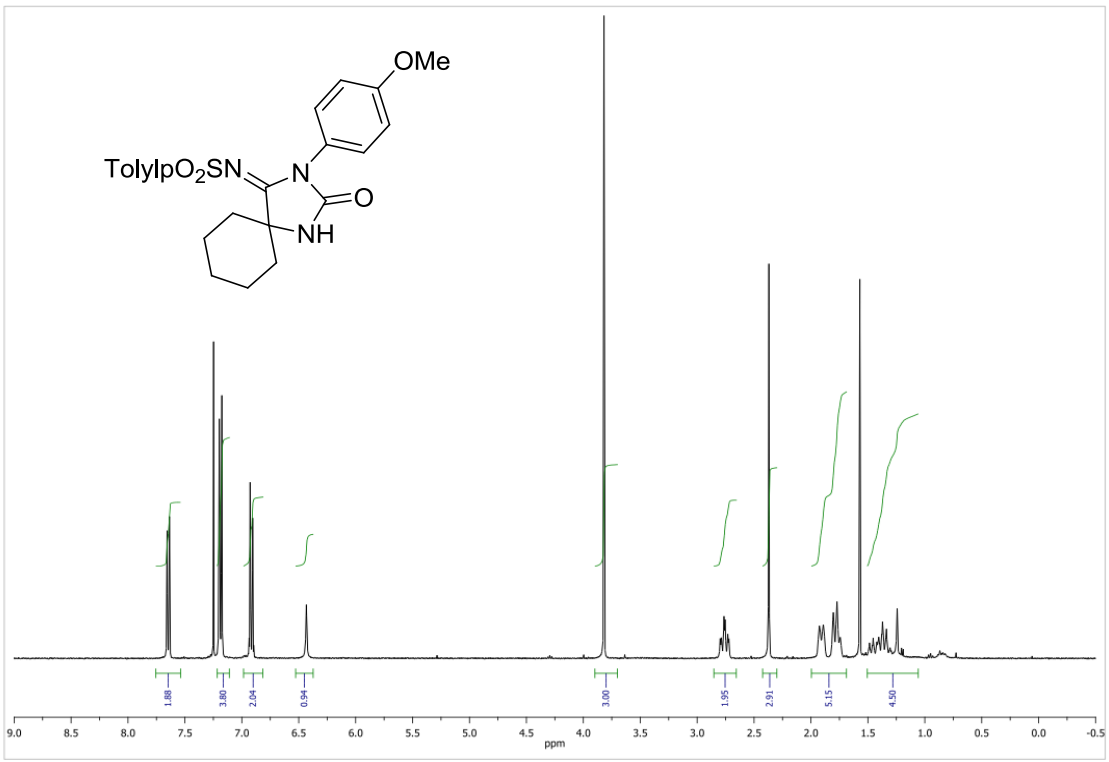


^{1}H NMR (300 MHz, $CDCl_3$)

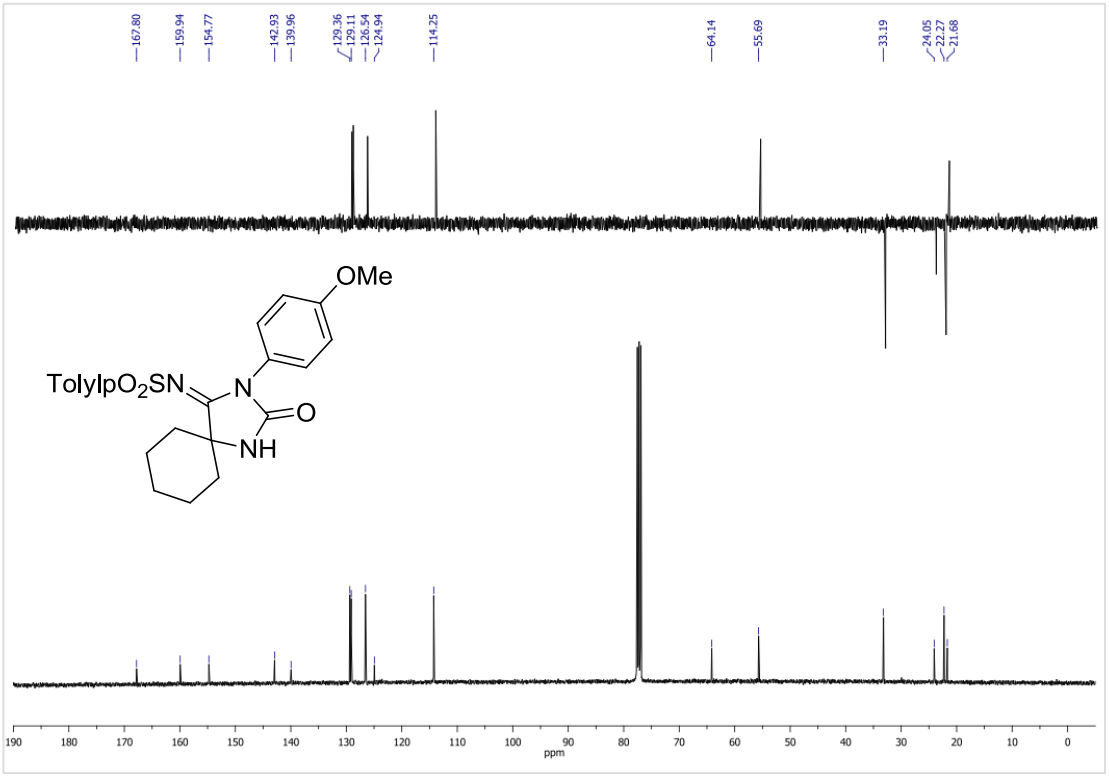


^{13}C NMR (75 MHz, $CDCl_3$)

