Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Enantioselective Isothiourea-Catalysed *trans*-Dihydropyridinone Synthesis using Saccharin-derived Ketimines: Scope and Limitations

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SUPPORTING INFORMATION

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General Information

Reactions involving moisture sensitive reagents were carried out under a nitrogen atmosphere using standard vacuum line techniques in addition to dry solvents. All glassware used was flame dried and cooled under vacuum. For moisture sensitive reactions, solvents (THF, CH_2Cl_2, toluene, hexane and Et_2O) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). Petrol is defined as petroleum ether 40-60 °C. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise.

Room temperature (RT) refers to 20-25 °C. Temperatures of 0 °C and −78 °C were obtained using ice/water and CO_2(s)/acetone baths respectively. Reflux conditions were obtained using an oil bath equipped with a contact thermometer. *Under reduced pressure* refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC_2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller.

Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F_{254} silica). Plates were visualised under UV light (254 nm) or by staining with either phosphomolybdic acid or $KMnO_4$ followed by heating. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated under a positive pressure of compressed air or on a Biotage® IsoleraTM 4, using Biotage® Snap Ultra or Biotage® KP Sil columns under the solvent system stated.

^1H, ^{13}C and ^{19}F nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (300 MHz, ^1H, 75 MHz ^{13}C, 282 MHz ^{19}F), Bruker Avance II 400 (400 MHz, ^1H, 101 MHz ^{13}C, 376 MHz ^{19}F) or a Bruker Avance II 400 (500 MHz, ^1H, 126 MHz ^{13}C, 470 MHz ^{19}F) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent as the internal standard. All coupling constants, *J*, are quoted in Hz. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), ABq (AB quartet), sept (septet), oct (octet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets, dt (doublet of triplets), dq (doublet of quartets) and td (triplet of doublets). The abbreviation Ar is used to denote aromatic, Ph to denote phenyl, Bn to denote benzyl, py to denote pyridyl and br to denote broad.

Infrared spectra (ν_{max}/cm^{-1}) were recorded on either a Perkin-Elmer Spectrum GX FT-IR spectrometer using a Shimadzu IRAffinity-1 using a Pike attenuated total reflectance (ATR) accessory. Only the characteristic peaks are quoted.

Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected. *Decomp* refers to decomposition.

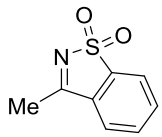
HPLC analyses were obtained on two separate machines; a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector while the temperature was assumed to be 20 °C; a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatograph, SIL-20AHT autosampler, CMB-20A communications bus module, SPD-M20A diode array detector and a CTO-20A column oven which allowed the temperature to be set from 25-40 °C. Separation was achieved using DAICEL CHIRALCEL OD-H and OJ-H columns or DAICEL CHIRALPAK AD-H, AS-H, IA, IB, IC and ID columns. All chiral HPLC traces were compared to the authentic racemic spectrum prepared in analogous fashion.

Mass spectrometry (*m/z*) data were acquired by electrospray ionisation (ESI), electron impact (EI), atmospheric solids analysis probe (ASAP) or nanospray ionisation (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews, low and high resolution ESI MS were carried out on a Micromass LCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution NSI MS was carried out on a Micromass Quattro II spectrometer and high resolution NSI MS on a Thermofisher LTQ Orbitrap XL spectrometer.

Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell at rt.

Preparation of Sulfonyl Imine Substrates

Methylbenzo[*d*]isothiazole 1,1-dioxide



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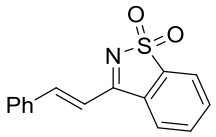
Following a literature procedure[1], in a flame-dried flask, saccharin (10 g, 54.5 mmol, 1.0 eq.) was dissolved in anhydrous THF (500 mL, 0.1 M) and cooled to 0 °C. Methylmagnesium bromide (0.3 M in ether, 36 mL, 109 mmol, 2.0 eq.) was added over 10 minutes. The reaction was allowed to warm to RT and stirred at RT for 17 hours. Sat. aq. NH_4Cl (200 mL) was added and the THF layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The combined organics were dried ($MgSO_4$), filtered and concentrated to dryness under reduced pressure. The crude material was purified by trituration with CH_2Cl_2 (20 mL) to give **38** as an off-white solid (5.34 g, 29.5 mmol, 54%). mp 198–202 °C {Lit.[1] 213–213.5 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.67 (3H, s, C*H*$_3$), 7.65–7.80 (3H, m, Ar*H*), 7.88–7.95 (1H, m, Ar*H*). All data in accordance with literature.[2]

General Procedure A: *Preparation of Sulfonyl Imine Substrates*

Following a literature procedure[3], compound **38** (1 eq.) was dissolved in ethanol (0.3 M) and heated to 80 °C. The aldehyde (1 eq.), acetic acid (10 mol%) and piperidine (10 mol%) were added. The reaction was stirred at 80 °C for 3 hours then cooled to 0 °C and filtered. The filter cake was washed with cold ethanol and, unless stated, was used without further purification.

(*E*)-3-Styrylbenzo[*d*]isothiazole 1,1-dioxide



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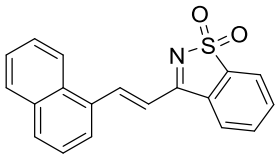
Following general procedure A, imine **38** (1.50 g, 8.25 mmol), benzaldehyde (0.84 mL, 8.25 mmol), acetic acid (48 µL, 0.28 mmol) and piperidine (84 µL, 0.28 mmol) gave the title compound as a yellow solid (1.49 g, 67%). mp 247–248 °C {Lit.[4] 245–247 °C}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 7.29 (1H, d, *J* 15.6, C(3)C*H*CH), 7.42–7.49 (3H, m, PhC*H* and ArC*H*), 7.70 (2H, dd, *J* 7.3, 2.3, PhC*H*), 7.76 (2H, dd, *J* 5.7, 3.0, ArC*H*), 7.88 (1H, dd, *J* 5.7, 3.0, Ar*H*), 7.92–7.99 (1H, m, Ar*H*), 8.31 (1H, d, *J* 15.6, C(3)CHC*H*). All data in accordance with literature.[4]

(*E*)-3-(2-(Naphthalen-1-yl)vinyl)benzo[*d*]isothiazole 1,1-dioxide



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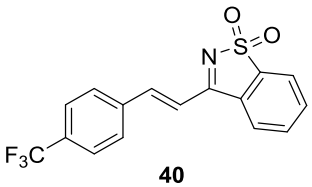
Following general procedure A, imine **38** (500 mg, 2.75 mmol), 1-naphthaldehyde (0.37 mL, 2.75 mmol), acetic acid (16 µL, 0.28 mmol) and piperidine (28 µL, 0.28 mmol) gave the title compound as an orange solid (580 mg, 1.8 mmol, 49%). mp 277−279 °C (EtOH); ν_{max} (ATR)/cm^{-1} 1610 (C=N); ^{1}H NMR (500 MHz, d_6-DMSO) δ_H: 7.65 (1H, ddd, *J* 8.0, 6.7, 1.1, Nap*H*), 7.68–7.75 (2H, m, Nap*H*), 7.96 (2H, pd, *J* 7.5, 1.3, Ar*H*), 8.01–8.08 (2H, m, C(3)C*H*CH + Nap*H*), 8.16 (1H, d, *J* 8.1, Nap*H*), 8.22 (1H, dd, *J* 6.5, 1.6, Ar*H*), 8.42 (2H, t, *J* 8.3, Nap*H*), 8.55 (1H, dd, *J* 6.7, 1.6, Ar*H*), 9.06 (1H, d, *J* 15.4, C(3)CHC*H*); ^{13}C NMR (126 MHz, d_6-DMSO) δ_C: 117.4 (C(3)*C*HCH), 122.6 (Ar*C*H), 123.1 (Nap*C*H), 125.8 (Nap*C*H), 125.9 (Ar*C*H), 126.6 (Nap*C*H), 127.0 (Nap*C*H), 127.8 (Nap*C*H), 128.9 (Nap*C*H), 130.8 (Nap*C*), 131.0 (Nap*C*), 131.2 (Ar*C*(4)), 132.2 (Nap*C*H), 133.4 (Nap*C*), 134.4 (Ar*C*H), 139.5 (Ar*C*(5)), 142.3 (C(3)CH*C*H), 167.7 (*C*(3)); HRMS (ASAP$^+$) $C_{19}H_{14}NO_2S$ $[M+H]^+$ found 320.0742, requires 320.0740 (+0.6 ppm).

(*E*)-3-(4-(Trifluoromethyl)styryl)benzo[*d*]isothiazole 1,1-dioxide



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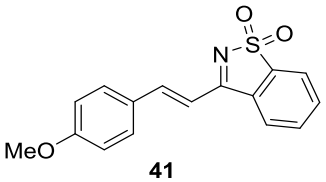
Following general procedure A, imine **38** (500 mg, 2.75 mmol), 4-(trifluoromethyl)benzaldehyde (0.38 mL, 2.75 mmol), acetic acid (16 µL, 0.28 mmol) and piperidine (28 µL, 0.28 mmol) gave the title compound as a white solid (610 mg, 1.8 mmol, 66%). mp 230−232 °C (EtOH); ν_{max} (ATR)/cm^{-1} 1628 (C=N); ^{1}H NMR (400 MHz, d_6-DMSO) δ_H: 7.89 (2H, d, *J* 8.1, Ar'C(3,5)*H*), 7.94 (1H, td, *J* 7.0, 1.4, Ar*H*), 7.97 (1H, td, *J* 7.5, 1.4, Ar*H*), 8.06 (1H, d, *J* 15.8, C(3)C*H*CH), 8.20−8.25 (3H, m, Ar'C(2,6)*H* and Ar*H*), 8.32 (1H, d, *J* 15.8, C(3)CHC*H*), 8.53 (1H, d, *J* 7.5, Ar*H*); ^{19}F NMR (376 MHz, d_6-DMSO) δ_F: −61.3 (Ar'CF_3); ^{13}C NMR (126 MHz, d_6-DMSO) δ_C: 118.6 (C(3)*C*HCH), 123.1 (Ar*C*H), 124.4 (q, *J* 272.4, CF_3), 126.3 (q, *J* 3.9, Ar'*C*(3,5)H), 126.4 (Ar*C*H), 130.5 (Ar'*C*(2,6)H), 131.2 (q, *J* 32.0, *C*CF$_3$), 131.3 (Ar*C*(4)), 134.9 (Ar*C*H), 135.0 (Ar*C*H), 138.8 (Ar'*C*(1)), 139.8 (Ar*C*(5)), 145.0 (C(3)CH*C*H), 168.1 (*C*(3)); HRMS (ASAP$^+$) $C_{16}H_{11}F_3NO_2S$ $[M+H]^+$ found 338.0462, requires 338.0457 (+1.5 ppm)

(*E*)-3-(4-Methoxystyryl)benzo[*d*]isothiazole 1,1-dioxide



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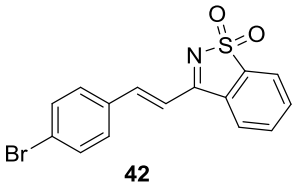
Following general procedure A, imine **38** (500 mg, 2.75 mmol), 4-methoxybenzaldehyde (0.33 mL, 2.75 mol), acetic acid (16 µL, 0.28 mmol) and piperidine (28 µL, 0.28 mmol) gave the title compound as yellow solid (593 mg, 2.0 mmol, 72%). mp 228−230 °C (EtOH) {Lit.[4] 229−232 °C}; ν_{max} (ATR)/cm^{-1} 1587 (C=N); ^{1}H NMR (500 MHz, d_6-DMSO) δ_H: 3.85 (3H, s, OC*H*$_3$), 7.09 (2H, d, *J* 8.3, Ar'C(3,5)*H*), 7.74 (1H, d, *J* 15.6, C(3)C*H*CH), 7.87–7.96 (2H, m, Ar*H*), 8.00 (2H, d, *J* 8.4, Ar'C(2,6)*H*), 8.16 (1H, d, *J* 6.9, Ar*H*), 8.25 (1H, d, *J* 15.5, C(3)CHC*H*), 8.48 (1H, d, *J* 7.3, Ar*H*); ^{13}C NMR (126 MHz, DMSO) δ_C: 55.6 (O*C*H$_3$), 112.1 (C(3)*C*HCH), 114.7 (Ar'*C*(3,5)H), 122.4 (Ar*C*H), 125.6 (Ar*C*H), 127.2 (Ar'*C*(1)), 131.3 (Ar*C*(4)), 132.0 (Ar'*C*(2,6)H), 134.2 (Ar*C*H), 134.2 (Ar*C*H), 139.6 (Ar*C*(5)), 147.3 (C(3)CH*C*H), 162.5 (Ar'*C*(4)OMe), 167.6 (*C*(3)); HRMS (NSI$^+$) $C_{16}H_{14}NO_3S$ $[M+H]^+$ found 300.0689, requires 300.0689 (+0.0 ppm). All data in accordance with literature.[4]

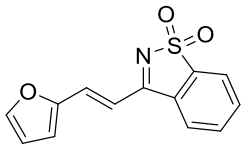
(*E*)-3-(4-Bromostyryl)benzo[*d*]isothiazole 1,1-dioxide



42

Following general procedure A, imine **38** (500 mg, 2.75 mmol), 4-bromobenzaldehyde (509 mg, 2.75 mmol), acetic acid (16 µL, 0.28 mmol) and piperidine (28 µL, 0.28 mmol) gave the title compound as an off-white solid (608 mg, 1.8 mmol, 64%). mp 256−260 °C (EtOH); ν_{max} (ATR)/cm^{-1} 1622 (C=N); ^{1}H NMR (500 MHz, d_6-DMSO) δ_H: 7.75 (2H, d, *J* 8.3, Ar'C(3,5)*H*), 7.89–8.00 (5H, m, Ar'C(2,6)*H* + C(3)C*H*CH + Ar*H*), 8.20 (1H, d, *J* 7.1, Ar*H*), 8.24 (1H, d, *J* 15.7, C(3)CHC*H*), 8.50 (1H, d, *J* 7.4, Ar*H*); ^{13}C NMR (126 MHz, d_6-DMSO) δ_C: 116.1 (C(3)*C*HCH), 122.6 (Ar*C*H), 125.4 (Ar'*C*(4)Br), 125.8 (Ar*C*H), 130.9 (Ar*C*(4)), 131.4 (Ar'*C*(2,6)H), 132.1 (Ar'*C*(3,5)H), 133.7 (Ar'*C*(1)), 134.4 (Ar*C*H), 134.4 (Ar*C*H), 139.5 (Ar*C*(5)), 145.5 (C(3)CH*C*H), 167.7 (*C*(3)); HRMS (ESI$^+$) $C_{15}H_{15}{}^{19}BrNO_2S$ $[M+H]^+$ found 347.9694, requires 347.9688 (+1.7 ppm).

(*E*)-3-(2-(Furan-2-yl)vinyl)benzo[*d*]isothiazole 1,1-dioxide



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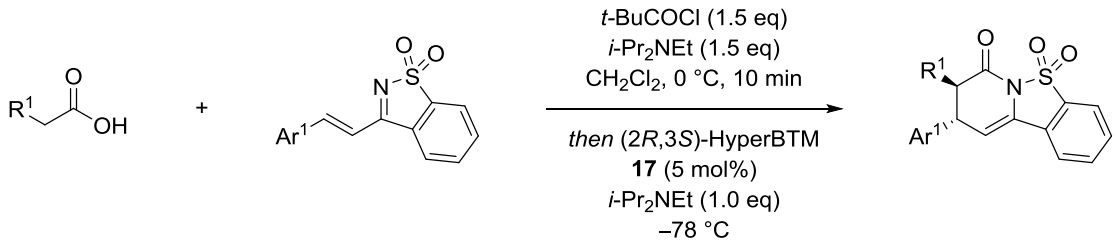
Following general procedure A, imine **38** (500 mg, 2.75 mmol), furfural (0.23 mL, 2.75 mmol), acetic acid (16 µL, 0.28 mmol) and piperidine (28 µL, 0.28 mmol) gave the title compound as a dark yellow solid (490 mg, 1.9 mmol, 69%). mp 230−233 °C (dec.) (EtOH); ν_{max} (ATR)/cm^{-1} 1618 (C=N); ^{1}H NMR (400 MHz, d_6-DMSO) δ_H: 6.80 (1 H, dd, *J* 3.5, 1.8, FurC(4)*H*), 7.30 (1 H, d, *J* 3.5, FurC(3)*H*), 7.46 (1 H, d, *J* 15.4, C(3)C*H*CH), 7.85–7.96 (2 H, m, Ar*H*), 8.10 (1H, d, *J* 1.8, FurC(5)*H*), 8.12 (1H, d, *J* 15.4, C(3)CHC*H*), 8.14–8.21 (1 H, m, Ar*H*), 8.39 (1 H, dd, *J* 5.7, 3.0, Ar*H*); ^{13}C NMR (100 MHz, d_6-DMSO) δ_C: 111.5 (C(3)*C*HCH), 113.9 (Fur*C*(4)H), 120.1 (Fur*C*(3)H), 122.4 (Ar*C*H), 125.5 (Ar*C*H), 130.8 (Ar*C*(4)), 132.6 (Fur*C*(5)H), 134.3 (Ar*C*H), 134.3 (Ar*C*H), 139.5 (Ar*C*(5)), 148.2 (C(3)CH*C*H), 151.2 (Fur*C*(2)), 167.3 (*C*(3)); HRMS (ESI$^+$) $C_{13}H_{10}NO_3S$ $[M+H]^+$ found 260.0378, requires 260.0376 (+0.8).

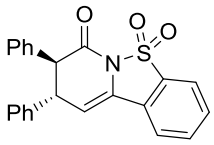
Isothiourea-Catalysed Michael Addition-Lactamisation

General procedure B: *Isothiourea-Catalysed Michael Addition-Lactamisation*



i-Pr$_2$NEt (1.5 eq.) and pivaloyl chloride (1.5 eq.) were added to a solution of requisite carboxylic acid (1.0 eq.) in CH_2Cl_2 (0.06 M) at 0 °C. The reaction mixture was allowed to stir at 0 °C for 10 min then cooled to −78 °C. The requisite Michael acceptor (1.0 eq.), (2*R*,3*S*)-HyperBTM **17** (5 mol%), and *i*-Pr$_2$NEt (1.0 eq.) were added and reaction stirred at −78 °C until complete by TLC analysis. The reaction mixture was quenched with aq. HCl (0.1 M) and extracted with CH_2Cl_2 (×3). The combined organics were dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the crude reaction mixture. Products were purified by Biotage® Isolera™ 4 in the solvent system reported.

(8*S*,9*S*)-8,9-Diphenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



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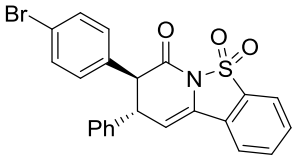
Following general procedure B, phenyl acetic acid (26 mg, 0.19 mmol), pivaloyl chloride (36 µL, 0.29 mmol) and *i*-Pr_2NEt (51 µL, 0.29 mmol) in CH_2Cl_2 (3.2 mL), (2*R*,3*S*)-HyperBTM **17** (3 mg, 0.01 mmol), cyclic sulfonyl imine **14** (50 mg, 0.19 mmol), *i*-Pr_2NEt (33 µL, 0.19 mmol) at −78 °C gave crude reaction mixture (85:15 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (53 mg, 73%) as a white solid (91:9 dr). mp 230-232 °C {Lit.[5] 232-233 °C}; $[\alpha]_D^{20}$ +134.0 (*c* 1.0, $CHCl_3$) {Lit.[5] $[\alpha]_D^{20}$ −177.0 (*c* 1.03, CH_2Cl_2) for 99% ee, 8*R*,9*R* isomer}; Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 254 nm, 30 °C) t_R (8*S*,9*S*): 13.1 min, t_R (8*R*,9*R*): 23.0 min; 95% ee; ^1H NMR (500 MHz, $CDCl_3$) δ_H: 4.06 (1H, d, *J* 7.2, C(8)*H*), 4.17 (1H, dd, *J* 7.2, 4.3, C(9)*H*), 6.14 (1H, d, *J* 4.3, C(10)*H*), 7.10−7.17 (4H, m, Ar*H*), 7.26−7.30 (6H, m, Ar*H*), 7.65 (1H, m, Ar*H*), 7.72−7.79 (2H, m, Ar*H*), 7.88−7.92 (1H, m, Ar*H*). All data in accordance with literature.[5]

(8*S*,9*S*)-8-(4-Bromophenyl)-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



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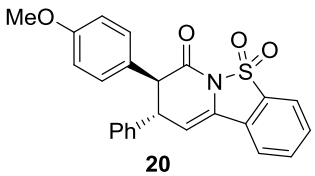
Following general procedure B, 4-bromophenyl acetic acid (80 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr_2NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **17** (5 mg, 0.019 mmol), cyclic sulfonyl imine **14** (100 mg, 0.37 mmol), *i*-Pr_2NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (89:11 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (129 mg, 75%) as a white solid (>95:5 dr). mp 182−184 °C; $[\alpha]_D^{20}$ +78.7 (*c* 0.1, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (80:20 hexane:IPA, flow rate 1 $mLmin^{-1}$, 254 nm, 30 °C) t_R (8*S*,9*S*): 44.6 min, t_R (8*R*,9*R*): 51.5 min; 97% ee; ν_{max} (ATR)/cm^{-1} 3028 (C-H), 1735 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ_H: 4.00 (1H, d, *J* 9.0, C(8)*H*), 4.17 (1H, dd, *J* 9.0, 3.8, C(9)*H*), 6.12 (1H, d, *J* 3.8, C(10)*H*), 6.99 (2H, d, *J* 8.4, Ar*H*), 7.07 (2H, d, *J* 6.6, Ar*H*), 7.24−7.30 (3H, m, Ar*H*), 7.38 (2H, d, *J* 8.4, Ar*H*), 7.65−7.69 (1H, m, Ar*H*), 7.73−7.75 (2H, m, Ar*H*), 7.89

(1H, d, *J* 7.9, Ar*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C:47.4 (*C*(9)H), 55.7 (*C*(8)H), 105.9 (*C*(10)H), 121.9 (Ar*C*H), 121.9 (Ar*C*H), 122.0 (Ar*C*(4)Br), 126.5 (Ar*C*(10b)), 127.7 (Ar*C*H), 128.0 (Ar*C*H), 129.3 (Ar*C*H), 129.7 (Ar*C*), 130.5 (Ar*C*H), 131.3 (Ar*C*H), 132.0 (Ar*C*H), 132.8 (Ar*C*), 134.3 (Ar*C*H), 135.0 (*C*(10a)), 140.3 (Ar*C*(4a)), 166.0 (*C*(7)); HRMS (NSI$^+$) $C_{23}H_{16}{}^{79}BrNO_3SNa^+$ [M+Na]$^+$, found 487.9913, requires 487.9926 (−2.7 ppm).

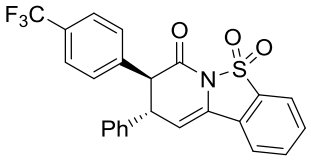
(8*S*,9*S*)-8-(4-Methoxyphenyl)-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



20

Following general procedure B, 4-methoxyphenyl acetic acid (61 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr_2NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **17** (5 mg, 0.019 mmol), cyclic sulfonyl imine **14** (100 mg, 0.37 mmol), *i*-Pr_2NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (>95:5 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (129 mg, 75%) as a white solid (>95:5 dr). mp 220−222 °C; $[\alpha]_D^{20}$ +54.4 (*c* 0.1, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 19.3 min, t_R (8*R*,9*R*): 26.6 min; >99% ee; ν_{max} (ATR)/cm^{-1} 2970 (C-H), 1751 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 3.76 (3H, s, ArOC*H*$_3$), 4.01 (1H, d, *J* 7.5, C(8)*H*), 4.13 (1H, dd, *J* 7.5, 4.4, C(9)*H*), 6.13 (1H, d, *J* 4.4, C(10)*H*), 6.79−6.82 (2H, m, C(8)Ar(3,5)*H*), 7.08−7.12 (4H, m, Ar*H*), 7.24−7.31 (3H, m, Ar*H*), 7.66 (1H, ddd, *J* 8.2, 5.9, 2.5, Ar*H*), 7.72−7.76 (2H, m, Ar*H*), 7.90 (1H, d, *J* 7.9, Ar*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 47.6 (*C*(9)H), 55.3 (*C*(8)H), 55.4 (ArO*C*H$_3$), 105.7 (*C*(10)H), 114.4 (C(8)Ar*C*(3,5)H), 121.8 (Ar*C*H), 122.0 (Ar*C*H), 126.7 (Ar*C*(10b)), 127.7 (Ar*C*H), 127.9 (Ar*C*H), 128.4 (Ar*C*H), 129.3 (Ar*C*H), 129.6 (Ar*C*H), 129.6 (Ar*C*), 131.2 (Ar*C*H), 132.9 (Ar*C*), 134.2 (*C*(10a)), 140.9 (Ar*C*(4a)), 159.2 (C(8)Ar*C*(4)), 166.7 (*C*(7)); HRMS (NSI$^+$) $C_{24}H_{19}NO_4SNa^+$ [M+Na]$^+$, found 440.0924, requires 440.0927 (−0.7 ppm).

