SUPPORTING INFORMATION

A rapid synthetic approach to the ABCD Core of the *Stemona* alkaloids

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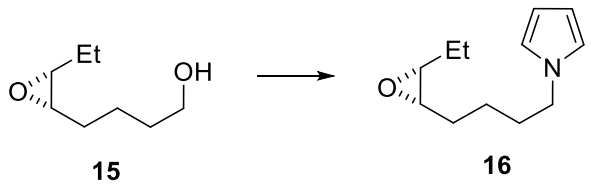
General experimental

All glassware was flame-dried and allowed to cool under vacuum before use. All chemicals were purchased from Aldrich, Alfa Aesar or Fisher without further purification except where specified. Anhydrous solvents were obtained from a purification column composed of activated alumina or distilled. Reagents requiring purification were done so according to Purification of Laboratory Chemicals (D. D. Perrin & W.L.F Armarego, 3rd Edition, Butterworth Heinemann, 1988). Flash chromatography was performed on silica gel (Merck Kieselgel 60 F254 230-400 mesh). TLC was performed on aluminium backed silica plates (0.2 mm, 60 F254) which were visualised at 256 nm or 365 nm followed by developing with either $KMnO_4$ or vanillin. Melting points were measured on a Stuart Scientific SMP10 melting point apparatus and are uncorrected. Infra-red spectra were recorded on the neat compounds using an ATR sampling accessory on a Perkin-Elmer Spectrum One spectrometer. Only strong and selected absorbances (ν_{max}) are reported. ^{1}H NMR spectra were carried out on Jeol Eclipse 400 or Varian 400 instruments. Chemical shifts (δ_H) are quoted in ppm, referenced to the indicated solvent. ^{13}C NMR spectra were recorded on Jeol Eclipse 400 or Varian 400 instruments. Chemical shifts (δ_C) are quoted in ppm referenced to the indicated solvent. ^{119}Sn NMR spectra were recorded on a Lambda 300 instrument. Chemical shifts (δ_{Sn}) are quoted in ppm referenced to $SnMe_4$. High resolution mass spectra were recorded on a Thermofisher LTQ Orbitrap XL spectrometer.

General Procedure 1 for stannane syntheses

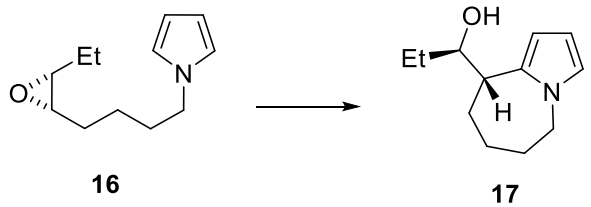
A solution of the relevant siloxyfuran (1.0 eq) and tetramethylethylenediamine (1.0 eq) in THF (5 mL/mmol of siloxyfuran), was cooled to 0 °C and $^{s}BuLi$ (1.4 M in hexanes, 1.0 eq) was added dropwise resulting in a yellow solution. After the addition, the reaction mixture was stirred at 0 °C for 2 h before adding tributyltin chloride (1.1 eq) and allowed to warm to room temperature . After stirring for 1 h, the solution had become a darker orange and was diluted with Et_2O and then quenched with a 1:1 solution of water/saturated aqueous $NaHCO_3$. The layers were separated and the aqueous layer was extracted twice with Et_2O. The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by Kugelrohr distillation.

(±)-1-(4-(3-Ethyloxiran-2-yl)butyl)-1*H*-pyrrole 16



Methanesulfonyl chloride (18.6 mL, 240 mmol) was added dropwise to a solution of epoxy alcohol **15** (23.1 g, 160 mmol) and triethylamine (33.5 mL, 240 mmol) in CH_2Cl_2 (150 mL) at 0 °C. The solution gradually became cloudy and yellow. The ice bath was removed and the mixture stirred at room temperature for 30 min. Water (150 mL) was added and the layers were separated. The product was extracted twice with CH_2Cl_2 (100 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow oil (35.6 g, 100%) which was set aside. Pyrrole (12.2 mL, 176 mmol) was added to a suspension of ground NaOH (13.4 g, 336 mmol) in DMSO (150 mL) and stirred for 30 min. The light brown/green solution was then cooled in an ice bath and the mesylate (35.6 g, 160 mmol) was added dropwise. The ice bath was allowed to slowly return to room temperature and stirred overnight. The reaction mixture was poured into water (300 mL) and the heat generated was allowed to dissipate before extracting the product thrice with Et_2O (200 mL) then drying ($MgSO_4$) the combined organic extracts and concentrating *in vacuo* to give **16** (26.9 g, 87%) as a pale yellow oil which was used in the next step without further purification. A sample was purified for characterisation by flash chromatography (3:7 Et_2O/petroleum ether, SiO_2). R_f 0.51 (1:1 Et_2O/petroleum ether); δ_H (400 MHz, $CDCl_3$) 6.65 (2 H, t, *J* 2.1, 2 x NCH), 6.14 (2 H, t, *J* 2.2, 2 x NCHC*H*), 3.90 (2 H, t, *J* 7.0, NCH_2), 2.92-2.84 (2 H, m, 2 x OCH), 1.85 (2 H, app. qn, *J* 7.0, NCH_2CH_2), 1.60-1.40 (6 H, m), 1.03 (3 H, t, *J* 7.6, CH_3); δ_C (100 MHz, $CDCl_3$) 120.6 (2 x NCH), 108.1 (2 x NCH*C*H), 58.4 (CH), 57.1 (CH), 49.6 (NCH_2), 31.5 (CH_2), 27.4 (CH_2), 24.1 (CH_2), 21.2 (CH_2), 10.7 (CH_3); *m/z* (%) (CI) 194.1 (70, $[M+H]^+$), 134.1 (20), 127.1 (20); HRMS (CI) Calc'd for $C_{12}H_{20}NO$ 194.1545, Found 194.1549.

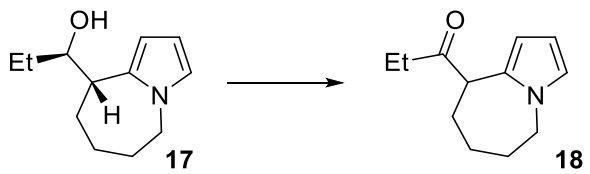
(±)-1-(6,7,8,9-Tetrahydro-5*H*-pyrrolo[1,2-*a*]azepin-9-yl)propan-1-ol 17



Indium(III) chloride (2.75 g, 12.4 mmol) was added to a solution of **16** (12.0 g, 62.1 mmol) in CH_2Cl_2 (2.4 L) in one portion. The clear yellow solution went orange and cloudy. The solution was stirred overnight until no more epoxide remained by TLC analysis. Water (500 mL) was added and the layers

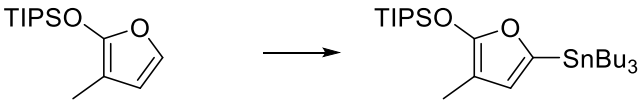
were separated. The product was extracted twice with CH_2Cl_2 (200 mL) then dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (CH_2Cl_2 → 1:9 Et_2O/CH_2Cl_2, SiO_2) gave **17** (9.44 g, 79%) as a pale yellow oil. R_f 0.35 (1:1 Et_2O/petroleum ether); ν_{max} (film)/cm^{-1} 3418 (O-H, br.), 1486, 1455, 1076, 969; δ_H (400 MHz, $CDCl_3$) 6.54 (1 H, dd, *J* 2.6, 1.9, NCH), 5.99 (1 H, dd, *J* 3.4, 2.6, NCHC*H*), 5.95 (1 H, dd, *J* 3.4, 1.9, $NCCH_{pyr}$), 4.06-3.86 (3 H, m, 2 x NCH_2, C*H*OH), 2.80 (1 H, m, C*H*CHOH), 1.91-1.66 (7 H, m), 1.48 (1 H, m, $CH_3CH_aH_b$), 1.06 (3 H, t, *J* 7.4, CH_3); δ_C (100 MHz, $CDCl_3$) 134.2 (N*C*CH), 122.7 (NCH), 108.1 (NC*C*H), 106.0 (NCH*C*H), 72.5 (br. HOCH), 50.2 (NCH_2), 45.0 (HOCH*C*H), 29.7 (CH_2), 29.4 (CH_2), 27.4 (br. CH_2), 26.4 (CH_2), 9.9 (CH_3); *m/z* (%) (CI) 194 (10, $[M+H]^+$), 176.1 (25, $[M-OH]^+$), 134.1 (100); HRMS (ESI) Calc'd for $C_{12}H_{19}NNaO$ 216.1359, Found 216.1366.

(±)-1-(6,7,8,9-Tetrahydro-5*H*-pyrrolo[1,2-*a*]azepin-9-yl)propan-1-one 18



Sulfur trioxide pyridine complex (23.0 g, 145 mmol) was added to stirred, anhydrous DMSO (40 mL) at room temperature under nitrogen. After 15 min the resulting solution was added dropwise to a stirred mixture of alcohol **17** (13.6 g, 70.5 mmol) and triethylamine (50 mL, 360 mmol) in anhydrous DMSO (28 mL) and DCM (150 mL) at 0 °C under nitrogen. The reaction was allowed to warm to room temperature , stirred for 4.5 h and quenched by the addition of water (150 mL). The mixture was extracted with Et_2O (3 × 150 mL) and the combined organic phase washed with water (150 mL) and brine (150 mL). Drying ($MgSO_4$) and evaporation gave a brown oil. Purification of the crude material by silica gel chromatography (EtOAc/petrol, 1:9 to 1:4 as eluent) afforded ketone **18** (10.96 g, 81%) as a light yellow oil. R_f 0.40 (1:4 EtOAc/petroleum ether); ν_{max} (film)/cm^{-1} 1708 (C=O), 1485, 1354, 1077; δ_H (400 MHz, $CDCl_3$) 6.55 (1 H, dd, *J* 2.7, 1.9, NCH), 5.98 (1 H, dd, *J* 3.4, 2.7, NCHC*H*), 5.82 (1 H, dd, 3.4, 1.9, $NCCH_{pyr}$), 3.93-3.88 (2 H, m, NCH_2), 3.84 (1 H, dd, *J* 7.6, 2.6, COCH), 2.49 (2 H, q, *J* 7.3, CH_3CH_2), 2.08 (1 H, m), 1.90 (1 H, m), 1.84-1.64 (4 H, m), 1.05 (3 H, t, *J* 7.3, CH_3); δ_C (100 MHz, $CDCl_3$) 211.3 (C=O), 131.8 (pyr-C), 122.5 (pyr-C), 108.1 (pyr-C), 106.1 (pyr-C), 51.2, 50.2, 35.0 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 27.5 (CH_2), 7.9 (CH_3); *m/z* (%) (CI) 192.1 (100, $[M+H]^+$), 134.1 (30), 93.1 (50); HRMS (CI) Calc'd for $C_{12}H_{18}NO$ 192.1388, Found 192.1391.

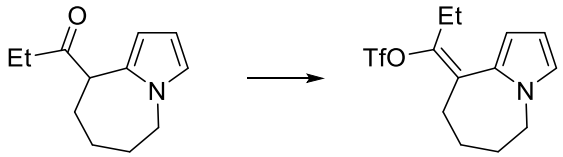
Triisopropyl((3-methyl-5-(tributylstannyl)furan-2-yl)oxy)silane 19[1]



S1 **19**

Synthesised according to **General Procedure 1** using siloxyfuran **S1**[2] (6.0 g, 23 mmol). Purification by Kugelrohr distillation (oven T = 200 °C, 2 mbar) to gave **19** (10.5 g, 84%) as a yellow oil. All data corresponded to that available in the literature.[1] ν_{max} (film)/cm^{-1} 1651, 1488, 1463, 1259, 881, 681; δ_H (400 MHz, $CDCl_3$) 6.29 (1 H, app. t, *J* 3.6, fur-CH), 1.83 (3 H, s, fur-CH_3), 1.64-1.48 (6 H, m, 3 x CH_2), 1.39-1.19 (11 H, m), 1.08 (18 H, d, *J* 7.3, 6 x TIPS CH_3), 1.01-0.95 (4 H, m), 0.88 (9 H, t, *J* 7.2, 3 x CH_3); $\delta^{119}{}_{Sn}$ (112 MHz, $CDCl_3$) -62.7.

(*E*)-1-(7,8-dihydro-5*H*-pyrrolo[1,2-*a*]azepin-9(6*H*)-ylidene)propyl trifluoromethanesulfonate S3

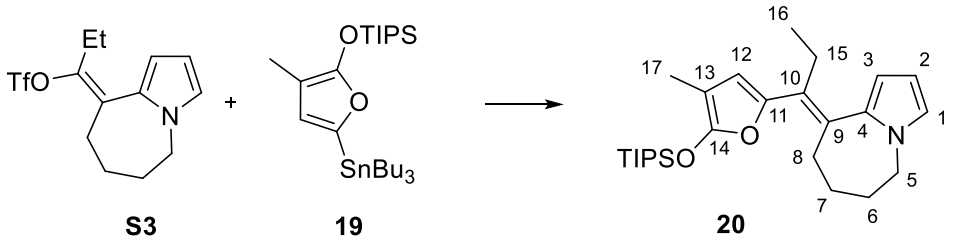


18 **S3**

Sodium hydride (60% dispersion in mineral oil, 1.15 g, 29 mmol) was added portionwise to a solution of ketone **18** (2.90 g, 15.2 mmol) in DMF (100 mL) and stirred at room temperature for 2 h. The dark green or sometimes orange solution was then cooled to 0 °C and *N*-phenyl-bis(trifluoromethanesulfonimide) (7.06 g, 19.8 mmol) was added in one portion. The ice bath was removed and the reaction mixture was stirred for 0.5 h before diluting with Et_2O (100 mL) and quenched (gas evolution) with dropwise addition of 1 M NaOH. After gas evolution had ended, NaOH (1 M, 200 mL) was added and the layers were separated. The product was extracted twice from the aqueous layer with Et_2O (150 mL) and the combined organic extracts were washed twice with NaOH (1 M, 50 mL) followed by water (50 mL) then dried ($MgSO_4$) and concentrated *in vacuo*. The crude orange oil **S3** (4.91 g, 100%) was used without further purification in the next step, or stored as a 0.5 M solution in THF in the freezer. R_f 0.37 (1:19 EtOAc/petroleum ether); δ_H (400 MHz, $CDCl_3$) 6.63 (1 H, t, *J* 2.2, NCH), 6.06-6.02 (2 H, m), 3.95-3.90 (2 H, m, NCH_2), 2.59 (2 H, q, *J* 7.4, CH_3CH_2), 2.53-2.45 (2 H, m, C=CCH_2CH_2), 1.87-1.78 (4 H, m), 1.16 (3 H, t, *J* 7.4, CH_3); δ_C (100 MHz, $CDCl_3$) 149.5 (CH_3CH_2C=C),

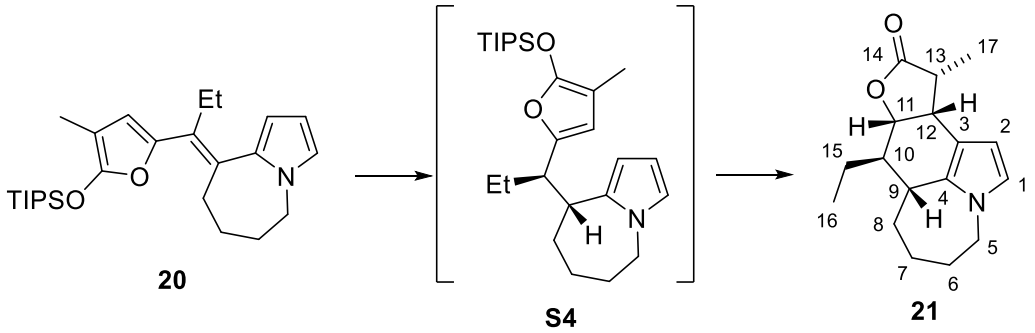
129.8 (N*C*CH), 126.6 (CH_3CH_2C=*C*), 123.3 (NCH), 118.4 (q, *J* 319.4, CF_3), 109.1 (pyr-C), 106.6 (pyr-C), 49.6 (NCH_2), 29.7 (C=C*C*H_2CH_2), 29.1 (CH_2), 27.5 (CH_2), 24.9 (CH_3*C*H_2), 12.0 (CH_3).

