

## Supporting Information

### New Synthetic Routes to (+)-Uleine and (-)-Tubifolidine: General Approach to 2-Azabicyclo[3.3.1]nonane Indole Alkaloids

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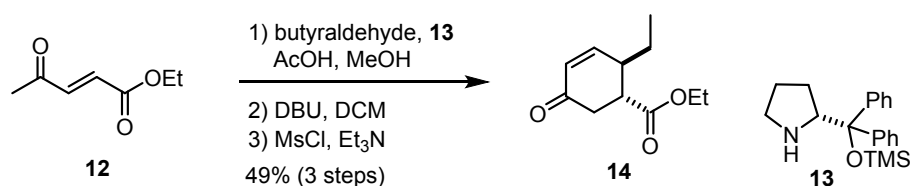
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## Experimental Section

### General information

Unless otherwise stated, reactions were performed under an argon atmosphere using freshly dried solvents. Tetrahydrofuran, dichloromethane, toluene, and ethyl ether were dried by passing through activated alumina columns. *N,N*-diisopropylethylamine was distilled over calcium hydride and stored over potassium hydroxide pellets in an amber glass bottle. Degassing was carried out by standard freeze-pumping-thaw cycle. All other commercially obtained reagents were used as received. Reactions at elevated temperatures were run in an oil bath. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). The TLC spots were visualized under UV lamp or using staining solutions such as ceric ammonium molybdate solution, *p*-anisaldehyde solution, ninhydrin solution or potassium permanganate solution. Flash column chromatography was performed with indicated solvents using silica gel (GS60 – 40/75) purchased from Fuji Silysia Chemical. <sup>1</sup>H NMR and <sup>13</sup>C spectra were recorded on Bruker Avance III HD spectrometer at 400MHz and 100MHz, respectively. Chemical shifts are reported relative to tetramethylsilane (0 ppm) or internal chloroform (<sup>1</sup>H,  $\delta$  = 7.26, <sup>13</sup>C,  $\delta$  = 77.16), internal DMSO (<sup>1</sup>H,  $\delta$  = 2.50, <sup>13</sup>C,  $\delta$  = 39.52) as indicated. Infrared spectra were recorded on Bruker LUMOS FT-IR spectrometer equipped with a microscope and mercury cadmium telluride (MCT) detector. Optical rotations were measured on a Jasco P-1020 polarimeter (light source= Na, 589nm). HRMS were measured by using ESI method at the Korean Basic Research Center, Ochang, Cheongju, Republic of Korea. Optical purity assay was conducted on Shimadzu HPLC (LC-20A Prominence Series) using Chiralpak® IA, AS (5  $\mu$ m particle size, 4.6 mm x 250 mm) with i-PrOH and n-hexane as mobile phases.

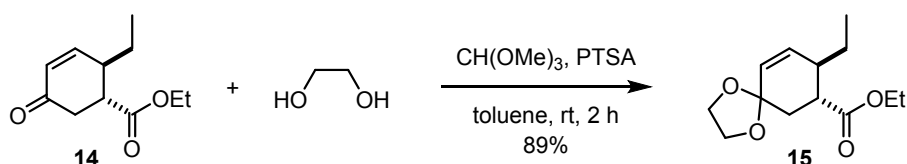
### Ethyl (1R,2R)-2-ethyl-5-oxocyclohex-3-ene-1-carboxylate (**14**)



Enone **14** was prepared in 93% ee by modification of the process reported in the literature.<sup>[1]</sup> To a solution of enoate **12** (7.15 g, 50.3 mmol), Hayashi-Jorgensen catalyst **13** (0.82 g, 2.5 mmol) and acetic acid (0.14 mL, 2.5 mmol) in MeOH (50 mL) was added butyraldehyde (9.1 mL, 100.6 mmol) at 0 °C. The resulting mixture was stirred for 1 h at 0 °C, warmed to rt and stirred for 20 h. The reaction mixture was then quenched with saturated NaHCO<sub>3</sub> (aq) solution and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/6) to give the corresponding Michael

adduct as a colorless oil. To a solution of the above Michael adduct dissolved in DCM (50 mL) was added DBU (15 mL, 101.6 mmol) at 0 °C. After 1 h at 0 °C, the solution was warmed to rt and stirred for 5 h. The reaction mixture was then quenched with saturated NaHCO<sub>3</sub> (aq) and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated and used directly for the next reaction without further purification. To a solution of crude aldol product in DCM (100 mL) were added MsCl (11.7 mL, 151 mmol) and Et<sub>3</sub>N (42.1 mL, 302 mmol) at 0 °C. After 1 h at 0 °C, the reaction mixture was warmed to rt and stirred for 12 h. The reaction mixture was then quenched with saturated NaHCO<sub>3</sub> (aq), and the mixture was extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/15) to give cyclohexenone **14** (4.84 g, 49% in 3 steps from **12**), along with cis-isomer **14'** (1.78 g, 18% from **12**) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.85 (dd, *J* = 10.2, 3.0 Hz, 1H), 6.01 (dd, *J* = 10.2, 2.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.89 (ddd, *J* = 9.4, 8.4, 6.0 Hz, 1H), 2.82 – 2.74 (m, 1H), 2.70 – 2.57 (m, 2H), 1.71 – 1.46 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 196.9, 173.4, 152.3, 129.0, 61.1, 45.1, 39.4, 38.9, 25.9, 14.2, 10.9; FT-IR (CH<sub>2</sub>Cl<sub>2</sub>) 2965, 2940, 2875, 1732, 1685, 1459, 1387, 1277, 1179, 1034, 861, 775 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>11</sub>H<sub>16</sub>NaO<sub>3</sub> [M+Na]<sup>+</sup> 219.0997, found 219.0998; [α]<sub>D</sub><sup>25</sup> = -131.3 (*c* 0.7, CHCl<sub>3</sub>); HPLC (Chiralpak IA, hexane/*i*-PrOH = 95:5, flow rate 1 mL/min, λ = 218 nm), *t*<sub>R</sub> = 6.41 (minor), 6.97 (major) min; ee = 93%.

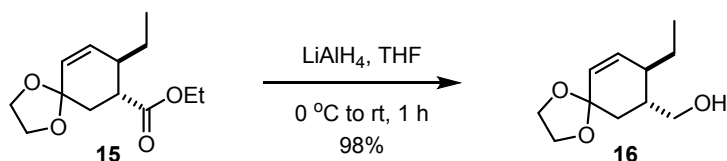
#### Ethyl (7R,8R)-8-ethyl-1,4-dioxaspiro[4.5]dec-9-ene-7-carboxylate (**15**)



To a solution of cyclohexenone **14** (3.56 g, 18.1 mmol) in toluene (18 mL) were added ethylene glycol (30 mL, 540.0 mmol), trimethyl orthoformate (2.18 mL, 20.0 mmol), and *p*-TsOH (345 mg, 1.8 mmol) at rt. After 2 h, the reaction mixture was quenched with saturated NaHCO<sub>3</sub> (aq) and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/20) to give acetal **15** (3.88 g, 89%) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.83 (dd, *J* = 10.2, 2.3 Hz, 1H), 5.60 (ddd, *J* = 10.2, 2.5, 1.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.04 – 3.89 (m, 4H), 2.64 (ddd, *J* = 12.6, 10.0, 3.6 Hz, 1H), 2.49 – 2.41 (m, 1H), 2.05 – 1.91 (m, 2H), 1.58 – 1.31 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 174.8, 135.0, 127.1, 105.3, 65.0, 64.7, 60.6, 44.1, 38.9, 36.5, 26.3, 14.4, 10.5; FT-IR (CH<sub>2</sub>Cl<sub>2</sub>) 2949, 2930, 2881, 1732, 1687, 1459, 1381, 1275, 1175, 1099, 1036, 920 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>13</sub>H<sub>20</sub>NaO<sub>4</sub> [M+Na]<sup>+</sup> 263.1259, found

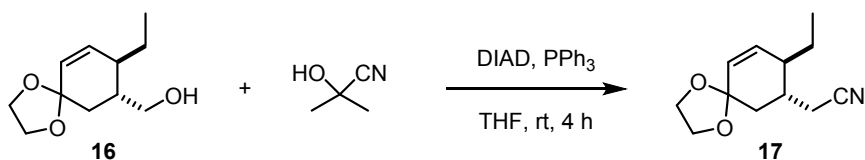
263.1259;  $[\alpha]_D^{27} = -44.1$  ( $c$  0.75,  $\text{CHCl}_3$ ).

**((7R, 8R)-8-Ethyl-1,4-dioxaspiro[4.5]dec-9-en-7-yl)methanol (**16**)**



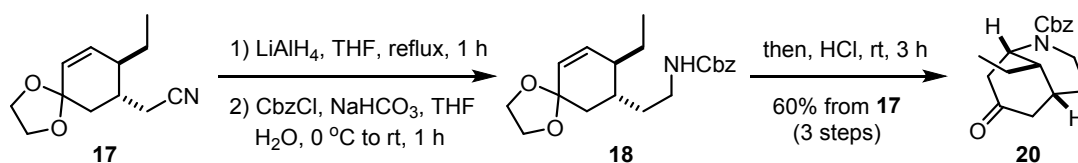
To a suspension of  $\text{LiAlH}_4$  (1.13 g, 29.8 mmol) in THF (50 mL) was cannulated acetal **15** (3.59 g, 14.9 mmol) at 0 °C. The reaction mixture was warmed to rt, stirred for 1 h, cooled to 0 °C and then quenched by sequentially adding  $\text{H}_2\text{O}$  (1.2 mL), 15%  $\text{NaOH}$  (aq) solution (1.2 mL), and  $\text{H}_2\text{O}$  (3.4 mL). The mixture was dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed ( $\text{EtOAc}/\text{hexane} = 1/1$ ) to give alcohol **16** (2.90 g, 98%) as a colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.86 (dd,  $J = 10.1, 3.0$  Hz, 1H), 5.61 (dd,  $J = 10.1, 1.4$  Hz, 1H), 4.05 – 3.81 (m, 4H), 3.78 – 3.59 (m, 2H), 2.01 (ddd,  $J = 13.1, 3.1, 0.9$  Hz, 1H), 1.97 – 1.84 (m, 2H), 1.77 (dd,  $J = 13.1, 9.3$  Hz, 1H), 1.71 (brs, 1H), 1.62 – 1.36 (m, 2H), 0.93 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  136.0, 126.8, 105.8, 64.9, 64.8, 64.5, 38.6, 37.9, 34.8, 25.5, 11.0; FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 3434, 2962, 2879, 1656, 1459, 1399, 1201, 1144, 1073, 1022, 957  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{11}\text{H}_{18}\text{NaO}_3$   $[\text{M}+\text{Na}]^+$  221.1154, found 221.1156;  $[\alpha]_D^{26} = -61.8$  ( $c$  0.69,  $\text{CHCl}_3$ ).

**2-((7R,8S)-8-Ethyl-1,4-dioxaspiro[4.5]dec-9-en-7-yl)acetonitrile (**17**)**

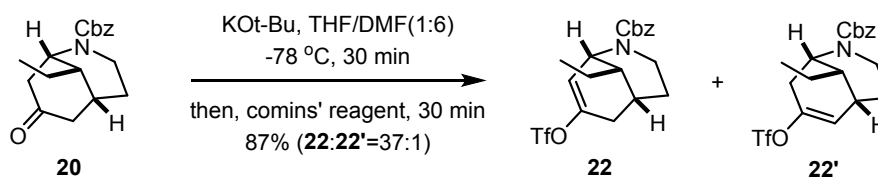


To a mixture of alcohol **16** (2.9 g, 14.6 mmol),  $\text{PPh}_3$  (11.5 g, 43.8 mmol), and acetone cyanohydrin (2.67 mL, 29.2 mmol) in THF (50 mL) was added DIAD (8.63 mL, 43.8 mmol) at 0 °C. The resulting mixture was warmed to rt, stirred for 4 h, quenched with saturated  $\text{NaHCO}_3$  (aq), and extracted with  $\text{EtOAc}$  (3 x 50 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed ( $\text{EtOAc}/\text{hexane} = 1/4$ ) to give nitrile **17** containing small amounts of inseparable byproducts. This mixture was used for the next reaction without further purification.

**Benzyl (1S,5R,9S)-9-ethyl-7-oxo-2-azabicyclo[3.3.1]nonane-2-carboxylate (**20**)**

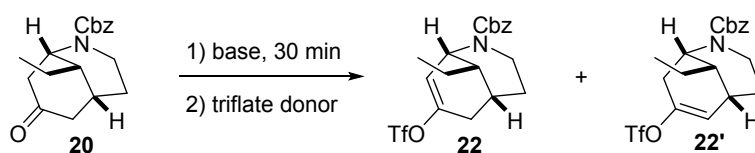


To a suspension of  $\text{LiAlH}_4$  (1.11 g, 29.2 mmol) in THF (50 mL) was cannulated nitrile **17** at 0 °C and the resulting mixture was heated under reflux. After 1 h, the reaction mixture was cooled to 0 °C and quenched by sequentially adding  $\text{H}_2\text{O}$  (1.1 mL), 15%  $\text{NaOH}$  (aq) solution (1.1 mL), and  $\text{H}_2\text{O}$  (3.3 mL). The mixture was warmed to rt, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and used for the next reaction without further purification. To this crude amine product were added THF (25.0 mL),  $\text{H}_2\text{O}$  (25.0 mL),  $\text{NaHCO}_3$  (1.84 g, 21.9 mmol) and benzyl chloroformate (3.1 mL, 21.9 mmol) slowly at 0 °C. The reaction mixture was then warmed to rt and stirred for 1 h. After completion of the reaction, the reaction mixture was added with hydrochloric acid (5 mL), stirred for 3 h, diluted with  $\text{H}_2\text{O}$  (50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/6) to give ketone **20** (2.70 g, 60%) as a colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  7.40 – 7.28 (m, 5H), 5.19 – 5.05 (m, 2H), 4.70 and 4.59 (2s, 1H), 4.10 and 4.01 (2dd,  $J$  = 14.5, 4.8 Hz, 1H), 2.96 – 2.78 (m, 1H), 2.65 – 2.49 (m, 2H), 2.48 – 2.26 (m, 3H), 1.91 – 1.66 (m, 3H), 1.62 – 1.44 (m, 2H), 1.08 – 0.97 (m, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  210.4, 209.9, 155.2, 154.9, 136.8, 136.6, 128.6, 128.1, 127.9, 127.8, 67.3, 52.1, 51.8, 42.0, 41.8, 41.7, 41.6, 41.4, 37.1, 36.9, 32.3, 32.1, 31.7, 31.6, 23.8, 11.6; FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 2952, 2938, 2881, 1695, 1424, 1344, 1232, 1116, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{18}\text{H}_{23}\text{NNaO}_3$   $[\text{M}+\text{Na}]^+$  324.1576, found 324.1577;  $[\alpha]_{\text{D}}^{25} = +63.6$  ( $c$  1.03,  $\text{CHCl}_3$ ).



isomer)  $\delta$  7.41 – 7.27 (m, 5H), 5.76 (d,  $J$  = 7.4 Hz, 1H), 5.09 (s, 2H), 4.74 (d,  $J$  = 5.0 Hz, 1H), 3.88 – 3.76 (m, 1H), 2.98 (m, 1H), 2.62 – 2.53 (m, 1H), 2.28 – 2.17 (m, 2H), 1.74 – 1.59 (m, 2H), 1.58 – 1.48 (m, 1H), 1.35 – 1.13 (m, 2H), 0.89 (t,  $J$  = 7.3 Hz, 3H); FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 3362, 2956, 2920, 1701, 1418, 1289, 1212, 1142, 1055, 887  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{19}\text{H}_{22}\text{F}_3\text{NNaO}_5\text{S}$   $[\text{M}+\text{Na}]^+$  456.1068, found 456.1071.

**Table 1. Preparation of enol triflate **22**<sup>a</sup>**

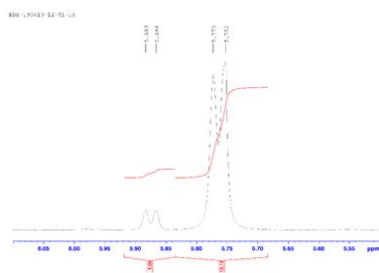


entry	conditions	yield ( <b>22</b> : <b>22'</b> ) <sup>b</sup>
1	KOt-Bu, THF, -78 °C, Comins' reagent, 30 min	84% (10:1)
2	KOt-Bu, THF, -78 °C, PhNTf <sub>2</sub> , 30 min	70% (N/A) <sup>c</sup>
3	LDA, THF, -78 °C, Comins' reagent, 3 h	30% (2:1)
4	LiHMDS, THF, -78 °C, Comins' reagent, 2 h	74% (6:1)
5	NaHMDS, THF, -78 °C, Comins' reagent, 30 min	84% (6:1)
6	KHMDS, THF, -78 °C, Comins' reagent, 30 min	83% (8:1)
7	KOt-Bu, THF, -95 °C, Comins' reagent, 30 min	89% (12:1)
8	KOt-Bu, THF, 0 °C, Comins' reagent, 30 min	80% (8:1)
9	KOt-Bu, THF/DMF (1:1), -78 °C, Comins', 30 min	89% (18:1)
10	KOt-Bu, THF/DMF (1:6), -78 °C, Comins', 30 min	87% (37:1)

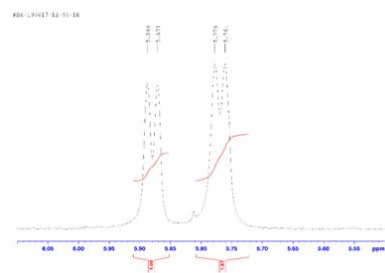
<sup>a</sup>Conditions: **20** (0.07 mmol), base (0.08 mmol), solvent (1.4 mL), 30 min, then triflate source (0.08 mmol). <sup>b</sup>Combined yields, the product ratios were determined using the <sup>1</sup>H NMR integrals of the vinyl protons **22** and **22'**, respectively. <sup>c</sup>Exact yield and ratio were not determined due to the inseparable byproducts.

#### <sup>1</sup>H NMR integrals of the vinyl protons (entries 1, 3 ~ 9)

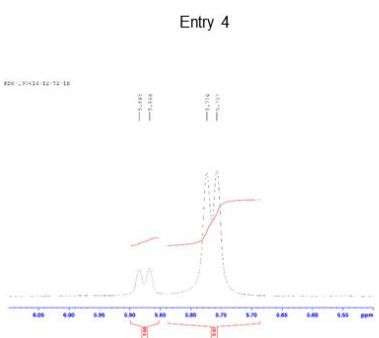
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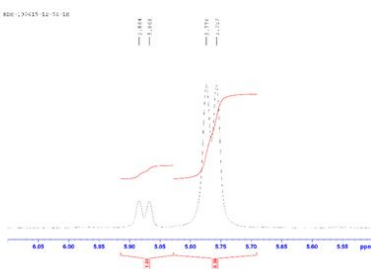
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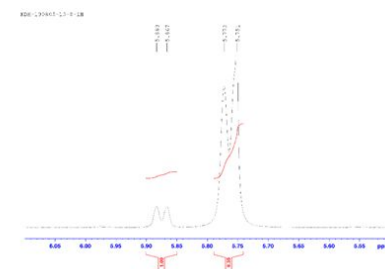
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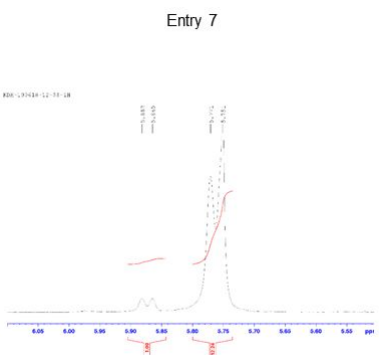
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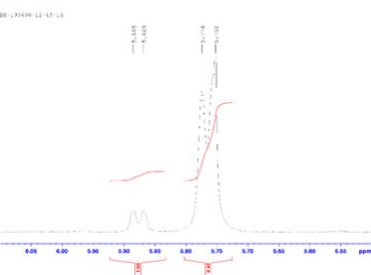
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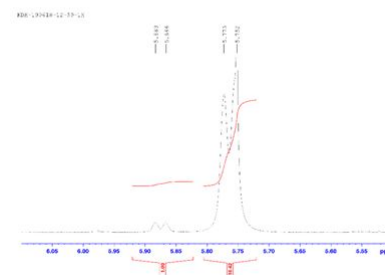
Entry 6



Entry 7



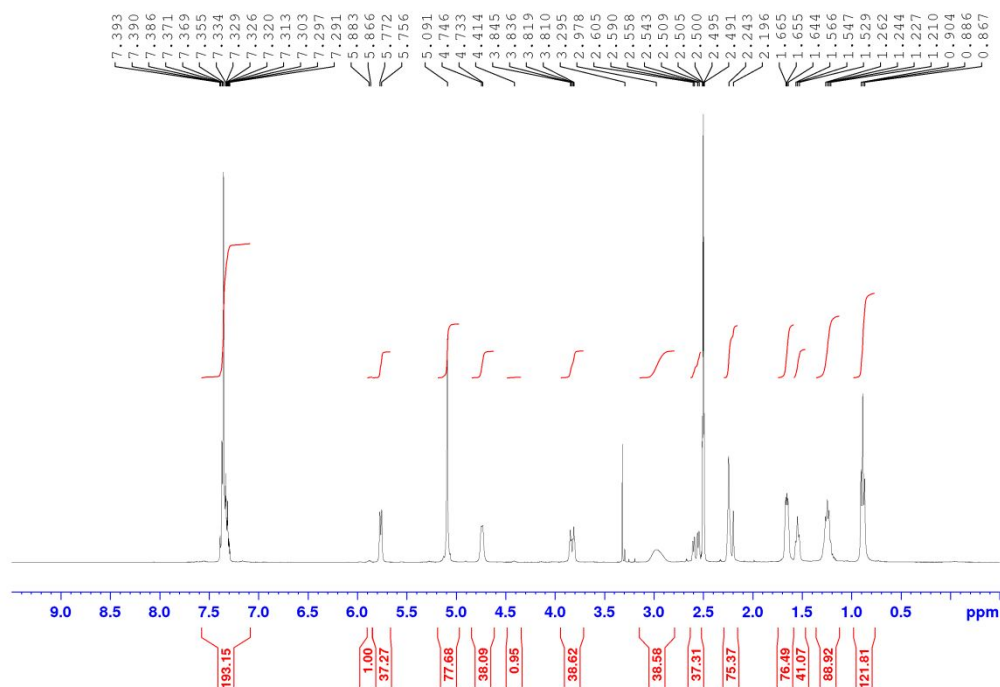
Entry 8



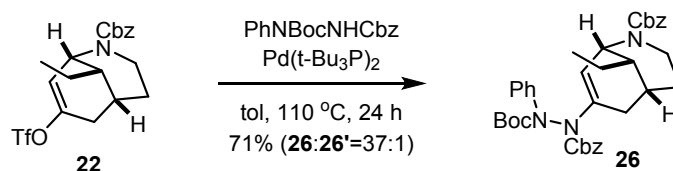
Entry 9

**Full <sup>1</sup>H NMR spectrum with integrals of the vinyl protons in entry 10 (22:22' = 37:1)**

KDH-SI-uleine-22-1H in DMSO



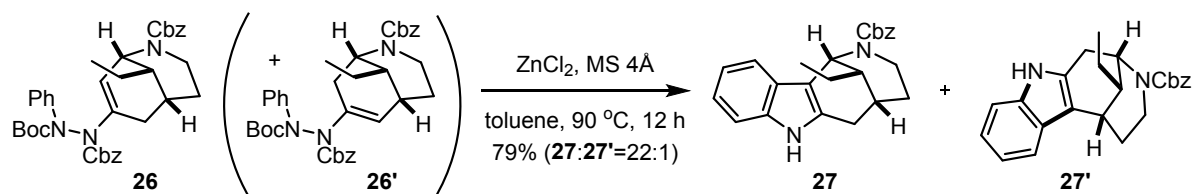
**1-Benzyl 2-(*tert*-butyl) 1-((1*R*,5*R*,9*S*)-2-((benzyloxy)carbonyl)-9-ethyl-2-azabicyclo[3.3.1]non-7-en-7-yl)-2-phenylhydrazine-1,2-dicarboxylate (**26**)**



To a Schlenk tube charged with enol triflate **22** (1.31 g, 3.02 mmol) were added  $\text{Pd}(\text{t-Bu}_3\text{P})_2$  (0.08 g, 0.15 mmol),  $\text{Cs}_2\text{CO}_3$  (1.97 g, 6.03 mmol),  $\text{PhNBocNHCbz}$  (1.14 g, 3.32 mmol) and toluene (15 mL) at rt. The resulting mixture was degassed with freeze-pump-thaw cycles ( $\times 2$ ). The reaction was heated at  $110^\circ\text{C}$  and stirred for 24 h. The reaction mixture was cooled to rt, filtered through a pad of silica gel with the aid of EtOAc (100 mL). The filtrate was concentrated and purified by flash column chromatography (EtOAc/Hexane = 1/10) to give ene-hydrazide **26** containing small amounts of regioisomer **26'** ( $\text{26:26'} = 37:1$ , 1.34 g, 2.14 mmol, 71% total yield) as yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ ) (spectral data contain the peaks corresponding to the Cbz rotamer and minor regio-isomer)  $\delta$  7.59 – 7.01 (m, 15H), 5.44 – 5.29 (m, 1H), 5.21 (s, 2H), 5.04 (s, 2H), 4.59 – 4.38 (m, 1H), 3.85 – 3.38 (m, 1H), 2.94 – 2.59 (m, 1H), 2.38 – 2.11 (m, 1H), 2.05 (s, 1H), 2.02 – 1.39 (m, 4H), 1.34 (s, 9H), 1.21 – 0.98 (m, 2H), 0.98 – 0.61 (m, 3H); FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 3028, 2965, 2926, 1726, 1493, 1303, 1161, 752,  $695\text{ cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{37}\text{H}_{43}\text{N}_3\text{NaO}_6$   $[\text{M}+\text{Na}]^+$  648.3050, found 648.3051.

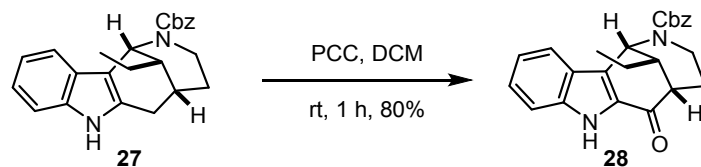


**Benzyl (1R,5R,12S)-12-ethyl-1,3,4,5,6,7-hexahydro-2H-1,5-methanoazocino[4,3-*b*]indole-2-carboxylate (**27**)**



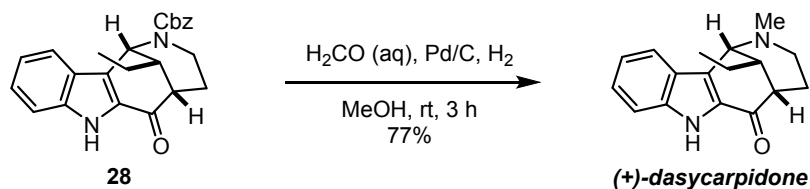
To a sealed tube charged with ZnCl<sub>2</sub> (0.61 g, 4.46 mmol) were added ene-hydrazide **26** (1.27 g, 2.03 mmol), molecular sieve (4Å, 1.00 g) and toluene (20 mL) at rt. The resulting solution was heated at 90 °C for 12 h, cooled to rt, quenched by saturated NaHCO<sub>3</sub> (aq), and extracted with EtOAc (3 x 20 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/4) to give indole **27** (0.58 g, 1.54 mmol, 76%) and regioisomer **27'** (0.02 g, 3%). **27**: yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 7.92 (s, 1H), 7.76– 7.24 (m, 7H), 7.16 – 6.89 (m, 2H), 5.61 and 5.47 (2d, *J* = 2.2 Hz, 1H), 5.33 and 5.22 (2d, *J* = 12.3 Hz, 0.9H), 5.17 and 5.04 (2d, *J* = 12.4 Hz, 1.1H), 3.88 and 3.78 (2dd, *J* = 13.5, 5.8 Hz, 1H), 3.07 – 2.94 (m, 1H), 2.76 – 2.61 (m, 1H), 2.55 (dd, *J* = 17.5, 5.4 Hz, 1H), 2.32 (s, 1H), 1.98 – 1.81 (m, 2H), 1.71 – 1.61 (m, 1H), 1.38 – 1.15 (m, 2H), 0.93 and 0.91 (2t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 155.5, 155.2, 137.2, 137.1, 136.3, 136.2, 135.6, 128.7, 128.5, 128.4, 128.2, 127.9, 127.8, 127.1, 126.9, 121.4, 121.3, 119.7, 119.6, 119.1, 118.4, 110.6, 110.5, 107.4, 106.9, 67.2, 67.0, 48.0, 47.7, 43.7, 43.4, 36.9, 36.8, 33.6, 33.4, 29.5 (x 2), 25.2, 23.6 (x 2), 12.0 (spectral data are identical to those reported in the literature<sup>[2]</sup>); [α]<sub>D</sub><sup>25</sup> = +89.1 (*c* 0.37, CHCl<sub>3</sub>), lit.<sup>[2b]</sup> [α]<sub>D</sub><sup>25</sup> = 89.0 (*c* 0.3, CHCl<sub>3</sub>), lit.<sup>[2c]</sup> [α]<sub>D</sub><sup>28</sup> = 89.4 (*c* 0.4, CHCl<sub>3</sub>); **27'**: yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 7.82 and 7.80 (2brs, 1H), 7.51 – 7.27 (m, 7H), 7.16 – 7.06 (m, 2H), 5.24 – 5.07 (m, 2H), 4.67 and 4.58 (2s, 1H), 3.94 and 3.86 (2dd, *J* = 13.3, 4.6 Hz, 1H), 3.31 (s, 1H), 3.13 – 2.98 (m, 1H), 2.77 (td, *J* = 13.0, 4.5 Hz, 1H), 2.70 – 2.56 (m, 1H), 1.96 – 1.69 (m, 3H), 1.34 – 1.19 (m, 1H), 0.93 and 0.92 (2t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 156.0, 155.5, 137.2, 137.1, 136.5, 132.5, 132.1, 128.7, 128.6, 128.1, 127.9, 127.3, 121.3, 119.4, 117.6, 110.8, 110.0, 67.1, 49.9, 49.7, 43.3, 43.1, 37.7, 31.1, 30.8, 29.1, 29.0, 26.5, 26.1, 23.8, 11.9.

**Benzyl (1R,5S,12S)-12-ethyl-6-oxo-1,3,4,5,6,7-hexahydro-2H-1,5-methanoazocino-[4,3-*b*]indole-2-carboxylate (**28**)**



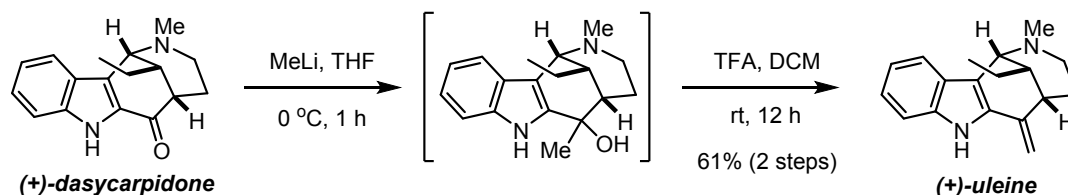
To a solution of indole **27** (505 mg, 1.35 mmol) in DCM (5 mL) was added PCC (581 mg, 2.7 mmol) at rt. The resulting mixture was stirred for 1 h and filtered through a pad of silica-gel with the aid of EtOAc (100 mL). The filtrate was concentrated and purified by flash column chromatography (EtOAc/Hexane = 1/4) to give **28** (419 mg, 1.08 mmol, 80%) as a yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 9.25 (brs, 1H), 8.01 – 7.43 (m, 3H), 7.42 – 7.24 (m, 5H), 7.22 – 6.93 (m, 1H), 5.86 and 5.69 (2d, *J* = 2.0 Hz, 1H), 5.37 and 5.23 (2d, *J* = 12.3 Hz, 0.8H), 5.19 and 5.06 (2d, *J* = 12.3 Hz, 1.2H), 4.02 and 3.90 (2dd, *J* = 13.8, 5.3 Hz, 1H), 2.86 – 2.69 (m, 2H), 2.27 – 2.16 (m, 1H), 2.13 – 1.87 (m, 2H), 1.48 – 1.29 (m, 2H), 0.93 and 0.92 (2t, *J* = 7.7 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 192.8, 155.7, 155.1, 138.7, 138.6, 136.7, 136.6, 132.5, 132.4, 128.8, 128.7, 128.6, 128.5, 128.1, 128.0, 127.5, 127.3, 125.4, 125.2, 122.7 (x 2), 122.0, 121.9, 121.4, 121.2, 112.9, 67.7, 67.4, 48.4, 48.2, 48.0, 47.8, 46.6, 36.8, 36.7, 30.1, 25.0, 24.9, 11.9 (spectral data are identical to those reported in the literature<sup>[2a]</sup>); [α]<sub>D</sub><sup>24</sup> = +232.6 (c 0.18, CHCl<sub>3</sub>), lit.<sup>[2c]</sup> [α]<sub>D</sub><sup>28</sup> = +231.8 (c 0.2, CHCl<sub>3</sub>).