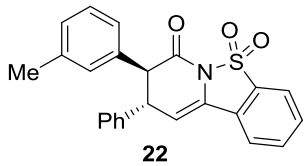
(8*S*,9*S*)-9-Phenyl-8-(4-(trifluoromethyl)phenyl)-8,9-dihydro-7*H* benzo[4,5]isothiazolo [2,3-*a*]pyridin-7-one 5,5-dioxide



21

Following general procedure B, 4-trifluoromethylphenyl acetic acid (76 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr_2NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **17** (5 mg, 0.019 mmol), cyclic sulfonyl imine **14** (100 mg, 0.37 mmol), *i*-Pr_2NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (>95:5 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (108 mg, 64%) as a white solid (>95:5 dr). mp 170−172 °C; $[\alpha]_D^{20}$ +59.7 (*c* 0.1, $CHCl_3$); Chiral HPLC analysis, Chiralpak IA (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 254 nm, 30 °C) t_R (8*S*,9*S*): 12.0 min, t_R (8*R*,9*R*): 15.9 min; 97% ee; ν_{max} (ATR)/cm^{-1} 3158 (C-H), 1707 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 4.13 (1H, d, *J* 9.3, C(8)*H*), 4.19 (1H, dd, *J* 9.3, 3.7, C(9)*H*), 6.16 (1H, d, *J* 3.7, C(10)*H*), 7.08−7.12 (2H, m, Ar*H*), 7.25−7.32 (5H, m, Ar*H*), 7.53 (2H, d, *J* 8.2, Ar*H*), 7.69 (1H, ddd, *J* 8.1, 6.3, 2.1, Ar*H*), 7.76−7.80 (2H, m, Ar*H*), 7.90 (1H, d, *J* 8.1, Ar*H*); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F:−62.7 (C*F*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 47.4 (*C*(8)H), 56.0 (*C*(9)H), 105.9 (*C*(10)H), 121.9 (Ar*C*H), 121.9 (Ar*C*H), 124.0 (q, *J* 272, *C*F_3), 125.7 (q, *J* 3.6, C(8)Ar*C*(3,5)H), 126.4 (Ar*C*(10b)), 127.7 (Ar*C*H), 128.1 (Ar*C*H), 129.3 (Ar*C*H), 129.3 (Ar*C*H), 129.7 (Ar*C*), 130.1 (q, *J* 33.0, C(8)Ar*C*(4)), 131.4 (Ar*C*H), 132.7 (*C*(10a)), 134.4 (Ar*C*H), 140.0 (Ar*C*), 140.1 (Ar*C*(4a)), 165.8 (*C*(7)); HRMS (NSI$^+$) $C_{24}H_{16}F_3NO_3SNa$ $[M+Na]^+$, found 478.0686, requires 478.0695 (−1.9 ppm).

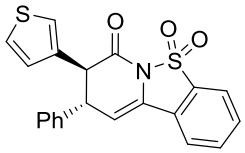
(8*S*,9*S*)-9-Phenyl-8-(*m*-tolyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



22

Following general procedure B, 3-methylphenyl acetic acid (56 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr_2NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **17** (5 mg, 0.019 mmol), cyclic sulfonyl imine **14** (100 mg, 0.37 mmol), *i*-Pr_2NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (94:6 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (105 mg, 71%) as a white solid (>95:5 dr). mp 174−177 °C {Lit.[5] 177−180 °C}; $[\alpha]_D^{20}$ +166.0 (*c* 1.0, $CHCl_3$) {Lit.[5] $[\alpha]_D^{20}$ −185.0 (*c* 1.03, $CHCl_3$) for 98% ee, 8*R*,9*R* isomer}; Chiral HPLC analysis, Chiralpak AD-H (70:30 hexane:IPA, flow rate 1 $mLmin^{-1}$, 254 nm, 30 °C) t_R (8*S*,9*S*): 14.6 min, t_R (8*R*,9*R*): 27.3 min; >99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: (500 MHz, $CDCl_3$) 2.31 (3H, s, C*H*$_3$), 4.05 (1H, d, *J* 7.1, C(8)*H*), 4.19 (1H, dd, *J* 7.1, 4.5, C(9)*H*), 6.16 (1H, d, *J* 4.5, C(10)*H*), 6.95-7.01 (1H, m, Ar*H*), 7.01-7.05 (1H, m, Ar*H*), 7.06-7.11 (1H, m, Ar*H*), 7.14–7.22 (3H, m, Ar*H*), 7.23-7.38 (3H, m, Ar*H*), 7.65–7.72 (1H, m, Ar*H*), 7.72–7.81 (2H, m, Ar*H*), 7.93 (1H, d, *J* 7.8, Ar*H*). All data in accordance with literature.[5]

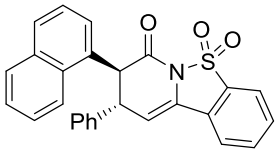
(8*S*,9*S*)-9-Phenyl-8-(thiophen-3-yl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



23

Following general procedure B, 3-thiopheneacetic acid (53 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr_2NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **17** (5 mg, 0.019 mmol), cyclic sulfonyl imine **14** (100 mg, 0.37 mmol), *i*-Pr_2NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (93:7 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (112 mg, 77%) as a white solid (>95:5 dr). mp 198−200 °C; $[\alpha]_D^{20}$ +79.3 (*c* 0.1, CH_2Cl_2); Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 254 nm, 30 °C) t_R (8*S*,9*S*): 21.7 min, t_R (8*R*,9*R*): 44.1 min; >99% ee; ν_{max} (ATR)/cm^{-1} 3001 (C-H), 1709 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 4.16−4.20 (2H, m, C(8)*H* and C(9)*H*), 6.15 (1H, d, *J* 4.6, C(10)*H*), 7.04−7.08 (2H, m, Ar*H*), 7.16−7.17 (2H, m, Ar*H*) 7.27−7.33 (4H, m, Ar*H*), 7.65 (1H, m, Ar*H*), 7.72 (2H, m, Ar*H*), 7.84 (1H, d, *J* 7.8, Ar*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 46.8 (*C*(9)H), 51.5 (*C*(8)H), 105.1 (*C*(10)H), 121.9 (Ar*C*H), 121.9 (Ar*C*H), 126.6 (Ar*C*H), 126.6 (Ar*C*(10b), 127.0 (Ar*C*H), 127.4 (Ar*C*H), 127.4 (Ar*C*H), 128.0 (Ar*C*H), 129.4 (Ar*C*H), 129.6 (Ar*C*), 131.3 (Ar*C*H), 132.8 (Ar*C*), 134.3 (Ar*C*H), 136.1 (*C*(10a)), 140.4 (Ar*C*(4a)), 165.9 (*C*(7)); HRMS (NSI$^+$) $C_{21}H_{16}NO_3S_2$ $[M+H]^+$, found 394.0561, requires 394.0572, (−2.8 ppm).

(8*S*,9*S*)-8-(Naphthalen-1-yl)-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide

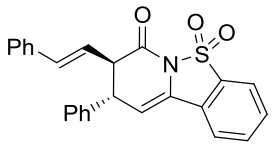


24

Following general procedure B, acid (93 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **14** (135 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 6 h gave crude reaction mixture (90:10 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (180 mg, 82 %) as a white solid (90:10 dr). mp 128−131°C {Lit.[5] 232−233 °C}; $[\alpha]_D^{20}$ +20 (*c* 0.6, $CHCl_3$) {Lit.[5] $[\alpha]_D^{20}$ −69 (*c* 1.10 $CHCl_3$)

for 96% ee, 8*R*,9*R* isomer}; Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C) t_R (8*S*,9*S*): 11.1 min, t_R (8*R*,9*R*): 40.2 min; 98% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.28 (1H, dd, *J* 5.9, 4.8, C(9)*H*), 4.78 (1H, d, *J* 5.9, C(8)*H*), 6.09 (1H, d, *J* 4.8, C(10)*H*), 7.14−7.21 (2H, m, Ar*H*), 7.22-7.38 (5H, m, Ar*H*), 7.44–7.55 (2H, m, Ar*H*), 7.65-7.70 (1H, m, Ar*H*), 7.72–7.84 (3H, m, Ar*H*), 7.87 (2H, d, *J* 8.4, Ar*H*), 7.94 (1H, d, *J* 7.8, Ar*H*). All data in accordance with literature.[5]

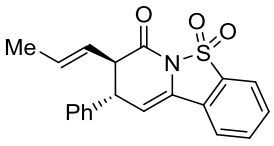
(8R,9S)-9-Phenyl-8-((E)-styryl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-one 5,5-dioxide



25

Following general procedure B, (*E*)-4-phenylbut-3-enoic acid (60 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr$_2$NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **53** (5 mg, 0.019 mmol), cyclic sulfonyl imine **617** (100 mg, 0.37 mmol), *i*-Pr$_2$NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (95:5 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (98 mg, 64%) as a white solid (95:5 dr). mp 204-206 °C; $[\alpha]_D^{20}$ +81.1 (*c* 1.0 CH_2Cl_2); Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*R*,9*S*): 15.6 min, t_R (8*S*,9*R*): 25.8 min; 71% ee; ^{1}H NMR (500 MHz, $CDCl_3$) 3.66 (1H, t, *J* 6.6, C(8)*H*), 3.96 (1H, t, *J* 5.0, C(8)*H*), 6.10 (1H, d, *J* 4.5, C(8)C(1)*H*), 6.17 (1H, dd, *J* 7.6, 15.9, C(8)C(2)*H*), 6.42 (1H, d, *J* 15.9, C(10)*H*), 7.20-7.34 (10H, m, Ar*H*), 7.61-7.64 (1H, m, Ar*H*), 7.70-7.72 (2H, m, Ar*H*), 7.85 (1H, d, *J* 7.8, Ar*H*); ^{13}C NMR (125 MHz, $CDCl_3$) 45.9 (*C*(9)H), 53.3 (*C*(8)H), 105.0 (C(8)*C*(1)H), 121.9 (Ar*C*H), 121.9 (Ar*C*H), 123.4 (C(8)*C*(2)H), 126.7 (Ar*C*H), 126.7 (Ar*C*H), 127.7 (Ar*C*H), 128.0 (Ar*C*), 128.2 (Ar*C*), 128.7 (Ar*C*H), 129.4 (Ar*C*H), 129.6 (Ar*C*), 131.2 (Ar*C*H), 132.8 (Ar*C*), 134.2 (Ar*C*H), 135.3 (Ar*C*H), 136.3 (*C*(10a)), 140.3 (Ar*C*), 166.2 (*C*(7)); HRMS (NSI$^+$) $C_{25}H_{20}NO_3S$ $[M+H]^+$, found 414.1139, requires 414.1158 (−4.5 ppm).

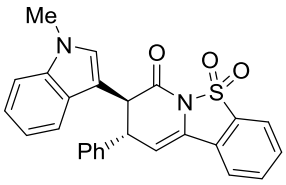
(8*R*,9*S*)-9-Phenyl-8-((*E*)-prop-1-en-1-yl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



26

Following general procedure B, (*E*)-pent-3-enoic acid (50 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **14** (135 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 7 h gave crude reaction mixture (96:4 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (135 mg, 77 %) as a white solid (>95:5 dr). mp 152−154 °C; $[\alpha]_D^{20}$ +215.8 (*c* 1.0, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 211 nm, 30 °C) t_R (8*S*,9*S*): 9.5 min, t_R (8*R*,9*R*): 16.1 min; 99% ee; ν_{max} (ATR)/cm^{-1} 3028 (C-H), 2916 (C=C), 1709 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 1.65 (3H, d, *J* 6.3, CH_3), 3.47 (1H, t, *J* 6.7, C(8)*H*), 3.84 (1H, app. t, *J* 5.3, C(9)*H*), 5.45–5.53 (1H, m, C*H*=CHCH$_3$), 5.55–5.65 (1H, m, CH=C*H*CH$_3$), 6.07 (1H, d, *J* 5.0, C(10)*H*), 7.15–7.20 (2H, m, Ph*H*), 7.25–7.30 (1H, m, Ph*H*), 7.30–7.36 (2H, m, Ph*H*), 7.65 (1H, ddd, *J* 8.2, 5.4, 3.0, Ar*H*), 7.70–7.76 (2H, m, Ar*H*), 7.88 (1H, dt, *J* 7.9, 1.0, Ar*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 18.3 (*C*H$_3$), 45.8 (*C*(9)H), 53.2 (*C*(8)H), 105.1 (*C*(10)H), 121.8 (Ar*C*H), 121.9 (Ar*C*H), 125.0 (*C*H=CHCH$_3$), 126.8 (Ar*C*(10b)), 127.6 (Ph*H*), 127.9 (Ph*H*), 129.3 (Ph*H*), 129.4 (Ph*C*), 131.1 (Ar*C*H), 131.7 (CH=*C*HCH$_3$), 132.8 (Ar*C*(10a)), 134.2 (Ar*C*H), 140.5 (Ar*C*(4a)), 166.7 (*C*(7)).

(8*S*,9*S*)-8-(1-Methyl-1*H*-indol-3-yl)-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide

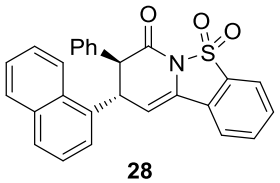


27

Following general procedure B, 1-methyl-3-indoleacetic acid (70 mg, 0.37 mmol), pivaloyl chloride (69 µL, 0.56 mmol) and *i*-Pr_2NEt (98 µL, 0.56 mmol) in CH_2Cl_2 (6 mL), (2*R*,3*S*)-HyperBTM **17** (5 mg, 0.019 mmol), cyclic sulfonyl imine **14** (100 mg, 0.37 mmol), *i*-Pr_2NEt (64 µL, 0.37 mmol) at −78 °C gave crude reaction mixture (80:20 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, hexane:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 1 CV)] gave the title compound (97 mg, 60%) as a white solid (89:11 dr). mp 236−238 °C; $[\alpha]_D^{20}$ +69.7 (*c* 1.0, CH_2Cl_2); Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 254 nm, 30 °C) t_R (8*S*,9*S*): 20.5 min, t_R (8*R*,9*R*): 50.8 min; >99% ee; ν_{max} (ATR)/cm^{-1} 3155 (C-H), 1705; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.69 (3H, s, NCH_3), 4.33 (1H, dd, *J* 5.6, 3.7, C(9)*H*), 4.42 (1H, d, *J* 3.7, C(8)*H*), 6.15 (1H, d, *J* 5.6, C(10)*H*), 6.94 (1H, s, indolyl(2)*H*), 7.16−7.20 (1H, m, Ar*H*), 7.24–7.27 (1H, m, Ar*H*), 7.25−7.39 (6H, m, Ar*H*), 7.67−7.70 (2H, m, Ar*H*), 7.75−7.78 (2H, m, Ar*H*), 7.92 (1H, d, *J* 7.8, Ar*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 33.0 (N*C*H$_3$), 46.7 (*C*(9)H), 48.0 (*C*(8)H), 105.2 (*C*(10)H), 109.8 (indolyl*C*(7)H), 110.3 (indolyl*C*(3)H), 119.0 (indolyl*C*(4)H), 119.8 (indolyl*C*(5)H),

121.9 (Ar*C*H), 121.9 (Ar*C*H), 122.3 (Ar*C*H), 126.3 (indolyl*C*(2)H), 126.6 (Ar*C*(10b)), 126.8 (Ar*C*), 127.4 (Ar*C*H), 128.0 (Ar*C*), 129.5 (Ar*C*H), 131.1 (Ar*C*H), 132.8 (Ar*C*), 134.2 (Ar*C*H), 137.1 (*C*(10a)), 141.0 (Ar*C*(4a)), 166.4 (*C*(7)); HRMS (NSI$^+$) $C_{26}H_{20}N_2O_3SNa$ $[M+Na]^+$, found 463.1078, requires 463.1087 (−1.9 ppm).

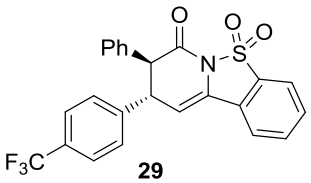
(8*S*,9*S*)-9-(Naphthalen-1-yl)-8-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



28

Following general procedure B, phenylacetic acid (68 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **39** (160 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 6 h gave crude reaction mixture (90:10 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (216 mg, 99%) as yellow solid (91:9 dr). mp 130−132 °C; $[\alpha]_D^{20}$ +99.6 (*c* 1.0, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (80:20 hexane:IPA, flow rate 1 $mLmin^{-1}$, 211 nm, 30 °C), t_R (8*R*,9*R*): 35.3 min, t_R (8*S*,9*S*): 39.7 min; >99% ee; ν_{max} (ATR)/cm^{-1} 3061 (C-H), 1705 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.32 (1H, d, *J* 4.8, C(8)*H*), 4.97 (1H, app. t, *J* 5.1, C(9)*H*), 6.26 (1H, d, *J* 5.1, C(10)*H*), 7.26–7.36 (6H, m, Ar*H*), 7.39 (1H, d, *J* 7.6, Ar*H*), 7.50–7.56 (2H, m, Ar*H*), 7.65–7.71 (1H, m, Ar*H*), 7.72−7.82 (3H, m, Ar*H*), 7.87–7.98 (3H, m, Ar*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 42.7 (*C*(9)H), 54.7 (*C*(8)H), 105.0 (*C*(10)H), 121.9 (Ar*C*H), 122.0 (Ar*C*H), 122.6 (Ar*C*H), 125.1 (Ar*C*H), 125.8 (Ar*C*H), 126.1 (Ar*C*(10b)), 126.6 (Ar*C*H), 126.9 (Ar*C*H), 128.0 (Ar*C*H), 128.2 (Ar*C*H), 128.7 (Ar*C*H), 129.2 (Ar*C*H), 129.6 (Ar*C*H), 130.2 (Ar*C*), 130.6 (Ar*C*), 131.3 (Ar*C*H), 132.8 (*C*(10a)), 134.3 (Ar*C*H), 134.5 (Ar*C*), 135.7 (Ph*C*), 137.1 (Ar*C*(4a)), 166.4 (*C*(7)), HRMS (ASAP) $C_{27}H_{20}NO_3S_2$ $[M+H]^+$, found 438.1169, requires 438.1158, (+2.5 ppm).

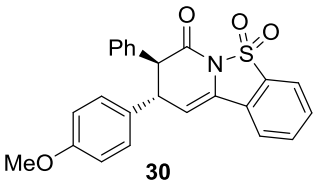
(8S,9S)-8-Phenyl-9-(4-(trifluoromethyl)phenyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-a]pyridin-7-one 5,5-dioxide



29

Following general procedure B, phenylacetic acid (68 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **40** (169 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 4 h gave crude reaction mixture (88:12 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (190 mg, 84%) as white solid (>95:5: dr). mp 208−212 °C; $[\alpha]_D^{20}$ +132.2 (*c* 1.0, $CHCl_3$); Chiral HPLC analysis, Chiralpak ID (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 220 nm, 30 °C), t_R (8*R*,9*R*): 16.9 min, t_R (8*S*,9*S*): 27.8 min; 95% ee; ν_{max} (ATR)/cm^{-1} 1707 (C=O); δ_H (400 MHz, $CDCl_3$) 4.03 (1H, d, *J* 8.4, C(8)*H*), 4.27 (1H, dd, *J* 8.4, 4.0, C(9)*H*), 6.13 (1H, d, *J* 4.1, C(10)*H*), 7.16 (2H, dd, *J* 7.5, 2.0, Ph*H*), 7.25 (2H, d, *J* 8.1, C(9)ArC(2,6)*H*), 7.29−7.33 (3H, m, Ph*H*), 7.55 (2H, d, *J* 8.1, C(9)ArC(3,5)*H*), 7.63–7.73 (1H, m, Ar*H*), 7.72–7.82 (2H, m, Ar*H*), 7.88 (1H, dt, *J* 8.0, 0.7, Ar*H*); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F: −62.61 (CF_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 47.2 (*C*(9)H), 55.8 (*C*(8)H), 104.7 (*C*(10)H), 121.9 (Ar*C*H), 122.0 (Ar*C*H), 124.0 (q, *J* 148.2, *C*F_3), 126.1 (q, *J* 4.2, C(9)Ar*C*(3,5)H), 126.3 (Ar*C*(4a)), 128.2 (C(9)Ar*C*(2,6)H), 128.2 (Ph*C*H), 128.6 (Ph*C*H), 129.0 (Ph*C*H), 130.1 (q, *J* 32.4, *C*CF_3), 130.2 (C(9)Ar*C*(1)), 131.5 (Ar*C*H), 132.8 (*C*(10a)), 134.4 (Ar*C*H), 135.6 (Ph*C*), 144.7 (Ar*C*(4a)), 166.0 (*C*(7)).

(8*S*,9*S*)-9-(4-Methoxyphenyl)-8-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide

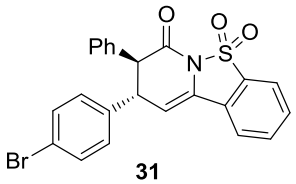


30

Following general procedure B, phenylacetic acid (68 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **41** (150 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 6 h gave crude reaction mixture (94:6 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (107 mg, 51%) as a yellow solid (>95:5 dr). mp 130−132 °C; $[\alpha]_D^{20}$ +175.0 (*c* 1.0, $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (80:20 hexane:IPA, flow rate 1 $mLmin^{-1}$, 220 nm, 30 °C) t_R (8*S*,9*S*): 56.7 min, t_R (8*R*,9*R*): 83.3 min; 99% ee; ν_{max} (ATR)/cm^{-1} 1707 (C=O), 1510; ^1H NMR (500 MHz, $CDCl_3$) δ_H: 3.77 (3H, s, O*C*H_3), 4.02 (1H, d, *J* 7.4, C(8)*H*), 4.12 (1H, dd, *J* 7.4, 4.4, C(9)*H*), 6.12 (1H, d, *J* 4.4, C(10)*H*), 6.81 (2H, d, *J* 8.7,C(9)ArC(3,5)*H*), 7.02 (2H, d, *J* 8.7, C(9)Ar(2,6)*H*), 7.16 (2H, dd, *J* 7.9, 1.7, Ph*H*), 7.21–7.30 (3H, m, Ph*H*), 7.66 (1H, ddd, *J* 8.2, 6.0, 2.4, Ar*H*), 7.70–7.77 (2H, m, Ar*H*), 7.89 (1H, d, *J* 7.9, Ar*H*); ^{13}C (126 MHz, $CDCl_3$) δ_C: 46.7 (*C*(9)), 55.4 (ArO*C*H_3), 56.3 (*C*(8)), 106.1 (*C*(10)), 114.6 (C(9)Ar*C*(3,5)H), 121.8 (Ar*C*H), 121.9 (Ar*C*H), 126.7

(Ar*C*(10b)), 127.9 (Ph*C*H), 128.5 (Ph*C*H), 128.7 (C(9)Ar*C*(2,6)H), 128.9 (Ph*C*H), 129.4 (Ar*C*(10a)), 131.2 (Ar*C*H), 132.7 (C(9)Ar*C*(1)), 132.8 (*C*(4a)), 134.2 (Ar*C*H), 136.5 (Ph*C*), 159.1 (C(9)Ar*C*(4)), 166.5 (*C*(7)); HRMS (pNSI) $C_{24}H_{20}NO_4S$ $[M+H]^+$ found 418.1105, requires 418.1108 (−0.7 ppm).