(*E*)-9-(1-(4-methyl-5-((triisopropylsilyl)oxy)furan-2-yl)propylidene)-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine 20



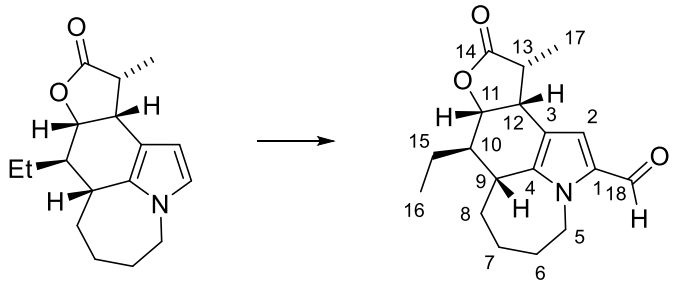
Stannane **19** (1.30 g, 2.4 mmol), enol triflate **S3** (710 mg, 2.2 mmol, 1.0 eq), powdered sodium hydroxide (96 mg, 2.4 mmol) and $Pd(PPh_3)Cl_2$ (2.0 mol%) were dissolved in THF (33 mL) and degassed by bubbling through N_2 for 10 min. The reaction was then heated at reflux for 1.5 h, cooled to room temperature and the reaction mixture was concentrated directly onto basic Al_2O_3 and purified by flash chromatography (1:9 CH_2Cl_2/petroleum ether with 1% NEt_3, SiO_2) to give **20** (665 mg, 78%) as a clear oil. R_f 0.56 (1:20 EtOAc/petroleum ether); δ_H (400 MHz, $CDCl_3$) 6.57 (1 H, dd, *J* 2.6, 1.9, H1), 6.14 (1 H, s, H12), 6.05 (1 H, dd, *J* 3.4 2.6, H2), 6.00 (1 H, dd, *J* 3.4, 1.9, H3), 3.90-3.84 (2 H, m, H5), 2.62-2.53 (2 H, m, H8), 2.49 (2 H, q, *J* 7.4, H15), 1.89 (3 H, s, H17), 1.83-1.70 (4 H, m, H6 & H7), 1.35-1.24 (3 H, m, 3 x TIPS CH), 1.12 (18 H, d, *J* 7.2, 6 x TIPS CH_3), 0.96 (3 H, t, *J* 7.4, H16); δ_C (100 MHz, $CDCl_3$) 152.2 (C14), 142.4 (C11), 135.8 (C4), 131.3 (C9), 127.6 (C10), 121.0 (C1), 114.2 (C12), 107.7 (pyr-C), 106.0 (pyr-C), 93.6 (C13), 49.3 (C5), 33.3 (CH_2), 29.7 (CH_2), 28.5 (CH_2), 25.6 (CH_2), 17.8 (6 x TIPS CH_3), 15.3 (C16), 12.6 (3 x TIPS CH), 8.7 (C17); *m/z* (%) (ESI) 466.3 (100, $[M+Na+O]^+$), 450.3 (20, $[M+Na]^+$), 428.3 (15, $[M+H]^+$); HRMS (ESI) Calc'd for $C_{26}H_{41}NNaO_2Si$ 450.2799, Found 450.2817.

(±)-8-Ethyl-11-methyl-5,6,7,7a,8,8a,11,11a-octahydroazepino[3,2,1-*hi*]furo[3,2-*e*]indol-10(4*H*)-one 21



Palladium hydroxide on carbon (200 mg, 20 wt%) was added to a solution of **20** (1.0 g, 2.34 mmol) in MeCN (75 mL). The solution was purged with N_2 three times before replacing the atmosphere with H_2 (1 atm). The reaction mixture was stirred vigorously and heated at 50 °C for 2 h. After allowing to cool, the mixture was filtered through basic alumina, washing though with $CHCl_3$, and concentrated *in vacuo* to give 820 mg of crude **S4**. Due to the instability of this compound, it was used directly in the next step without purification. Tin(IV) chloride (0.44 mL, 3.7 mmol) was added to a solution of (±)-BINOL (1.17 g, 4.09 mmol) in CH_2Cl_2 (50 mL) and stirred for 10 min before cooling to -60 °C. A solution of **S4** (800 mg, 1.86 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise and the solution stirred at -60 °C for 1 h, after which time TLC indicated no starting material remained. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and allowed to warm to room temperature . Water (20 mL) and saturated aqueous NH_4Cl (20 mL) were added and the layers were separated. The aqueous layer was extracted twice with CH_2Cl_2 (30 mL) and the combined organic extracts were washed with brine. The mixture was dried ($MgSO_4$), concentrated *in vacuo* and purified by flash chromatography (5% EtOAc/10% CH_2Cl_2/petroleum ether, SiO_2) to give **21** (270 mg, 53% from **20**) as colourless plates, m.p. 137-138 °C (from EtOAc/petroleum ether). R_f 0.22 (10% EtOAc/20% CH_2Cl_2/petroleum ether); ν_{max} (film)/cm^{-1} 1766 (C=O), 1687 (br.), 1177 (C-O), 996; δ_H (500 MHz, $CDCl_3$) 6.46 (1 H, d, *J* 2.8, H1), 5.85 (1 H, d, *J* 2.8, H2), 4.59 (1 H, br. t, *J* 5.0, H11), 3.93 (1 H, br. dd, *J* 14.0, 5.2, H5$_a$), 3.81 (1 H, br. dd, *J* 14.0, 11.5, H5$_b$), 3.50 (1 H, br. dd, *J* 7.1, 5.0, H12), 2.95 (1 H, qn, *J* 7.1, H13), 2.55 (1 H, d, *J* 10.8, H9), 2.15 (1 H, m, H10), 2.03 (1 H, m, H7$_a$), 1.90 (1 H, m, H6$_a$), 1.83 (1 H, m, H8$_a$), 1.63-1.47 (2 H, m, H8$_b$, H7$_b$), 1.46-1.32 (3 H, m, H15, H6$_b$), 1.35 (3 H, d, *J* 7.1, H17), 1.01 (3 H, t, *J* 7.4, H16); δ_C (100 MHz, $CDCl_3$) 179.3 (C14), 131.9 (C4), 120.4 (C1), 108.7 (C3), 106.4 (C2), 81.6 (C11), 49.5 (C5), 44.4 (C10), 41.9 (C13), 37.2 (C9), 37.1 (C12), 36.6 (C8), 31.3 (C7), 29.5 (C6), 24.2 (C15), 12.5 (C16), 11.8 (C17); *m/z* (%) (CI) 274.2 (100, $[M+H]^+$), 200.1 (50); HRMS (CI) Calc'd for $C_{17}H_{24}NO_2$ 274.1807, Found 274.1805; Anal. Calc'd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12 Found: C, 75.30; H, 8.51; N, 5.20.

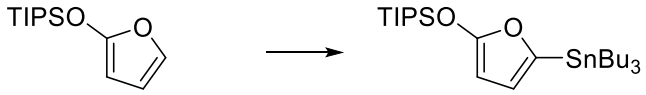
(±)-8-Ethyl-11-methyl-10-oxo-4,5,6,7,7a,8,8a,10,11,11a-decahydroazepino[3,2,1-*hi*]furo[3,2-*e*]indole-2-carbaldehyde 22



21 **22**

Oxalyl chloride (62 µl, 0.73 mmol) was added to cooled (<5 °C) DMF (56 µl, 0.73 mmol) and the resulting white solid was agitated by magnetic stirring at room temperature for 10 min before dissolving in CH_2Cl_2 (3.0 mL). A solution of **21** (166 mg, 0.61 mmol) in CH_2Cl_2 (0.5 mL) was added and the solution became homogeneous and yellow. After stirring for 15 min, NaOAc (1 M, 3.0 mL) was added and the reaction mixture was stirred for a further 30 min before adding Et_2O (10 mL) and separating the layers. The aqueous layer was extracted twice with Et_2O (5 mL) and the combined organic extracts were washed twice with saturated aqueous $NaHCO_3$ (5 mL) then H_2O (5 mL). The mixture was dried ($MgSO_4$) and concentrated *in vacuo* to give **22** (184 mg, 84%) as yellow cylinders, m.p. 175-178 °C (from EtOAc/petroleum ether). R_f 0.40 (1:1 EtOAc/petroleum ether); δ_H (400 MHz, $CDCl_3$) 9.40 (1 H, s, H18), 6.67 (1 H, s, H2), 5.59 (1 H, dd, *J* 14.5 5.6, $H5_a$), 4.64 (1 H, t, *J* 4.2, H11), 3.67 (1 H, dd, *J* 14.5 11.4, $H5_b$), 3.48 (1 H, dd, *J* 7.4, 4.5, H12), 3.02 (1 H, qn, *J* 7.2, H13), 2.65 (1 H, d, *J* 2.4, H9), 2.27 (1 H, m, H10), 2.03 (1 H, m, $H7_a$), 1.94 (1 H, m, $H6_a$), 1.85 (1 H, m, $H8_a$), 1.70-1.52 (2 H, m, $H8_b$, $H7_b$), 1.40-1.31 (2 H, m, $H15_a$, $H6_b$) 1.36 (3 H, d, *J* 7.2, H17), 1.23 (1 H, m, $H15_b$), 1.02 (3 H, t, *J* 7.4, H16); δ_C (100 MHz, $CDCl_3$) 179.2 (C18), 178.1 (C14), 144.2 (C4), 130.9 (C1), 124.8 (C2), 111.1 (C3), 80.5 (C11), 45.7 (C5), 43.9 (C10), 41.5 (C13), 37.2 (C9), 36.4 (C12), 35.5 (C8), 31.2 (C7), 28.5 (C6), 24.2 (C15), 12.5 (C16), 11.6 (C17); *m/z* (%) (CI) 302.2 (100, $[M+H]^+$), 228.2 (10); HRMS (CI) Calc'd for $C_{18}H_{24}NO_3$ 302.1756, Found 302.1749. Anal. Calc'd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65 Found: C, 72.61; H, 7.74; N, 4.52.

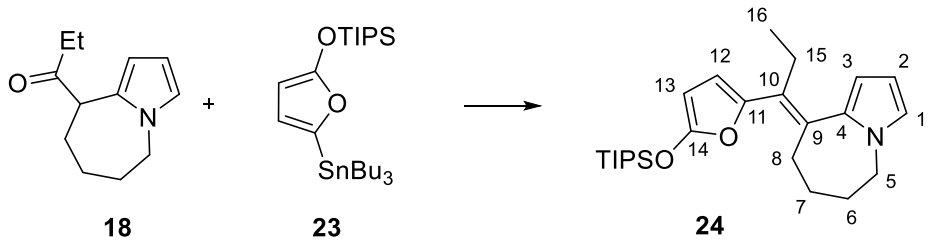
Triisopropyl((5-(tributylstannyl)furan-2-yl)oxy)silane 23



S2 **23**

Synthesised according to **General Procedure 1** using siloxyfuran **S2**[3] (5.9 g, 24 mmol). Purification by Kugelrohr distillation (oven T = 200 °C, 2 mbar) to gave **23** (12.8 g, 97%) as a yellow oil. ν_{max} (film)/cm^{-1} 1611, 1523, 1486, 1463, 1254, 837, 690, 665; δ_H (400 MHz, $CDCl_3$) 6.39 (1 H, app. q, *J* 3.3, SnCCH), 5.14 (1 H, app. q, *J* 3.0, TIPSOCC*H*), 1.65-1.46 (6 H, m, 3 x CH_2), 1.38-1.18 (11 H, m, 3 x CH_2, 3 x CH), 1.09 (18 H, d, *J* 7.4, 6 x TIPS CH_3), 1.03-0.99 (4 H, m), 0.88 (9 H, t, *J* 7.4, 3 x CH_3); δ_C (100 MHz, $CDCl_3$) 161.5 (TIPSOC), 148.6 (TIPSOC*C*H), 123.8 (d, *J* 22.5, SnC*C*H), 83.8 (d, *J* 31.9, SnC), 29.1 (t, *J* 10.7, 3 x CH_2), 27.4 (br., 3 x CH_2), 17.7 (m, 6 x TIPS CH_3), 13.8 (m, 3 x CH_2), 12.4 (br., 3 x TIPS CH), 10.2 (m, 3 x CH_2); *m/z* (ESI) No molecular ion observed, presumably due to its instability.

