Supporting Information

Structure-Stability Relationship of NLRP3 Inflammasome-Inhibiting Sulfonylureas

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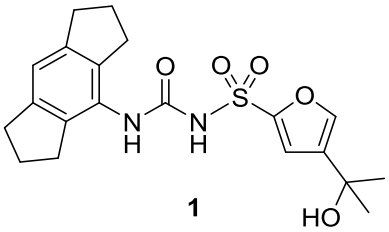
Content

General Information

Chemicals were purchased from ABCR, Acros Organics, BLDpharm, Carl Roth, Enamine, Fisher Scientific, Sigma Aldrich, Tokyo Chemical Industry and VWR Chemicals. Indane (**13**), thiophene-3-carboxylic acid (**19**) and, 9-nitroanthracene (**23**), 3,4-dichloroaniline (**27**), and 3-ethyl furoate (**29**) were commercially available. 4-Isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**), 9-isocyanato-1,2,3,4,5,6,7,8-octahydroanthracene (**26**), and 1,2-dichloro-4-isocyanatobenzene (**28**) were prepared as noted below and used in the next steps without further purification.

Thin layer chromatography was carried out with pre-coated silica gel (60 F254) aluminum sheets from Merck. Detection was performed with UV light at 254 and 360 nm or with $AgNO_3$ staining. Acros Organics silica gel 60 (70–230 mesh) was taken for preparative column chromatography. Preparative silica gel flash column chromatography was performed on an Interchim Puriflash PF420 system with diode-array detection (DAD) from 200 to 400 nm. Melting points were measured on a Büchi 510 oil bath apparatus. HR-ESI-MS spectra were recorded on a Bruker micrOTOF-Q mass spectrometer coupled with a HPLC Dionex UltiMate 3000 or a LTQ Orbitrap XL. ESI-MS mass spectra were recorded on an API2000 mass spectrometer coupled with an Agilent HPLC HP1100 using an EC50/2 Nucleodur C18 Gravity 3 µm column or on a Agilent Infinity Lab LC/MSD-system coupled with a Agilent HPLC 1260 Infinity II using a EC50/2 Nucleodur C18 Gravity 3 µm column. The purity of synthesized compounds was determined by HPLC-DAD. NMR spectra were recorded on a Bruker Avance DRX 500 (500 MHz ^{1}H NMR, 126 MHz ^{13}C NMR) and a Bruker Avance III 600 (600 MHz ^{1}H NMR, 151 MHz ^{13}C NMR). Chemical shifts are given in parts per million (ppm) referring to the signal center using the solvent peaks for reference: DMSO-d_6 (2.49/39.7).

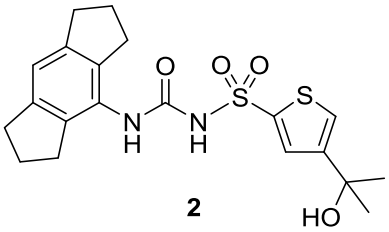
Preparation of Compounds



1

***N*-((1,2,3,5,6,7-Hexahydro-*s*-indacen-4-yl)carbamoyl)-4-(2-hydroxypropan-2-yl)furan-2-sulfonamide (1).** Under nitrogen, triphosgene (BTC, 267 mg, 0.9 mmol) was dissolved in dry THF (20 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (182 mg, 1.8 mmol) was added. 1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (**17**, 156 mg, 0.9 mmol) was dissolved in dry THF (20 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (20 mL), filtered and concentrated to yield 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**). 4-(2-Hydroxypropan-2-yl)furan-2-sulfonamide (**31**, 185 mg, 0.9 mmol) was dissolved in dry THF (10 mL). NaH (60% dispersion in mineral oil, 65 mg, 1.6 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**) was dissolved in dry THF (5 mL) and added in one portion. The reaction mixture was stirred for 2 h at room temperature under nitrogen. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (15 mL) and acidified with 2N HCl. The precipitate was collected, washed with H_2O (3 × 5 mL), dried, and washed with hexane (3 × 5 mL). It was dried under high vacuum to yield **1** as a white solid (336 mg).

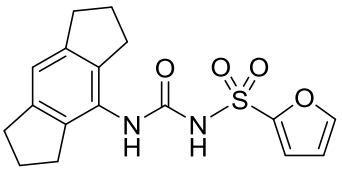
Yield 92%; mp: >140 °C (decomposition), lit.[1] mp: 239 °C (sodium salt); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 1.39 (s, 6H), 1.94 (quint, J = 7.4 Hz, 4H), 2.59 (t, J = 7.3 Hz, 4H), 2.79 (t, J = 7.4 Hz, 4H), 5.11 (s, 1H), 6.95 (s, 1H), 7.26 (s, 1H), 7.82 (s, 1H), 8.10 (s, 1H), 10.97 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 25.00, 30.05, 30.92, 32.41, 66.55, 116.50, 118.12, 128.43, 137.14, 137.30, 141.97, 143.10, 147.22, 148.36; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 4.08 min, 96% purity, *m/z* $[M+H]^+$ calcd for $C_{20}H_{24}N_2O_5S$ 405.1, found 405.2; **HRMS (ESI)** *m/z* $[M+Na]^+$ calcd for $C_{20}H_{24}N_2O_5S$ 427.1298, found 427.1310.



2

***N*-((1,2,3,5,6,7-Hexahydro-*s*-indacen-4-yl)carbamoyl)-4-(2-hydroxypropan-2-yl)thiophene-2-sulfonamide (2).** Under nitrogen, triphosgene (BTC, 534 mg, 1.8 mmol) was dissolved in dry THF (30 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (364 mg, 3.6 mmol) was added. 1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (**17**, 312 mg, 1.8 mmol) was dissolved in dry THF (30 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (30 mL), filtered and concentrated to yield 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**). 4-(2-Hydroxypropan-2-yl)thiophene-2-sulfonamide (**22**, 376 mg, 1.7 mmol) was dissolved in dry THF (15 mL). NaH (60 % dispersion in mineral oil, 130 mg, 3.24 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture was stirred for 2 h at room temperature under nitrogen atmosphere. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (30 mL) and acidified with 2 N HCl. The precipitate was collected and dried under high vacuum. The crude product was purified by silica column chromatography using petroleum ether/EtOAc (1+1) as eluent to yield **2** as a grey solid (492 mg).

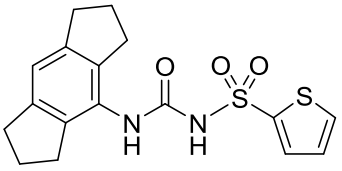
Yield 69%; mp: >130 °C (decomposition), lit.[2] mp: 133-134 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.42 (s, 6H), 1.94 (quint, J = 7.3 Hz, 4H), 2.59 (t, J = 7.4 Hz, 4H), 2.79 (t, J = 7.4 Hz, 4H), 5.23 (s, 1H), 6.94 (s, 1H), 7.69 – 7.71 (m, 1H), 7.76 – 7.77 (m, 1H), 8.10 (s, 1H), 10.60 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.98, 30.06, 31.32, 32.40, 69.32, 118.02, 126.46, 128.55, 131.85, 137.21, 139.85, 143.07, 148.85, 152.47; **LC-MS (ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 9.85 min, 97% purity, *m/z* $[M+H]^+$ calcd for $C_{20}H_{24}N_2O_4S_2$ 421.1, found 421.4; **HRMS (ESI)** *m/z* $[M+Na]^+$ calcd for $C_{20}H_{24}N_2O_4S_2$ 443.1070, found 443.1092.



3

***N*-((1,2,3,5,6,7-Hexahydro-*s*-indacen-4-yl)carbamoyl)furan-2-sulfonamide (3).** Under nitrogen, triphosgene (BTC, 202 mg, 0.68 mmol) was dissolved in dry THF (15 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (138 mg, 1.36 mmol) was added. 1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (**17**, 118 mg, 0.68 mmol) was dissolved in dry THF (15 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (10 mL), filtered and concentrated to yield 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**). Furan-2-sulfonamide (111 mg, 0.68 mmol) was dissolved in dry THF (15 mL). NaH (60% dispersion in mineral oil, 49 mg, 1.22 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**) was dissolved in dry THF (3.5 mL) and added in one portion. The reaction mixture was stirred for 2 h at room temperature under nitrogen atmosphere. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (15 mL) and acidified with 2 N HCl. The built precipitate was collected, washed with H_2O and EtOAc and was dried under high vacuum to yield **3** as a white solid (204 mg).

Yield 87%; mp: 210-212 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.95 (quint, J = 7.4 Hz, 4H), 2.59 (t, J = 7.4 Hz, 4H), 2.79 (t, J = 7.3 Hz, 4H), 6.72 (dd, J = 3.2, 1.9 Hz, 1H), 6.95 (s, 1H), 7.26 (d, J = 3.7 Hz, 1H), 8.03 (s, 1H), 8.11 (s, 1H), 10.91 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.98, 30.00, 32.39, 111.70, 117.77, 118.09, 128.41, 137.25, 143.08, 147.47, 147.50, 148.35; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 9.57 min, 96% purity, *m/z* $[M+H]^+$ calcd for $C_{17}H_{18}N_2O_4S$ 347.1, found 347.2; **HRMS (ESI)** *m/z* $[M+H]^+$ calcd for $C_{17}H_{18}N_2O_4S$ 347.1060, found 347.1075, lit.[3] *m/z* $[M-H]^-$ calcd 345.0987, found 345.0866.

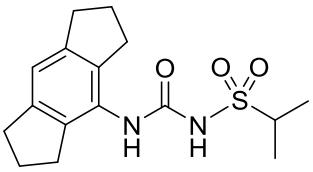


4

***N*-((1,2,3,5,6,7-Hexahydro-*s*-indacen-4-yl)carbamoyl)thiophene-2-sulfonamide (4).** Under nitrogen, triphosgene (BTC, 534 mg, 1.8 mmol) was dissolved in dry THF (30 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (364 mg, 3.6 mmol) was added. 1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (**17**, 312 mg, 1.8 mmol) was dissolved in dry THF (30 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (30 mL), filtered and concentrated to yield 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**). Thiophene-2-sulfonamide (294 mg, 1.8 mmol) was dissolved in dry THF (15 mL). NaH (60% dispersion in mineral oil, 130 mg, 3.24 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture was stirred for 4 h at room temperature under nitrogen. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (30 mL) and

acidified with 2 N HCl. The precipitate was collected, washed with H_2O (3 × 5 mL) and dried under high vacuum to yield **4** as a white solid (542 mg).

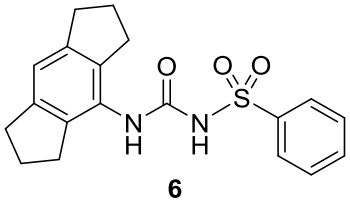
Yield 83%; mp: >230 °C (decomposition); **^{1}H NMR** (600 MHz, DMSO-d_6) δ 1.94 (quint, J = 7.5 Hz, 4H), 2.58 (t, J = 7.4 Hz, 4H), 2.79 (t, J = 7.4 Hz, 4H), 6.94 (s, 1H), 7.19 (dd, J = 5.0, 3.8 Hz, 1H), 7.77 (dd, J = 3.7, 1.4 Hz, 1H), 8.01 (dd, J = 5.0, 1.4 Hz, 1H), 8.11 (s, 1H), 10.88 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 25.00, 30.05, 32.41, 118.05, 127.27, 128.52, 133.48, 133.98, 137.21, 140.39, 143.09, 148.87; **LC-MS (ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 9,95 min, 97% purity, *m/z* $[M+H]^+$ calcd for $C_{17}H_{18}N_2O_3S_2$ 363.1, found 363.2; **HRMS (ESI)** *m/z* $[M+Na]^+$ calcd for $C_{17}H_{18}N_2O_3S_2$ 385.0658, found 385.0651, lit.[3] *m/z* $[M+H]^+$ calcd 363.0832, found 363.0819.



5

***N*-((1,2,3,5,6,7-Hexahydro-*s*-indacen-4-yl)carbamoyl)propane-2-sulfonamide (5).** Under nitrogen, triphosgene (BTC, 202 mg, 0.68 mmol) was dissolved in dry THF (15 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (138 mg, 1.36 mmol) was added. 1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (**17**, 118 mg, 0.68 mmol) was dissolved in dry THF (15 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (10 mL), filtered and concentrated to yield 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**). Propane-2-sulfonamide (84 mg, 0.68 mmol) was dissolved in dry THF (10 mL). NaH (60 % dispersion in mineral oil, 49 mg, 1.22 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**) was dissolved in dry THF (3.5 mL) and added in one portion. The reaction mixture was stirred for 2 h at room temperature under nitrogen atmosphere. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (15 mL) and acidified with 2 N HCl. The precipitate was collected, washed with H_2O (3 × 5 mL), dried, and washed with EtOAc (3 × 5 mL). It was dried under high vacuum to yield **5** as a white solid (216 mg).

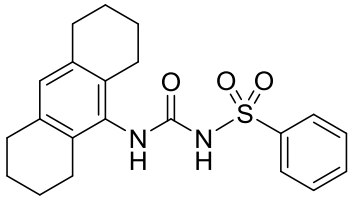
Yield 99%; mp: 178-180 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 1.31 (d, J = 6.9 Hz, 6H), 1.99 (quint, J = 7.6 Hz, 4H), 2.70 (t, J = 7.2 Hz, 4H), 2.81 (t, J = 7.3 Hz, 4H), 3.70 (quint, J = 7.0 Hz, 1H), 6.96 (s, 1H), 8.16 (s, 1H), 10.21 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 15.67, 25.04, 30.16, 32.43, 52.57, 117.99, 128.66, 137.15, 143.11, 149.63; **LC-MS (ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 210-400 nm), t_R= 10.76 min, 93% purity, *m/z* $[M+H]^+$ calcd for $C_{16}H_{22}N_2O_3S$ 323.1, found 323.1; **HRMS (ESI)** *m/z* $[M+H]^+$ calcd for $C_{16}H_{22}N_2O_3S$ 323.1424, found 323.1433.



6

***N*-((1,2,3,5,6,7-Hexahydro-*s*-indacen-4-yl)carbamoyl)benzenesulfonamide (6).** Under nitrogen, triphosgene (BTC, 534 mg, 1.8 mmol) was dissolved in dry THF (30 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (364 mg, 3.6 mmol) was added. 1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (**17**, 312 mg, 1.8 mmol) was dissolved in dry THF (30 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (30 mL), filtered and concentrated to yield 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**). Benzenesulfonamide (252 mg, 1.6 mmol) was dissolved in dry THF (15 mL). NaH (60% dispersion in mineral oil, 115 mg, 2.9 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 4-isocyanato-1,2,3,5,6,7-hexahydro-*s*-indacene (**18**) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture was stirred for 4 h at room temperature under nitrogen. The organic solvent was removed under reduced pressure. The residue was partitioned between EtOAc (50 mL) and saturated NH_4Cl solution (50 mL). The organic layer was separated. The aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography using petroleum ether/EtOAc (1+1) as eluent to yield **6** as a white solid (334 mg).

Yield 59%; mp: >230°C (decomposition); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.91 (quint, J = 7.4 Hz, 4H), 2.53 (t, J = 7.4 Hz, 4H), 2.77 (t, J = 7.4 Hz, 4H), 6.92 (s, 1H), 7.59 – 7.72 (m, 3H), 7.95 (d, J = 7.8 Hz, 2H), 8.09 (s, 1H), 10.69 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.95, 29.99, 32.38, 117.97, 127.15, 128.52, 128.95, 133.18, 137.16, 140.01, 143.04, 148.94; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 20 min, DAD 220-400 nm), t_R= 8.58 min, 98% purity, *m/z* $[M+H]^+$ calcd for $C_{19}H_{20}N_2O_3S$ 357.1, found 357.2; **HRMS (ESI)** *m/z* $[M+Na]^+$ calcd for $C_{19}H_{20}N_2O_3S$ 379.1087, found 379.1103, lit.[4] MS (ESI) *m/z* $[M+H]^+$ calcd 357.13, found 357.05.

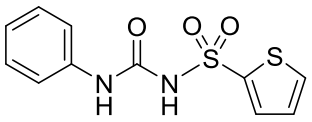


7

***N*-((1,2,3,4,5,6,7,8-Octahydroanthracen-9-yl)carbamoyl)benzenesulfonamide (7).** Under nitrogen, triphosgene (BTC, 267 mg, 0.9 mmol) was dissolved in dry THF (20 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (182 mg, 1.8 mmol) was added. 1,2,3,4,5,6,7,8-Octahydroanthracen-9-amine (**25**, 181 mg, 0.9 mmol) was dissolved in dry THF (20 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (20 mL), filtered and concentrated to yield 9-isocyanato-1,2,3,4,5,6,7,8-octahydroanthracene (**26**). Benzenesulfonamide (142 mg, 0.9 mmol) was dissolved in dry THF (10 mL). NaH (60% dispersion in

mineral oil, 65 mg, 1.6 mmol) was added and the reaction mixture was stirred at 0 °C under nitrogen for 30 min. The crude 9-isocyanato-1,2,3,4,5,6,7,8-octahydroanthracene (**26**) was dissolved in dry THF (5 mL) and added in one portion. The reaction mixture was stirred for 2 h at room temperature under nitrogen. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (15 mL) and acidified with 2 N HCl. The precipitate was collected, washed with H_2O (3 × 5 mL), dried, and washed with hexane (3 × 5 mL). It was dried under high vacuum to yield **7** as a white solid (295 mg).

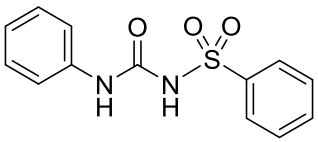
Yield 85%; mp: >220 °C (decomposition); **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.53 – 1.62 (m, 8H), 2.09 – 2.34 (m, 4H), 2.56 – 2.61 (m, 4H), 6.69 (s, 1H), 7.58 – 7.64 (m, 2H), 7.67 – 7.73 (m, 2H), 7.90 – 7.96 (m, 2H), 10.87 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 22.43, 22.57, 24.24, 28.72, 127.24, 128.22, 128.98, 131.62, 132.87, 133.22, 134.06, 140.02, 149.61; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 5.36 min, 99% purity, *m/z* $[M+H]^+$ calcd for $C_{21}H_{24}N_2O_3S$ 385.2, found 385.2; **HRMS(ESI)** *m/z* $[M+Na]^+$ calcd for $C_{21}H_{24}N_2O_3S$ 407.1400, found 407.1401.



8

***N*-(Phenylcarbamoyl)thiophene-2-sulfonamide (8).** Thiophene-2-sulfonamide (490 mg, 3 mmol) was dissolved in dry THF (15 mL). NaH (60 % dispersion in mineral oil, 216 mg, 5.4 mmol) was added and the reaction mixture was stirred at 0 °C under argon for 30 min. Phenyl isocyanate (357 mg, 3 mmol) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture was stirred for 4 h at room temperature under argon. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (30 mL) and acidified with 2 N HCl. The precipitate was collected, washed with H_2O (3 × 5 mL), dried, and washed with CH_2Cl_2 (3 × 5 mL). It was dried under high vacuum to yield a white solid (358 mg).

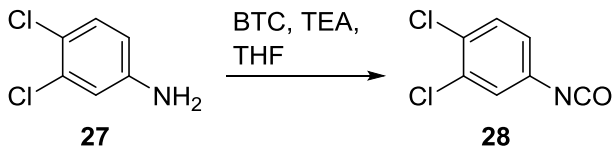
Yield 42%; mp: 160-162 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 7.02 – 7.05 (m, 1H), 7.20 (dd, *J* = 5.0, 3.8 Hz, 1H), 7.26 – 7.29 (m, 2H), 7.36 – 7.38 (m, 2H), 7.80 (dd, *J* = 3.8, 1.5 Hz, 1H), 8.01 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.84 (s, 1H), 10.94 (s, 1H), lit.[5] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.04 (d, *J* = 7.3 Hz, 1H), 7.20 (dd, *J* = 4.9, 3.9 Hz, 1H), 7.28 (t, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 2H), 7.81 (dd, *J* = 3.8, 1.3 Hz, 1H), 8.02 (dd, *J* = 5.0, 1.3 Hz, 1H), 8.89 (s, 1H), 10.94 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 119.07, 123.31, 127.40, 128.82, 133.69, 134.14, 137.92, 140.30, 149.21; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 5.21 min, 100% purity, *m/z* $[M+Na]^+$ calcd for $C_{11}H_{10}N_2O_3S_2$ 283.0, found 283.1; **HRMS(ESI)** *m/z* $[M+Na]^+$ calcd for $C_{11}H_{10}N_2O_3S_2$ 305.0036, found 305.0025.



9

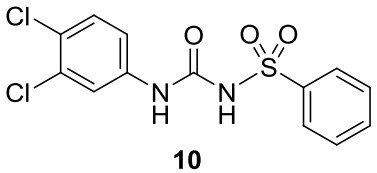
***N*-(Phenylcarbamoyl)benzenesulfonamide (9).** Benzenesulfonamide (472 mg, 3 mmol) was dissolved in dry THF (15 mL). NaH (60 % dispersion in mineral oil, 216 mg, 5.4 mmol) was added and the reaction mixture was stirred at 0 °C under argon for 30 min. Phenyl isocyanate (357 mg, 3 mmol) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture stirred for 4 h at room temperature under argon. The reaction was quenched by dropwise adding of H_2O (1 mL) and the organic solvent was removed under reduced pressure. The residue was partitioned between EtOAc (100 mL) and saturated NH_4Cl solution (100 mL). The organic layer was separated. The aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography using petroleum ether/EtOAc (2+1) as eluent to yield **9** as a white solid (497 mg).

Yield 60%; mp: 156-158 °C, lit.[6] mp: 158-160 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 6.99 – 7.02 (m, 1H), 7.23 – 7.27 (m, 2H), 7.31 – 7.35 (m, 2H), 7.60 – 7.64 (m, 2H), 7.67 – 7.71 (m, 1H), 7.96 – 7.98 (m, 2H), 8.81 (s, 1H), 10.72 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 118.93, 123.14, 127.35, 128.77, 128.99, 133.21, 138.04, 140.12, 149.45; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 6.38 min, 100% purity, *m/z* $[M+H]^+$ calcd for $C_{13}H_{12}N_2O_3S$ 277.1, found 277.2; **HRMS(ESI)** *m/z* $[M+Na]^+$ calcd for $C_{13}H_{12}N_2O_3S$ 299.0461, found 299.0476.



27 **28**

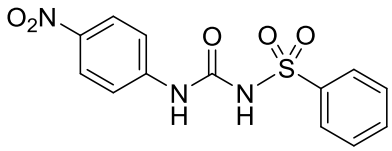
Scheme S1. Synthesis of 3,4-dichloroisocyanate 28



10

***N*-((3,4-Dichlorophenyl)carbamoyl)benzenesulfonamide (10).** Under argon, triphosgene (BTC, 534 mg, 1.8 mmol) was dissolved in dry THF (30 mL). The mixture was stirred and cooled to 0 °C for 30 min. TEA (364 mg, 3.6 mmol) was added. 3,4-Dichloroaniline (**27**, 297 mg, 1.8 mmol) was dissolved in dry THF (30 mL) and dropwise added over 30 min. The mixture was stirred for additional 30 min at room temperature and then 30 min at 75 °C. The solvent was evaporated and the residue was taken up in dry THF (30 mL), filtered and the filtrate was concentrated to yield 1,2-dichloro-4-isocyanatobenzene (**28**). Benzenesulfonamide (283 mg, 1.8 mmol) was dissolved in dry THF (15 mL). NaH (60% dispersion in mineral oil, 130 mg, 3.24 mmol) was added and the reaction mixture was stirred at 0 °C under argon for 30 min. The crude 1,2-dichloro-4-isocyanatobenzene (**28**) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture was stirred for 4 h at room temperature under argon. The reaction was quenched by dropwise adding of H_2O (1 mL) and the organic solvent was removed under reduced pressure. The residue was partitioned between EtOAc (100 mL) and saturated NH_4Cl solution (100 mL). The organic layer was separated. The aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica column chromatography using petroleum ether/EtOAc (1+1) as eluent to yield a white solid (216 mg).

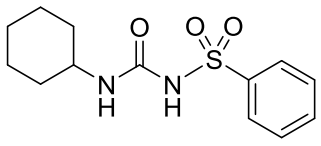
Yield 35%; mp: 168-170 °C, lit.[6] mp: 194-195 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ7.24 – 7.33 (m, 1H), 7.43 – 7.54 (m, 1H), 7.59 – 7.64 (m, 2H), 7.65 – 7.73 (m, 2H), 7.90 – 8.00 (m, 2H), 9.14 (s, 1H), 11.10 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 118.97, 119.93, 124.23, 127.31, 128.91, 130.54, 130.95, 133.00, 138.73, 140.51, 150.31; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 9.31 min, 100% purity, *m/z* $[M+H]^+$ calcd for $C_{13}H_{10}Cl_2N_2O_3S$ 345.0, found 345.1; **HRMS(ESI)** *m/z* $[M+Na]^+$ calcd for $C_{13}H_{10}Cl_2N_2O_3S$ 388.9501, found 388.9511.



11

***N*-((4-Nitrophenyl)carbamoyl)benzenesulfonamide (11).** Benzenesulfonamide (472 mg, 3 mmol) was dissolved in dry THF (15 mL). NaH (60 % dispersion in mineral oil, 216 mg, 5.4 mmol) was added and the reaction mixture was stirred at 0 °C under argon for 30 min. 4-Nitrophenyl isocyanate (492 mg, 3 mmol) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture stirred for 4 h at room temperature under argon. The organic solvent was removed under reduced pressure. The residue was dispersed in H_2O (30 mL) and acidified with 2 N HCl. The precipitate was collected, washed with H_2O (3 × 5 mL) and was dried under high vacuum to yield **11** as a yellow solid (713 mg).