#### (+)-Dasycarpidone



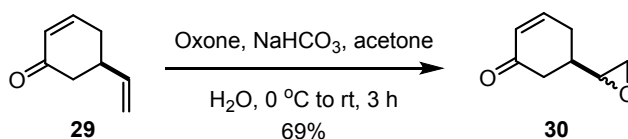
To a solution of **28** (201 mg, 0.52 mmol), Pd/C (50 mg) in MeOH (10 ml) was added formaldehyde (1.15 mL, 37% w/v aqueous solution, 15.5 mmol) at rt under hydrogen atmosphere. The reaction mixture was stirred for 3 h and then filtered through a pad of Celite with the aid of EtOAc (50 mL). The filtrate was washed with 1.0 M NaOH (aq), dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and purified by flash column chromatography (DCM/MeOH = 20/1) to give (+)-dasycarpidone (107 mg, 0.4 mmol, 77%) as a white foamy solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.63 (brs, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.39 (td, *J* = 8.2, 1.1 Hz, 1H), 7.19 (td, *J* = 8.0, 1.1 Hz, 1H), 4.29 (d, *J* = 2.4 Hz, 1H), 2.72 – 2.68 (m, 1H), 2.61 – 2.55 (m, 1H), 2.38 – 2.33 (m, 1H), 2.32 (s, 3H), 2.19 – 2.02 (m, 2H), 1.95 – 1.89 (m, 1H), 1.36 – 1.22 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 193.5, 138.3, 133.0, 127.8, 126.9, 122.0, 121.1, 120.0, 112.9, 56.5, 49.8, 46.6, 46.2, 44.2, 30.4, 25.1, 12.0 (spectral data are identical to those reported in literature<sup>[2a, 3]</sup>); [α]<sub>D</sub><sup>24</sup> = +65.1 (c 1.30, CHCl<sub>3</sub>), lit.<sup>[2c]</sup> [α]<sub>D</sub><sup>30</sup> = +63.1 (c 0.7, CHCl<sub>3</sub>), lit.<sup>[3d]</sup> [α]<sub>D</sub><sup>26</sup> = +64.7 (c 1.02, CHCl<sub>3</sub>).

### (+)-Uleine



To a solution of (+)-dasycarpidone (20 mg, 0.076 mmol) in THF (2.5 mL) was added MeLi (0.14 mL, 0.23 mmol, 1.6 M solution in Et<sub>2</sub>O) at 0 °C. The resulting mixture was stirred at 0 °C for 1 h and then quenched with saturated NH<sub>4</sub>Cl (aq) solution (0.5 mL), diluted with DCM (10 mL), dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated in vacuo. The crude mixture was used for next reaction without further purification. To a solution of the above crude tertiary alcohol product in DCM (2.5 mL) was added TFA (0.03 mL, 0.38 mmol) and the resulting mixture was stirred at rt. After 12 h, the reaction mixture was quenched with saturated NaHCO<sub>3</sub> (aq), and extracted with DCM (3 x 5 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (DCM/MeOH = 20/1) to give (+)-uleine (12 mg, 61%, 2 steps) as a yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.25 (brs, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.19 (td, *J* = 8.0, 1.0 Hz, 1H), 7.10 (td, *J* = 8.0, 1.0 Hz, 1H), 5.27 (s, 1H), 5.00 (s, 1H), 4.11 (brs, 1H), 2.73 – 2.65 (m, 1H), 2.58 – 2.43 (m, 1H), 2.31 (s, 3H), 2.19 – 1.97 (m, 3H), 1.76 – 1.64 (m, 1H), 1.12 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 138.7, 136.8, 135.4, 129.5, 122.9, 120.1, 119.7, 110.9, 107.7, 107.1, 56.8, 46.4, 46.1, 44.4, 39.6, 34.7, 24.5, 11.9 (spectral data are identical to those reported in the literature<sup>[3c,4]</sup>); [α]<sub>D</sub><sup>26</sup> = +18.9 (*c* 0.33, CHCl<sub>3</sub>), lit.<sup>[2c]</sup> [α]<sub>D</sub><sup>27</sup> = +18.2 (*c* 0.3, CHCl<sub>3</sub>).

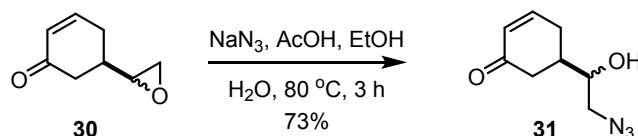
### (R)-5-((S)-Oxiran-2-yl)cyclohex-2-en-1-one (**30**)



Olefin **29** was prepared in 98% ee by following the procedure reported in the literature<sup>[5]</sup> (HPLC (Chiralpak AS-3, hexane/*i*-PrOH = 90:10, flow rate 1 mL/min, λ = 222 nm), *t*<sub>R</sub> = 7.17 (minor), 8.00 (major) min; ee = 98%; [α]<sub>D</sub><sup>23</sup> = -48.1 (*c* = 0.19, CHCl<sub>3</sub>), lit.<sup>[5]</sup> [α]<sub>D</sub> = -47.6 (*c* = 0.32, CHCl<sub>3</sub>)). To a flask charged with olefin **29** (2.9 g, 23.9 mmol), NaHCO<sub>3</sub> (8.0 g, 95.6 mmol) in acetone (60 mL) was added Oxone (22.0 g, 71.7 mmol) in H<sub>2</sub>O (60 mL) at 0 °C. The resulting solution was warmed to rt, stirred for 3 h, then quenched with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (aq) and extracted with ether (3 x 100 mL). The combined organic solution was washed with brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (ether/pentane = 1/2) to give epoxide **30** as an inseparable diastereomeric

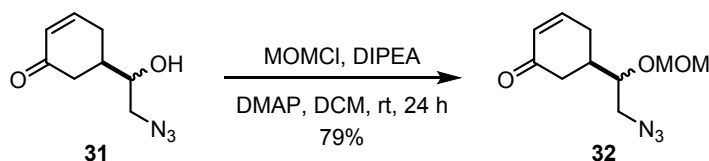
mixture (ratio = 1.4:1, 2.3 g, 16.5 mmol, 69% total yield) as a colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  7.03 – 6.94 (m, 1H), 6.06 (d,  $J$  = 10.0 Hz, 1H), 2.97 – 2.88 (m, 1H), 2.83 – 2.76 (m, 1H), 2.64 – 2.43 (m, 3H), 2.42 – 2.26 (m, 2H), 2.24 – 1.98 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  198.2, 198.1, 148.9, 148.5, 130.3, 130.1, 54.6, 54.5, 46.1, 45.6, 40.5, 40.0, 37.9, 37.0, 28.5, 28.3; FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 3295, 2926, 2848, 1679, 1389, 1250, 863, 736  $\text{cm}^{-1}$ .

**(R)-5-(2-Azido-1-hydroxyethyl)cyclohex-2-en-1-one (31)**



To a solution of epoxide **30** (2.3 g, 16.5 mmol) in ethanol/ $\text{H}_2\text{O}$  (4:1, 82 mL) were added  $\text{NaN}_3$  (1.3 g, 19.8 mmol) and AcOH (1.1 mL, 19.8 mmol). The resulting solution was heated at 80  $^\circ\text{C}$  for 3 h, cooled to rt, quenched with saturated  $\text{NaHCO}_3$  (aq), and extracted with ether (3 x 50 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (ether/pentane = 1/2) to give azide **31** as an inseparable diastereomeric mixture (ratio = 1.4:1, 2.2 g, 12.0 mmol, 73% total yield) as yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  7.06 – 6.94 (m, 1H), 6.06 (d,  $J$  = 10.9 Hz, 1H), 3.75 – 3.64 (m, 1H), 3.52 – 3.35 (m, 2H), 2.63 – 2.44 (m, 1H), 2.43 – 2.33 (m, 3H), 2.32 – 2.22 (m, 1H), 2.20 (t,  $J$  = 4.8 Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  199.5, 199.2, 150.0, 149.5, 129.8, 129.6, 72.7 (x 2), 54.9, 41.0, 39.0, 38.4 (x 2), 28.7, 26.9; FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 3422, 2932, 1201, 1669, 1612, 1275, 1103  $\text{cm}^{-1}$ .

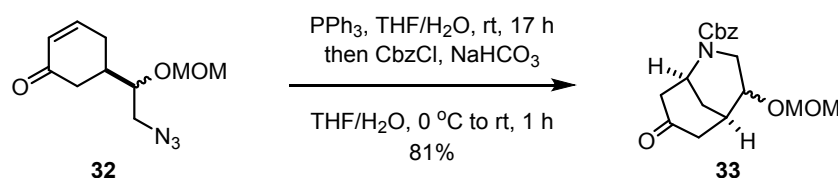
**(R)-5-(2-Azido-1-(methoxymethoxy)ethyl)cyclohex-2-en-1-one (32)**



To a solution of azide **31** (1.4 g, 7.9 mmol) in DCM (26 mL) were added DIPEA (5.5 mL, 31.6 mmol), DMAP (96 mg, 0.79 mmol) and MOMCl (1.8 mL, 23.7 mmol) at 0  $^\circ\text{C}$ . The resulting mixture was warmed to rt, stirred for 24 h, quenched with saturated  $\text{NaHCO}_3$  (aq) and extracted with DCM (3 x 50 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/3) to give MOM ether as an inseparable diastereomeric mixture (ratio = 1.4:1, 1.4 g, 6.23 mmol, 79% total yield) as a yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  7.04 – 6.95 (m, 1H), 6.09 – 6.02 (m, 1H), 4.80 – 4.73 (m, 1H), 4.71 – 4.65 (m, 1H), 3.63 – 3.56 (m, 1H), 3.53 – 3.45 (m, 1H), 3.43 (s, 3H), 3.41 –

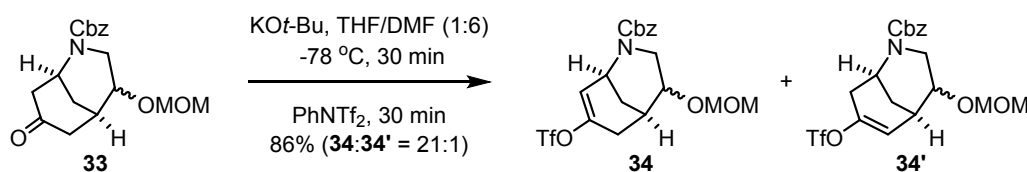
3.34 (m, 1H), 2.66 – 2.40 (m, 3H), 2.39 – 2.24 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  198.9, 198.8, 149.5, 149.1, 130.0, 129.8, 97.1, 79.2, 79.0, 56.3 (x 2), 52.0 (x 2), 40.9, 39.5, 37.2 (x 2), 28.6, 27.2; FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 2926, 2903, 2105, 1681, 1450, 1389, 1257, 1150, 1028, 918, 738  $\text{cm}^{-1}$ .

**Benzyl (1S,5R)-4-(methoxymethoxy)-7-oxo-2-azabicyclo[3.3.1]nonane-2-carboxylate (**33**)**



To a solution of MOM ether **32** (1.10 g, 4.9 mmol) in THF/ $\text{H}_2\text{O}$  (6:1, 16 mL) was added  $\text{PPh}_3$  (1.90 g, 7.3 mmol) at rt. The resulting mixture was stirred for 17 at rt until the starting material is completely consumed (monitored by TLC). The reaction mixture was then cooled to 0  $^\circ\text{C}$ , and added with  $\text{NaHCO}_3$  (0.62 g, 7.3 mmol) and  $\text{CbzCl}$  (1.03 mL, 7.3 mmol). The resulting solution was warmed to rt, stirred for 1 h, diluted with water (10 mL) and extracted with EtOAc (3 x 50 mL). The removed organic solution was washed with brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/3) to give ketone **33** as an inseparable diastereomeric mixture (ratio = 1.4:1, 1.30 g, 3.96 mmol, 81% total yield) as a colorless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , deduced from the mixture) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  7.40 – 7.27 (m, 5H), 5.19 – 5.06 (m, 2H), 4.93 – 4.55 (m, 3H), 4.33 – 4.11 (m, 1H), 3.81 – 3.52 (m, 1H), 3.39 – 3.26 (m, 3H), 2.97 – 2.83 (m, 1H), 2.72 – 2.29 (m, 5.5H), 2.08 – 1.63 (m, 1.5H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , deduced from the mixture)  $\delta$  209.4, 208.9, 155.6, 155.4, 136.6, 136.5, 128.6 (x 2), 128.2 (x 2), 128.0 (x 2), 95.6, 95.4, 95.0, 94.9, 73.7, 73.2, 72.8, 72.4, 67.6, 67.5, 67.4, 55.8, 55.7, 55.6, 48.3, 47.9, 47.8, 47.6, 46.5, 46.2, 44.6, 42.0, 41.7, 41.4, 41.0, 40.2, 33.6, 33.5, 30.7, 30.4, 26.2, 26.1 (spectral data contain the peaks corresponding to the Cbz rotamer); FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 2930, 2899, 1699, 1422, 1220, 1114, 1036, 920, 697  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{18}\text{H}_{23}\text{NNaO}_5$   $[\text{M}+\text{Na}]^+$  356.1474, found 356.1473.

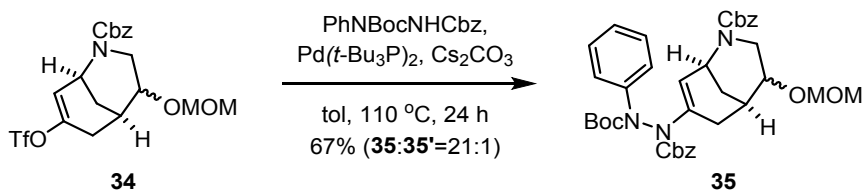
**Benzyl (1S,5R)-4-(methoxymethoxy)-7-(((trifluoromethyl)sulfonyl)oxy)-2-azabicyclo[3.3.1]non-7-ene-2-carboxylate (**34**)**



To a solution of ketone **33** (1.32 g, 3.96 mmol) in THF (3 mL) and DMF (17 mL) was added  $\text{KOt-Bu}$

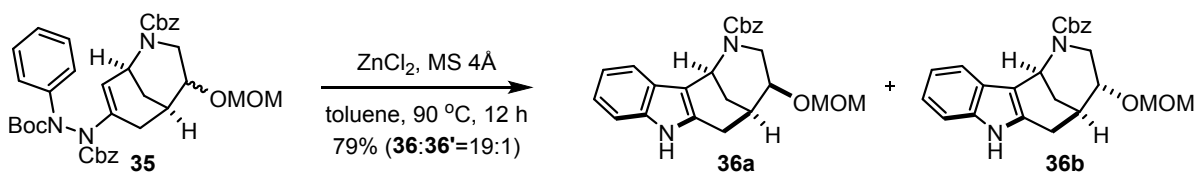
(4.8 mmol) in THF/DMF (1:6, 34 mL) at -78 °C via a cannula over 10 min. The resulting mixture was stirred for 30 min at -78 °C and cannulated with a solution of PhNTf<sub>2</sub> (1.70 g, 4.8 mmol) in THF/DMF (1:6, 20 mL) at -78 °C. After 30 min at -78 °C, the reaction mixture was quenched with saturated NH<sub>4</sub>Cl (aq) solution and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/10) to give inseparable mixture of enol-triflate **34** and its regioisomer **34'** (21:1, 1.59 g, 3.41 mmol, 86% total yield) as a colorless oil. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, 60 °C, deduced from the mixture) δ 7.42 – 7.27 (m, 5H), 5.91 – 5.82 (m, 1H), 5.18 – 5.05 (m, 2H), 4.93 – 4.78 (m, 1H), 4.71 – 4.56 (m, 1H), 4.11 – 3.93 (m, 1H), 3.72 – 3.56 (m, 1H), 3.33 – 3.18 (m, 3H), 3.10 – 2.47 (m, 5H), 2.47 – 2.26 (m, 1H), 2.09 – 1.43 (m, 2H) (spectral data contain the peaks corresponding to the minor regio-isomer); FT-IR (CHCl<sub>3</sub>) 2360, 1701, 1419, 1213, 1144, 1042 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>19</sub>H<sub>22</sub>F<sub>3</sub>NNaO<sub>7</sub>S [M+Na]<sup>+</sup> 488.0967, found 488.0968.

**1-Benzyl 2-(*tert*-butyl) 1-((1*S*,5*R*)-2-((benzyloxy)carbonyl)-4-(methoxymethoxy)-2-azabicyclo-[3.3.1]non-7-en-7-yl)-2-phenylhydrazine-1,2-dicarboxylate (**35**)**



To a Schlenk tube charged with enol triflate **34** (1.58 g, 3.4 mmol) (containing small amounts of **34'**) were added Pd(*t*-Bu<sub>3</sub>P)<sub>2</sub> (0.09 g, 0.17 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2.20 g, 6.8 mmol), PhNBocNHCbz (1.30 g, 3.7 mmol) and toluene (17 mL) at rt. The resulting mixture was degassed with freeze-pump-thaw cycles (× 2). The reaction mixture was then heated at 110 °C. After 24 h, the reaction mixture was cooled to rt and filtered through a pad of silica-gel with the aid of EtOAc (100 mL). The filtrate was concentrated and chromatographed (EtOAc/Hexane = 1/4) to give an inseparable mixture of ene-hydrazide **35** and regioisomer **35'** (21:1, 1.50 g, 2.3 mmol, 67% total yield) as a yellow oil. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, 60 °C, deduced from the mixture) (spectral data contain the peaks corresponding to the minor regio-isomer) δ 7.59 – 7.08 (m, 15H), 5.63 – 5.47 (m, 1H), 5.27 – 5.16 (m, 2H), 5.13 – 4.99 (m, 2H), 4.72 – 4.51 (m, 3H), 3.91 – 3.70 (m, 1H), 3.59 – 3.33 (m, 1H), 3.29 – 3.16 (m, 3H), 2.91 – 2.78 (m, 0.5H), 2.77 – 2.53 (m, 1H), 2.48 – 1.94 (m, 3H), 1.73 – 1.51 (m, 1H), 1.43 – 1.39 (m, 0.5H), 1.38 – 1.28 (m, 9H); FT-IR (CHCl<sub>3</sub>) 1723, 1311, 1248, 1158, 1038 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>34</sub>H<sub>45</sub>N<sub>3</sub>NaO<sub>8</sub> [M+Na]<sup>+</sup> 680.2948, found 680.2949.

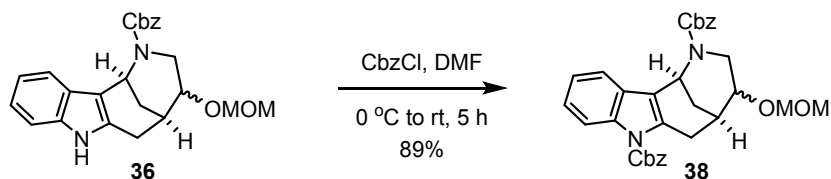
**Benzyl (1*S*,5*R*)-4-(methoxymethoxy)-1,3,4,5,6,7-hexahydro-2*H*-1,5-methano-azocino[4,3-*b*]indole-2-carboxylate (**36a**)**



To a sealed tube charged with  $\text{ZnCl}_2$  (0.64 g, 4.7 mmol) were added ene-hydrazide **35** (1.40 g, 2.13 mmol), molecular sieve (4Å, 1.00 g) and toluene (11 mL) at rt. The resulting solution was heated at 90 °C for 12 h, cooled to rt, quenched by adding saturated  $\text{NaHCO}_3$  (aq) solution, and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/3) to give indole **36** (0.64 g, 1.58 mmol, 74%) as a pale yellow solid and its regioisomer **36'** (0.03 g, 0.08 mmol, 4%) as a yellow oil. (Although the stereochemistry of the –OMOM group has no consequence for the next reaction, the diastereomers **36a** and **36b** were separated for the structural characterizations. They were in fact re-combined for the next reaction.) **36a**: pale yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  7.99 and 7.98 (2brs, 1H), 7.72 – 7.38 (m, 3H), 7.37 – 7.21 (m, 4H), 7.19 – 6.88 (m, 2H), 5.68 and 5.54 (2s, 1H), 5.32 and 5.20 (2d,  $J$  = 12.5 Hz, 1H), 5.17 and 5.06 (2d,  $J$  = 12.5 Hz, 1H), 4.79 – 4.63 (m, 2H), 4.07 and 3.95 (2dd,  $J$  = 13.0, 6.0 Hz, 1H), 3.87 – 3.74 (m, 1H), 3.37 (s, 3H), 3.21 – 3.05 (m, 1H), 2.91 – 2.74 (m, 1H), 2.61 (s, 1H), 2.57 – 2.43 (m, 1H), 2.09 – 1.92 (m, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  155.2, 155.1, 136.9, 136.1, 136.0, 135.9, 128.7, 128.6, 128.5, 128.3, 128.0, 127.8, 126.1, 125.9, 121.6, 121.5, 119.9, 119.7, 119.0, 118.3, 110.6, 110.5, 109.2, 108.8, 95.6, 95.4, 74.4, 74.0, 67.5, 67.1, 55.7, 43.3, 43.0, 41.3, 41.0, 31.4, 31.0, 30.9, 21.4 (x 2); FT-IR ( $\text{CH}_2\text{Cl}_2$ ) 3743, 3315, 2360, 1685, 1457, 1422, 1239, 1040, 746  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_4$   $[\text{M}+\text{Na}]^+$  429.1790, found 429.1793;  $[\alpha]_{\text{D}}^{22}$  = -37.2 ( $c$  0.79,  $\text{CHCl}_3$ ); **36b**: yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  8.01 and 8.00 (2brs, 1H), 7.71 – 7.38 (m, 3H), 7.37 – 7.25 (m, 4H), 7.23 – 6.90 (m, 2H), 5.74 and 5.60 (2s, 1H), 5.34 and 5.20 (2d,  $J$  = 12.4 Hz, 1H), 5.17 and 5.04 (2d,  $J$  = 12.4 Hz, 1H), 4.78 and 4.71 (2d,  $J$  = 7.0 Hz, 1H), 4.67 and 4.64 (2d,  $J$  = 7.0 Hz, 1H), 4.06 and 3.97 (2d,  $J$  = 14.5 Hz, 1H), 3.66 and 3.56 (2s, 1H), 3.45 – 3.27 (m, 3H), 3.19 – 3.04 (m, 1H), 2.79 and 2.73 (2dd,  $J$  = 14.5, 2.2 Hz, 1H), 2.64 and 2.59 (2d,  $J$  = 3.0 Hz, 1H), 2.50 (s, 1H), 2.49 – 2.42 (m, 1H), 1.79 – 1.63 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) (spectral data contain the peaks corresponding to the Cbz rotamer)  $\delta$  155.8, 155.6, 137.0, 136.2, 136.1, 134.8, 134.7, 128.7, 128.6, 128.5, 128.3, 127.9, 127.8, 126.1, 125.9, 121.8, 121.6, 120.0, 119.8, 119.1, 118.5, 110.6 (x 2), 109.4, 109.0, 94.9, 94.8 (x 2), 74.5, 74.2, 67.4, 67.0, 55.7, 55.6, 43.9, 43.5, 41.4, 41.1, 31.2, 31.0, 27.5, 27.2, 26.7, 26.6;  $[\alpha]_{\text{D}}^{22}$  = -31.8 ( $c$  0.79,  $\text{CHCl}_3$ ).

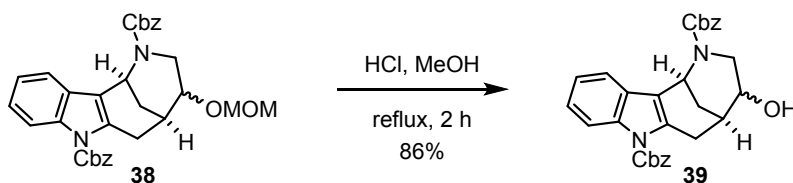
**Dibenzyl (1S,5R)-4-(methoxymethoxy)-3,4,5,6-tetrahydro-1H-1,5-methano-azocino[4,3-*b*]indole-**

### 2,7-dicarboxylate (**38**)



To a solution of indole **36** (577 mg, 1.42 mmol) in DMF (7.0 mL) was added NaH (60%, 85 mg, 2.1 mmol) at 0 °C. After 30 min, the reaction mixture was added with CbzCl (0.3 mL, 2.1 mmol) at 0 °C and stirred for 5 h. The reaction mixture was then quenched with saturated NH<sub>4</sub>Cl (aq) solution and extracted with EtOAc (3 x 20 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/4) to give indole **38** as a mixture of two diastereomers (683 mg, 1.3 mmol, 89%) as a yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, deduced from the mixture) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 8.14 – 8.03 (m, 1H), 7.71 – 7.46 (m, 4H), 7.45 – 7.38 (m, 4H), 7.37 – 7.27 (m, 3H), 7.25 – 6.99 (m, 2H), 5.73 – 5.40 (m, 3H), 5.39 – 5.03 (m, 2H), 4.79 – 4.62 (m, 2H), 4.15 – 3.64 (m, 1H), 3.83 – 3.51 (m, 1H), 3.49 – 3.26 (m, 4H), 3.08 – 2.92 (m, 1H), 2.83 – 2.71 (m, 0.5H), 2.66 – 2.39 (m, 2H), 1.74 – 1.61 (m, 0.5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, deduced from the mixture) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 155.3, 155.1, 154.7, 151.9, 151.8, 141.1, 137.6, 136.8 (x2), 136.7 (x2), 136.5 (x2), 136.0, 135.9, 135.1 (x2), 135.0, 128.9 (x2), 128.8 (x2), 128.7 (x2), 128.6, 128.5 (x2), 128.4, 128.0, 127.9, 127.8, 127.7, 127.6, 127.0, 124.3, 124.2, 124.1, 123.4 (x2), 123.2, 123.1, 119.1, 119.0, 118.5, 118.3, 116.1, 115.8, 115.7, 115.6, 115.2, 95.6, 95.4, 94.9, 94.8, 74.4, 74.2, 73.9, 68.8, 67.7, 67.5, 67.2, 67.1, 65.3, 55.7, 55.5, 43.4, 43.0, 42.8, 42.5, 41.5, 41.4, 41.1 (x2), 31.2, 31.1, 31.0, 30.9, 30.2, 29.8, 29.5, 29.4, 26.3, 26.0, 24.2; FT-IR (CH<sub>2</sub>Cl<sub>2</sub>) 3038, 2940, 1734, 1695, 1457, 1352, 1214, 1108, 1040, 752 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>32</sub>H<sub>32</sub>N<sub>2</sub>NaO<sub>6</sub> [M+Na]<sup>+</sup> 563.2158, found 563.2158.

### Dibenzyl (1*S*,5*R*)-4-hydroxy-3,4,5,6-tetrahydro-1*H*-1,5-methanoazocino[4,3-*b*]indole-2,7-dicarboxylate (**39**)

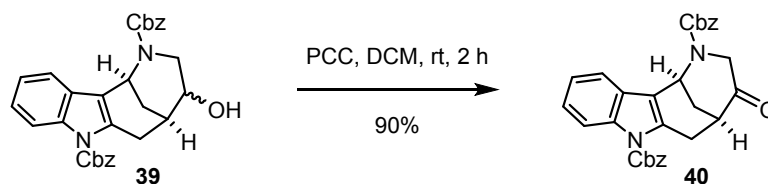


To a solution of indole **38** (612 mg, 1.1 mmol) in MeOH (11 mL) was added HCl (35% aqueous solution, 0.9 mL) at 0 °C. The resulting solution was heated under reflux for 3 h, cooled to rt, quenched with saturated NaHCO<sub>3</sub> (aq) solution and extracted with EtOAc (3 x 20 mL). The combined organic solution



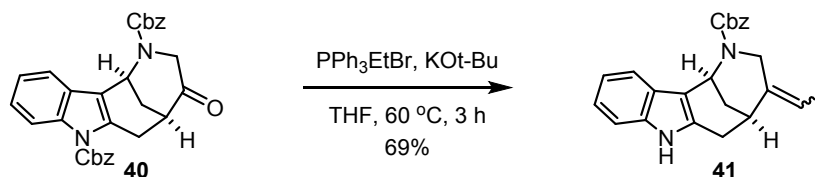
was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/1) to give indole **39** as a mixture of two diastereomers (483 mg, 0.97 mmol, 86%) as a colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, deduced from the mixture) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 8.13 – 8.04 (m, 1H), 7.70 – 7.42 (m, 4H), 7.41 – 7.31 (m, 4H), 7.30 – 6.98 (m, 5H), 5.71 – 5.36 (m, 3H), 5.36 – 5.00 (m, 2H), 4.11 – 3.66 (m, 2H), 3.54 – 3.21 (m, 1H), 3.07 – 2.92 (m, 1H), 2.91 – 2.77 (m, 0.5H), 2.72 – 2.12 (m, 3H), 1.98 – 1.88 (m, 1H), 1.73 – 1.57 (m, 0.5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, deduced from the mixture) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 156.1, 155.9, 155.1, 154.8, 151.8, 137.8, 137.6, 136.7 (x2), 136.6, 136.5, 135.9, 135.2, 135.0, 128.9 (x2), 128.8 (x2), 128.7, 128.5 (x2), 128.4, 128.1, 128.0, 127.9 (x2), 127.8, 127.7, 124.4, 124.2, 124.1, 123.5, 123.4, 123.2, 123.1, 119.2, 119.0, 118.4, 118.2, 115.8, 115.7, 115.6, 115.2, 69.6, 68.9, 68.8, 68.5, 67.7, 67.4, 67.3, 44.4, 44.2, 43.8, 43.3, 43.0, 42.9, 42.8, 42.4, 32.9 (x2), 32.6, 23.5, 30.4, 29.9, 29.4, 29.4, 25.9, 25.6, 23.6; FT-IR (CHCl<sub>3</sub>) 3743, 2360, 1556, 1515 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>30</sub>H<sub>29</sub>N<sub>2</sub>O<sub>5</sub> [M+H]<sup>+</sup> 497.2076, found 497.2075.

**Dibenzyl (1S,5R)-4-oxo-3,4,5,6-tetrahydro-1H-1,5-methanoazocino[4,3-*b*]indole-2,7-dicarboxylate (**40**)**



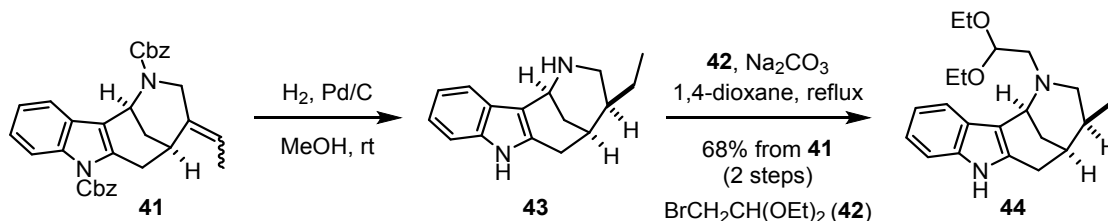
To a solution of indole **39** (0.45 g, 0.9 mmol) in DCM (9 mL) was added PCC (2.0 g, 9.1 mmol) at rt. The resulting mixture was stirred for 2 h and filtered through a pad of silica gel with the aid of EtOAc (50 mL). The filtrate was concentrated and purified by flash column chromatography (EtOAc/Hexane = 1/4) to give ketone **40** (0.41 g, 0.8 mmol, 90%) as a yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 8.16 – 8.04 (m, 1H), 7.84 – 7.25 (m, 12H), 7.23 – 6.98 (m, 1H), 5.83 and 5.68 (2s, 1H), 5.53 – 5.08 (m, 4H), 4.42 and 4.30 (2d, *J* = 19.8 Hz, 1H), 3.52 and 3.43 (2d, *J* = 19.8 Hz, 1H), 3.39 – 3.21 (m, 2H), 3.03 (s, 1H), 2.45 – 2.12 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (spectral data contain the peaks corresponding to the Cbz rotamer) δ 208.5, 208.1, 154.5, 154.0, 151.6, 136.3, 136.2, 135.3, 135.2, 134.9, 134.8, 129.1, 129.0 (x2), 128.9 (x2), 128.8 (x2), 128.7, 128.3, 128.0, 127.9, 127.6, 125.0, 124.9, 123.7, 123.4, 119.8, 118.8, 117.0, 116.2, 115.8, 115.6, 69.2, 69.1, 68.1, 67.7, 51.9, 42.9, 42.3, 42.0, 41.8, 31.7, 31.6, 29.4, 28.8; FT-IR (CHCl<sub>3</sub>) 3743, 2941, 2360, 1734, 1699, 1397, 1313, 1212, 754 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>30</sub>H<sub>27</sub>N<sub>2</sub>O<sub>5</sub> [M+H]<sup>+</sup> 495.1920, found 495.1919; [α]<sub>D</sub><sup>22</sup> = -48.4 (*c* 0.6, CHCl<sub>3</sub>).

**Benzyl (1S,5R)-4-ethylidene-1,3,4,5,6,7-hexahydro-2H-1,5-methanoazocino[4,3-*b*]indole-2-carboxylate (41)**



To a solution of  $\text{PPh}_3\text{EtBr}$  (876 mg, 2.4 mmol) in THF (4 mL) was added  $\text{KO}t\text{-Bu}$  (1.0 M solution, 2.3 mL, 2.3 mmol) at 0 °C. After 30 min, ketone **40** (389 mg, 0.8 mmol) dissolved in THF (4 mL) was cannulated into the mixture at 0 °C. The resulting mixture was heated at 60 °C for 3 h, cooled to rt, quenched with saturated  $\text{NaHCO}_3$  (aq) solution and extracted with EtOAc (3 x 20 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/8) to give **41** (*E/Z* mixture ~1:6, 202 mg, 0.5 mmol, 69%) as a yellow solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , deduced from the mixture) (spectral data contains the peaks corresponding to the Cbz rotamer and minor diastereomer)  $\delta$  7.89 (brs, 1H), 7.76 – 7.22 (m, 7H), 7.17 – 6.91 (m, 2H), 5.79 and 5.66 (2t,  $J$  = 2.8 Hz, 1H), 5.41 (q,  $J$  = 6.7 Hz, 1H), 5.38 – 5.05 (m, 2H), 4.72 and 4.62 (2d,  $J$  = 15.4 Hz, 0.85 H, *Z* isomer), 4.24 and 4.14 (2d,  $J$  = 14.9 Hz, 0.15H, *E* isomer), 3.46 – 3.07 (m, 2H), 2.93 (s, 1H), 2.71 – 2.59 (m, 1H), 2.14 – 1.91 (m, 2H), 1.69 – 1.53 (m, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , deduced from the mixture) (spectral data contains the peaks corresponding to the Cbz rotamer and minor diastereomer)  $\delta$  155.2, 155.0, 137.2, 137.1 (x2), 136.9, 136.2, 136.1, 135.8, 135.7, 135.6, 128.7, 128.6 (x2), 128.5, 128.3, 127.9, 127.7, 126.4, 126.2, 121.7, 121.6, 120.1, 120.0, 119.8, 119.5, 119.4, 119.3, 118.6, 110.6, 110.5, 109.7, 109.2, 67.4, 67.3, 66.9, 46.1, 44.2, 44.1, 43.9, 39.2 (x2), 36.9, 36.8, 33.0, 32.8, 32.2, 31.0, 29.1, 28.2, 28.1, 12.9, 12.8, 12.6, 12.5; FT-IR ( $\text{CHCl}_3$ ) 3743, 2360, 1679, 1420, 1244, 1216, 744  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) Calcd for  $\text{C}_{24}\text{H}_{24}\text{N}_2\text{NaO}_2$   $[\text{M}+\text{Na}]^+$  395.1735, found 395.1735.