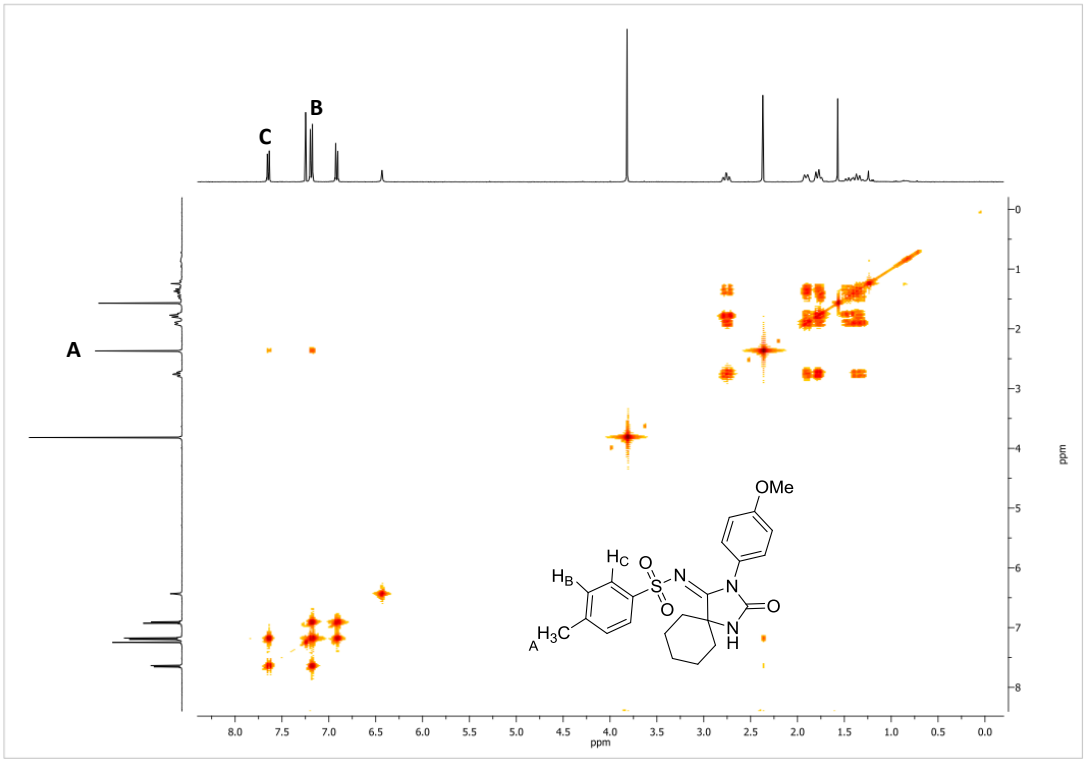
3-(4-Methoxyphenyl)-4-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-2-one (3i).



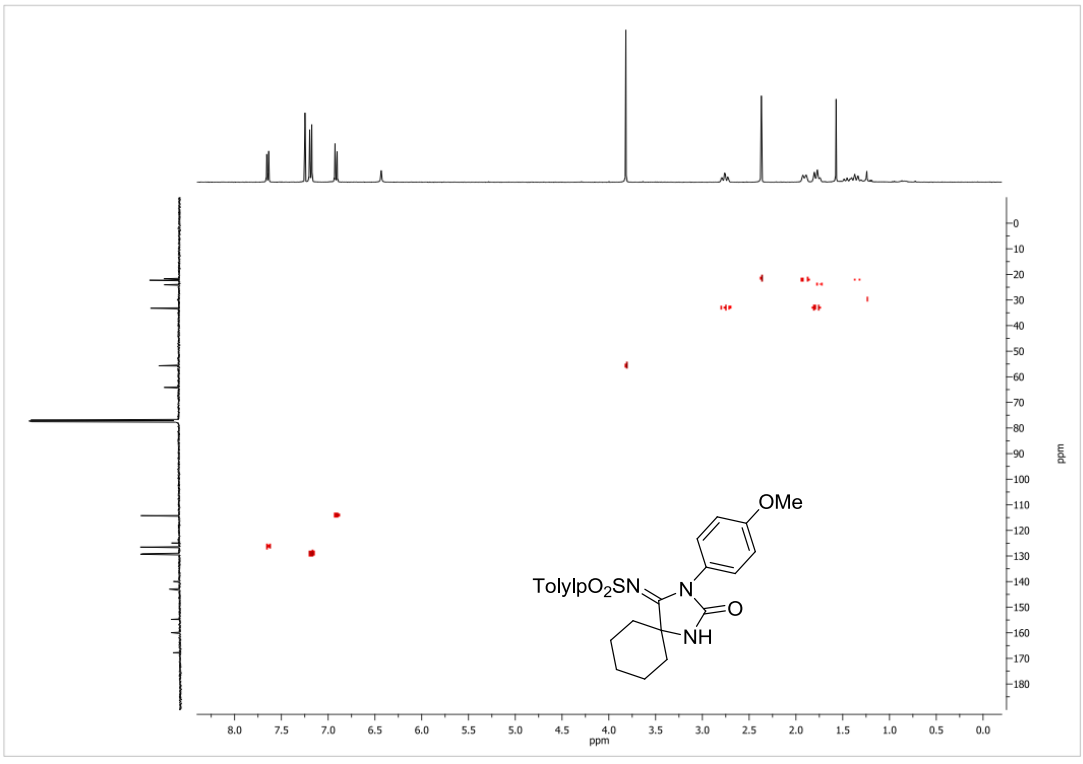
^{1}H NMR (400 MHz, $CDCl_3$)