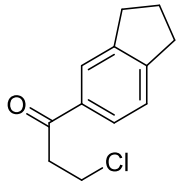
Yield 74%; mp: >230 °C (decomposition), lit.[7] mp: 244-245 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 7.58 – 7.60 (m, 2H), 7.63 – 7.66 (m, 2H), 7.70 – 7.73 (m, 1H), 7.98 – 8.00 (m, 2H), 8.14 – 8.17 (m, 2H), 9.57 (s, 1H), 11.17 (s, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 118.51, 124.95, 127.47, 129.09, 133.51, 139.65, 142.12, 144.55, 149.39; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 7.41 min, 98% purity, *m/z* $[M+H]^+$ calcd for $C_{13}H_{11}N_3O_5S$ 322.1, found 322.2; **HRMS(ESI)** *m/z* $[M-H]^-$ calcd for $C_{13}H_{10}N_3O_5S$ 320.0347, found 320.0347.



12

***N*-(Cyclohexylcarbamoyl)benzenesulfonamide (12).** Benzenesulfonamide (472 mg, 3 mmol) was dissolved in dry THF (15 mL). NaH (60 % dispersion in mineral oil, 216 mg, 5.4 mmol) was added and the reaction mixture was stirred at 0 °C under argon for 30 min. Cyclohexyl isocyanate (376 mg, 3 mmol) was dissolved in dry THF (7.5 mL) and added in one portion. The reaction mixture stirred for 4 h at room temperature under argon. The reaction was quenched by dropwise adding of H_2O (1 mL) and the organic solvent was removed under reduced pressure. The residue was partitioned between EtOAc (100 mL) and saturated NH_4Cl solution (100 mL). The organic layer was separated. The aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to yield **12** as a white solid (813 mg).

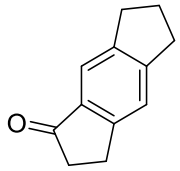
Yield 96%; mp: 190-192 °C, lit.[8] mp: 188-189 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.05 – 1.16 (m, 4H), 1.19 – 1.24 (m, 2H), 1.46 – 1.51 (m, 1H), 1.55 – 1.60 (m, 2H), 1.62 – 1.67 (m, 2H), 6.33 (d, *J* = 7.9 Hz, 1H), 7.58 – 7.63 (m, 2H), 7.65 – 7.70 (m, 1H), 7.88 – 7.91 (m, 2H), 10.32 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.10, 24.92, 32.20, 48.05, 127.09, 128.93, 133.07, 140.25, 150.37; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 200-400 nm), t_R= 9.21 min, 99% purity, *m/z* $[M+H]^+$ calcd for $C_{13}H_{18}N_2O_3S$ 283.1, found 283.0; **HRMS(ESI)** *m/z* $[M+Na]^+$ calcd for $C_{13}H_{18}N_2O_3S$ 305.0930, found 305.0942.



14

3-Chloro-1-(2,3-dihydro-1*H*-inden-5-yl)propan-1-one (14). $AlCl_3$ (2.9 g, 22 mmol) was dispersed in dry CH_2Cl_2 (20 mL) and cooled to -10 °C under nitrogen. Indane (**13**, 2.4 g, 20 mmol) and 3-chloropropionyl chloride (2.5 g, 20 mmol) were dissolved in dry CH_2Cl_2 (20 mL) and added dropwise over 1 h. The mixture was allowed to warm to room temperature and was stirred for 18 h. The solution was carefully added to 2 N HCl (25 mL) at -10 °C. The organic layer was separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with saturated sodium bicarbonate solution (50 mL) and brine (50 mL), dried over Na_2SO_4, filtered and concentrated to yield **14** as a beige solid (3.65 g).

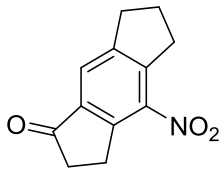
Yield 88%; mp: 66-68 °C, lit.[1] mp: 64-66 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 2.05 (quint, J = 7.5 Hz, 2H), 2.92 (t, J = 7.5 Hz, 4H), 3.50 (t, J = 6.3 Hz, 2H), 3.91 (t, J = 6.3 Hz, 2H), 7.36 (d, J = 7.8 Hz, 1H), 7.73 – 7.79 (m, 1H), 7.83 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.90, 31.95, 32.40, 39.60, 40.63, 123.76, 124.37, 126.45, 134.81, 144.43, 150.05, 196.56; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 11.65 min, 99% purity, *m/z* $[M+H]^+$ calcd for $C_{12}H_{13}ClO$ 209.1, found 209.0.



15

3,5,6,7-Tetrahydro-*s*-indacen-1(2*H*)-one (15). 3-Chloro-1-(2,3-dihydro-1*H*-inden-5-yl)propan-1-one (**14**, 2.9 g, 14 mmol) was added under stirring to concentrated H_2SO_4 (20 mL). The mixture was stirred for 48 h at 55 °C. The mixture was slowly poured onto crushed ice and the built precipitate was collected. The crude brown product was purified by silica gel flash column chromatography using a gradient of 100% petroleum ether to 25% EtOAc as eluent to yield **15** as a light beige solid (2.06 g).

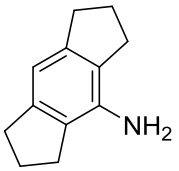
Yield 85%; mp: 80-82 °C, lit.[9] mp: 80-81 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 2.05 (quint, J = 7.4 Hz, 2H), 2.58 – 2.64 (m, 2H), 2.87 (t, J = 7.4 Hz, 2H), 2.91 (t, J = 7.4 Hz, 2H), 3.00 – 3.04 (m, 2H), 7.38 (s, 1H), 7.43 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 25.03, 25.35, 31.43, 32.43, 36.30, 118.01, 122.32, 135.48, 143.54, 152.32, 154.28, 205.47; **LC-MS(ESI)** (90% H_2O with 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 6.05 min, 100% purity, *m/z* $[M+H]^+$ calcd for $C_{12}H_{12}O$ 173.1, found 173.1.



16

4-Nitro-3,5,6,7-tetrahydro-*s*-indacen-1(2*H*)-one (16). 3,5,6,7-Tetrahydro-*s*-indacen-1(2*H*)-one (**15**, 517 mg, 3 mmol) was dissolved in dry CH_2Cl_2 (12 mL), acetic anhydride (8 mL) and acetic acid (6 mL) at 0 °C. Fuming nitric acid (1.2 mL) was added dropwise over 2 h at 0 °C. The reaction mixture was allowed to stir for 1 h at 0 °C. The solution was poured onto crushed ice and was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (50 mL) and brine (50 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel column chromatography using petroleum ether / EtOAc (4+1) as eluent to yield **16** as a yellow resin (276 mg).

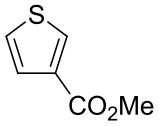
Yield 42%; lit.[1] mp: 99-101 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 2.13 (quint, J = 7.6 Hz, 2H), 2.70 – 2.75 (m, 2H), 2.89 (t, J = 7.5 Hz, 2H), 3.03 (t, J = 7.5 Hz, 2H), 3.08 – 3.13 (m, 2H), 7.66 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.96, 25.10, 28.81, 32.78, 36.81, 125.34, 125.47, 135.64, 155.47, 156.67, 201.03. One aromatic ^{13}C signal is missing. **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 6.08 min, 99% purity, *m/z* $[M+H]^+$ calcd for $C_{12}H_{11}NO_3$ 218.1, found 218.1.



17

1,2,3,5,6,7-Hexahydro-*s*-indacen-4-amine (17). $Pd(OH)_2$ on carbon (Pearlman's catalyst, 50% water wet, 55 mg) was placed in a Schlenk flask under H_2. A mixture of 4-nitro-3,5,6,7-tetrahydro-*s*-indacen-1(2*H*)-one (**16**, 217 mg, 1 mmol) and methanesulfonic acid (1.06 g, 1.1 mmol) was added by syringe and the mixture was allowed to stir for 18 h at room temperature under H_2 (1 atm, balloon). The reaction mixture was filtered through celite and the filtrate was evaporated. The crude product was purified by silica gel column chromatography using petroleum ether / EtOAc (1+1) + 1% TEA as eluent to yield **17** as a colourless solid (96 mg).

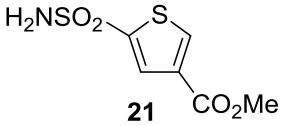
Yield 55%; mp: 88-90 °C, lit.[1] mp: 88-89 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.96 (quint, J = 7.4 Hz, 4H), 2.58 (t, J = 7.3 Hz, 4H), 2.71 (t, J = 7.4 Hz, 4H), 4.48 (s, 2H), 6.34 (s, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 24.90, 28.85, 32.57, 108.27, 124.72, 139.59, 142.43; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 6.90 min, 98% purity, *m/z* $[M+H]^+$ calcd for $C_{12}H_{15}N$ 174.1, found 174.1.



20

Methyl thiophene-3-carboxylate (20). Thiophene-3-carboxylic acid (**19**, 1.92 g, 15 mmol) was dissolved in MeOH (30 mL). Concentrated H_2SO_4 (1.5 mL) was added and the mixture was refluxed for 18 h. The reaction mixture was concentrated and neutralized with saturated $NaHCO_3$ solution (20 mL). The aqueous phase was extracted with EtOAc (3 × 50 mL), dried over Na_2SO_4 and concentrated to yield **20** as a light-yellow liquid (2.07 g).

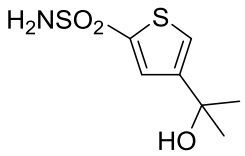
Yield 97%; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 3.80 (s, 3H), 7.46 (dd, J = 5.1, 1.3 Hz, 1H), 7.65 (dd, J = 5.1, 3.0 Hz, 1H), 8.34 (dd, J = 3.1, 1.3 Hz, 1H), lit.[10] ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.30 (dd, J = 5.1, 3.2 Hz, 1H), 7.52 (dd, J = 5.1, 1.2 Hz, 1H), 8.10 (dd, J = 3.2, 1.2 Hz, 1H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 51.65, 127.32, 127.62, 132.70, 133.67, 162.48; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 8.56 min, 100% purity, *m/z* $[M+H]^+$ calcd for $C_6H_6O_2S$ 143.0, found 143.0.



21

Methyl 5-sulfamoylthiophene-3-carboxylate (21). Chlorosulfonic acid (10.5 g, 90 mmol) was stirred at 0 °C under argon atmosphere. Methyl thiophene-3-carboxylate (**20**, 2.13 g, 15 mmol) was added dropwise at 0 °C over 30 min. The reaction mixture was heated to 60 °C for 3 h. The solution was slowly poured onto crushed ice and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The crude intermediate methyl 5-(chlorosulfonyl)thiophene-3-carboxylate was dissolved in dry MeCN (30 mL) and ammonia gas was added (1 atm, balloon). The reaction mixture was stirred for 1 h at room temperature. The organic phase was evaporated. The precipitate was collected, washed with water (20 mL) and hexane (20 mL). The product was dried under high vacuum to yield **21** as a white solid (510 mg).

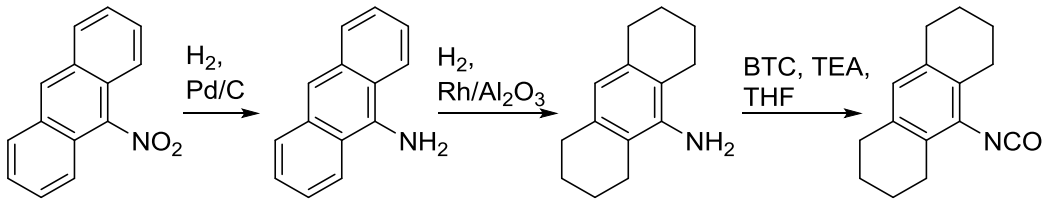
Yield 15%; mp: 128-130 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 3.83 (s, 3H), 7.81 – 7.82 (m, 3H), 8.55 (d, J = 1.5 Hz, 1H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 52.14, 129.19, 132.01, 137.47, 146.98, 161.65; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 210-400 nm), t_R= 5.71 min, 99% purity, *m/z* $[M+H]^+$ calcd for $C_6H_7NO_4S_2$ 222.0, found 221.9.



22

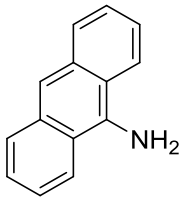
4-(2-Hydroxypropan-2-yl)thiophene-2-sulfonamide (22). Methyl 5-sulfamoylthiophene-3-carboxylate (**21**, 487 mg, 2.2 mmol) was dissolved in dry THF (10 mL) and placed under nitrogen atmosphere. The solution was cooled to 0 °C. CH_3MgBr (3 M in Et_2O, 7.33 mL, 22 mmol) was added carefully. The reaction mixture was allowed to stir at room temperature for 2 h. The reaction was quenched with saturated NH_4Cl solution (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel flash column chromatography using a gradient from petroleum ether to petreoleum ether / EtOAc (1+1) to yield **22** as a white solid (413 mg).

Yield 85%; mp: 108-110 °C; **^{1}H NMR** (600 MHz, DMSO-d_6) δ 1.42 (s, 6H), 5.19 (s, 1H), 7.52 (d, J = 1.7 Hz, 1H), 7.55 (d, J = 1.7 Hz, 1H), 7.58 (s, 2H); **^{13}C NMR** (151 MHz, DMSO-d_6) δ 31.39, 69.30, 123.61, 128.84, 145.04, 152.36; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeOH + 2 mM NH_4Ac in 10 min, then 100% MeOH + 2 mM NH_4Ac to 20 min, DAD 220-400 nm), t_R= 4.62 min, 99% purity, *m/z* $[M+NH_4]^+$ calcd for $C_7H_{11}NO_3S_2$ 239.1, found 238.9.



23 **24** **25** **26**

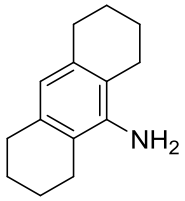
Scheme S2. Synthesis of 1,2,3,4,5,6,7,8-octahydroanthracen-9-amine 25



24

Anthracen-9-amine (24). 9-Nitroanthracene (**23**, 893 mg, 4 mmol) was dispersed in dry EtOH (20 mL) and treated with 10% Pd/C (89 mg) under H_2 (1 atm, balloon) for 24 h. The reaction mixture was filtered through celite and was concentrated. The crude product was purified by silica gel flash column chromatography using a gradient from 100% CH_2Cl_2 to 3% MeOH to yield **24** as a yellow solid (360 mg).

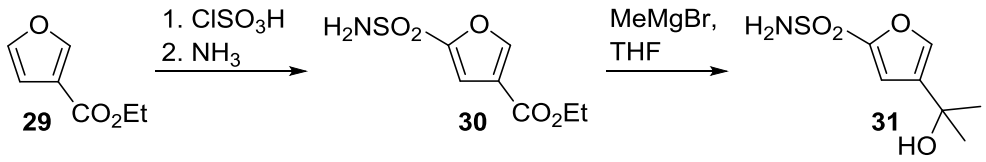
Yield 47%; mp: 144-146 °C, lit.[11] mp: 148-151 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 6.58 (s, 2H), 7.27 – 7.31 (m, 2H), 7.37 – 7.41 (m, 2H), 7.63 (s, 1H), 7.84 (d, J = 8.4 Hz, 2H), 8.34 (d, J = 8.8 Hz, 2H); **^{13}C NMR** (126 MHz, DMSO-d_6) δ 111.96, 116.68, 122.08, 123.08, 125.23, 128.00, 132.13, 141.19; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 6.74 min, 88% purity, *m/z* $[M+H]^+$ calcd for $C_{14}H_{11}N$ 194.1, found 194.1.



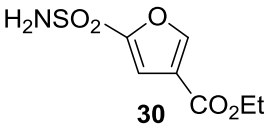
25

1,2,3,4,5,6,7,8-Octahydroanthracen-9-amine (25). Anthracen-9-amine (**24**, 348 mg, 1.8 mmol) was dissolved in dry EtOH (15 mL) and treated with Rh 5% on activated Al_2O_3 under H_2 for 48 h. The suspension was filtered through celite and was concentrated. The crude product was purified by silica gel flash column chromatography using a gradient of petroleum ether / EtOAc (4+1) to petroleum ether / EtOAc (1+1) to yield **25** as a white solid (313 mg).

Yield 86%; mp: 84-86 °C, lit.[12] mp: 83-84 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.59 – 1.64 (m, 4H), 1.70 – 1.76 (m, 4H), 2.33 (t, J = 6.5 Hz, 4H), 2.54 (t, J = 6.2 Hz, 4H), 4.24 (s, 2H), 6.06 (s, 1H), **^{13}C NMR** (126 MHz, DMSO-d_6) δ 22.68, 23.05, 23.77, 29.37, 116.96, 117.55, 133.26, 142.83; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 7.91 min, 95% purity, *m/z* $[M+H]^+$ calcd for $C_{14}H_{19}N$ 202.2, found 202.1.

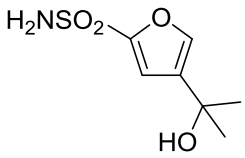


Scheme S3. Synthesis of the sulfonamide building block 31 for sulfonylurea 1



Ethyl 5-sulfamoylfuran-3-carboxylate (30). This compound was synthesized as described elsewhere.[13] 3-Ethyl furoate (**29**, 1.45 mL, 10.7 mmol) was dissolved in dry CH_2Cl_2 (20 mL) under nitrogen. The solution was cooled to -30 °C and chlorosulfonic acid (0.75 mL, 11.5 mmol) was added dropwise over 10 min at -30 °C. The reaction was allowed to warm to room temperature and was stirred for 72 h. The mixture was cooled to -10 °C and dry pyridine (0.95 mL, 11.7 mmol) was added slowly over 10 min. PCl_5 (2.45 g, 11.7 mmol) was added in portions at -10 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 18 h. The reaction was quenched by dropwise addition to ice-cool water (50 mL) over 30 min. The mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with water (50 mL), dried over Na_2SO_4, filtered and concentrated to yield the crude intermediate ethyl 5-(chlorosulfonyl)furan-3-carboxylate. The crude intermediate was dissolved in dry THF (20 mL) and cooled to -78 °C. Ammonia gas was liquefied at -78 °C and 10 mL were added to the reaction at -78 °C. The reaction mixture was allowed to slowly warm to room temperature and was stirred for 18 h. The reaction mixture was concentrated under vacuum and the crude product was purified by silica gel flash column chromatography using a gradient of 100 % CH_2Cl_2 to 10% MeOH to yield **30** as a light beige solid (845 mg).

Yield 36%; mp: 130-132 °C, lit.[1] mp: 131-132.5 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.26 – 1.30 (m, 3H), 4.24 – 4.29 (m, 2H), 7.11 – 7.13 (m, 1H), 7.96 (s, 2H), 8.63 – 8.64 (m, 1H), **^{13}C NMR** (126 MHz, DMSO-d_6) δ 14.12, 60.77, 111.58, 119.59, 150.40, 153.50, 161.33; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 2.76 min, 98% purity, *m/z* $[M+NH_4]^+$ calcd for $C_7H_9NO_5S$ 237.1, found 237.1.



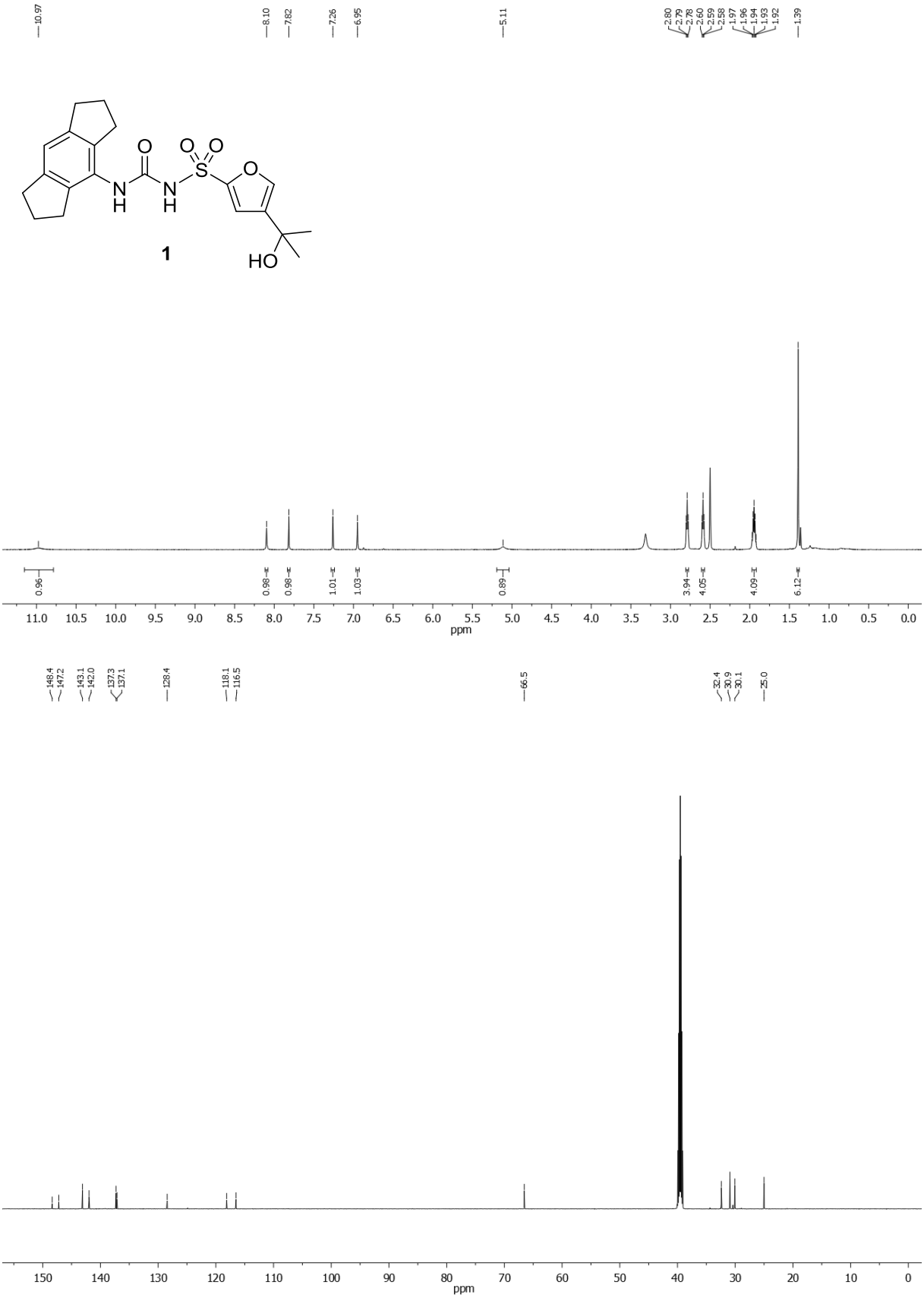
31

4-(2-Hydroxypropan-2-yl)furan-2-sulfonamide (31). Ethyl 5-sulfamoylfuran-3-carboxylate (**30**, 482 mg, 2.2 mmol) was dissolved in dry THF (10 mL) under nitrogen. The solution was cooled to 0 °C. CH_3MgBr (3 M solution in Et_2O, 7.33 mL, 22 mmol) was carefully added at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched with saturated NH_4Cl solution (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel flash column chromatography using a gradient of 100% CH_2Cl_2 to 10% MeOH to yield **31** as a beige solid (375 mg).

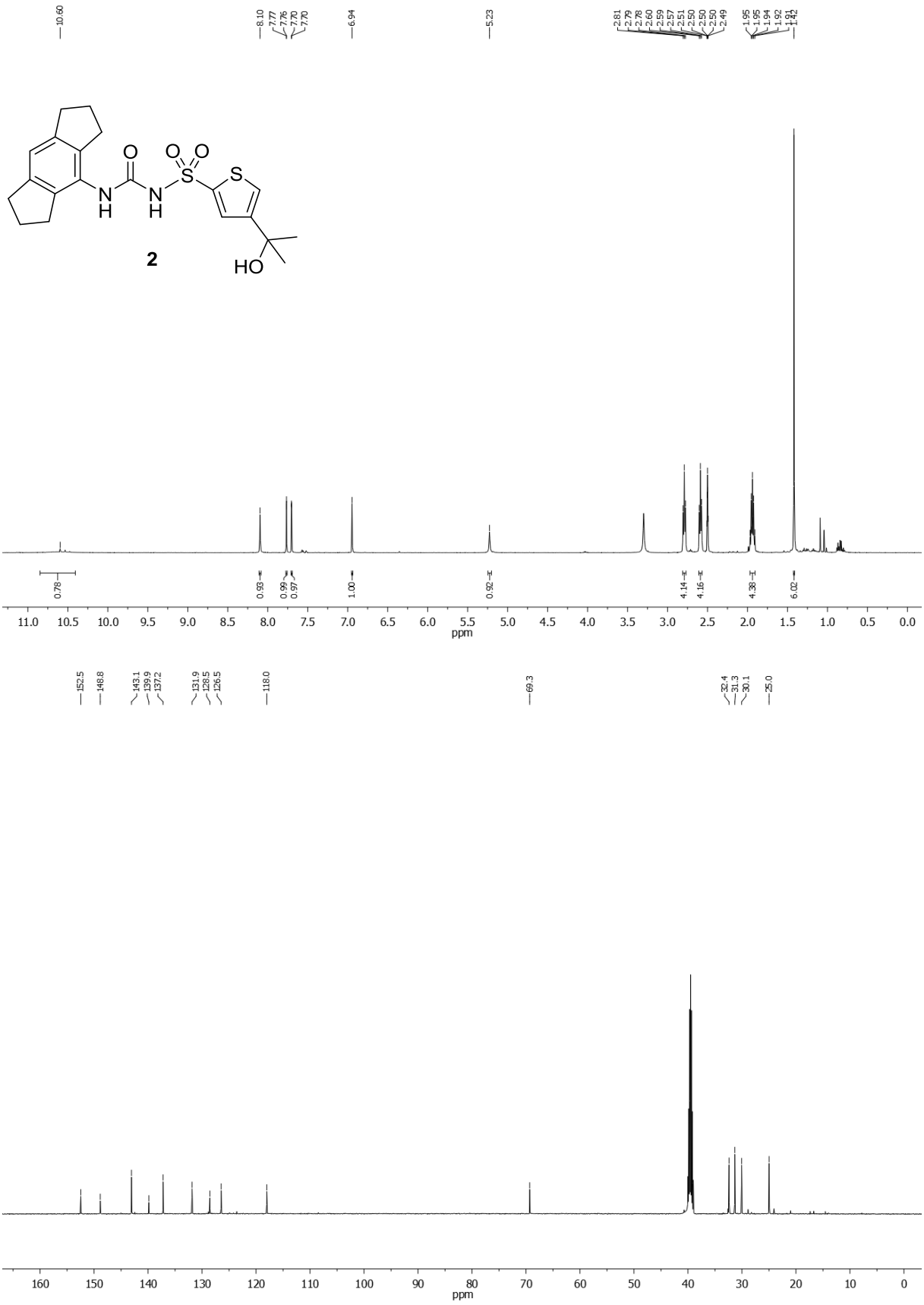
Yield 83%; mp: 100-102 °C; lit.[1] mp: 99.5-101.5 °C; **^{1}H NMR** (500 MHz, DMSO-d_6) δ 1.38 – 1.39 (m, 6H), 5.08 (d, J = 1.5 Hz, 1H), 6.94 – 6.96 (m, 1H), 7.66 – 7.69 (m, 3H), **^{13}C NMR** (126 MHz, DMSO-d_6) δ 30.97, 66.57, 112.11, 136.56, 140.26, 151.69; **LC-MS(ESI)** (90% H_2O + 2 mM NH_4Ac to 100% MeCN in 10 min, then 100% MeCN to 15 min, DAD 200-600 nm), t_R= 0.84 min, 100% purity, *m/z* $[M-H]^-$ calcd for $C_7H_{11}NO_4S$ 204.0, found 204.0.