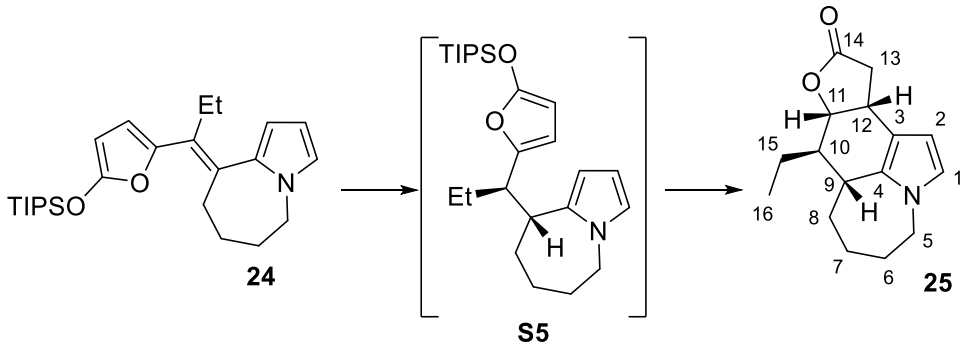
(*E*)-9-(1-(5-((triisopropylsilyl)oxy)furan-2-yl)propylidene)-6,7,8,9-tetrahydro-5*H*-pyrrolo[1,2-*a*]azepine 24



To a stirred solution of ketone **18** (10.9 g, 57.1 mmol) in anhydrous DMF (300 mL) at room temperature under nitrogen was added sodium hydride (4.32 g of a 60% dispersion in mineral oil, 110 mmol) portionwise. After stirring for 2 h the reaction was cooled to 0 °C and $PhNTf_2$ (26.5 g, 74.1 mmol) added in one portion. The reaction was warmed to room temperature , stirred for 30 min, diluted with Et_2O (300 mL) and quenched by the cautious addition of 1M aq. NaOH (600 mL). The phases were separated, the aqueous phase extracted with Et_2O (2 × 200 mL) and the combined organic phase warmed with 1M aq. NaOH (2 × 200 mL) and water (200 mL). Drying ($MgSO_4$) and evaporation afforded the crude compound (17.45 g) which was used directly in the following step. Crude triflate and stannane **23** (33.0 g, 62.3 mmol) were dissolved in anhydrous THF and the solution degassed by sparging with nitrogen. Powdered sodium hydroxide (2.75 g, 62.3 mmol) and $Pd(PPh_3)_2Cl_2$ (890 mg, 1.27 mmol) were added and the stirred mixture heated to reflux. After 3 h the reaction was cooled to room temperature and stirred overnight. After 16 h the mixture was dry loaded onto basic alumina, and purified by silica gel chromatography (DCM in petrol containing 1% Et_3N, 0% to 10% as eluent) to afford the title compound (15.8 g, 67% over two steps) as a light yellow oil. ν_{max} (film)/cm^{-1} 1613, 1543, 1463, 1264, 999; δ_H (400 MHz, $CDCl_3$) 6.59 (1 H, dd, *J* 2.6, 1.8, H1), 6.23 (1 H, d, *J* 3.3, H12), 6.07 (1 H, dd, *J* 2.6, 3.5, H2), 6.03 (1 H, dd, *J* 3.5, 1.8, H3), 5.23 (1 H, d, *J* 3.3, H13), 3.92-3.86 (2 H, m, H5), 2.63-

2.55 (2 H, br. s, H8), 2.52 (2 H, q, *J* 7.4, H15), 1.85-1.73 (4 H, m, H6 & H7), 1.37-1.26 (3 H, m, 3 x TIPS CH), 1.14 (18 H, d, *J* 7.3, 3 x TIPS CH_3), 0.98 (3 H, t, *J* 7.4, H16); δ_C (100 MHz, $CDCl_3$) 156.1 (C14), 143.8 (C11), 135.7 (C4), 131.3 (C9), 128.5 (C10), 121.1 (C1), 111.2 (C12), 107.7 (pyr-C), 106.0 (pyr-C), 85.5 (C13), 49.4 (C5), 33.4 (CH_2), 29.7 (CH_2), 28.6 (CH_2), 25.7 (CH_2), 17.7 (6 x TIPS CH_3), 15.2 (C16), 12.4 (3 x TIPS CH); *m/z* (%) (ESI) 452.3 (100, $[M+Na+O]^+$), 436.3 (40, $[M+Na]^+$), 414.3 (10, $[M+H]^+$); HRMS (ESI) Calc'd for $C_{25}H_{39}NNaO_2Si$ 436.2642, Found 436.2662.

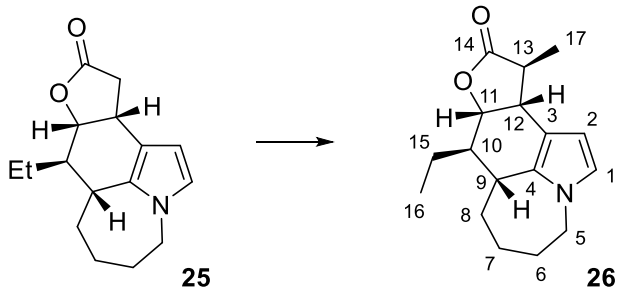
(±)-8-Ethyl-5,6,7,7a,8,8a,11,11a-octahydroazepino[3,2,1-*hi*]furo[3,2-*e*]indol-10(4*H*)-one 25



Palladium hydroxide on carbon (242 mg, 20 wt%) was added to a solution of **24** (1.21 g, 2.91 mmol) in MeCN (90 mL). The solution was purged with N_2 three times before replacing the atmosphere with H_2 (1 atm). The reaction mixture was stirred vigorously and heated at 50 °C for 2 h. After allowing to cool the mixture was filtered through basic alumina, washing though with $CHCl_3$, and concentrated *in vacuo* to give 1.2 g of crude **S5**. Due to the instability of this compound, it was used directly in the next step without purification (~80% by ^{1}H NMR). Tin(IV) chloride (0.68 mL, 5.8 mmol) was added to a solution of (±)-BINOL (1.83 g, 6.39 mmol) in CH_2Cl_2 (60 mL) and stirred for 10 min before cooling to -78 °C. A solution of **S5** (1.2 g, 2.9 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise and the solution was allowed to warm slowly to -40 °C over 2 h, after which time TLC indicated no starting material remained. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and allowed to warm to room temperature. Water (20 mL) and saturated aqueous NH_4Cl (20 mL) were added and the layers were separated. The aqueous layer was extracted twice with CH_2Cl_2 (30 mL) and the combined organic extracts were washed twice with 1 M aqueous NaOH (20 mL) followed by brine. The mixture was dried ($MgSO_4$), concentrated *in vacuo* and purified by flash chromatography (1:5 EtOAc /petroleum ether, SiO_2) to give **25** (462 mg, 61% from **24**) as colourless cubes, m.p. 115-117 °C (from EtOAc/petroleum ether). R_f 0.25 (1:5 EtOAc /petroleum ether); ν_{max} (film)/cm^{-1} 1795 (C=O), 1110 (C-O), 933; δ_H (400 MHz, $CDCl_3$) 6.48 (1 H, d, *J* 2.8, H1), 5.82 (1 H, d, *J* 2.8, H2), 4.65 (1 H, t, *J* 4.9, H11), 3.94 (1 H, br. dd, *J* 13.9,

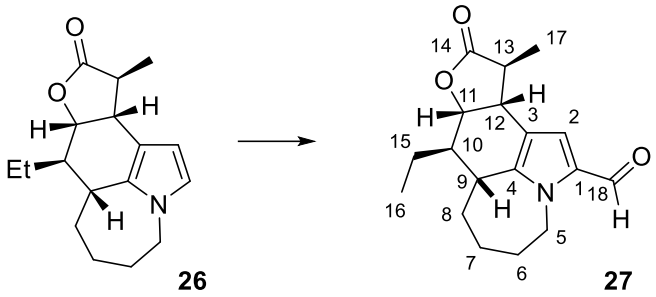
5.1, H5$_a$), 3.80 (1 H, dd, *J* 13.9, 11.4, H5$_b$), 3.49 (1 H, m, H12), 2.87 (1 H, dd, *J* 16.8, 7.4, H13$_a$), 2.60 (1 H, dd, *J* 16.8, 2.4, H13$_b$), 2.57 (1 H, m, H9), 2.13 (1 H, m, H10), 2.05 (1 H, m, H7$_a$), 1.94-1.83 (2 H, m, H8$_a$, H6$_a$), 1.56-1.48 (2 H, m, H8$_b$, H7$_b$), 1.48-1.35 (3 H, m, H15, H6$_b$), 1.02 (3 H, t, *J* 7.4, H16); δ_C (100 MHz, $CDCl_3$) 177.1 (C14), 131.2 (C4), 121.6 (C1), 113.2 (C3), 104.4 (C2), 83.0 (C11), 49.8 (C5), 44.3 (C10), 38.7 (C13), 37.0 (C9), 36.4 (C8), 32.6 (C12), 31.2 (C7), 29.7 (C6), 24.0 (C15), 12.4 (C16); *m/z* (%) (CI) 260.2 (100, $[M+H]^+$), 200.1 (20); HRMS (CI) Calc'd for $C_{16}H_{22}NO_2$ 260.1651, Found 260.1645; Anal. Calc'd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40 Found: C, 75.18; H, 8.19; N, 5.48.

(±)-(13-*Epi*-197) 26



A solution of **25** (215 mg, 0.83 mmol) in THF (17 mL) was cooled to -78 °C and LiHMDS (1.0 M in THF, 870 µl, 0.87 mmol) was added dropwise. The mixture was stirred at -78 °C for 45 min before adding methyl iodide (150 µl, 2.34 mmol) slowly and stirring below -60 °C for 1 h. The reaction was then quenched with saturated aqueous NH_4Cl (10 mL) and allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted twice with CH_2Cl_2 (10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude material by flash chromatography (3:7 EtOAc/petroleum ether, SiO_2) gave **26** (180 mg, 79%) as yellow needles, m.p. 147-149 °C (from EtOAc/petroleum ether). R_f 0.32 (1:4 EtOAc/petroleum ether); ν_{max} (film)/cm^{-1} 1769 (C=O), 1681, 1178 (C-O), 993; δ_H (400 MHz, $CDCl_3$) 6.50 (1 H, d, *J* 2.7, H1), 5.89 (1 H, d, *J* 2.7, H2), 4.62 (1 H, dd, *J* 8.5, 7.0, H11), 4.00 (1 H, br. dd, *J* 14.3, 5.7, H5$_a$), 3.78 (1 H, dd, *J* 14.3, 11.3, H5$_b$), 3.14 (1 H, br. t, *J* 7.0, H12), 2.61-2.50 (2 H, m, H13, H9), 2.16-2.02 (2 H, m, H8$_a$, H7$_a$), 1.96 (1 H, m, H6$_a$), 1.80 (1 H, m, H10), 1.73-1.51 (4 H, m, H15, H7$_b$, H6$_b$), 1.40 (3 H, d, *J* 7.5, H17), 1.28 (1 H, m, H8$_b$), 1.00 (3 H, t, *J* 7.6, H16); δ_C (100 MHz, $CDCl_3$) 180.0 (C14), 131.6 (C4), 122.3 (C1), 114.8 (C3), 104.7 (C2), 80.0 (C11), 50.8 (C5), 43.7 (C10), 43.2 (C13), 41.6 (C12), 36.7 (C9), 34.8 (C8), 30.7 (C7), 29.7 (C6), 22.5 (C15), 14.4 (C17), 10.7 (C16); *m/z* (%) (CI) 274.1 (100, $[M+H]^+$), 200.1 (50); HRMS (CI) Calc'd for $C_{17}H_{24}NO_2$ 274.1807, Found 274.1804; Anal. Calc'd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12 Found: C, 74.46; H, 8.60; N, 5.17.

(±)-(13-*Epi*-198) 27



Oxalyl chloride (98 µl, 1.2 mmol) was added to cooled (<5 °C) DMF (90 µl, 1.2 mmol) and the resulting white solid was agitated by magnetic stirring at room temperature for 10 min before dissolving in CH_2Cl_2 (7.0 mL). A solution of **26** (270 mg, 0.97 mmol) in CH_2Cl_2 (1.0 mL) was added and the solution became homogeneous and yellow. After stirring for 15 min, NaOAc (1 M, 5.0 mL) was added and the reaction mixture was stirred for a further 30 min before adding Et_2O (20 mL) and separating the layers. The aqueous layer was extracted twice with Et_2O (10 mL) and the combined organic extracts were washed twice with saturated aqueous $NaHCO_3$ (5 mL) then H_2O (10 mL). The mixture was dried ($MgSO_4$) and concentrated *in vacuo* to give **27** (250 mg, 86%) as yellow cylinders, m.p. 131-133 °C (from EtOAc/petroleum ether). R_f 0.44 (4:1 EtOAc/petroleum ether); ν_{max} (film)/cm^{-1} 1768 (C=O lac), 1651 (C=O ald), 1179 (C-O), 996; δ_H (400 MHz, $CDCl_3$) 9.40 (1 H, s, H18), 6.68 (1 H, s, H2), 5.57 (1 H, br. dd, *J* 14.1, 5.7, H5$_a$), 4.69 (1 H, t, *J* 6.0, H11), 3.66 (1 H, dd, *J* 14.1, 11.0, H5$_b$), 3.12 (1 H, t, *J* 6.0, H12), 2.67-2.59 (2 H, m, H13, H9), 2.12-2.00 (2 H, m, H10, H7$_a$), 2.00-1.91 (2 H, m, H8$_a$, H6$_a$), 1.64-1.41 (5 H, m, H15, H8$_b$, H7$_b$, H6$_b$), 1.42 (3 H, d, *J* 7.3, H17), 1.02 (3 H, t, *J* 7.5, H16); δ_C (100 MHz, $CDCl_3$) 179.2 (C18), 179.1 (C14), 143.5 (C4), 131.8 (C1), 122.8 (C2), 116.4 (C3), 79.5 (C11), 46.5 (C5), 44.1 (C13), 43.6 (C10), 40.0 (C12), 36.9 (C9), 34.6 (C8), 30.8 (C7), 28.4 (C6), 23.4 (C15), 14.8 (C17), 11.5 (C16); *m/z* (%) (CI) 302.1 (100, $[M+H]^+$), 228.1 (40); HRMS (CI) Calc'd for $C_{18}H_{24}NO_3$ 302.1756, Found 302.1746; Anal. Calc'd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65 Found: C, 72.06; H, 7.74; N, 4.85.

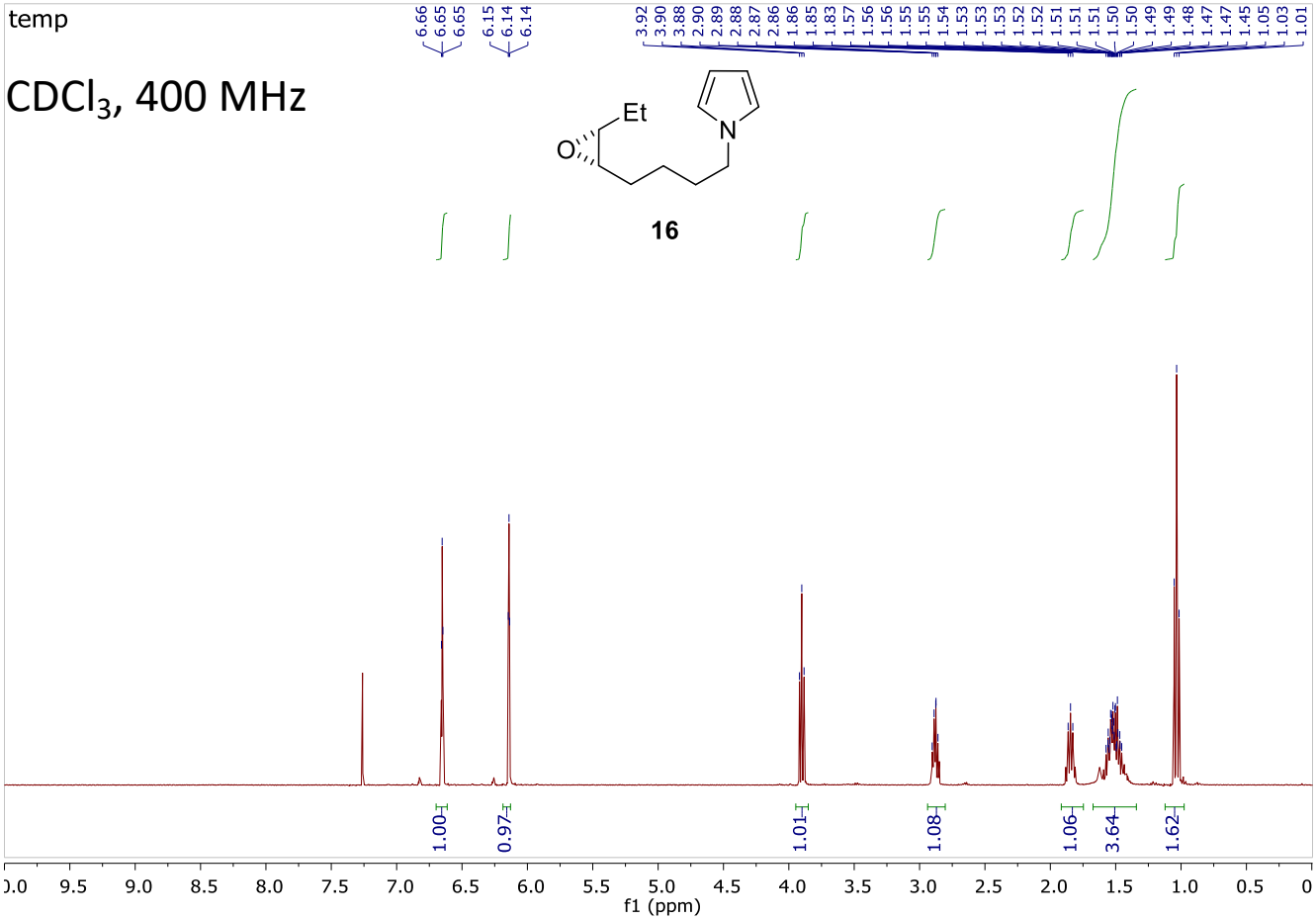
References.