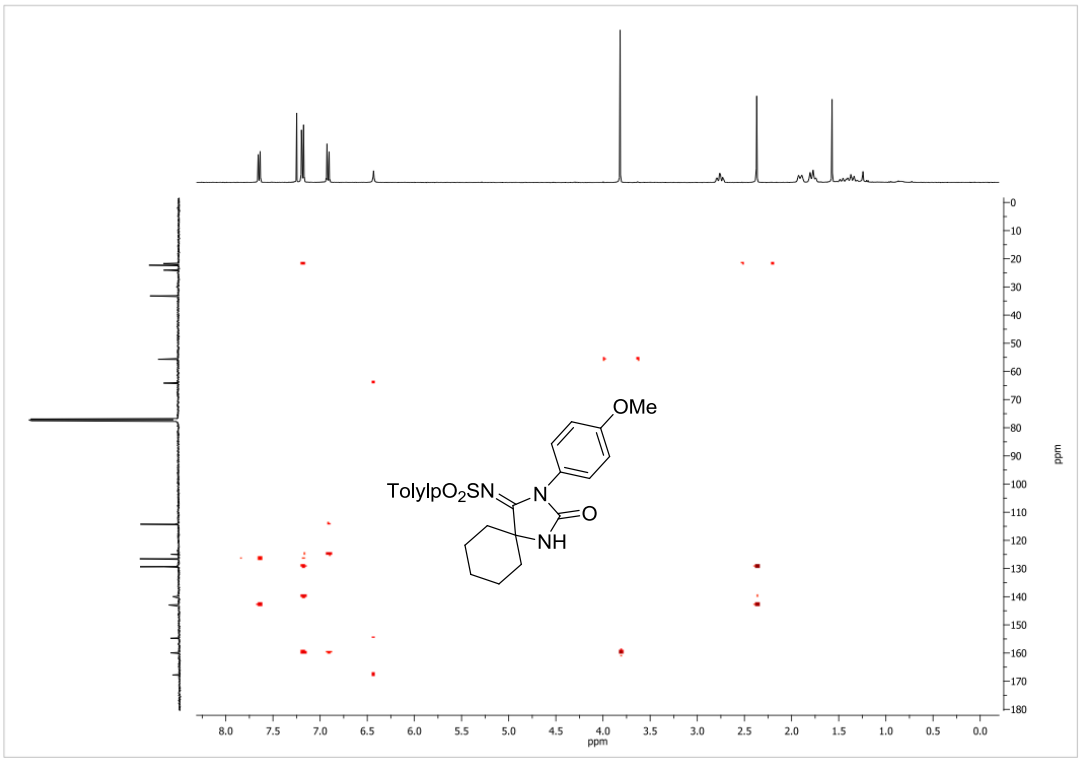
^{13}C NMR (100 MHz, $CDCl_3$)