NMR data

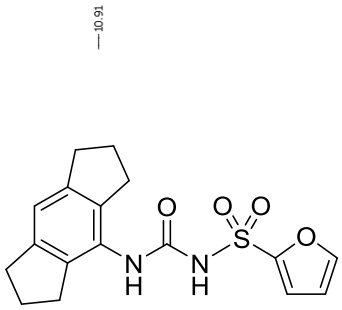
^{1}H and ^{13}C NMR spectra of compound **1**



^{1}H and ^{13}C NMR spectra of compound **2**



^{1}H and ^{13}C NMR spectra of compound **3**



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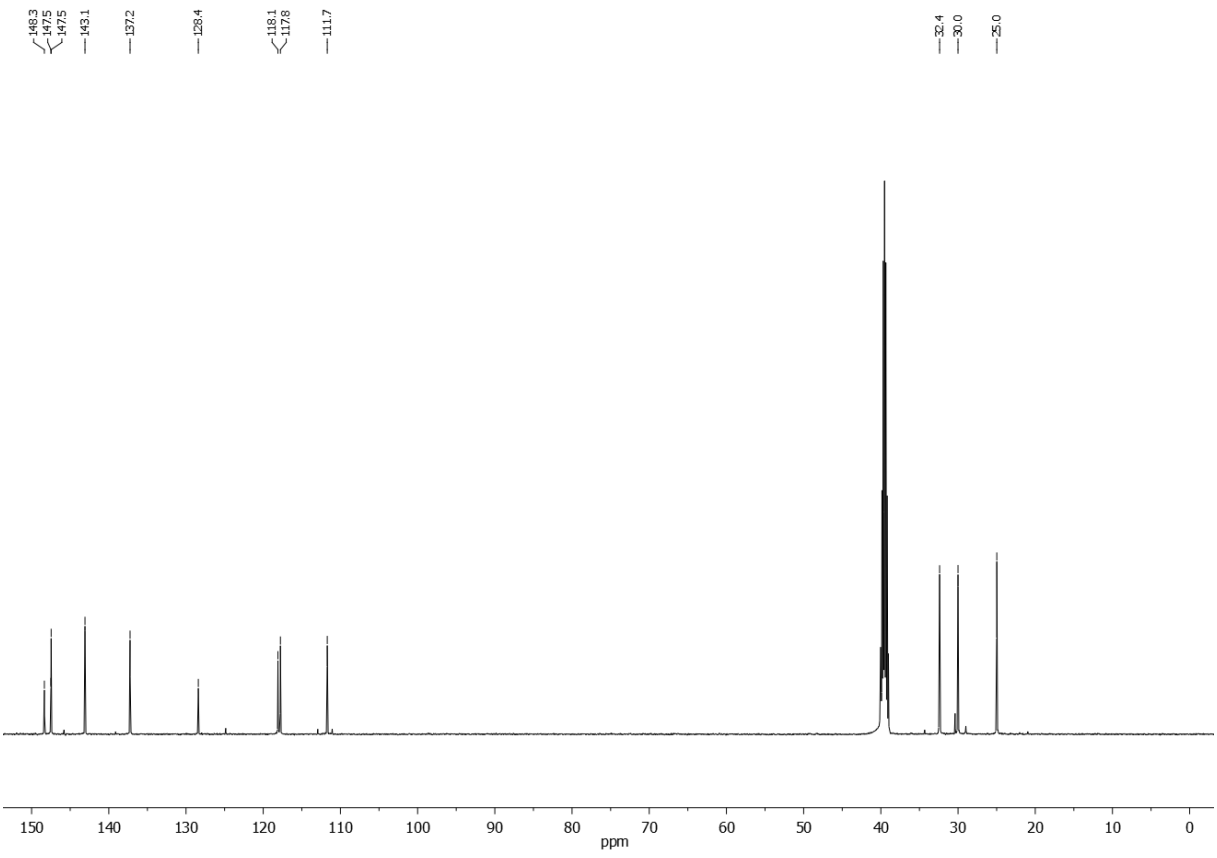
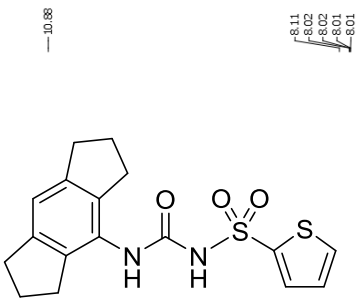


^{1}H and ^{13}C NMR spectra of compound **4**



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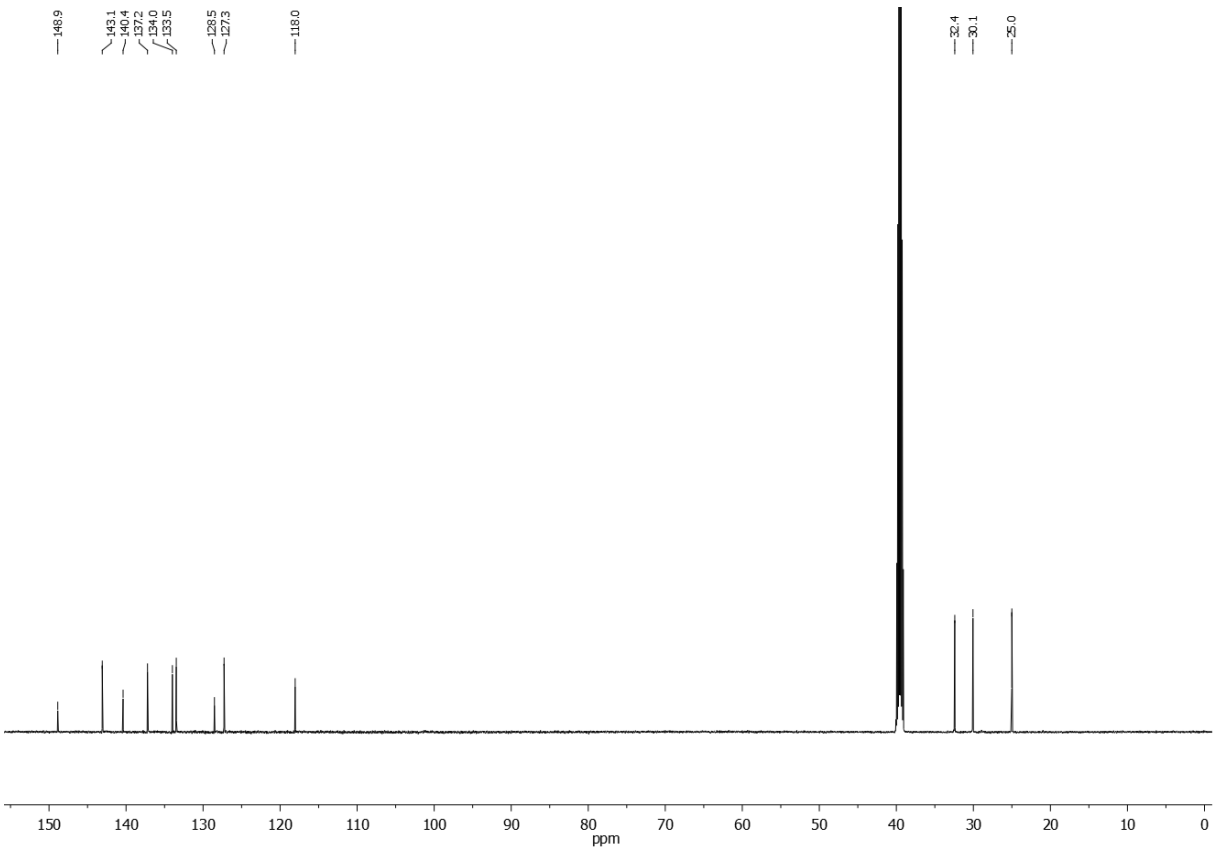
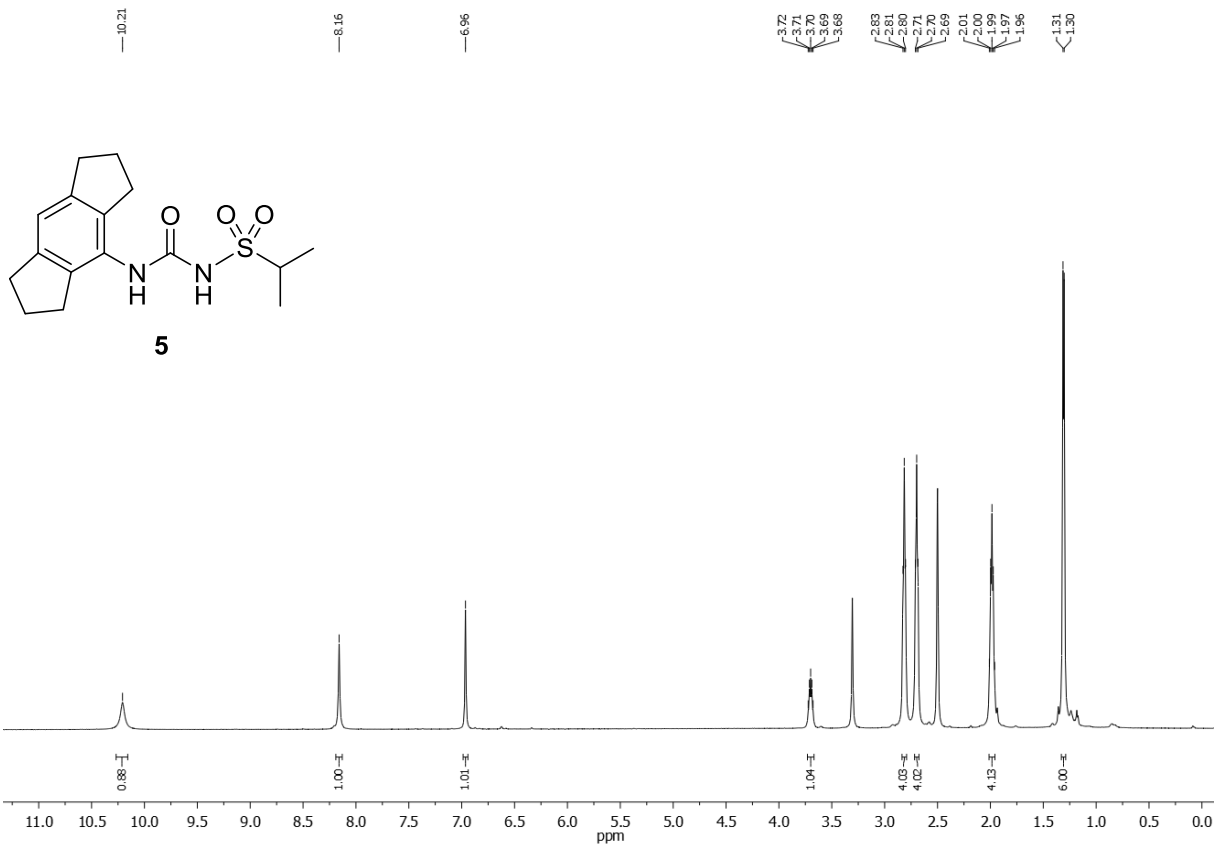


^{1}H and ^{13}C NMR spectra of compound **5**



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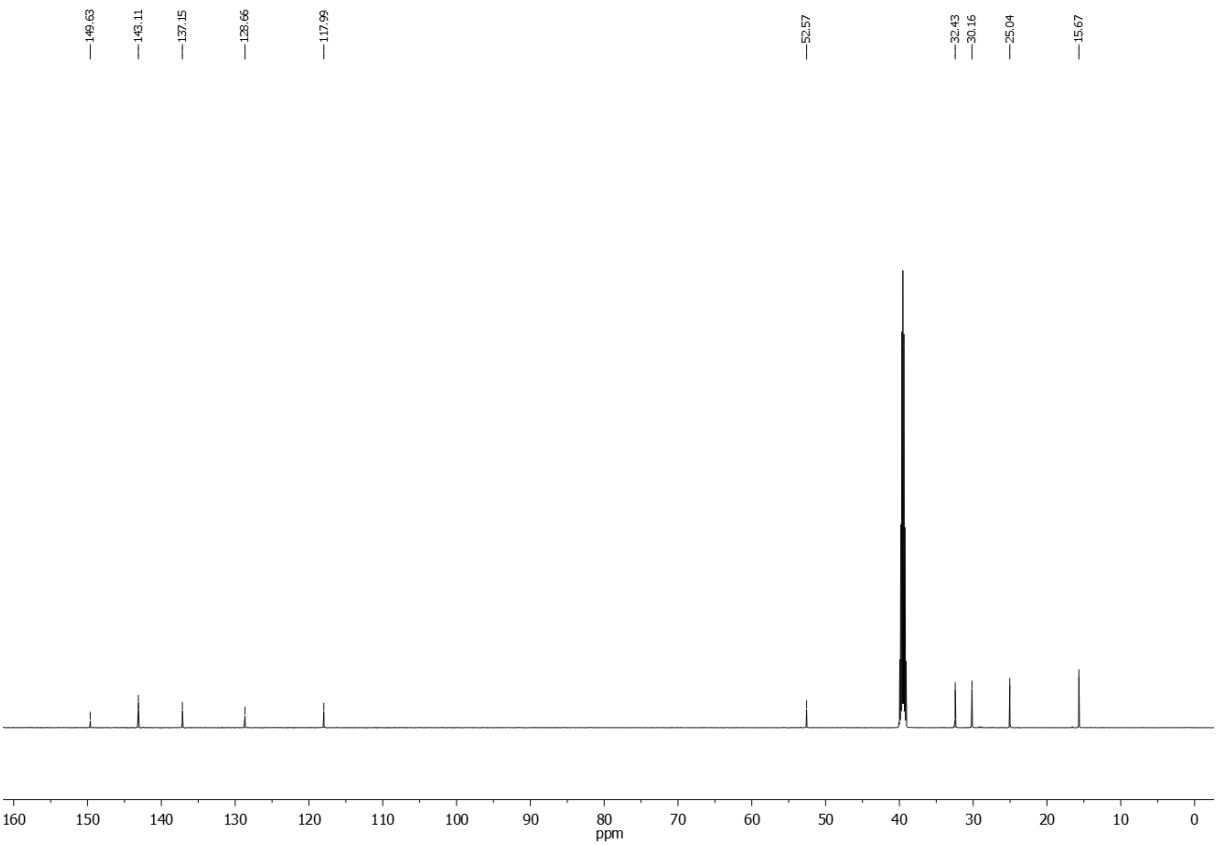
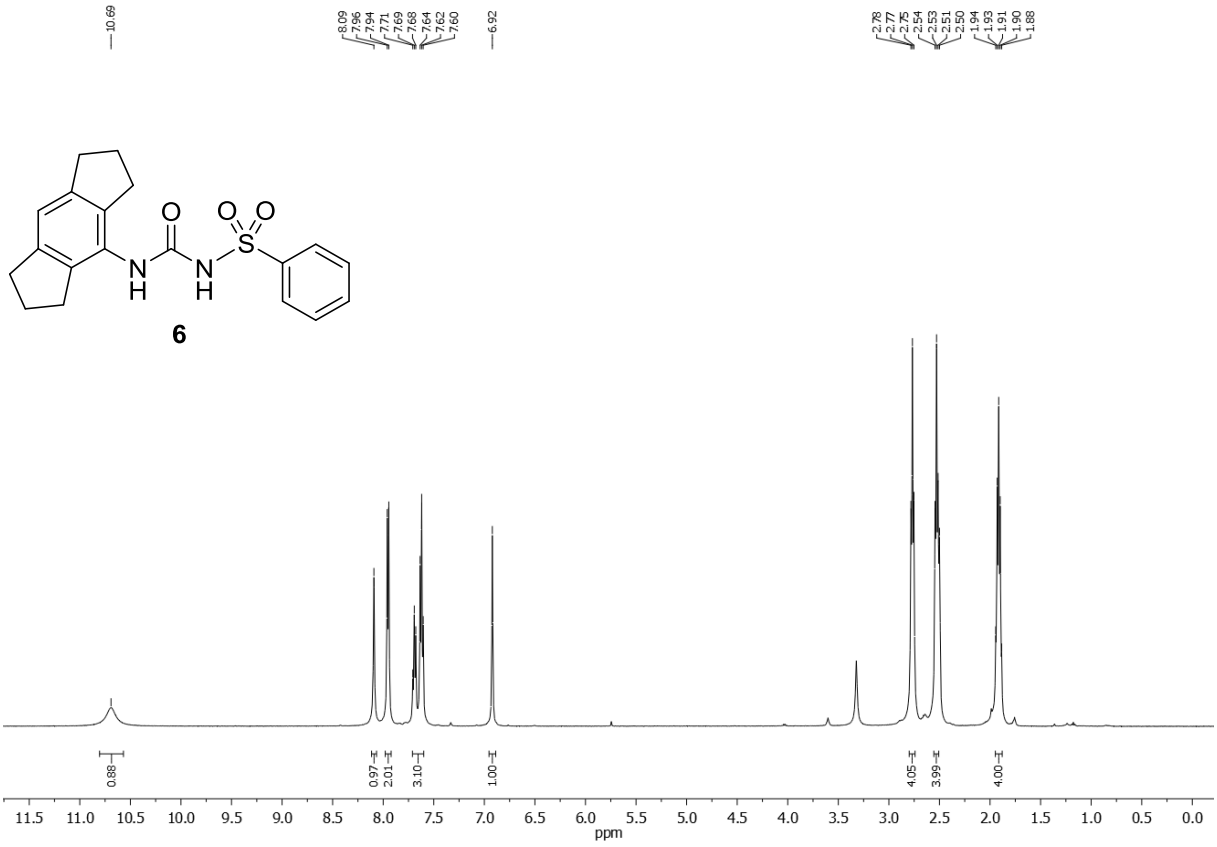
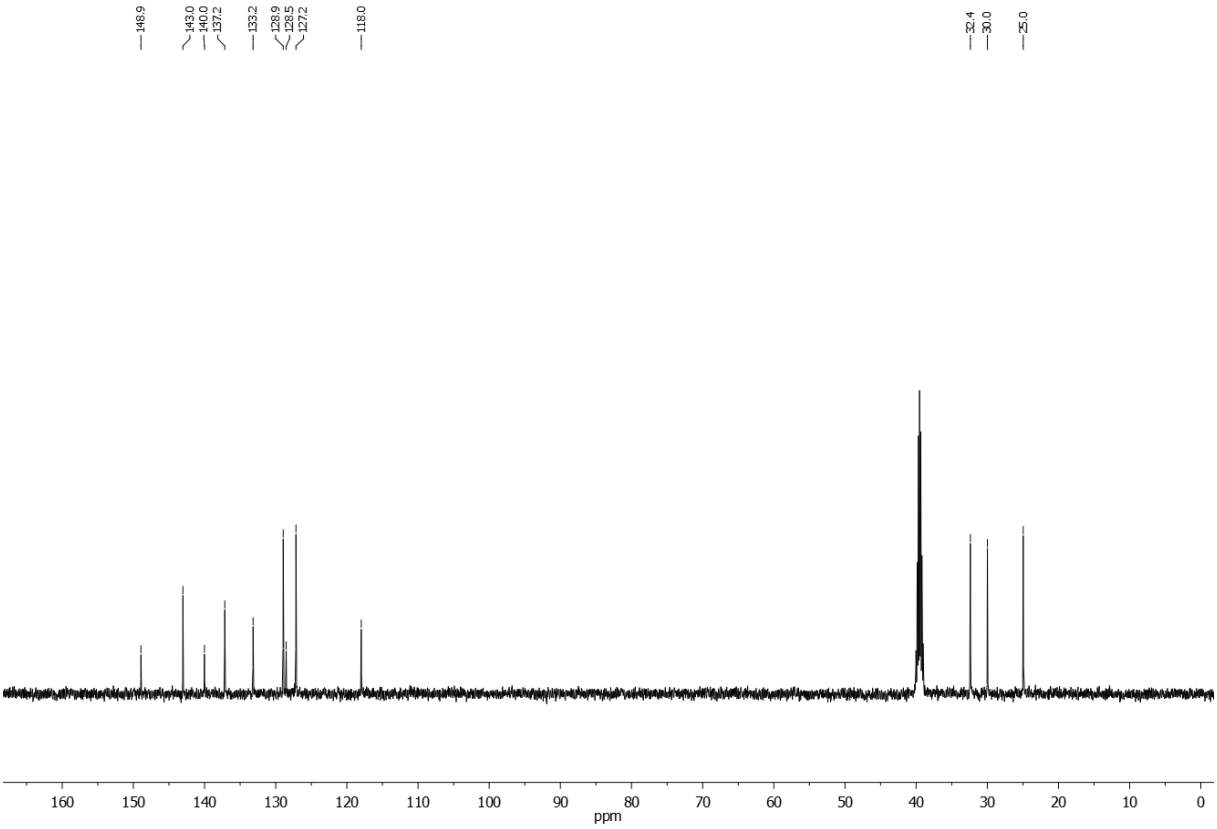
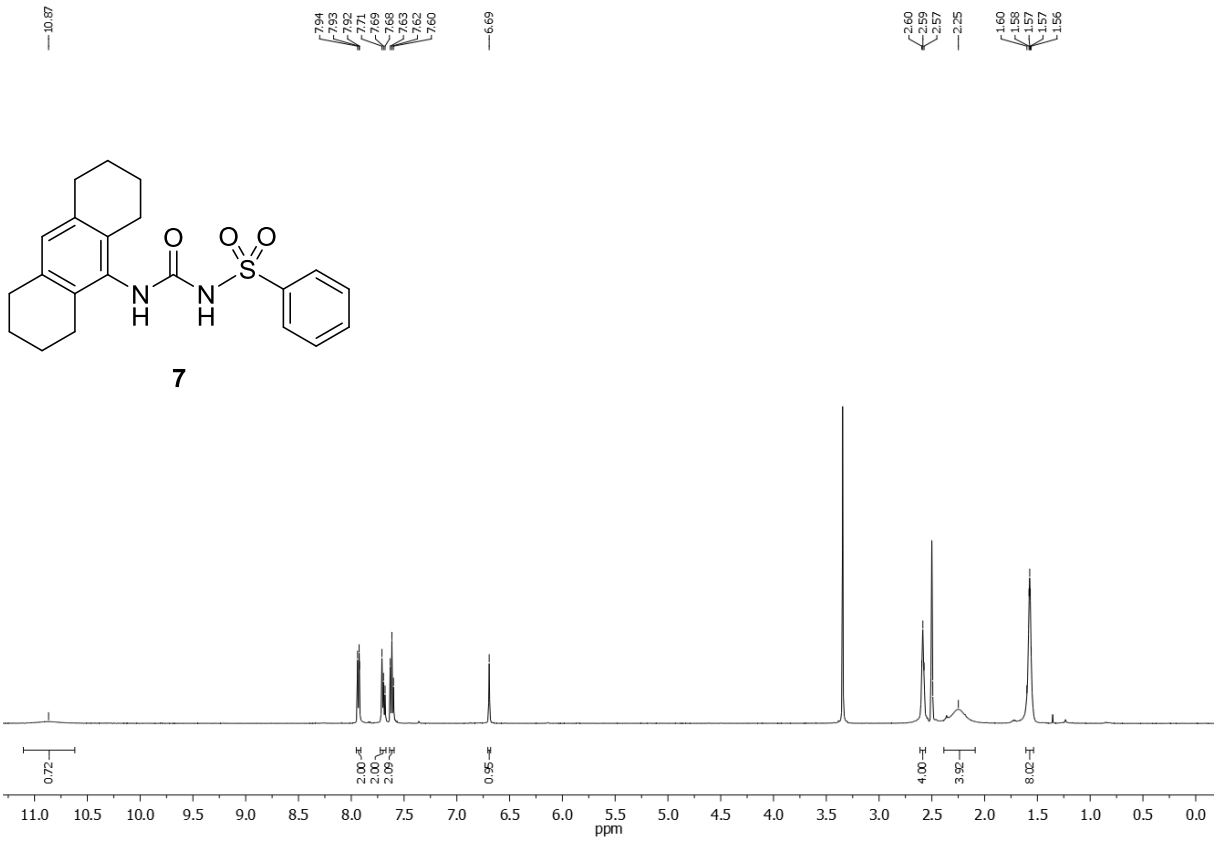