1. Liras, S.; Lynch, C. L.; Fryer, A. M.; Vu, B. T.; Martin, S. F. *J. Am. Chem. Soc.* **2001**, *123*, 5918.

2. Synthesised from 2(5*H*)-furanone in 98% yield according to the procedure given reference 4.

3. Synthesised from 3-methyl-2(5*H*)-furanone in 99% yield according to the procedure given in reference 4.

4. Martin, S. F.; Barr, K. J.; Smith, D. W.; Bur, S. K. *J. Am. Chem. Soc*. **1999**, *121*, 6990.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N
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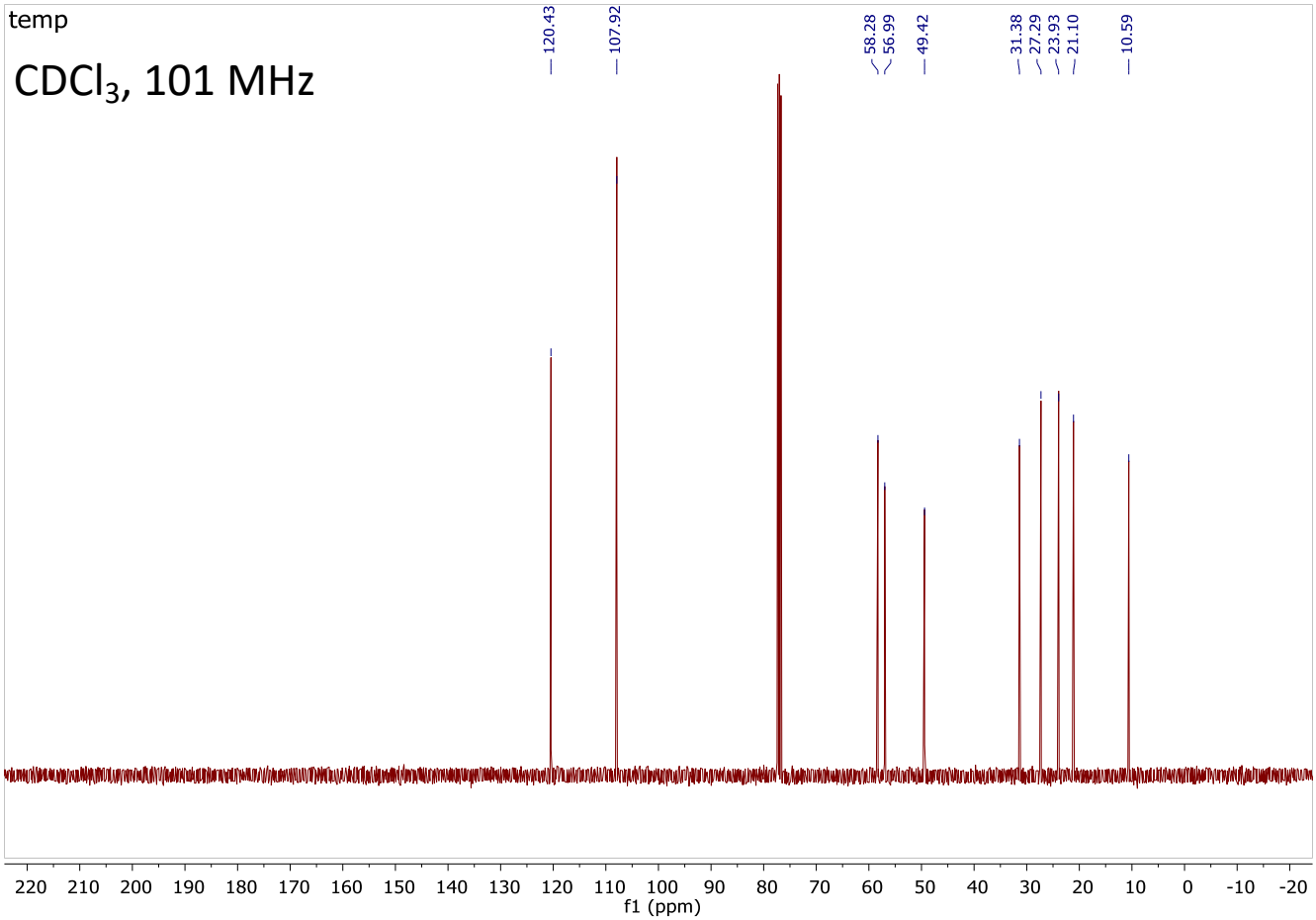
1.00 0.97 1.01 1.08 1.06 3.64 1.62
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)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27.29
23.93
21.10
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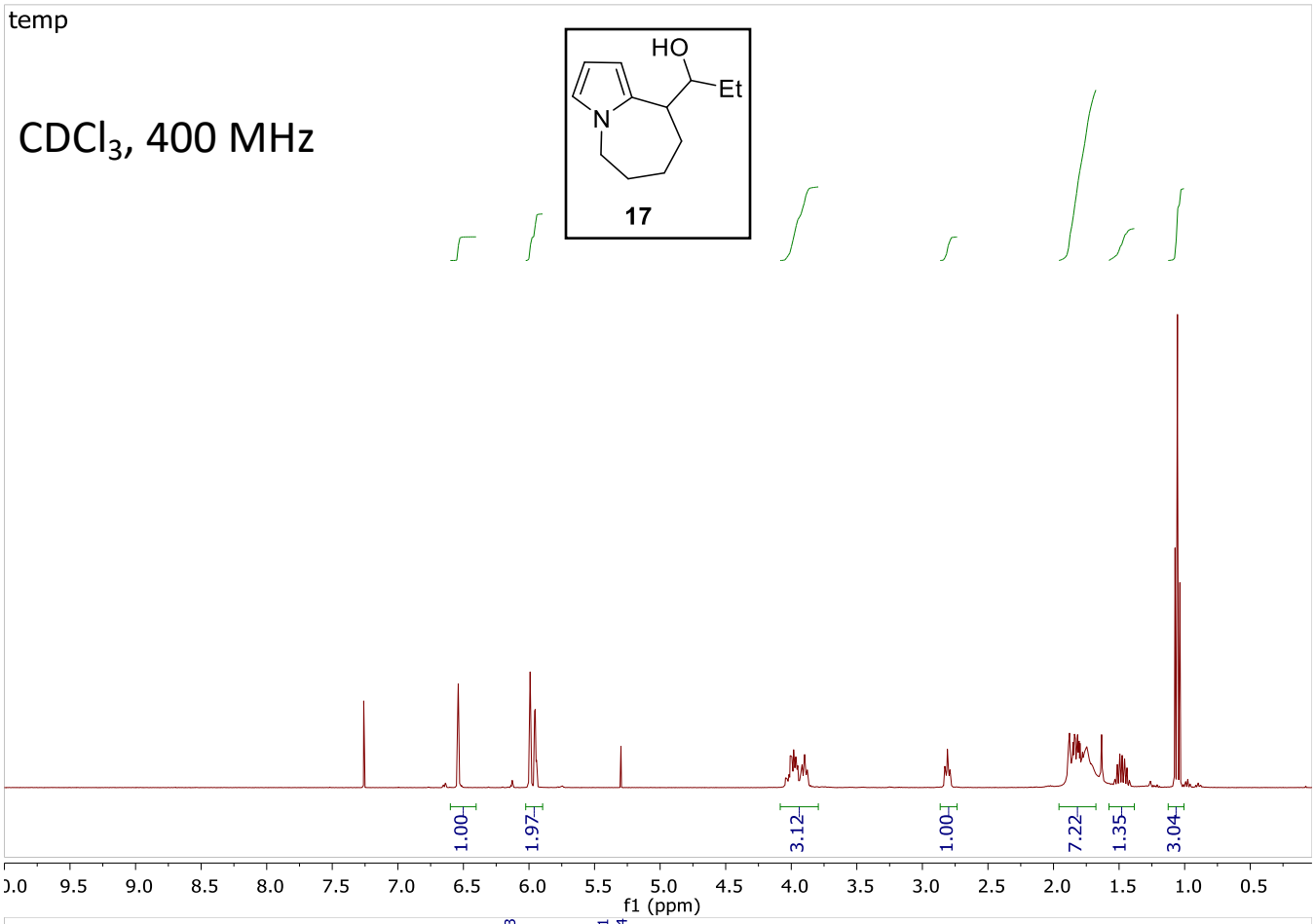
f1 (ppm)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Et
N
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1.97
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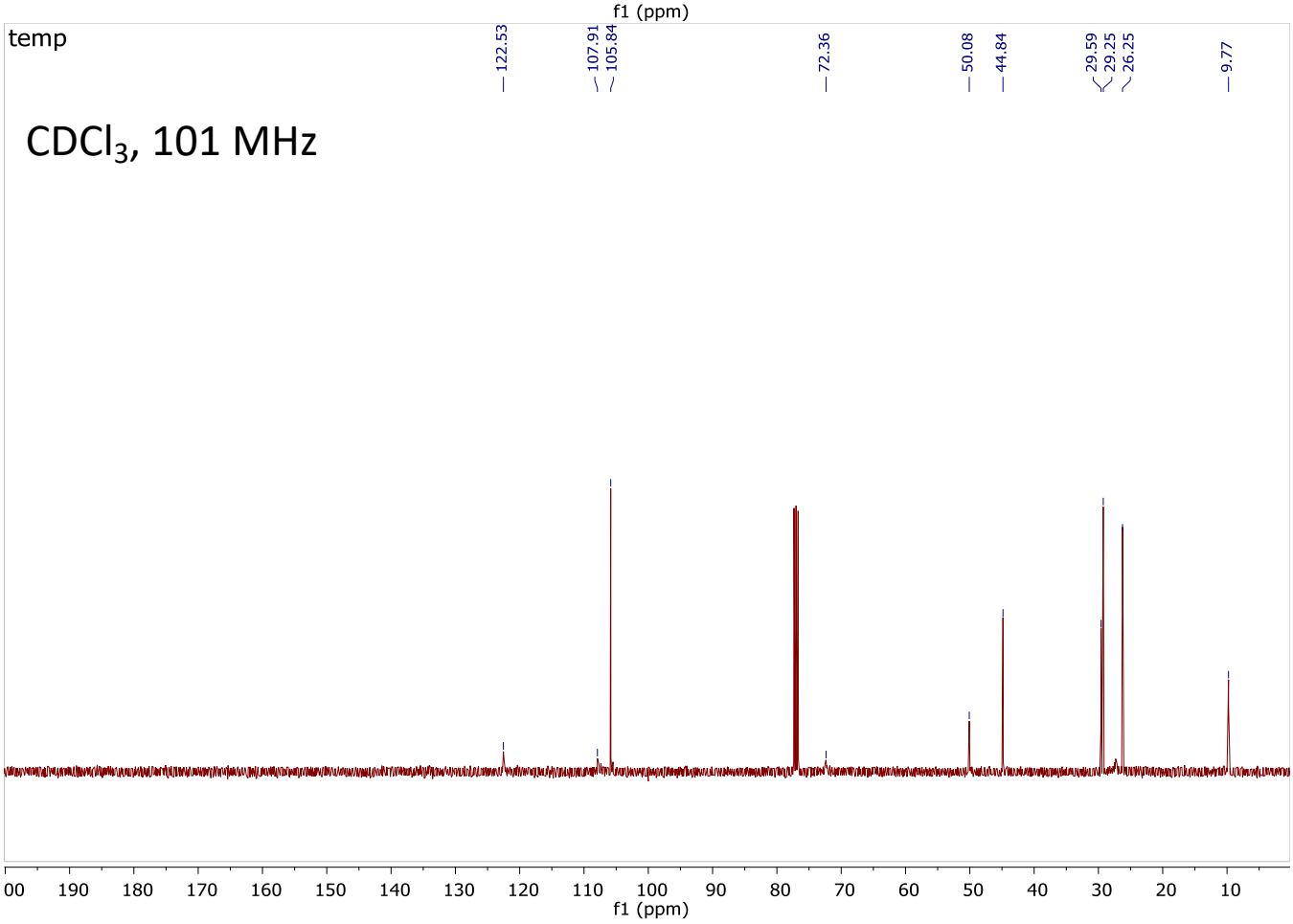
1.00
7.22
1.35
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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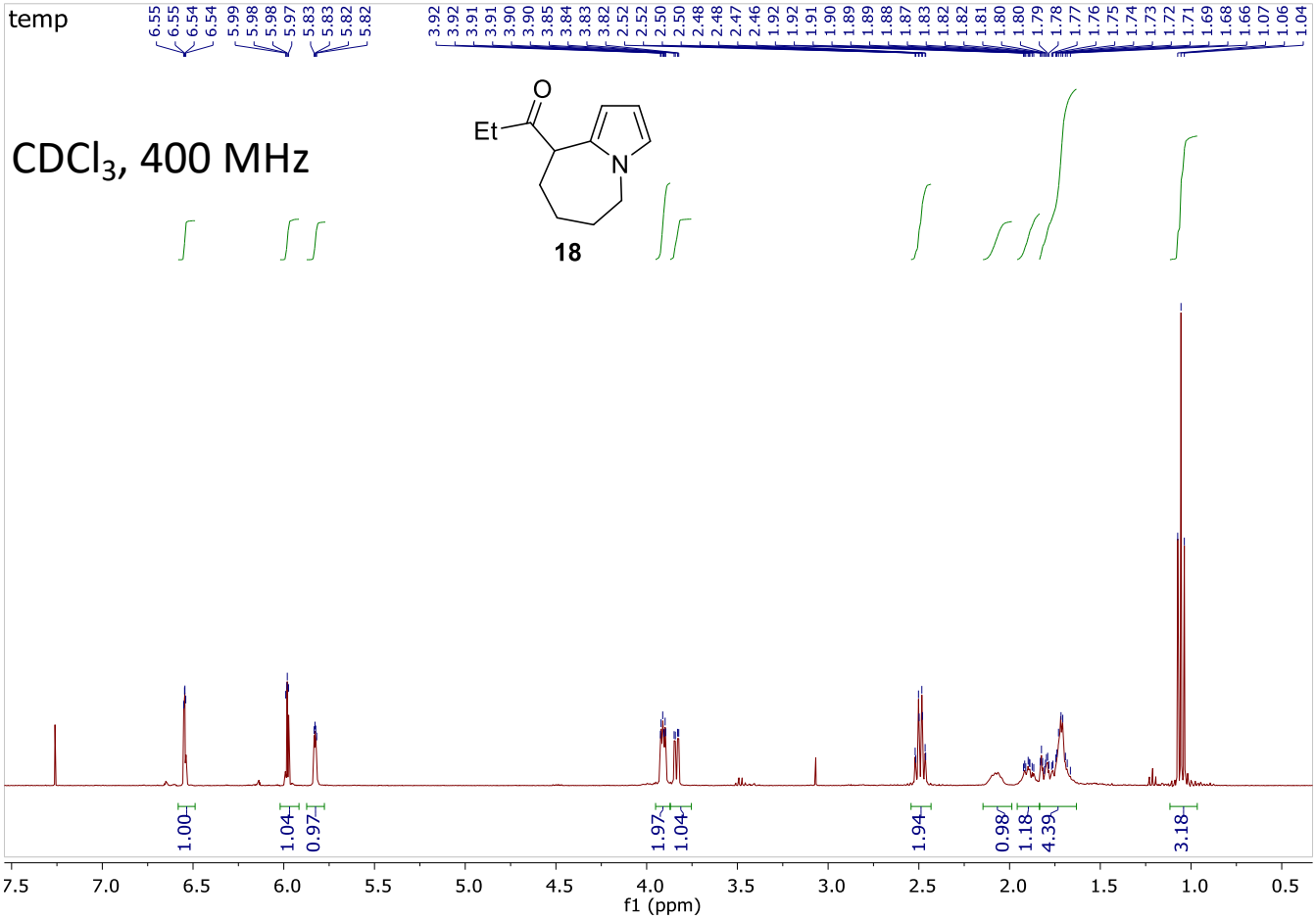
f1 (ppm)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O