COSY

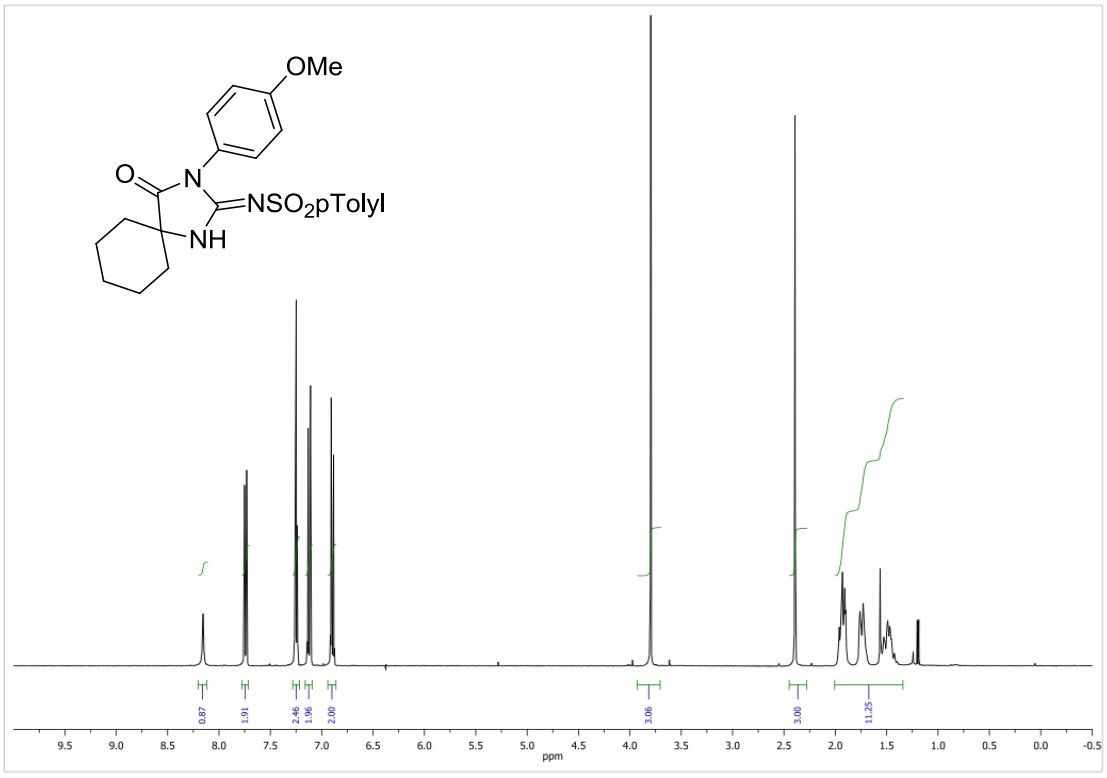


HMQC

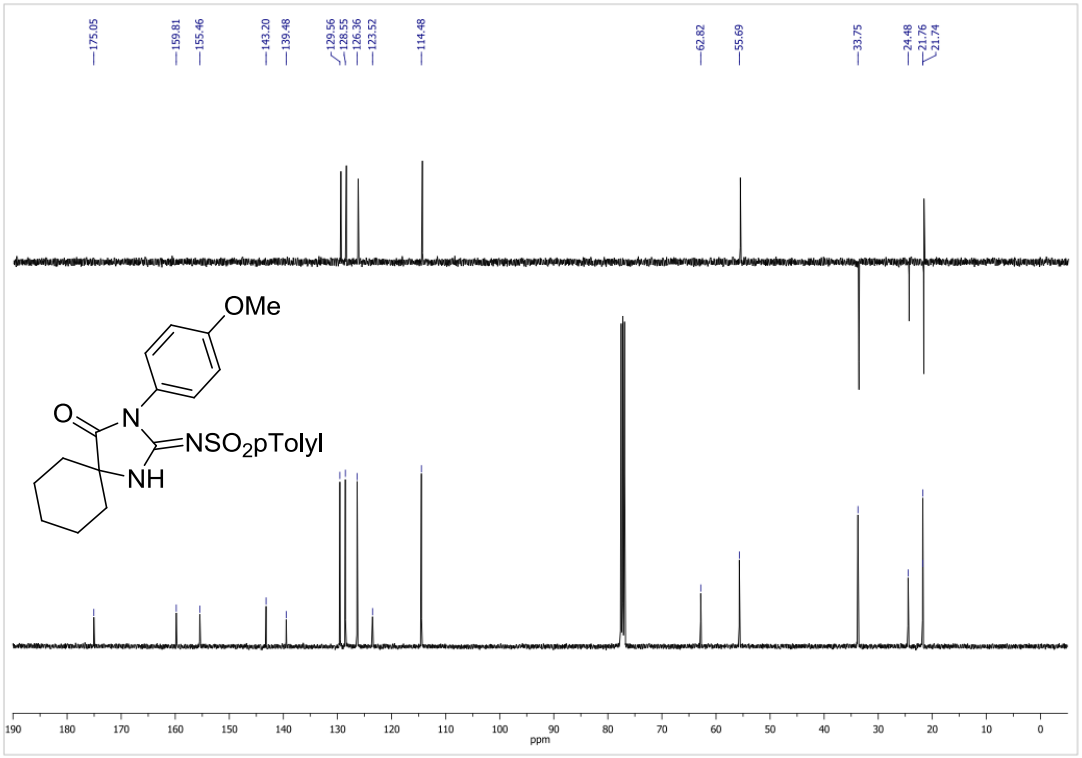


HMBC

3-(4-Methoxyphenyl)-2-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-4-one (4i).

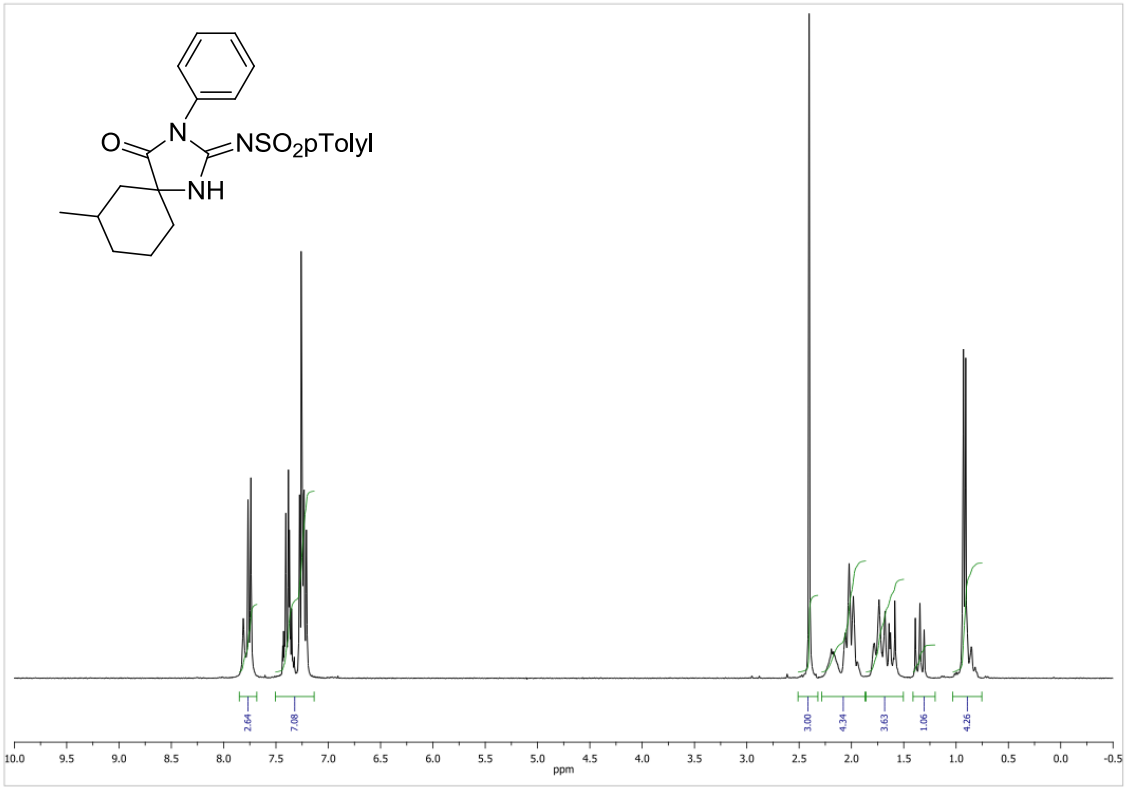


^{1}H NMR (400 MHz, $CDCl_3$)