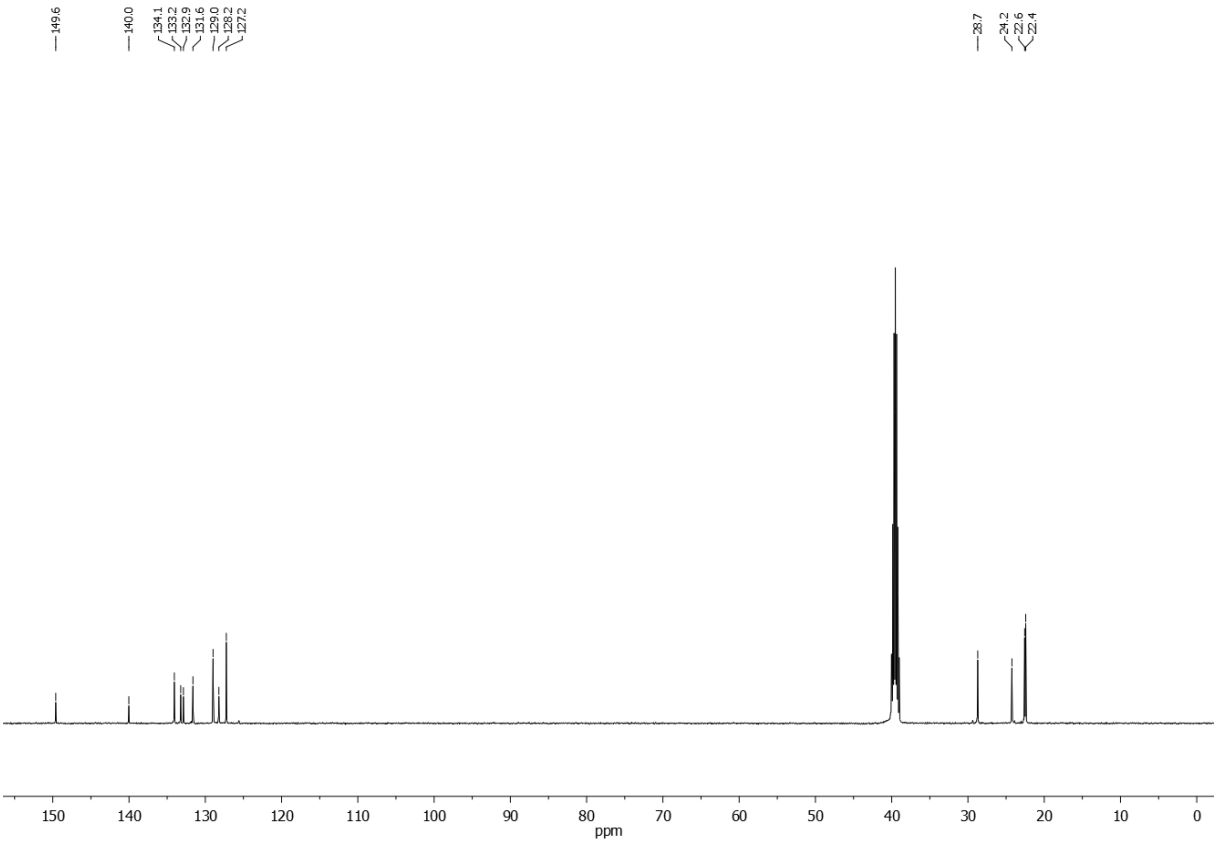
^{1}H and ^{13}C NMR spectra of compound **6**



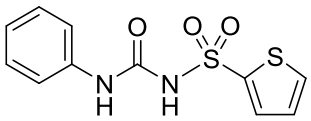


^{1}H and ^{13}C NMR spectra of compound **7**





^{1}H and ^{13}C NMR spectra of compound **8**



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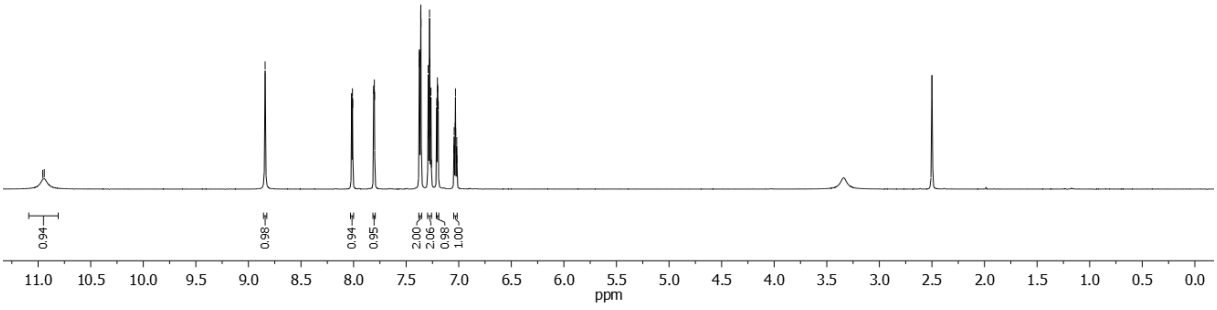
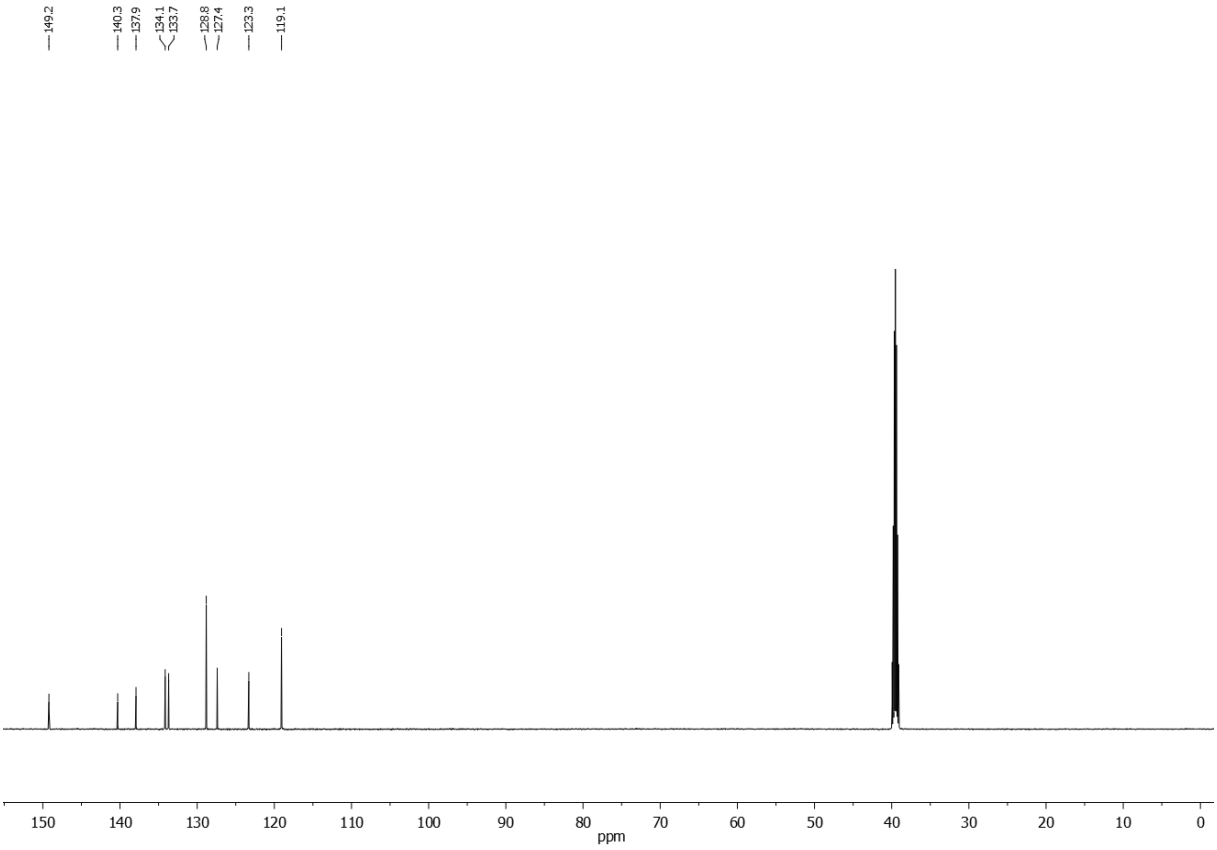
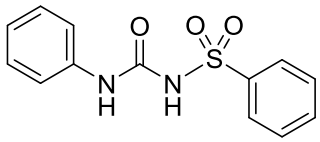




^{1}H and ^{13}C NMR spectra of compound **9**



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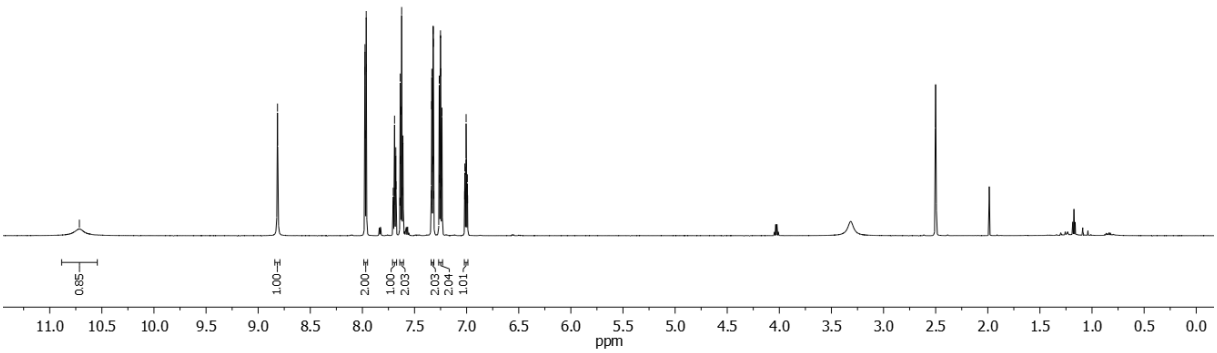
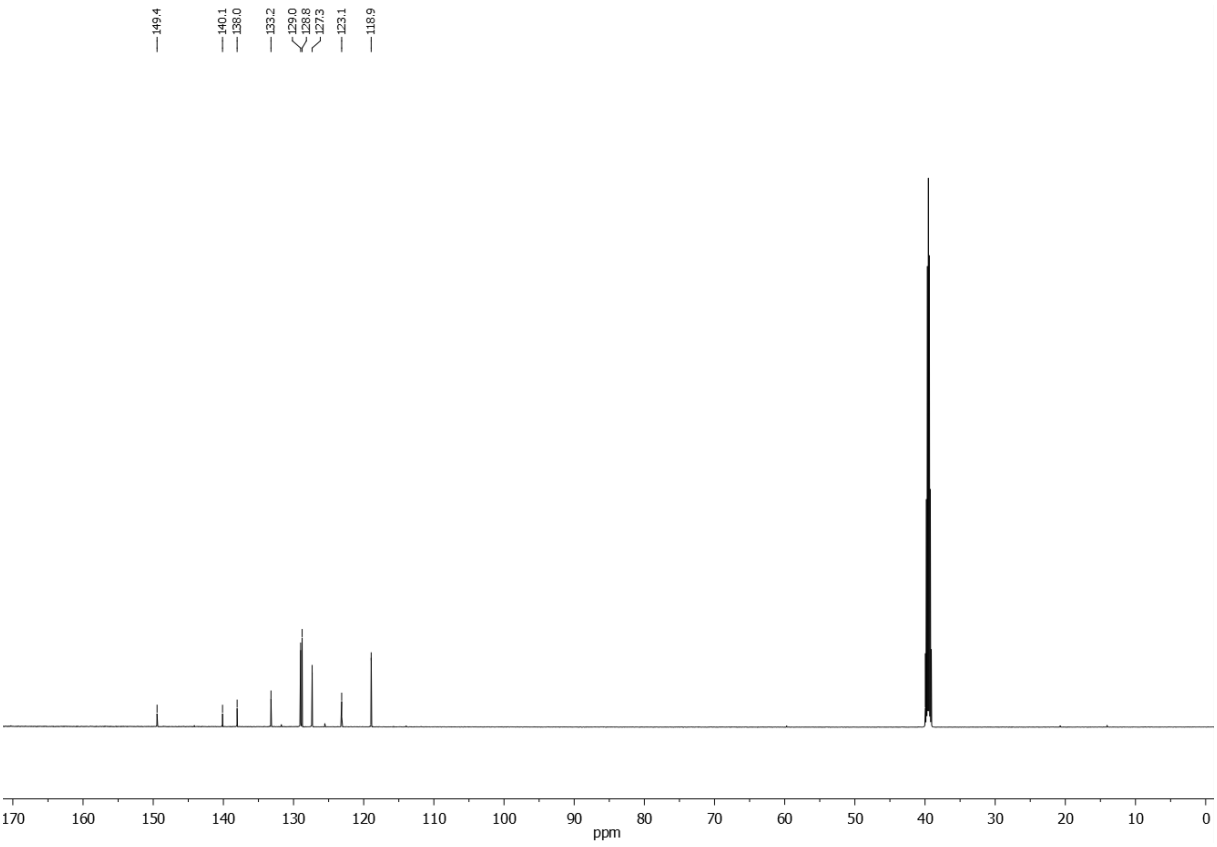
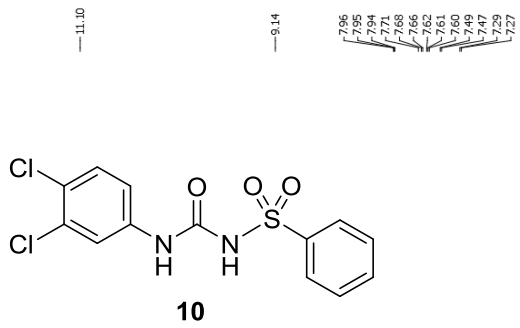




^{1}H and ^{13}C NMR spectra of compound **10**



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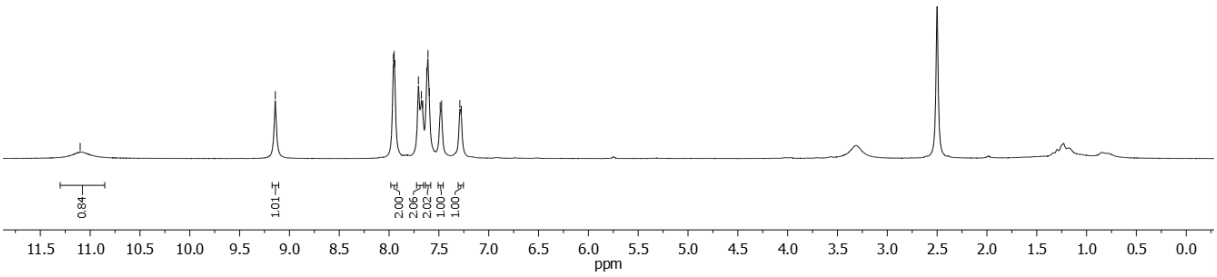
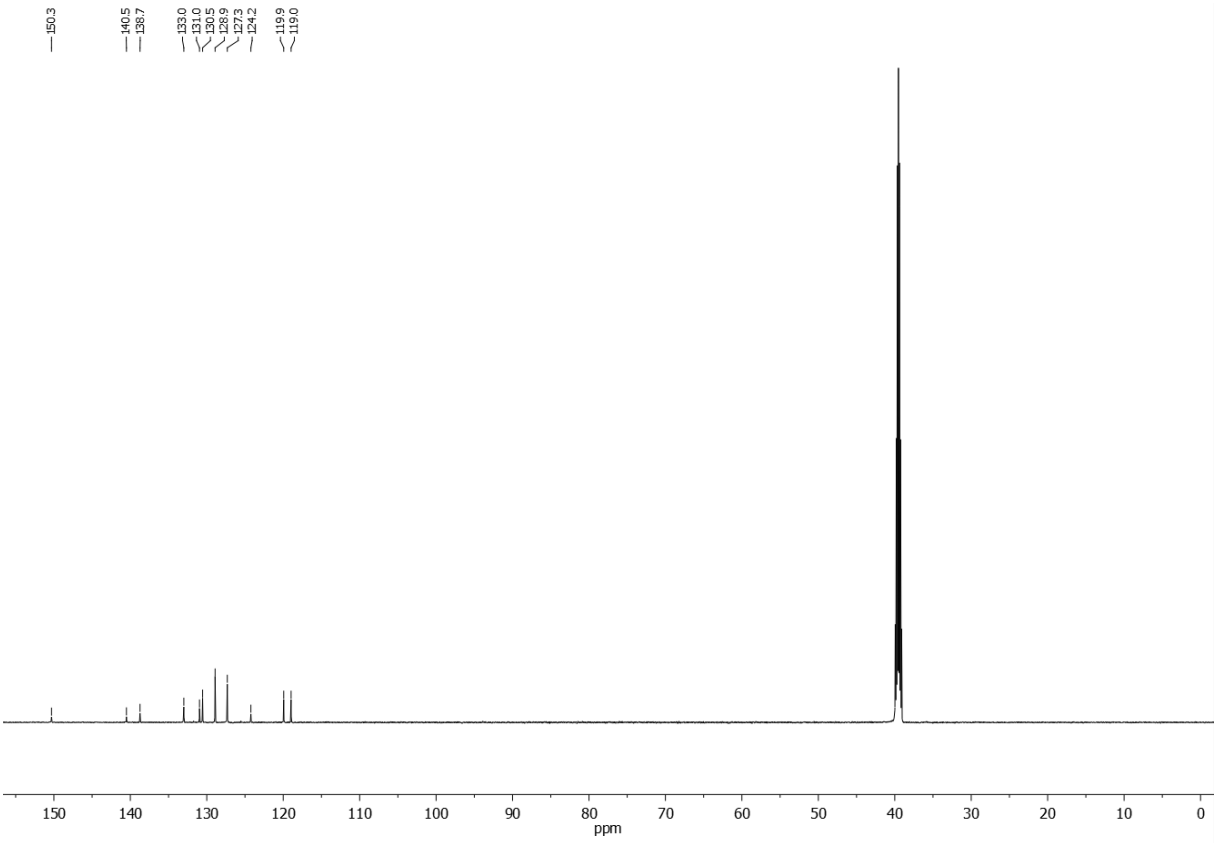
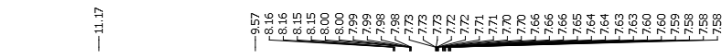
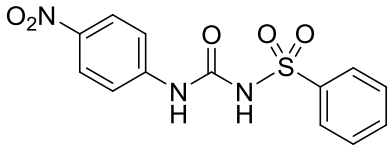




^{1}H and ^{13}C NMR spectra of compound **11**





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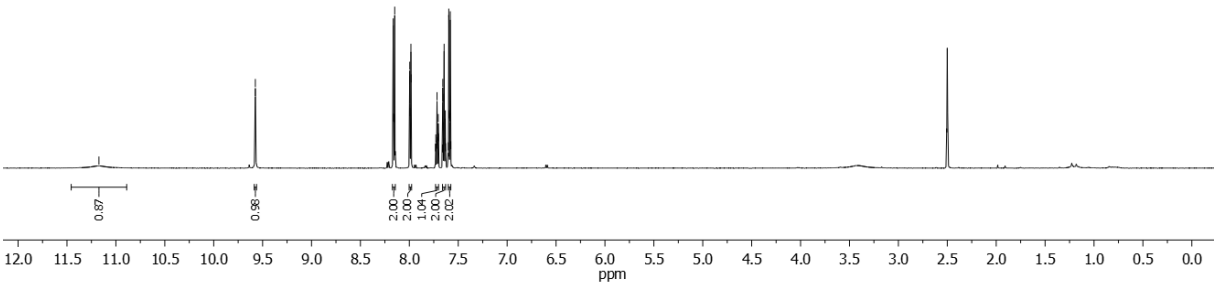
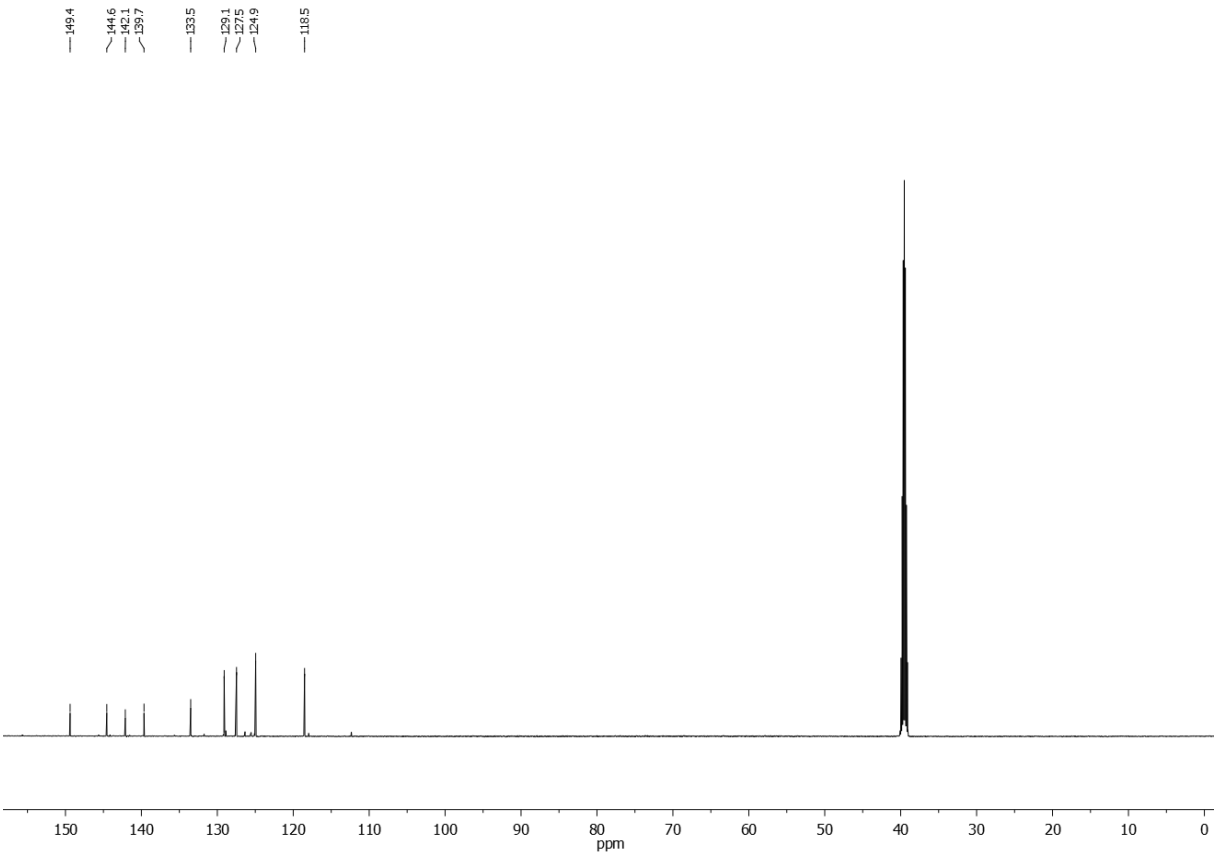
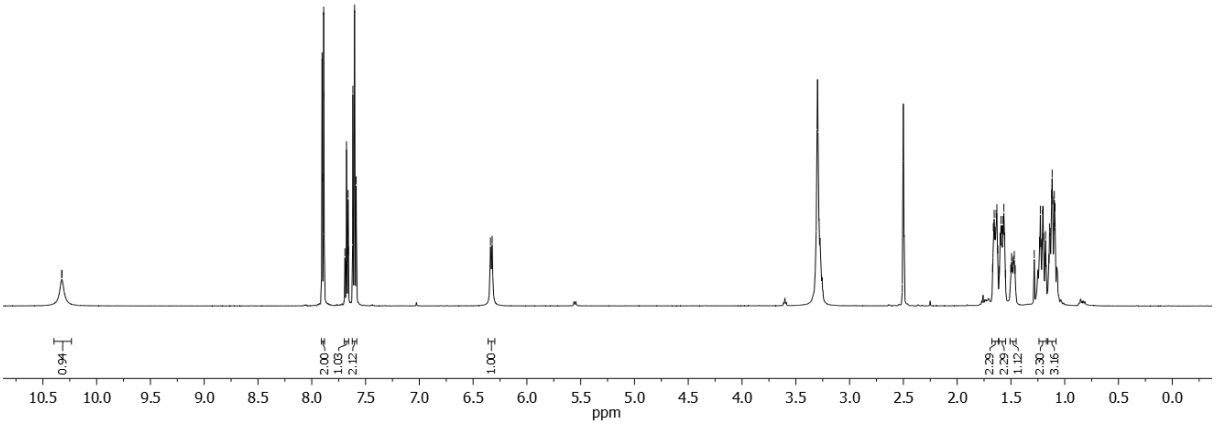
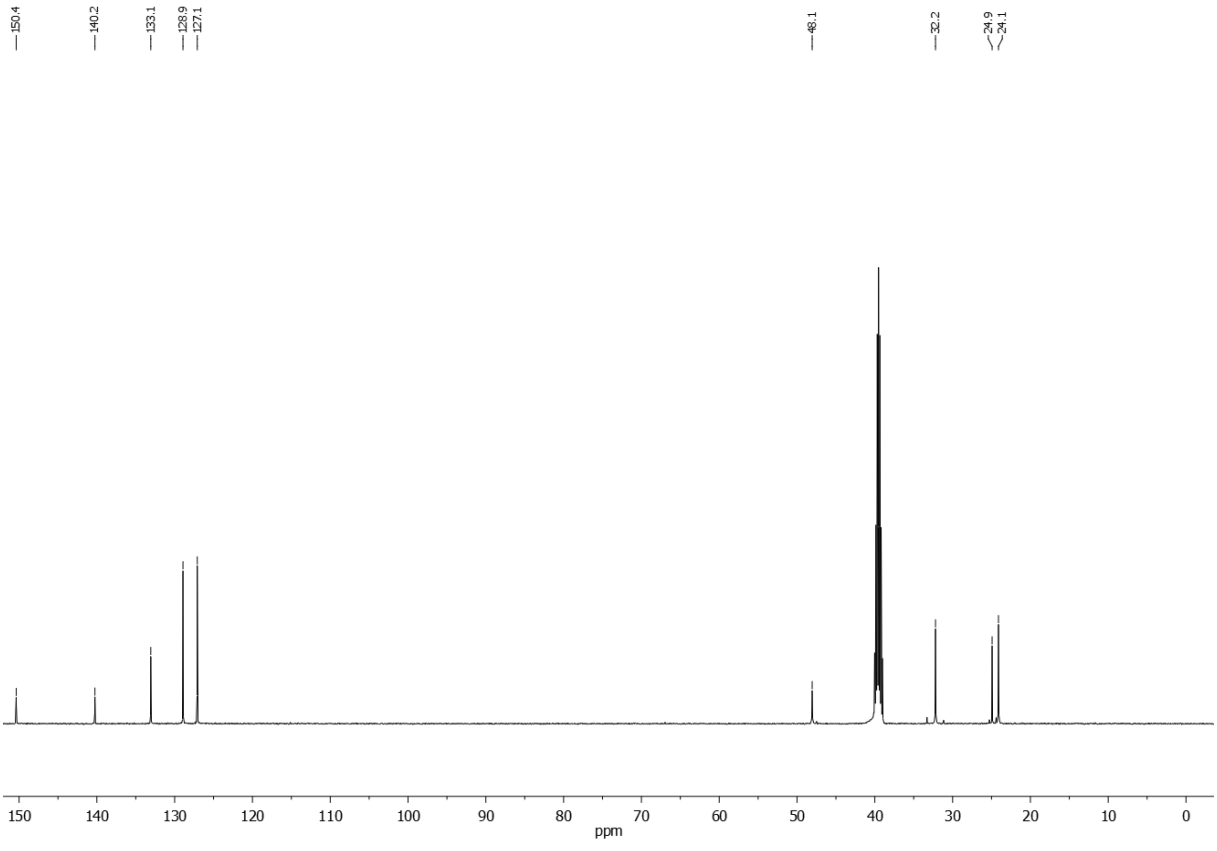