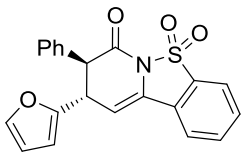
(8*S*,9*S*)-9-(4-Bromophenyl)-8-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



31

Following general procedure B, phenylacetic acid (68 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **42** (174 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 6 h gave crude reaction mixture (94:6: dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (160 mg, 69%) as a white solid (>95:5 dr). mp 130−132 °C; $[\alpha]_D^{20}$+130.0 (*c* 1.0, $CHCl_3$) {Lit.[5] $[\alpha]_D^{20}$ −159 (*c* 1.03, $CHCl_3$) for 99% ee, 8*R*,9*R* isomer}; Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 $mLmin^{-1}$, 211 nm, 30 °C) t_R (8*S*,9*S*): 17.2 min, t_R (8*R*,9*R*): 21.4 min; 99% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.97 (1H, d, *J* 8.3, C(8)*H*), 4.14 (1H, dd, *J* 8.3, 4.1, C(9)*H*), 6.08 (1H, d, *J* 4.1, C(10)*H*), 6.92–6.98 (2H, m, Ar*H*), 7.12 (2H, dd, *J* 7.4, 2.1, Ar*H*), 7.22–7.33 (3H, m, Ar*H*), 7.36–7.46 (2H, m, Ar*H*), 7.62–7.69 (1H, m, Ar*H*), 7.71–7.79 (2H, m, Ar*H*), 7.88 (1H, d, *J* 7.8, Ar*H*). All data in accordance with literature.[5]

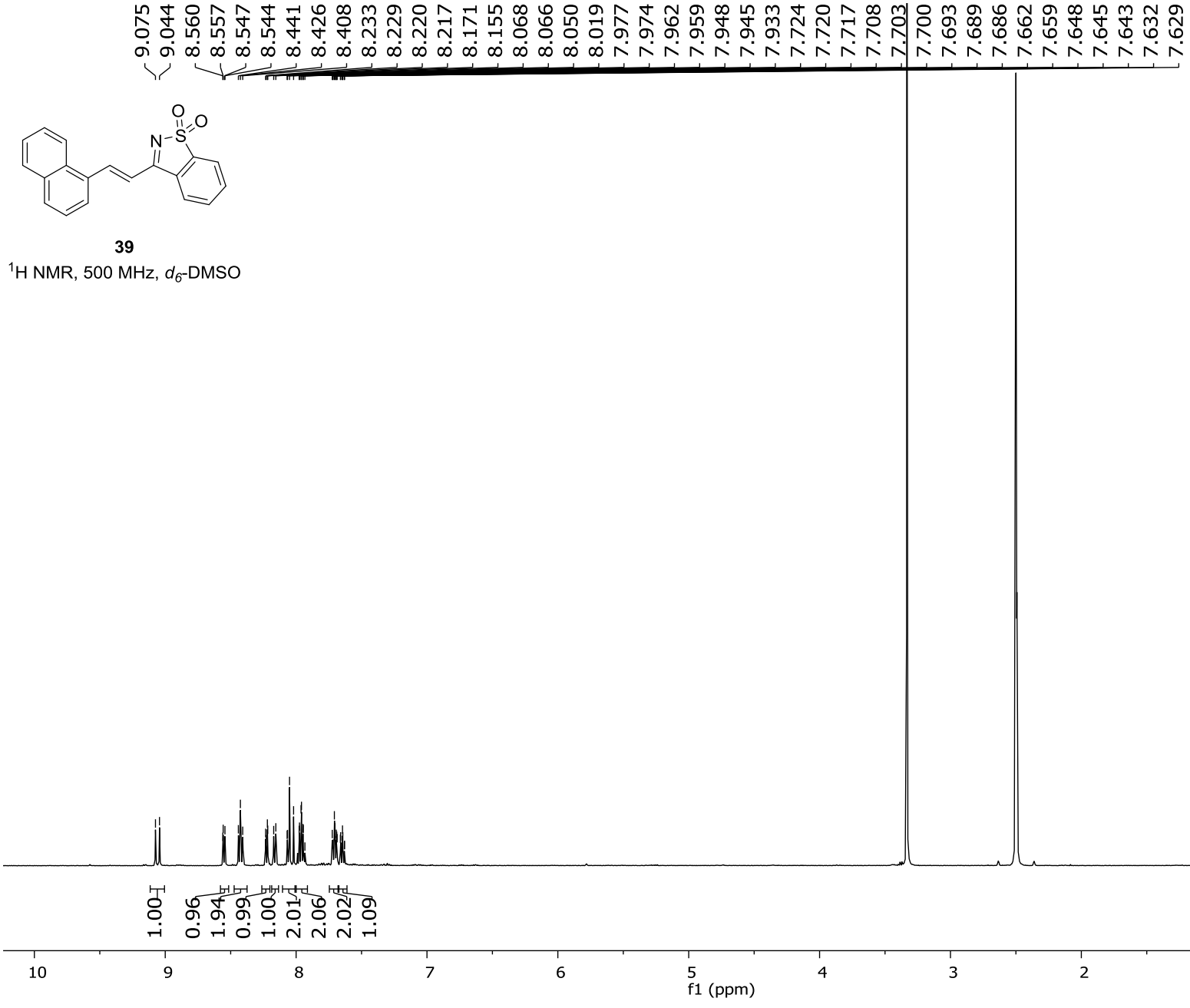
(8*S*,9*S*)-9-(Furan-2-yl)-8-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide



32

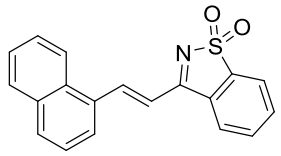
Following general procedure B, phenylacetic acid (68 mg, 0.50 mmol), pivaloyl chloride (92 µL, 0.75 mmol) and *i*-Pr_2NEt (131 µL, 0.75 mmol) in CH_2Cl_2 (8.3 mL), (2*R*,3*S*)-HyperBTM **17** (7.7 mg, 0.025 mmol), cyclic sulfonyl imine **43** (129 mg, 0.50 mmol), *i*-Pr_2NEt (87 µL, 0.50 mmol) at −78 °C for 6 h gave crude reaction mixture (93:7 dr). Purification by Biotage® Isolera™ 4 [SNAP 25 g, 75 mL^{-1}, petrol:EtOAc (97:3 4 CV, 97:3 to 50:50 10 CV, 50:50 4 CV)] gave the title compound (174 mg, 92 %) as an off-white solid (>95:5: dr). mp 130−132 °C; $[\alpha]_D^{20}$ +119.4 (*c* 1.0 $CHCl_3$); Chiral HPLC analysis, Chiralpak AD-H (60:40

hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C) t_R (8*S*,9*S*): 13.1 min, t_R (8*R*,9*R*): 23.8 min; 90% ee; ν_{max} (ATR)/cm^{-1} 3601 (C-H), 1707 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) 4.26−4.32 (2H, m, *J* 2.8, C(8)*H* + C(9)*H*), 6.09 (1H, d, *J* 3.2, FurC(3)*H*), 6.09–6.16 (1H, m, C(10)*H*), 6.29 (1H, dd, *J* 3.3, 1.9, FurC(4)*H*), 7.25–7.35 (5H, m, Ph*H*), 7.39 (1H, dd, *J* 1.9, 0.7, FurC(5)*H*), 7.68 (1H, ddd, *J* 8.2, 6.3, 2.2, Ar*H*), 7.73–7.81 (2H, m, Ar*H*), 7.90 (1H, dt, *J* 7.8, 0.8, Ar*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C: 40.5 (C(9)), 52.6 (C(8)), 102.3 (Fur*C*(3)H), 107.1 (*C*(10)), 110.6 (Fur*C*(4)H), 121.9 (Ar*C*H), 122.0 (Ar*C*H), 126.5 (Ar*C*(10b)), 128.0 (Ph*C*H), 128.2 (Ph*C*H), 129.1 (Ph*C*H), 130.1 (*C*(10a)), 131.4 (Ar*C*H), 132.9 (Ar*C*(4a)), 134.3 (Ar*C*H), 136.1 (Ph*C*), 142.8 (Fur*C*(5)H), 152.3 (Fur*C*(2)), 166.2 (*C*(7)).



39

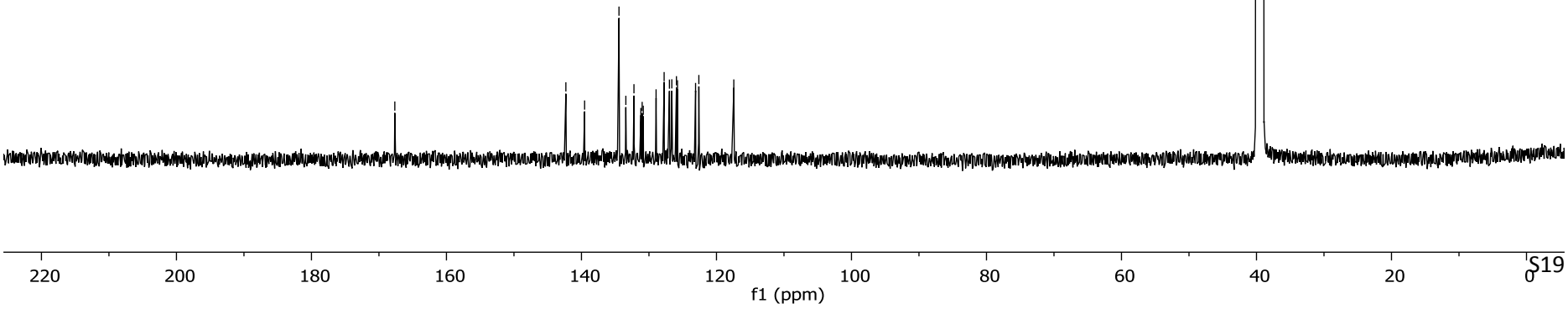
^{1}H NMR, 500 MHz, d_6-DMSO

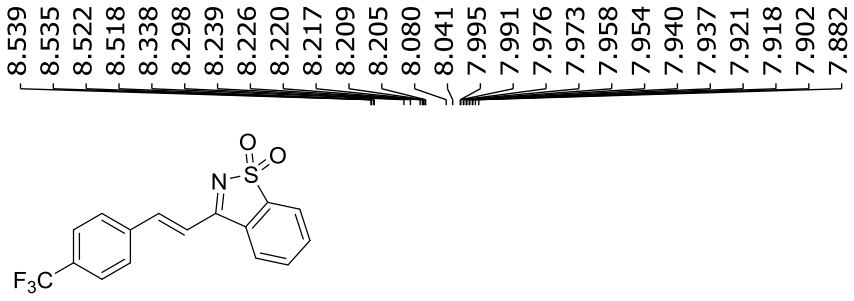


39

^{13}C NMR, 126 MHz, d_6-DMSO

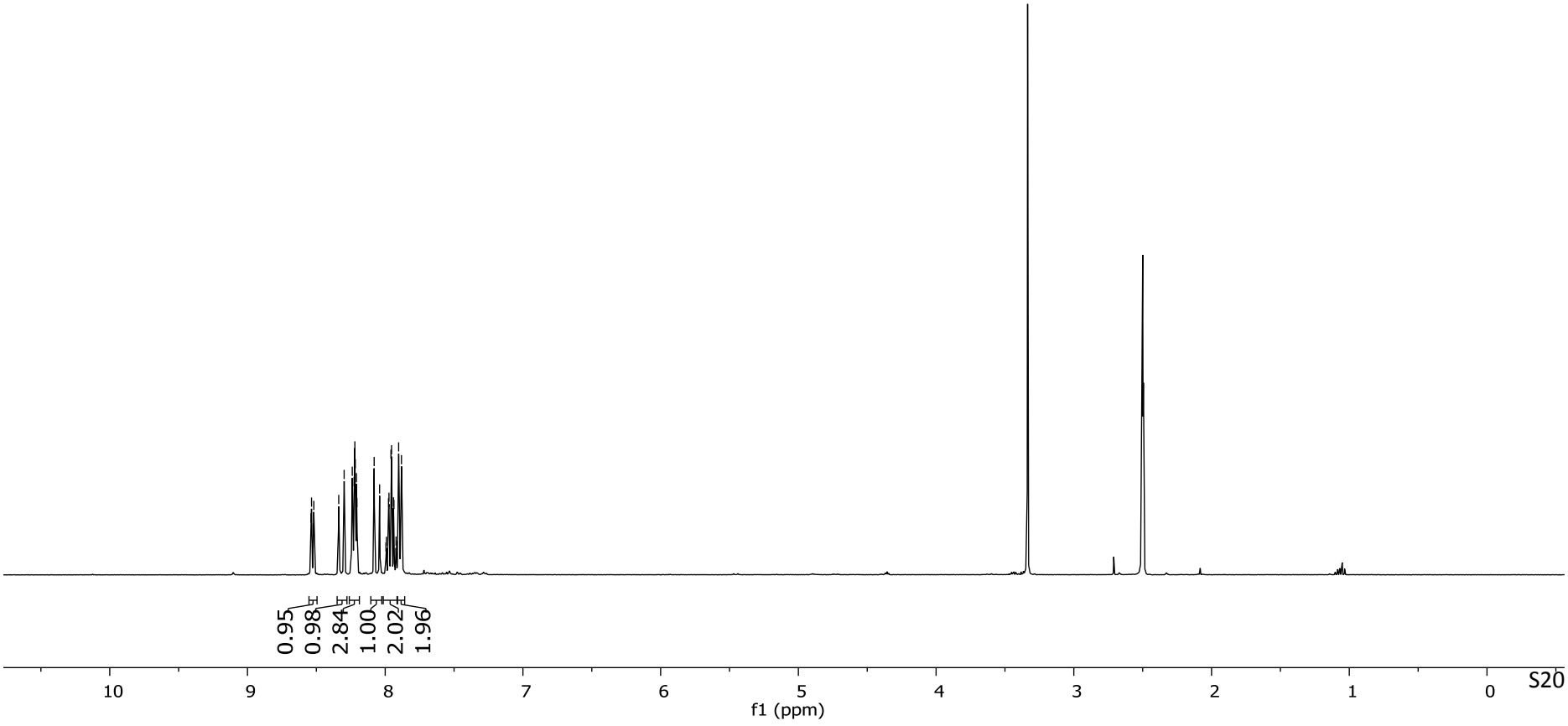
167.651
142.310
139.536
134.442
133.424
132.222
131.199
131.008
130.845
128.947
127.754
126.968
126.614
125.932
125.775
123.096
122.610
117.432

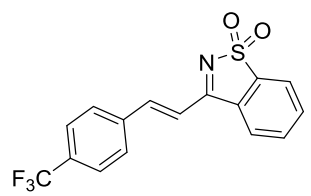




40

^{1}H NMR, 400 MHz, d_6-DMSO





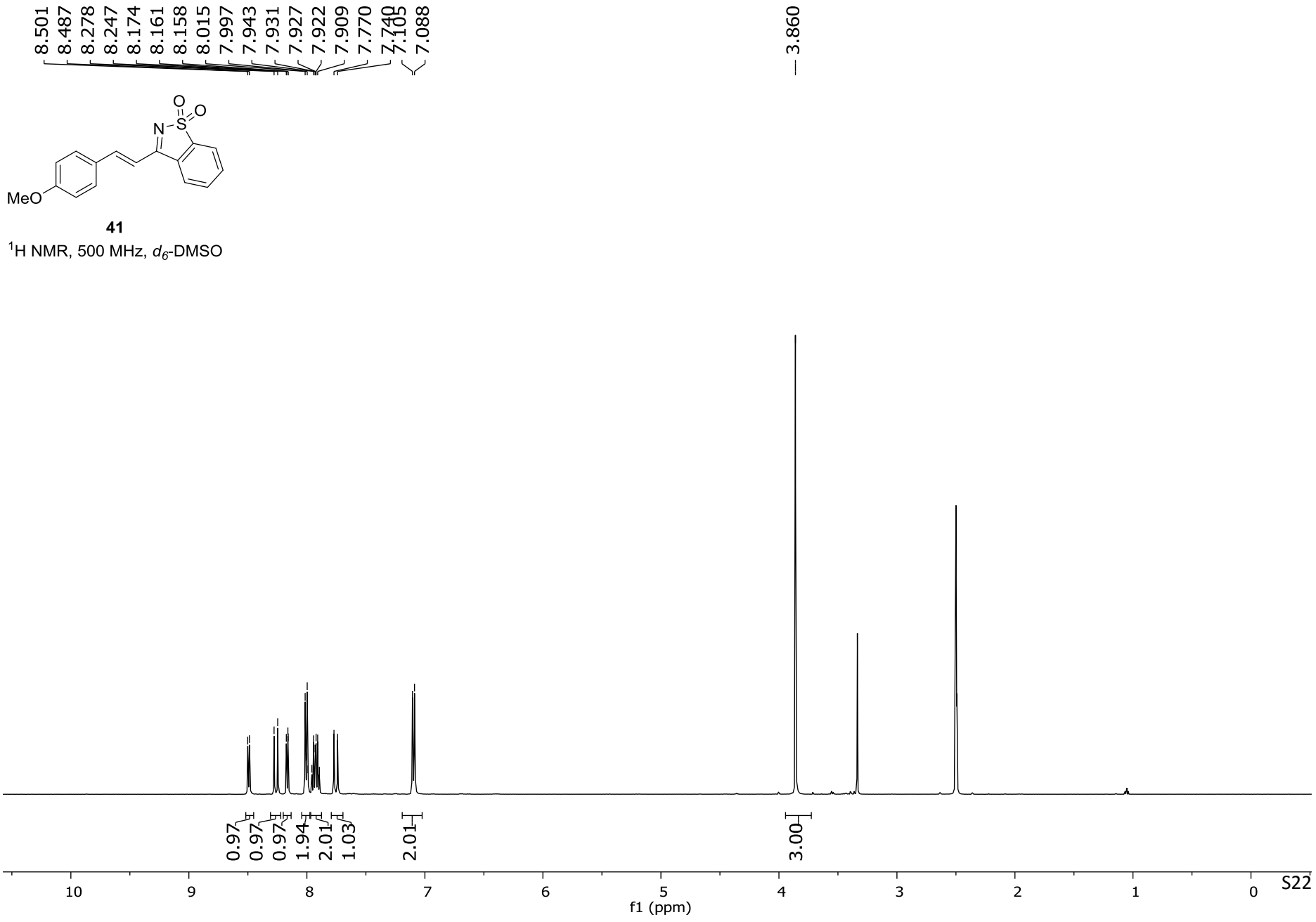
40

^{13}C NMR, 101 MHz, d_6-DMSO

167.661
144.556
139.395
138.308
134.527
134.483
131.155
130.901
130.824
130.648
130.394
130.063
127.233
125.975
125.915
125.908
125.886
125.068
122.902
122.688
120.736
118.194

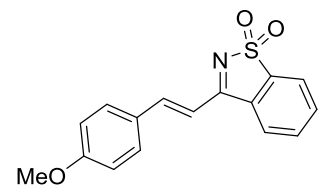
200 180 160 140 120 100 80 60 40 20

f1 (ppm)