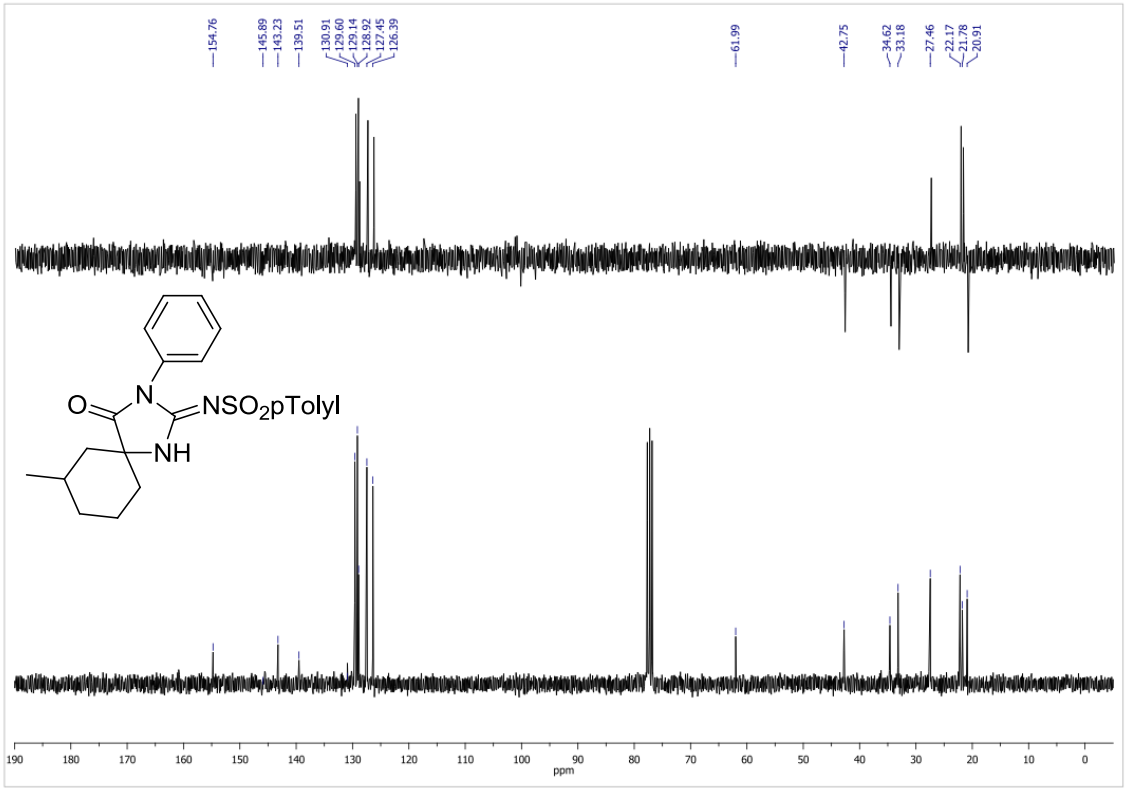


^{13}C NMR (100 MHz, $CDCl_3$)

7-Methyl-3-phenyl-2-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-4-one (4j).

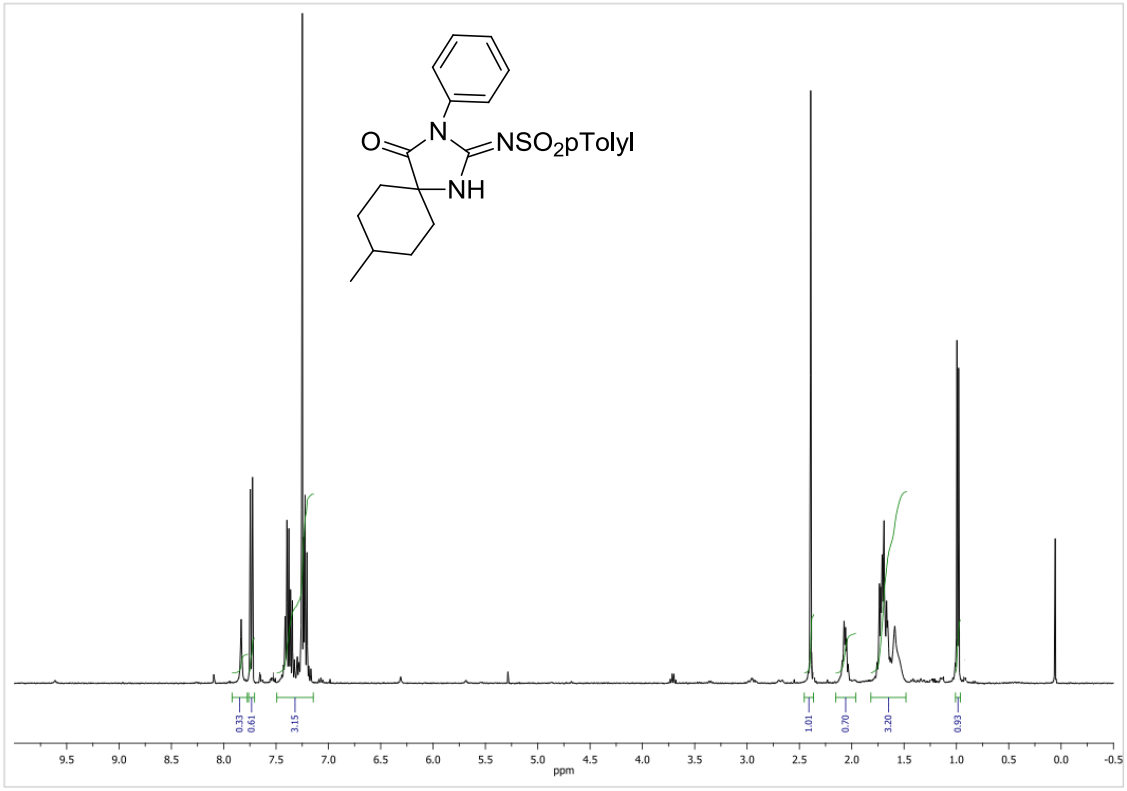


^{1}H NMR (300 MHz, $CDCl_3$)