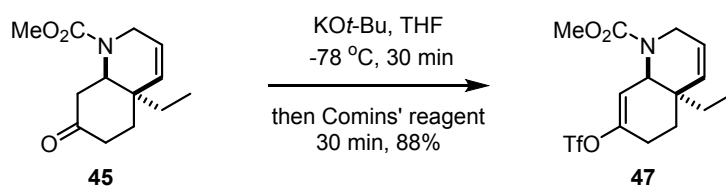
**(1S,4S,5R)-2-(2,2-diethoxyethyl)-4-ethyl-2,3,4,5,6,7-hexahydro-1H-1,5-methanoazocino[4,3-*b*]indole (44)**



To a mixture of olefin **41** (33 mg, 0.09 mmol), Pd/C (10 mg) and MeOH (3 mL) was charged  $\text{H}_2$  gas (1 atm) by using a balloon at rt. After 16 h at rt, the reaction mixture was filtered through a pad of Celite with MeOH (30 mL). The filtrate was concentrated in vacuo and used for next step without further

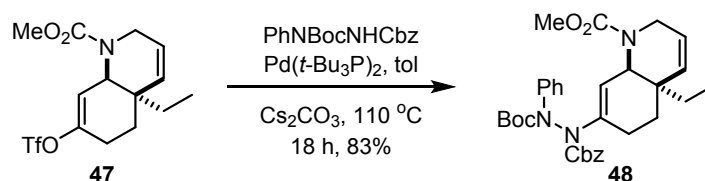
purification. The crude product **43** was dissolved in 1,4-dioxane (1.8 mL) and added with bromoacetaldehyde diethyl acetal **42** (0.02 mL, 0.14 mmol), Na<sub>2</sub>CO<sub>3</sub> (19 mg, 0.18 mmol). The resulting mixture was heated under reflux for 21 h, quenched with water and extracted with EtOAc (3 x 20 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/1) to give acetal **44** (22 mg, 0.06 mmol, 68%) as a yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (brs, 1H), 7.69 – 7.62 (m, 1H), 7.31 – 7.27 (m, 1H), 7.13 – 7.04 (m, 2H), 4.74 (t, *J* = 5.1 Hz, 1H), 4.29 (s, 1H), 3.79 – 3.48 (m, 4H), 2.94 (dd, *J* = 13.4, 5.6 Hz, 1H), 2.81 – 2.68 (m, 2H), 2.60 (d, *J* = 7.0 Hz, 1H), 2.27 – 2.12 (m, 3H), 2.06 – 1.98 (m, 1H), 1.90 (td, *J* = 12.2, 3.0 Hz, 1H), 1.82 – 1.73 (m, 1H), 1.33 – 1.21 (m, 5H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H) (spectral data are identical to those reported in the literature<sup>[6]</sup>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 136.6, 135.9, 128.4, 120.9, 119.8, 119.0, 110.3, 107.6, 102.5, 61.8, 61., 59.4, 51.6, 51.2, 41.8, 34.5, 29.0, 24.9, 22.8, 15.6, 15.5, 11.7; FT-IR (CH<sub>2</sub>Cl<sub>2</sub>) 2928, 2852, 1738, 1463, 1373, 1246, 1059, 742 cm<sup>-1</sup>; HRMS (ESI-TOF) Calcd for C<sub>22</sub>H<sub>33</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 357.2542, found 357.2546; [α]<sub>D</sub><sup>22</sup> = +19.4 (c 0.18, CHCl<sub>3</sub>).

**Methyl (4aR,8aR)-4a-ethyl-7-(((trifluoromethyl)sulfonyl)oxy)-4a,5,6,8a-tetrahydro-quinoline-1(2H)-carboxylate (**47**)**



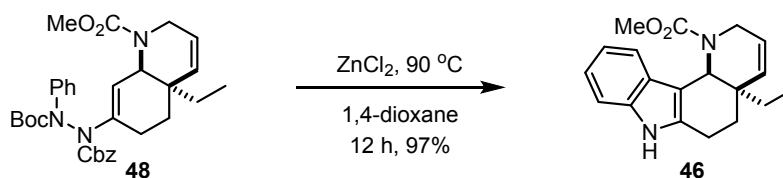
To a solution of ketone **45** (200 mg, 0.84 mmol) in THF (8.4 mL) was added KO*t*-Bu (1.0 M solution, 1.0 mL, 1.0 mmol) at -78 °C. The resulting mixture was stirred for 30 min and treated with a solution of Comins' reagent (397 mg, 1.0 mmol) in THF (8.4 mL) via cannula at -78 °C. The reaction mixture was further stirred at the same temperature for 30 min, quenched with saturated NH<sub>4</sub>Cl (aq) solution and extracted with EtOAc (3 x 50 mL). The combined organic solution was washed with NaHCO<sub>3</sub> (aq), brine, dried over anhydrous MgSO<sub>4</sub>, filtered, concentrated in vacuo and chromatographed (EtOAc/Hexane = 1/20) to give enol-triflate **47** (274 mg, 0.74 mmol) as colorless oil. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>, 85 °C) δ 5.73 (ddd, *J* = 10.3, 4.0, 2.2 Hz, 1H), 5.56 (t, *J* = 2.3 Hz, 1H), 5.46 (d, *J* = 10.3 Hz, 1H), 4.80 (s, 1H), 4.15 and 4.1 (2dd, *J* = 4.0, 2.3 Hz, 1H), 3.68 (s, 3H), 3.52 – 3.43 (m, 1H), 2.42 – 2.29 (m, 1H), 2.26 – 2.16 (m, 1H), 1.81 (ddd, *J* = 13.5, 5.4, 2.0 Hz, 1H), 1.70 (ddd, *J* = 13.4, 11.6, 5.5 Hz, 1H), 1.55 – 1.32 (m, 2H), 0.84 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>, 85 °C) δ 155.0, 150.0, 128.9, 123.5, 119.3, 118.5, 116.1, 52.2, 52.0, 36.5, 31.6, 29.8, 23.8, 7.4; HRMS (ESI-TOF) Calcd for C<sub>14</sub>H<sub>18</sub>F<sub>3</sub>NNaO<sub>5</sub>S [M+Na]<sup>+</sup> 392.0755, found 392.0757.

**1-Benzyl 2-(*tert*-butyl) 1-((4aR,8aR)-4a-ethyl-1-(methoxycarbonyl)-1,2,4a,5,6,8a-hexahydroquinolin-7-yl)-2-phenylhydrazine-1,2-dicarboxylate (**48**)**



To a Schlenk tube charged with triflate **47** (227 mg, 0.62 mmol) were added  $\text{Pd}(t\text{-Bu}_3\text{P})_2$  (16 mg, 0.03 mmol),  $\text{Cs}_2\text{CO}_3$  (400 mg, 1.2 mmol),  $\text{PhNBocNHCBz}$  (231 mg, 0.68 mmol) and toluene (6.2 mL) at rt. The resulting mixture was degassed two times by freeze-pump-thaw cycles. The reaction was heated at 110 °C for 24 h, cooled to rt, and filtered through a pad of silica gel with the aid of EtOAc (50 mL). The filtrate was concentrated and purified by flash column chromatography (EtOAc/Hexane = 1/10) to give ene-hydrazide **48** (287 mg, 0.51 mmol, 83%) as yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ , 85 °C)  $\delta$  7.41 – 7.15 (m, 10H), 5.59 – 5.47 (m, 1H), 5.39 – 5.30 (m, 1H), 5.27 – 5.09 (m, 3H), 4.66 – 4.54 (m, 1H), 4.01 – 3.89 (m, 1H), 3.66 – 3.58 (m, 3H), 3.34 – 3.09 (m, 1H), 2.35 – 1.98 (m, 2H), 1.73 – 1.63 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO-d}_6$ , 85 °C)  $\delta$  155.0, 153.0, 151.8, 151.7, 140.2, 138.9, 138.8, 135.5, 135.4, 12.5, 129.4, 128.0, 127.8, 127.5, 127.4, 127.3, 125.1, 123.2, 123.0, 122.7, 119.8, 81.4, 67.3, 67.2, 52.6, 51.7, 36.3, 36.2, 32.1, 30.3, 29.9, 27.3, 27.2, 22.7, 22.3, 7.5; HRMS (ESI-TOF) Calcd for  $\text{C}_{32}\text{H}_{39}\text{N}_3\text{NaO}_6$   $[\text{M}+\text{Na}]^+$  584.2737, found 584.2741.

**Methyl (4aR,11cS)-4a-ethyl-2,4a,5,6,7,11c-hexahydro-1H-pyrido[3,2-*c*]carbazole-1-carboxylate (**46**)**



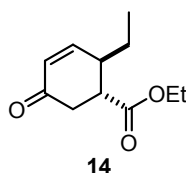
To a sealed tube charged with  $\text{ZnCl}_2$  (76 mg, 0.56 mmol) were added ene-hydrazide **48** (143 mg, 0.25 mmol) and 1,4-dioxane (2.5 mL). The resulting solution was heated at 90 °C for 12 h, cooled to rt, quenched by saturated  $\text{NaHCO}_3$  (aq) solution, and extracted with EtOAc (3 x 30 mL). The combined organic solution was washed with  $\text{NaHCO}_3$  (aq), brine, dried over anhydrous  $\text{MgSO}_4$ , filtered, concentrated in vacuo and chromatographed (EtOAc/hexane = 1/4) to give indole **46** (77 mg, 0.25 mmol, 97%) as yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-d}_6$ , 85 °C)  $\delta$  10.5 (brs, 1H), 7.26 (d,  $J$  = 8.0 Hz, 1H), 7.11 (d,  $J$  = 7.9 Hz, 1H), 6.99 (td,  $J$  = 7.1, 1.2 Hz, 1H), 6.90 (td,  $J$  = 8.0, 1.1 Hz, 1H), 5.58 – 5.49 (m, 2H), 5.41 (s, 1H), 4.10 (dd,  $J$  = 18.3, 2.3 Hz, 1H), 3.81 (s, 3H), 2.97 (d,  $J$  = 18.3 Hz, 1H), 2.68 – 2.55 (m, 2H), 1.89 (ddd,  $J$  = 13.2, 4.8, 2.4 Hz, 1H), 1.79 (ddd,  $J$  = 13.2, 11.0, 6.5 Hz, 1H), 1.66 – 1.46

(m, 2H), 0.95 (t,  $J = 7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ , 85 °C)  $\delta$  155.5, 135.8, 135.7, 130.1, 126.0, 123.6, 119.6, 118.2, 116.5, 110.4, 106.2, 51.8, 39.3, 39.1, 38.6, 31.9, 31.0, 19.2, 7.7 (spectral data are identical to those reported in the literature<sup>[7]</sup>).

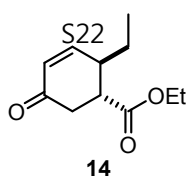
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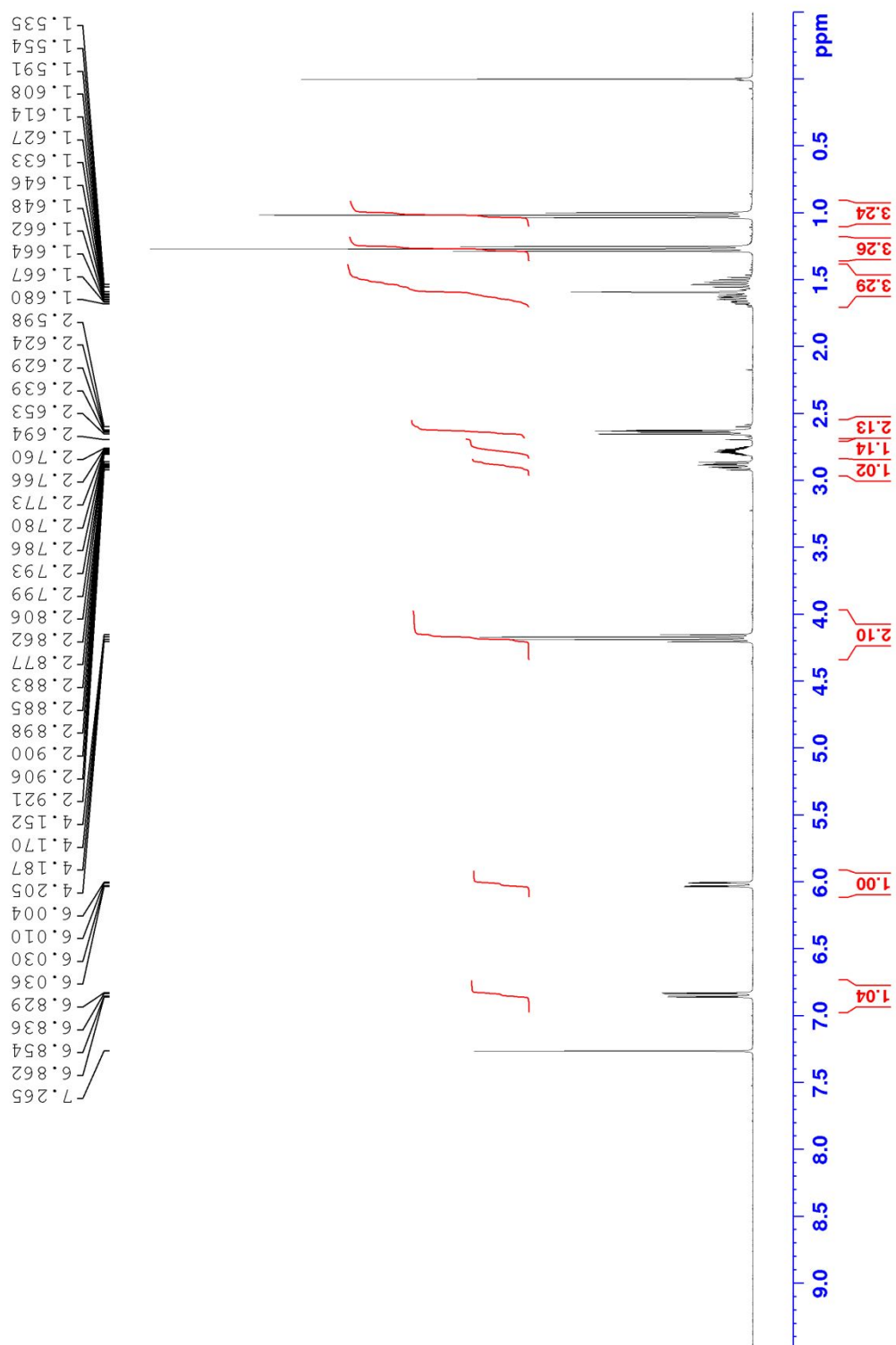
## $^1\text{H}$ -NMR of Compound 14 (400 MHz, $\text{CDCl}_3$ )

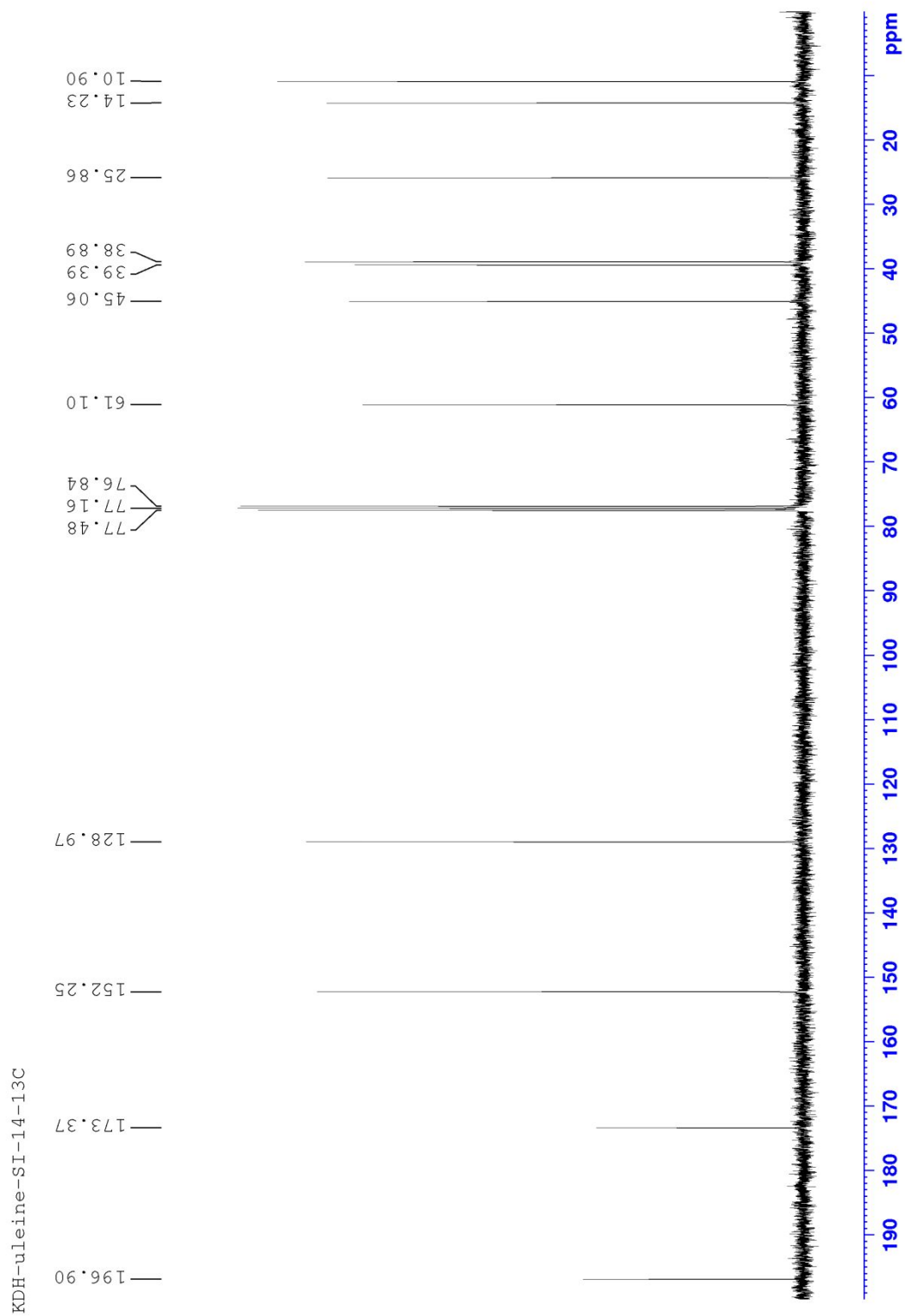


**<sup>13</sup>C-NMR of Compound 14 (100 MHz, CDCl<sub>3</sub>)**



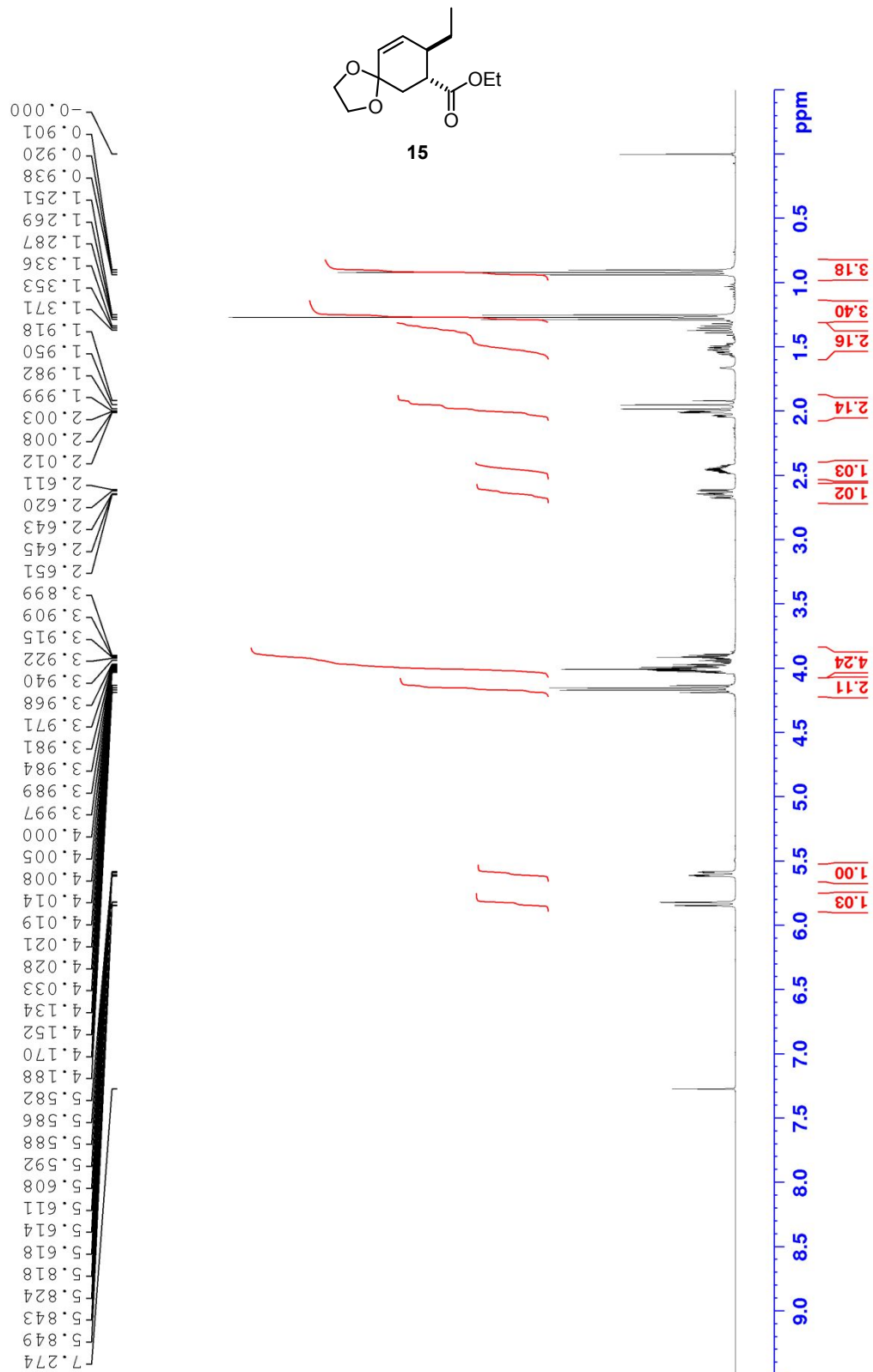
KDH-uleine-SI-14-1H



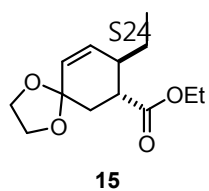


<sup>1</sup>H-NMR of Compound 15 (400 MHz, CDCl<sub>3</sub>)

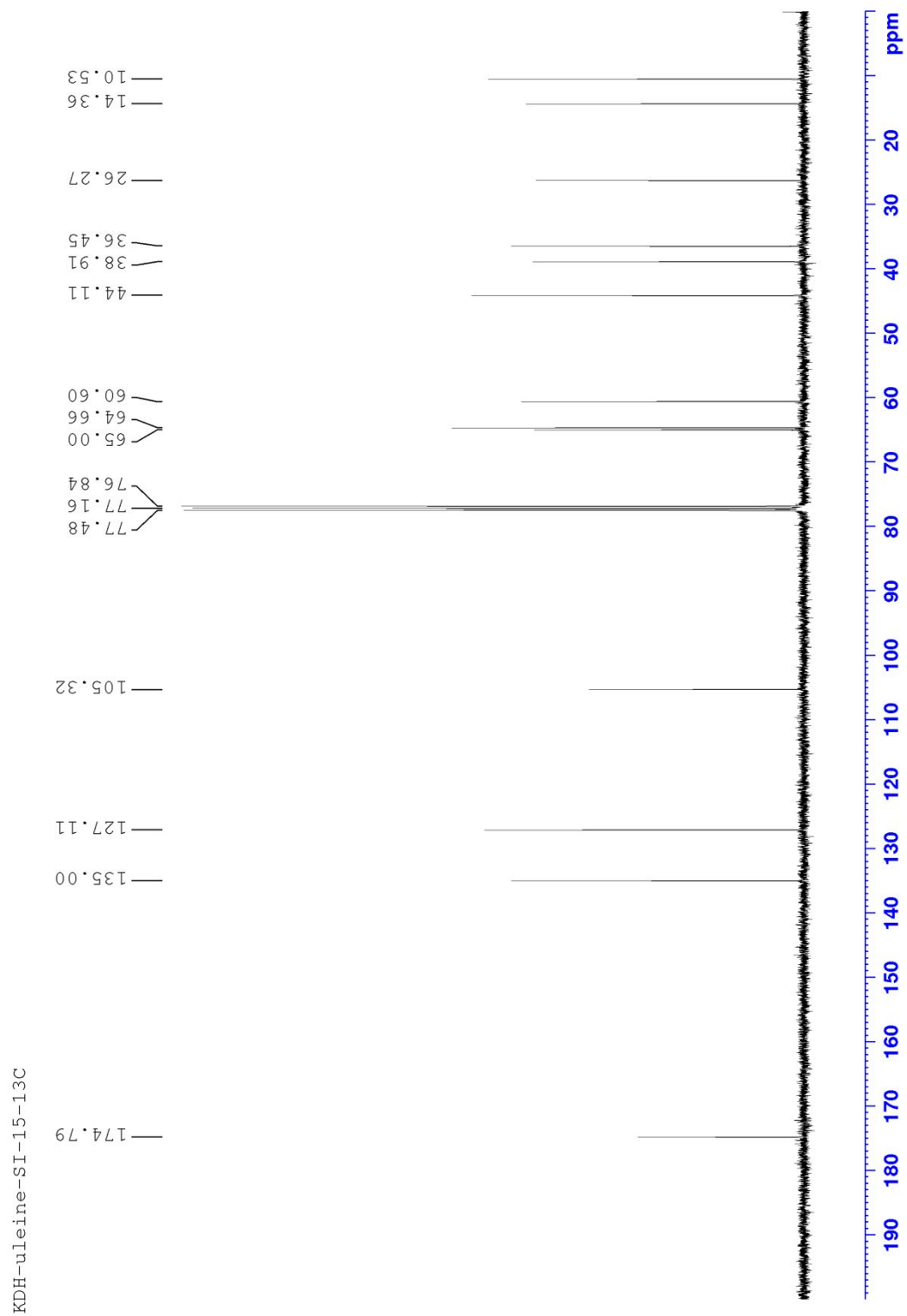
KDH-uleine-SI-15-1H



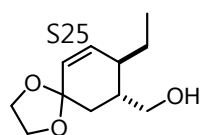
**<sup>13</sup>C-NMR of Compound 15 (100 MHz, CDCl<sub>3</sub>)**



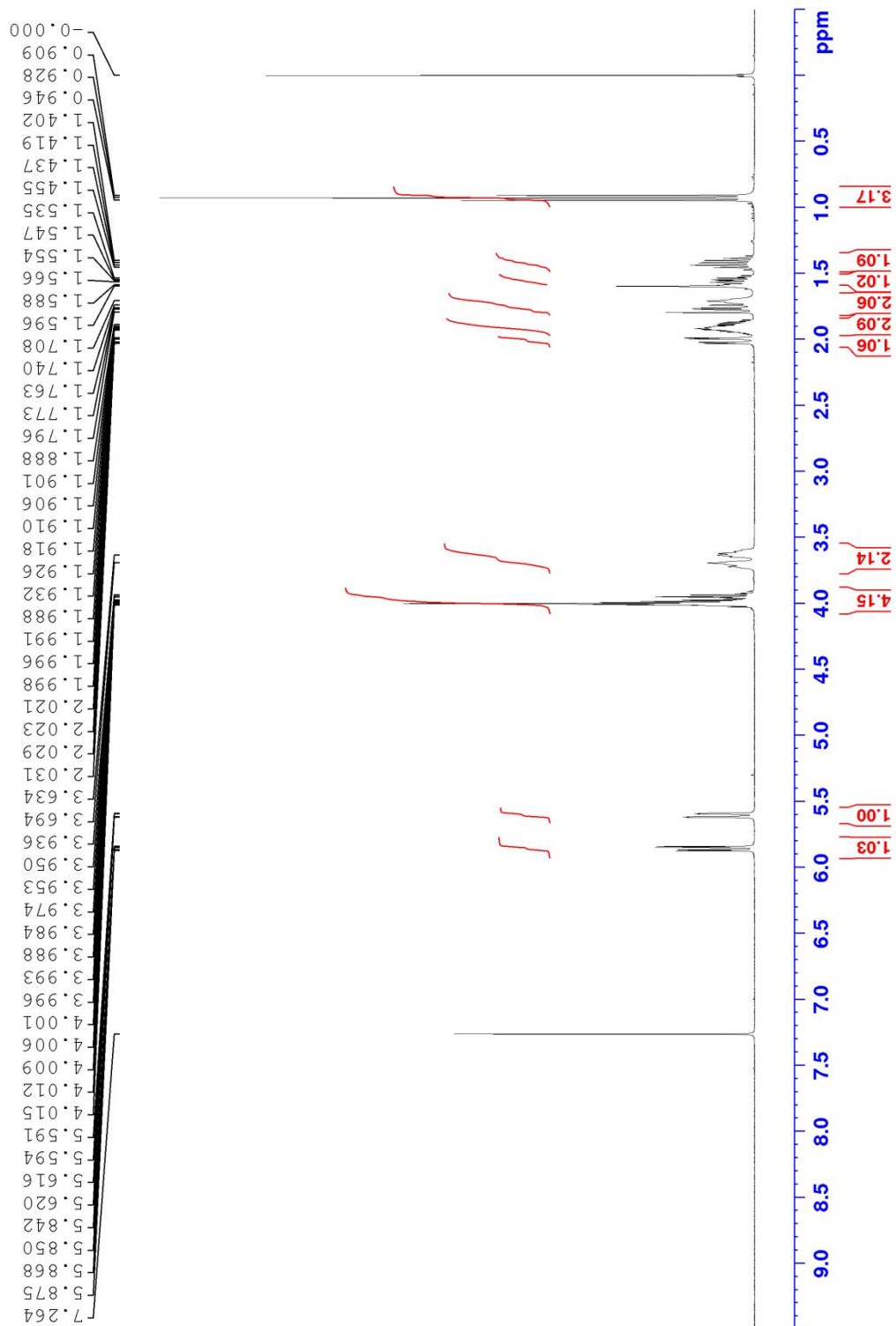




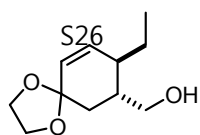
<sup>1</sup>H NMR of Compound 16 (400 MHz, CDCl<sub>3</sub>)



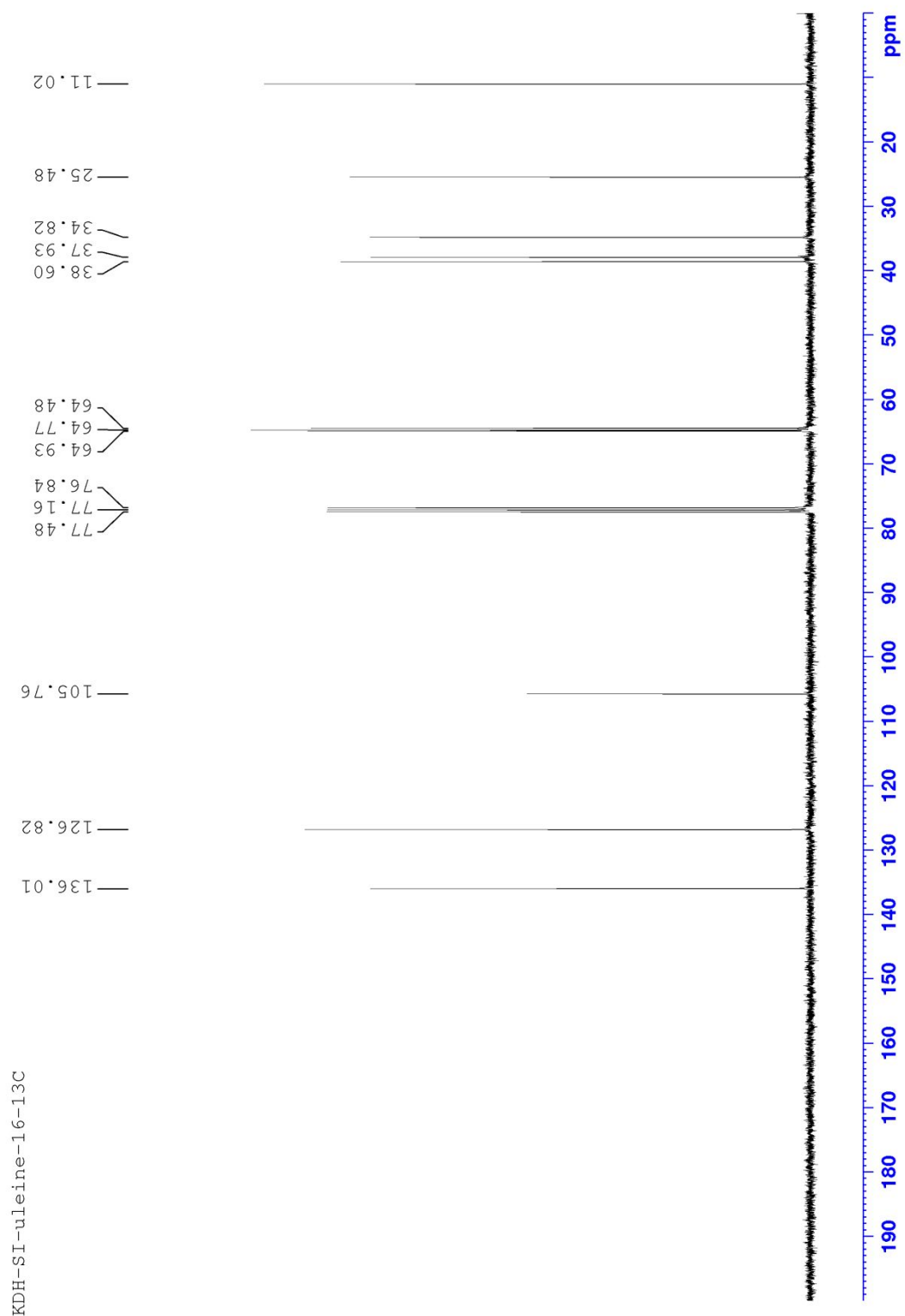
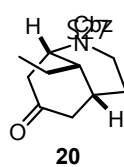
KDH-SI-uleine-16-1H