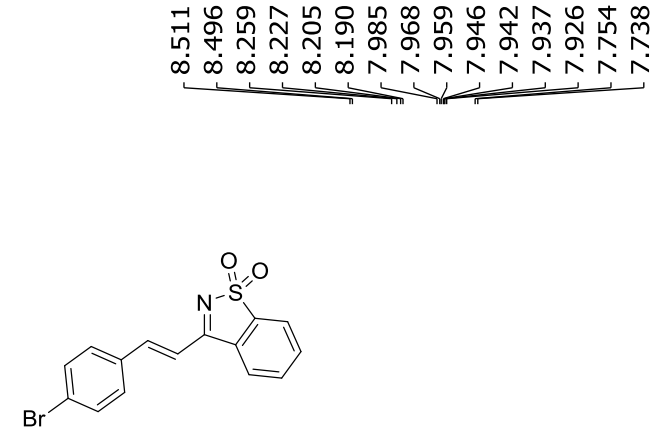
41

^{1}H NMR, 500 MHz, d_6-DMSO



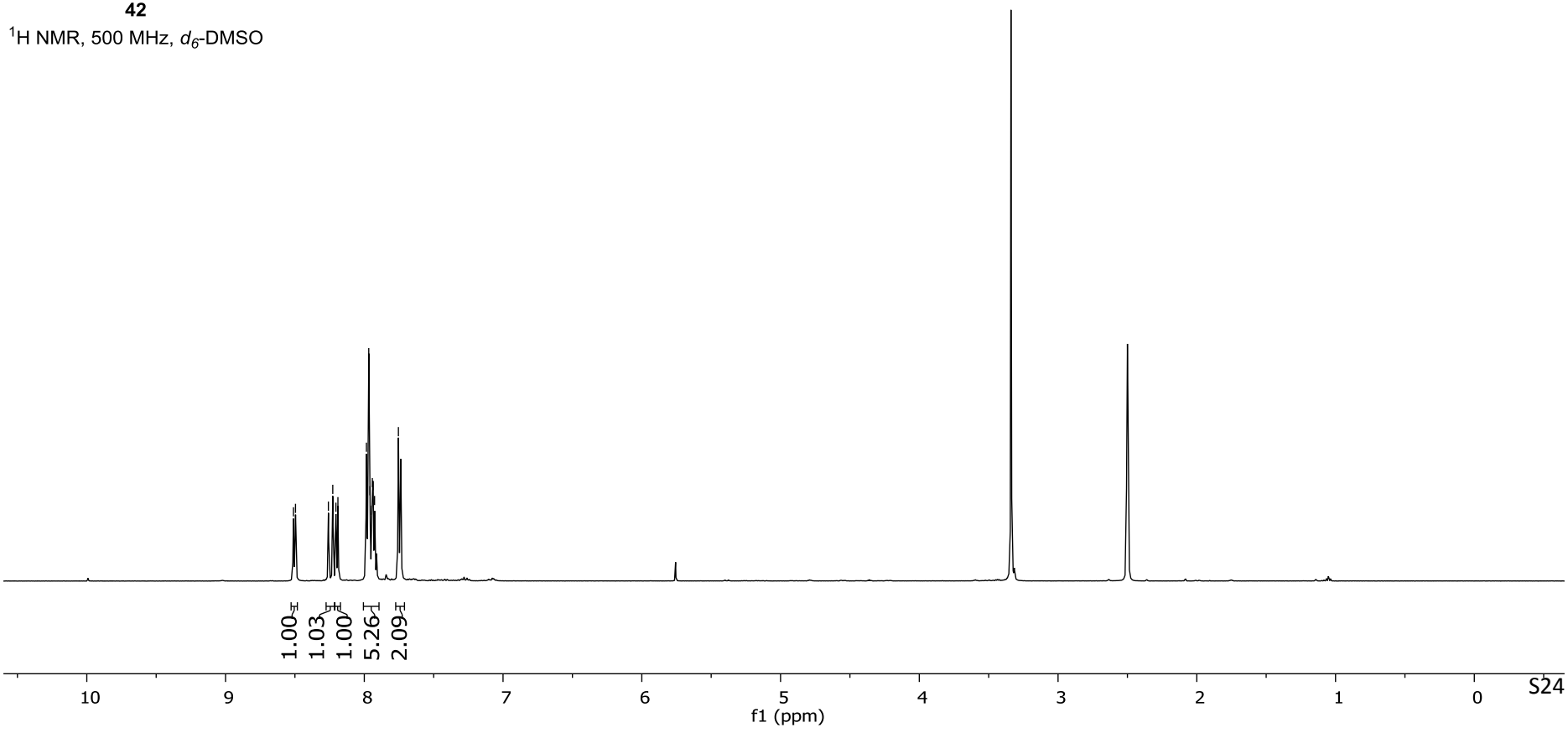
41

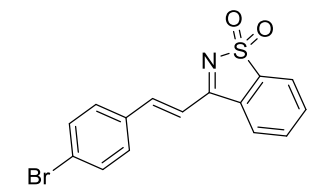
^{13}C NMR, 126 MHz, d_6-DMSO



42

^{1}H NMR, 500 MHz, d_6-DMSO



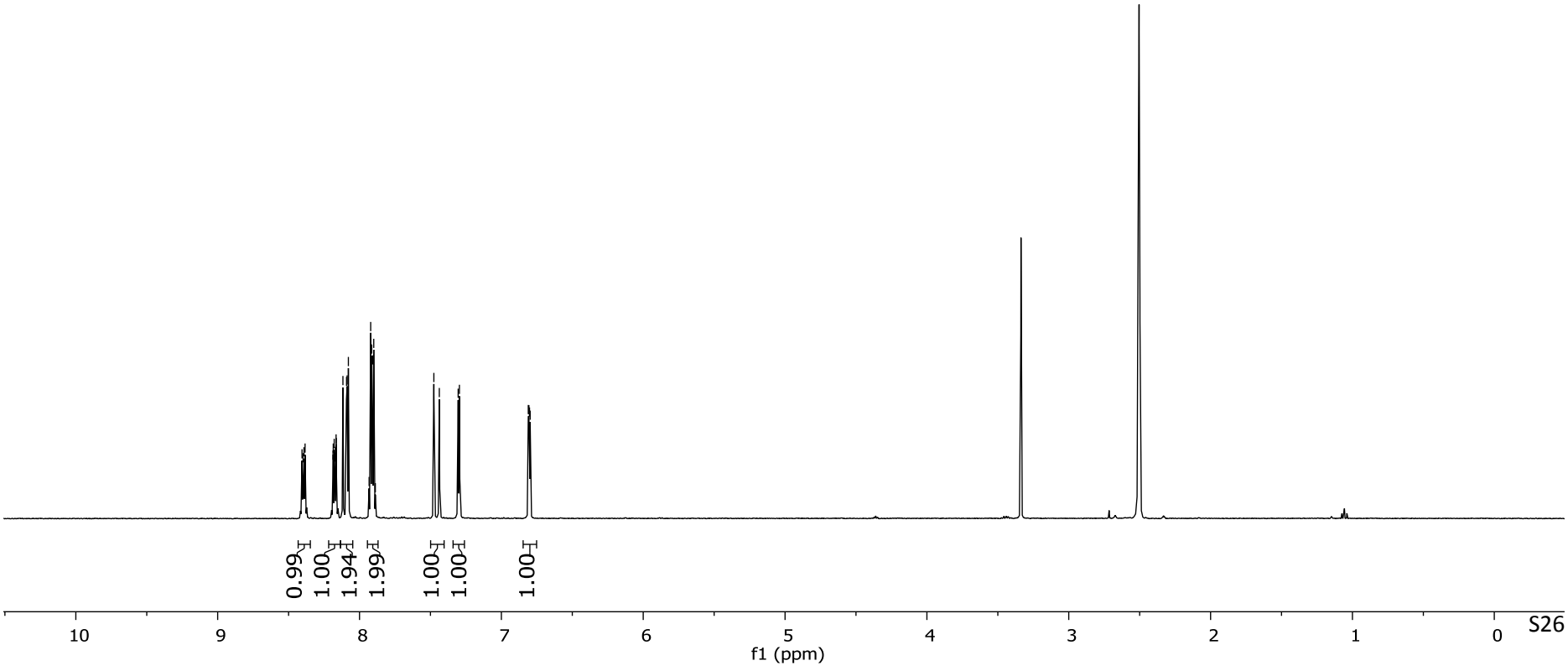


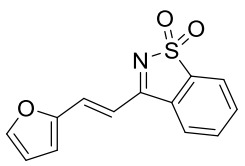
42

^{13}C NMR, 126 MHz, d_6-DMSO

43

^{1}H NMR, 400 MHz, d_6-DMSO





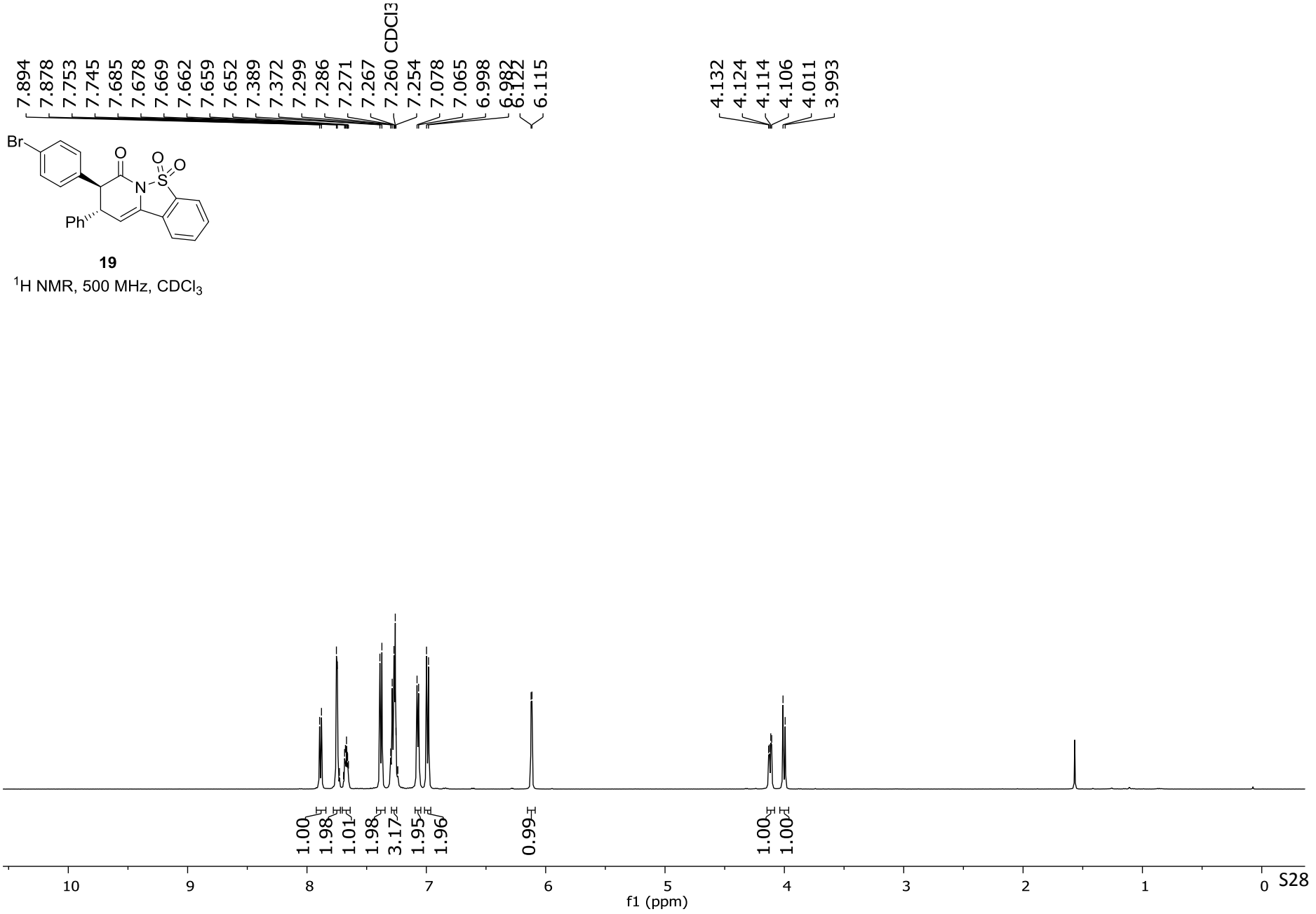
43

^{13}C NMR, 101 MHz, d_6-DMSO

167.326
151.150
148.185
139.542
134.326
134.253
132.621
130.840
125.523
122.443
120.071
113.926
111.453

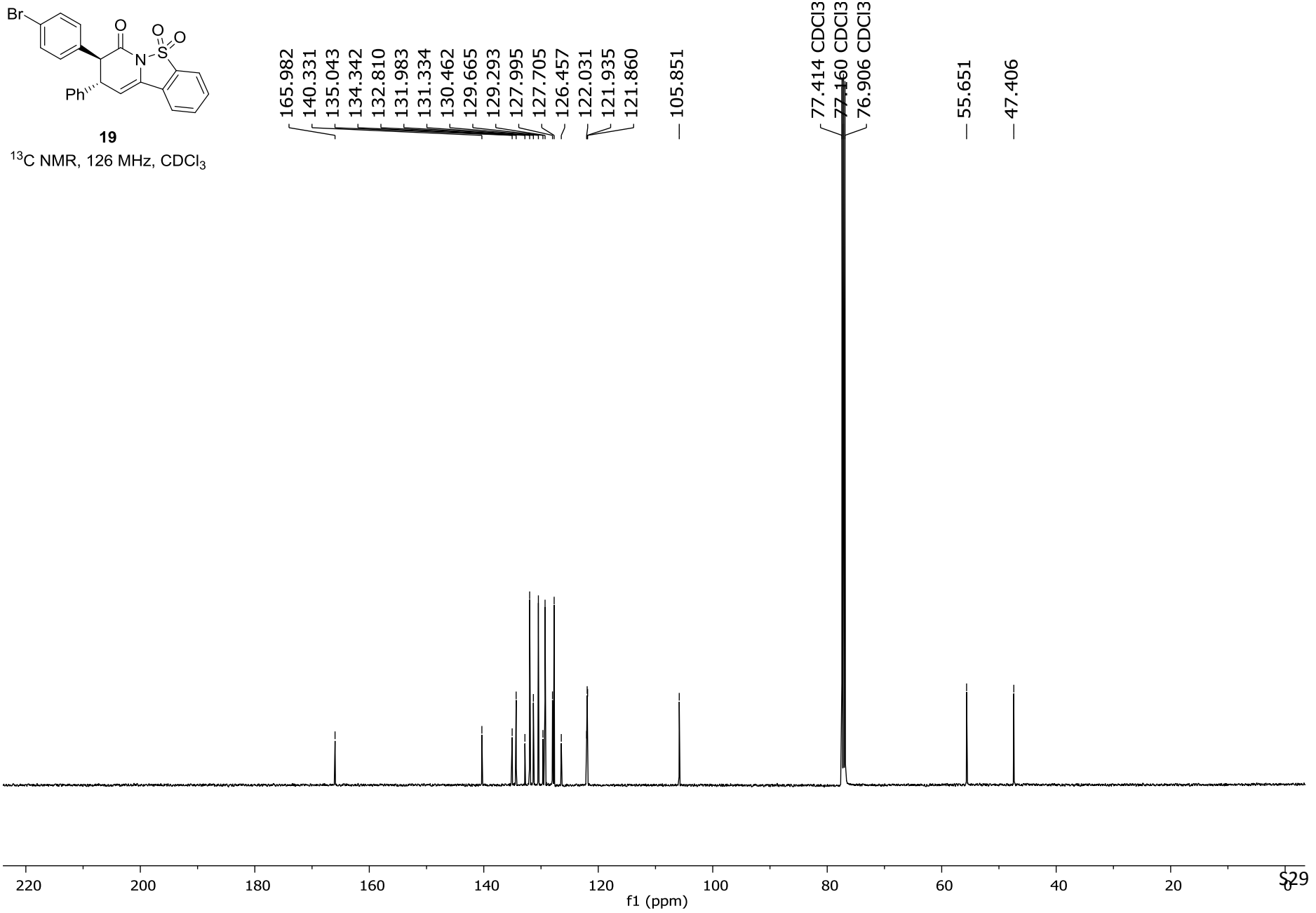
220 200 180 160 140 120 100 80 60 40 20 0

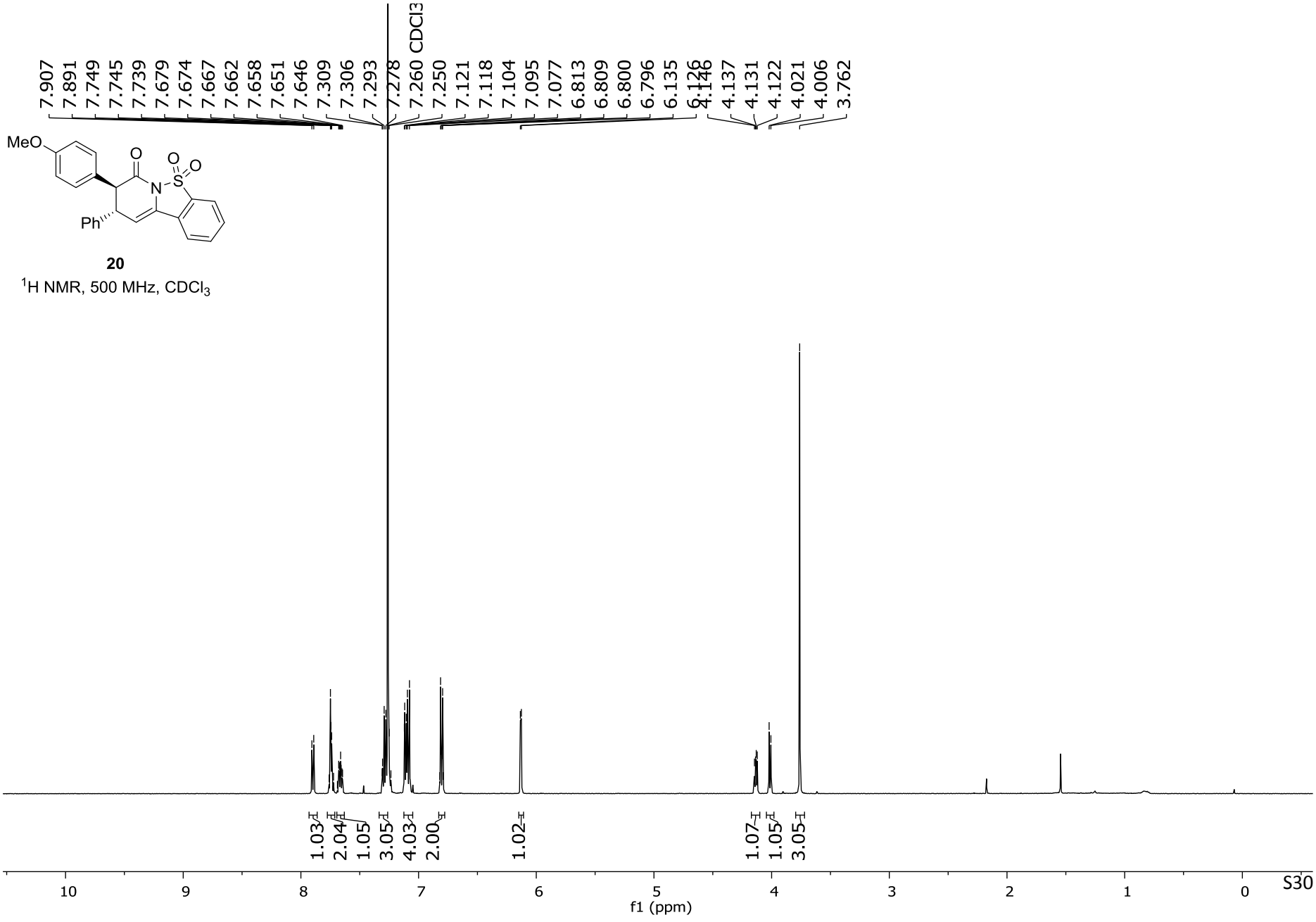
f1 (ppm)



19

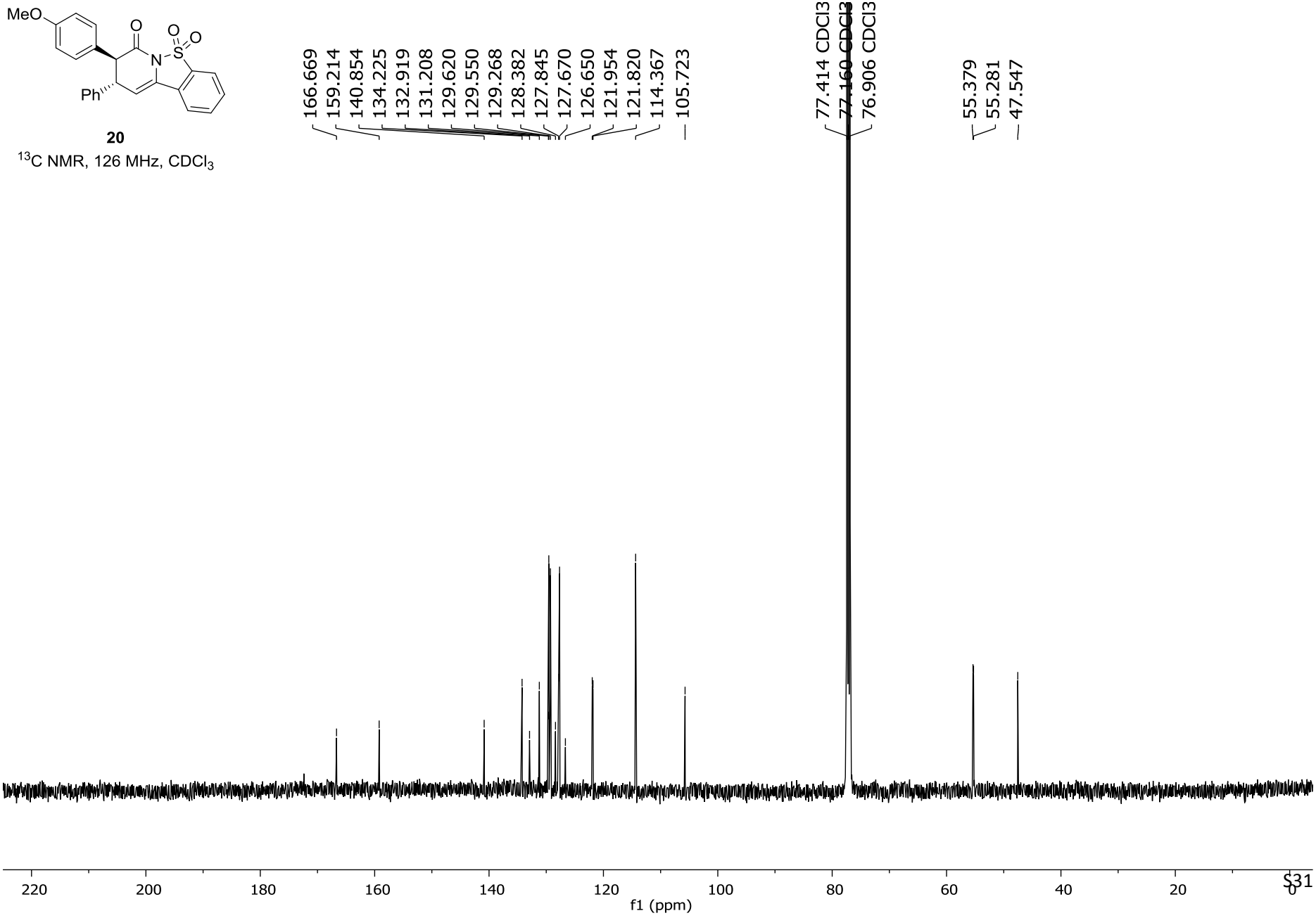
^{1}H NMR, 500 MHz, $CDCl_3$

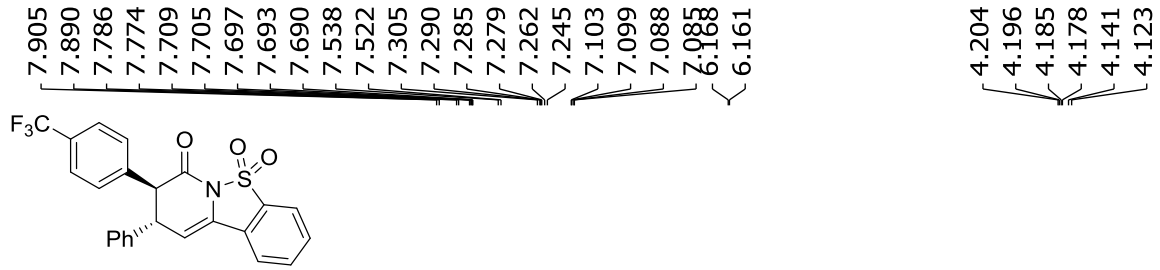

Br
O
O
O
N
S
Ph
19
13C NMR, 126 MHz, CDCl3
165.982
140.331
135.043
134.342
132.810
131.983
131.334
130.462
129.665
129.293
127.995
127.705
126.457
122.031
121.935
121.860
105.851
77.414 CDCl3
77.160 CDCl3
76.906 CDCl3
55.651
47.406
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



20

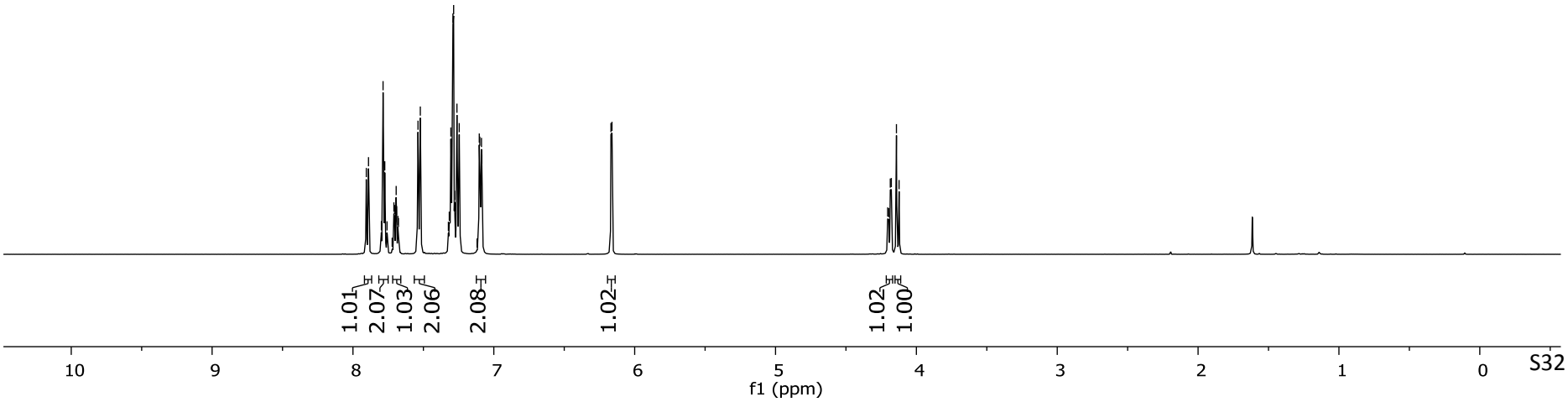
^{1}H NMR, 500 MHz, $CDCl_3$

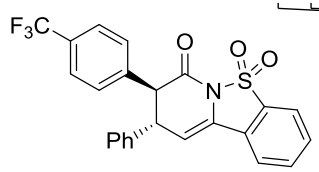

MeO
O
O
O
N
S
Ph
20
^{13}C NMR, 126 MHz, CDCl$_3$
166.669
159.214
140.854
134.225
132.919
131.208
129.620
129.550
129.268
128.382
127.845
127.670
126.650
121.954
121.820
114.367
105.723
77.414 CDCl3
77.160 CDCl3
76.906 CDCl3
55.379
55.281
47.547
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