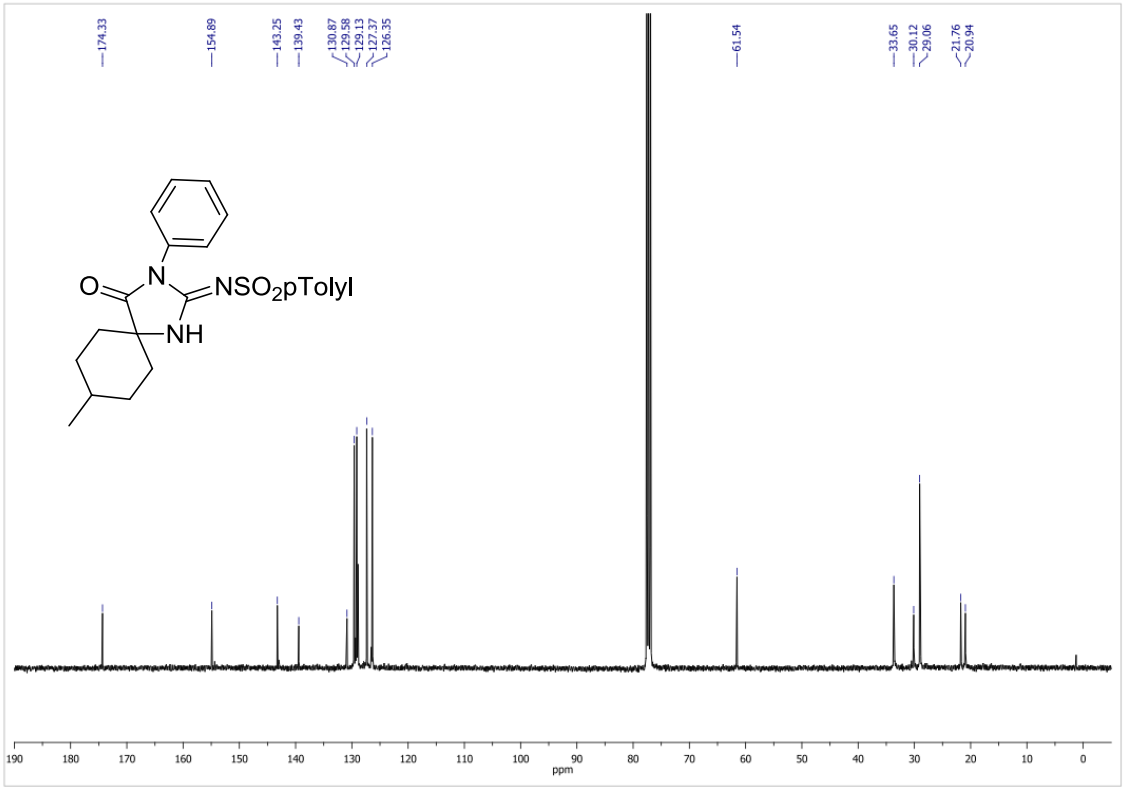


^{13}C NMR (75 MHz, $CDCl_3$)

8-Methyl-3-phenyl-2-[(4-tolylsulfonyl)imino]-1,3-diazaspiro[4.5]decan-4-one (4k).

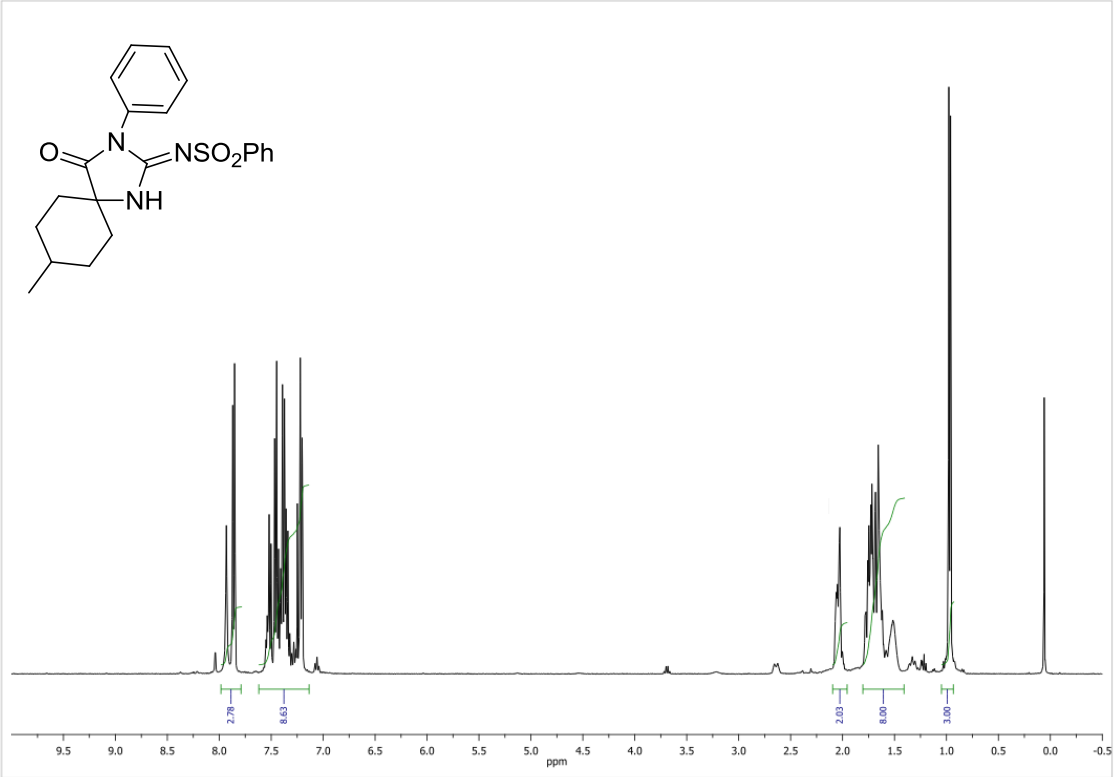


^{1}H NMR (300 MHz, $CDCl_3$)