N
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1.04
1.94
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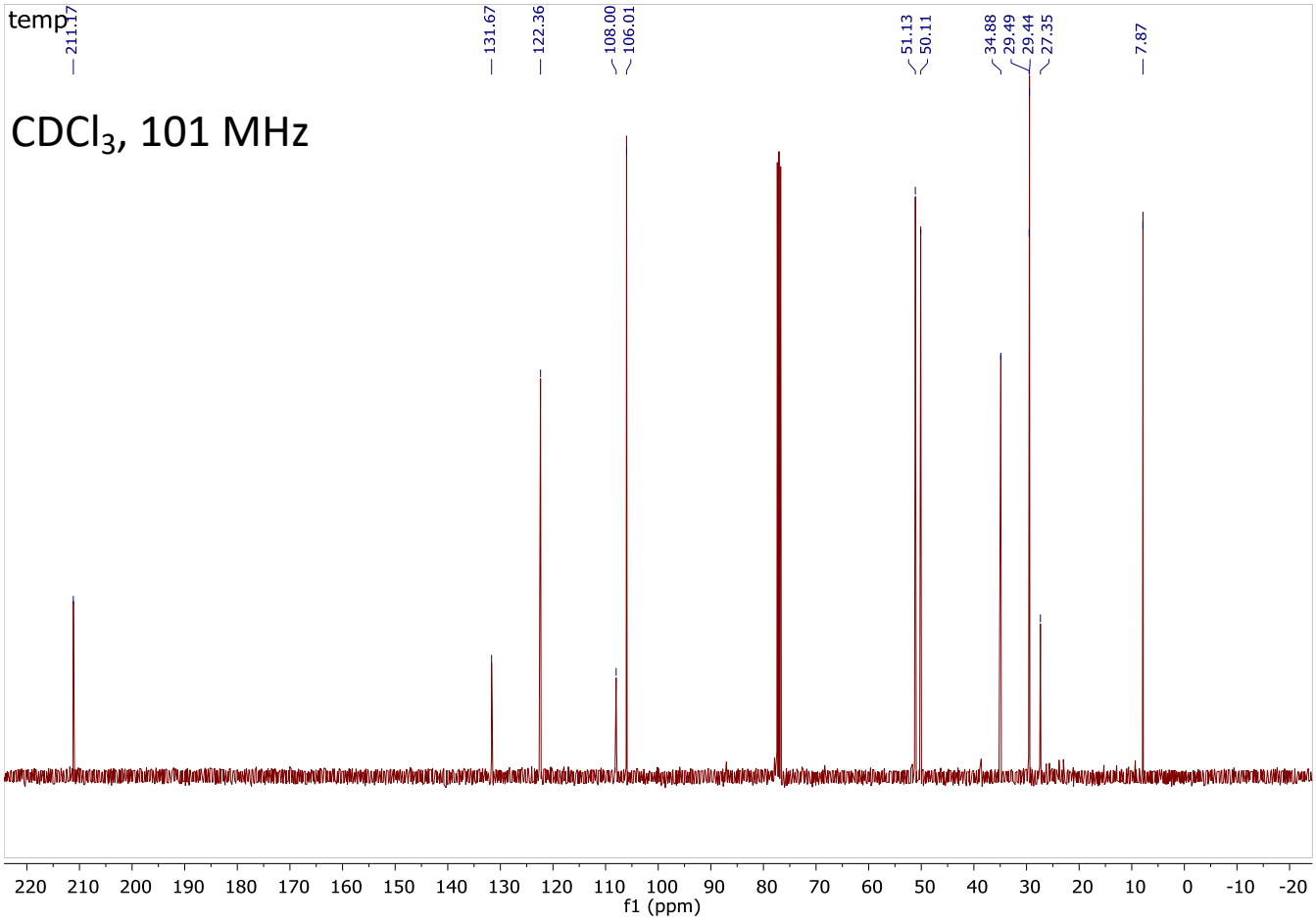
1.18
4.39
3.18
f1 (ppm)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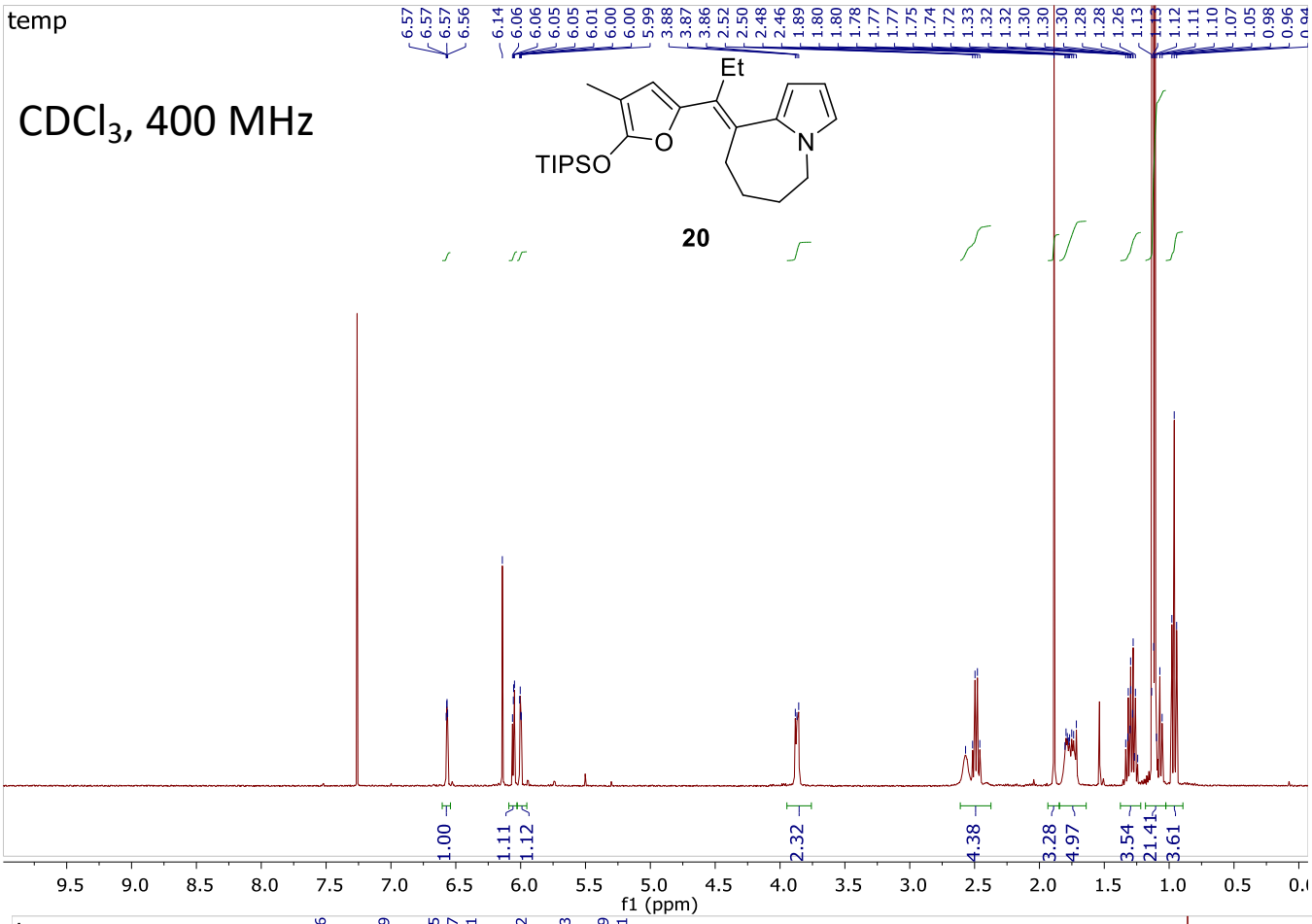
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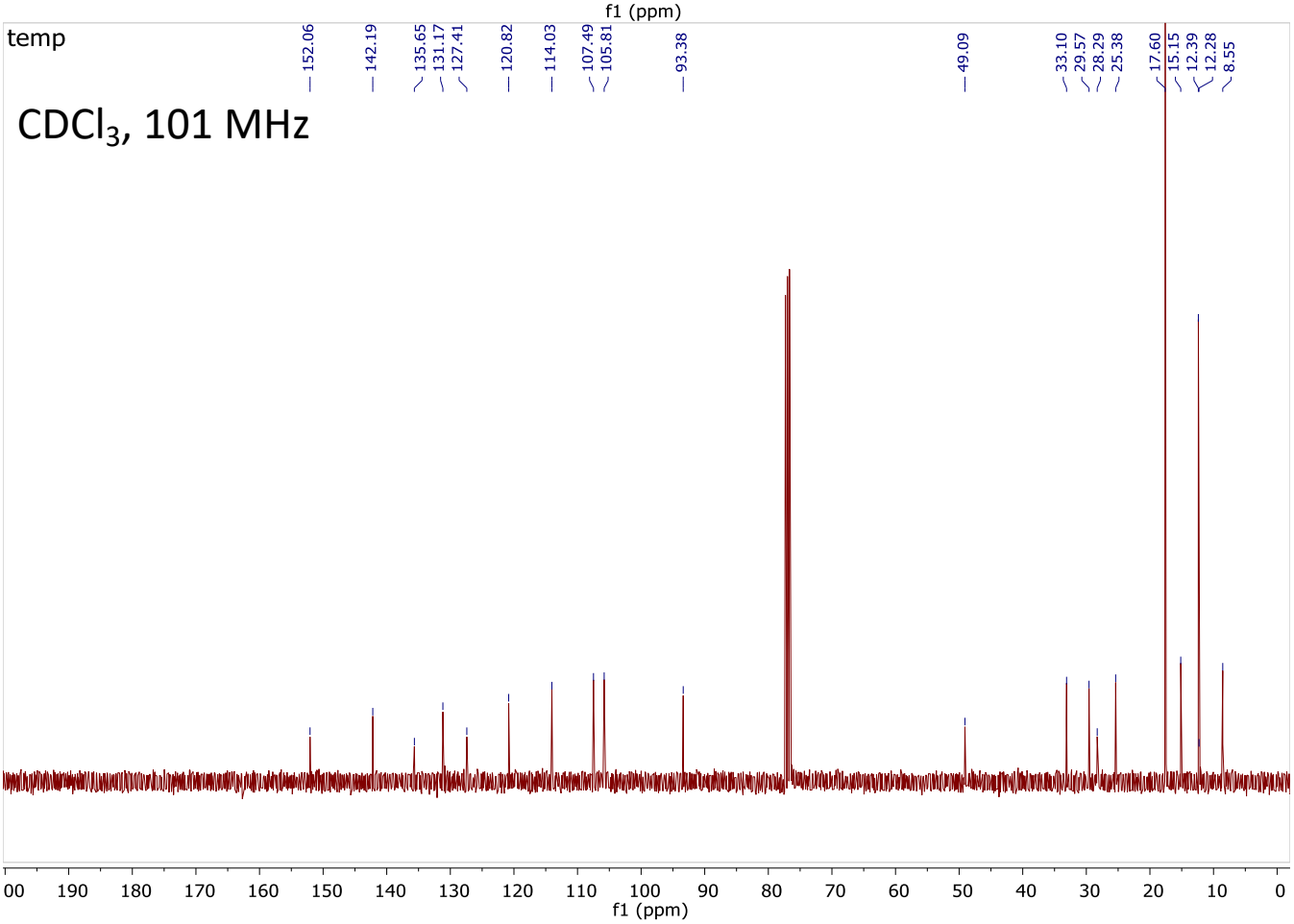
f1 (ppm)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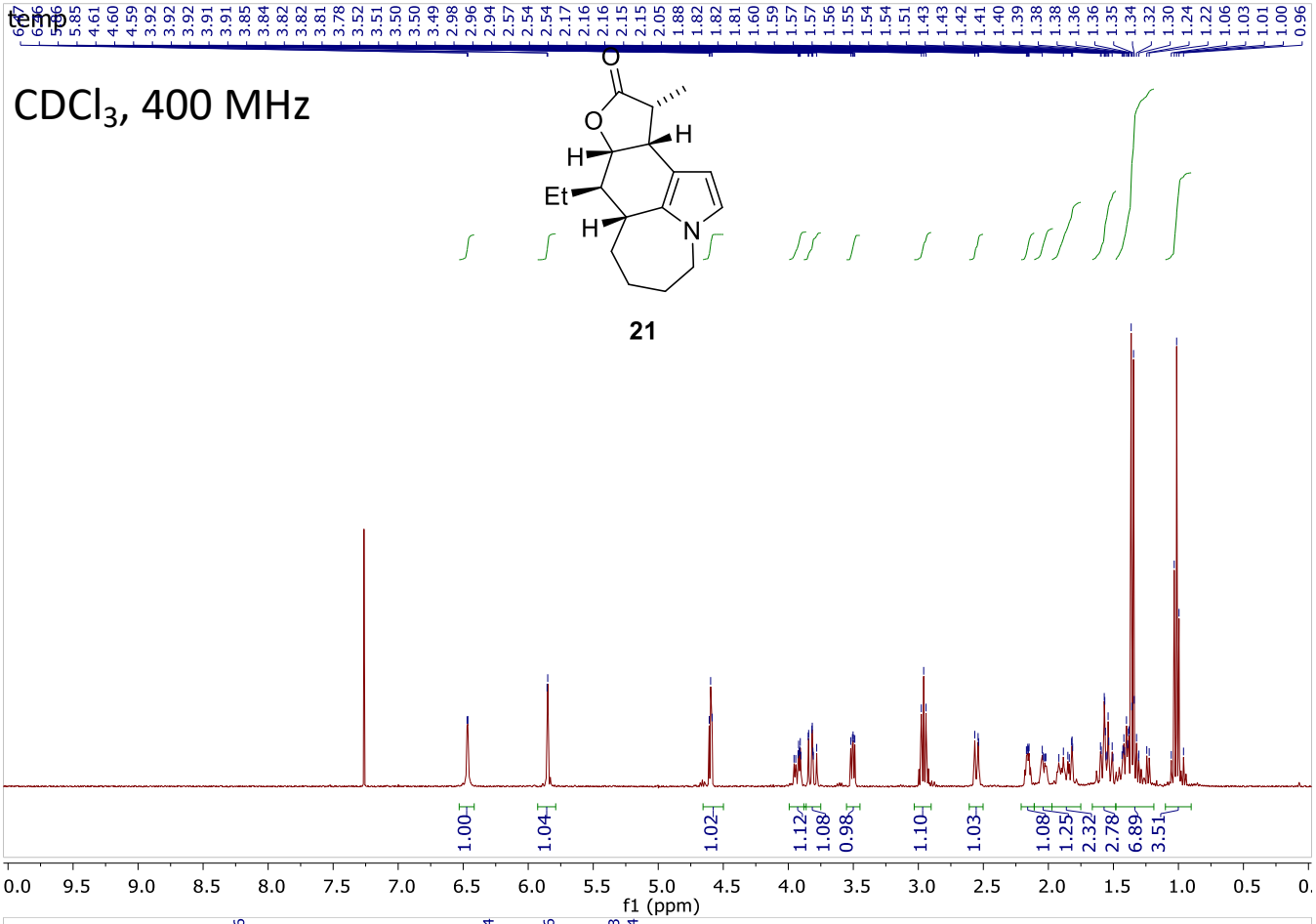
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H
Et
H
N
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1.04
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1.10
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1.08
1.25
2.32
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6.89
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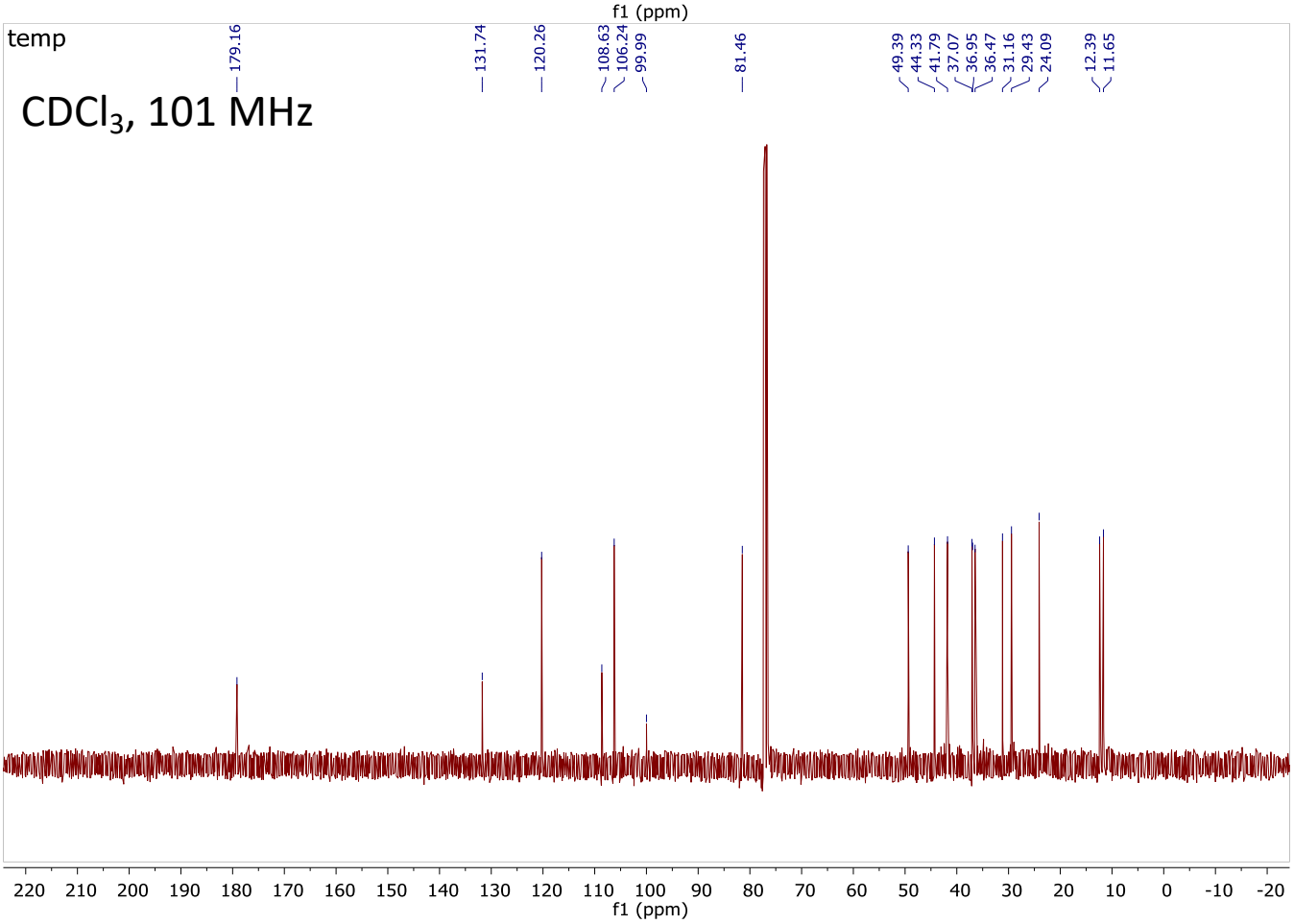
f1 (ppm)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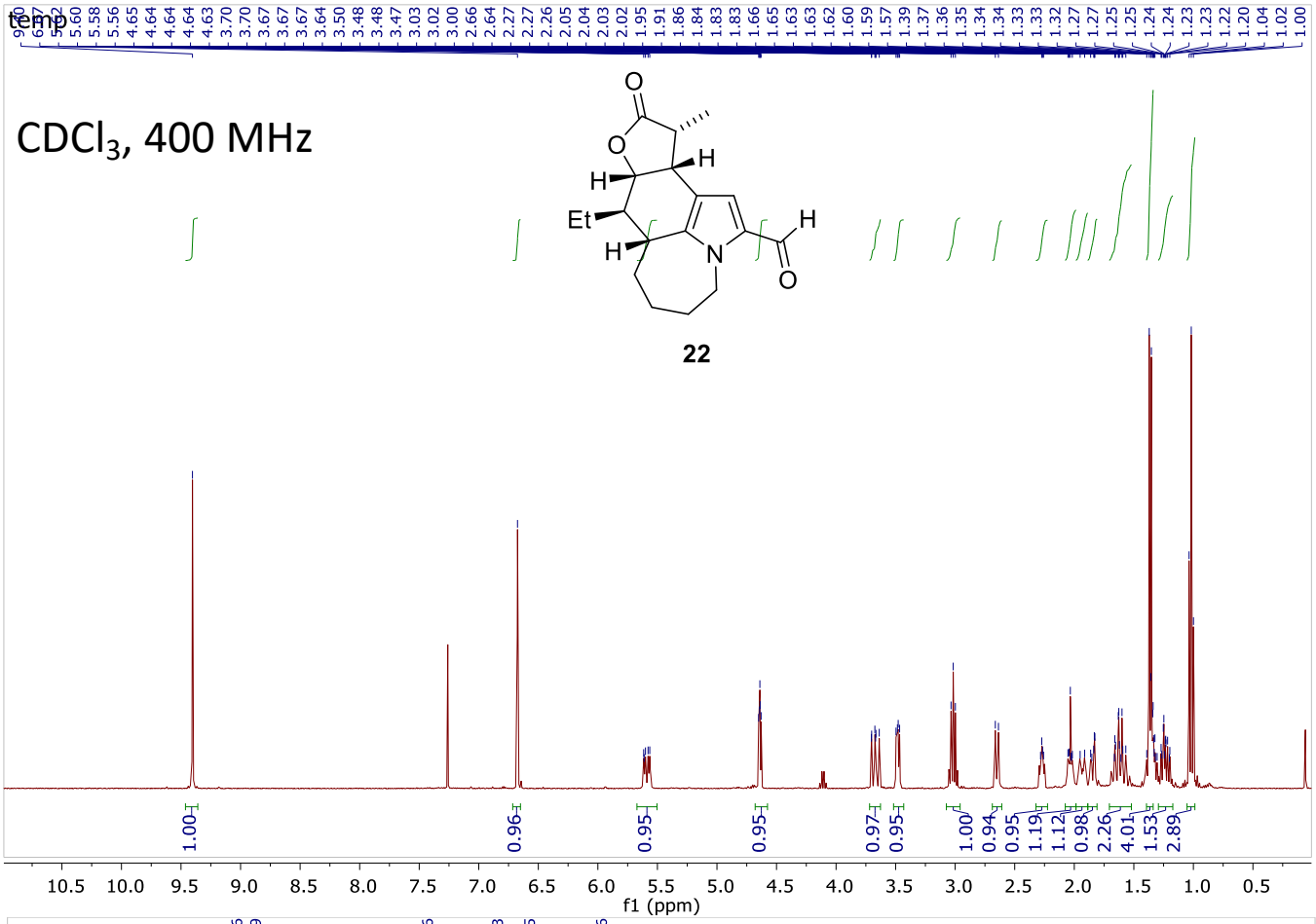
11.65
f1 (ppm)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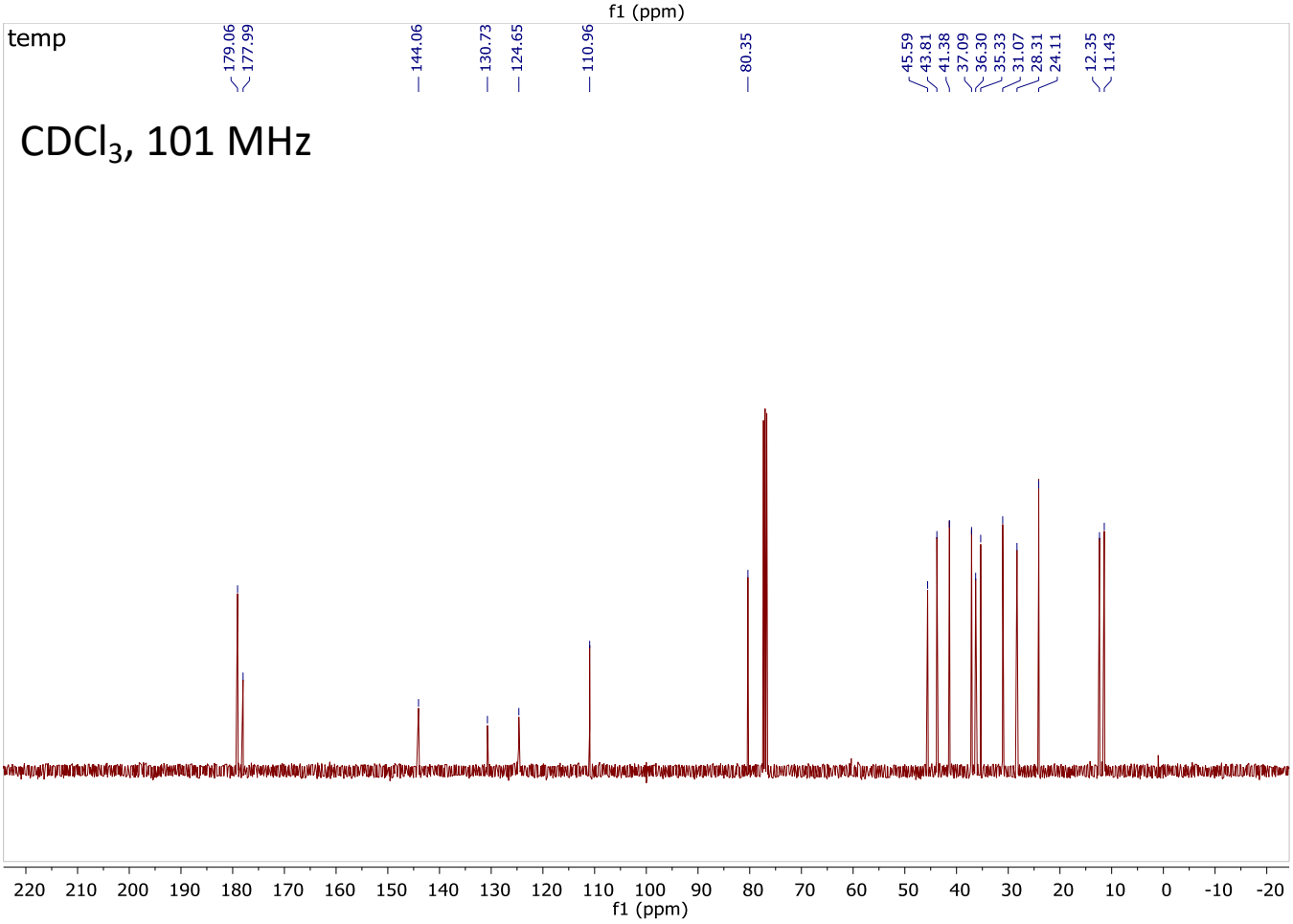
2.89
f1 (ppm)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35.33
31.07
28.31
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f1 (ppm)