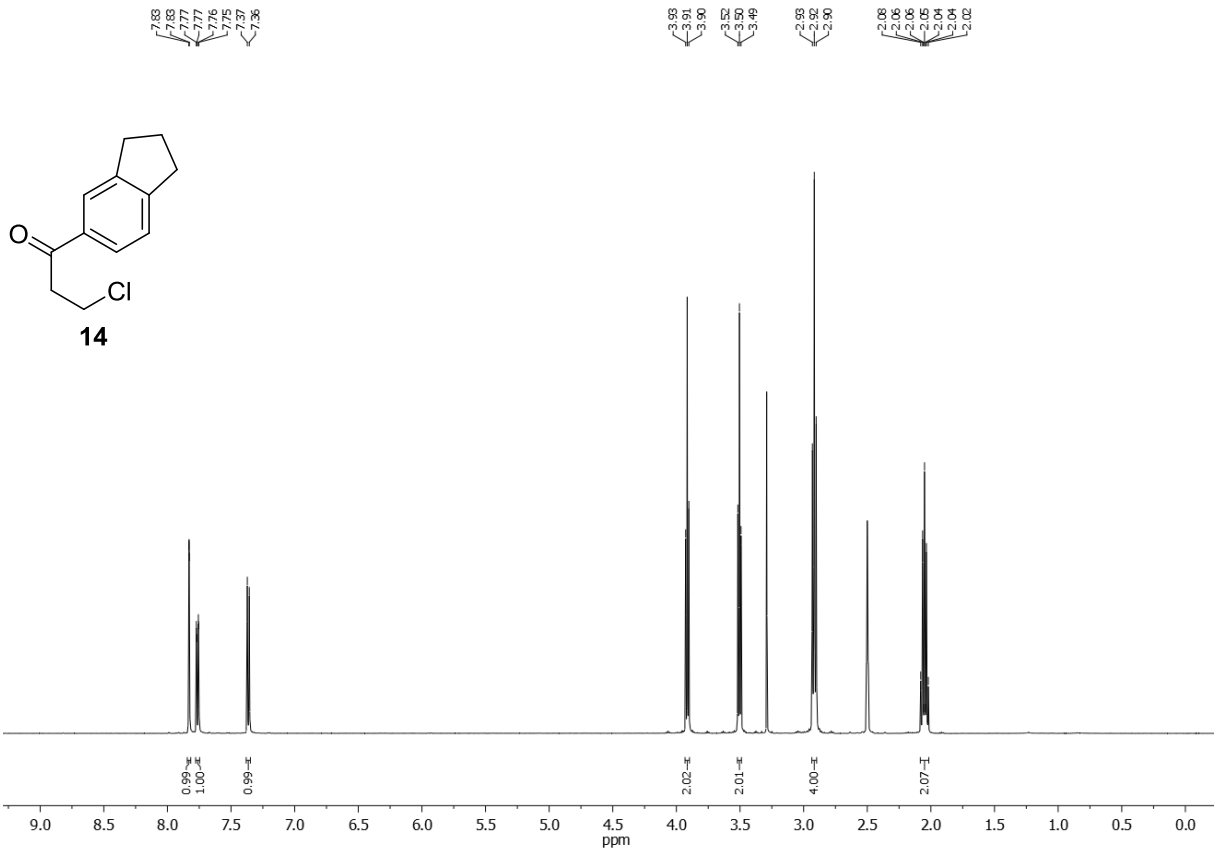
^{1}H and ^{13}C NMR spectra of compound **12**

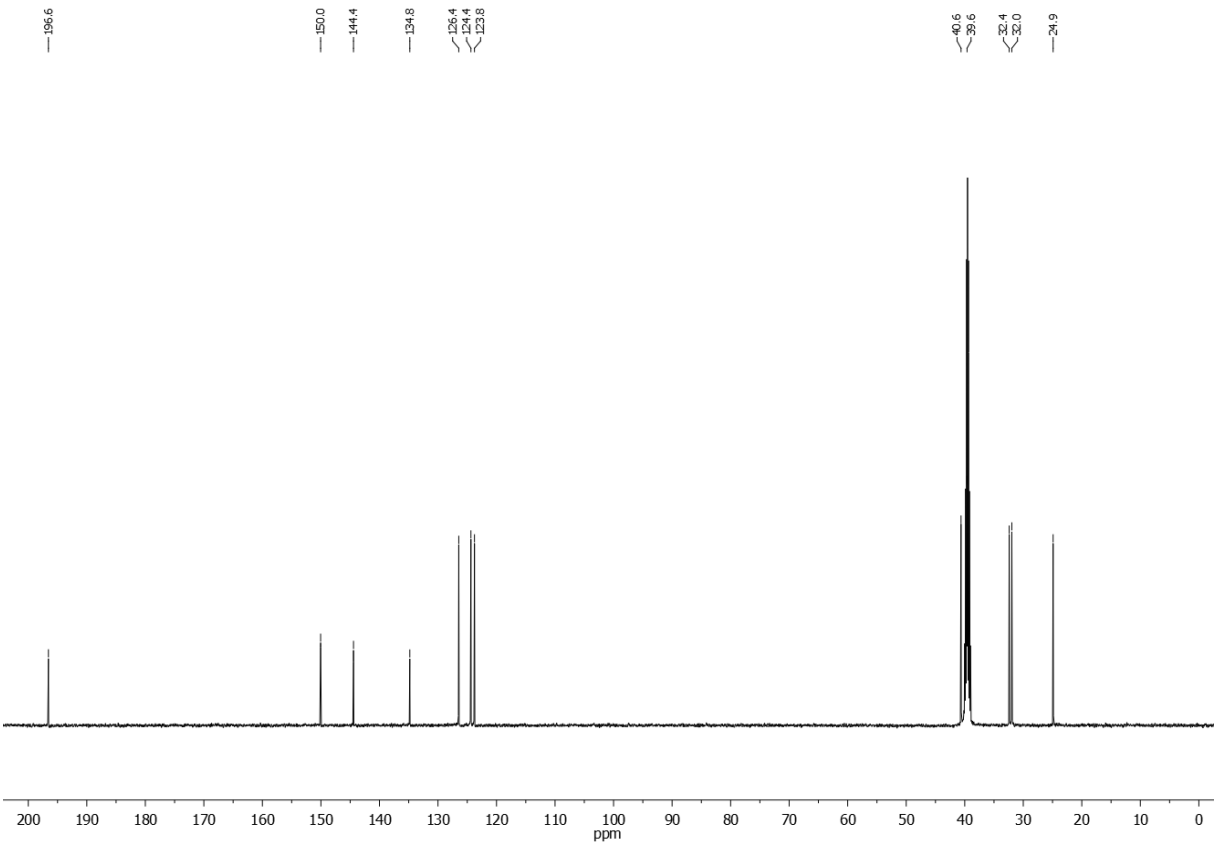
12





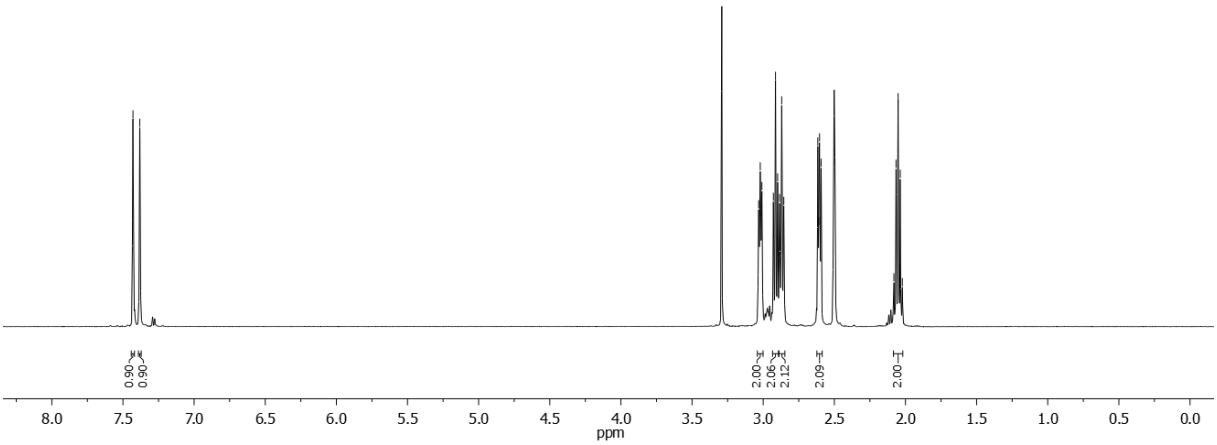
^{1}H and ^{13}C NMR spectra of compound **14**

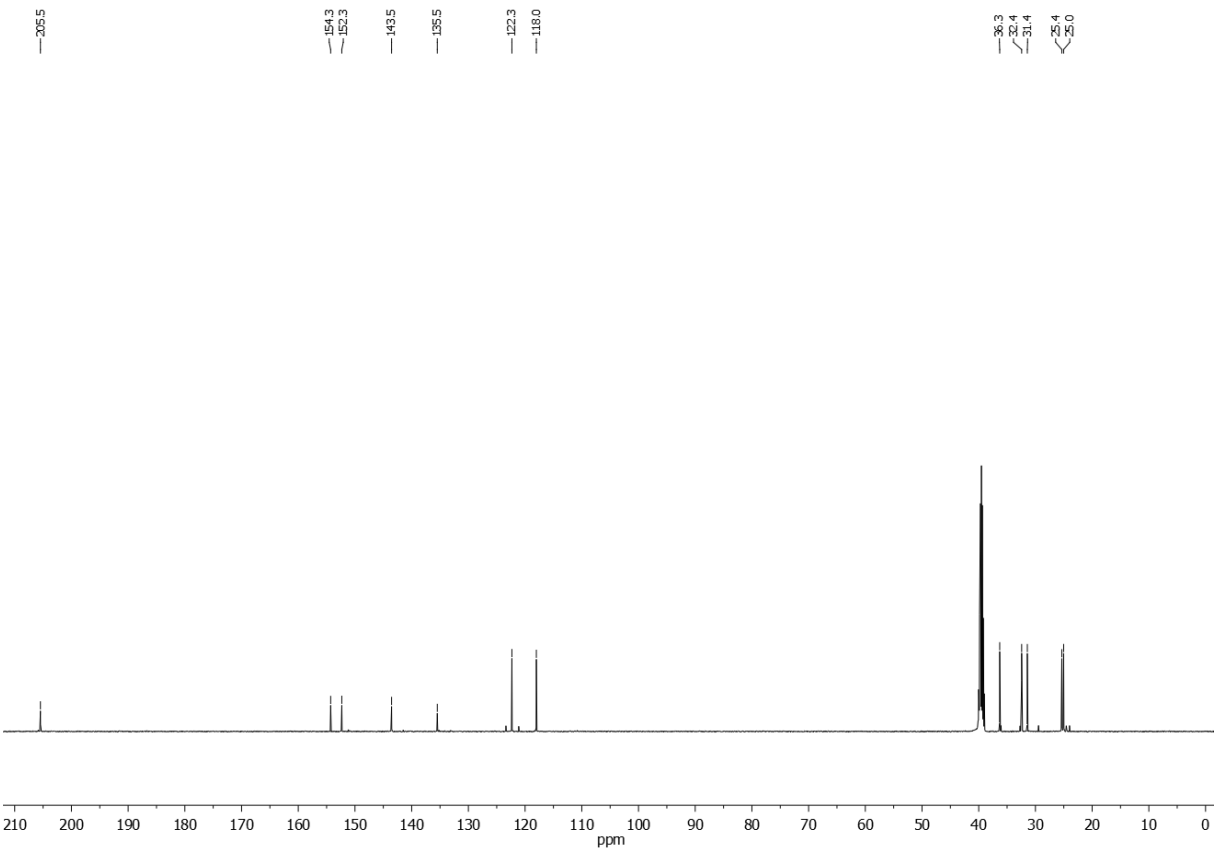




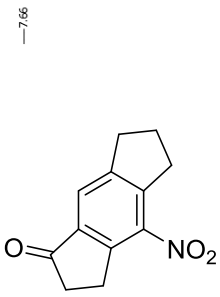
^{1}H and ^{13}C NMR spectra of compound **15**

15

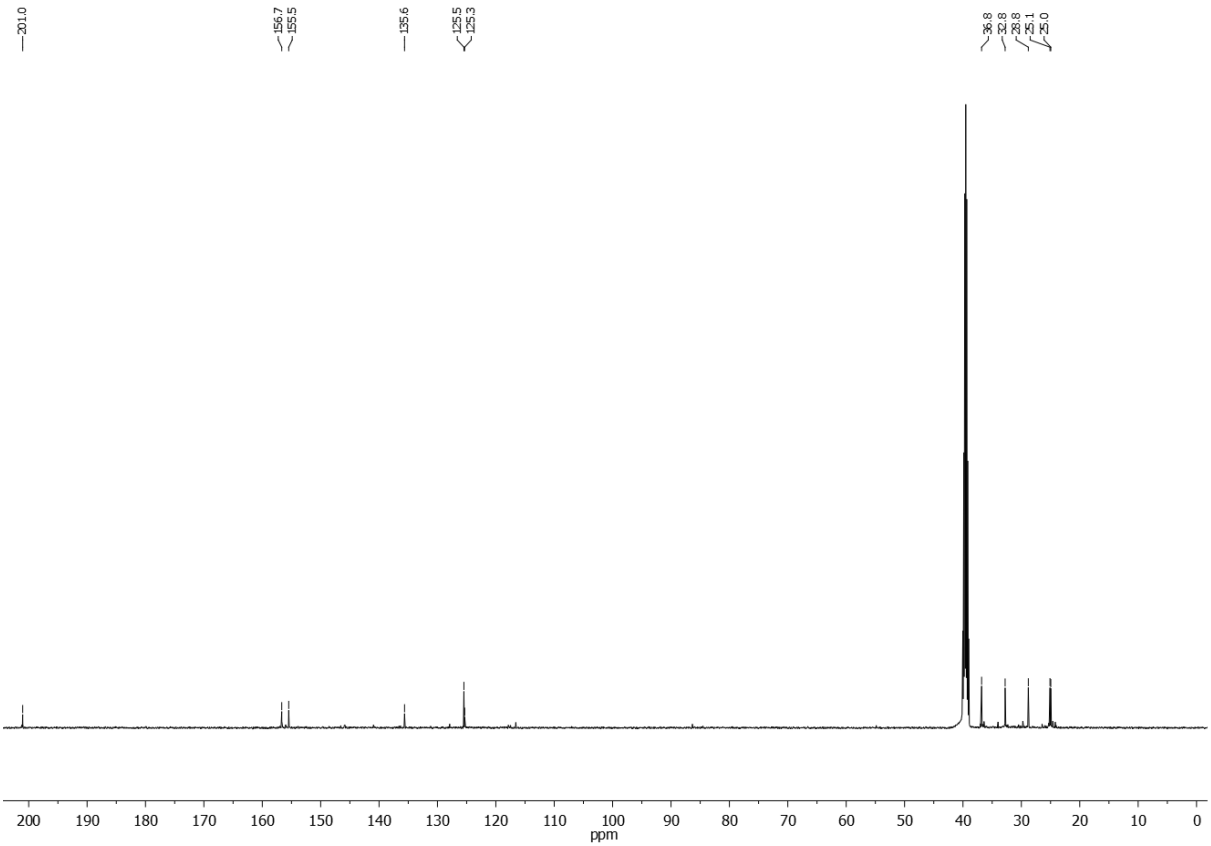




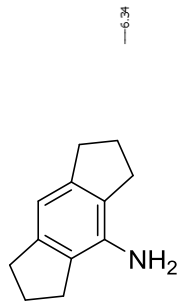
^{1}H and ^{13}C NMR spectra of compound **16**



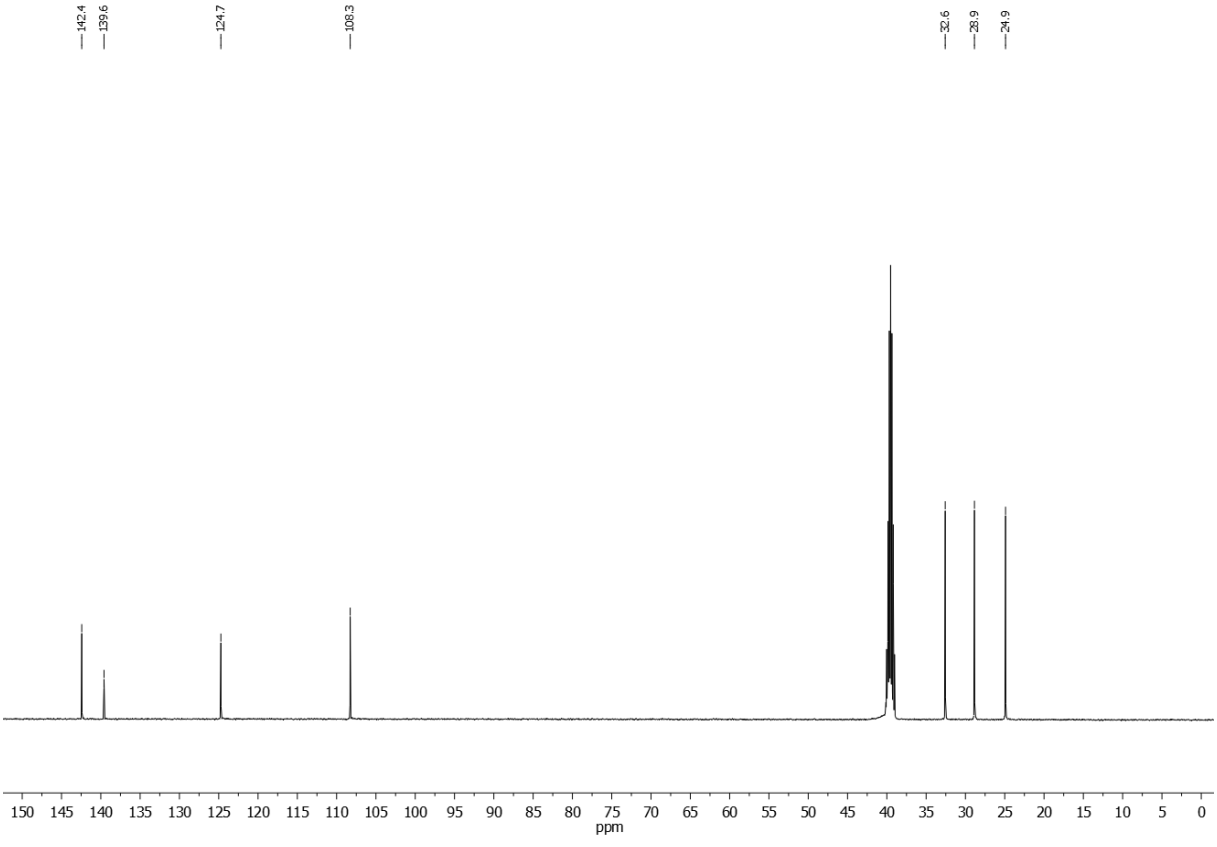
16



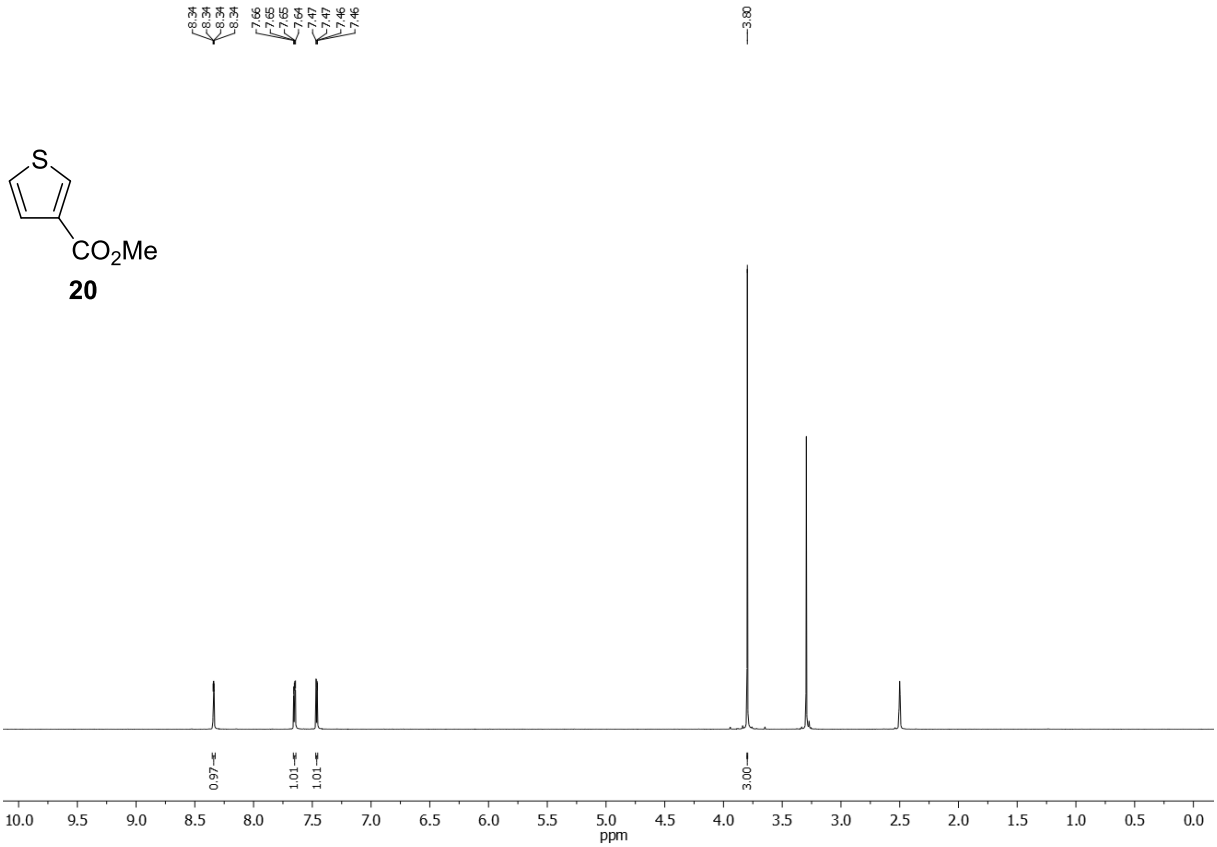
^{1}H and ^{13}C NMR spectra of compound **17**