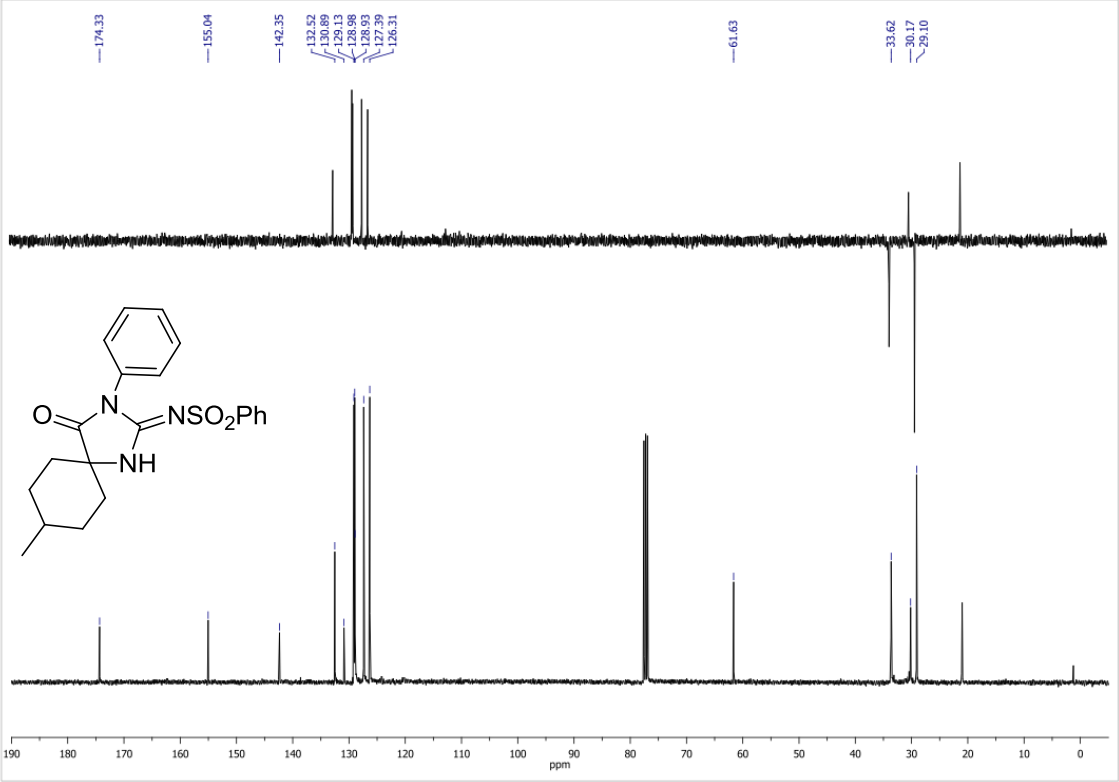


^{13}C NMR (75 MHz, $CDCl_3$)

8-Methyl-3-phenyl-2-phenylsulfonylimino-1,3-diazaspiro[4.5]decan-4-one (4l).



^{1}H NMR (400 MHz, $CDCl_3$)



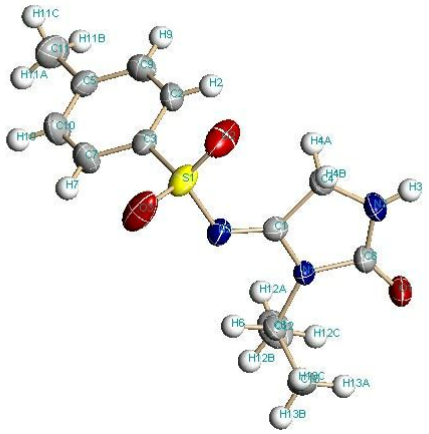
^{13}C NMR (100 MHz, $CDCl_3$)

Crystal Structure Determination for Compound 3c

Crystallographic data are presented in Tables 1-**check last table**. A single crystal of **3c** was coated in **high-vacuum grease** and mounted on a glass fibre. X-ray measurements were made using a Bruker SMART CCD area-detector diffractometer with Mo-K_α radiation (λ = 0.71073 Å).[2] Intensities were integrated[3] from several series of exposures, each exposure covering 0.3° in ω, and the total data set being a **hemisphere**. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements.[4] The structure was solved by **direct methods** and refined by least squares on weighted F^2 values for all reflections (see Table 1).[5]

All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. All hydrogen atoms were constrained to ideal geometries and refined with fixed isotropic displacement parameters.

Refinement proceeded smoothly to give the residuals shown in Table 1. Complex neutral-atom scattering factors were used.[6]



[2] SMART diffractometer control software, Bruker Analytical X-ray Instruments Inc., Madison, WI, 2000.
[3] SAINT integration software, Siemens Analytical X-ray Instruments Inc., Madison, WI, 2000.
[4] G. M. Sheldrick. *SADABS: A program for absorption correction with the Siemens SMART system;* University of Göttingen: Germany, 2001.
[5] *SHELXTL program system version 6.1;* Bruker Analytical X-ray Instruments Inc., Madison, WI, 1998.
[6] *International Tables for Crystallography*, Kluwer, Dordrecht, 1992, vol. C.

Table 1. Crystal data and structure refinement for **3c**.

Identification code	datosm
Empirical formula	C13 H17 N3 O3 S
Formula weight	295.36
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	a = 15.939(3) Å α = 90°
	b = 5.4586(9) Å β = 96.807(3)°
	c = 16.280(3) Å γ = 90°
Volume	1406.5(4) $Å^3$
Z	4
Density (calculated)	1.395 Mg/m^3
Absorption coefficient	0.241 mm^{-1}
F(000)	624
Crystal size	0.90 x 0.10 x 0.10 mm
θ range for data collection	1.29 to 25.00°
Index ranges	-18<=h<=18, -6<=k<=6, -19<=l<=19
Reflections collected	13033
Independent reflections	2489 [R_{int} = 0.0756]
Completeness to θ = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.614130
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2489 / 0 / 184
Goodness-of-fit on F^2	S = 1.049
R indices [for 1910 reflections with I>2σ(I)]	R_1 = 0.0475, wR_2 = 0.1129
R indices (for all 2489 data)	R_1 = 0.0663, wR_2 = 0.1280
Weighting scheme	$w^{-1} = \sigma^2(F_o^2) + (aP)^2 + (bP)$,
	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
	a = **0.0494**, b = **0.61210**
Largest diff. peak and hole	0.288 and -0.258 $eÅ^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **3c**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
S(1)	2279(1)	13466(1)	4242(1)	48(1)
O(1)	4620(1)	5958(4)	5945(1)	55(1)
O(2)	2736(1)	13260(4)	3541(1)	69(1)
O(3)	2136(1)	15873(4)	4549(2)	72(1)
N(1)	3631(1)	9050(4)	5654(1)	35(1)
N(2)	2704(1)	11911(4)	5034(1)	40(1)
N(3)	4290(2)	7589(4)	4644(1)	51(1)
C(1)	3286(2)	10303(4)	4978(1)	34(1)
C(2)	1213(2)	10009(5)	3493(2)	47(1)
C(3)	1291(2)	12041(5)	3996(2)	39(1)
C(4)	3718(2)	9407(5)	4258(2)	44(1)
C(5)	-263(2)	9728(5)	3631(2)	46(1)
C(6)	3384(2)	9377(5)	6495(2)	42(1)
C(7)	589(2)	12936(6)	4309(2)	56(1)
C(8)	4231(2)	7344(5)	5449(2)	41(1)
C(9)	441(2)	8882(5)	3315(2)	50(1)
C(10)	-176(2)	11781(6)	4128(2)	60(1)
C(11)	-1103(2)	8468(7)	3439(2)	69(1)
C(12)	2969(2)	7086(6)	6778(2)	72(1)
C(13)	4133(2)	10234(7)	7084(2)	64(1)