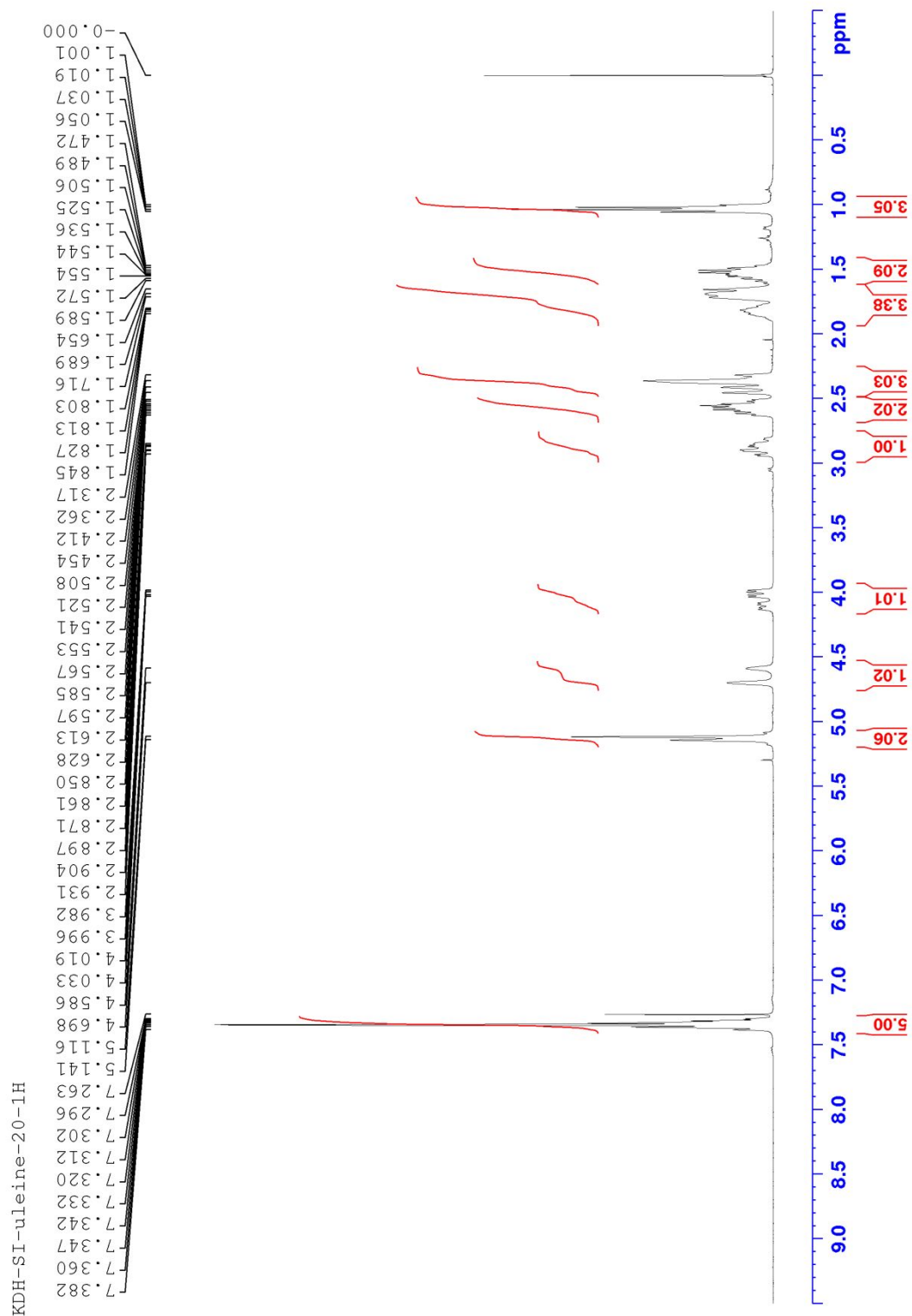
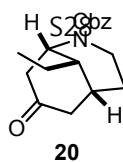
$^{13}\text{C}$  NMR of Compound 16 (100 MHz,  $\text{CDCl}_3$ )

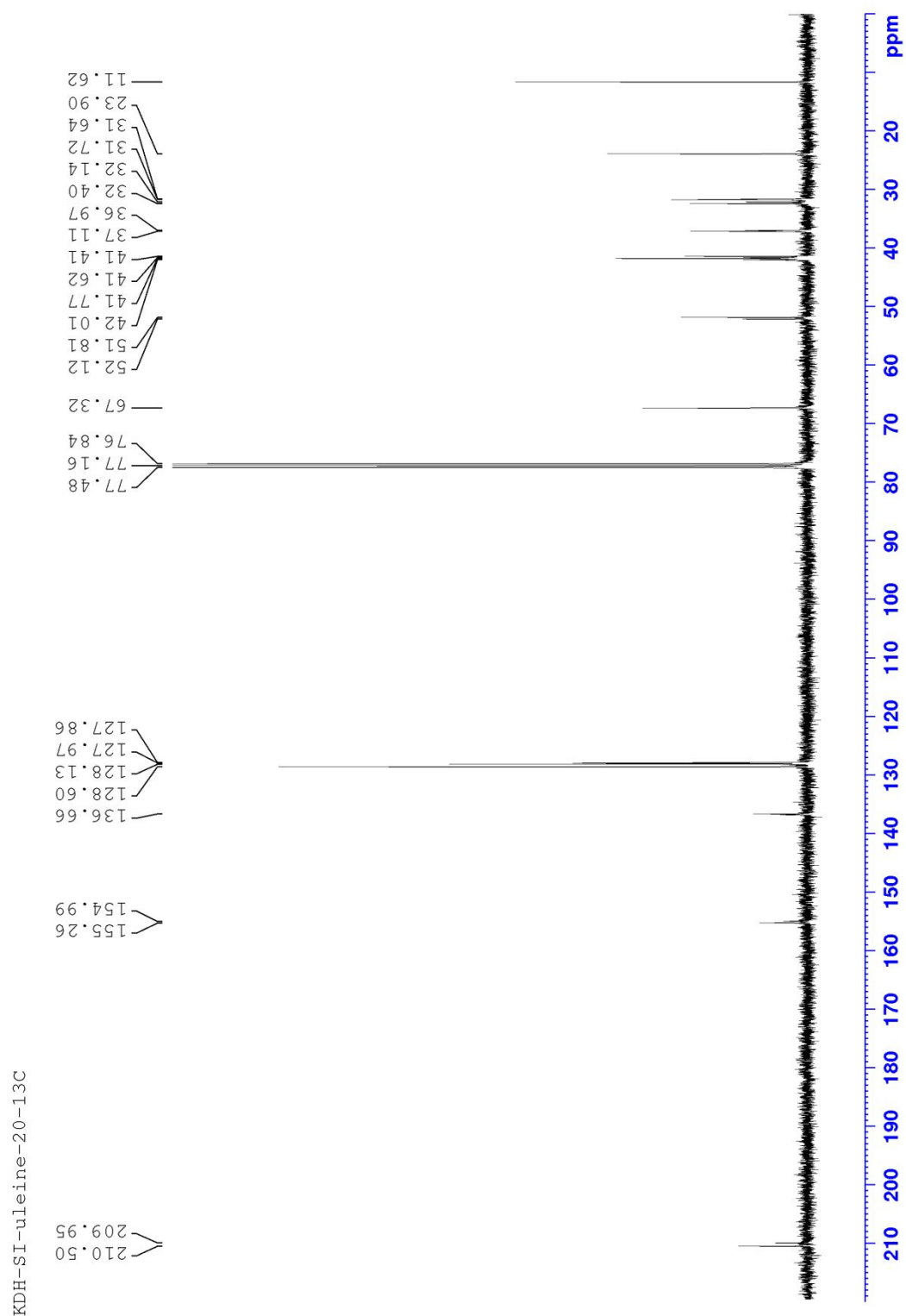


<sup>1</sup>H NMR of Compound 20 (400 MHz, CDCl<sub>3</sub>)



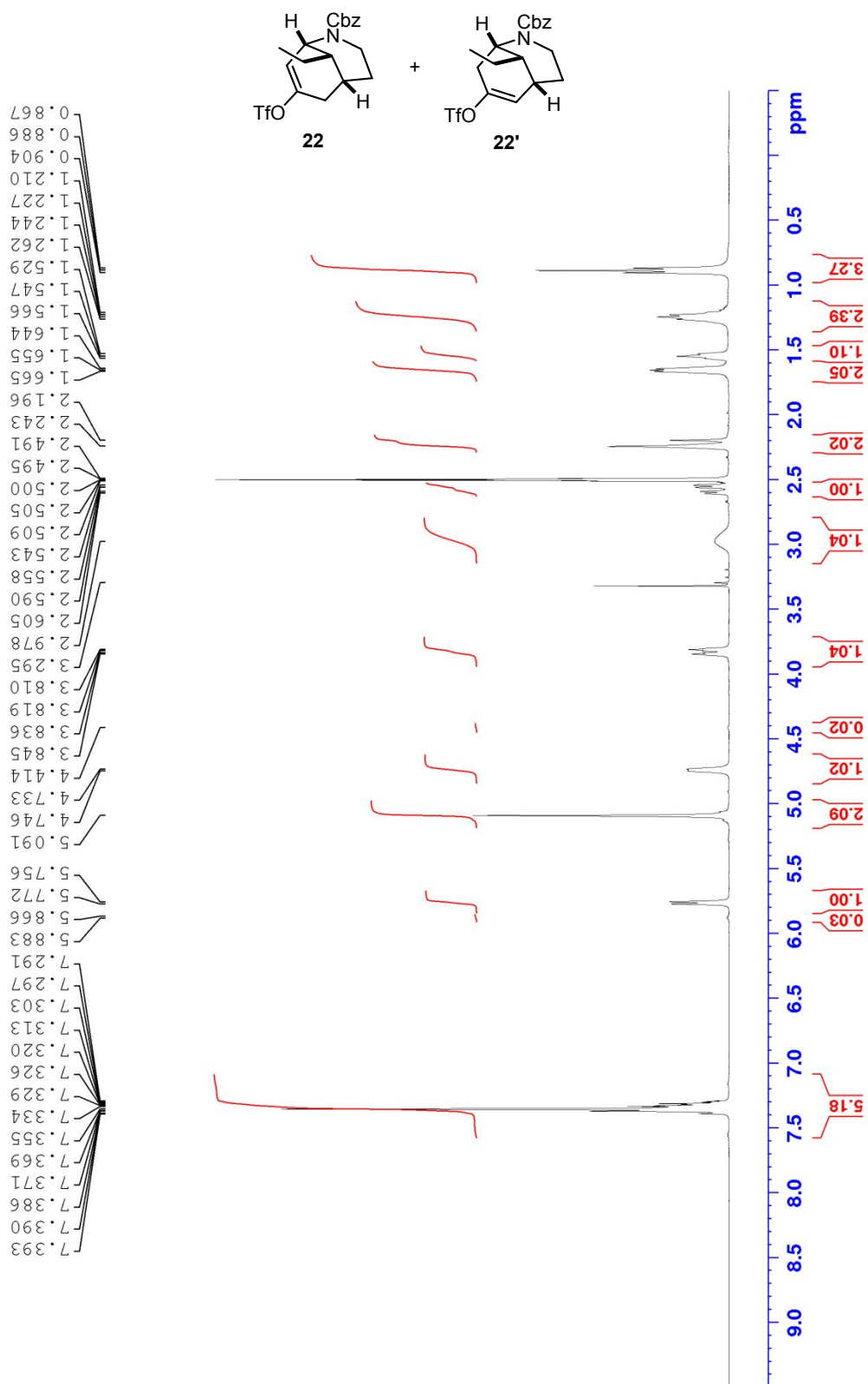
**$^{13}\text{C}$  NMR of Compound 20 (100 MHz,  $\text{CDCl}_3$ )**





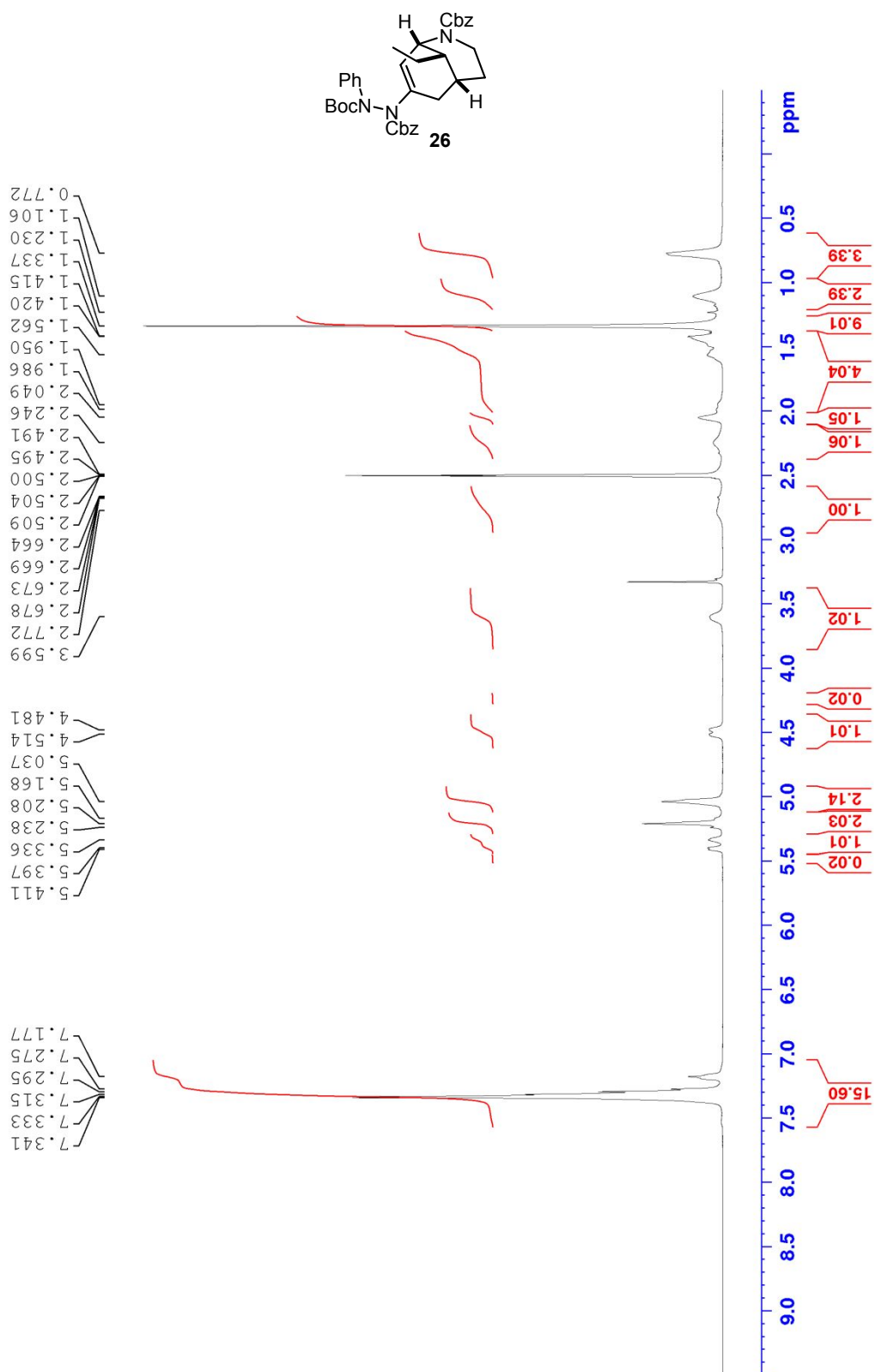
**$^1\text{H}$  NMR of Compound 22 (+22') (400 MHz, DMSO- $\text{d}_6$ )**

KDH-SI-uleineine-22-1H in DMSO

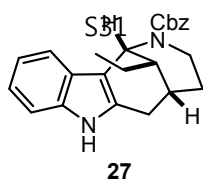


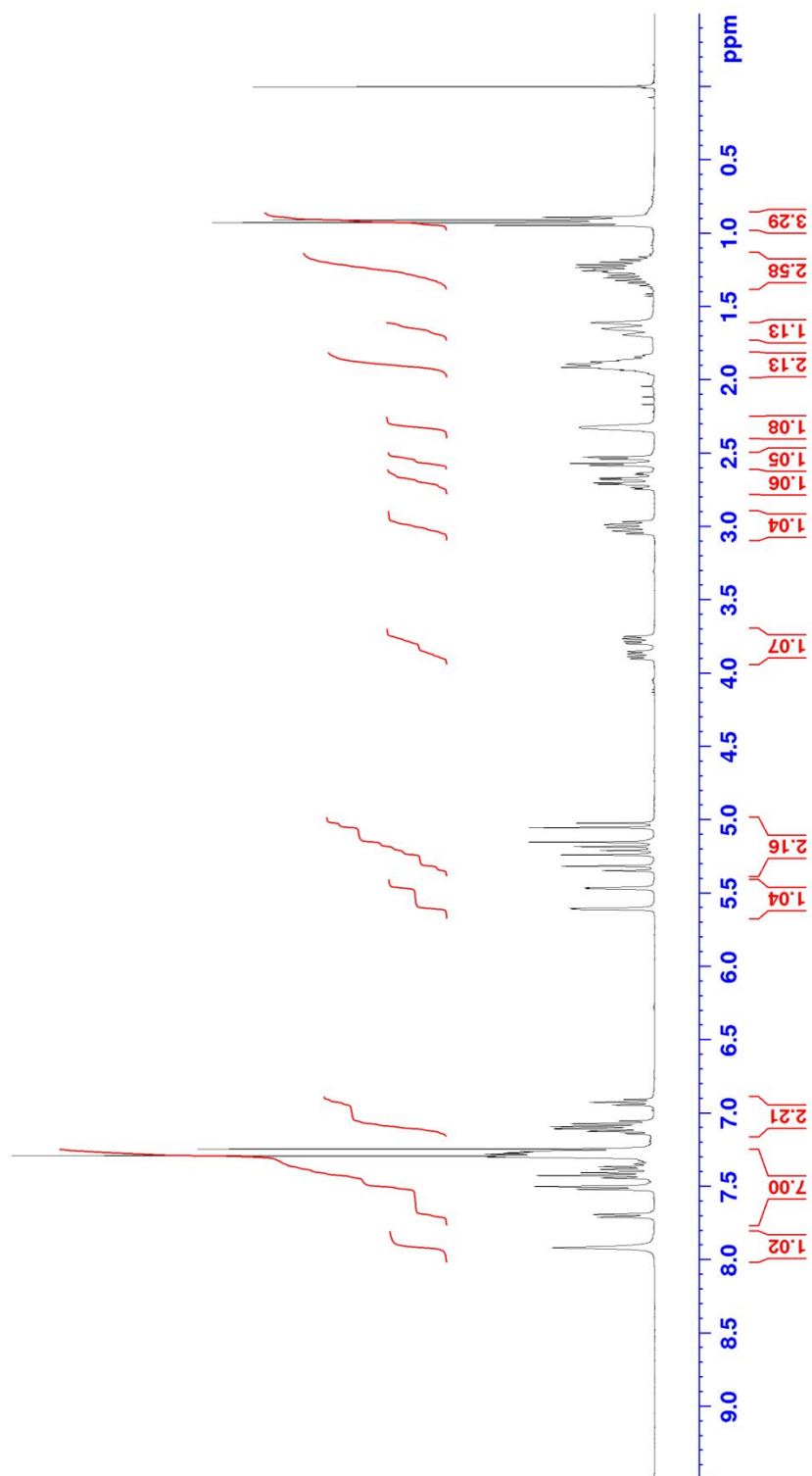
<sup>1</sup>H NMR of Compound 26 (400 MHz, DMSO-d<sub>6</sub>)

KDH-SI-uleineine-26-1H-DMSO



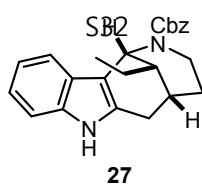
<sup>1</sup>H NMR of Compound 27 (400 MHz, CDCl<sub>3</sub>)





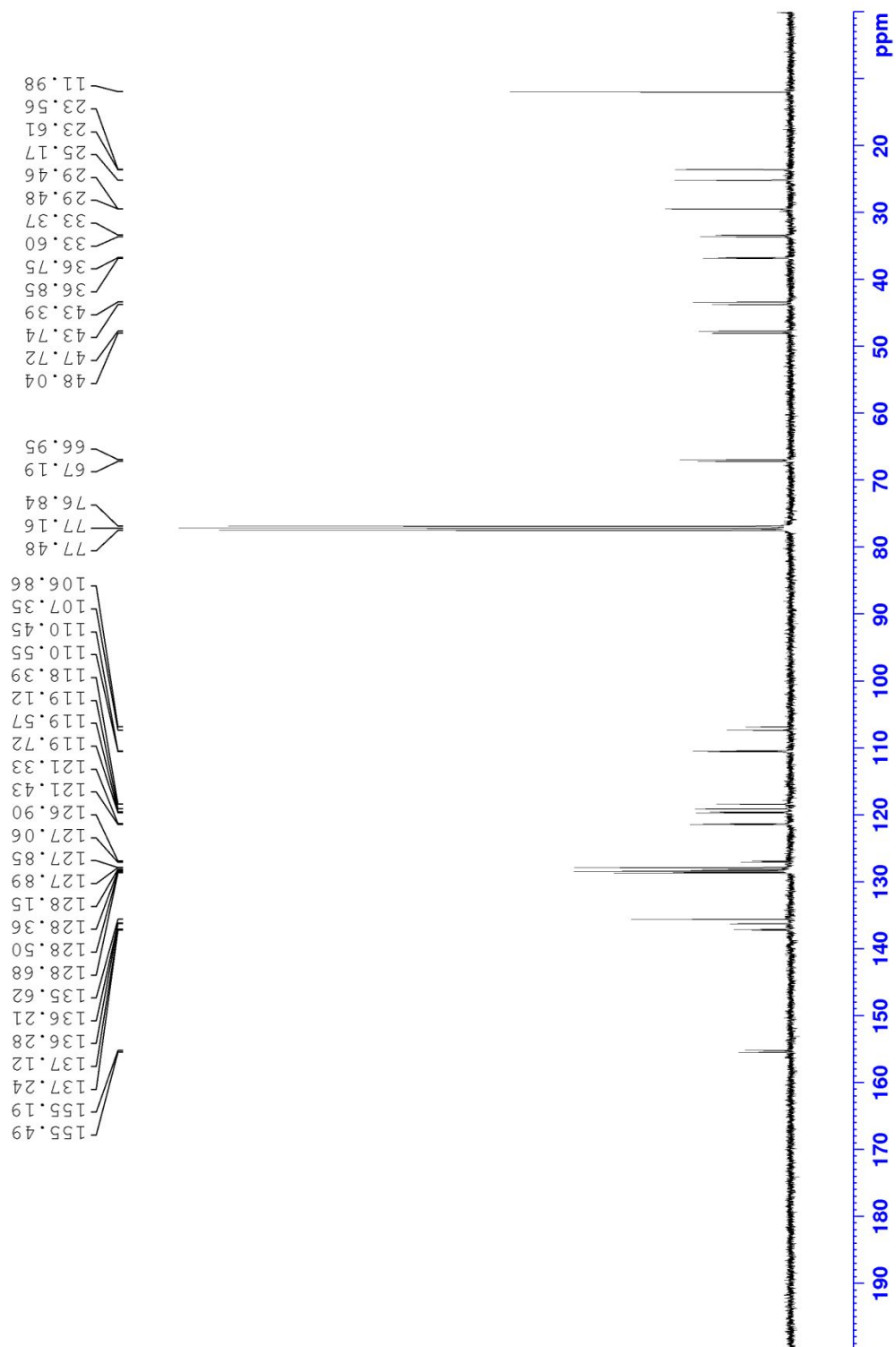
KDH-SI-uleine-27-1H

**<sup>13</sup>C NMR of Compound 27 (100 MHz, CDCl<sub>3</sub>)**

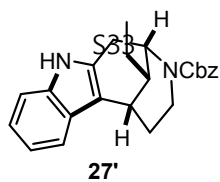




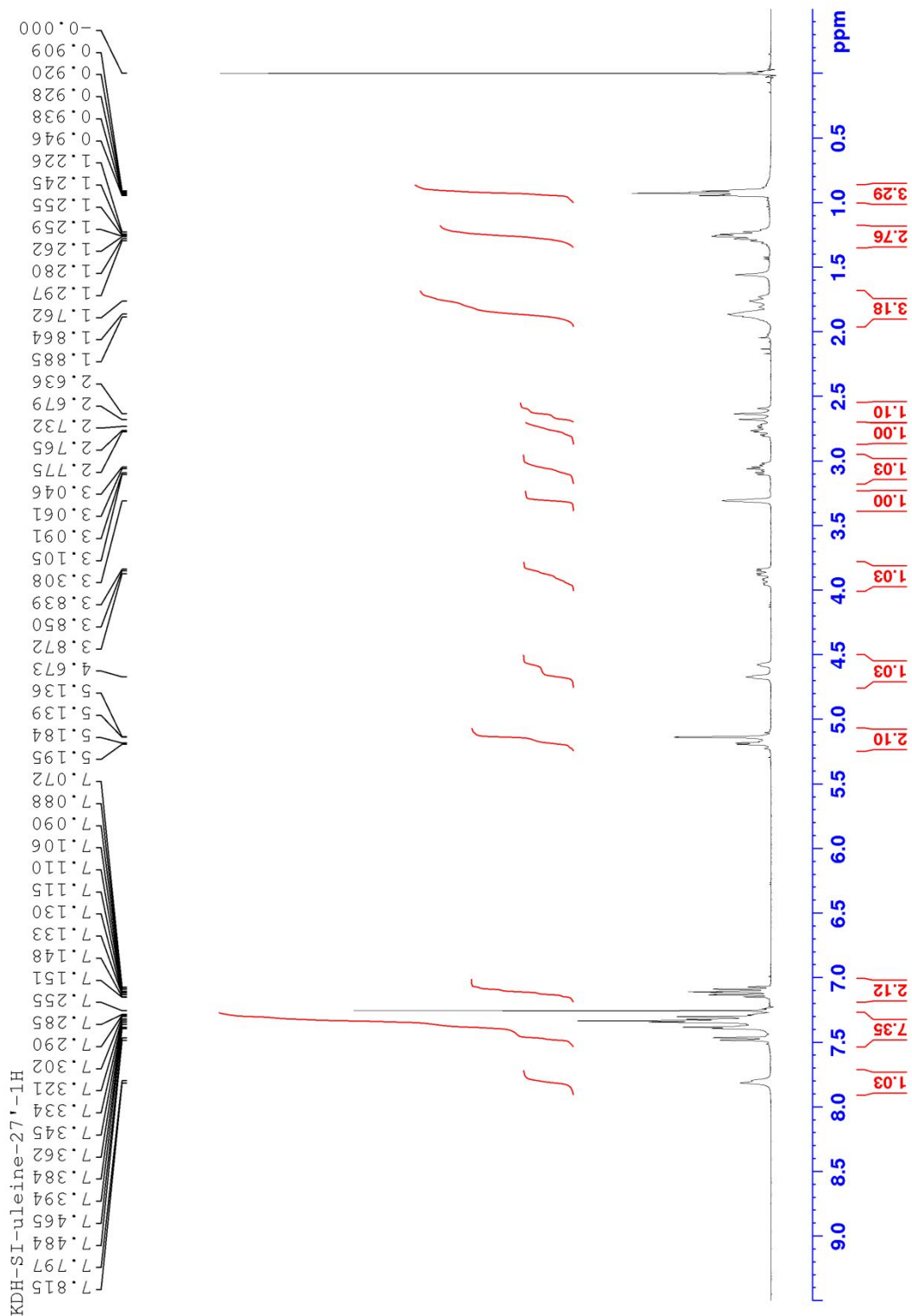
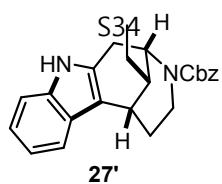
KDH-SI-uleine-27-13C



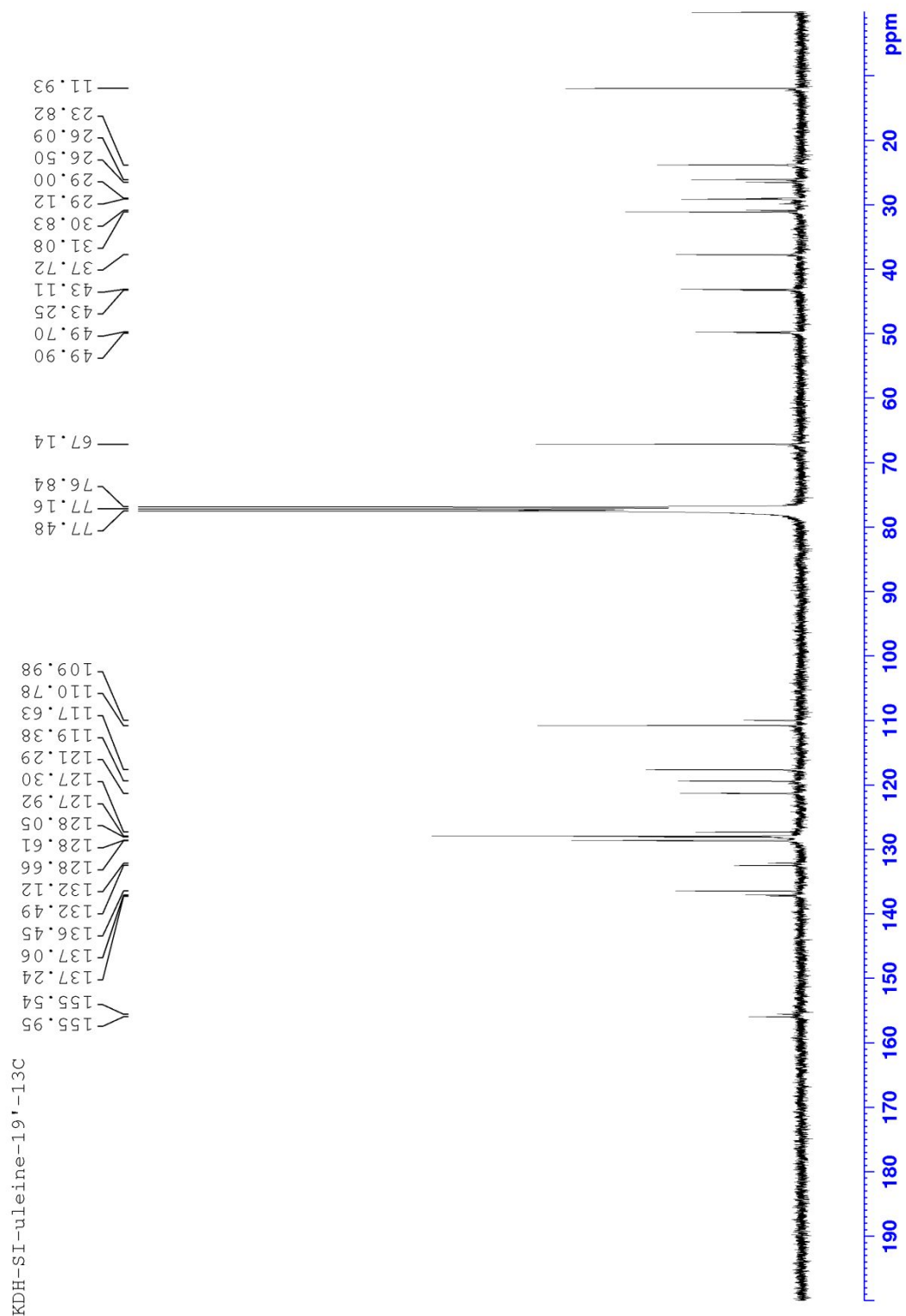
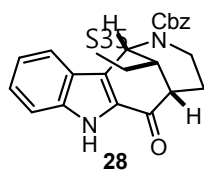
<sup>1</sup>H NMR of Compound 27' (400 MHz, CDCl<sub>3</sub>)