21

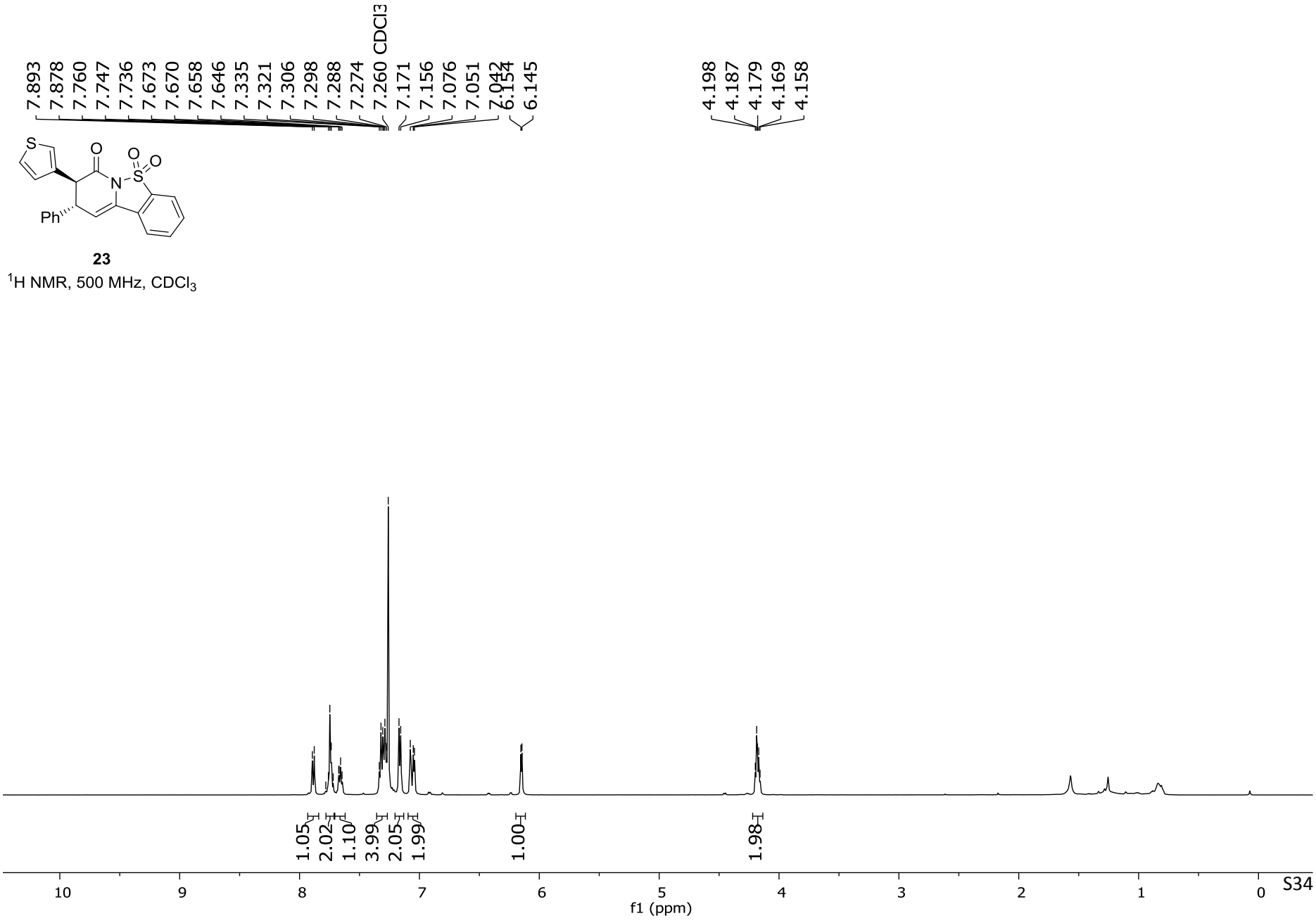
^{1}H NMR, 500 MHz, $CDCl_3$





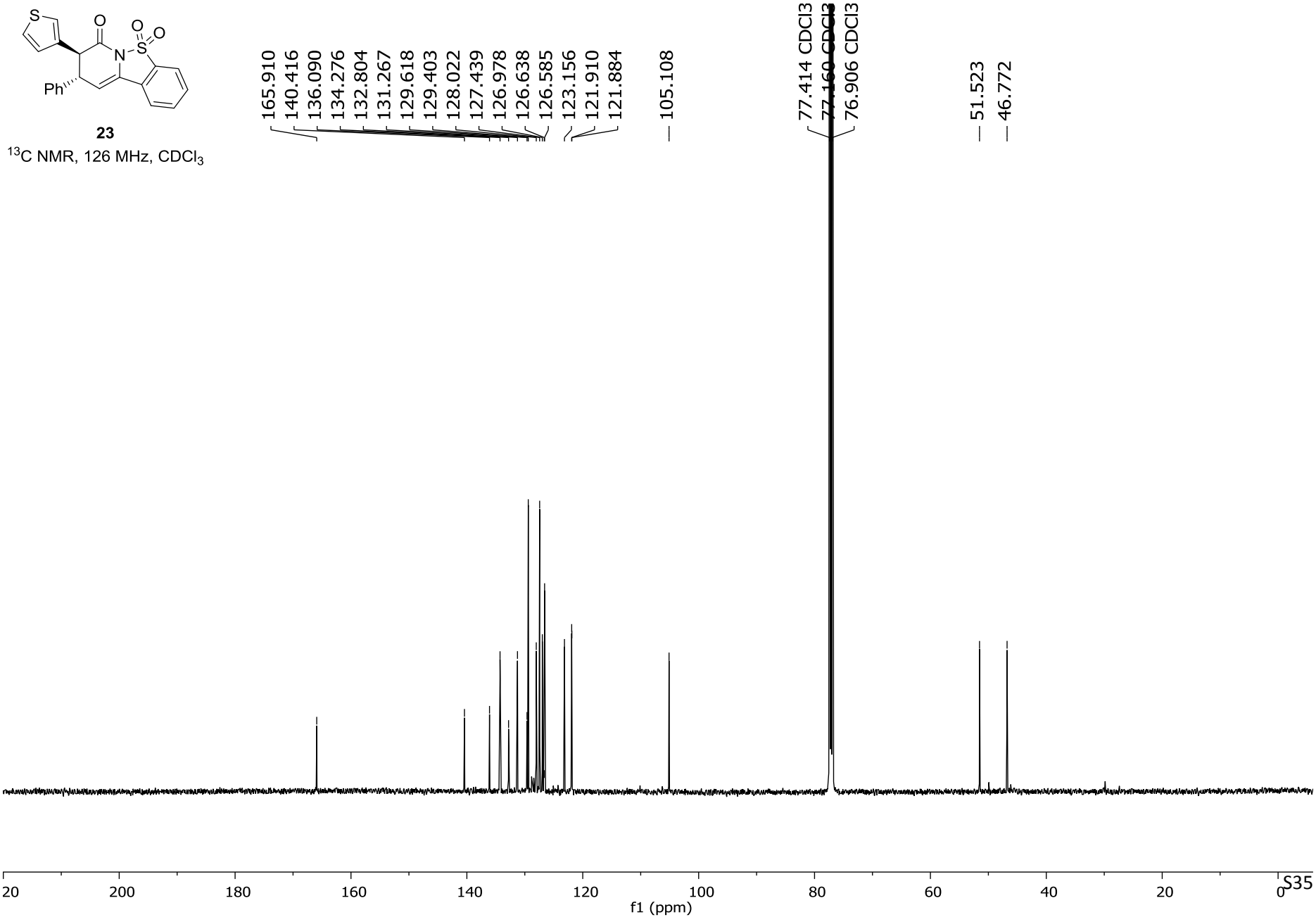
21

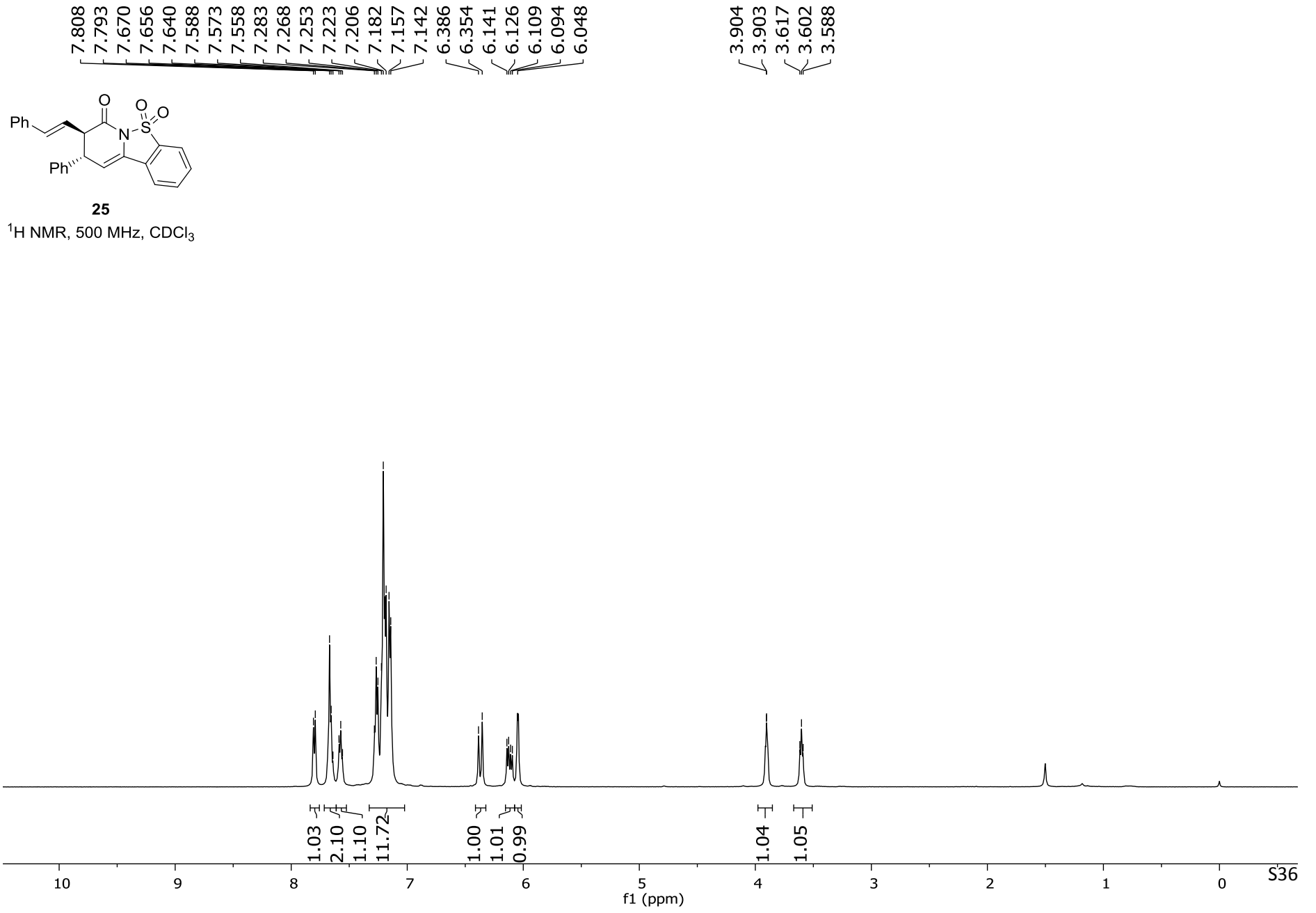
^{13}C NMR, 126 MHz, $CDCl_3$



23

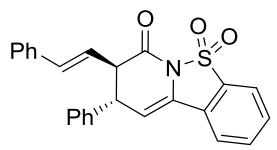
^{1}H NMR, 500 MHz, $CDCl_3$


S
O
O
O
N
S
Ph
23
13C NMR, 126 MHz, CDCl3
165.910
140.416
136.090
134.276
132.804
131.267
129.618
129.403
128.022
127.439
126.978
126.638
126.585
123.156
121.910
121.884
105.108
77.414 CDCl3
77.160 CDCl3
76.906 CDCl3
51.523
46.772
f1 (ppm)



25

^{1}H NMR, 500 MHz, $CDCl_3$

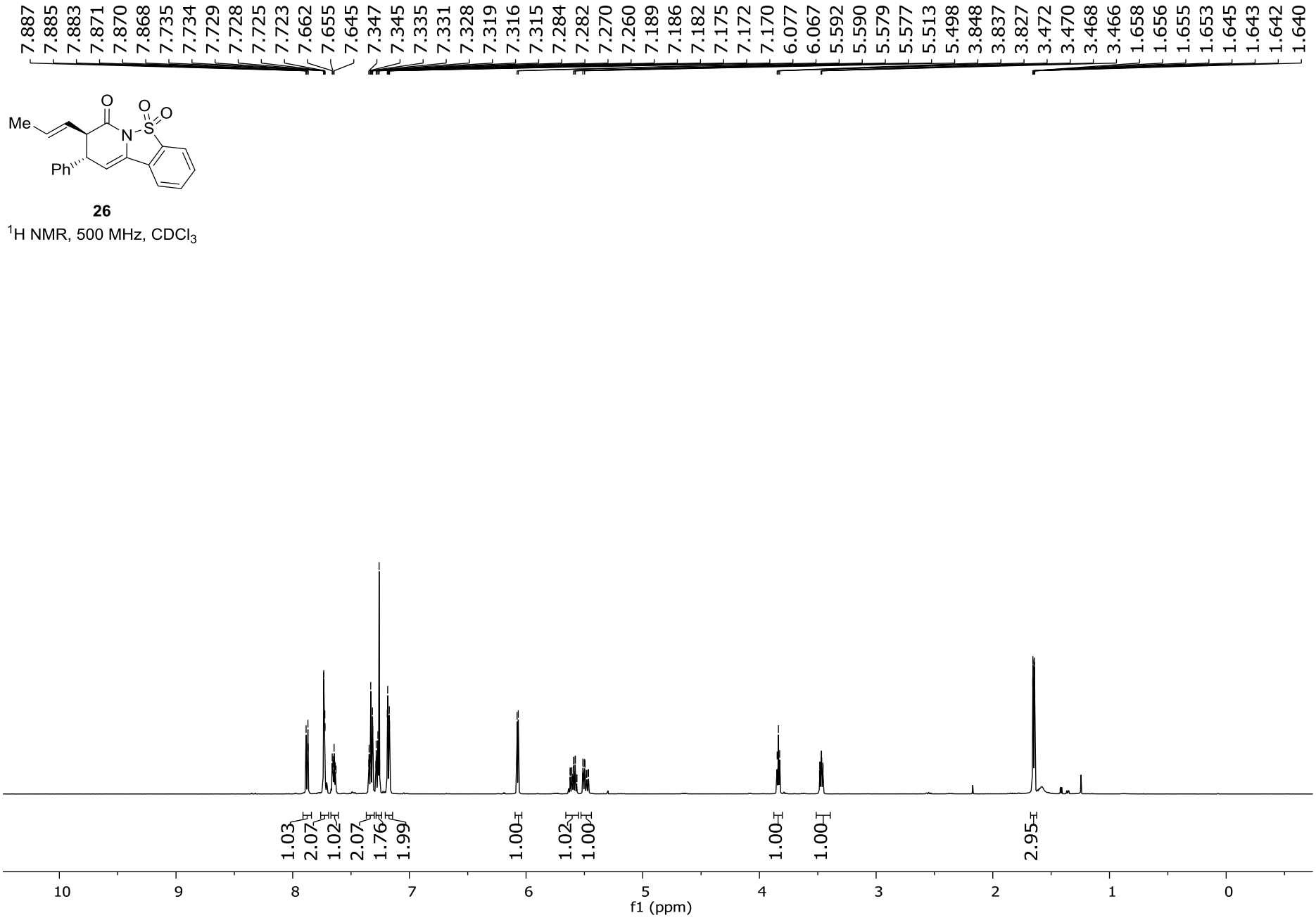


25

^{13}C NMR, 101 MHz, $CDCl_3$

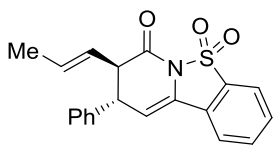
166.244
140.291
136.263
135.303
134.234
132.841
131.232
129.577
129.403
128.654
128.167
128.017
127.678
126.688
123.397
121.879
105.029
53.302
45.912

220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



26

^{1}H NMR, 500 MHz, $CDCl_3$

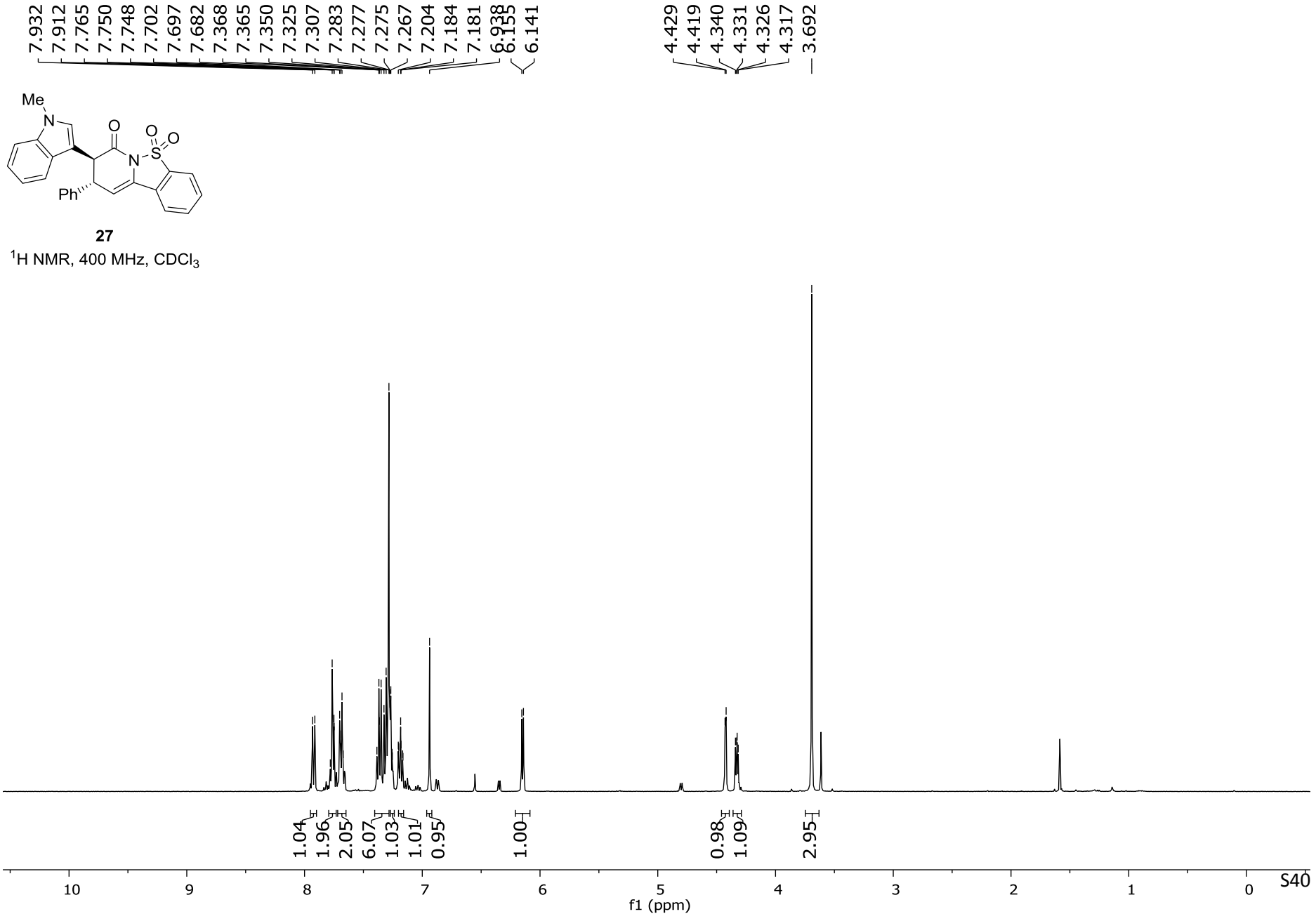


26

^{1}H NMR, 500 MHz, $CDCl_3$

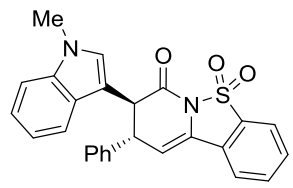
166.739
140.537
134.175
132.816
131.697
131.133
129.390
129.302
127.864
127.601
126.769
125.000
121.871
121.786
105.073
53.171
45.813
18.262

220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



27

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

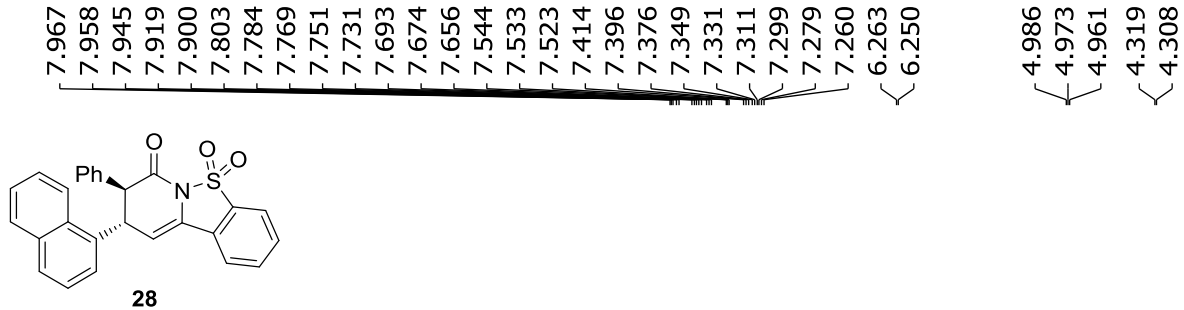


27

^{13}C NMR, 101 MHz, $CDCl_3$

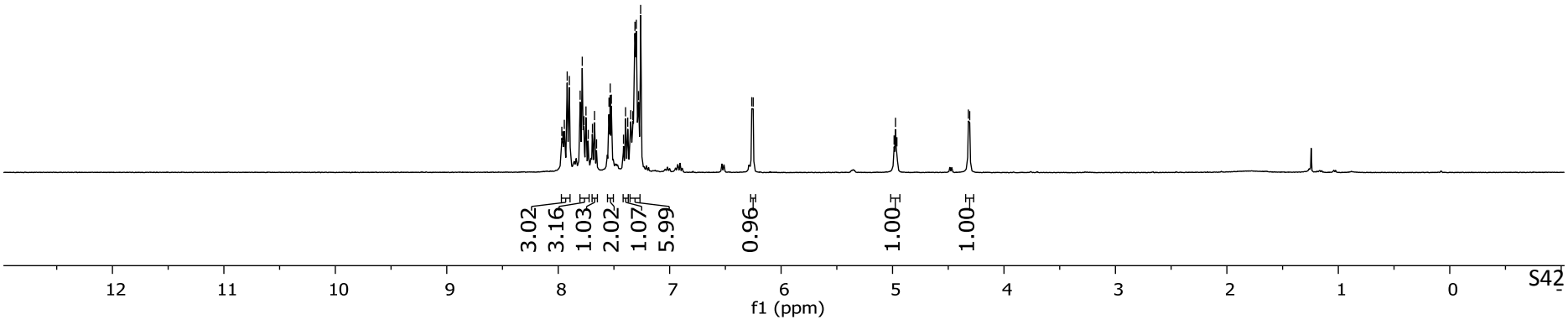
166.352
140.962
137.065
134.213
132.840
131.138
129.471
127.938
127.358
126.827
126.598
126.296
122.314
121.903
121.851
119.793
118.984
110.285
109.760
105.181
77.478 CDCl3
77.160 CDCl3
76.843 CDCl3
47.991
46.672
32.974

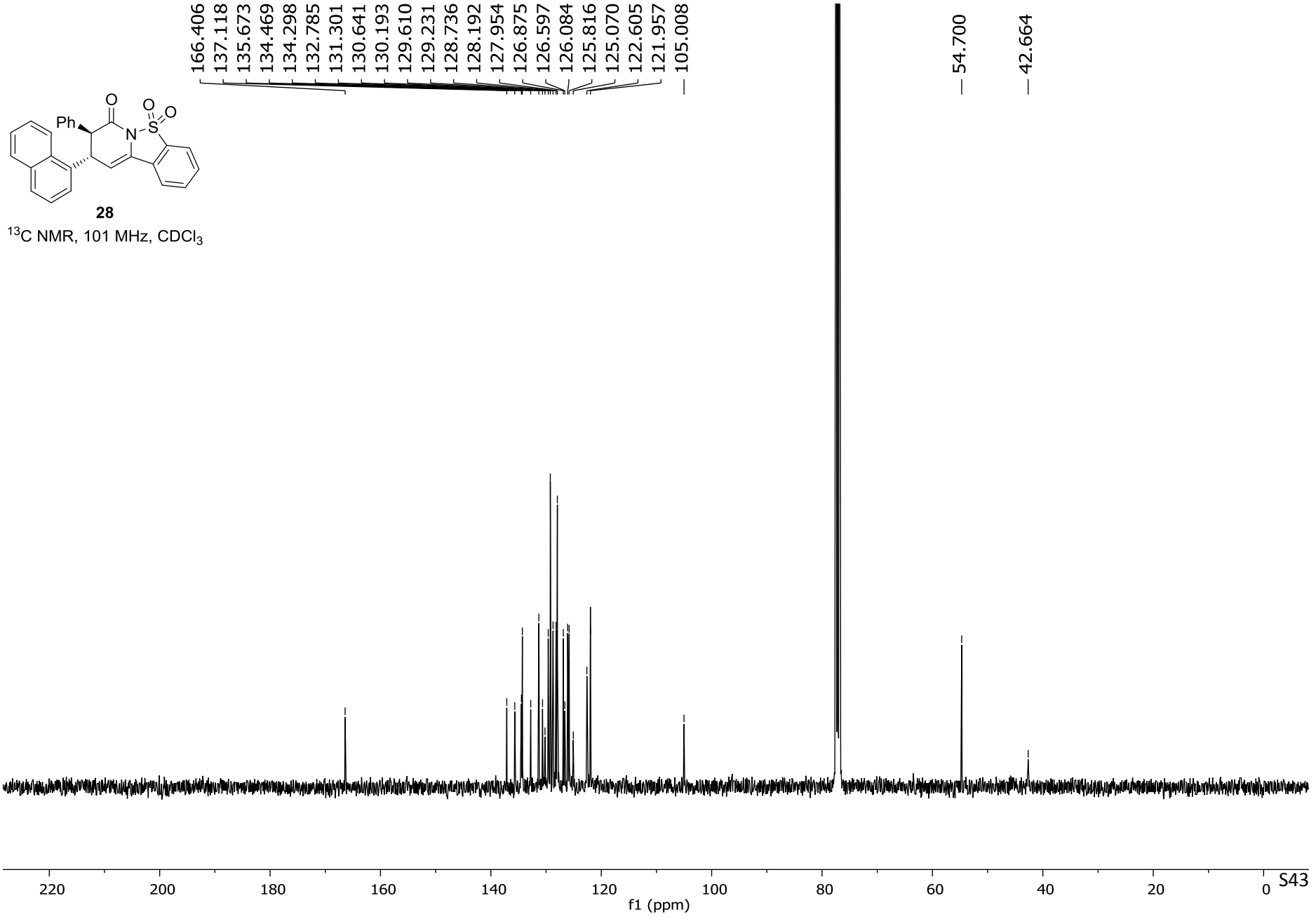
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

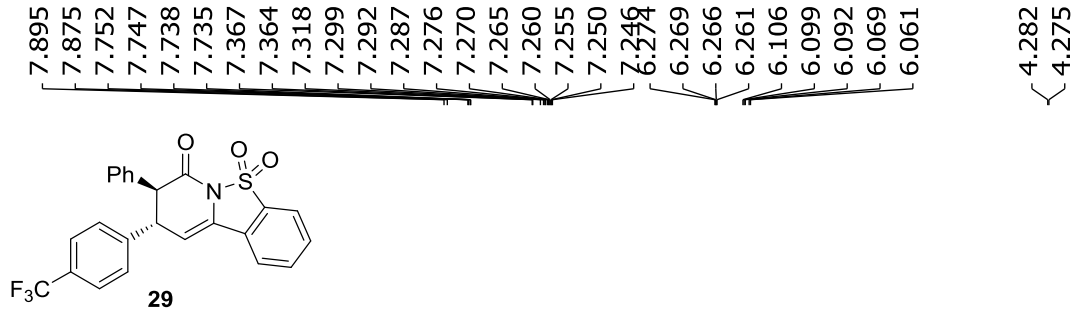


28

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

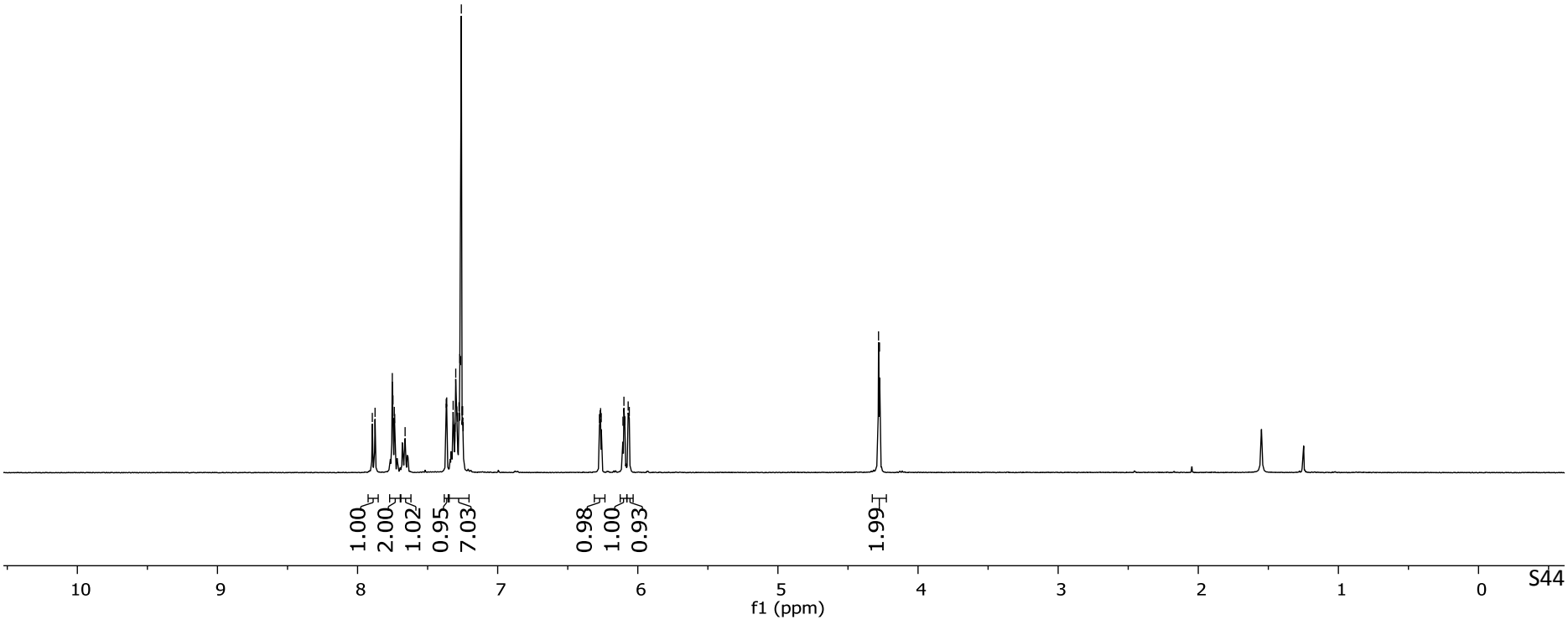


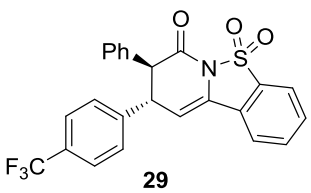

166.406
137.118
135.673
134.469
134.298
132.785
131.301
130.641
130.193
129.610
129.231
128.736
128.192
127.954
126.875
126.597
126.084
125.816
125.070
122.605
121.957
105.008
54.700
42.664
Ph
O
O
O
N
S
28
13C NMR, 101 MHz, CDCl3
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