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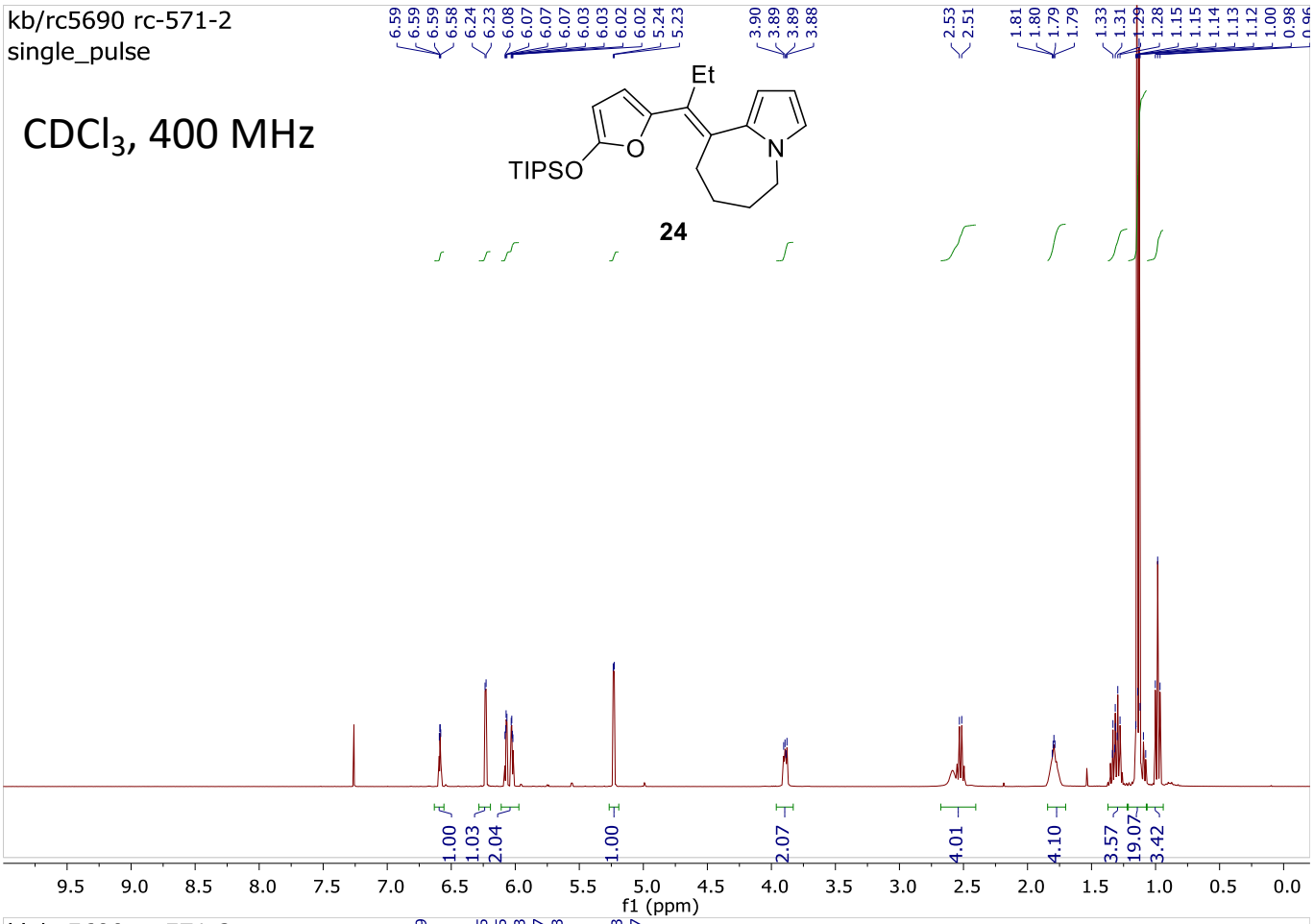
$CDCl_3$, 400 MHz