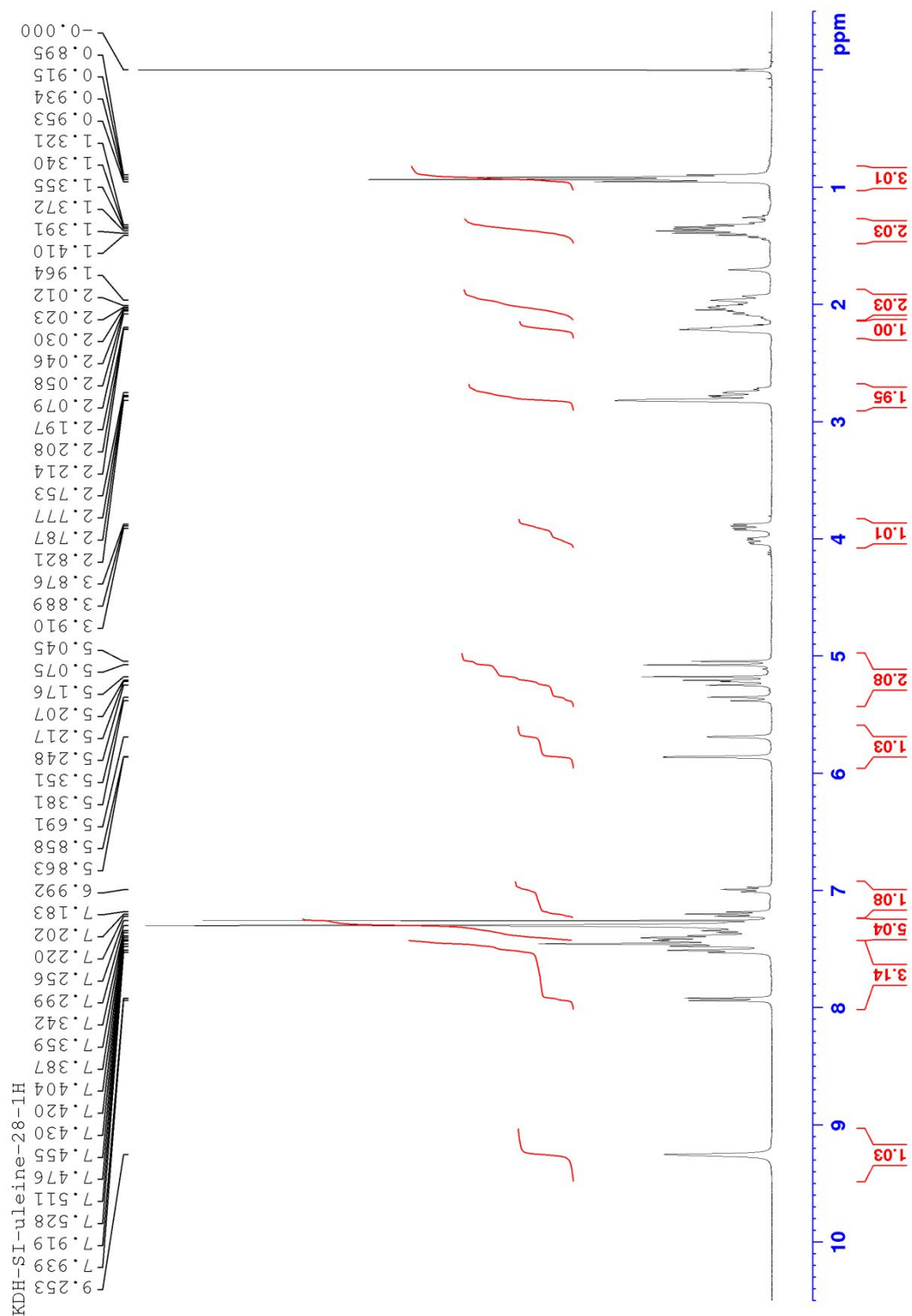
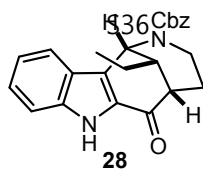
<sup>13</sup>C NMR of Compound 27' (100 MHz, CDCl<sub>3</sub>)



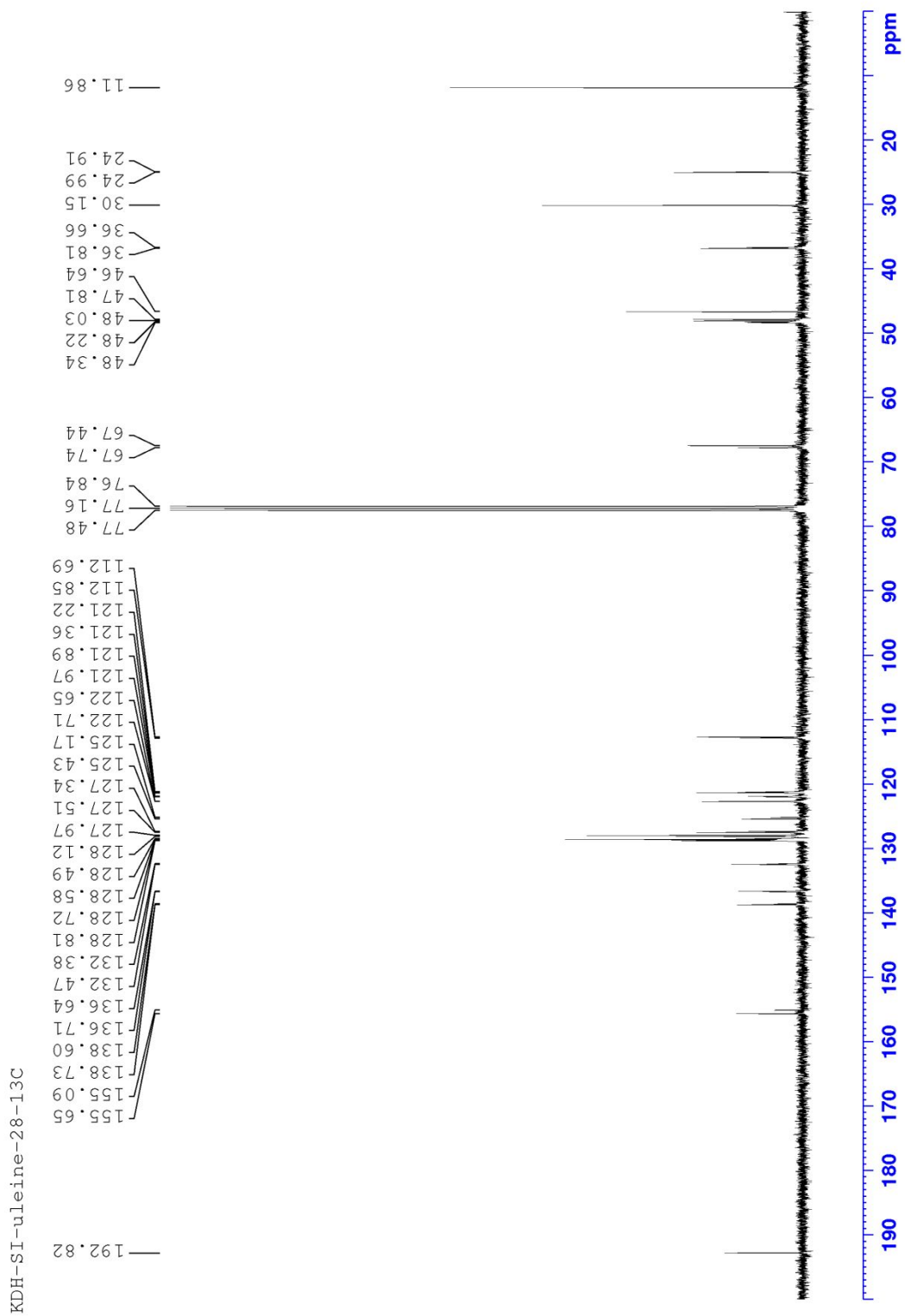
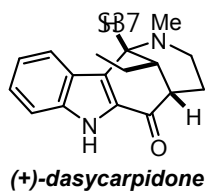
<sup>1</sup>H NMR of Compound 28 (400 MHz, CDCl<sub>3</sub>)



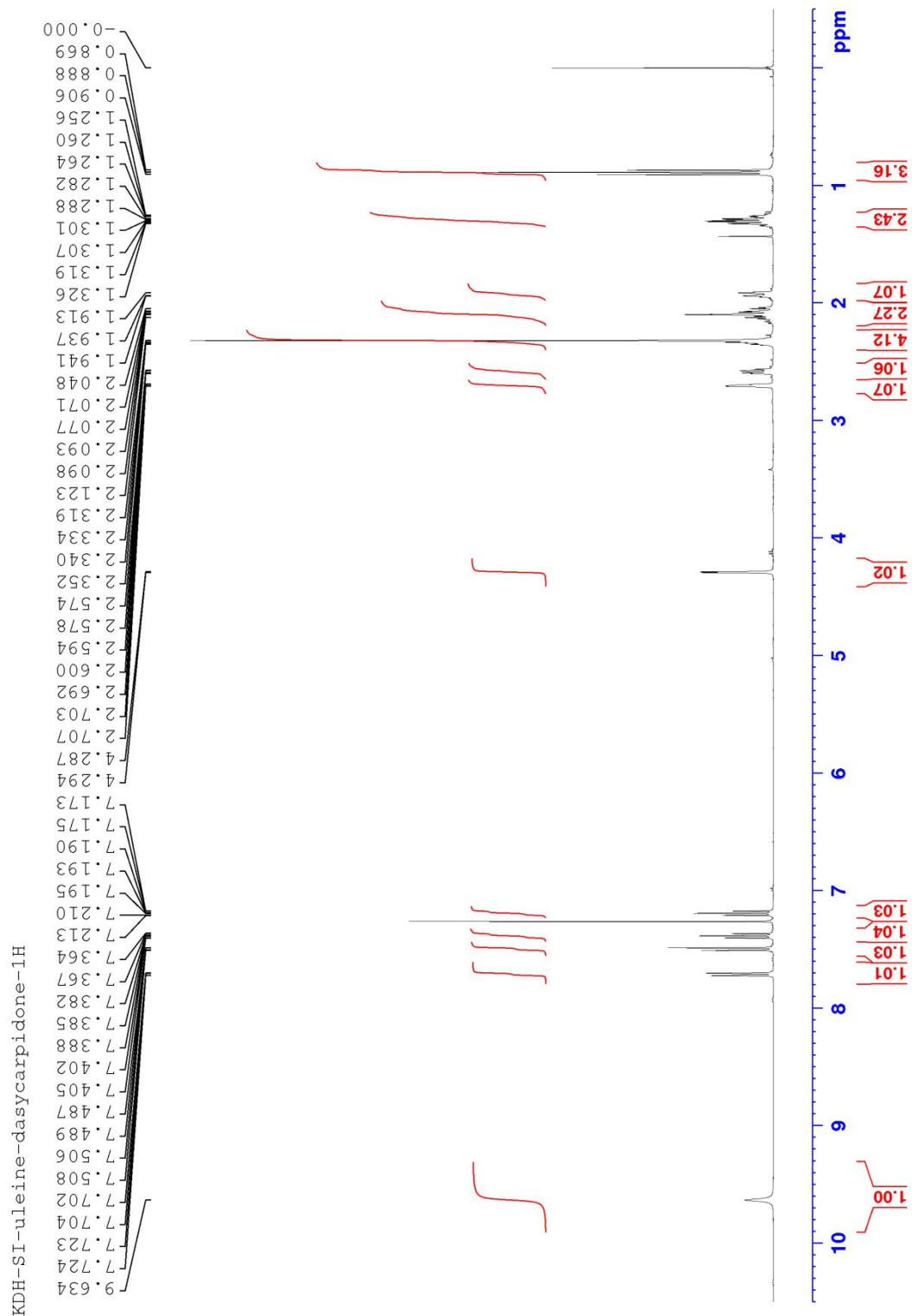
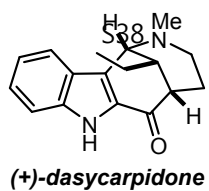
**$^{13}\text{C}$  NMR of Compound 28 (100 MHz,  $\text{CDCl}_3$ )**



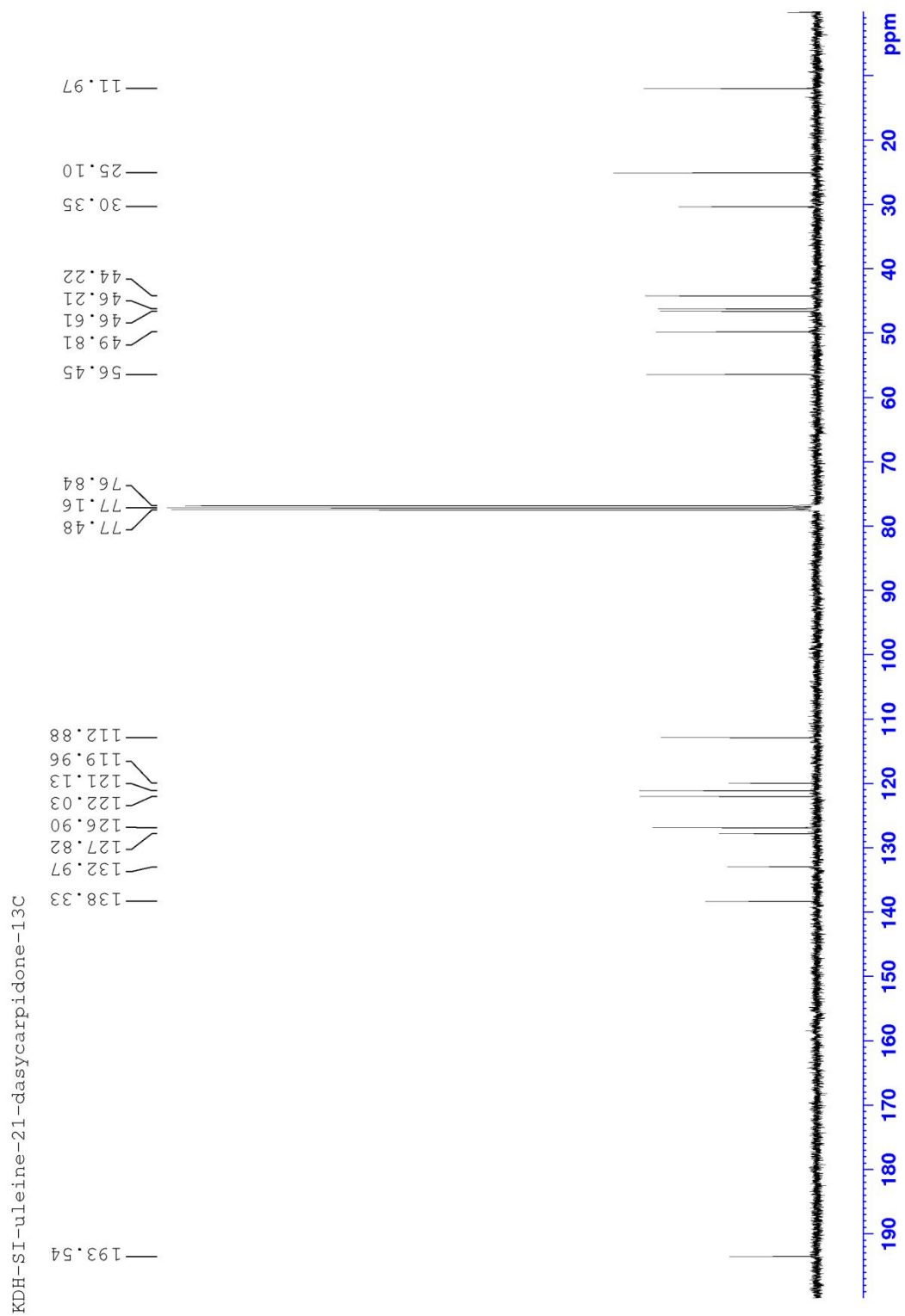
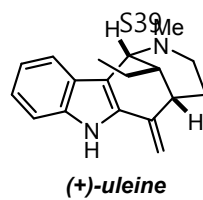
**<sup>1</sup>H NMR of (+)-Dasycarpidone (400 MHz, CDCl<sub>3</sub>)**

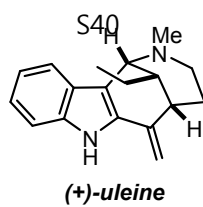


<sup>13</sup>C NMR of (+)-Dasycarpidone (100 MHz, CDCl<sub>3</sub>)

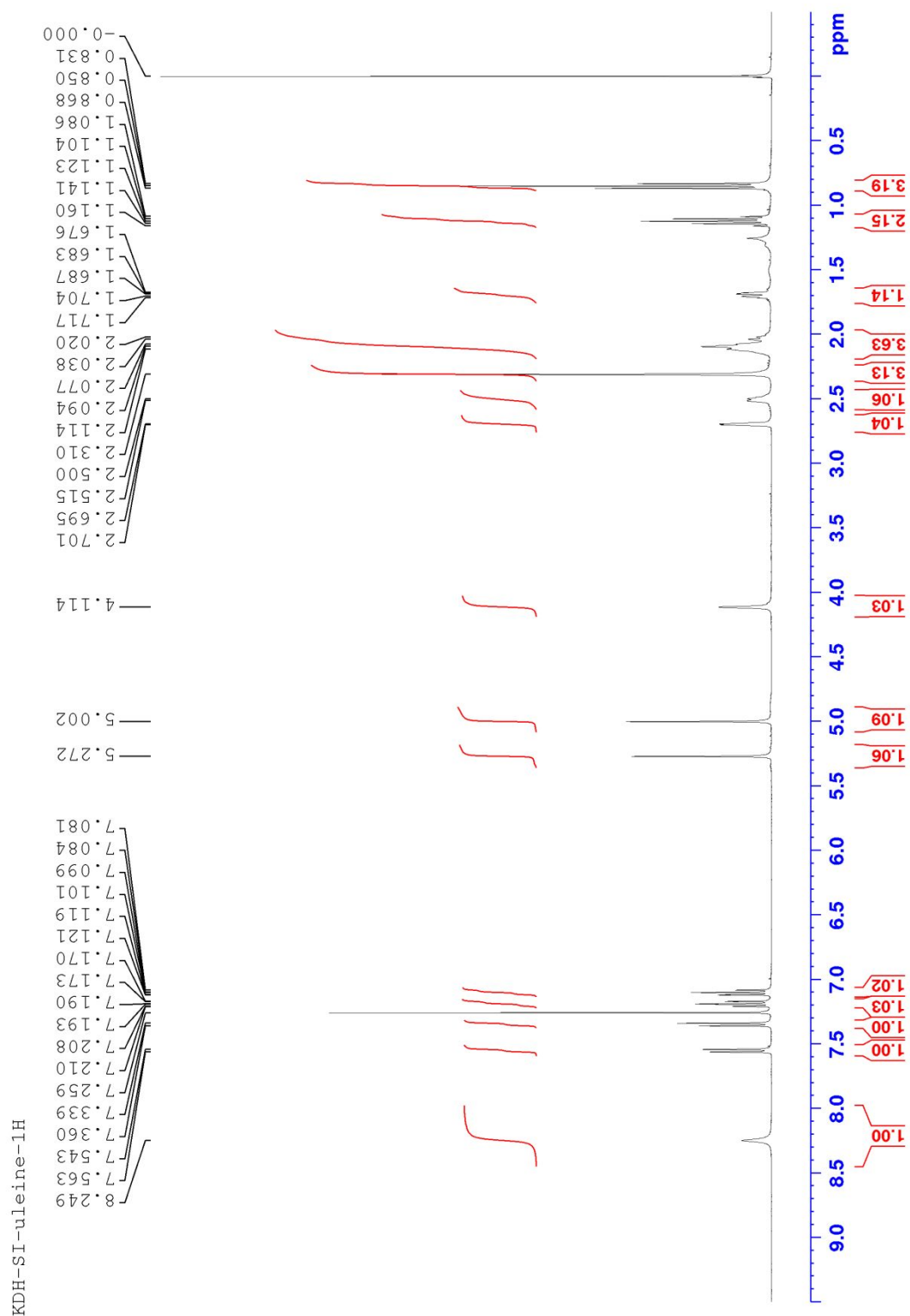


**<sup>1</sup>H NMR of (+)-Uleine (400 MHz, CDCl<sub>3</sub>)**



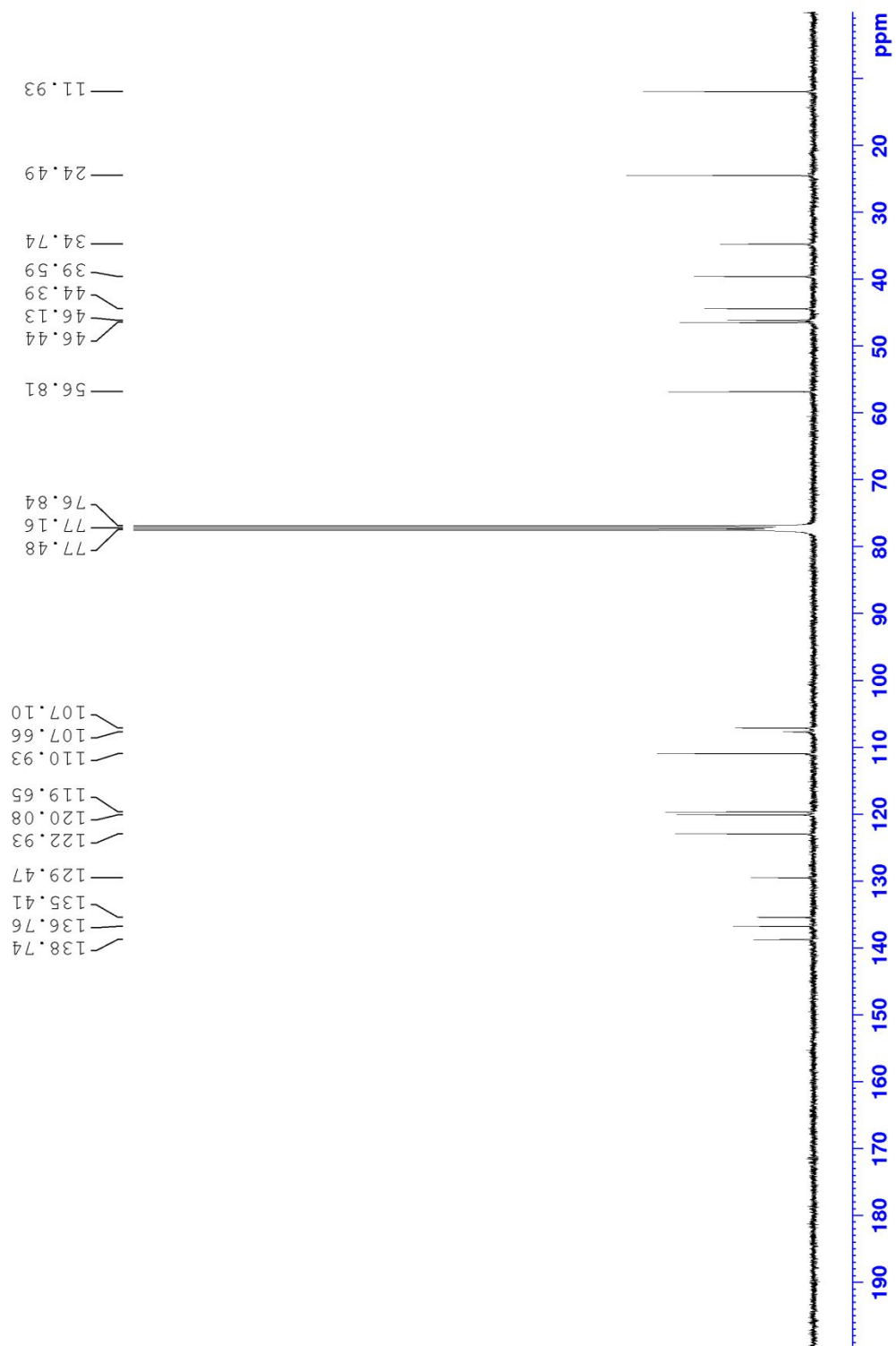


**$^{13}\text{C}$  NMR of (+)-Uleine (100 MHz,  $\text{CDCl}_3$ )**

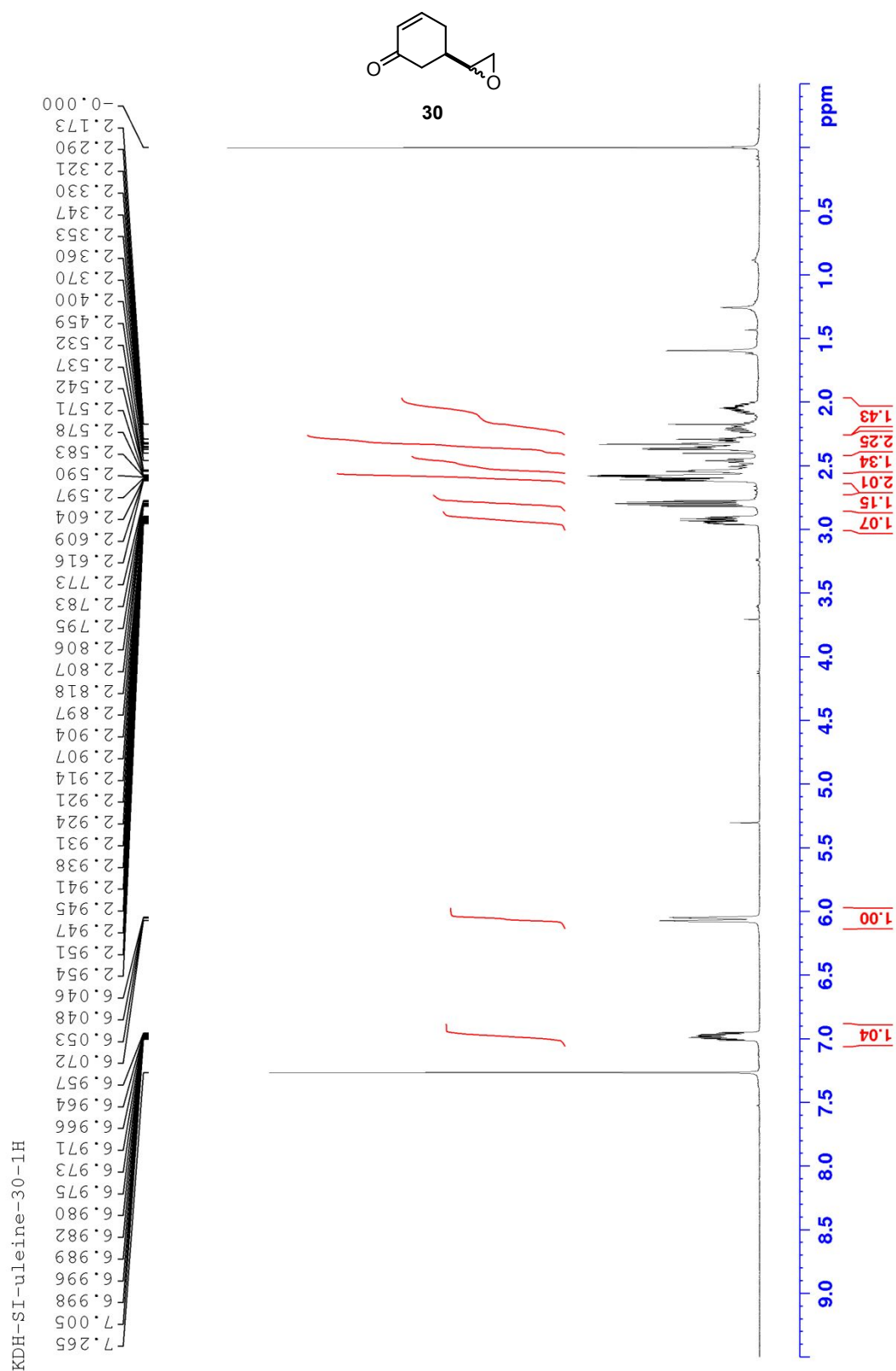




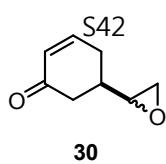
KDH-SI-uleine-13C



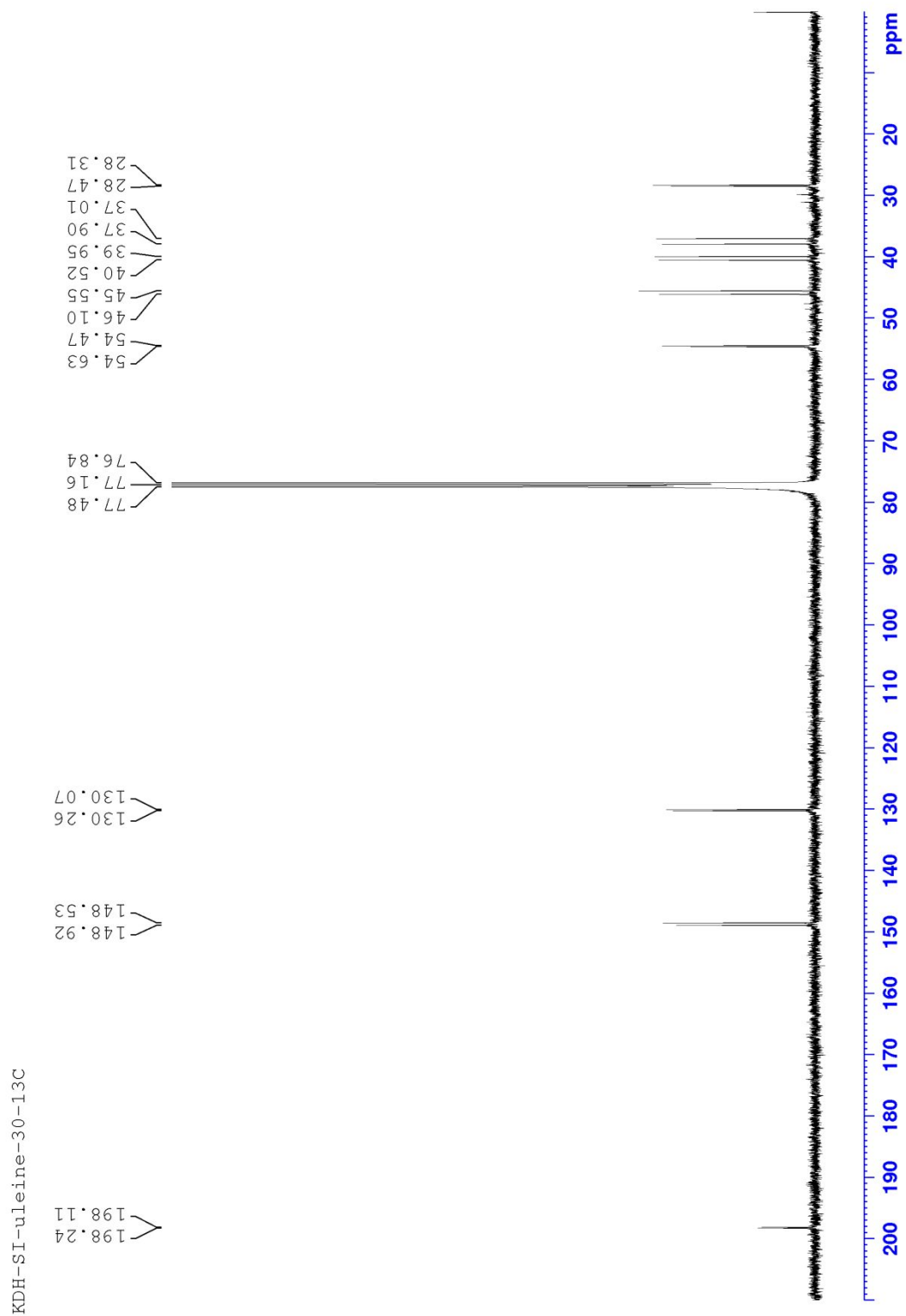
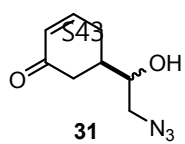
<sup>1</sup>H NMR of Compound 30 (400 MHz, CDCl<sub>3</sub>)