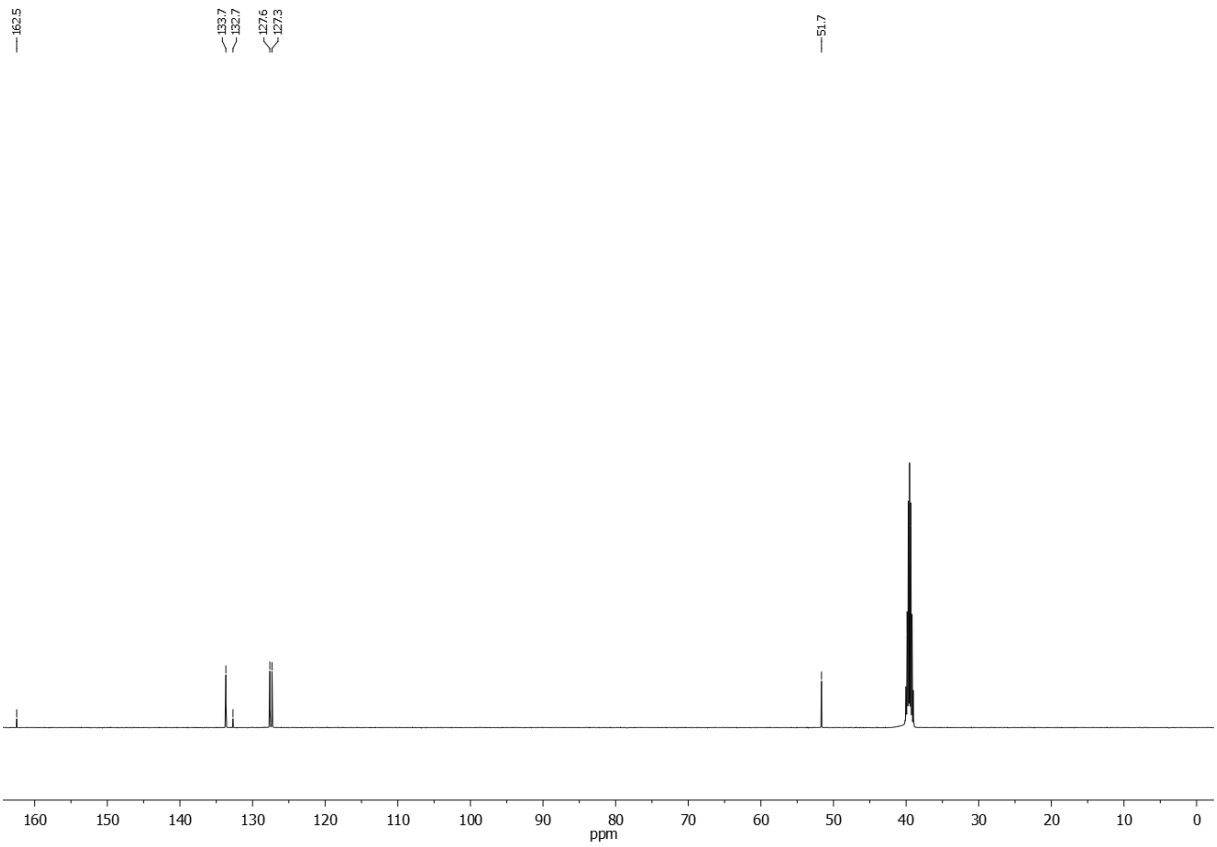


17

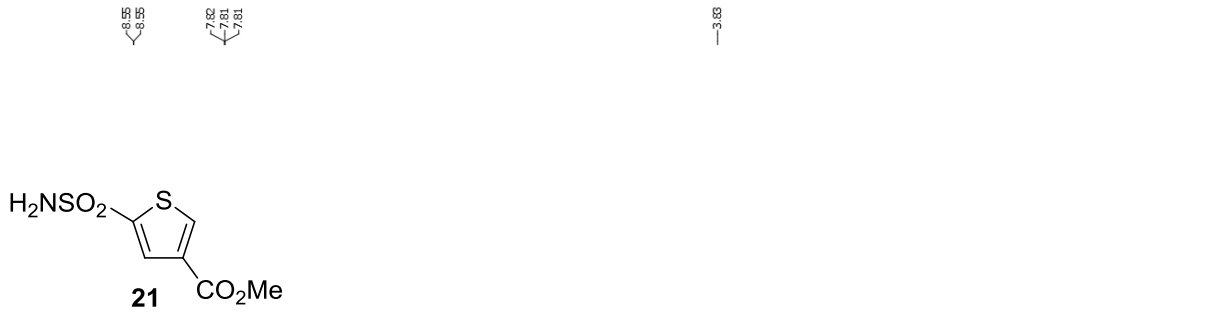


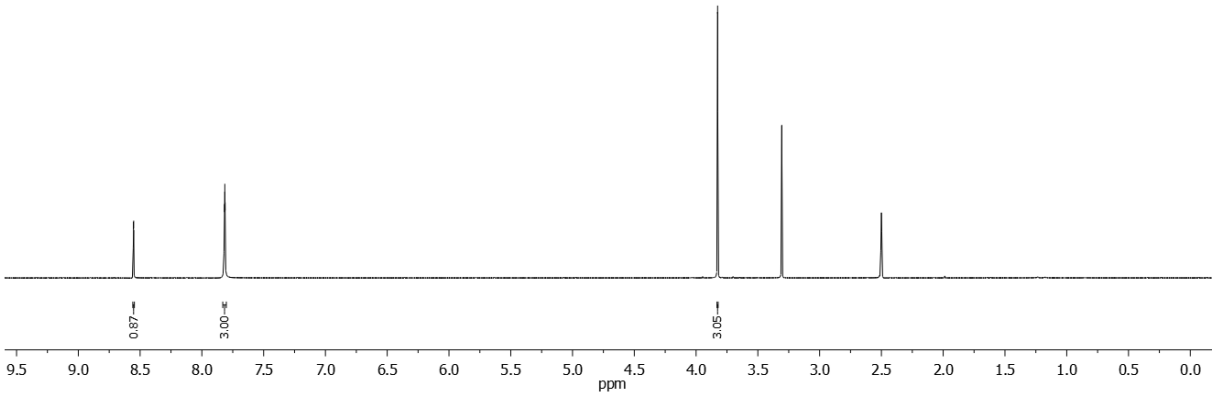
^{1}H and ^{13}C NMR spectra of compound **20**

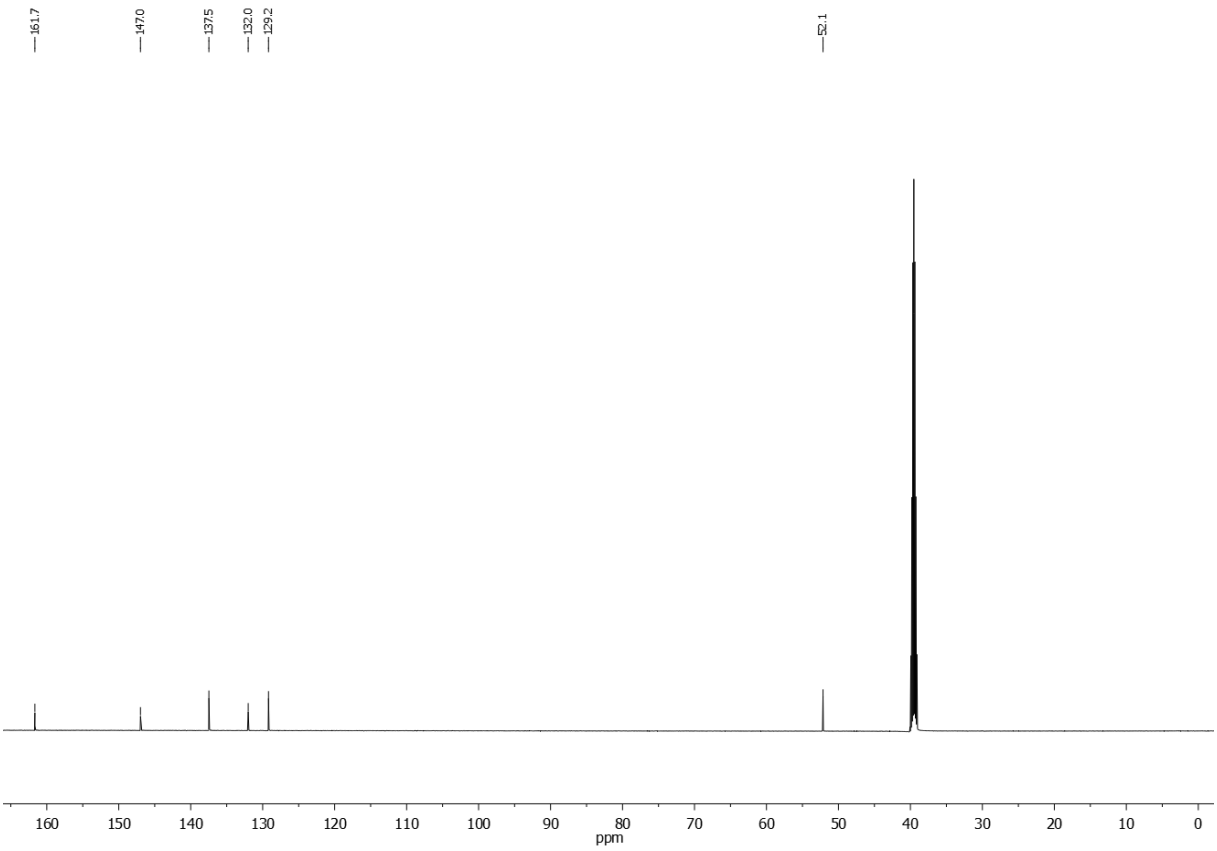




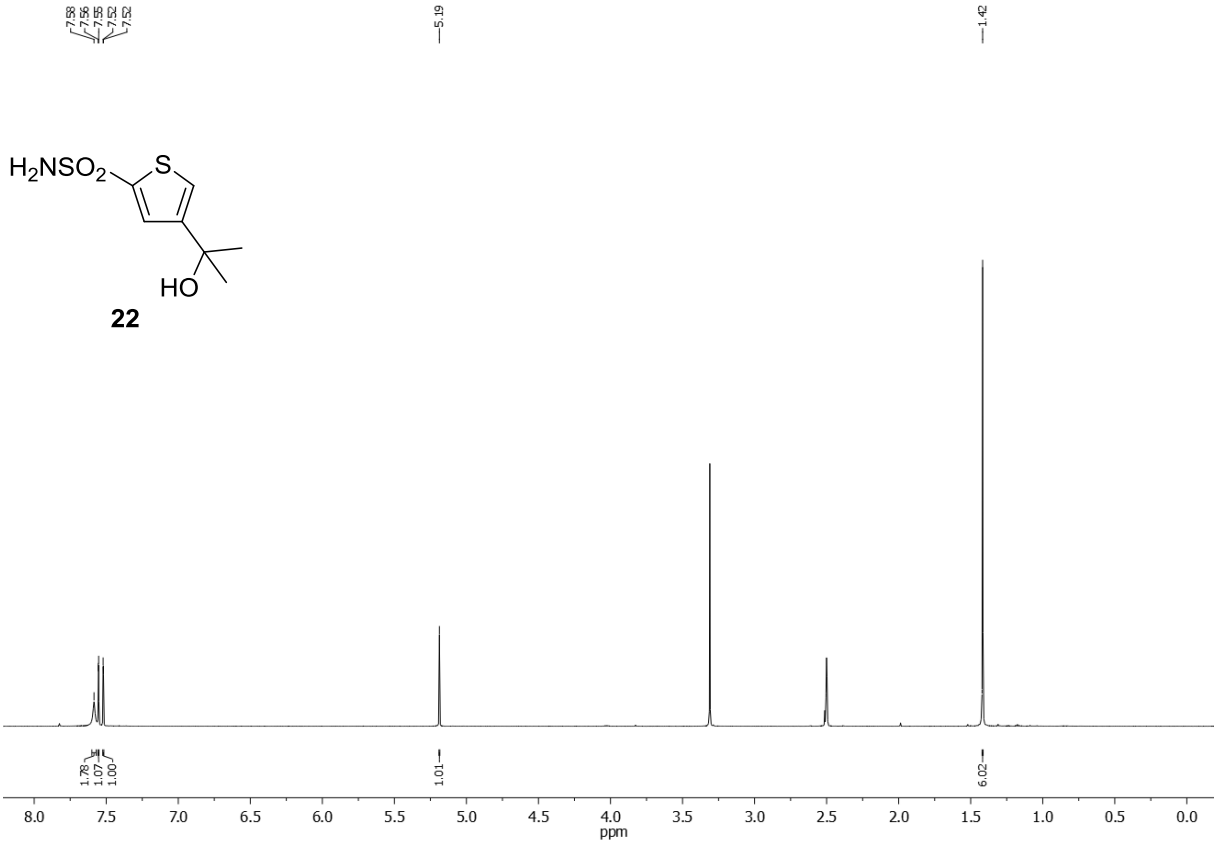
^{1}H and ^{13}C NMR spectra of compound **21**

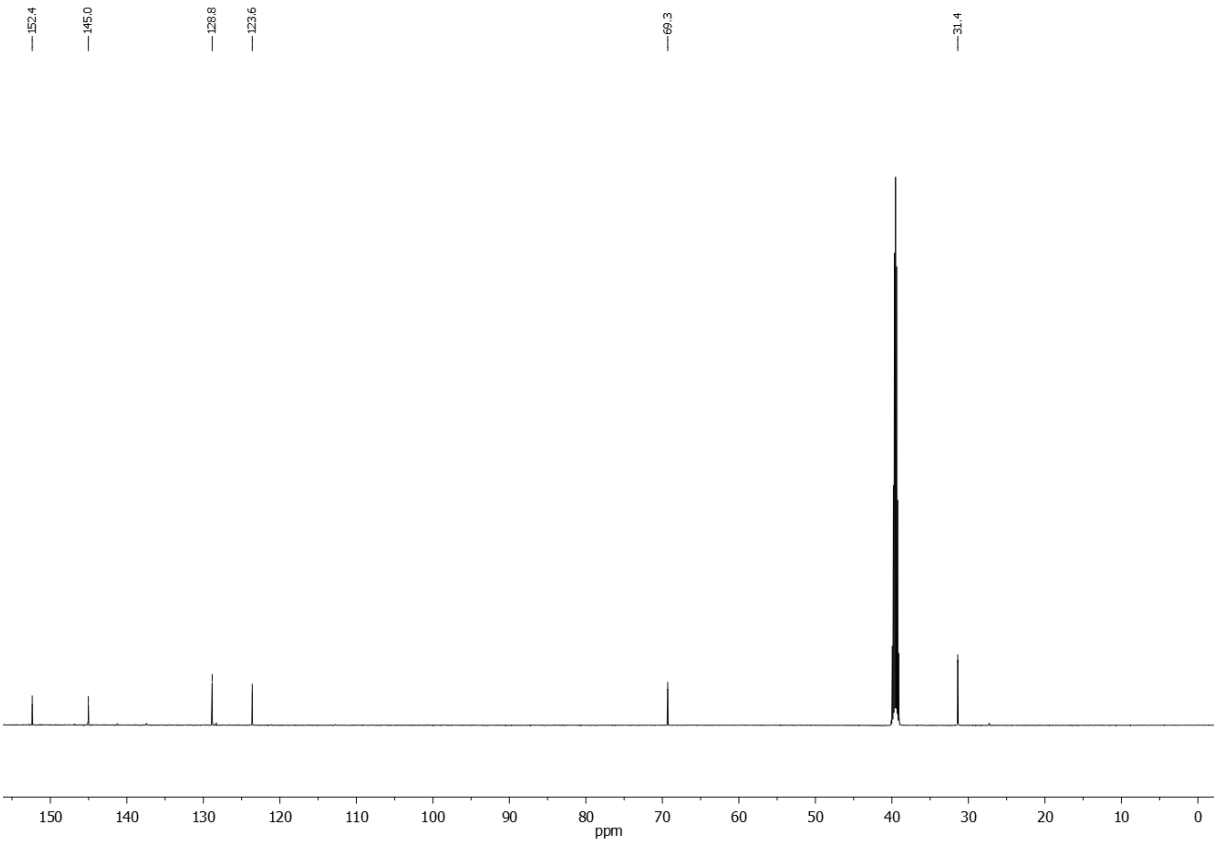




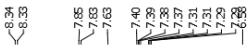


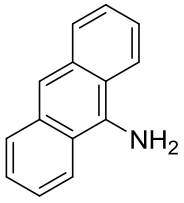
^{1}H and ^{13}C NMR spectra of compound **22**



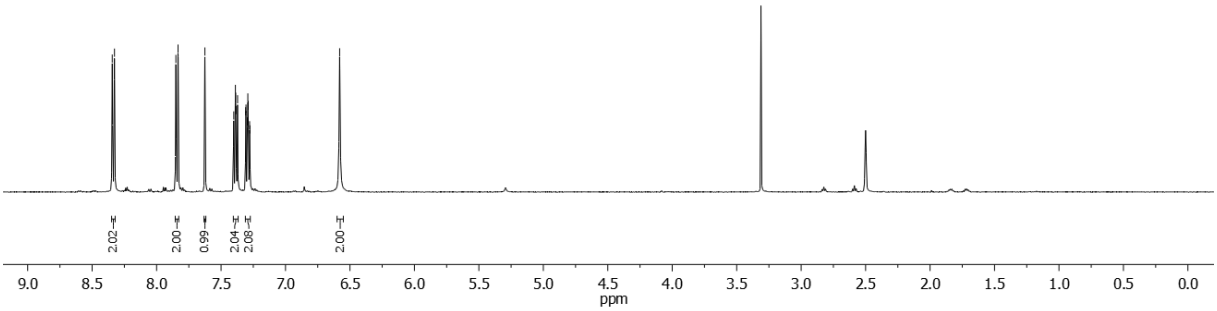


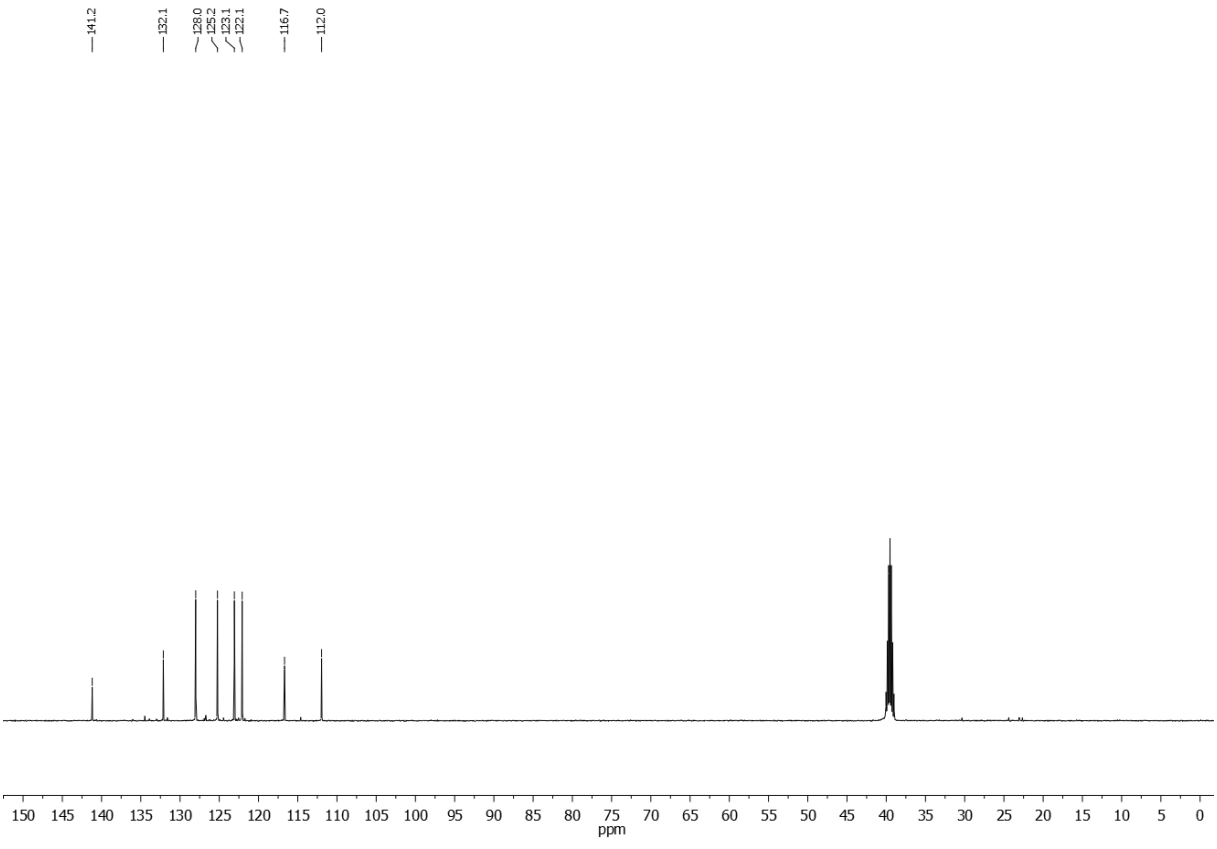
^{1}H and ^{13}C NMR spectra of compound **24**



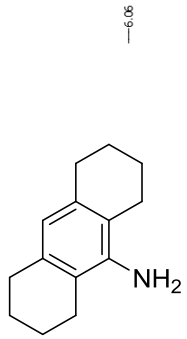


24

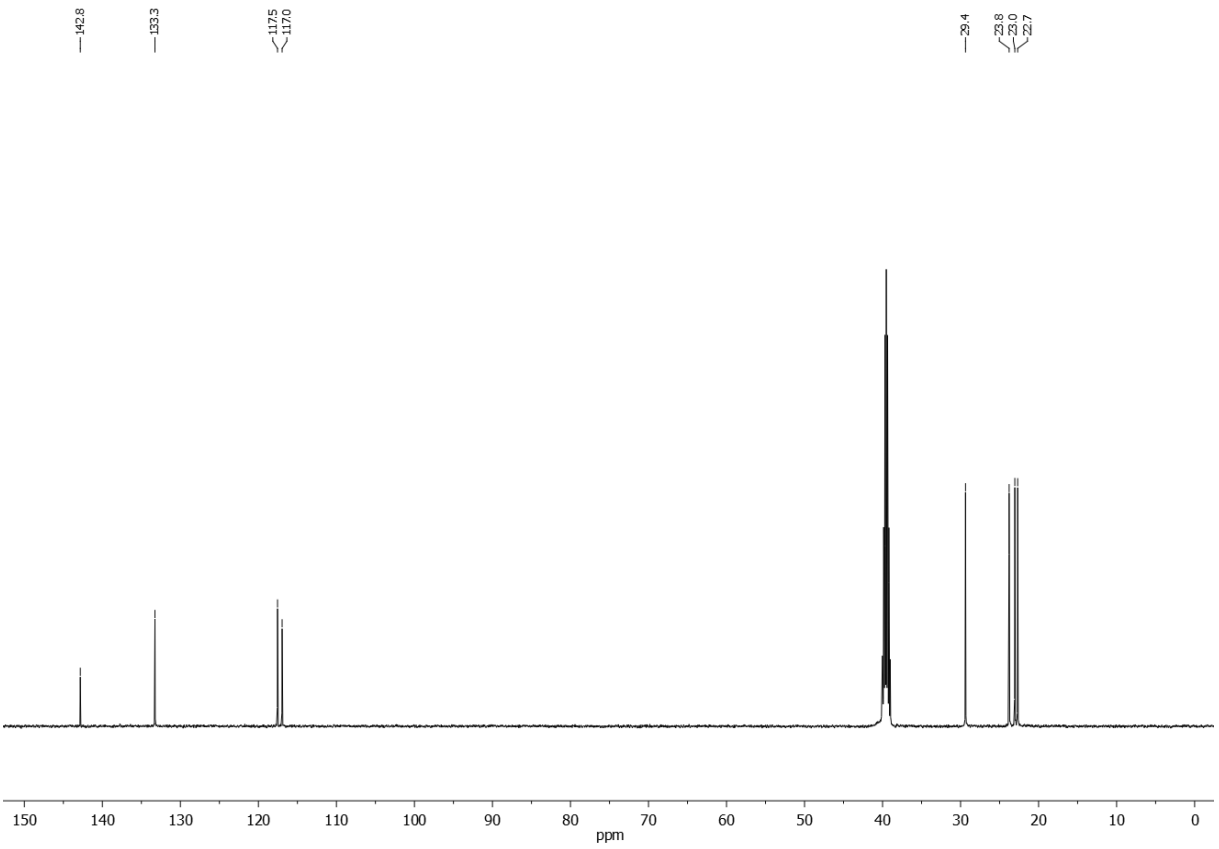




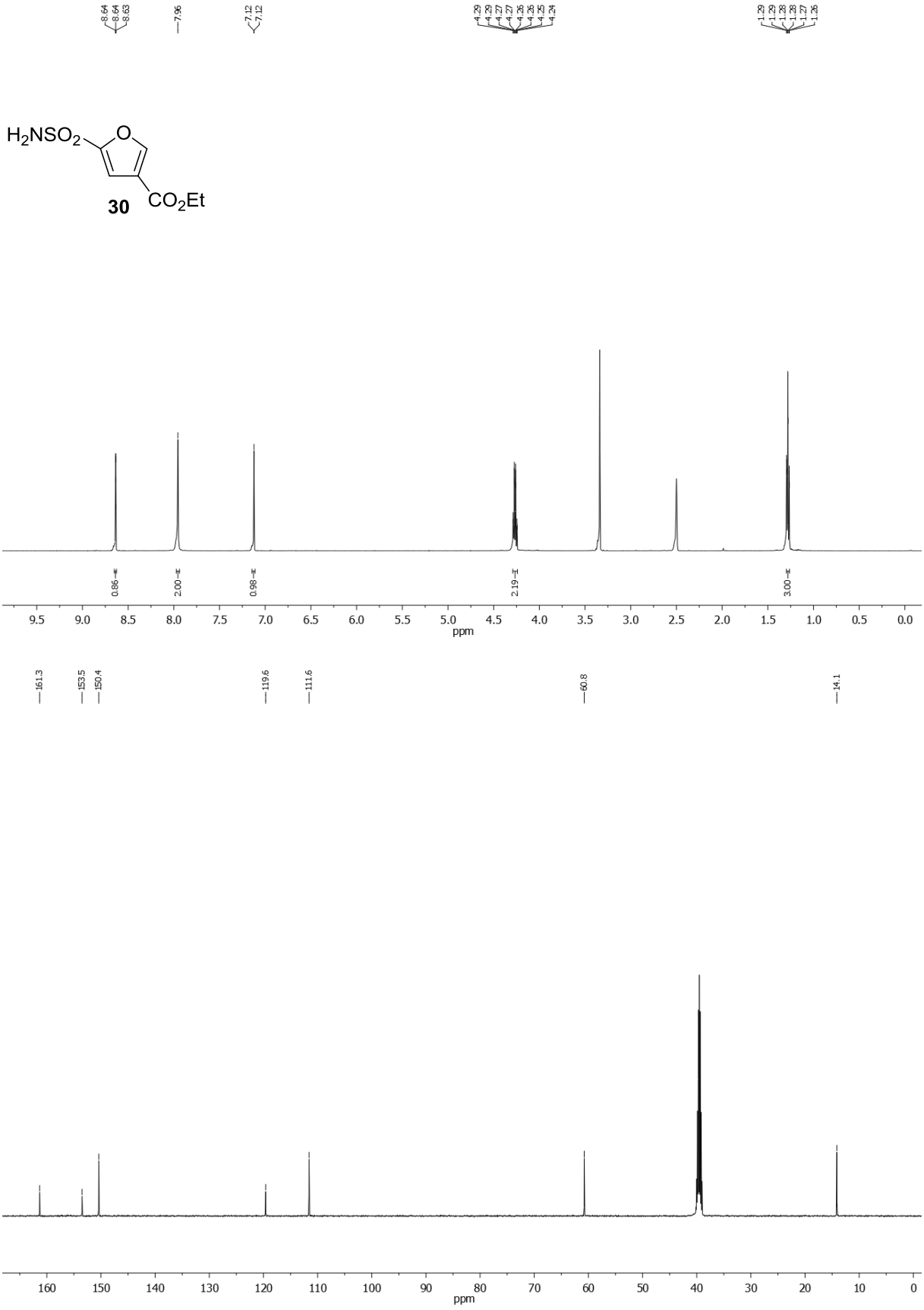
^{1}H and ^{13}C NMR spectra of compound **25**