Crystal Structure Determination for Compound 4f

Crystallographic data are presented in Tables 1-**check last table**. A single crystal of **4f** was coated in **high-vacuum grease** and mounted on a glass fibre. X-ray measurements were made using a Bruker SMART CCD area-detector diffractometer with Mo-K_α radiation (λ = 0.71073 Å).[2] Intensities were integrated[3] from several series of exposures, each exposure covering 0.3° in ω, and the total data set being a **hemisphere**. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements.[4] The structure was solved by **direct methods** and refined by least squares on weighted F^2 values for all reflections (see Table 1).[5]

All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. All hydrogen atoms were constrained to ideal geometries and refined with fixed isotropic displacement parameters.

Refinement proceeded smoothly to give the residuals shown in Table 1. Complex neutral-atom scattering factors were used.[6]

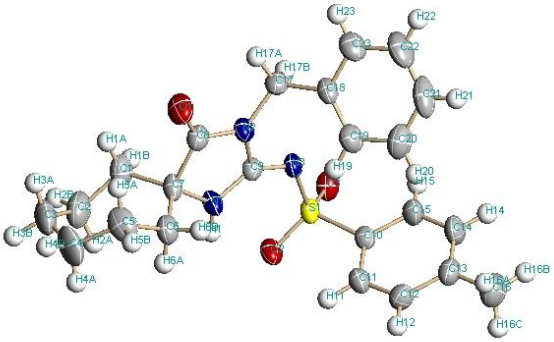


Table 1. Crystal data and structure refinement for **4f**.

Identification code	datosm
Empirical formula	C23 H27 N3 O3 S
Formula weight	425.54
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 13.1137(14) Å α = 90°
	b = 6.2475(7) Å β = 113.906(2)°
	c = 14.2342(16) Å γ = 90°
Volume	1066.1(2) $Å^3$
Z	2
Density (calculated)	1.326 Mg/m^3
Absorption coefficient	0.182 mm^{-1}
F(000)	452
Crystal size	0.9 x 0.10 x 0.10 mm
θ range for data collection	1.56 to 25.00°
Index ranges	-15<=h<=15, -7<=k<=7, -16<=l<=16
Reflections collected	10556
Independent reflections	3769 [R_{int} = 0.1630]
Completeness to θ = 25.00°	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3769 / 1 / 273
Goodness-of-fit on F^2	S = 1.008
R indices [for 3267 reflections with I>2σ(I)]	R_1 = 0.0722, wR_2 = 0.1506
R indices (for all 3769 data)	R_1 = 0.0774, wR_2 = 0.1536
Weighting scheme	$w^{-1} = \sigma^2(F_o^2) + (aP)^2 + (bP)$,
	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
	a = 0.084000, b = 0.00000
Absolute structure (Flack) parameter	0.42(11)
Largest diff. peak and hole	0.482 and -0.224 $eÅ^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **4f**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
S(1)	6236(1)	3828(1)	4818(1)	33(1)
O(1)	2412(3)	1743(5)	852(2)	58(1)
O(2)	5523(2)	5144(4)	5119(2)	44(1)
O(3)	6913(2)	2287(4)	5546(2)	44(1)
N(1)	3762(2)	4165(5)	3236(2)	38(1)
N(2)	4120(3)	1956(5)	2206(2)	36(1)
N(3)	5592(3)	2593(4)	3748(2)	34(1)
C(1)	1842(4)	2712(7)	2675(3)	55(1)
C(2)	1051(4)	3908(11)	2966(4)	70(1)
C(3)	33(4)	4771(9)	2032(4)	72(1)
C(4)	232(4)	6600(10)	1437(4)	80(2)
C(5)	1119(4)	6260(9)	1025(3)	65(1)
C(6)	2294(4)	6104(6)	1848(3)	46(1)
C(7)	2683(3)	3921(7)	2362(2)	38(1)
C(8)	3010(3)	2443(6)	1685(2)	39(1)
C(9)	4562(3)	2972(5)	3153(2)	32(1)
C(10)	7124(3)	5517(6)	4501(3)	34(1)
C(11)	6806(3)	7576(6)	4190(3)	42(1)
C(12)	7432(3)	8791(7)	3819(3)	45(1)
C(13)	8401(4)	8009(6)	3770(3)	45(1)
C(14)	8727(4)	5970(6)	4128(3)	50(1)
C(15)	8100(3)	4697(6)	4492(3)	45(1)
C(16)	9036(5)	9375(7)	3331(4)	66(1)
C(17)	4714(3)	398(6)	1854(3)	40(1)
C(18)	5529(3)	1296(6)	1451(3)	38(1)

C(19)	5960(4)	3332(7)	1651(3)	48(1)
C(20)	6752(4)	3992(9)	1296(3)	61(1)
C(21)	7098(4)	2629(11)	732(3)	68(1)
C(22)	6676(5)	630(11)	538(4)	70(1)
C(23)	5884(4)	-46(8)	891(3)	55(1)