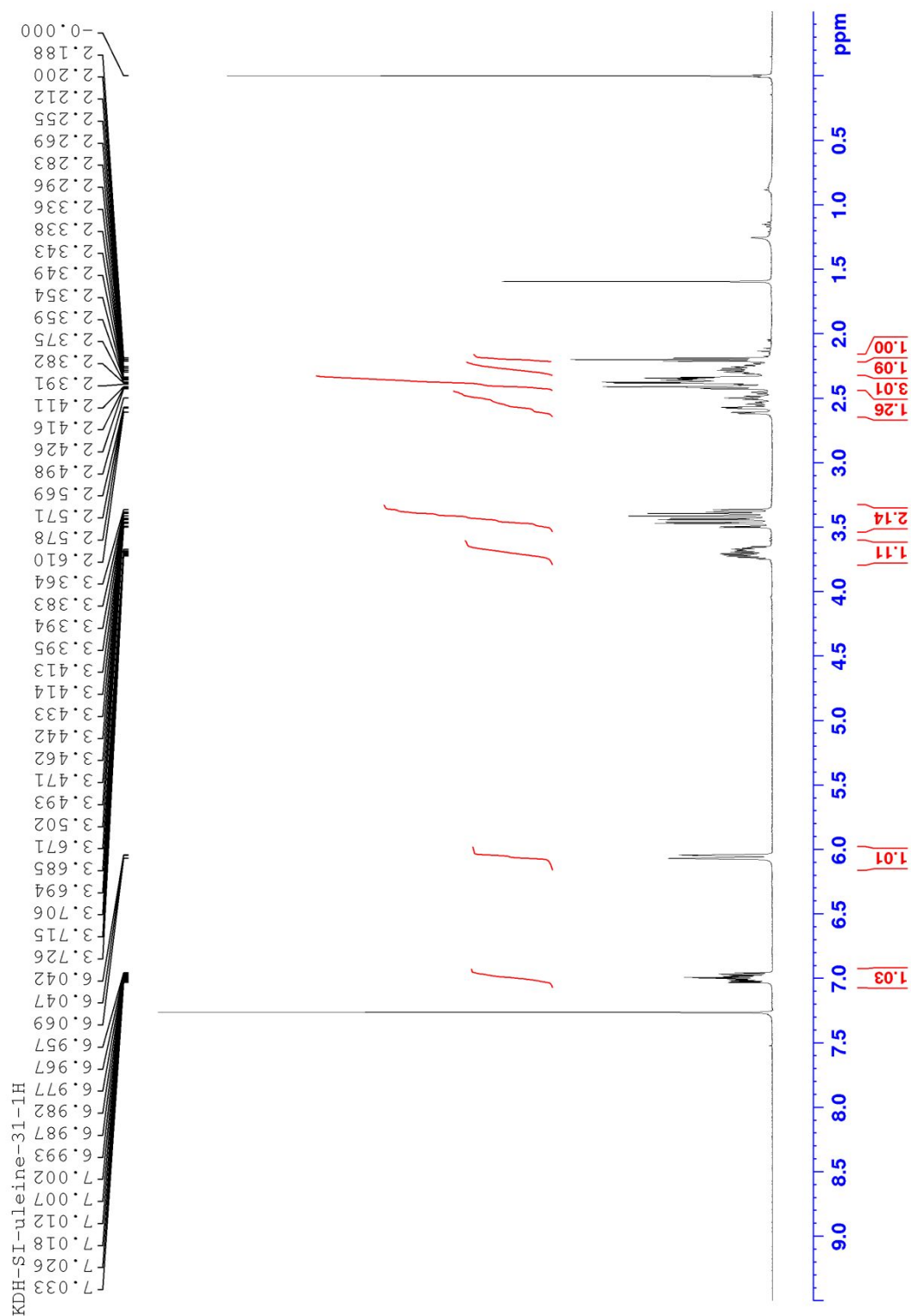


**<sup>13</sup>C NMR of Compound 30 (100 MHz, CDCl<sub>3</sub>)**

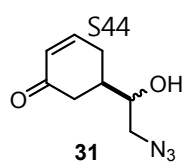


**<sup>1</sup>H NMR of Compound 31 (400 MHz, CDCl<sub>3</sub>)**

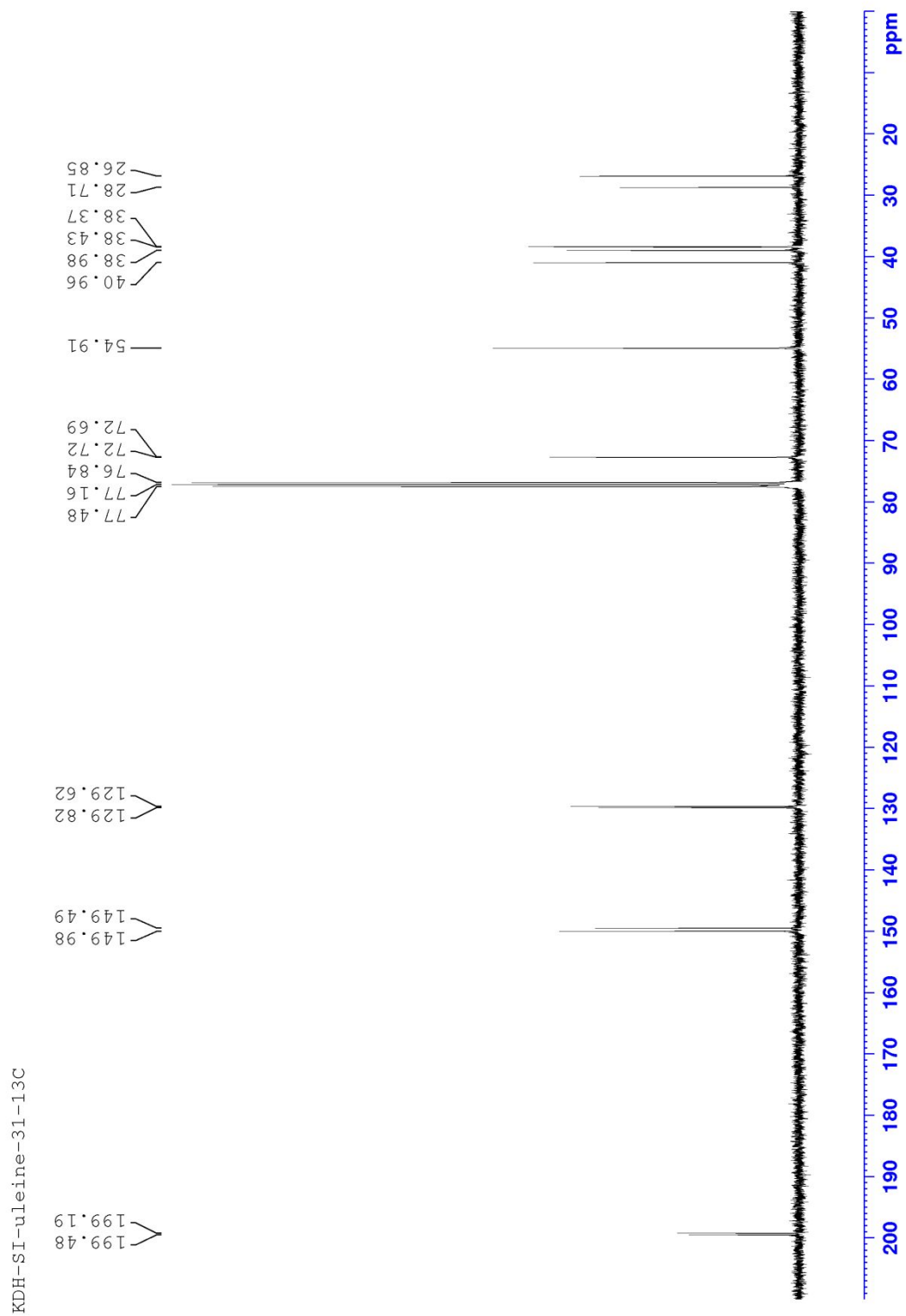
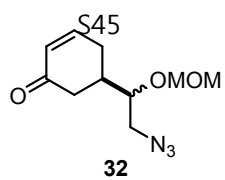




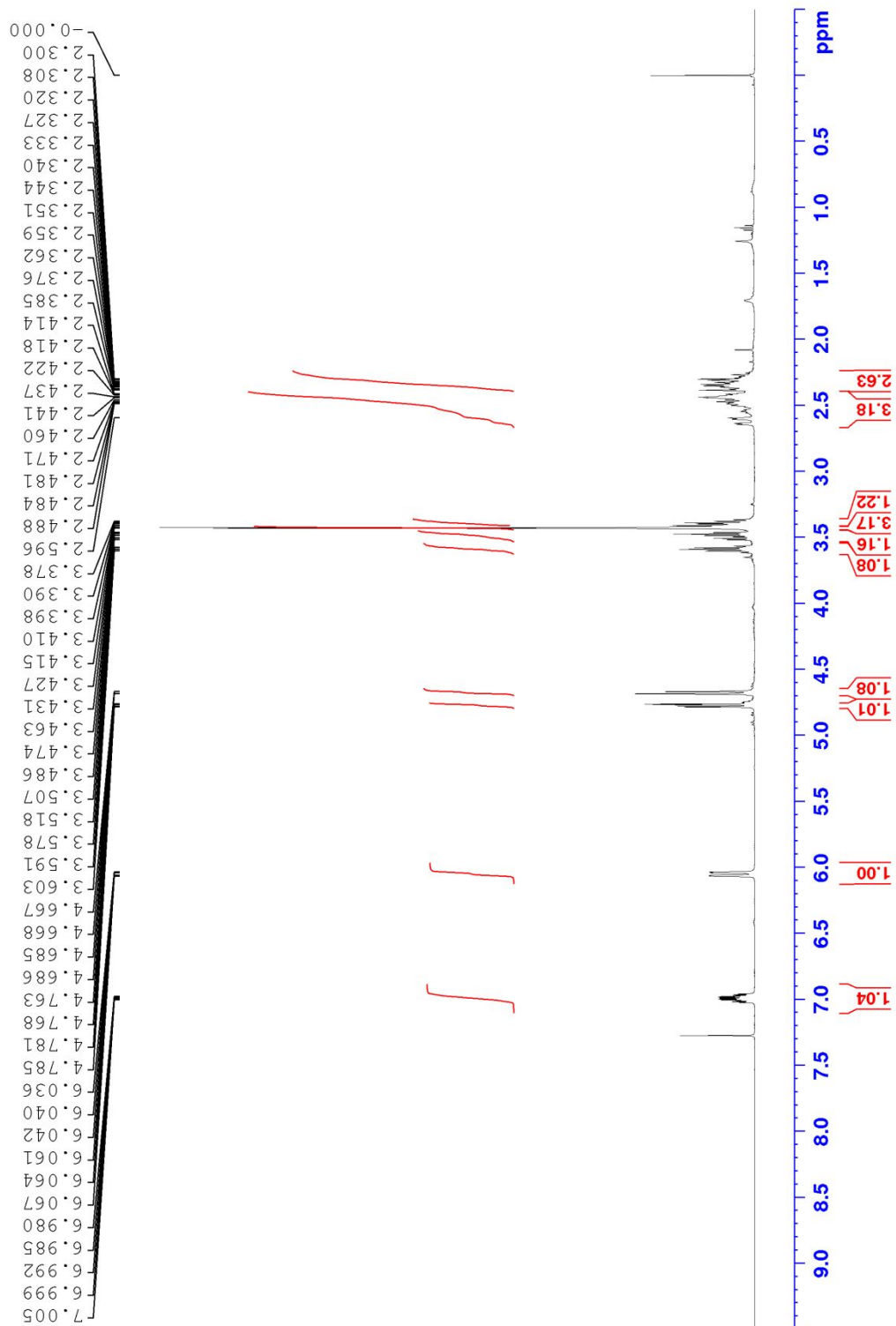
$^{13}\text{C}$  NMR of Compound 31 (100 MHz,  $\text{CDCl}_3$ )



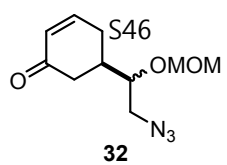
<sup>1</sup>H NMR of Compound 32 (400 MHz, CDCl<sub>3</sub>)



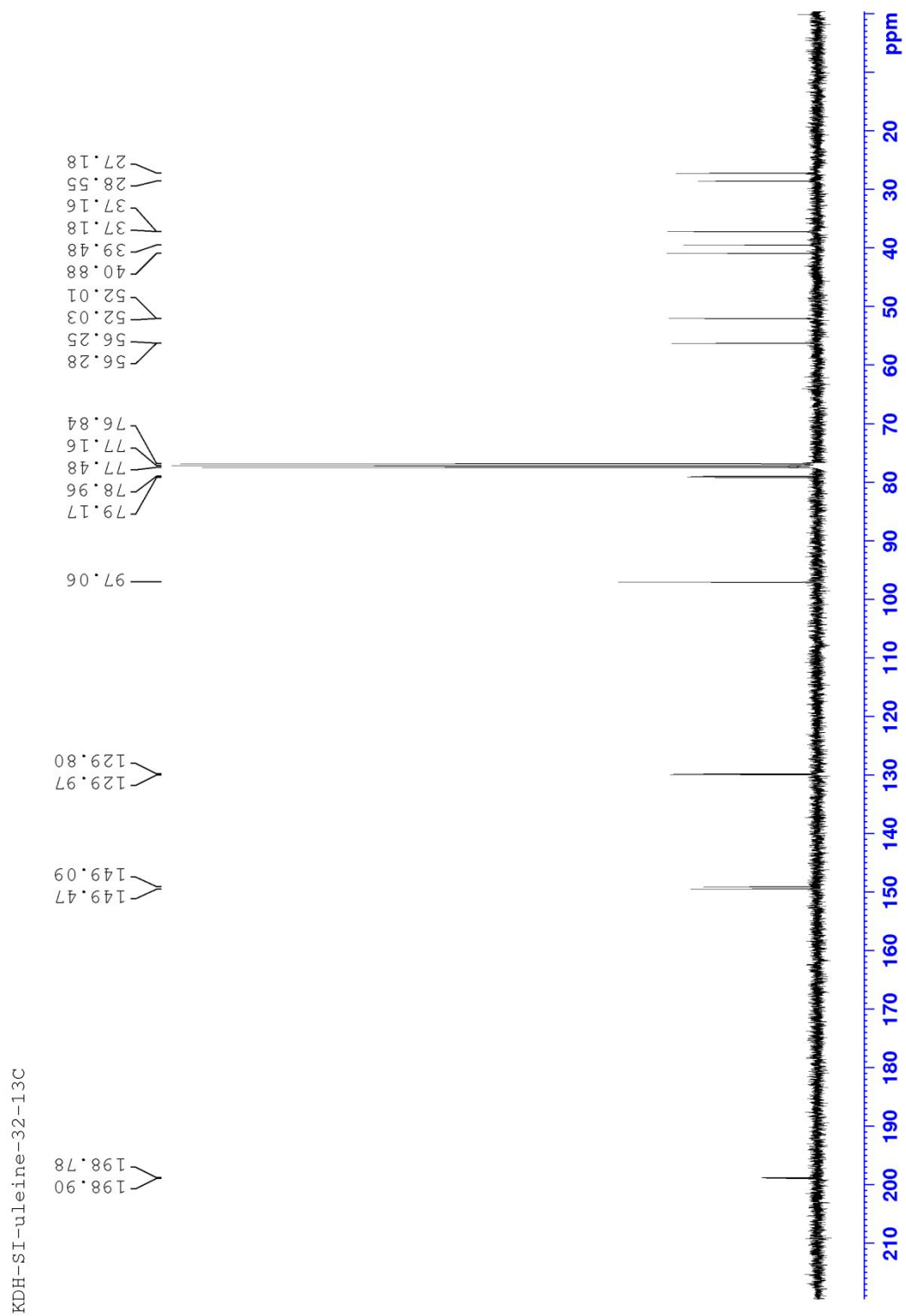
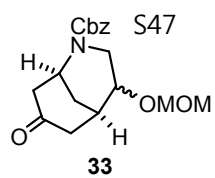
KDH-SI-uleine-32-1H

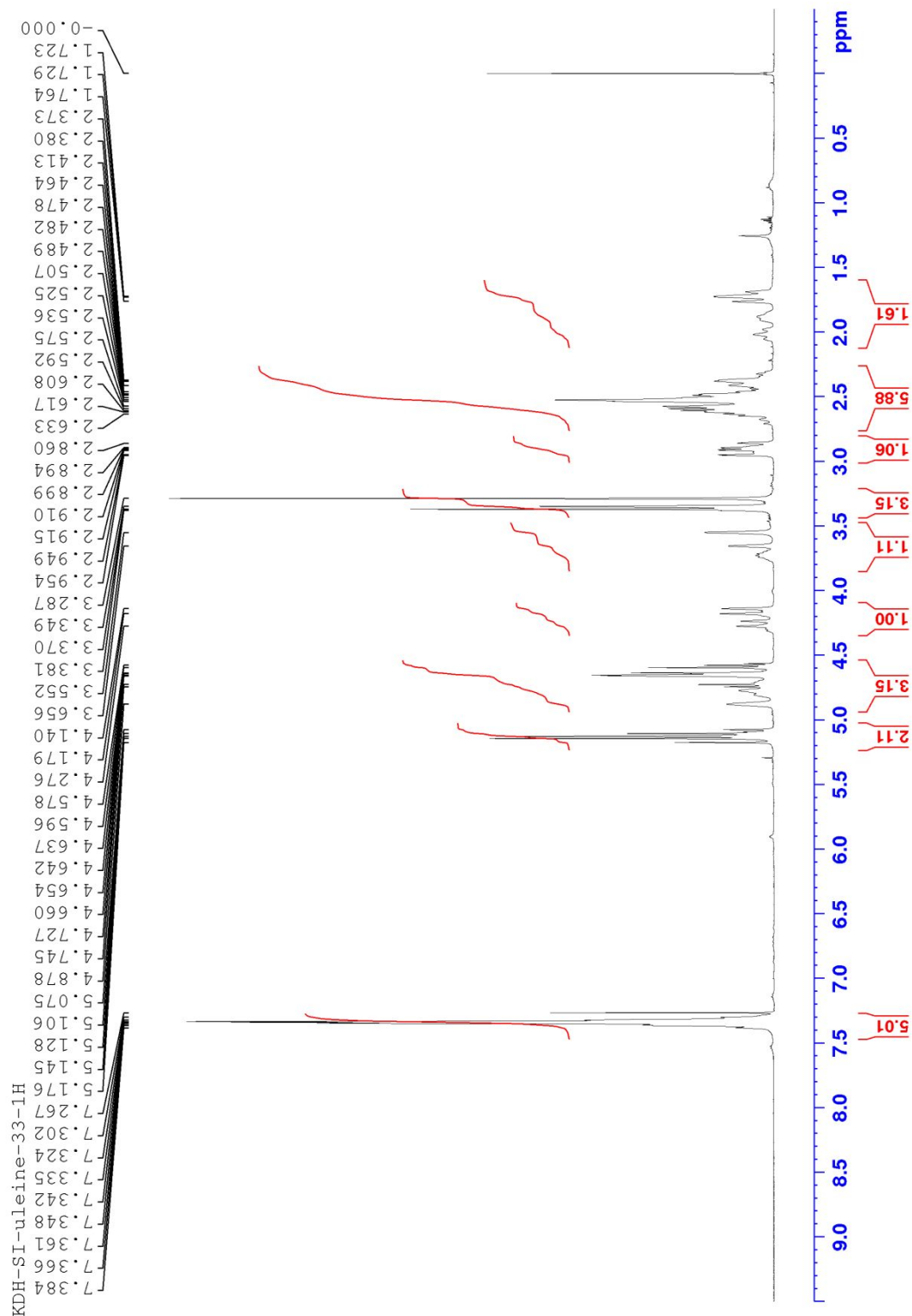


$^{13}\text{C}$  NMR of Compound 32 (100 MHz,  $\text{CDCl}_3$ )

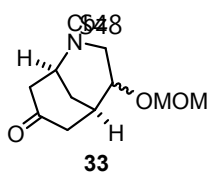


**<sup>1</sup>H NMR of Compound 33 (400 MHz, CDCl<sub>3</sub>)**



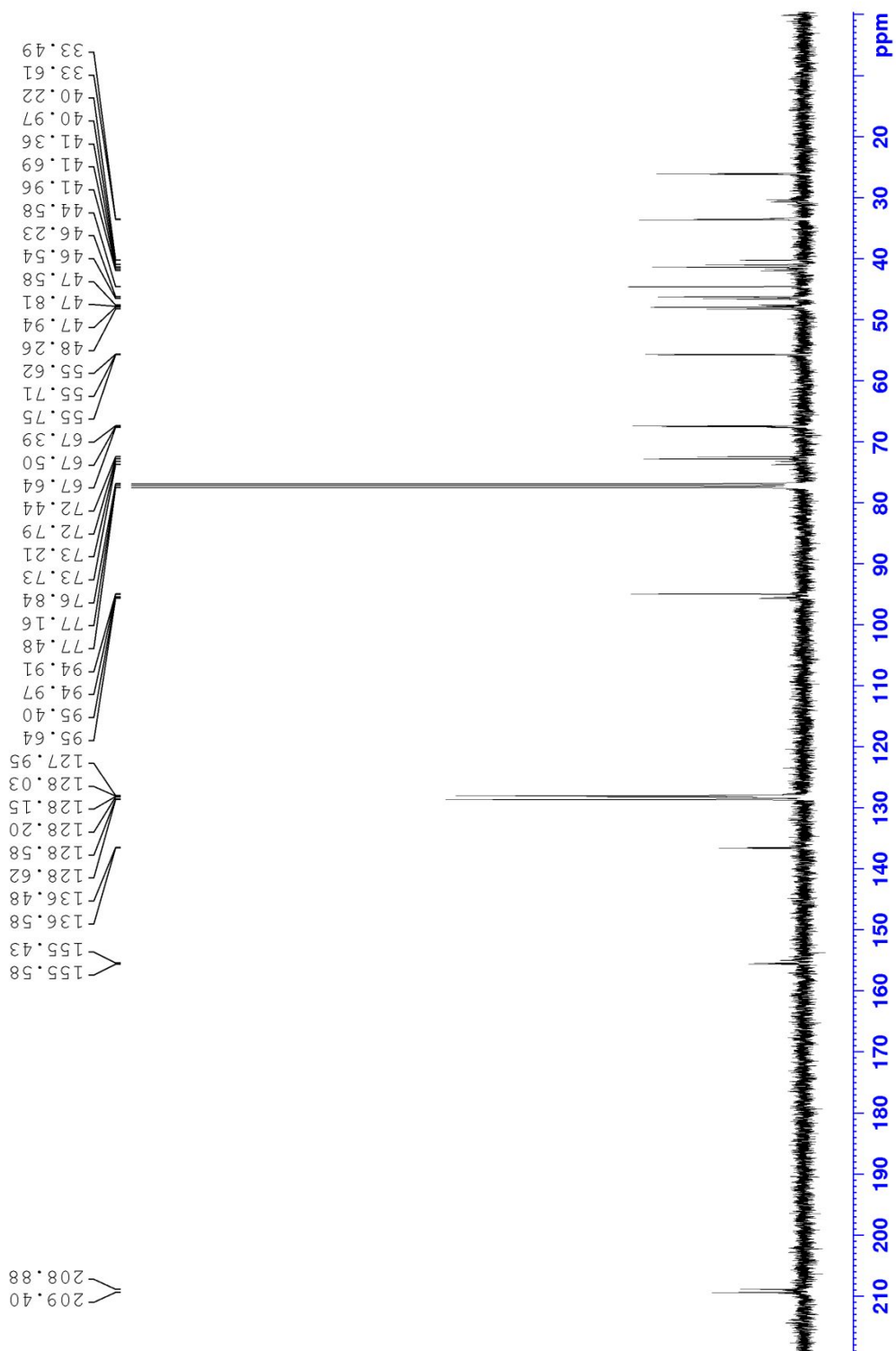


$^{13}\text{C}$  NMR of Compound 33 (100 MHz,  $\text{CDCl}_3$ )

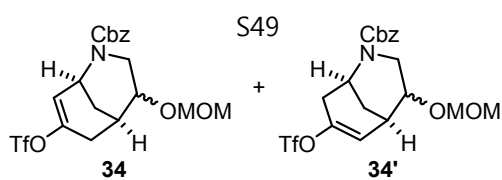




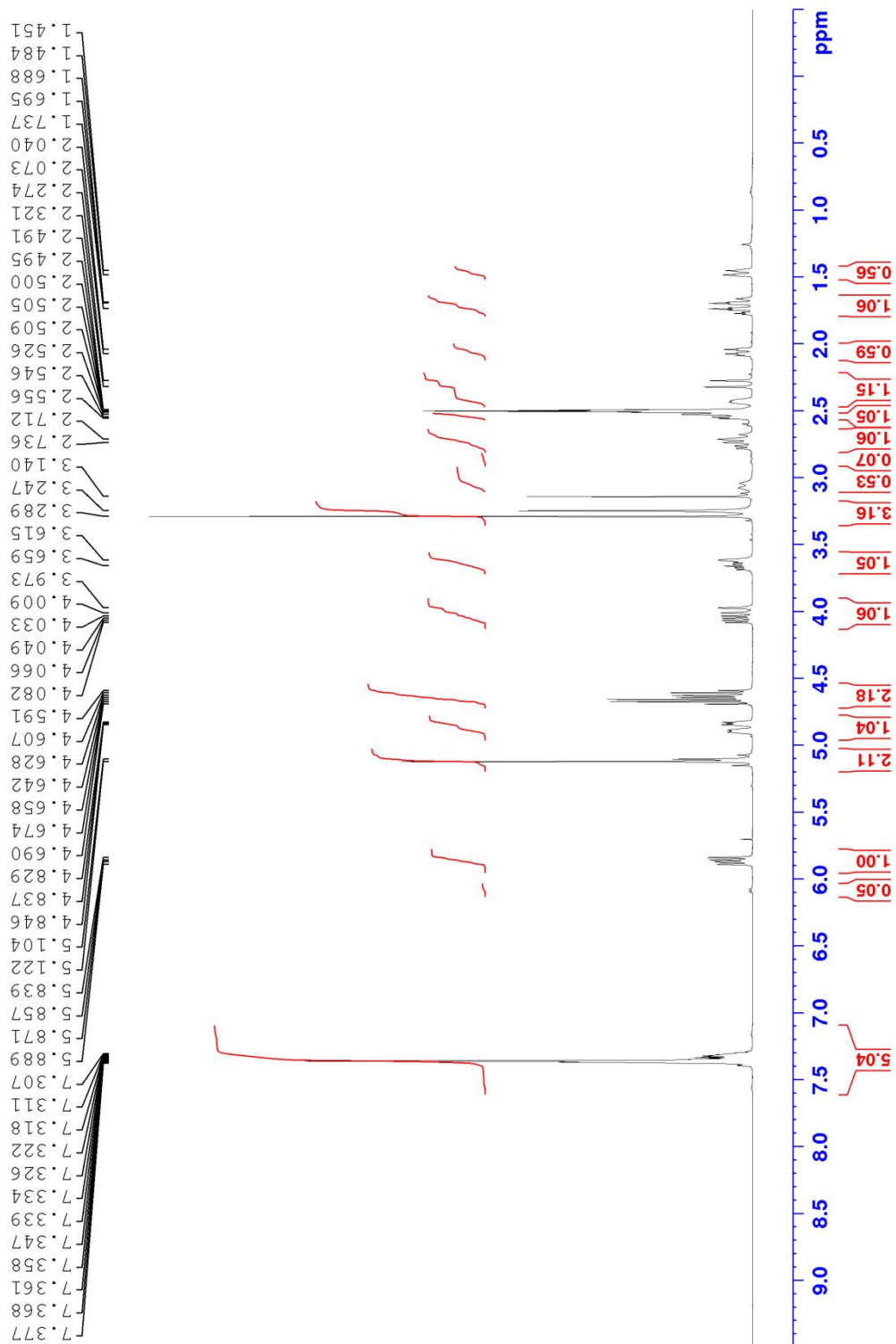
KDH-SI-uleine-33-13C



<sup>1</sup>H NMR of Compound 34 (+34') (400 MHz, DMSO-d<sub>6</sub> at 60 °C)

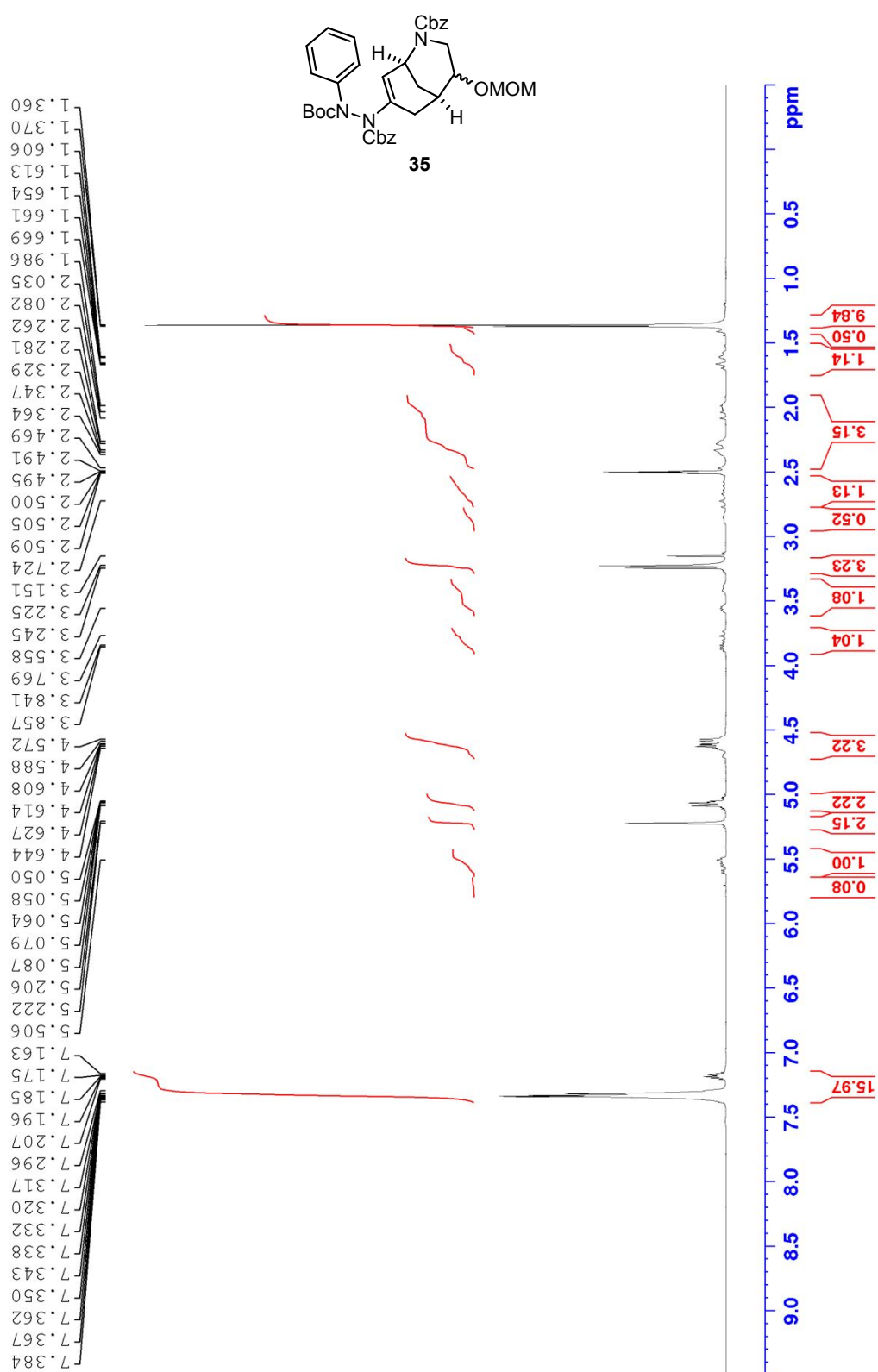


KDH-SI-uleine-34-1H-DMSO-temp.60

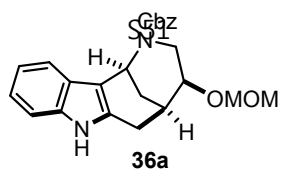


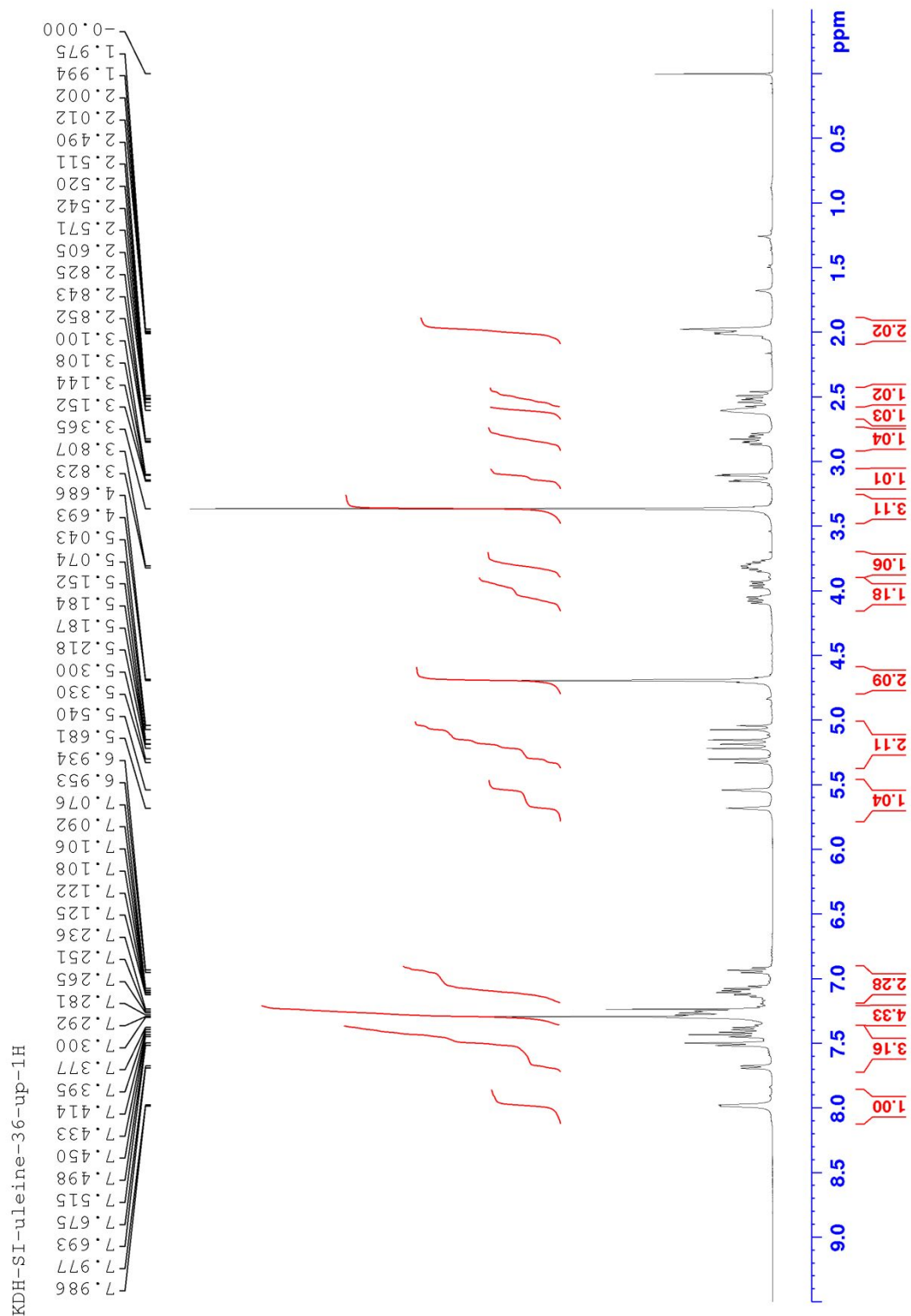
<sup>1</sup>H NMR of Compound 35 (400 MHz, DMSO-d<sub>6</sub>, 60 °C)