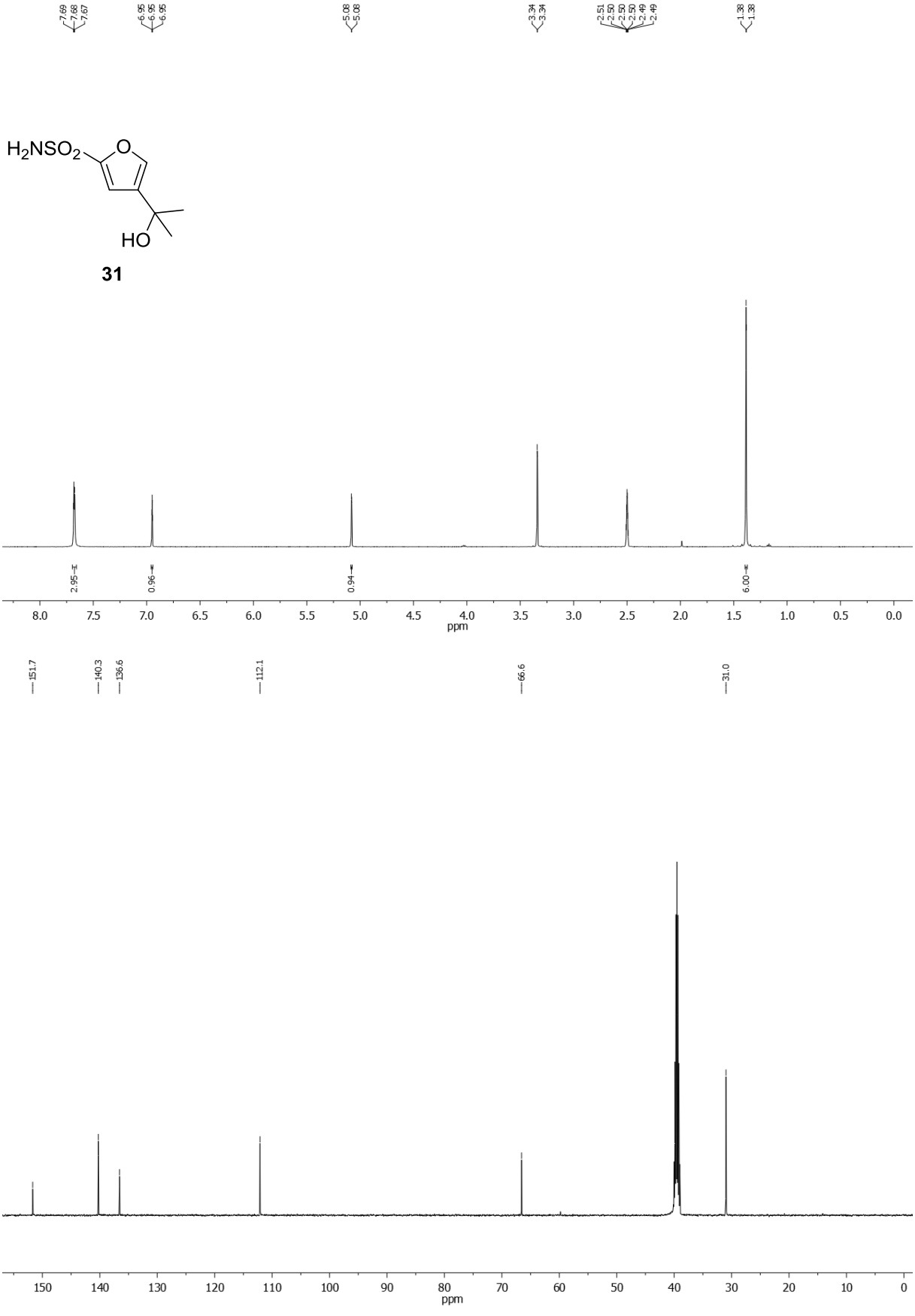
25



^{1}H and ^{13}C NMR spectra of compound **30**



^{1}H and ^{13}C NMR spectra of compound **31**



HPLC Stability Measurements

HPLC measurements for compounds **1**-**6** and **8**-**12** were performed on a Merck-Hitachi LaChrom Elite instrument (Hitachi High-Tech Corporation, Tokyo, Japan) equipped with a L-2130 HPLC pump (with inline degasser), a L-2200 autosampler, a L-2300 column oven and a L-2455 diode array detector (DAD). Chromatograms were monitored at 205 nm. The HPLC was equipped with a RP-18 column (4 µm, 125 × 4 mm, Nucleosil, Machery-Nagel, Düren, Germany). The column oven was adjusted to 37 °C. Chromatograms were obtained using the program EZChrom Elite (version 3.3.2, Agilent, Santa Clara, USA).

HPLC measurements for compound **7** were performed on a Jasco HPLC 2000 instrument (Jasco, Pfungstadt, Germany) equipped with a LG-2080-02S ternary low-pressure gradient unit, a DG-2080-53 degasser, a PU-2080 HPLC pump, a CO-2060 column oven and a UV-2075 UV detector. Chromatograms were monitored at 205 nm. The column oven was adjusted to 37 °C. Chromatograms were obtained using the program ChromPass (version 1.8.6.1, Jasco, Pfungstadt, Germany).

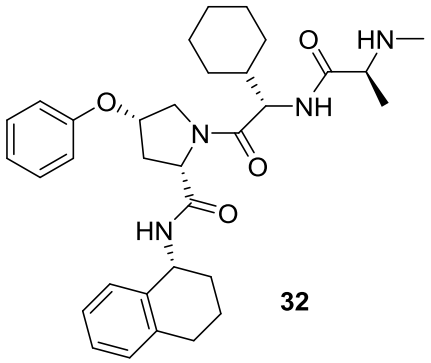
Chromatograms were recorded under isocratic conditions, using 60% H_2O_{dd} and 40% MeCN (v/v) (compound **1**), 55% H_2O_{dd} and 45% MeCN (v/v) (compounds **6**, **7**, **8**, **11**, **12**), 50% H_2O_{dd} and 50% MeCN (v/v) (compound **9**), 45% H_2O_{dd} and 55% MeCN (v/v) (compound **10**), respectively, the flow rate was 1.0 mL/min. Chromatograms of compound **4** were recorded using a linear gradient from 55% H_2O_{dd} and 45% MeCN (v/v) to 75% H_2O_{dd} and 25% MeCN, the flow rate was 1.2 mL/min. Chromatograms of compound **2** were recorded under isocratic conditions, using 63% H_2O_{dd} and 37% MeCN (v/v), the flow rate was 1.5 mL/min. Chromatograms of compound **3** and **5** were recorded under isocratic conditions, using 50% H_2O_{dd}, 30% MeCN (v/v) and 20% MeOH (v/v) (compound **3**) and 50% H_2O_{dd}, 35% MeCN (v/v) and 15% MeOH (v/v) (compound **5**), respectively, the flow rate was 1.5 mL/min. Each eluent (except for MeOH) contained 0.1% TFA.

Sample preparation and incubation for stability measurements

Five different buffers/solutions were prepared with H_2O_{dd} as follows and adusted with a Metrohm 691 pH Meter.

pH = 8.4, 20 mM Tris-HCl buffer, 150 mM NaCl
pH = 7.4, 12 mM phosphate buffer, 2,7 mM KCl, 137 mM NaCl
pH = 6.0, 12 mM phosphate buffer, 2,7 mM KCl, 137 mM NaCl
pH = 4.0, 10 mM NaOAc / AcOH
pH = 1.0, 100 mM HCl

Compound **32** served as an internal standard. The preparation is reported elsewhere.[14]



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Stock solutions of all test compounds and of the internal standard compound were prepared in MeCN. For incubations, 400 µL of the corresponding buffer and 100 µL of the solutions of the respective test compound and of the internal standard compound were added. The final incubation volume was 500 µL. The final concentrations of the test compound and the internal standard were 0.1 mM each. The concentration of MeCN was 20% (v/v). Incubations were performed at 37 °C using an Eppendorf Thermomixer comfort with 300 rpm. Aliquots of 20 µL were injected into the HPLC system at the beginning of the incubations and in 60 min intervals over 8 h.

Areas under the curve (AUCs) of the resulting chromatograms were determined for the respective test compound and the internal standard. Ratios were calculated using the following equation 1,

$$\text{ratio} = \frac{\frac{\text{AUC}_{\text{compd}}\,(\text{t})}{\text{AUC}_{\text{IS}}\,(\text{t})} \times 100\%}{\frac{\text{AUC}_{\text{compd}}\,(\text{t}_0)}{\text{AUC}_{\text{IS}}\,(\text{t}_0)}} \qquad (1)$$

where AUC_{compd} (t) is the area under the curve of the compound at time t, and AUC_{IS} (t) is the area under the curve of the internal standard at time t, AUC_{compd} (t_0) is the area under the curve of the compound at time t = 0 h, and AUC_{IS} (t_0) is the area under the curve of the internal standard at time t = 0 h.

Ratio values at nine different time points were plotted *versus* incubation time and fitted to the equation of exponential decay. From the obtained pseudo-first order rate constants, *k*, the half-lives, $t_{1/2}$, were calculated using equation 2.

$$t_{1/2} = \frac{\ln(2)}{k} \qquad (2)$$

Sample preparation and incubation for decomposition analysis of sulfonylurea 2

The chromatograms for the analysis of decomposition products of sulfonylurea **2** were recorded using a linear gradient (flow rate= 1.4 mL/min) starting with 80% H_2O_{dd} and 20% MeCN (v/v) to 55% H_2O_{dd} and 45% MeCN within 12.5 min and back to 80% H_2O_{dd} and 20% MeCN (v/v) within 10.5 min at 23.0 min. The eluents contained 0.1% TFA.

Stock solutions of the sulfonylurea **2** and the respective spiking compounds **17**, **22** and of the internal standard compound were prepared in MeCN. For incubations, 400 µL of 100 mM HCl (pH = 1.0) and 100 µL of the solutions of the respective compounds (either compound **2** alone, compound **2** together with compound **17** or compound **2** together with compound **22**) and of the internal standard compound were added. The final incubation volume was 500 µL. The final concentrations of the compounds and the internal standard were 0.1 mM each. Incubations were performed at 37 °C using an Eppendorf Thermomixer comfort with 300 rpm. Aliquots of 20 µL were injected into the HPLC at 0 h or 2 h of incubation.

Figures S1-S12. Time course of decomposition of compounds 1-12

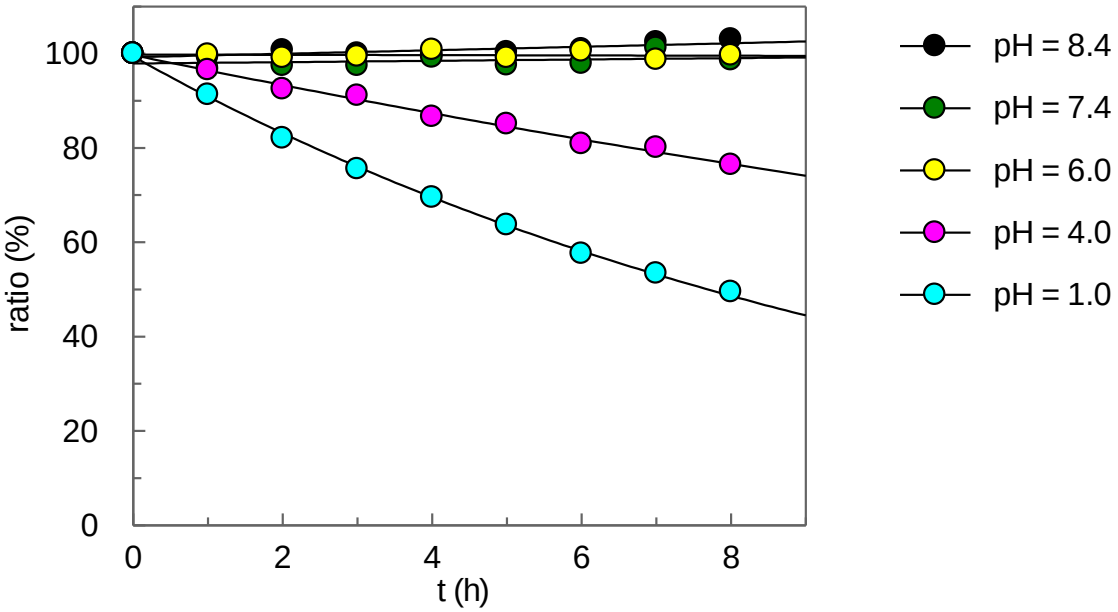


Figure S1. Time course of decomposition of MCC950 (**1**). Compound **1** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted *versus* incubation time.

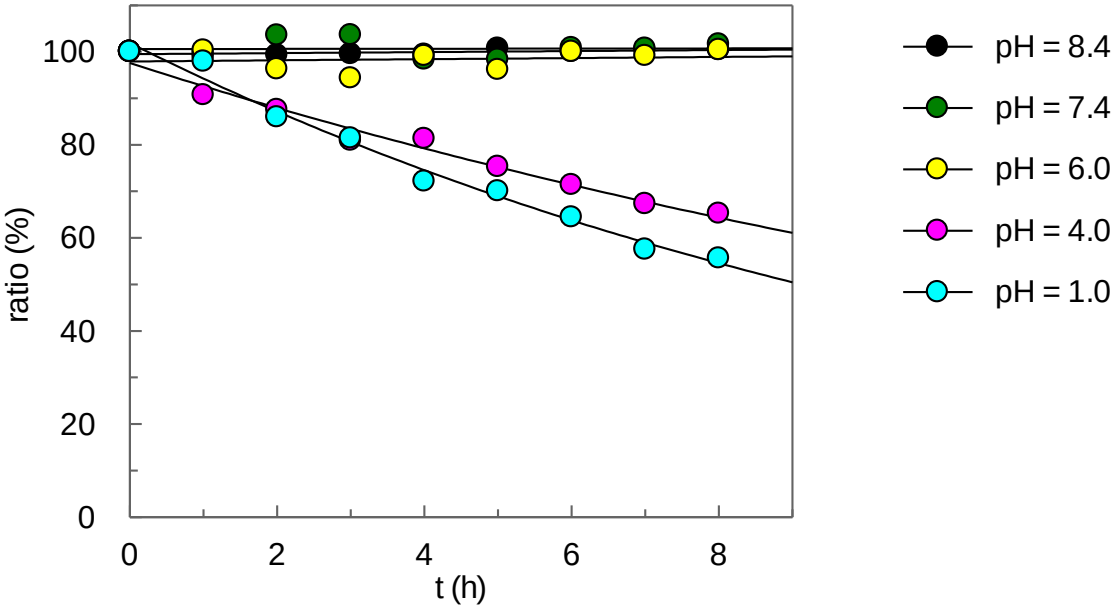


Figure S2. Time course of decomposition of sulfonylurea **2**. Compound **2** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

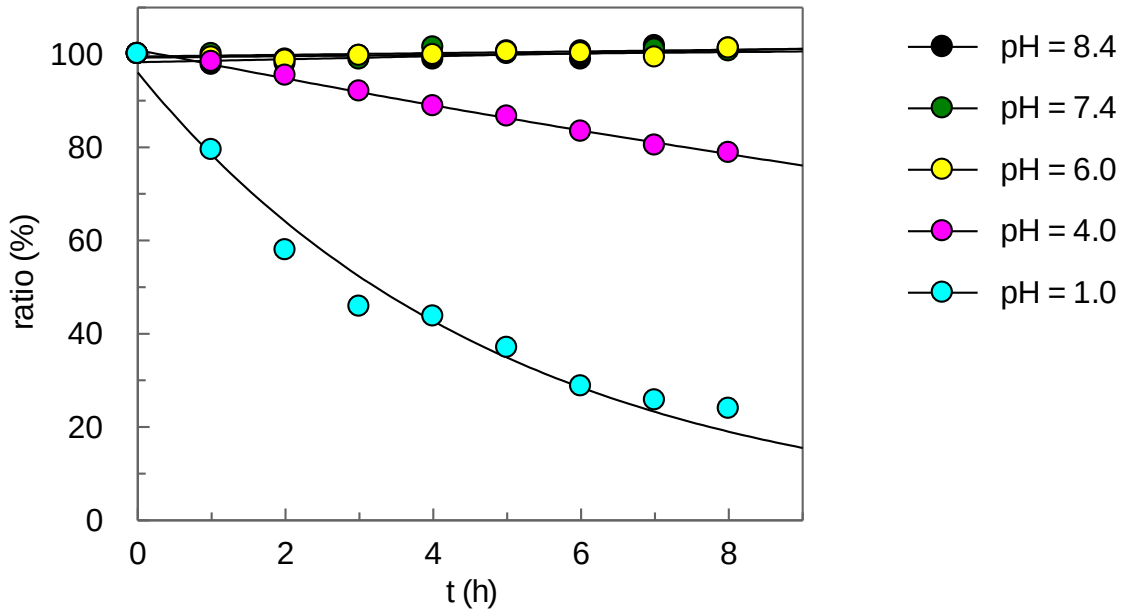


Figure S3. Time course of decomposition of sulfonylurea **3**. Compound **3** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

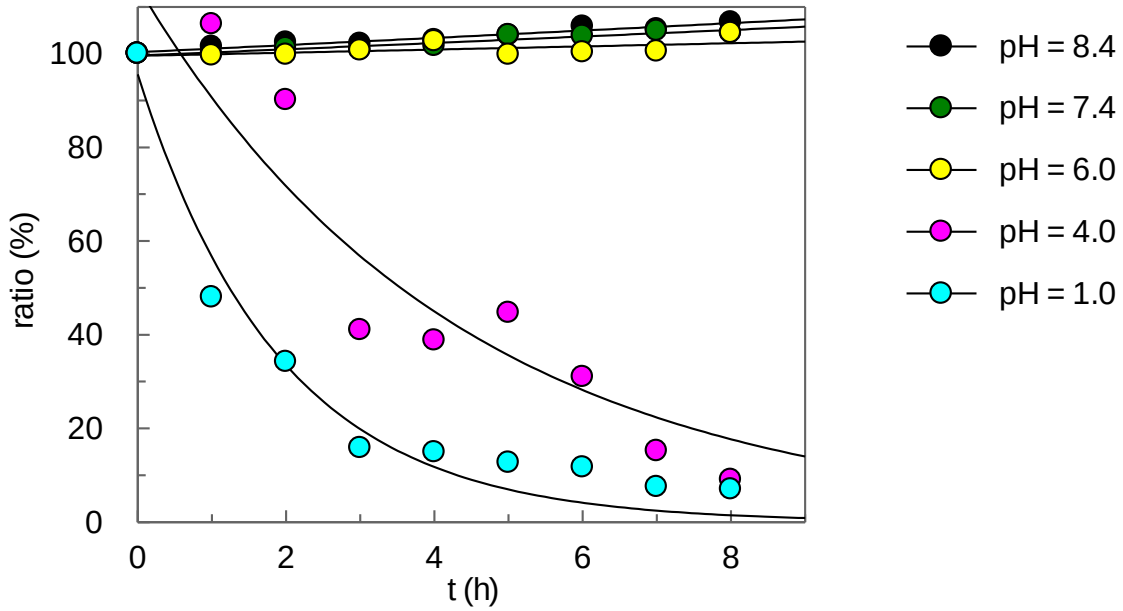


Figure S4. Time course of decomposition of sulfonylurea **4**. Compound **4** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

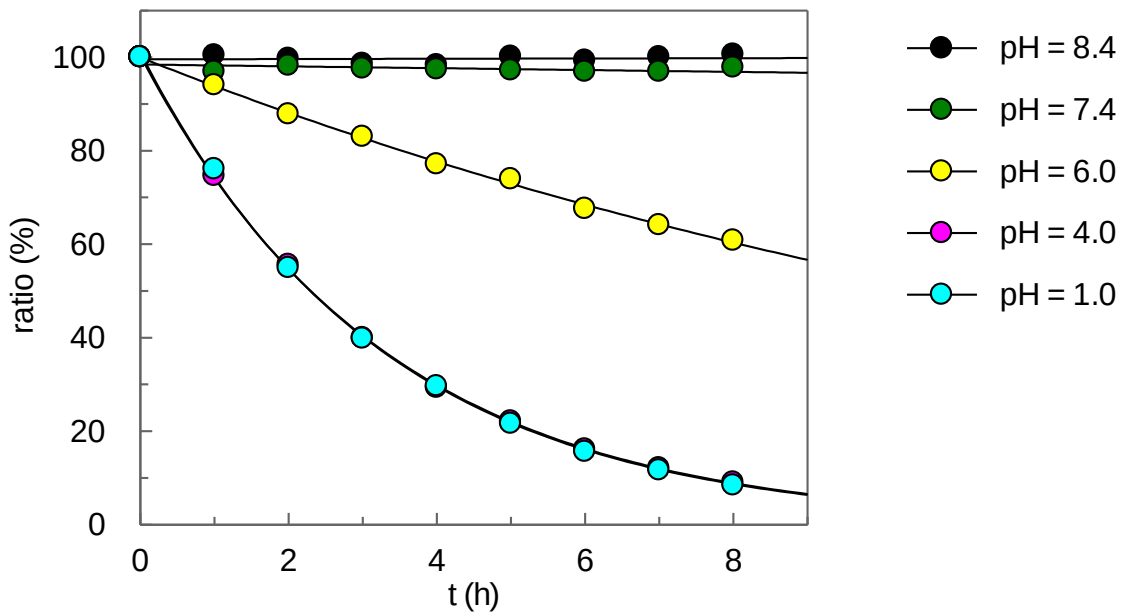


Figure S5. Time course of decomposition of sulfonylurea **5**. Compound **5** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

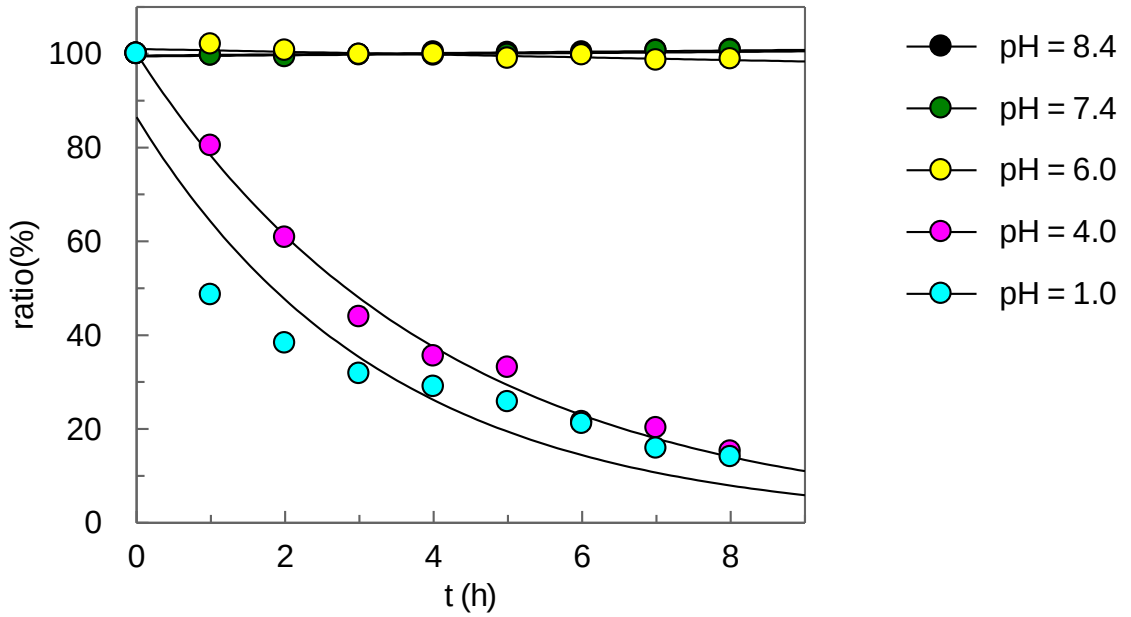


Figure S6. Time course of decomposition of sulfonylurea **6**. Compound **6** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