24



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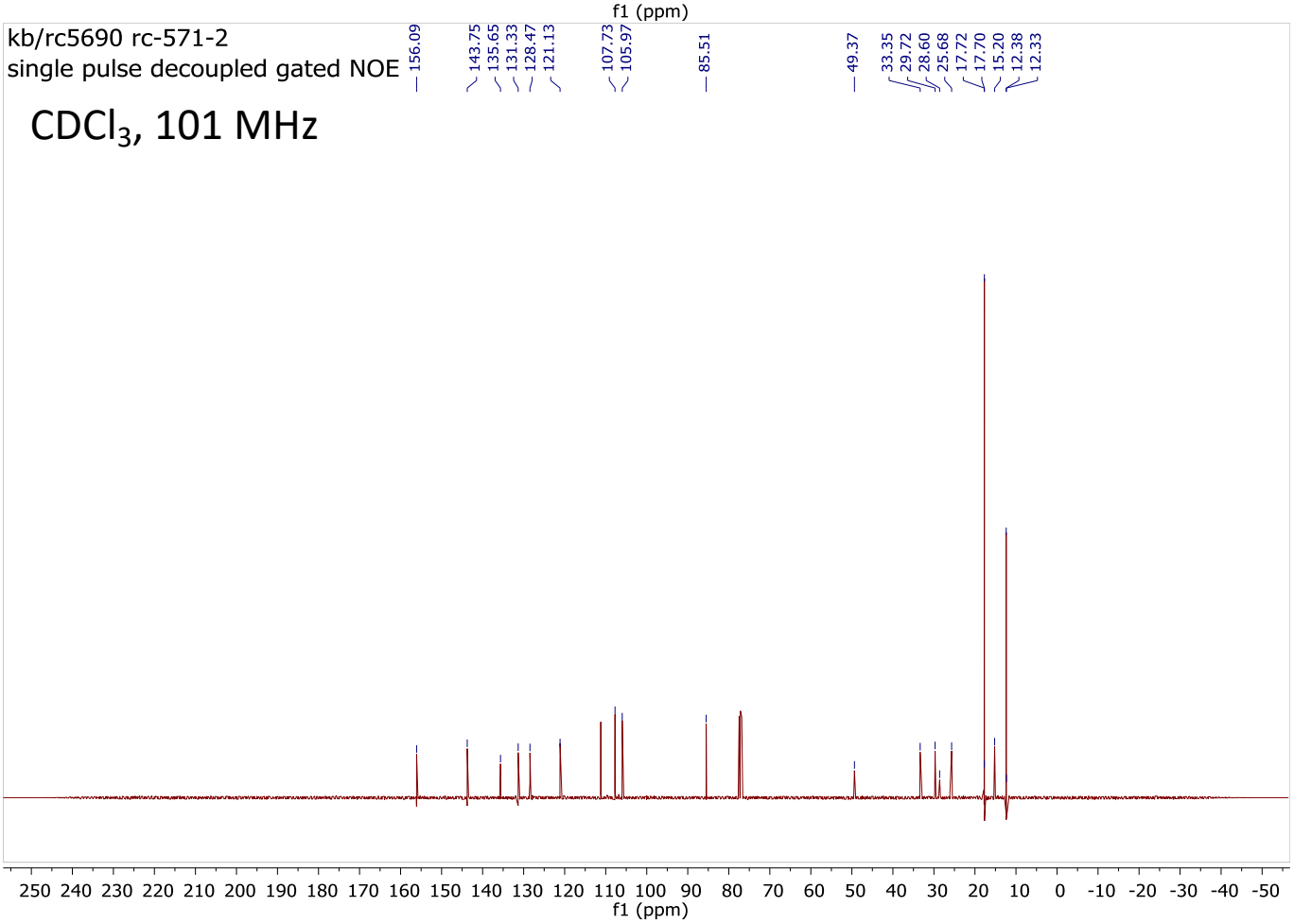
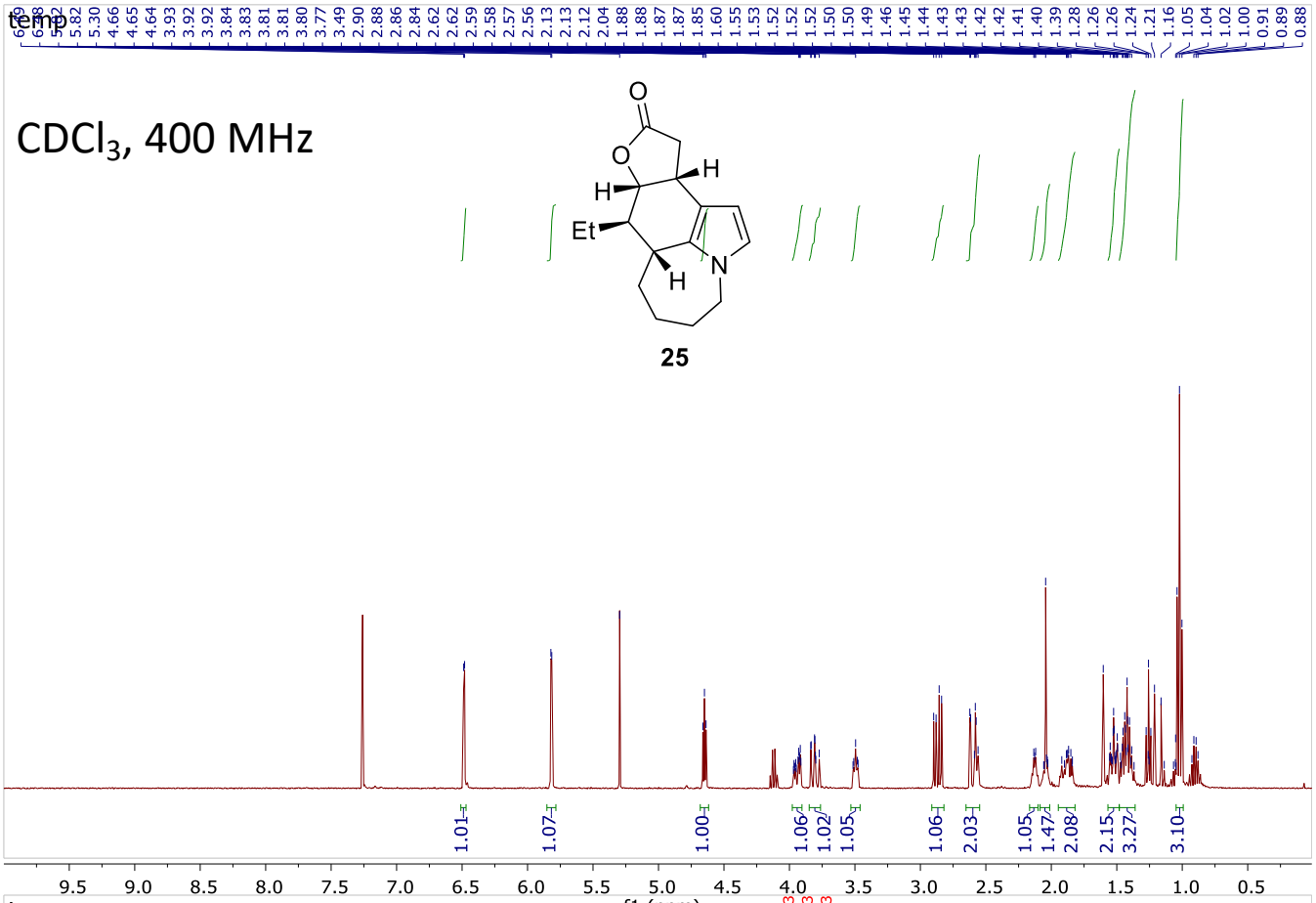
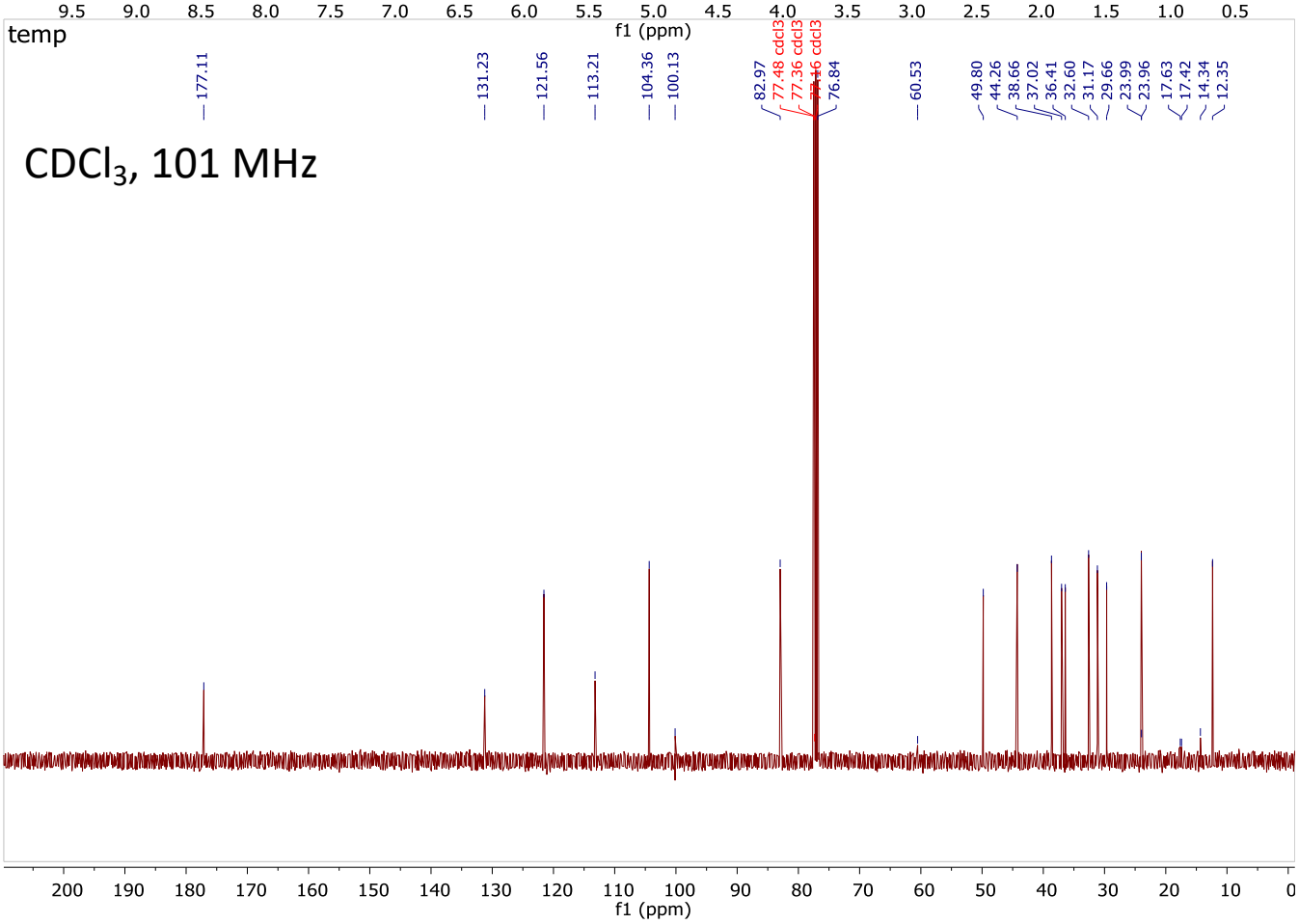
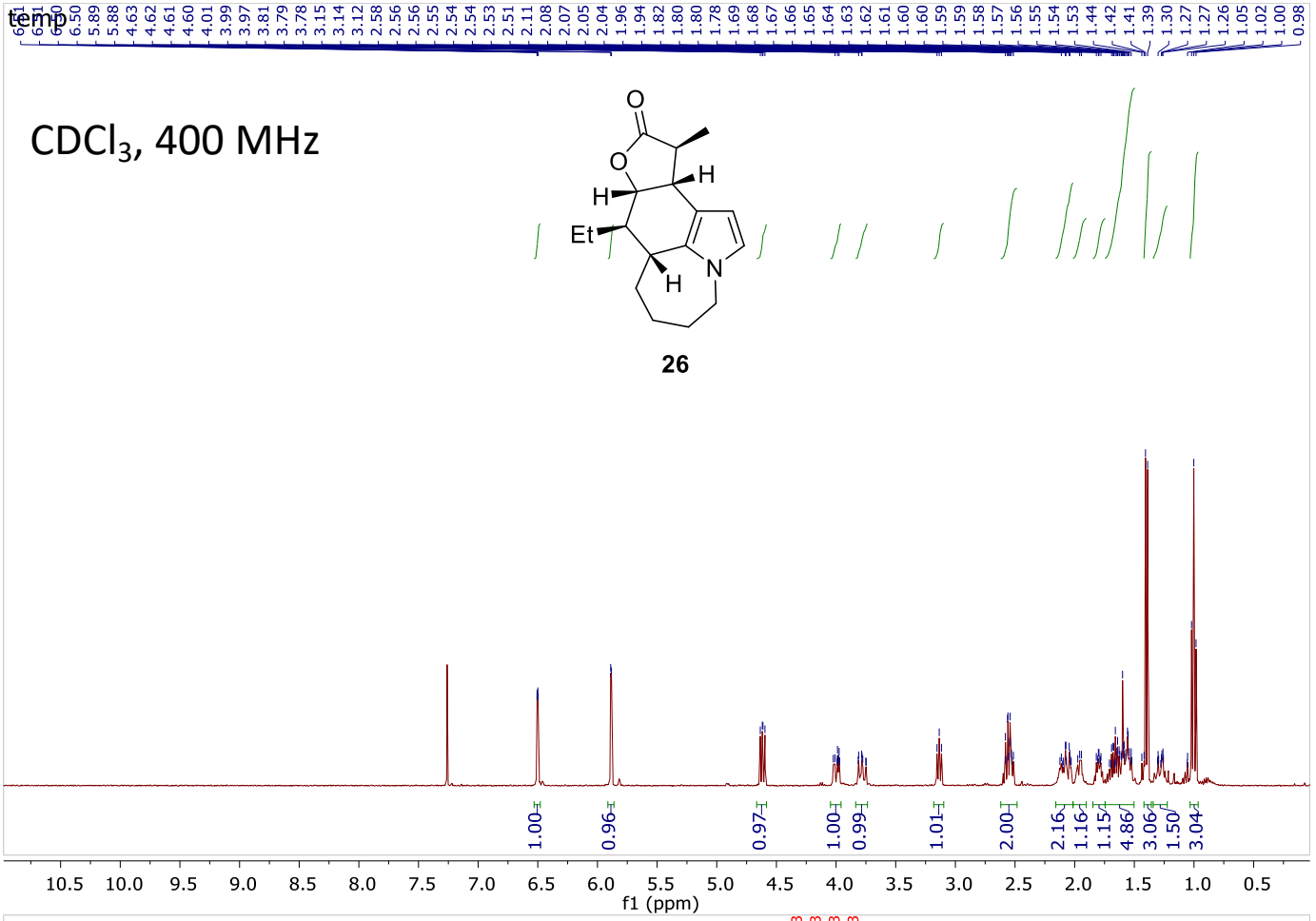
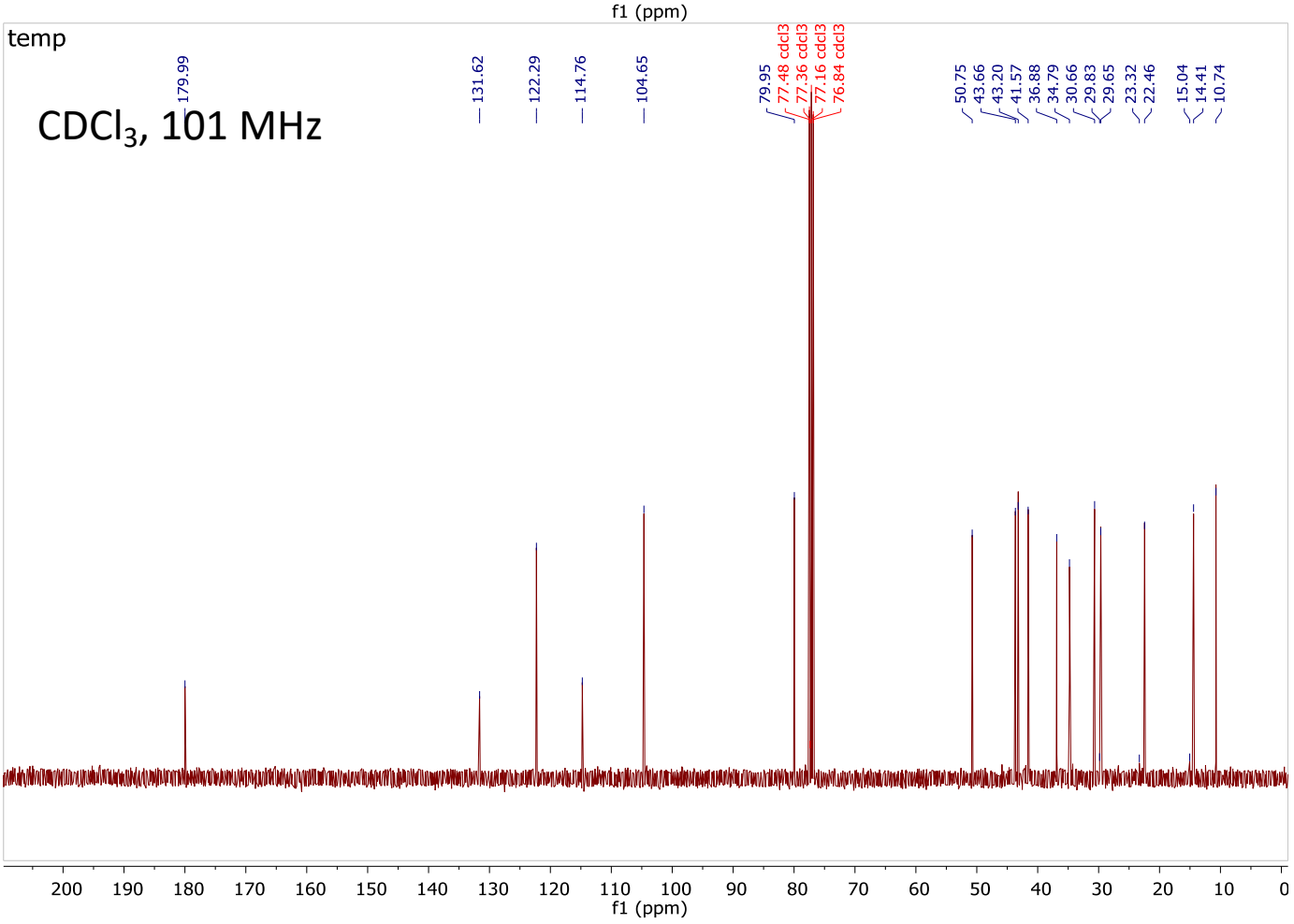
$CDCl_3$, 101 MHz