KDH-SI-uleine-35-1H-DMSO-temp60

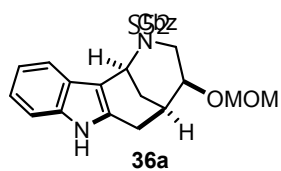


**<sup>1</sup>H NMR of Compound 36a (400 MHz, CDCl<sub>3</sub>)**

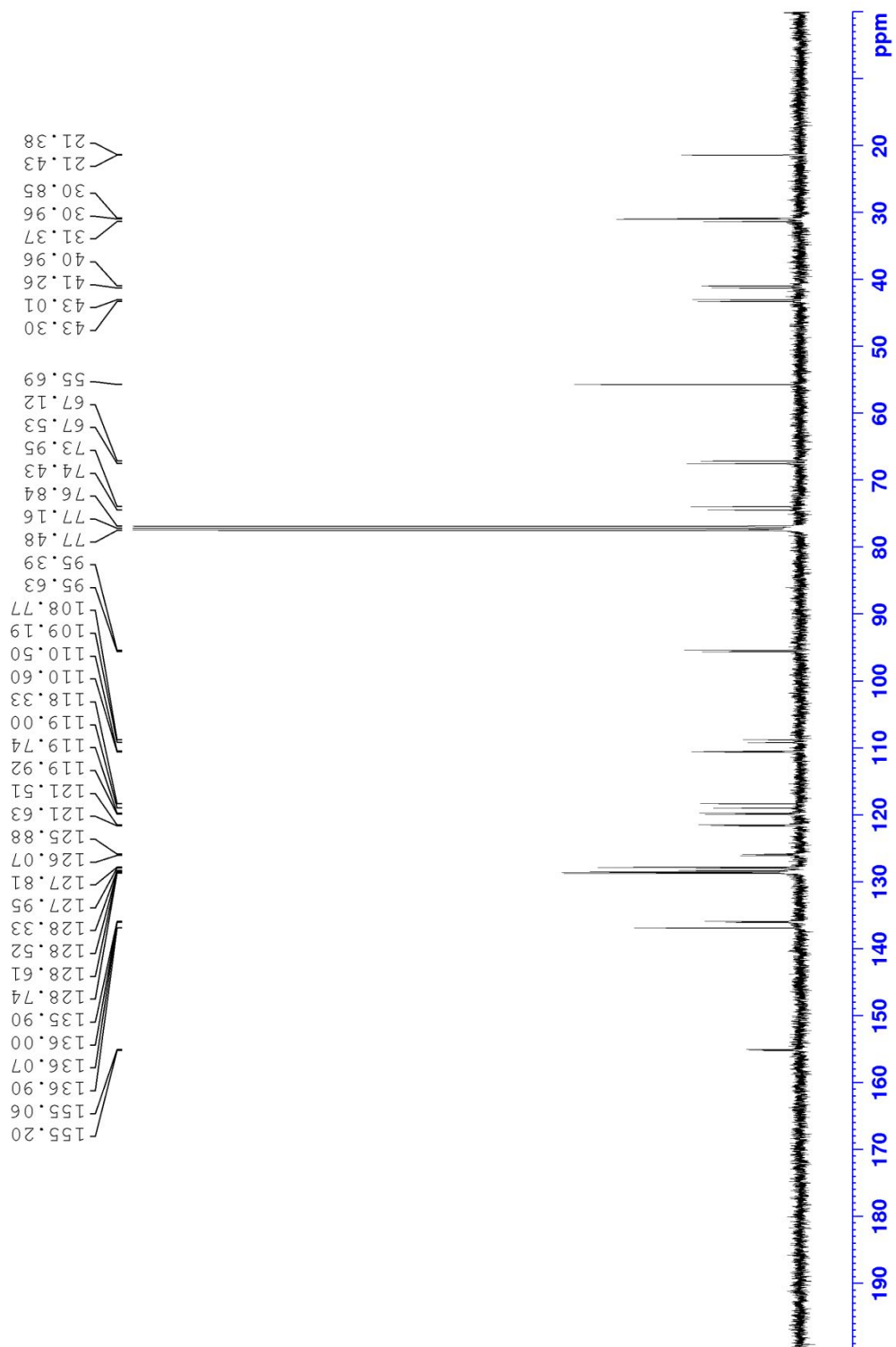




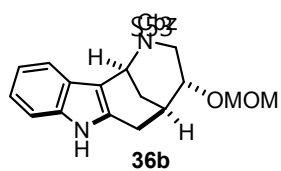
$^{13}\text{C}$  NMR of Compound 36a (100 MHz,  $\text{CDCl}_3$ )

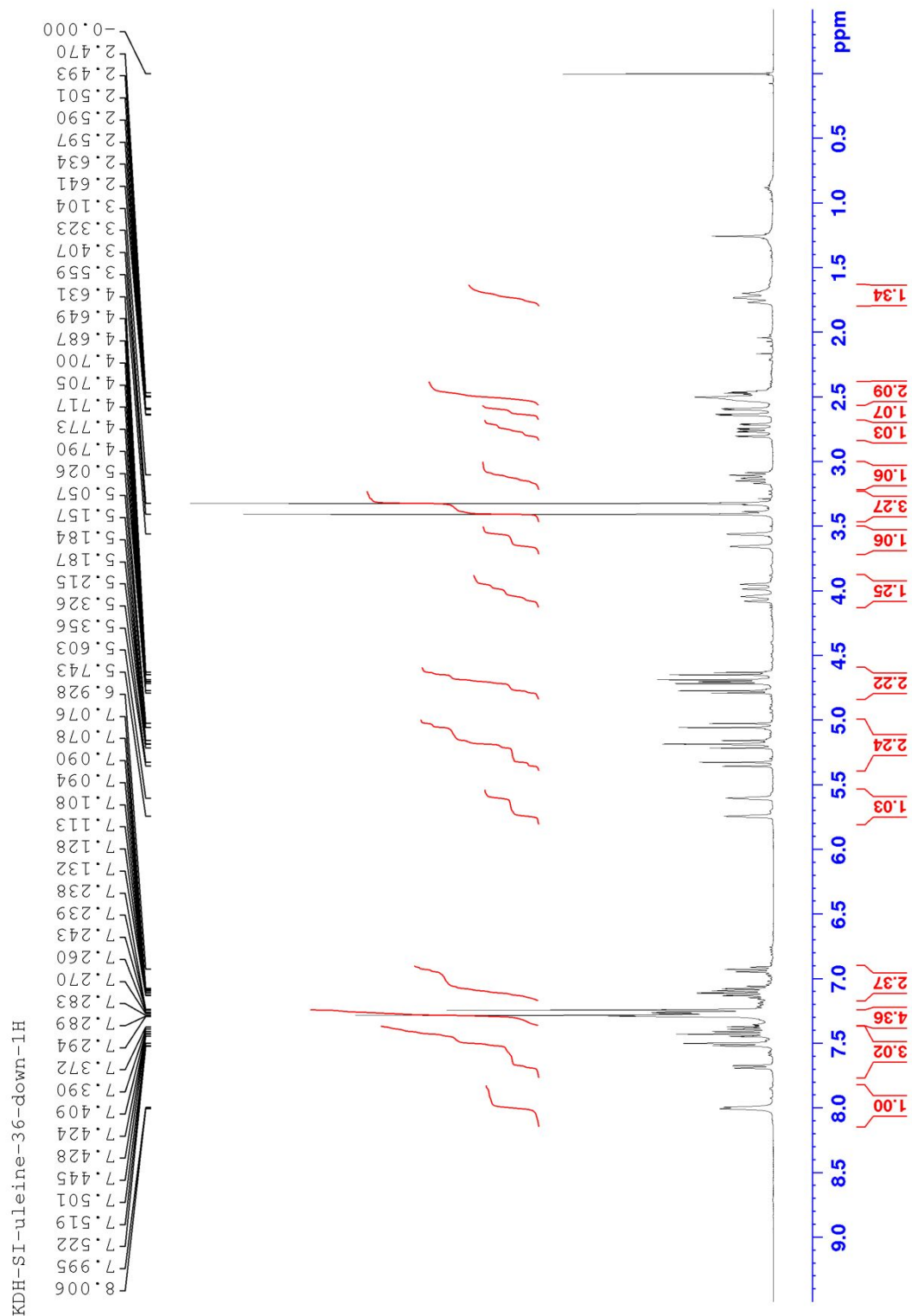


KDH-SI-uleine-36-up-13C

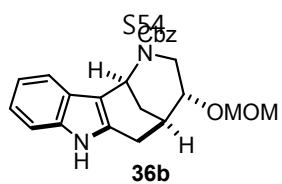


<sup>1</sup>H NMR of Compound 36b (400 MHz, CDCl<sub>3</sub>)

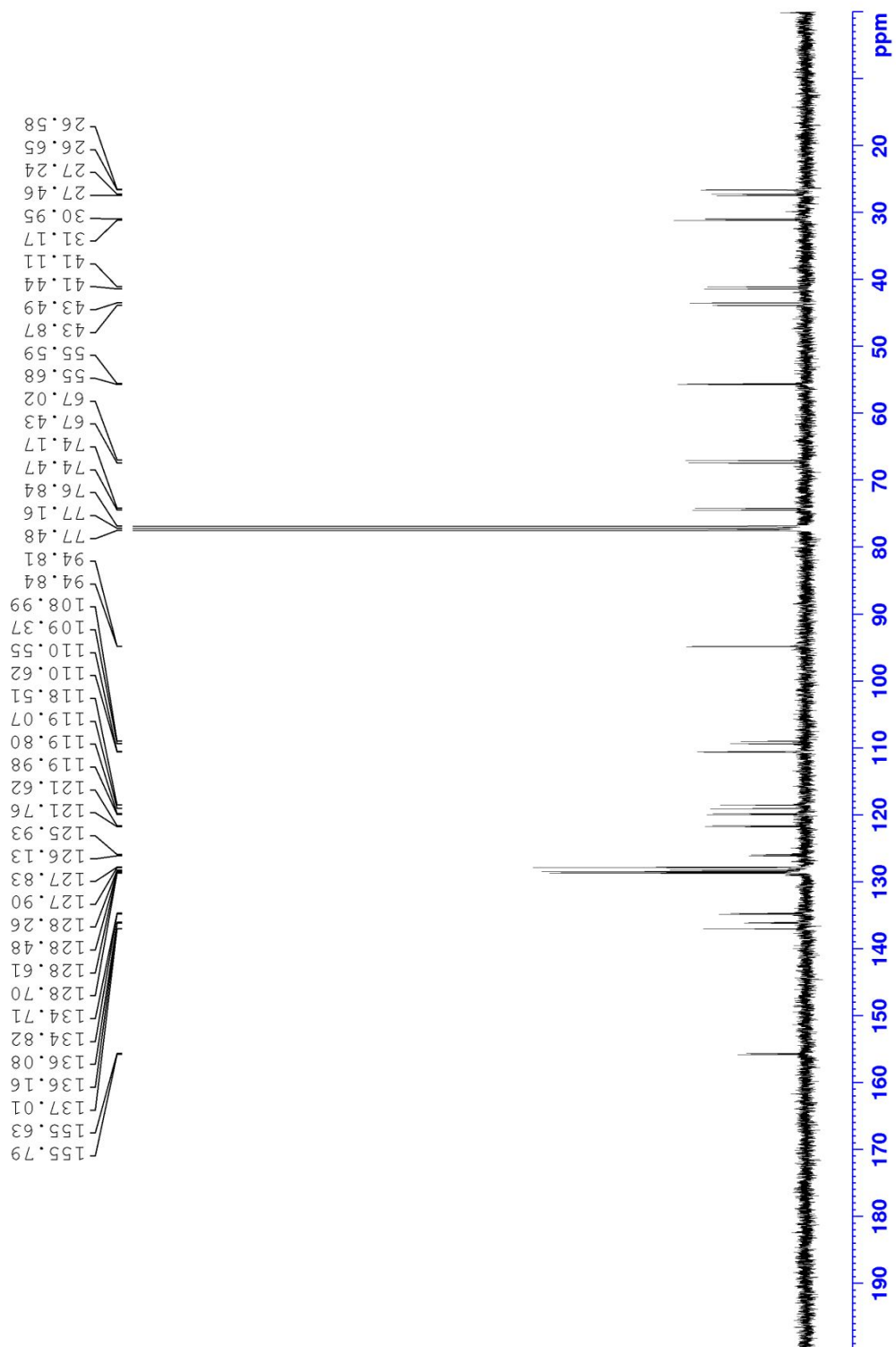




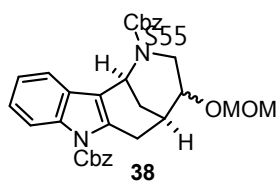
$^{13}\text{C}$  NMR of Compound 36b (100 MHz,  $\text{CDCl}_3$ )



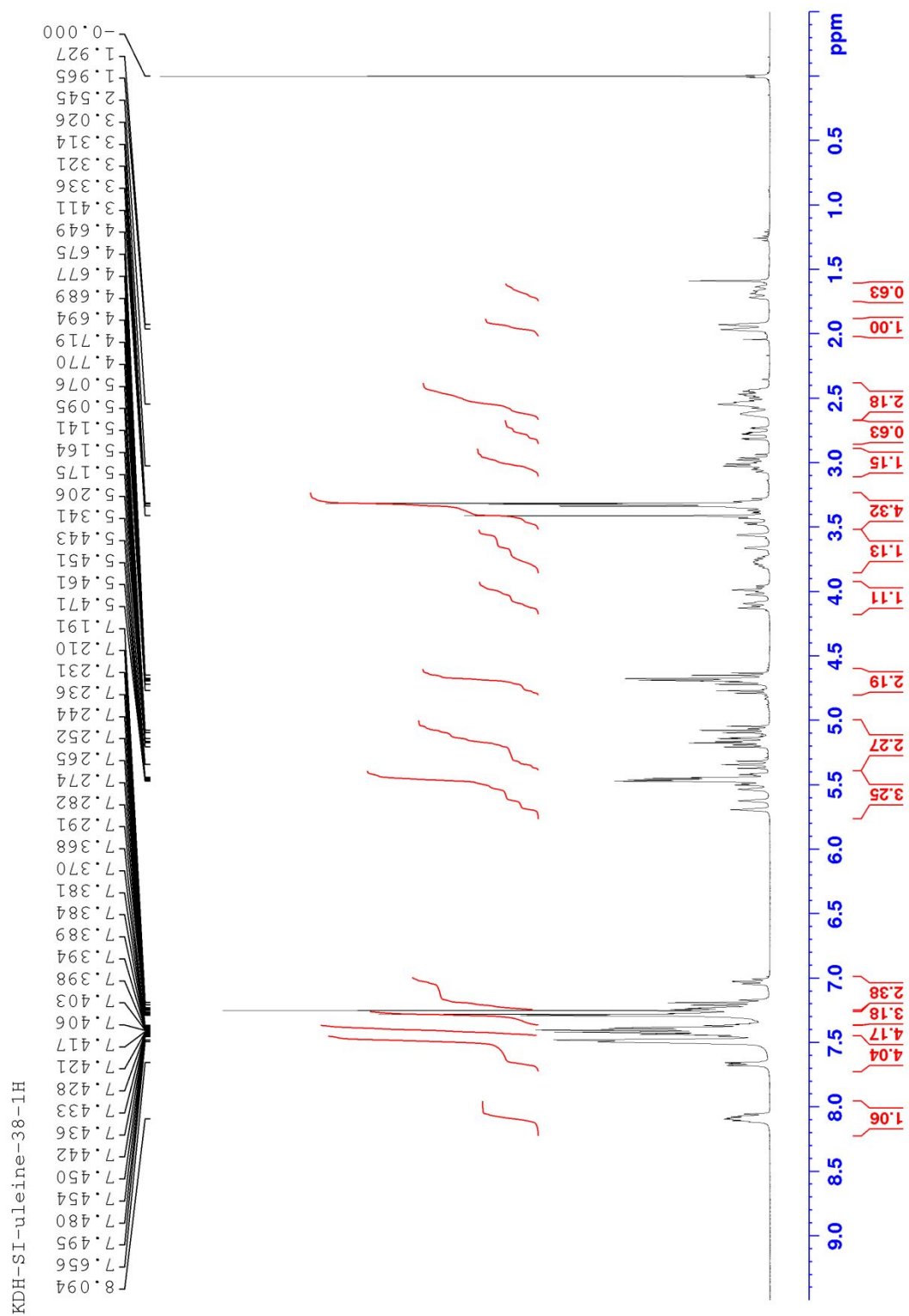
KDH-SI-uleine-36-down-13C



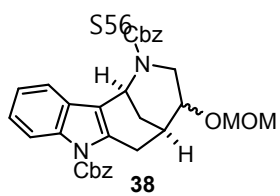
<sup>1</sup>H NMR of Compound 38 (400 MHz, CDCl<sub>3</sub>)





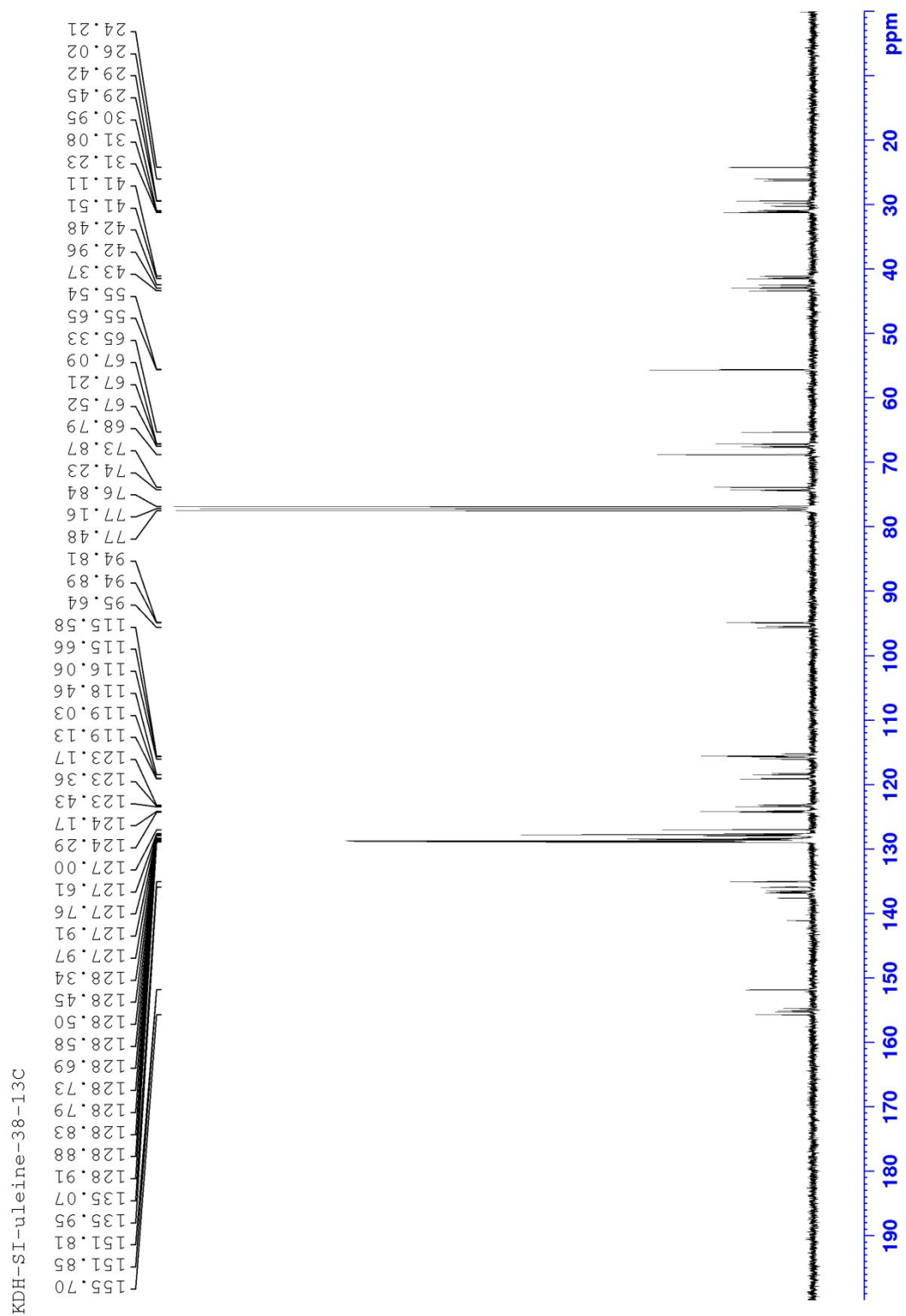
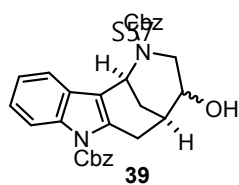


$^{13}\text{C}$  NMR of Compound 38 (100 MHz,  $\text{CDCl}_3$ )

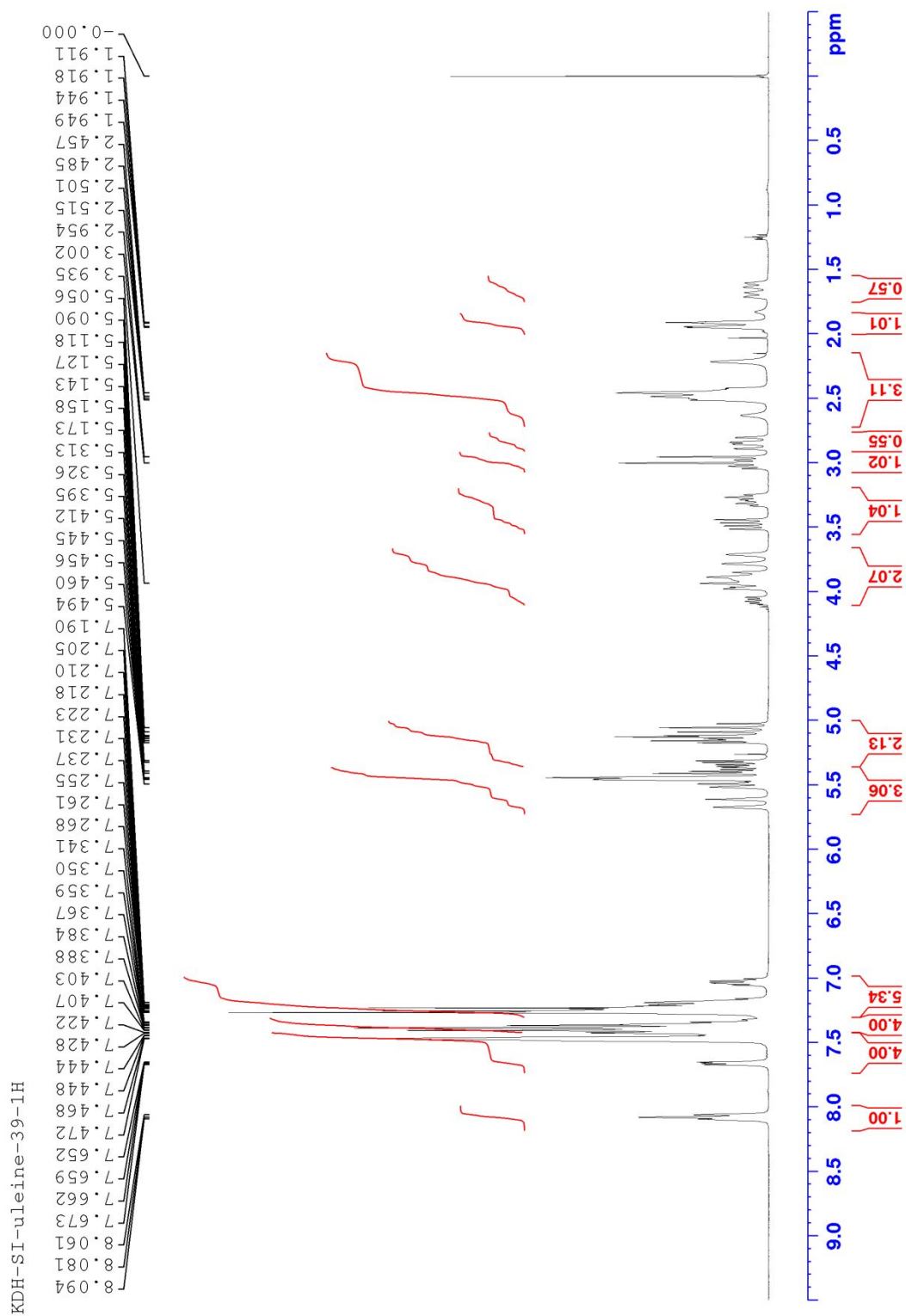
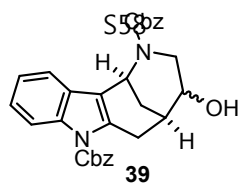




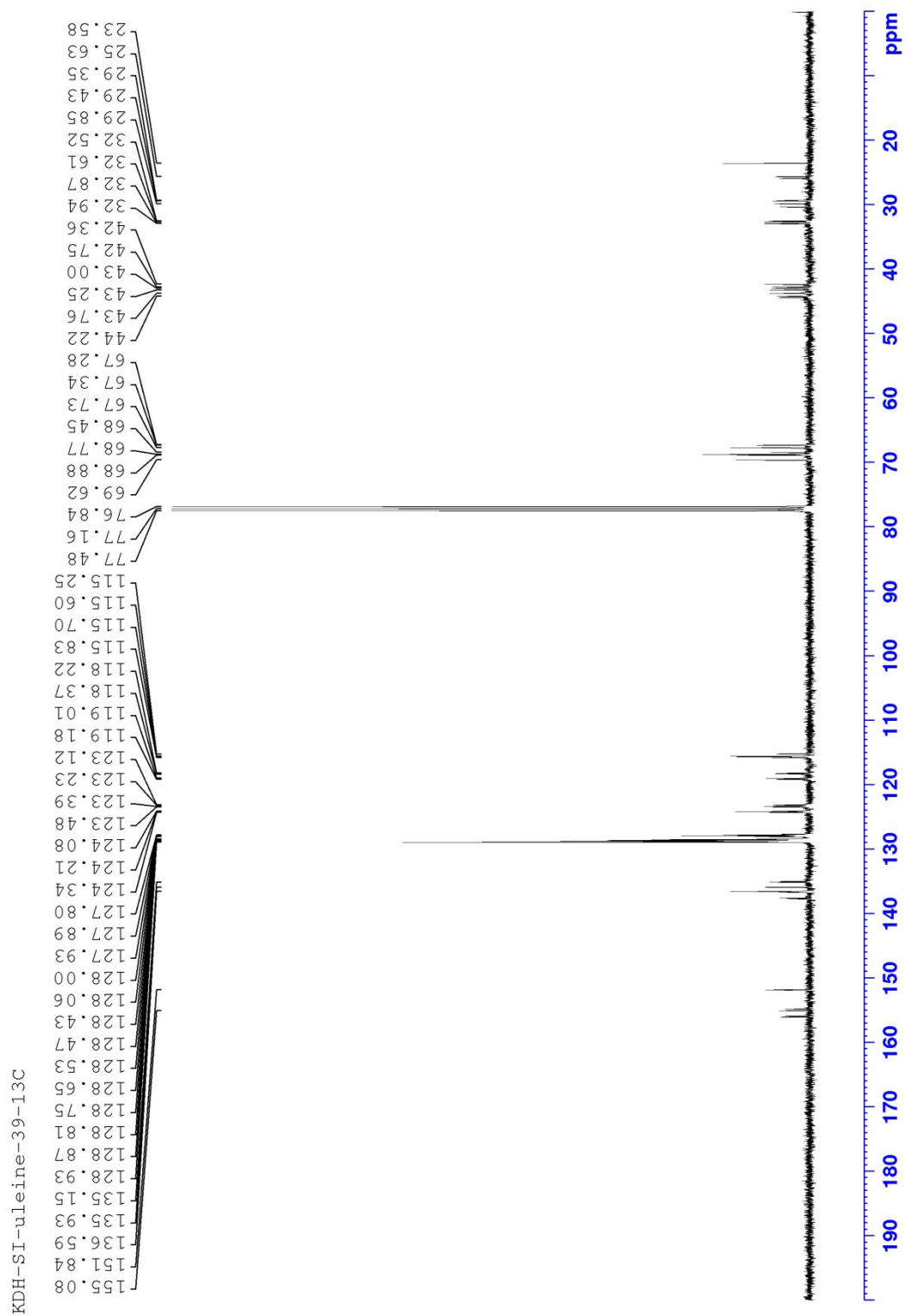
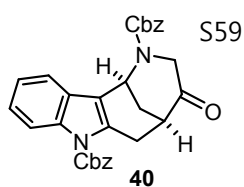
<sup>1</sup>H NMR of Compound 39 (400 MHz, CDCl<sub>3</sub>)

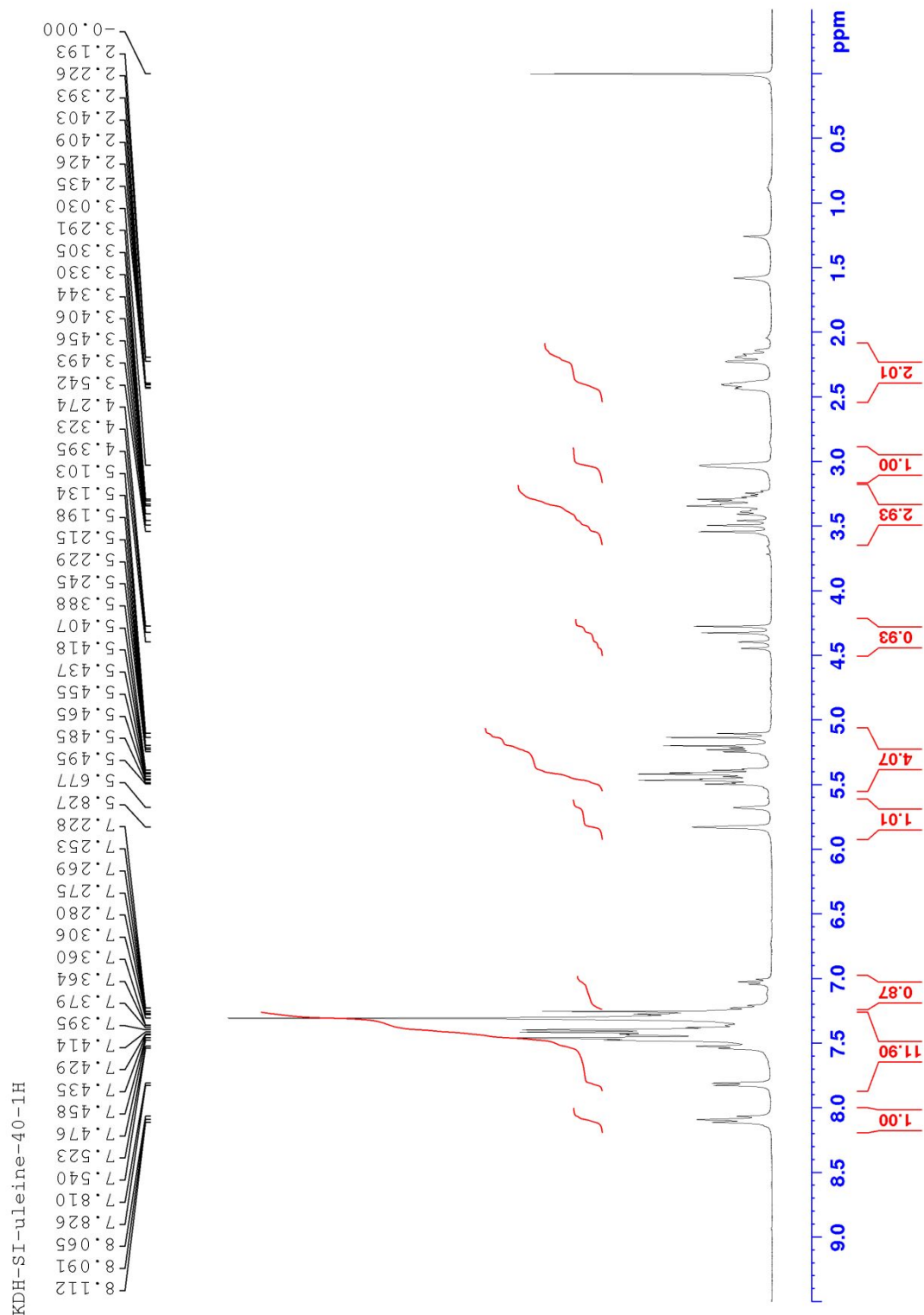


**<sup>13</sup>C NMR of Compound 39 (100 MHz, CDCl<sub>3</sub>)**

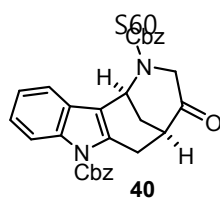


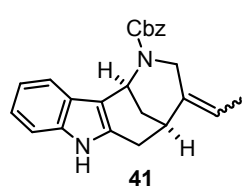
<sup>1</sup>H NMR of Compound 40 (400 MHz, CDCl<sub>3</sub>)



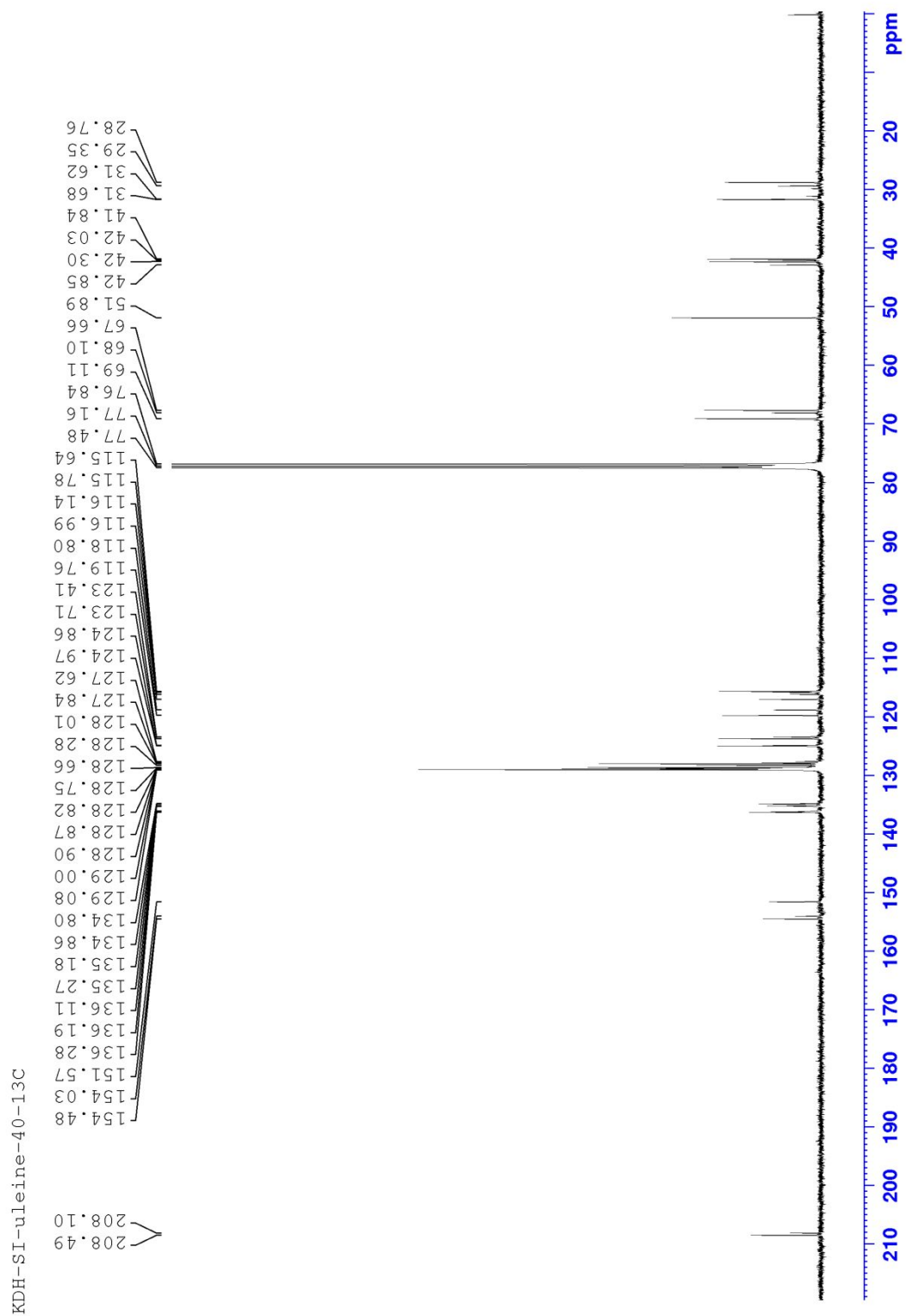


$^{13}\text{C}$  NMR of Compound 40 (100 MHz,  $\text{CDCl}_3$ )