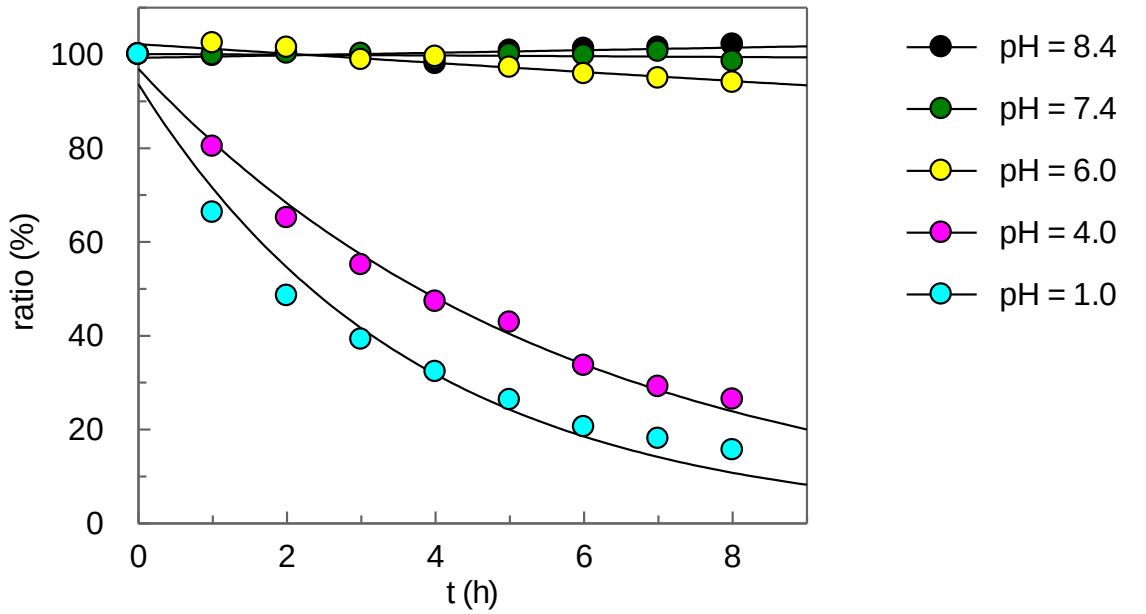


Figure S7. Time course of decomposition of sulfonylurea **7**. Compound **7** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

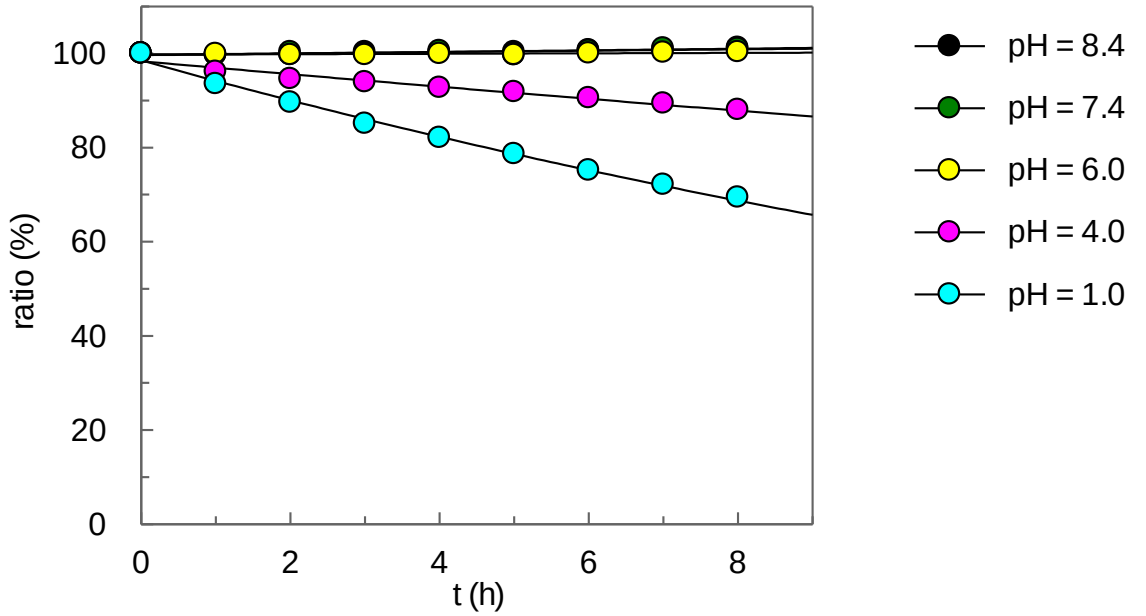


Figure S8. Time course of decomposition of sulfonylurea **8**. Compound **8** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

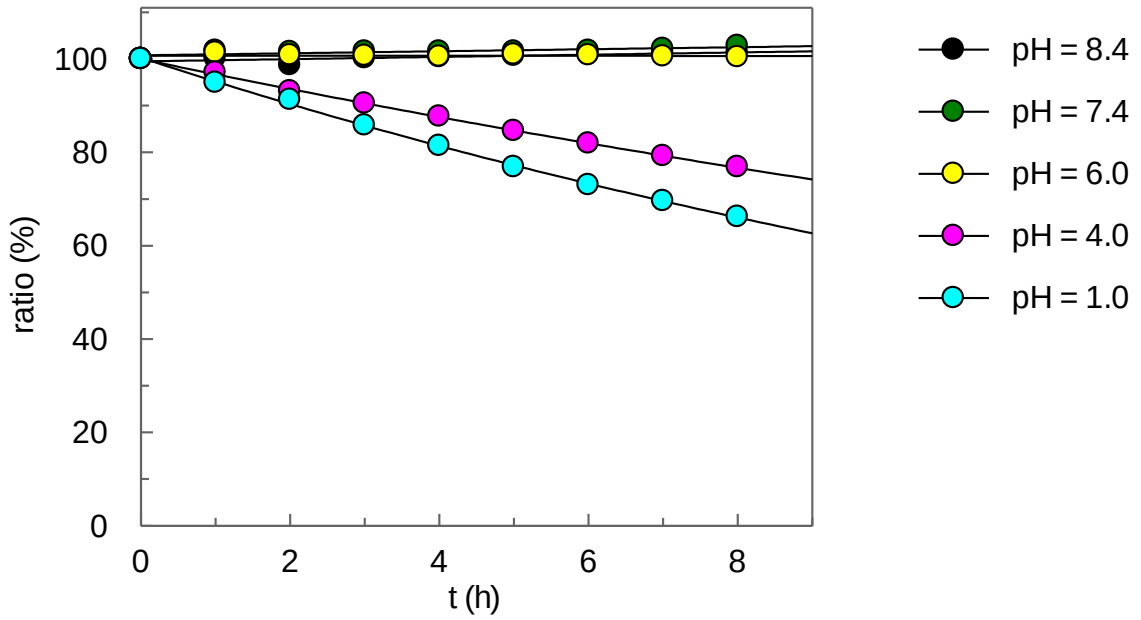


Figure S9. Time course of decomposition of sulfonylurea **9**. Compound **9** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

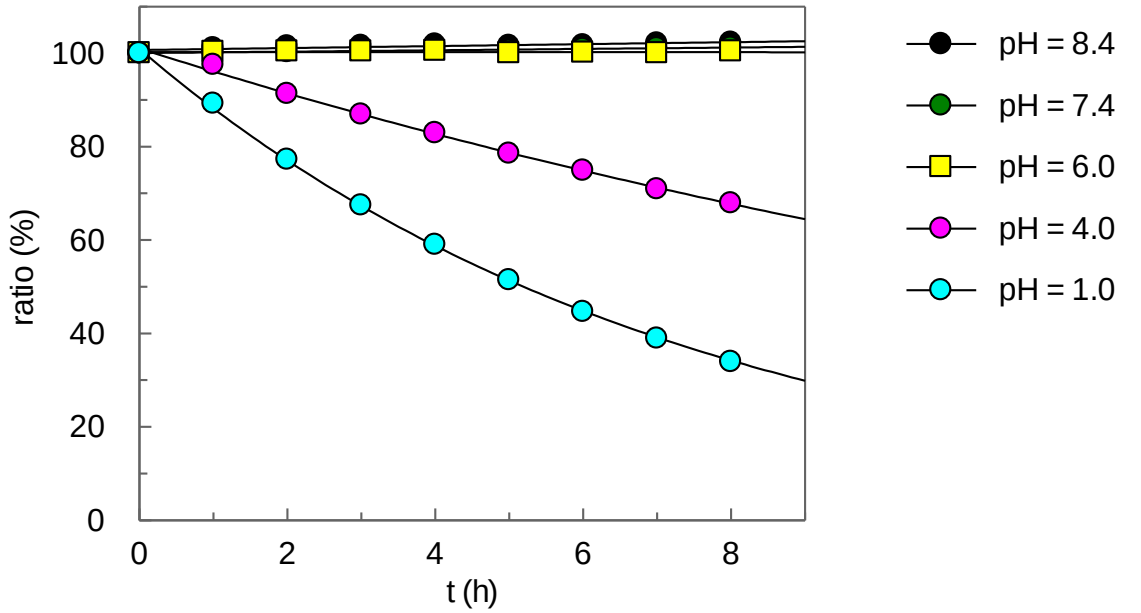


Figure S10. Time course of decomposition of sulfonylurea **10**. Compound **10** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

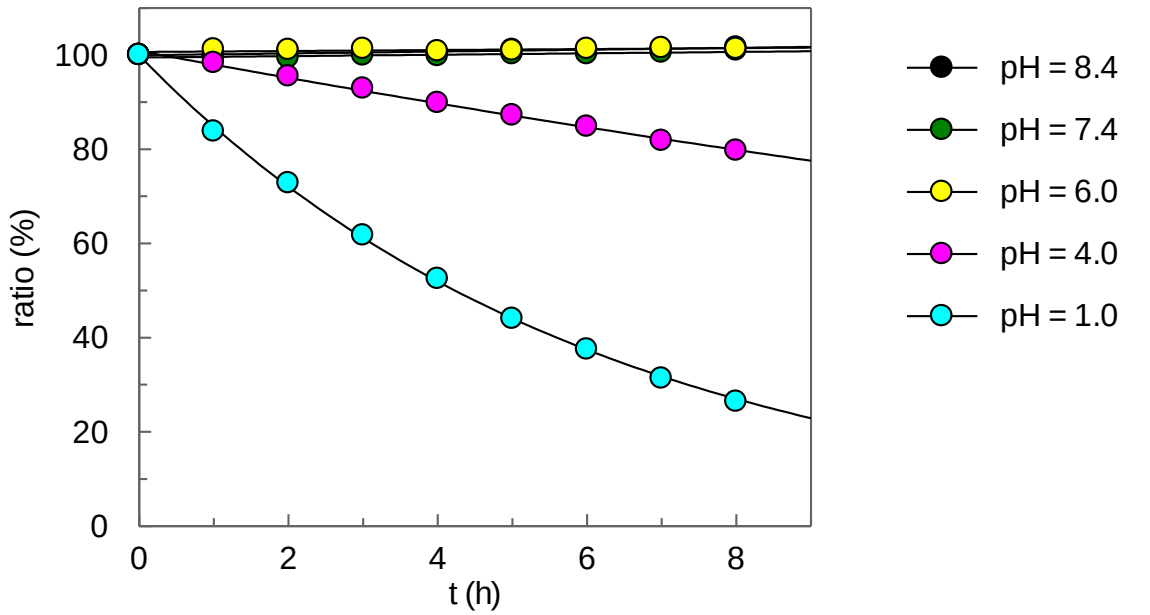


Figure S11. Time course of decomposition of sulfonylurea **11**. Compound **11** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

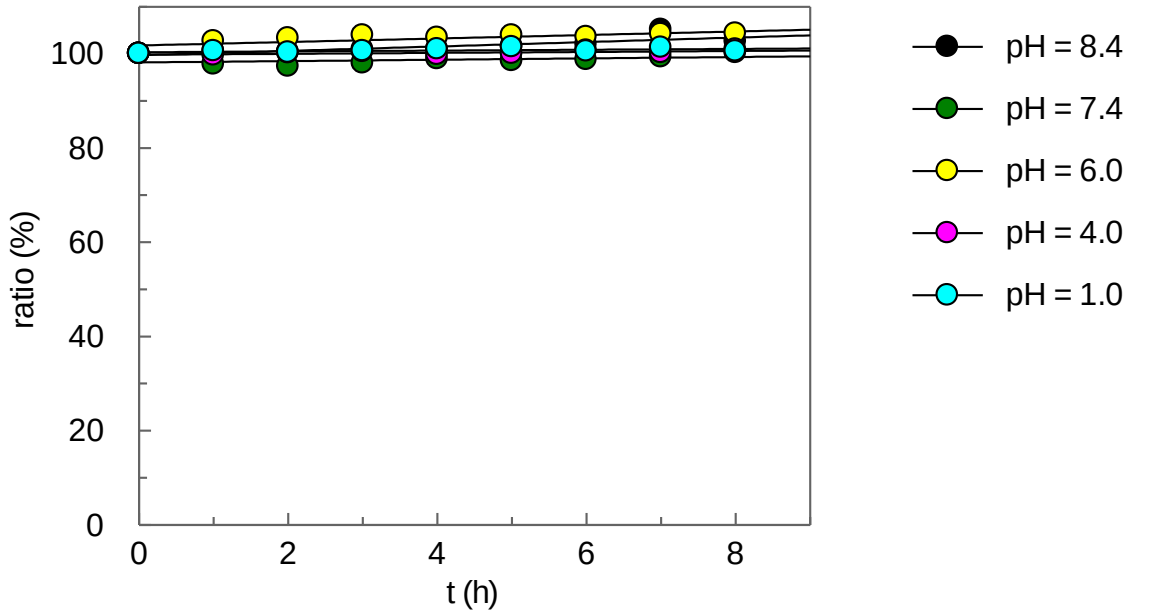
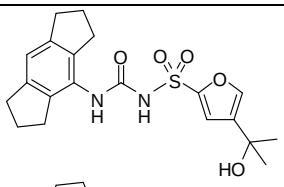
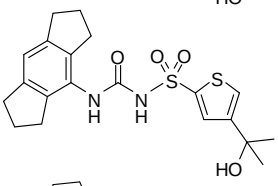
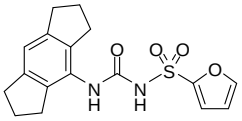
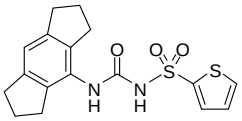
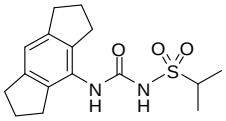
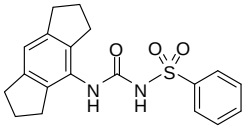
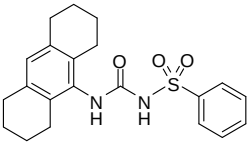
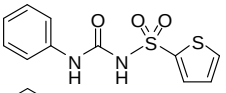
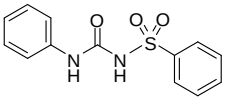
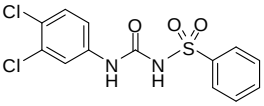
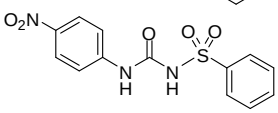
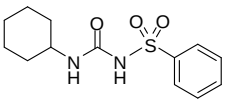


Figure S12. Time course of decomposition of sulfonylurea **12**. Compound **12** (0.1 mM) was incubated at 37 °C for 8 h at five different pH values in the presence of an internal standard (0.1 mM) and subjected to HPLC analysis. The ratio is plotted versus incubation time.

Table S1. Sulfonylureas prepared and their chemical stability

compd		ratio of compound concentration after 8 h (%)[a] half-life (h)[b]				
		pH = 1.0	pH = 4.0	pH = 6.0	pH = 7.4	pH = 8.4
1		ratio = 50% $t_{1/2}$ = 7.8 h	ratio = 76% $t_{1/2}$ = 21.1 h	ratio = 100% $t_{1/2}$ = n.d.	ratio = 99% $t_{1/2}$ = n.d.	ratio = 103% $t_{1/2}$ = n.d.
2		ratio = 56% $t_{1/2}$ = 8.9 h	ratio = 65% $t_{1/2}$ = 13.3 h	ratio = 100% $t_{1/2}$ = n.d.	ratio = 102% $t_{1/2}$ = n.d.	ratio = 100% $t_{1/2}$ = n.d.
3		ratio = 24% $t_{1/2}$ = 3.4 h	ratio = 79% $t_{1/2}$ = 22.1 h	ratio = 101% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.
4		ratio = 7% $t_{1/2}$ = 1.3 h	ratio = 9% $t_{1/2}$ = 3.0 h	ratio = 104% $t_{1/2}$ = n.d.	ratio = 104% $t_{1/2}$ = n.d.	ratio = 107% $t_{1/2}$ = n.d.
5		ratio = 8% $t_{1/2}$ = 2.3 h	ratio = 9% $t_{1/2}$ = 2.3 h	ratio = 61% $t_{1/2}$ = 11.0 h	ratio = 98% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.
6		ratio = 14% $t_{1/2}$ = 2.3 h	ratio = 15% $t_{1/2}$ = 2.8 h	ratio = 99% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.
7		ratio = 16% $t_{1/2}$ = 2.6 h	ratio = 26% $t_{1/2}$ = 4.0 h	ratio = 94% $t_{1/2}$ = n.d.	ratio = 99% $t_{1/2}$ = n.d.	ratio = 102% $t_{1/2}$ = n.d.
8		ratio = 69% $t_{1/2}$ = 15.4 h	ratio = 88% $t_{1/2}$ = 49.2 h	ratio = 100% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.
9		ratio = 66% $t_{1/2}$ = 13.3 h	ratio = 77% $t_{1/2}$ = 20.9 h	ratio = 100% $t_{1/2}$ = n.d.	ratio = 103% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.
10		ratio = 34% $t_{1/2}$ = 5.1 h	ratio = 68% $t_{1/2}$ = 13.9 h	ratio = 100% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.	ratio = 102% $t_{1/2}$ = n.d.
11		ratio = 26% $t_{1/2}$ = 4.2 h	ratio = 80% $t_{1/2}$ = 23.7 h	ratio = 101% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.	ratio = 102% $t_{1/2}$ = n.d.
12		ratio = 101% $t_{1/2}$ = n.d.	ratio = 101% $t_{1/2}$ = n.d.	ratio = 104% $t_{1/2}$ = n.d.	ratio = 100% $t_{1/2}$ = n.d.	ratio = 103% $t_{1/2}$ = n.d.

[a]Areas under the curve (AUCs) of the chromatograms after 8 h incubation at the indicated pH were determined for the test compound and the internal standard. Ratios were calculated as a measure of compound stability using eq 1. [b]Ratio values at nine different time points were plotted *versus* incubation time and fitted to the equation of exponential decay. Half-lives, $t_{1/2}$, were calculated using eq 2. [c]Not detectable; no decomposition observed within 8 h.

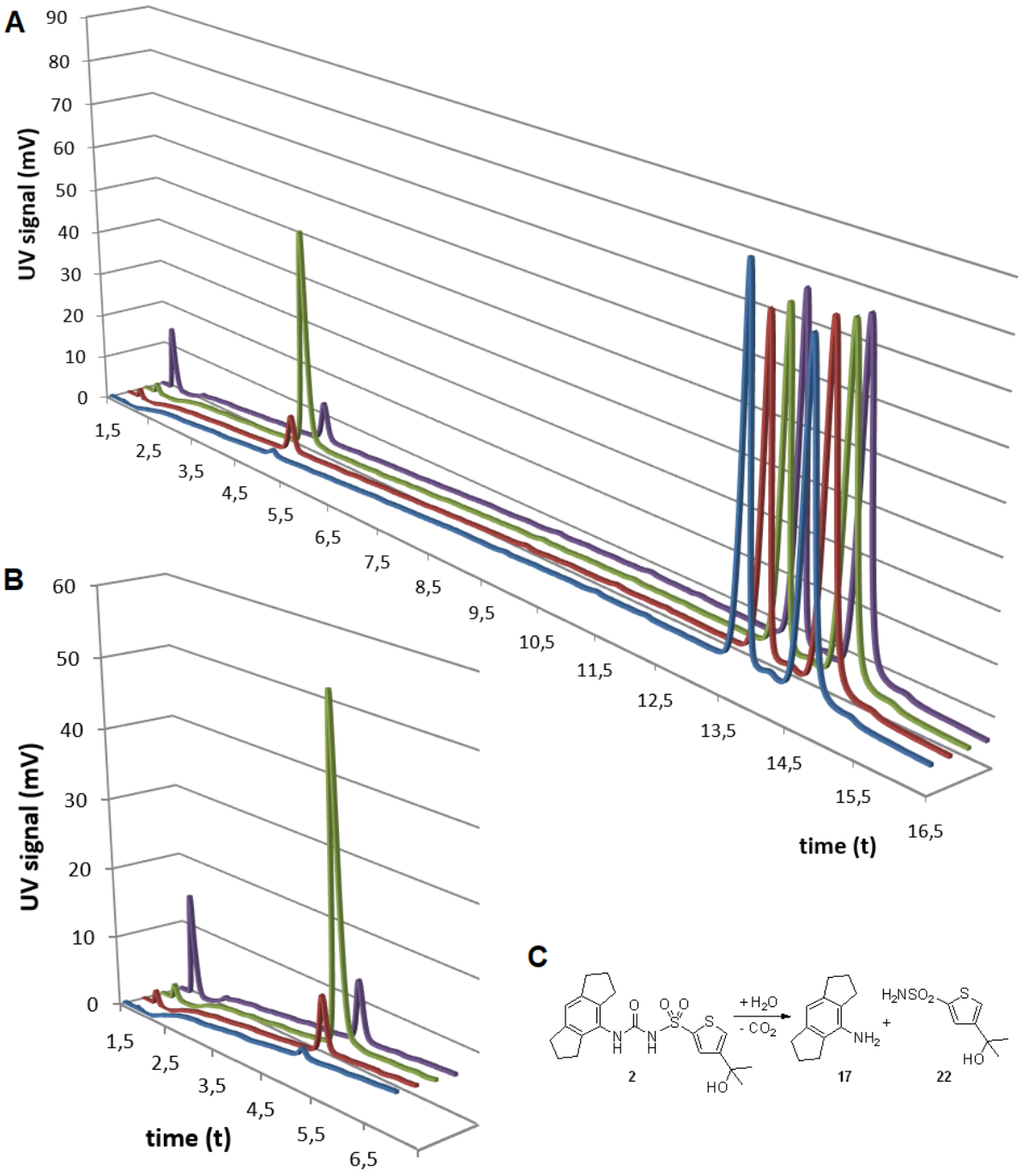


Figure S13. (**A**) Chromatograms for decomposition analysis of sulfonylurea **2** from 1.5 min to 16.5 min and (**B**) sections from 1.5 min to 7.0 min. Compound **2** eluted at 13.8 min, 1,2,3,5,6,7-hexahydro-*s*-indacen-4-amine (**17**) at 5.3 min, 4-(2-hydroxypropan-2-yl)thiophene-2-sulfonamide (**22**) at 1.8 min and the internal standard **32** at 14.7 min. Blue: Compound **2** after 0 h of incubation. Red: Compound **2** after 2 h of incubation. Green: Compound **2** spiked with **17** after 2 h of incubation. Purple: Compound **2** spiked with **22** after 2 h of incubation. (**C**) Decomposition reaction of sulfonylurea **2**.

Surface Plasmon Resonance Spectroscopy

Surface plasmon resonance spectroscopy (SPR) experiments were performed at 25 °C on a Biacore 8K device (GE Healthcare) that was equipped with a streptavidin functionalized sensor chip (Series S Sensor Chip SA, Cytiva). The system was flushed with running buffer (10 mM HEPES pH 7.4, 200 mM NaCl, 0.5 mM ADP, 0.5 mM dithiothreitol (DTT), 2 mM $MgCl_2$, 1 g/L carboxymethyl dextran (CMD), 0.05% Tween20, 2% DMSO) before the sensor chip was conditioned with three consecutive injections of 1 M NaCl in 50 mM NaOH (1 min, 10 µL/min). Biotinylated NLRP3-NACHT protein was recombinantly expressed in HEK-293T cells and after purification immobilized onto the sensor chip at 2 µL/min for 3000 s. Residual streptavidin binding sites were blocked by for consecutive injections of Biotin-PEG (1 µM, M_n 2,300 Da) for 2 min at 10 µL/min. Binding of compounds was measured in single cycle mode by injecting increasing concentrations of 2.3 to 600 nM at 30 µL/min (associatin 240 s, dissociation 60/360 s). Data were collected at a rate of 10 Hz, double referenced by blank cycle and reference flow cell subtraction and corrected by a 4-point solvent correction. For determination of binding constants, processed data were fitted to a 1:1 interaction model using the Biacore Insight Evaluation Software (version 3.0.12.15655).

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