29

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



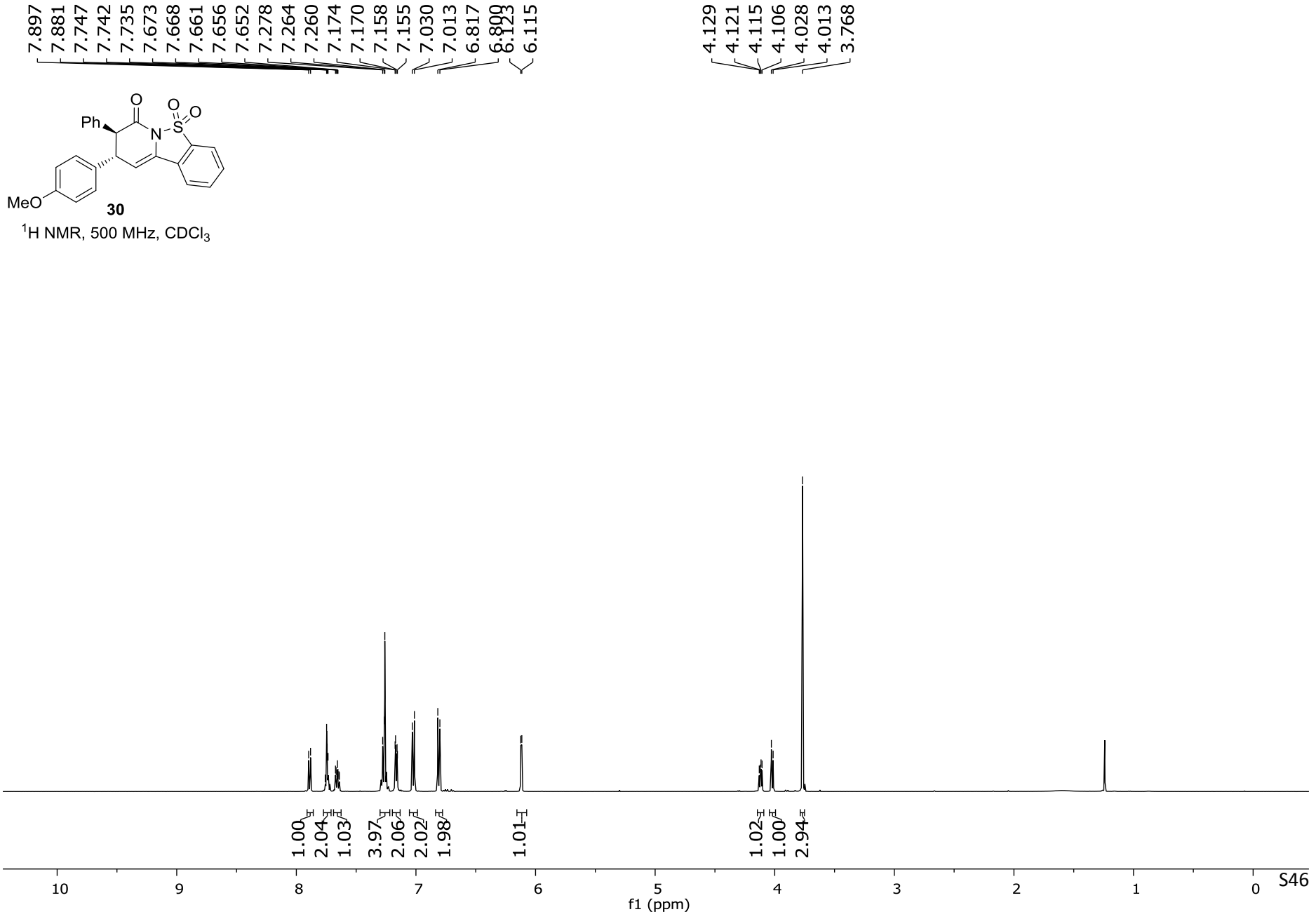


29

^{13}C NMR, 126 MHz, $CDCl_3$

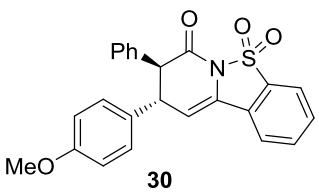
166.035
144.735
135.649
134.397
132.829
131.484
130.468
130.211
130.177
129.950
129.690
129.021
128.570
128.169
127.220
126.299
126.171
126.145
126.114
126.079
125.853
122.889
121.954
121.900
120.723
104.667
55.800
47.223

220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)



30

^{1}H NMR, 500 MHz, $CDCl_3$

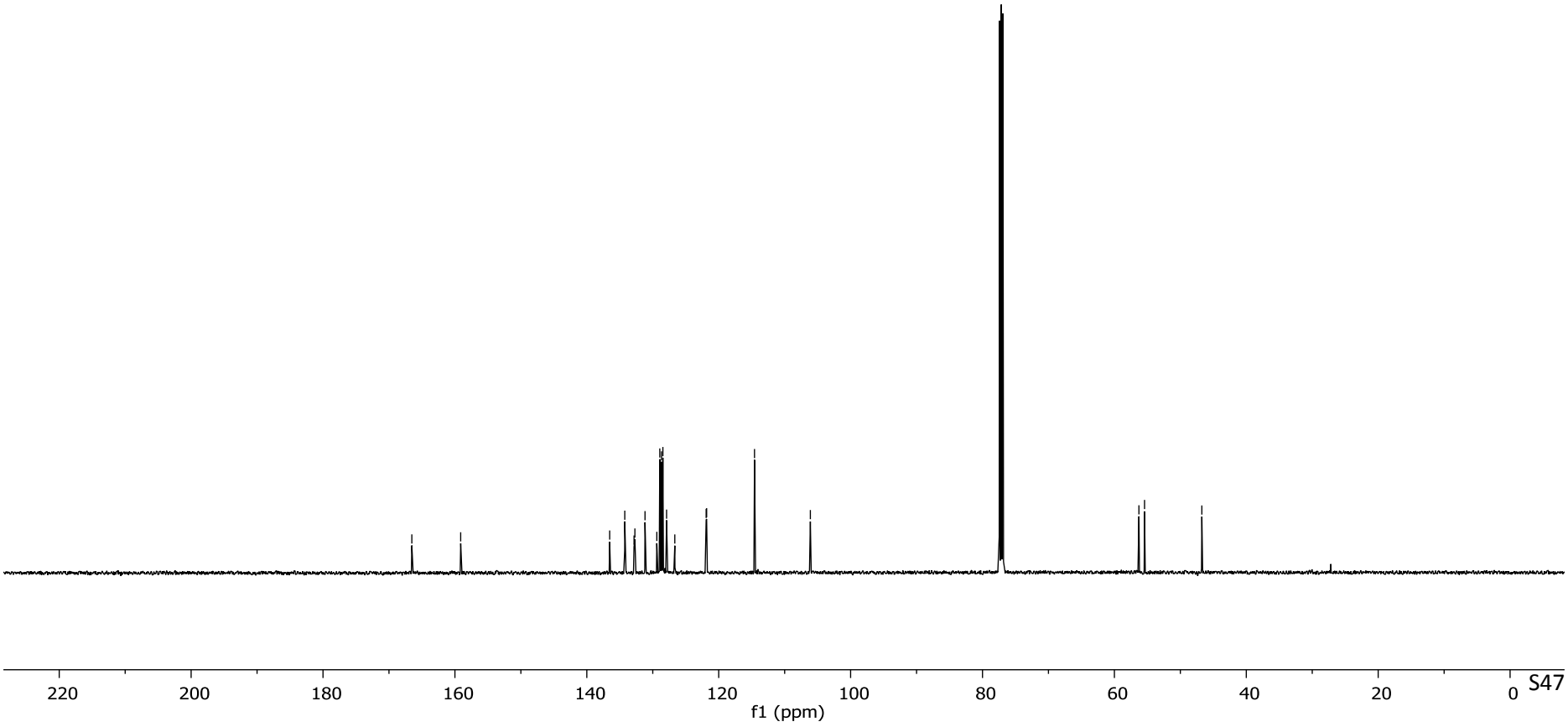


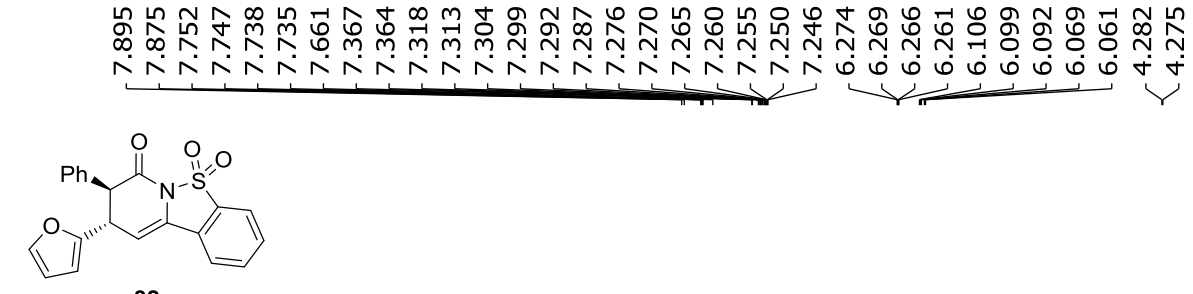
30

^{13}C NMR, 126 MHz, $CDCl_3$

166.533
159.125
136.533
134.242
132.840
132.708
131.173
129.384
128.933
128.674
128.463
127.904
126.658
121.904
121.831
114.571
106.104

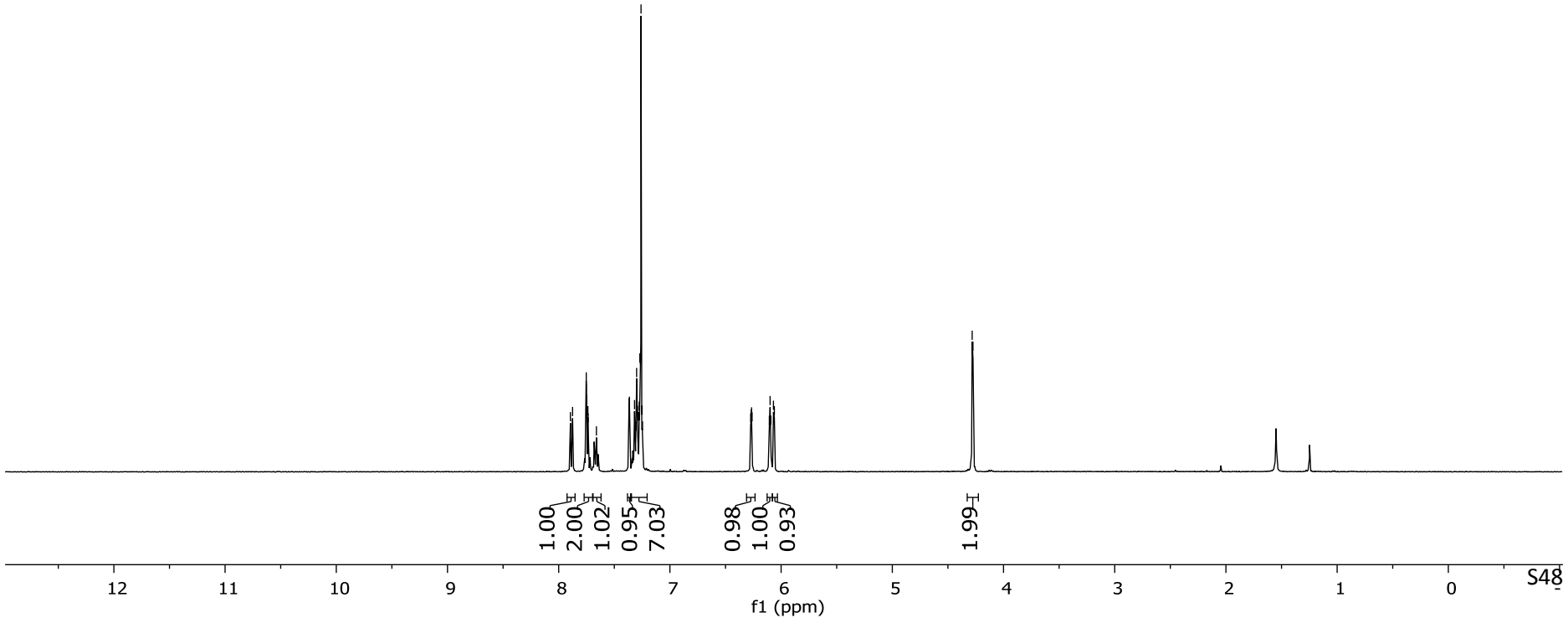
56.279
55.428
46.738

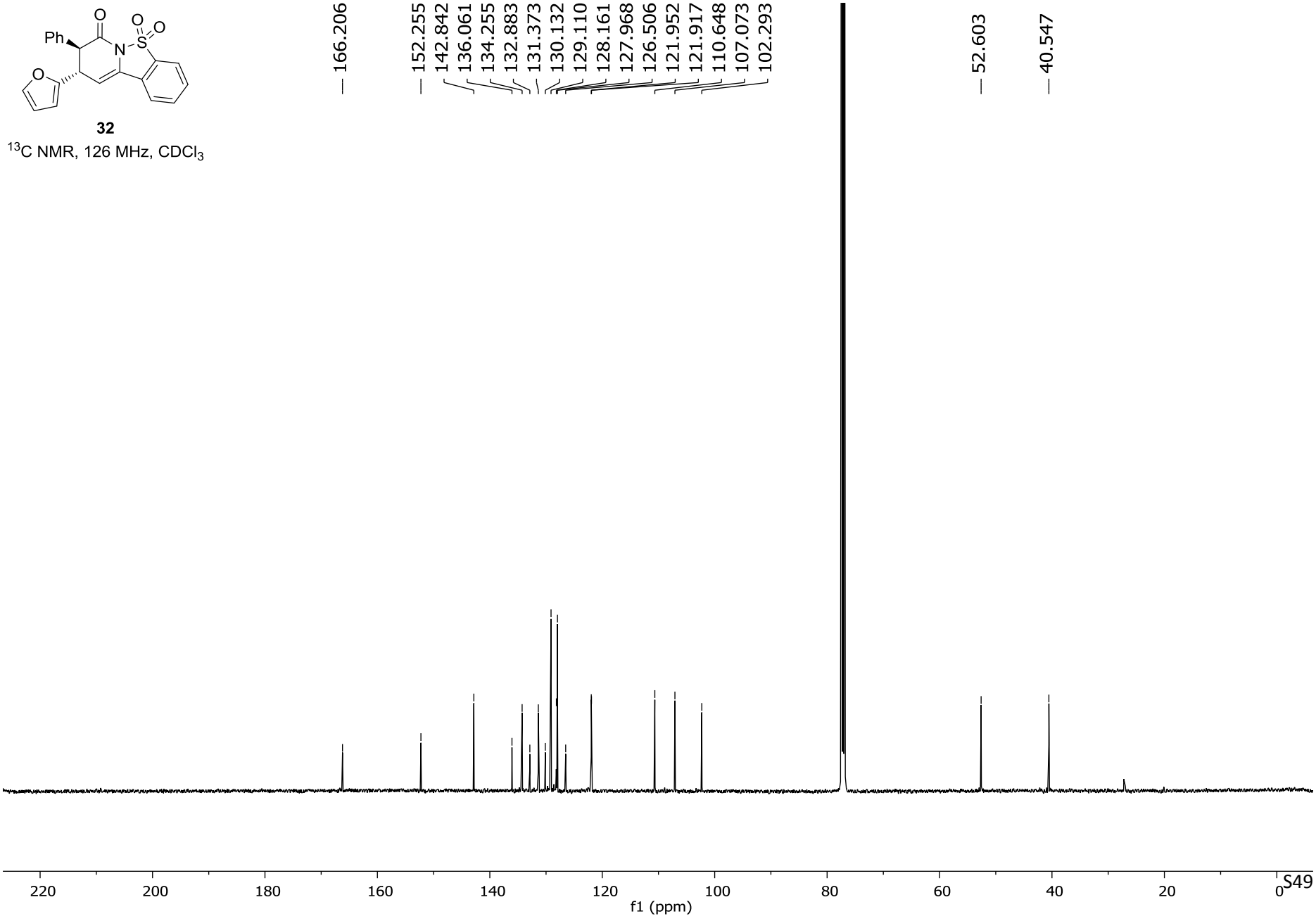




32

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



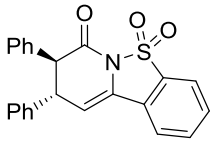


32

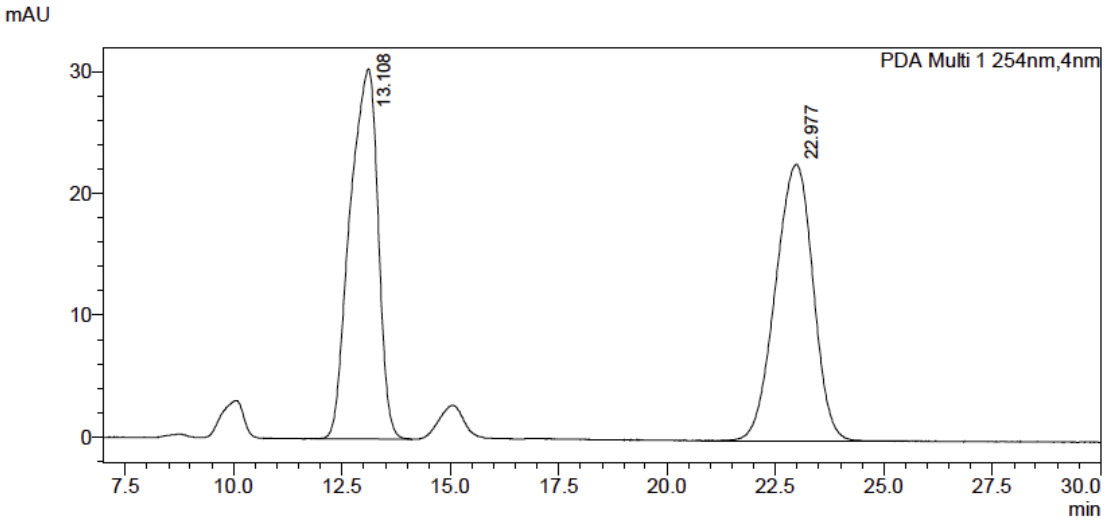
^{13}C NMR, 126 MHz, $CDCl_3$

HPLC Data

HPLC data for **15**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 13.1 min, t_R (8*R*,9*R*): 23.0 min; 95% ee.

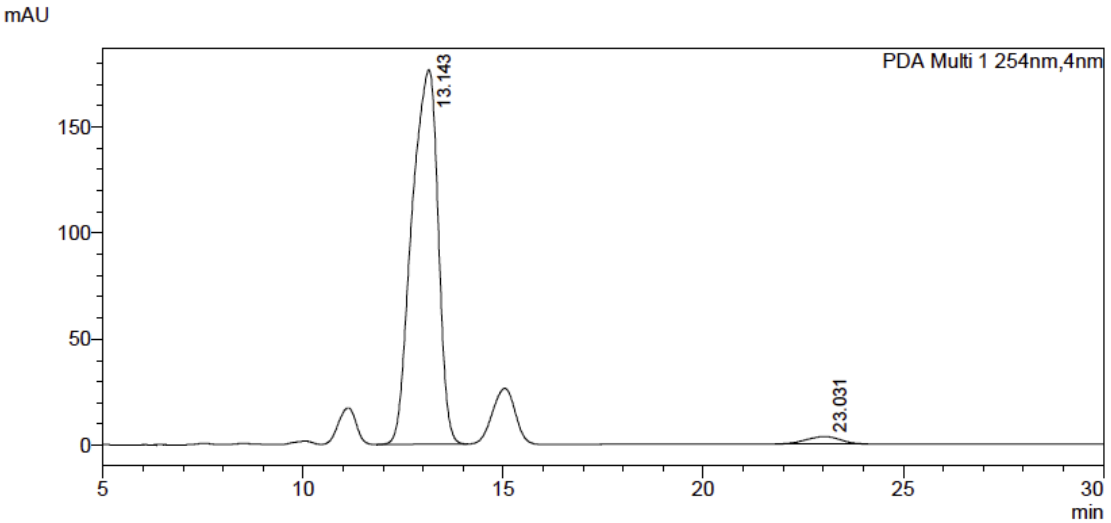


15



PDA Ch1 254nm

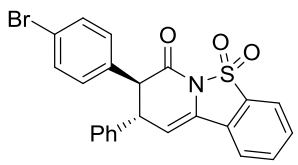
Peak#	Ret. Time	Area%
1	13.108	50.011
2	22.977	49.989
Total		100.000



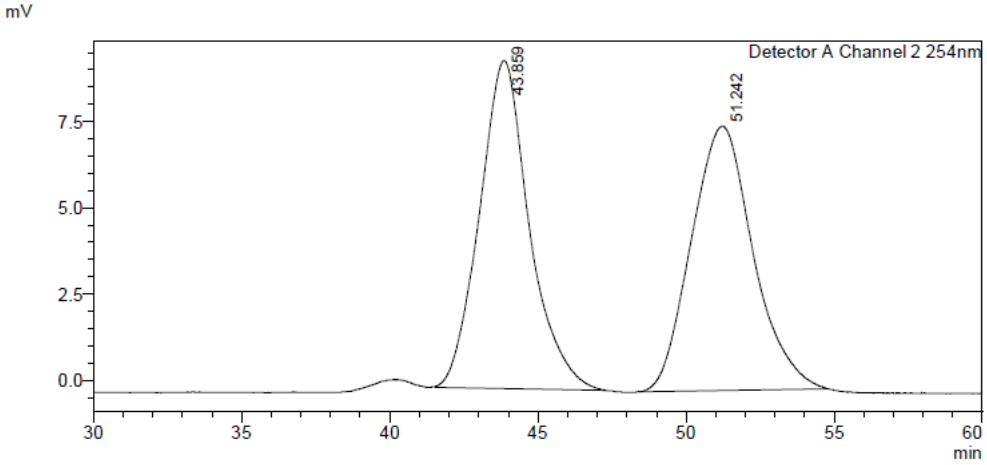
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	13.143	97.540
2	23.031	2.460
Total		100.000

HPLC data for **19**: Chiralpak AD-H (80:20 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 44.6 min, t_R (8*R*,9*R*): 51.5 min; 97% ee.