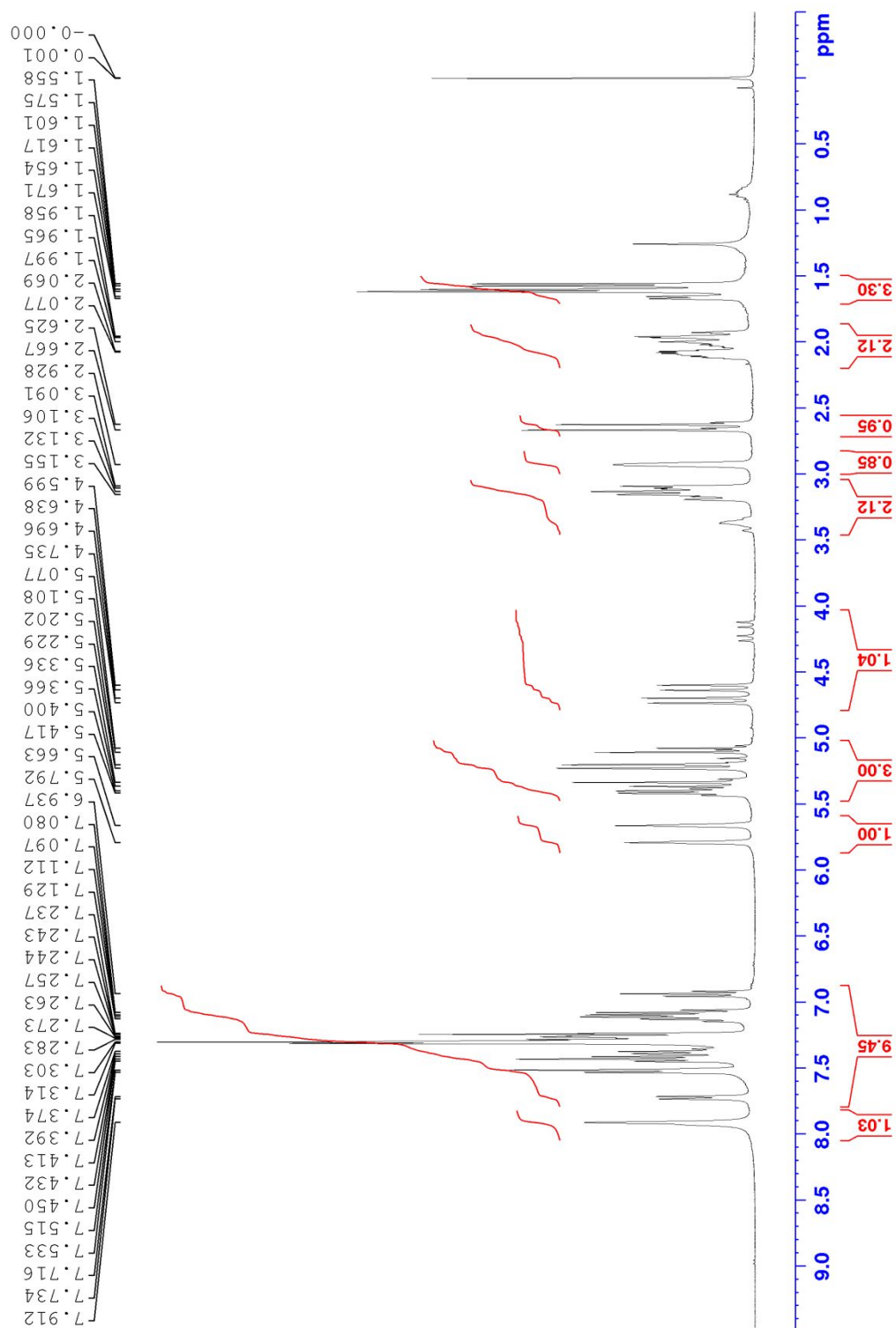




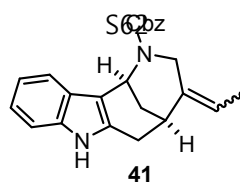
<sup>1</sup>H NMR of Compound 41 (400 MHz, CDCl<sub>3</sub>)

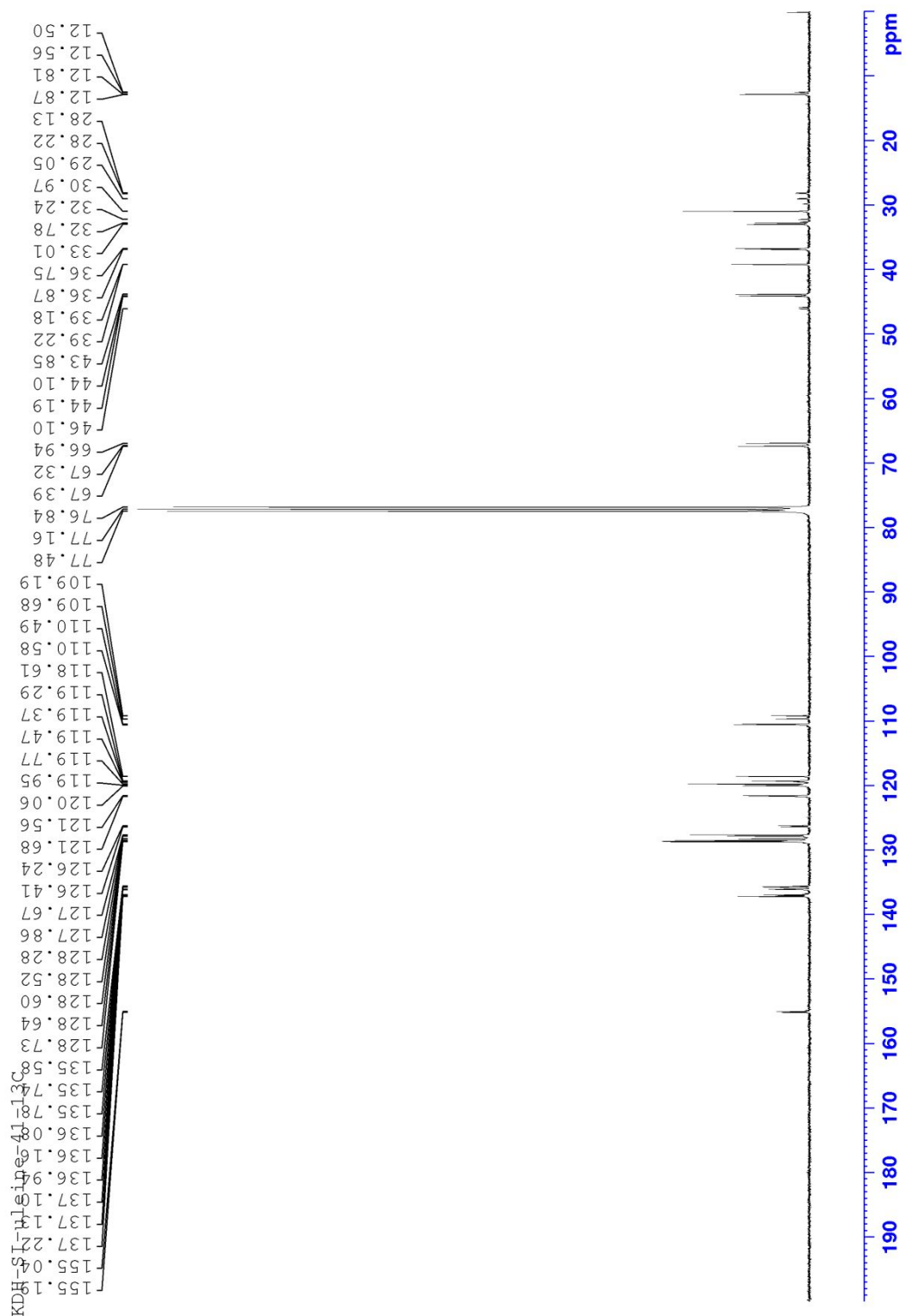


KDH-SI-uleine-41-1H

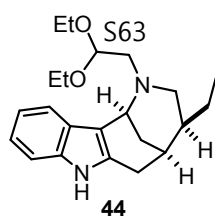


$^{13}\text{C}$  NMR of Compound 41 (100 MHz,  $\text{CDCl}_3$ )

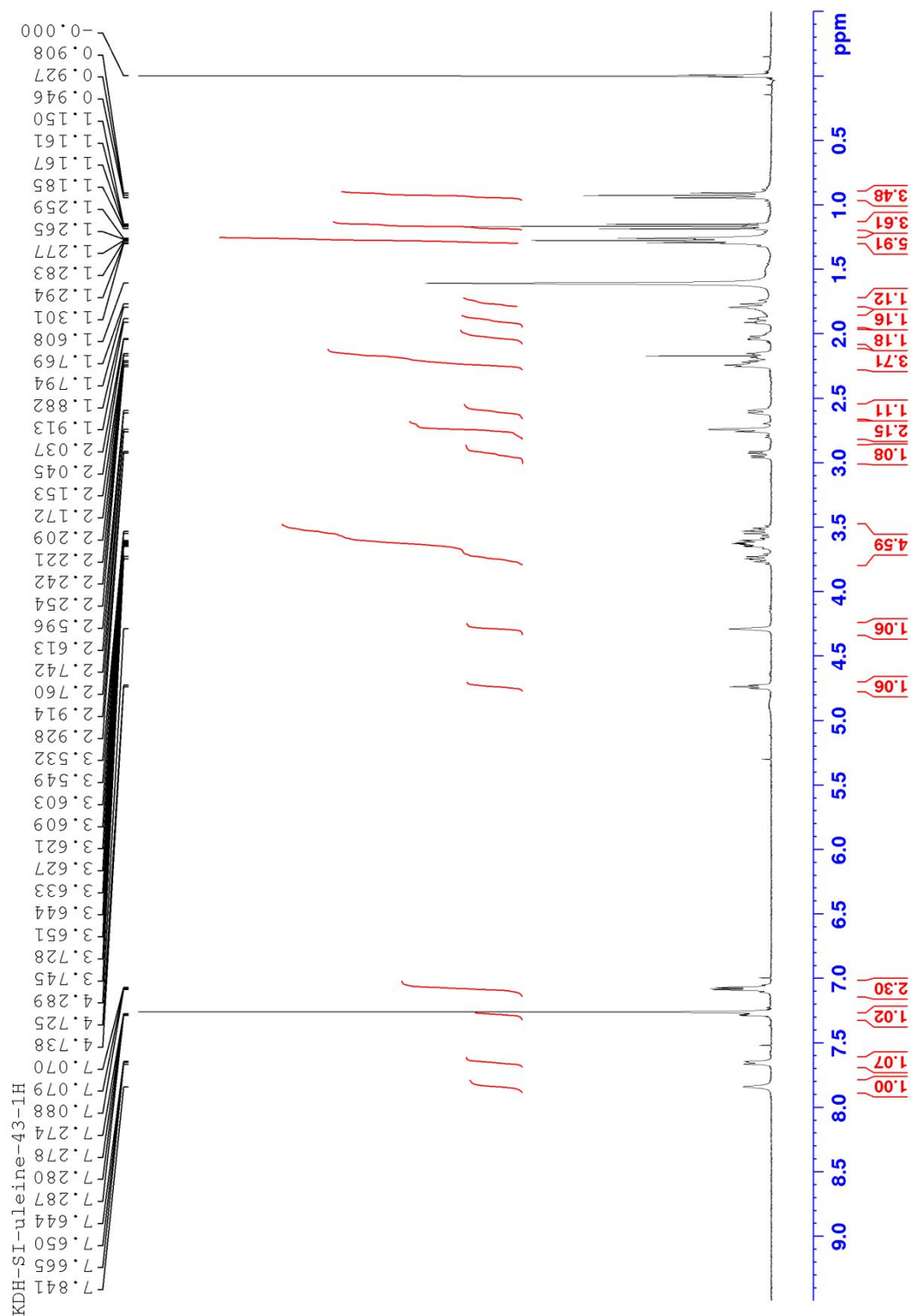




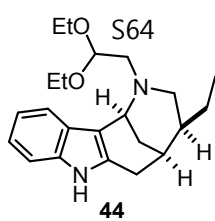
**<sup>1</sup>H NMR of Compound 44 (400 MHz, CDCl<sub>3</sub>)**





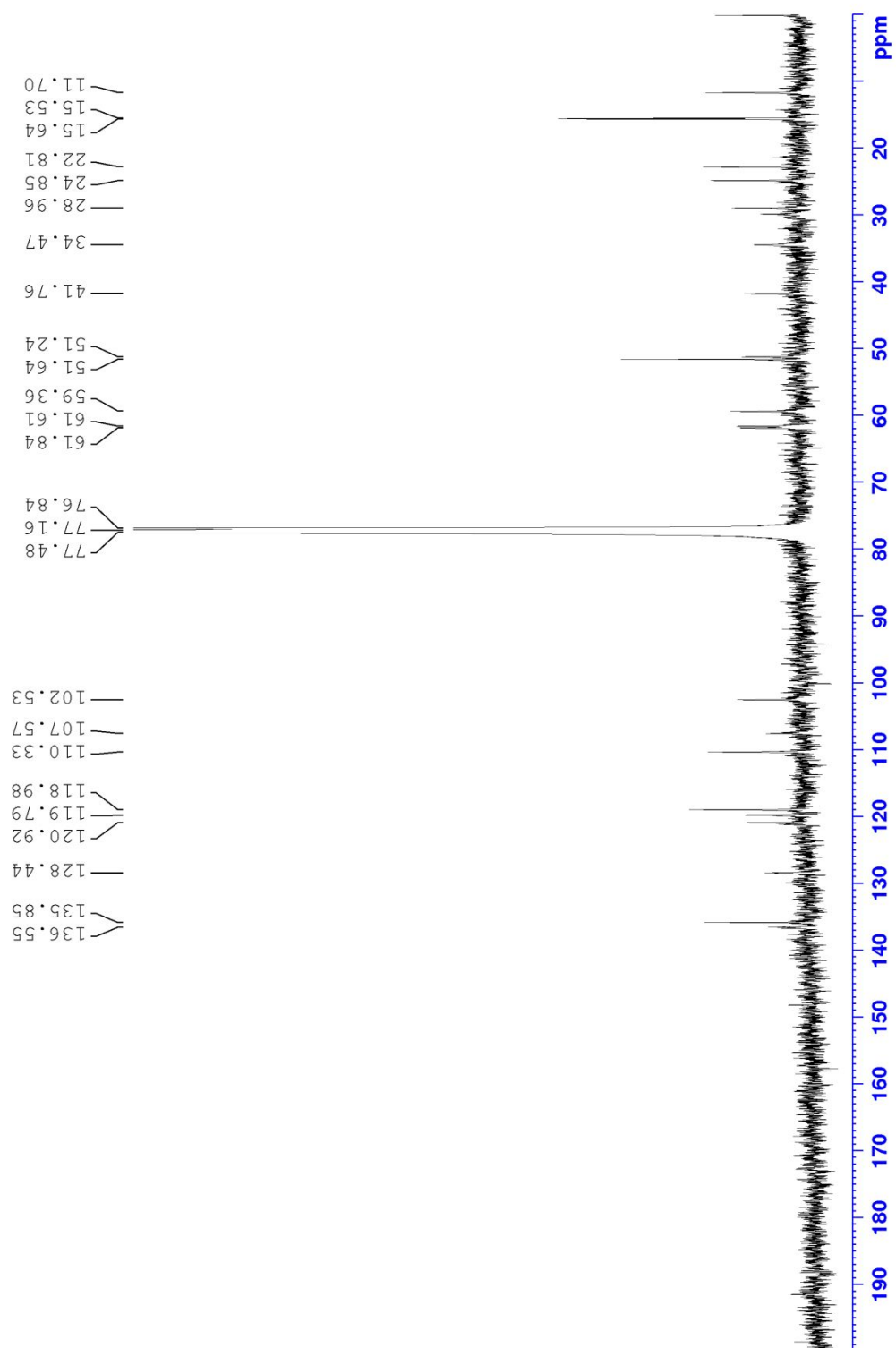


$^{13}\text{C}$  NMR of Compound 41 (100 MHz,  $\text{CDCl}_3$ )



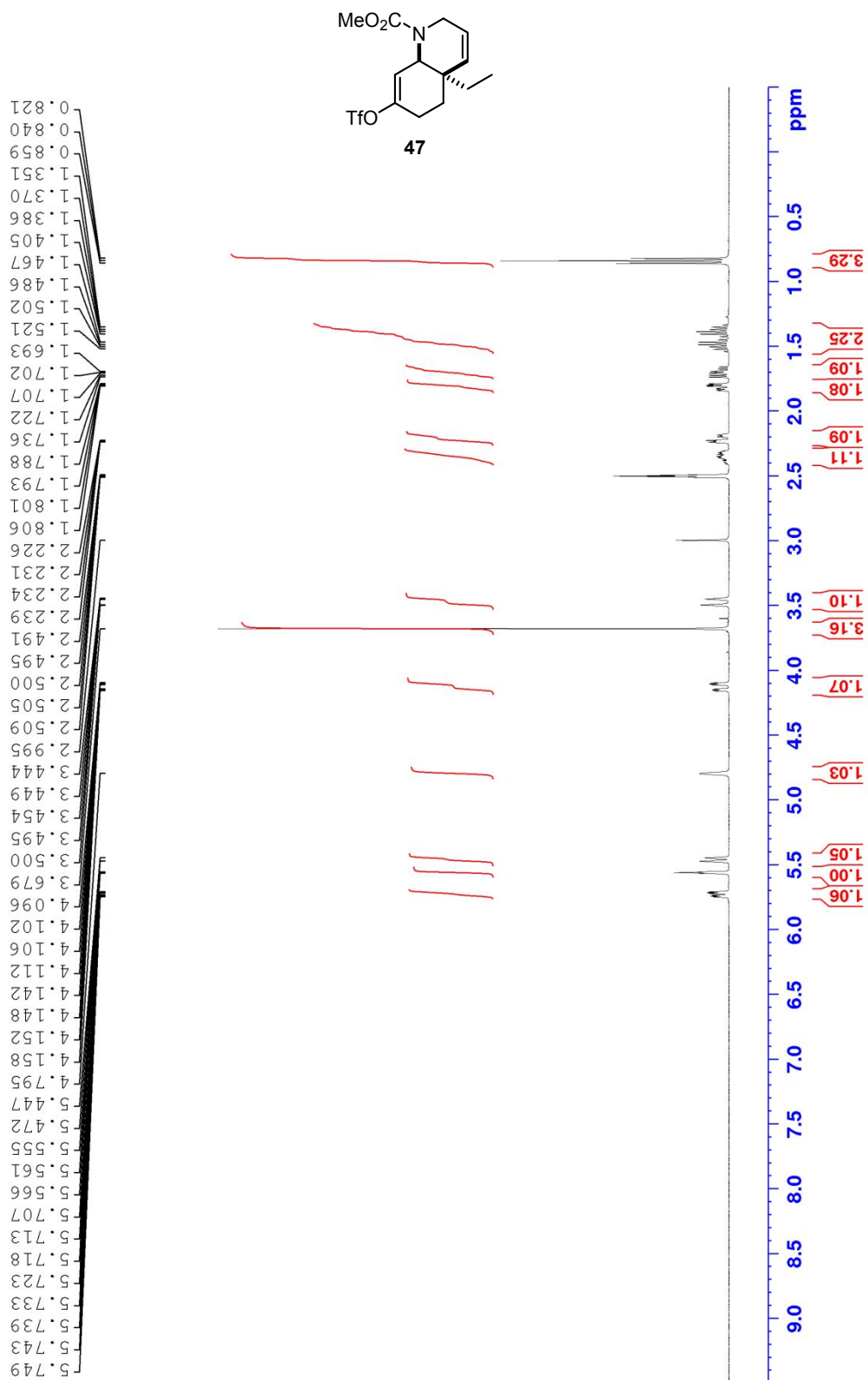


KDH-SI-uleine-43-13C

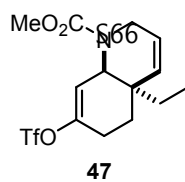


<sup>1</sup>H NMR of Compound 47 (400 MHz, DMSO-d<sub>6</sub> at 85 °C)

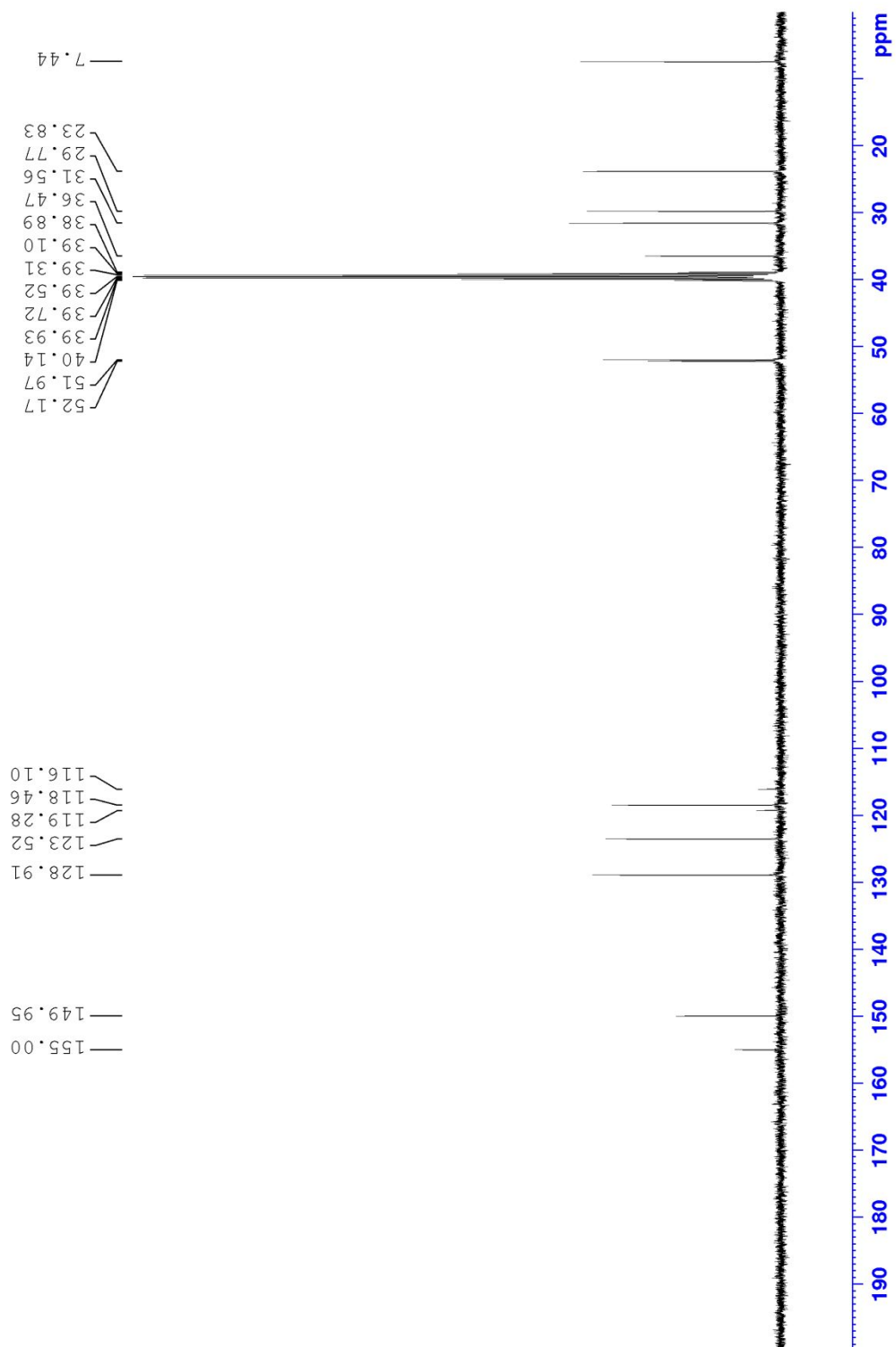
KDH-SI-uleine-46-1H-85



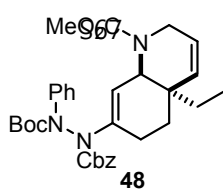
<sup>13</sup>C NMR of Compound 47 (100 MHz, DMSO-d<sub>6</sub> at 85 °C)



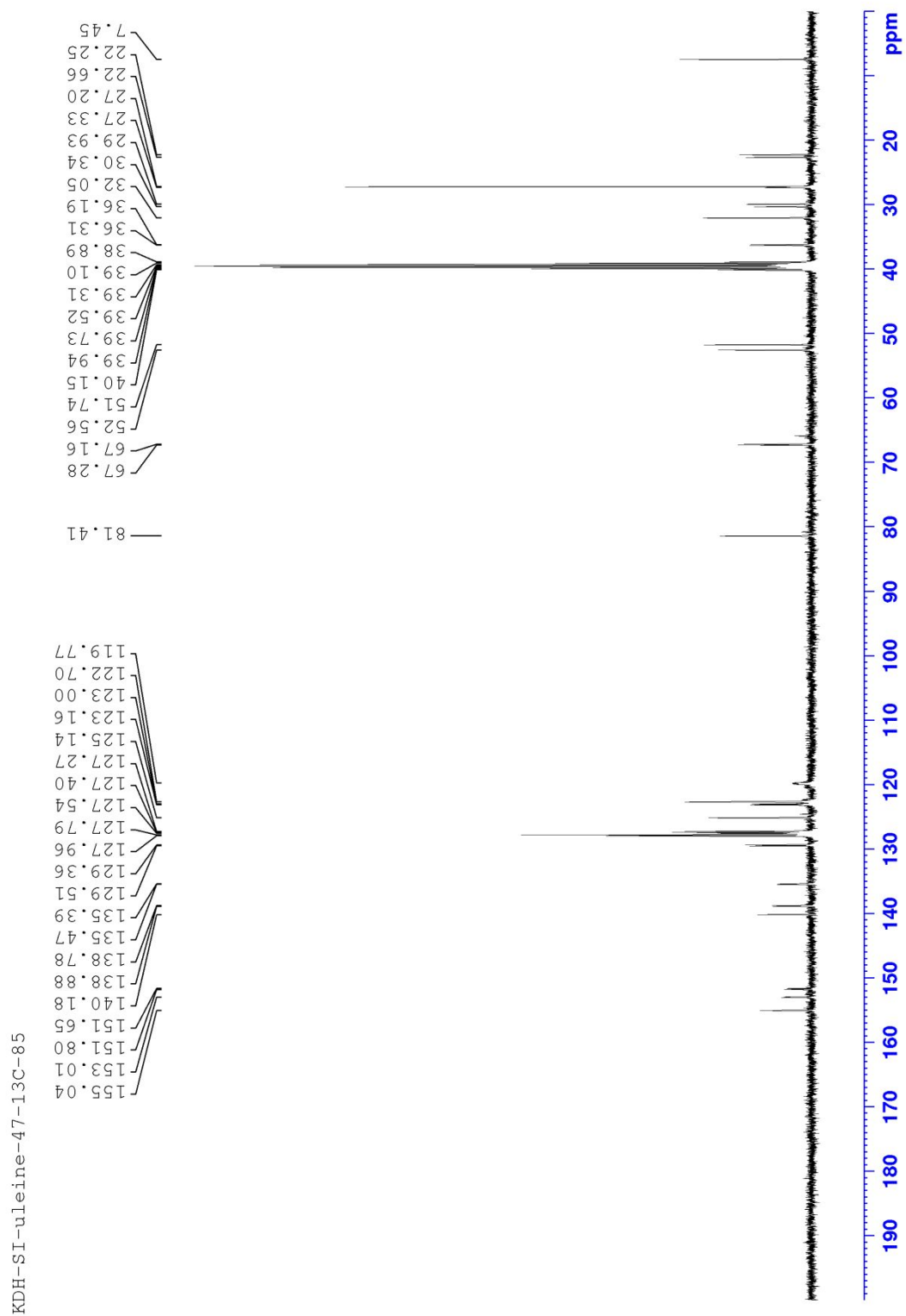
KDH-SI-uleine-46-13C-85



<sup>1</sup>H NMR of Compound 48 (400 MHz, DMSO-d<sub>6</sub> at 85 °C)

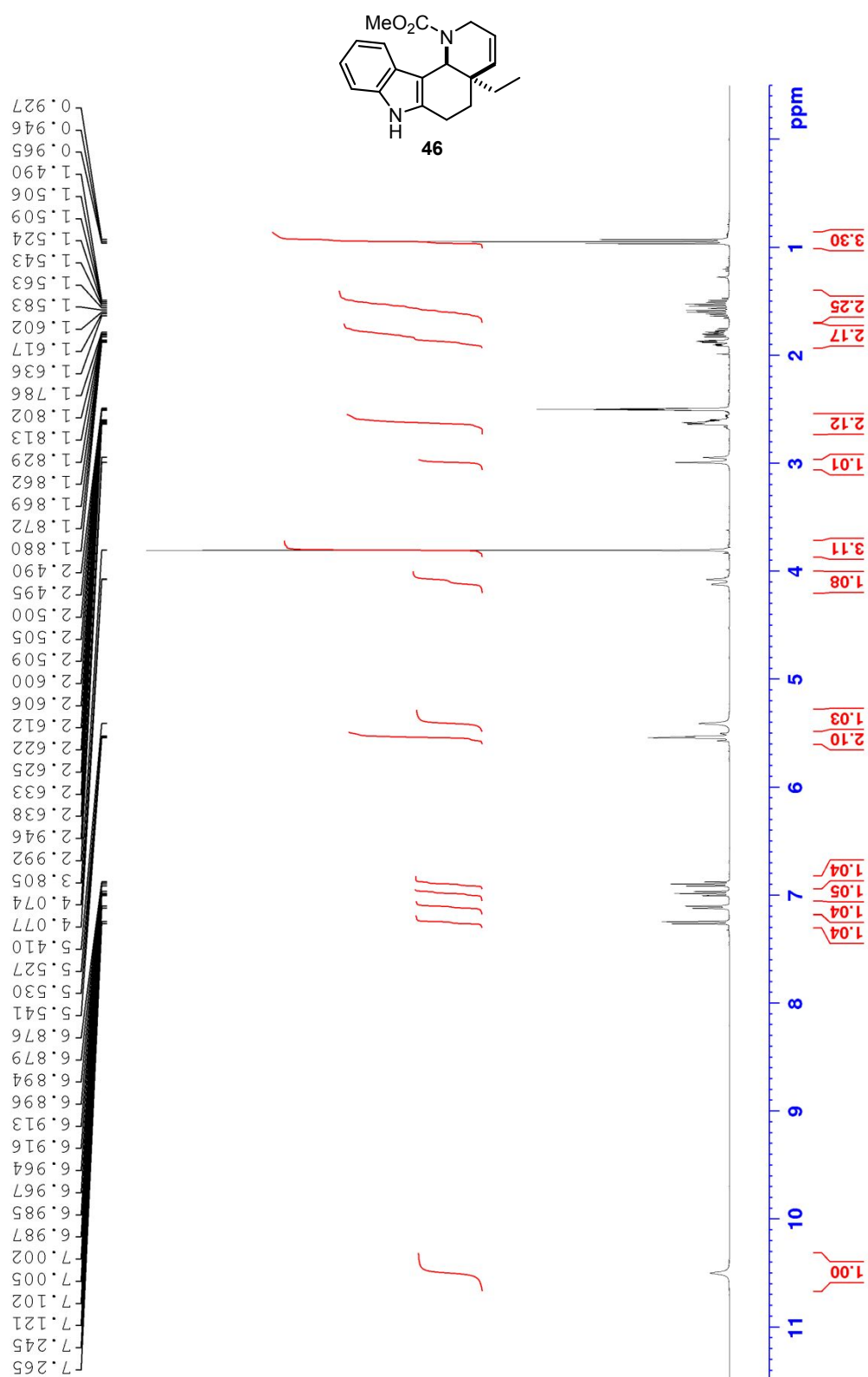






<sup>1</sup>H NMR of Compound 46 (400 MHz, DMSO-d<sub>6</sub> at 85 °C)

KDH-SI-uleine-45-1H-85



**<sup>13</sup>C NMR of Compound 46 (100 MHz, DMSO-d<sub>6</sub> at 85 °C)**

KDH-SI-uleine-46-13C-85