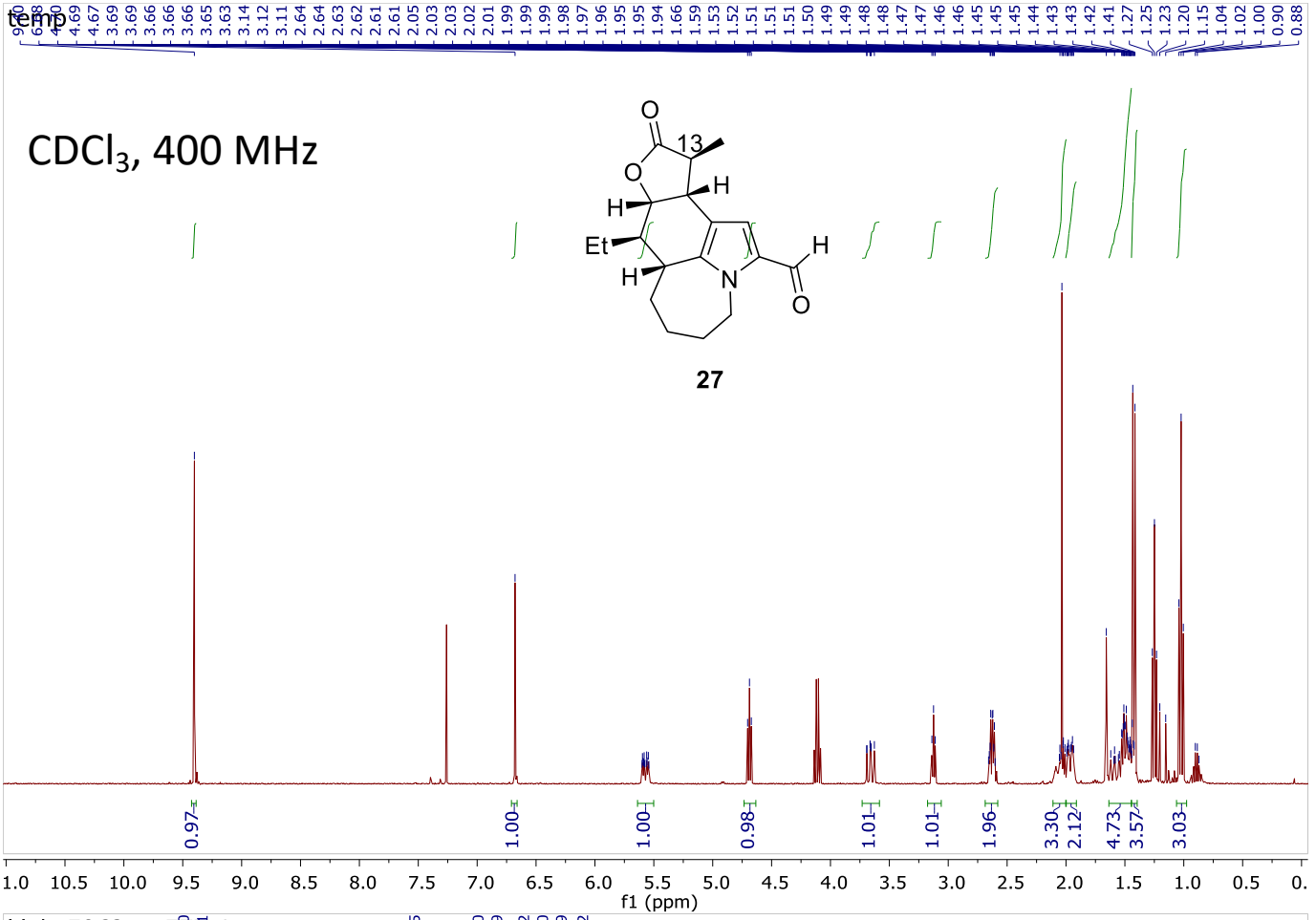


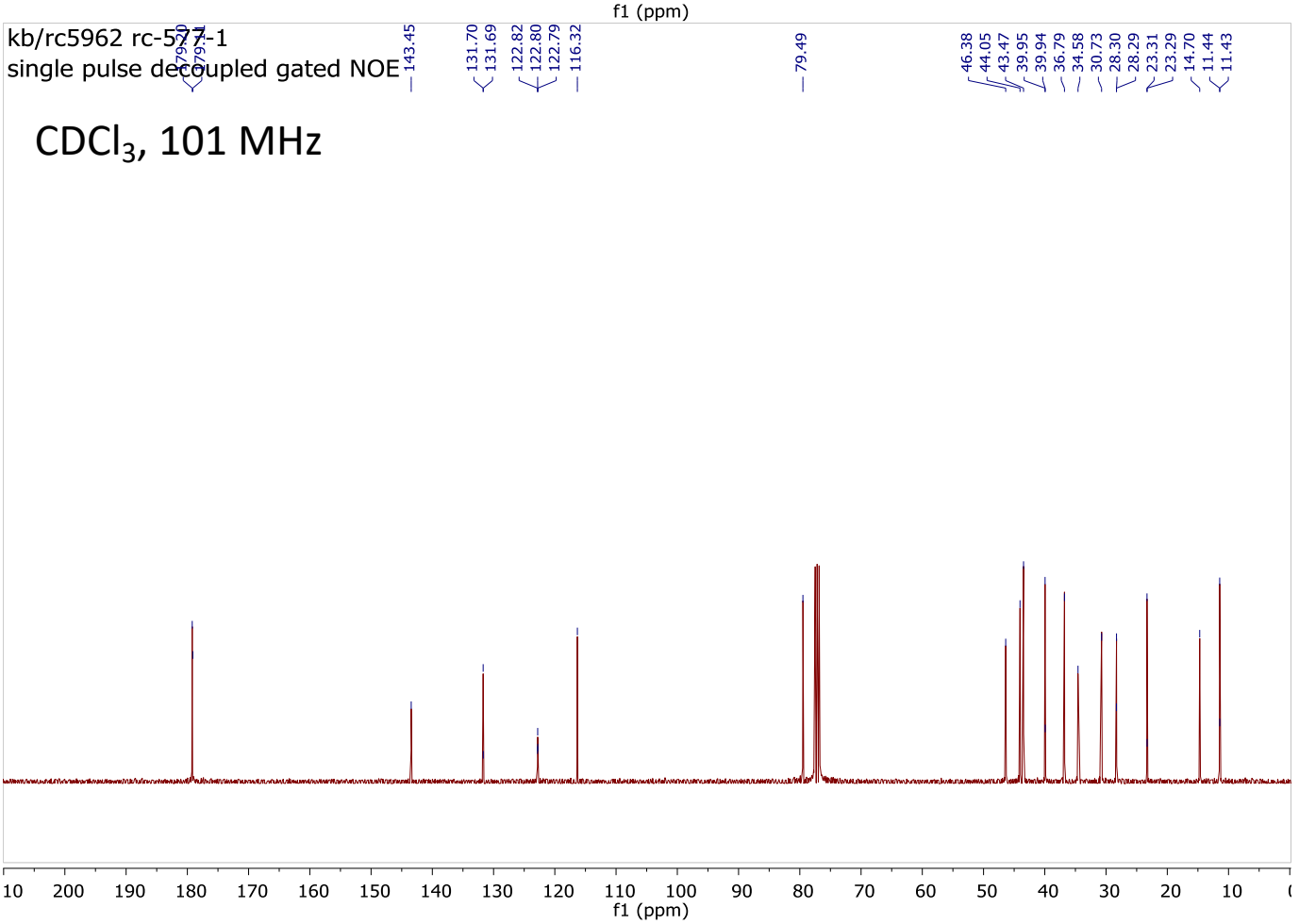

temp
CDCl3, 400 MHz
O
O
H
H
Et
H
N
25
1.01
1.07
1.00
1.06
1.02
1.05
1.06
2.03
1.05
1.47
2.08
2.15
3.27
3.10
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


temp
CDCl3, 101 MHz
177.11
131.23
121.56
113.21
104.36
100.13
82.97
77.48 cdcl3
77.36 cdcl3
77.16 cdcl3
76.84
60.53
49.80
44.26
38.66
37.02
36.41
32.60
31.17
29.66
23.99
23.96
17.63
17.42
14.34
12.35
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


temp
CDCl3, 400 MHz
O
O
H
H
Et
H
N
26
1.00
0.96
0.97
1.00
0.99
1.01
2.00
2.16
1.16
1.15
4.86
3.06
1.50
3.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


temp
CDCl3, 101 MHz
179.99
131.62
122.29
114.76
104.65
79.95
77.48 cdcl3
77.36 cdcl3
77.16 cdcl3
76.84 cdcl3
50.75
43.66
43.20
41.57
36.88
34.79
30.66
29.83
29.65
23.32
22.46
15.04
14.41
10.74
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


temp
CDCl3, 400 MHz
O
13
O
H
H
Et
H
H
N
H
O
27
0.97
1.00
1.00
0.98
1.01
1.01
1.96
3.30
2.12
4.73
3.57
3.03
f1 (ppm)


kb/rc5962 rc-577-1
single pulse decoupled gated NOE
143.45
131.70
131.69
122.82
122.80
122.79
116.32
79.49
46.38
44.05
43.47
39.95
39.94
36.79
34.58
30.73
28.30
28.29
23.31
23.29
14.70
11.44
11.43
CDCl3, 101 MHz
f1 (ppm)