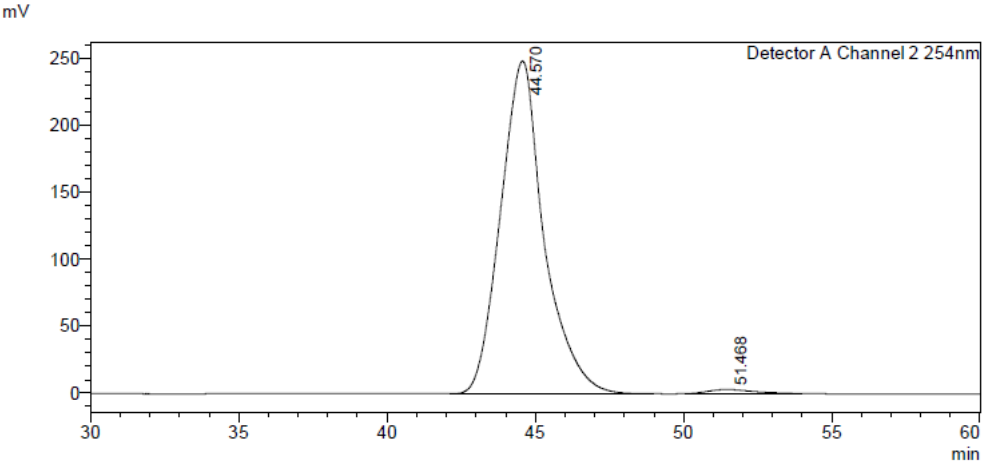


19



Detector A Channel 2 254nm

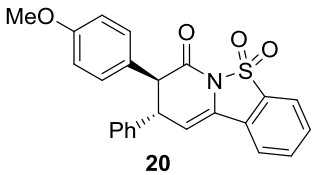
Peak#	Ret. Time	Area%
1	43.859	49.984
2	51.242	50.016
Total		100.000



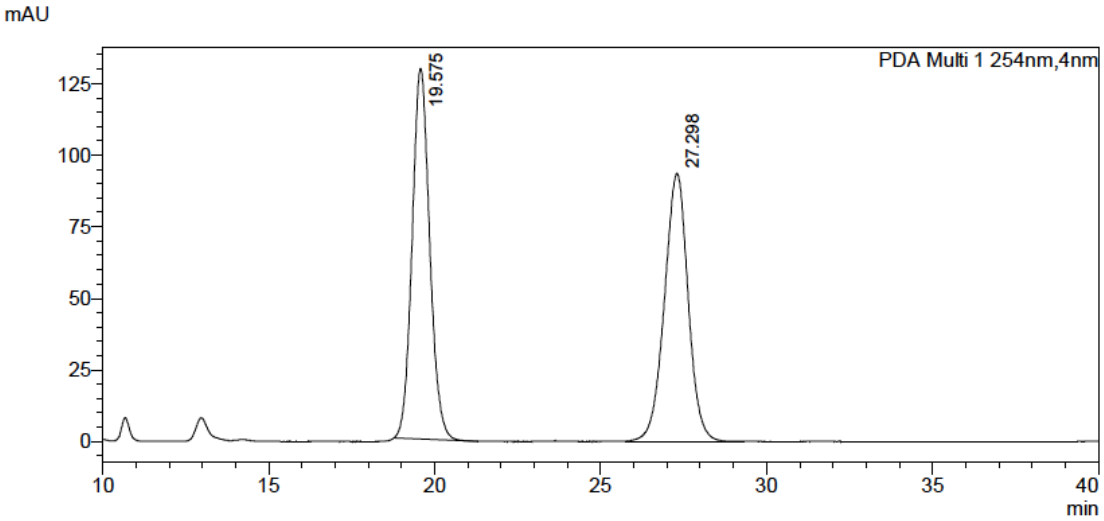
Detector A Channel 2 254nm

Peak#	Ret. Time	Area%
1	44.570	98.802
2	51.468	1.198
Total		100.000

HPLC data for **20**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 19.3 min, t_R (8*R*,9*R*): 26.6 min; >99% ee.

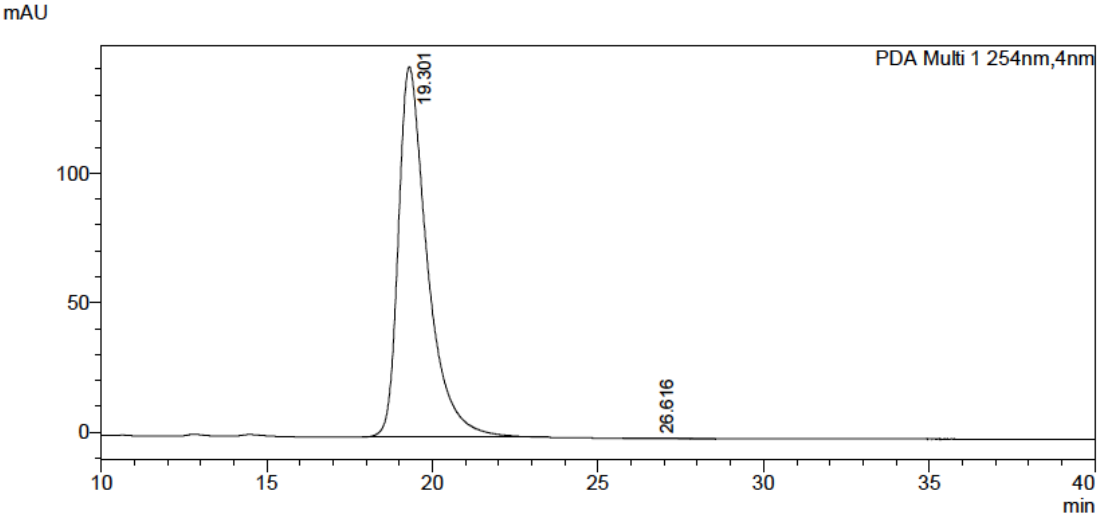


20



PDA Ch1 254nm

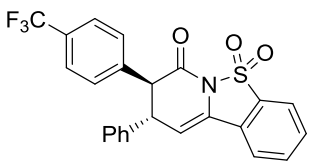
Peak#	Ret. Time	Area%
1	19.575	50.621
2	27.298	49.379
Total		100.000



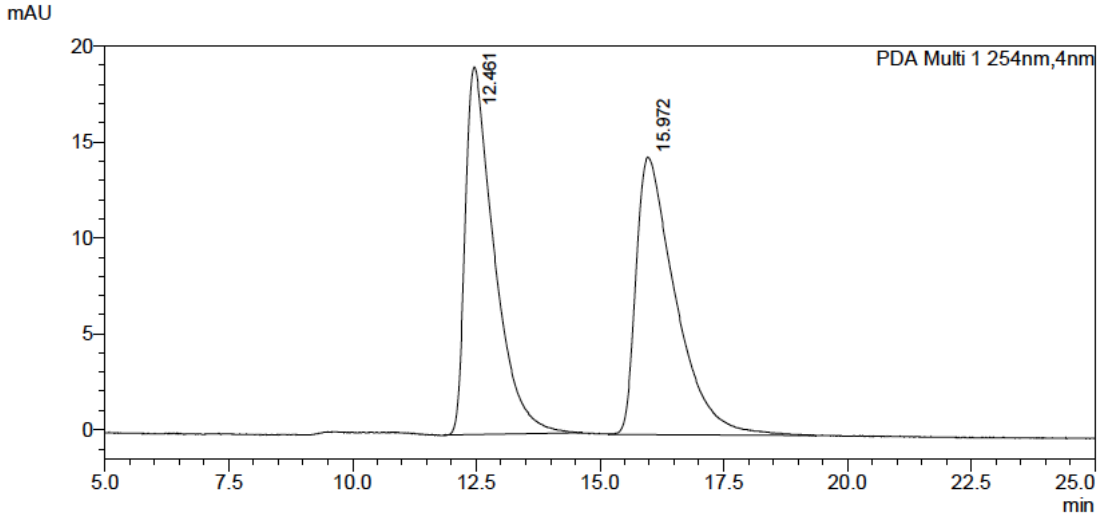
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	19.301	99.925
2	26.616	0.075
Total		100.000

HPLC data for **21**: Chiralpak IA (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 12.0 min, t_R (8*R*,9*R*): 15.9 min; 97% ee.

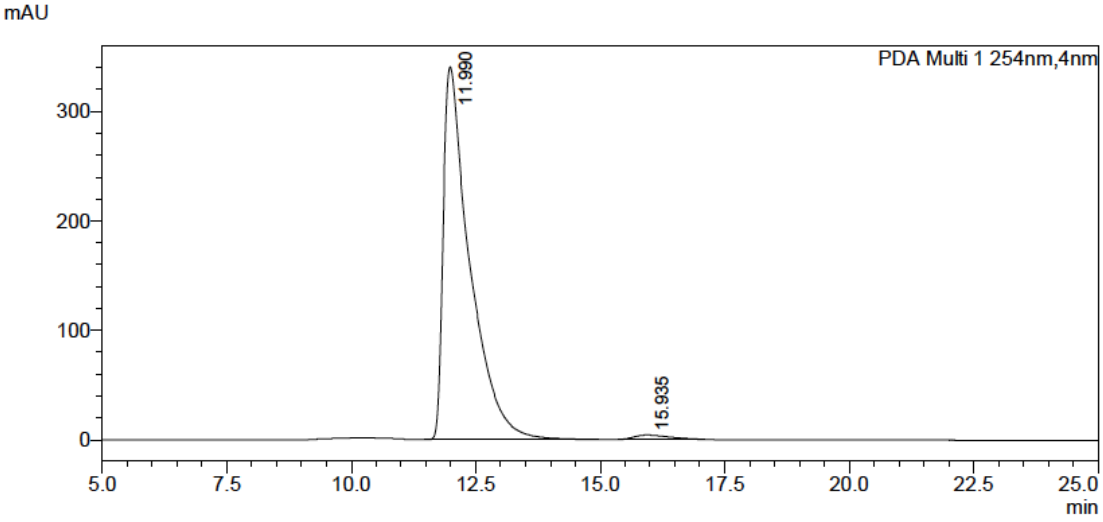


21



PDA Ch1 254nm

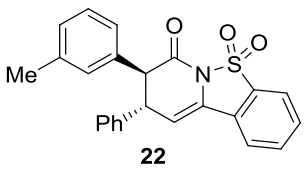
Peak#	Ret. Time	Area%
1	12.461	49.322
2	15.972	50.678
Total		100.000



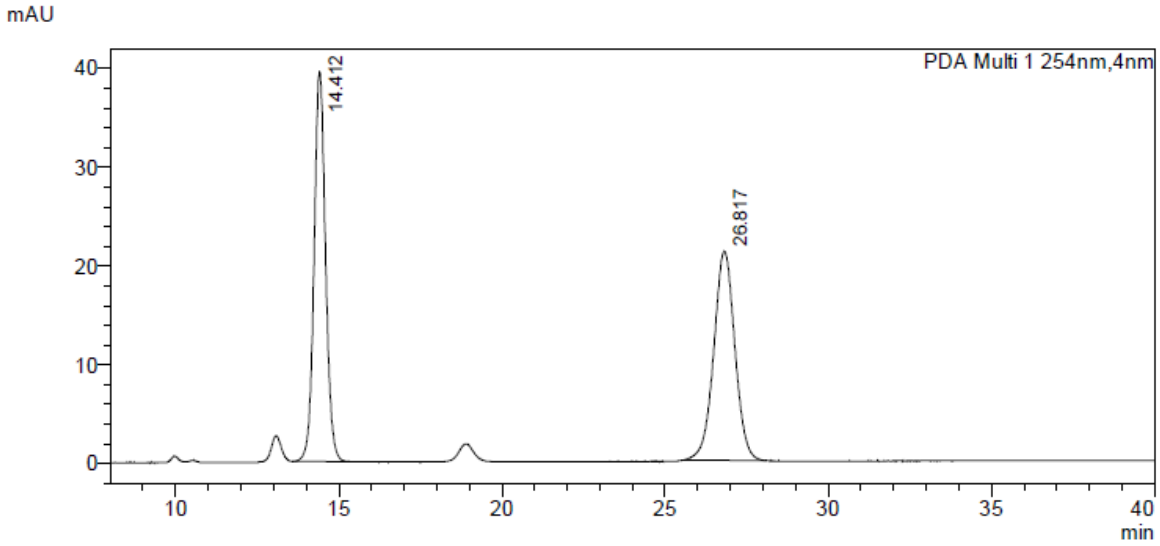
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.990	98.480
2	15.935	1.520
Total		100.000

HPLC data for **22**: Chiralpak AD-H (70:30 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 14.6 min, t_R (8*R*,9*R*): 27.3 min; >99% ee



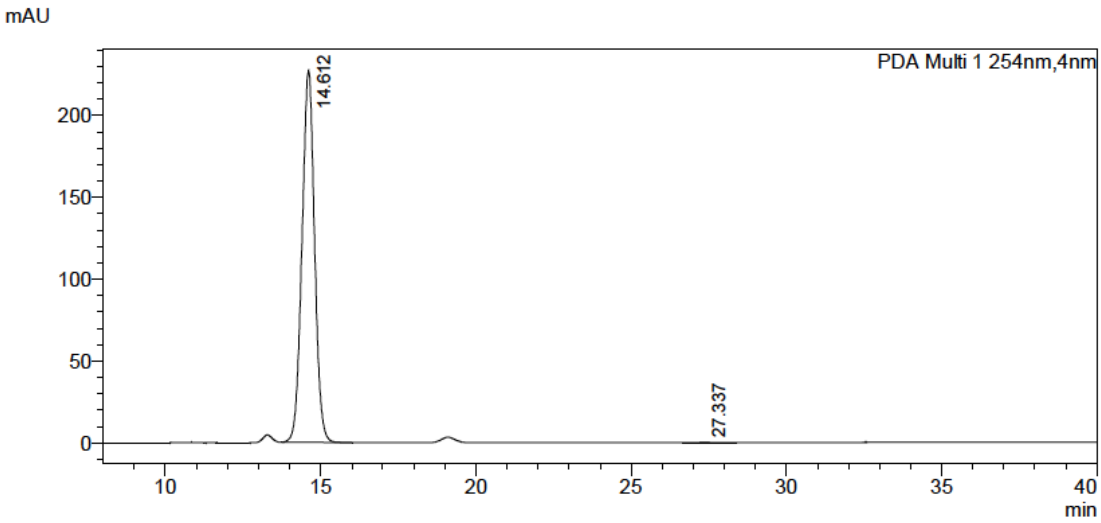
22



<Peak Table>

PDA Ch1 254nm

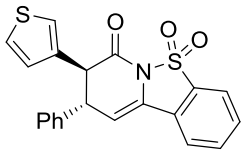
Peak#	Ret. Time	Area%
1	14.412	50.230
2	26.817	49.770
Total		100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	14.612	99.870
2	27.337	0.130
Total		100.000

HPLC data for 23: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 21.7 min, t_R (8*R*,9*R*): 44.0 min; >99% ee.



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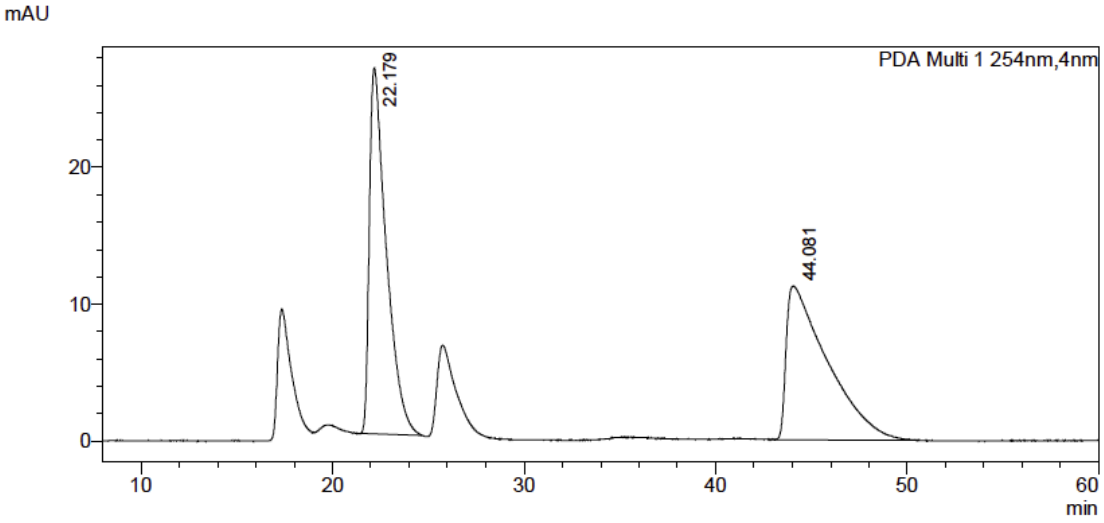
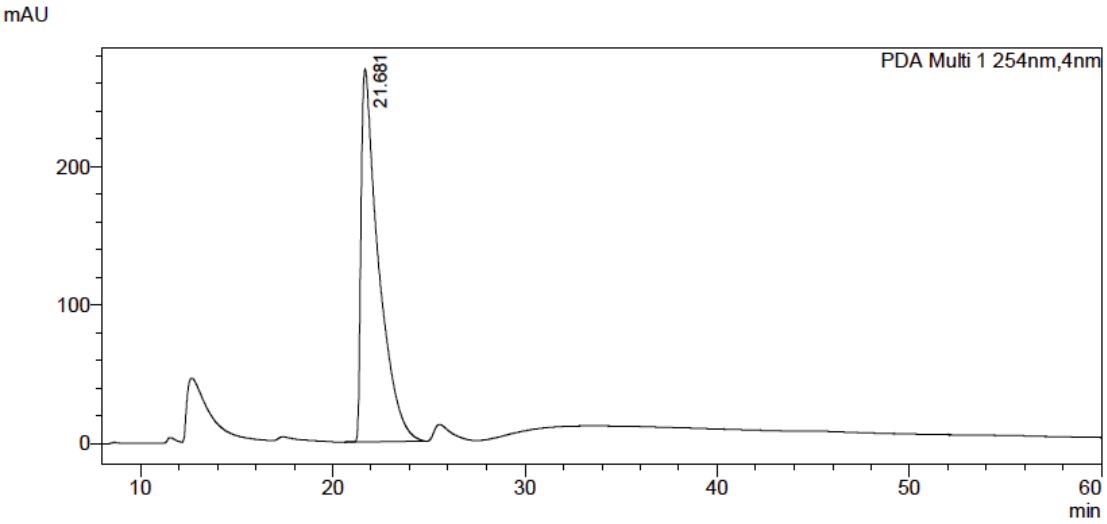


PDA Ch1 254nm

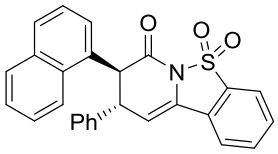
Peak#	Ret. Time	Area%
1	22.179	49.495
2	44.081	50.505
Total		100.000



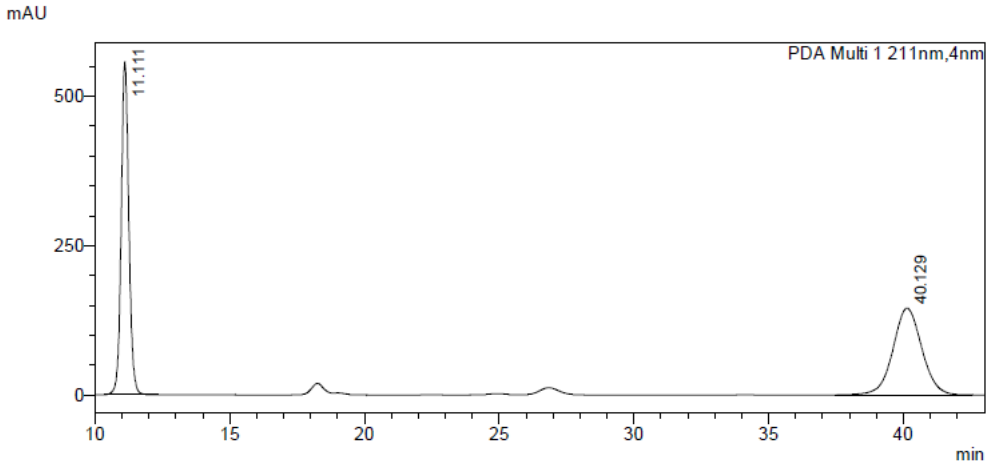
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	21.681	100.000
Total		100.000

HPLC data for **24**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C) t_R (8*S*,9*S*): 11.1 min, t_R (8*R*,9*R*): 40.2 min; 98% ee



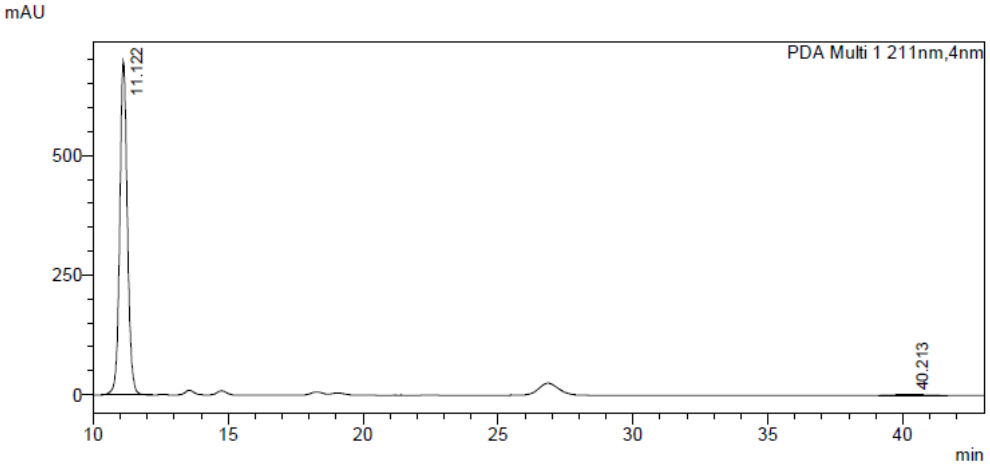
24



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.111	50.377
2	40.129	49.623
Total		100.000

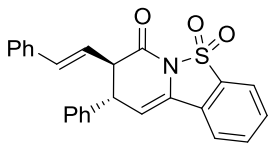


<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	11.122	98.965
2	40.213	1.035
Total		100.000

HPLC data for **25**: Chiral HPLC analysis, Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*R*,9*S*): 15.6 min, t_R (8*S*,9*R*): 25.8 min; 71% ee



25

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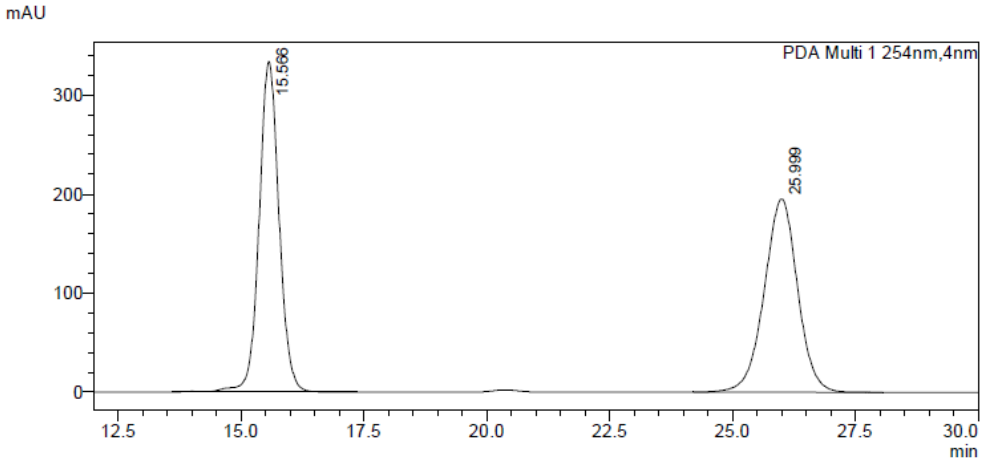
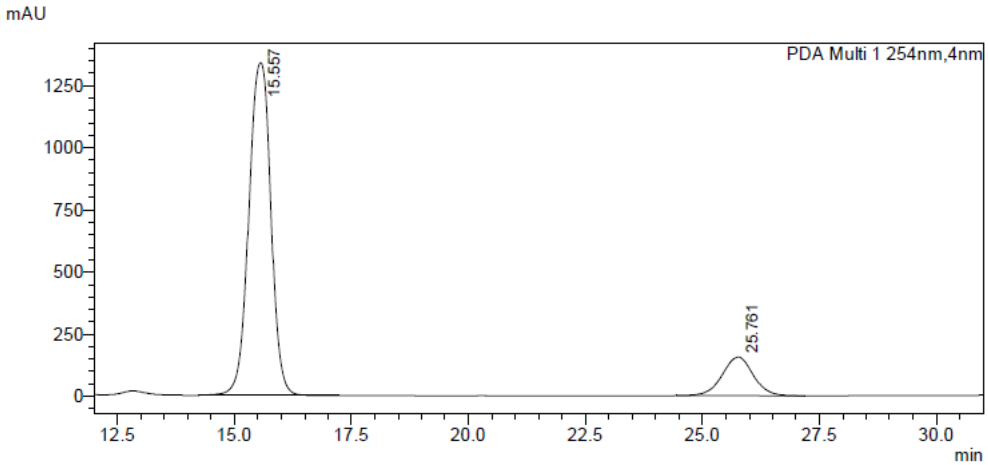


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.566	50.619
2	25.999	49.381
Total		100.000

<Chromatogram>

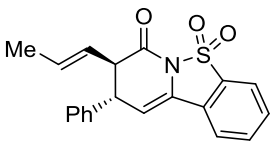


<Peak Table>

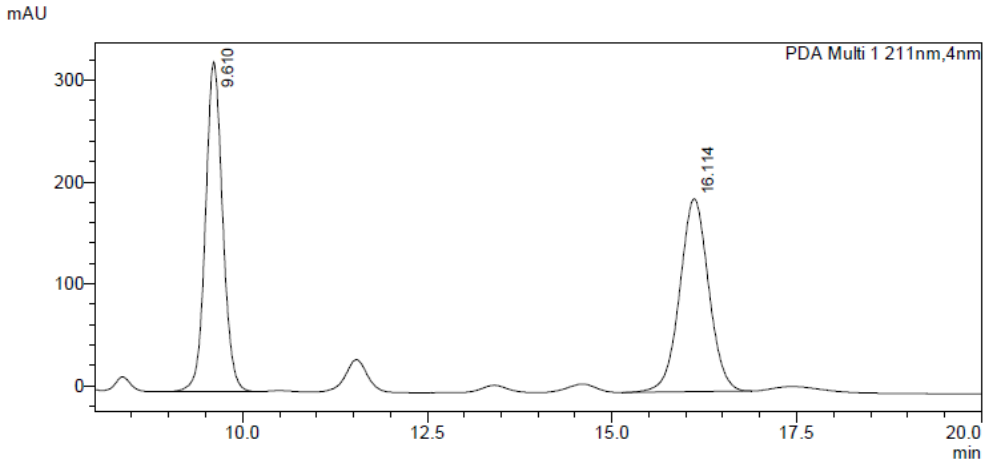
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.557	85.946
2	25.761	14.054
Total		100.000

HPLC data for **26**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C); t_R (8*S*,9*S*): 9.5 min, t_R (8*R*,9*R*): 16.1 min; 99% ee



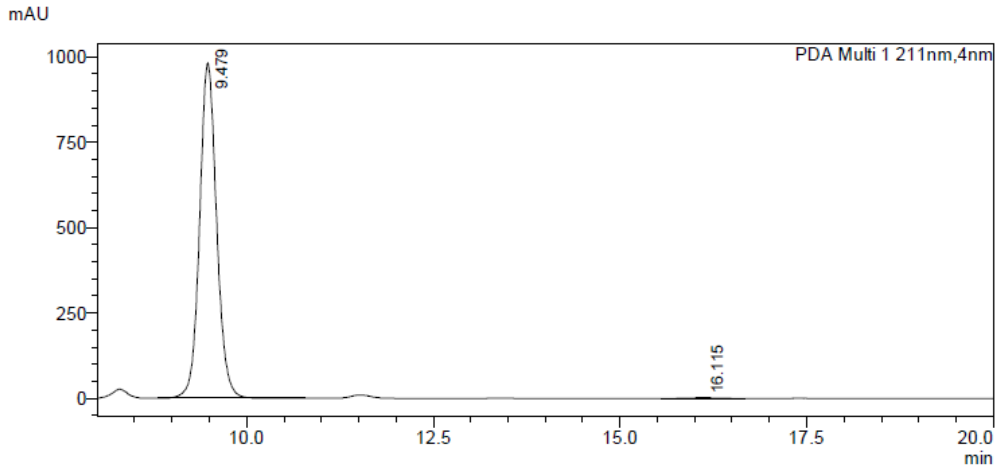
26



<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.610	50.280
2	16.114	49.720
Total		100.000

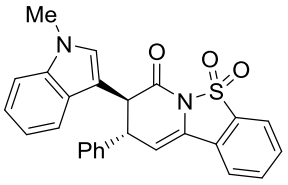


<Peak Table>

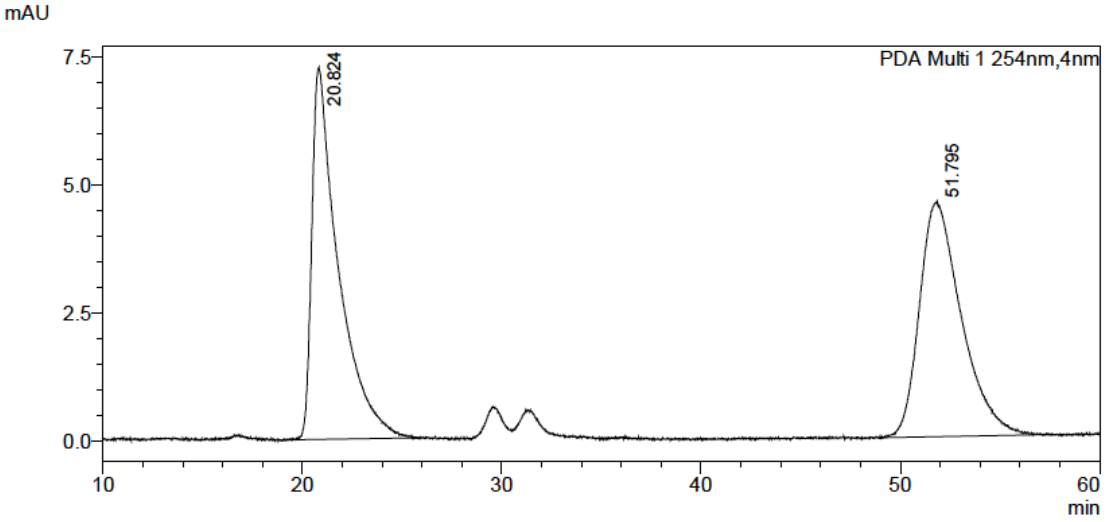
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	9.479	99.665
2	16.115	0.335
Total		100.000

HPLC data for **27**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 254 nm, 30 °C) t_R (8*S*,9*S*): 12.0 min, t_R (8*R*,9*R*): 15.9 min; >99% ee.

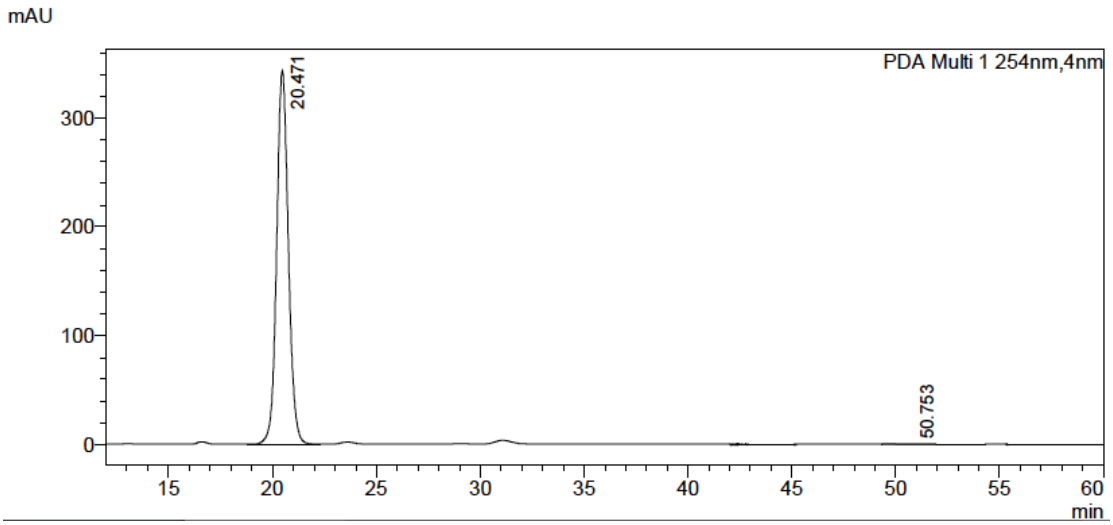


27



PDA Ch1 254nm

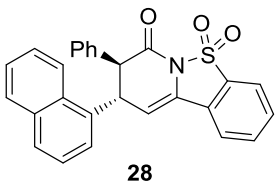
Peak#	Ret. Time	Area%
1	20.824	50.083
2	51.795	49.917
Total		100.000



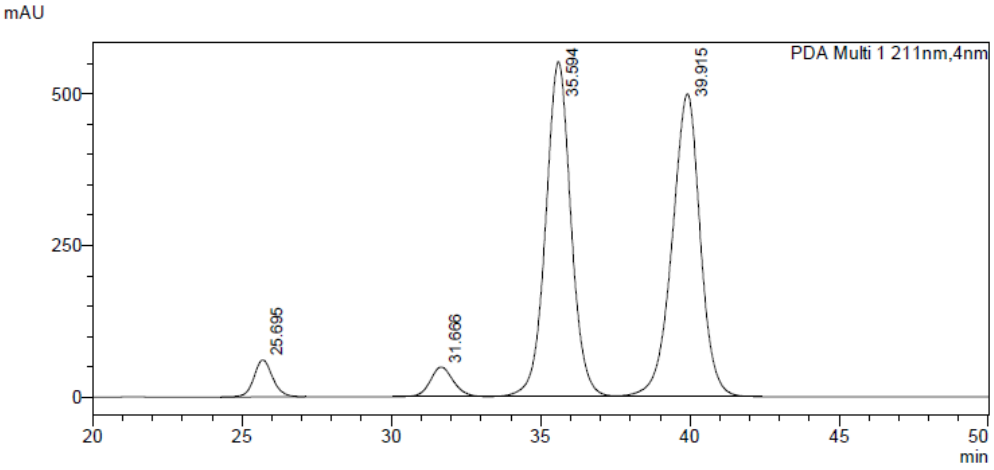
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	20.471	99.713
2	50.753	0.287
Total		100.000

HPLC data for **28**: Chiralpak AD-H (80:20 hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C), t_R (8*R*,9*R*): 35.5 min, t_R (8*S*,9*S*): 39.7 min; >99% ee



28

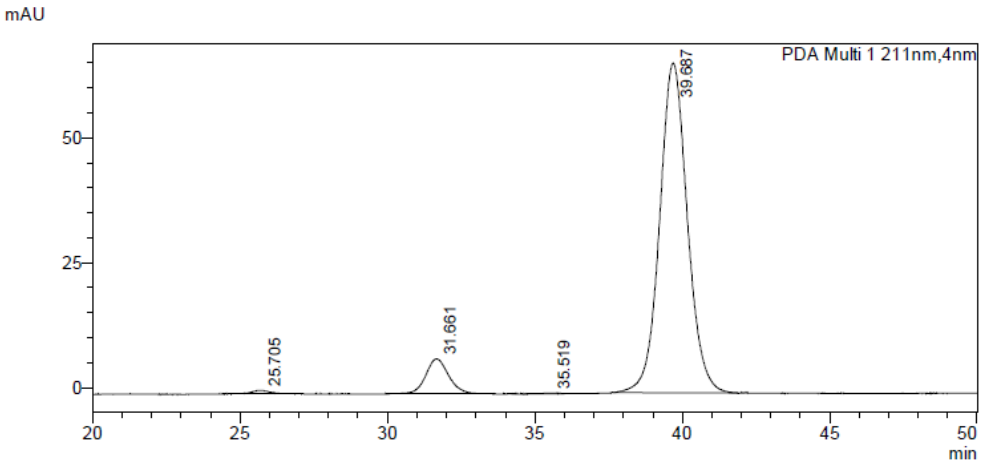


<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	25.695	3.737
2	31.666	3.743
3	35.594	46.148
4	39.915	46.372
Total		100.000

<Chromatogram>

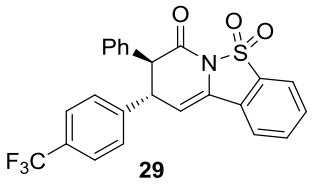


<Peak Table>

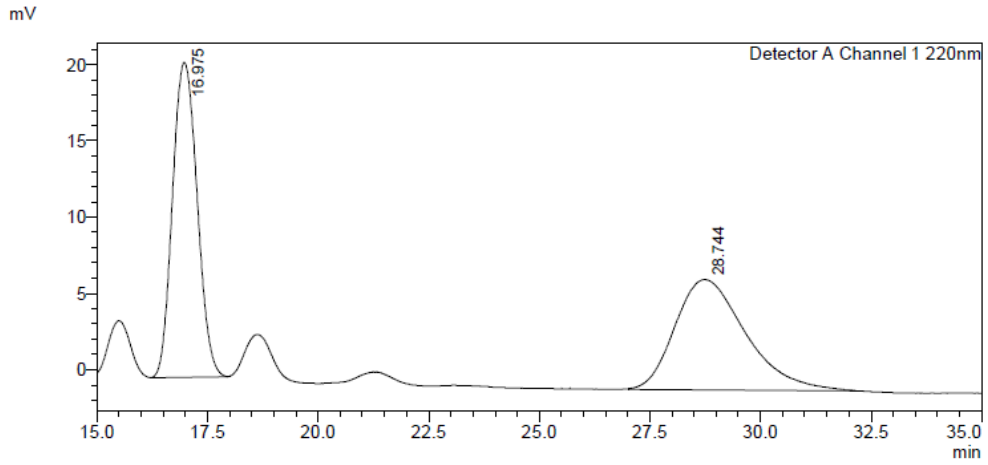
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	25.705	0.459
2	31.661	7.709
3	35.519	0.128
4	39.687	91.704
Total		100.000

HPLC data for **29**: Chiralpak ID (80:20 hexane:IPA, flow rate 1 mLmin^{-1}, 220 nm, 30 °C), t_R (8*R*,9*R*): 16.9 min, t_R (8*S*,9*S*): 27.8 min; 95% ee

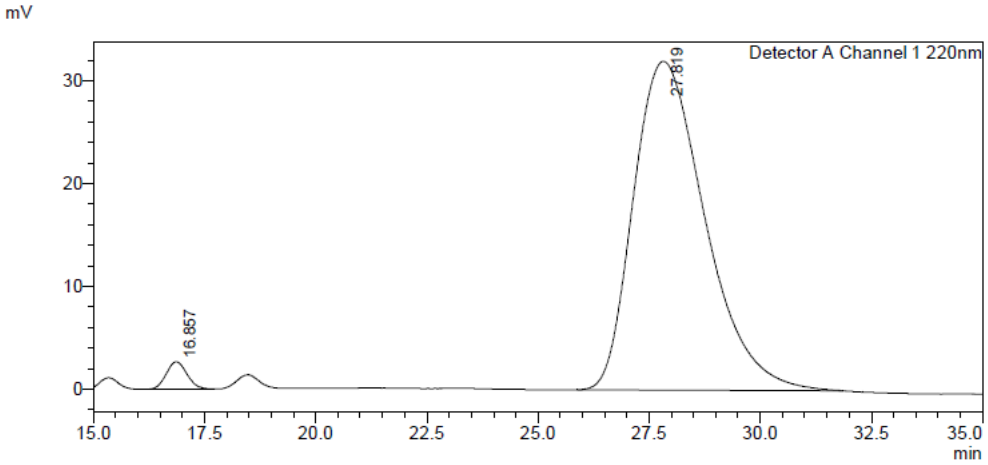


29



Detector A Channel 1 220nm

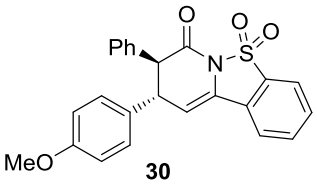
Peak#	Ret. Time	Area%
1	16.975	49.817
2	28.744	50.183
Total		100.000



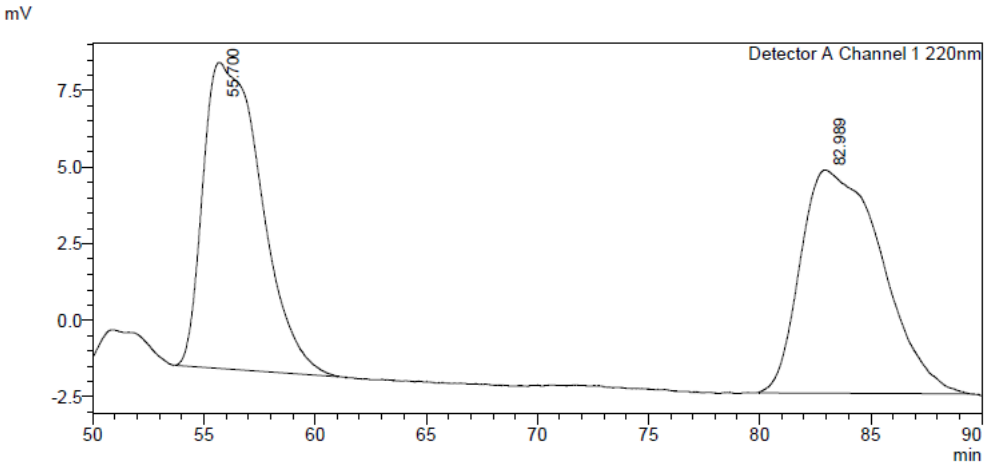
Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	16.857	2.378
2	27.819	97.622
Total		100.000

HPLC data for **30**: Chiralpak AD-H (80:20 hexane:IPA, flow rate 1 mLmin^{-1}, 220 nm, 30 °C) t_R (8*S*,9*S*): 56.7 min, t_R (8*R*,9*R*): 83.3 min; 99% ee

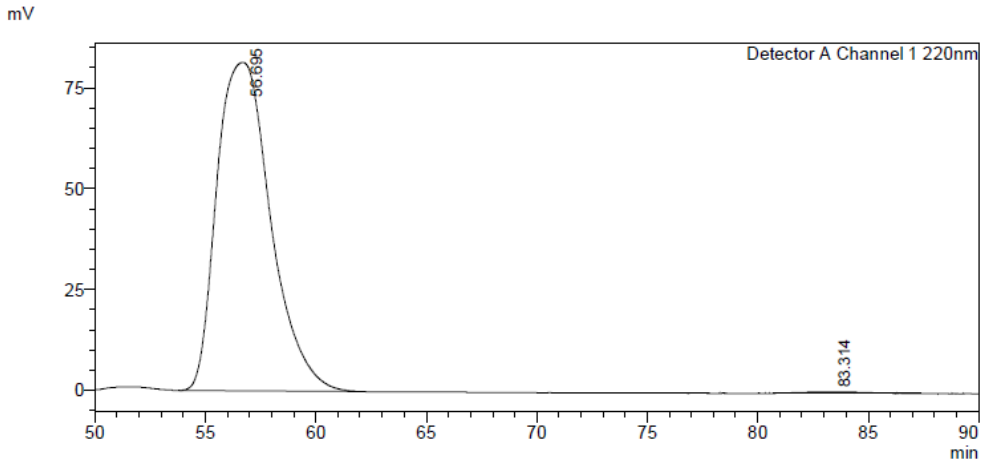


30



Detector A Channel 1 220nm

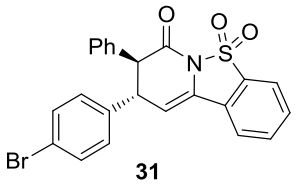
Peak#	Ret. Time	Area%
1	55.700	49.505
2	82.989	50.495
Total		100.000



Detector A Channel 1 220nm

Peak#	Ret. Time	Area%
1	56.695	99.455
2	83.314	0.545
Total		100.000

HPLC data for **31**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C) t_R (8*S*,9*S*): 17.2 min, t_R (8*R*,9*R*): 21.4 min; 99% ee



31

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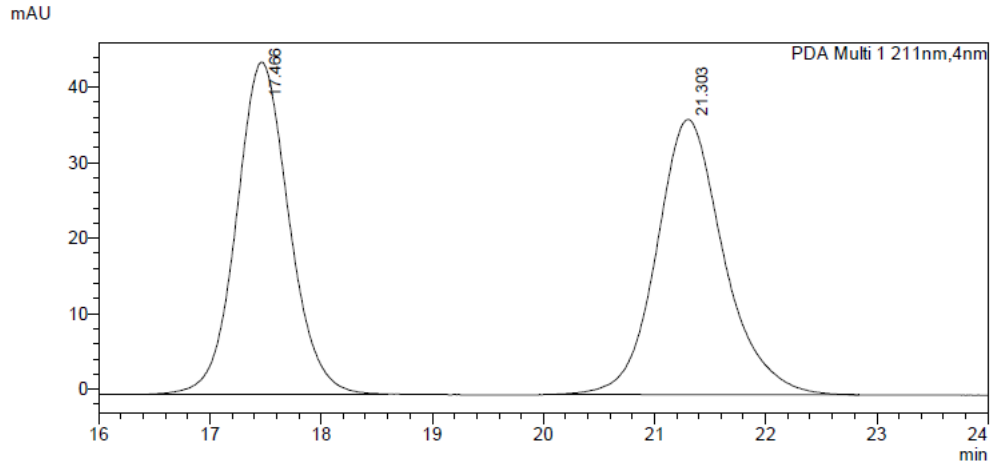
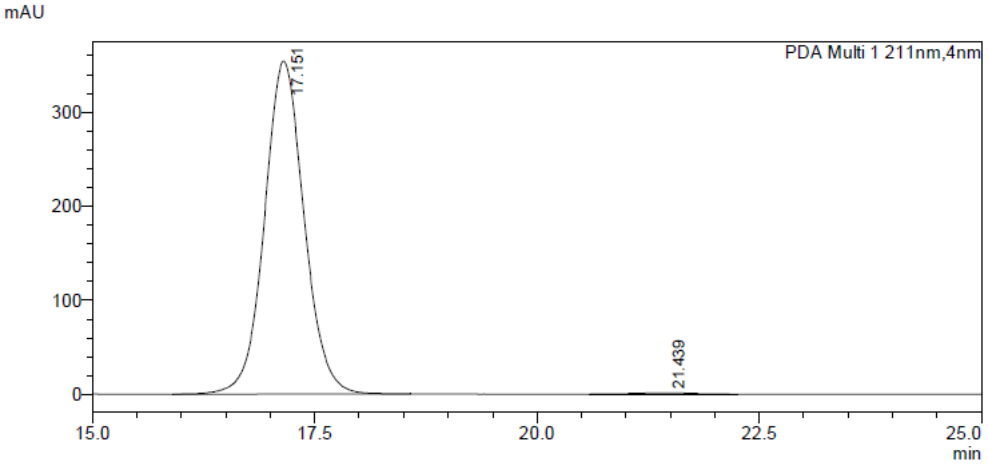


<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.466	48.564
2	21.303	51.436
Total		100.000

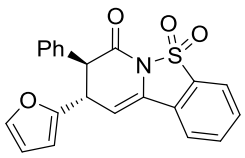


<Peak Table>

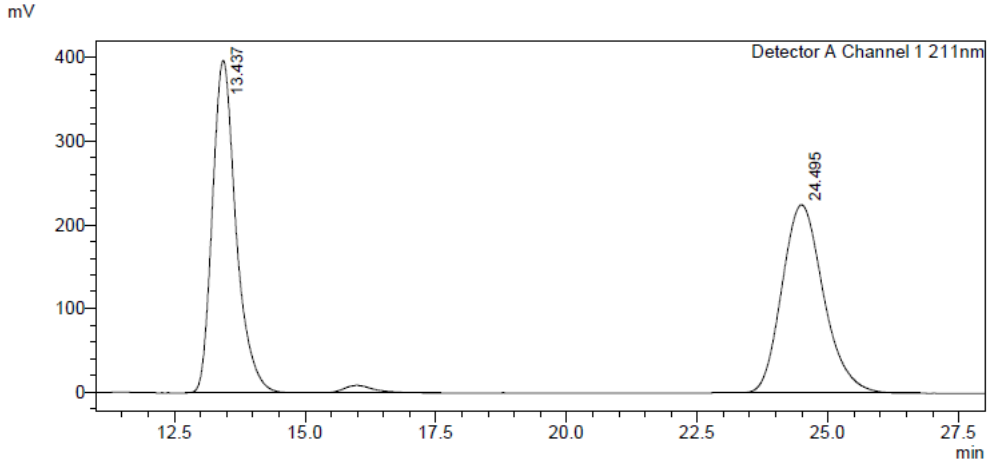
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	17.151	99.451
2	21.439	0.549
Total		100.000

HPLC data for **32**: Chiralpak AD-H (60:40 hexane:IPA, flow rate 1 mLmin^{-1}, 211 nm, 30 °C) t_R (8*S*,9*S*): 13.1 min, t_R (8*R*,9*R*): 23.8 min; 95% ee

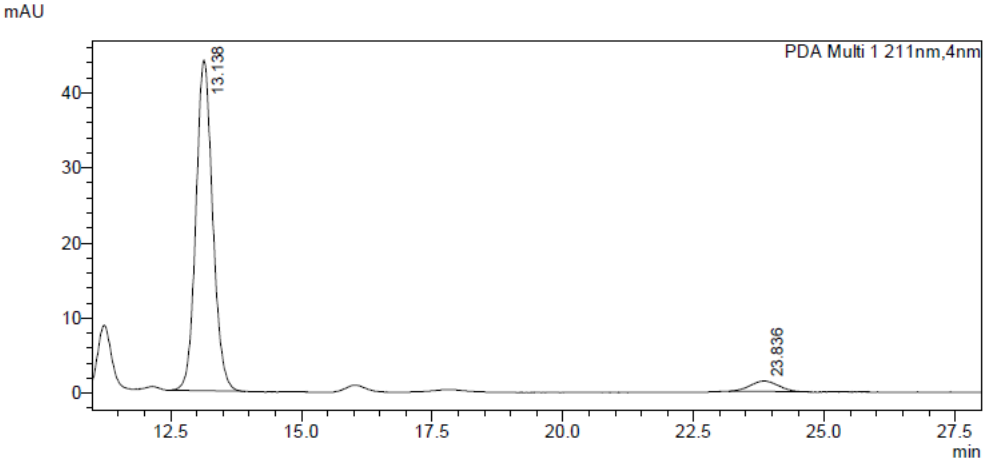


32



Detector A Channel 1 211nm

Peak#	Ret. Time	Area%
1	13.437	50.059
2	24.495	49.941
Total		100.000



PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.138	94.976
2	23.836	5.024
Total		100.000

References and Notes

[1] Q. -R. Zhang, J.-R. Huang, W. Zhang, L. Dong, *Org. Lett.* **2014**, *16*, 1684-1687.

[2] M. Rommel, T. Fukuzumi, J. W. Bode, *J. Am. Chem. Soc.* **2008**, *130*, 17266-17267.

[3] X. Feng, Z. Zhou, C. Ma, X. Yin, R. Li, L. Dong, Y.-C. Chen, *Angew. Chem. Int. Ed.* **2013**, *52*, 14173-14176.

[4] R. A. Abramovitch, I. Shinkai, B. J. Mavunkel, K. M. More, S. O'Connor, G. H. Ooi, W. T. Pennington, P. C. Srinivasan, J. R. Stowers, *Tetrahedron* **1996**, *52*, 3339-3354.

[5] J. Izquierdo, M. A. Pericàs, *ACS Catalysis* **2016**, *6*, 348-356.