Supporting Information

Highly Selective Domino Multi-Cyclizations for Forming Polycyclic Fused Acridines and Azaheterocyclic Skeletons

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Experimental

General information

Microwave irradiation was carried out with Initiator 2.5 Microwave Synthesizers from Biotage, Uppsala, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm^{-1}. ^1H NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in DMSO-d_6 (or $DCCl_3$ or CD_3COOD) with chemical shift (δ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QⅡ HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

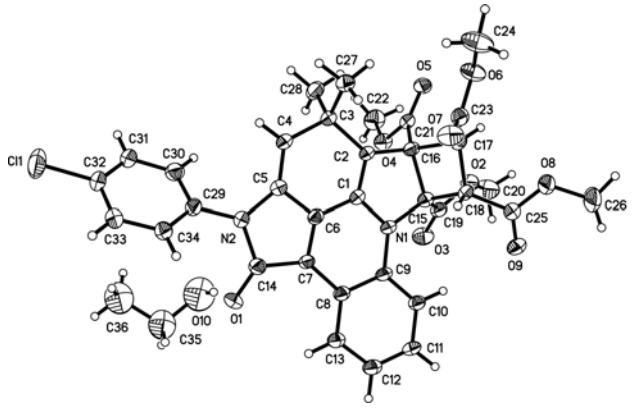


Fig 1, X-ray Structure of Hexacyclic Fused Acridines **4a**

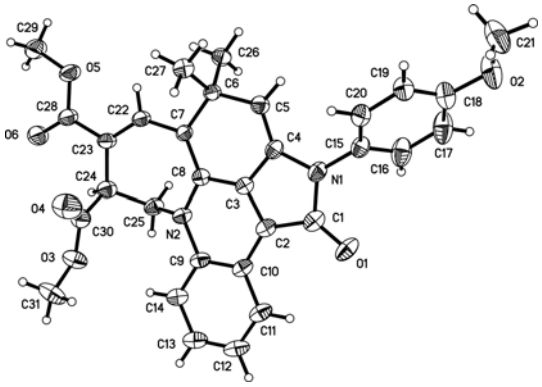


Fig 2, X-ray Structure of Product **5i**

Crystal data for **4a**: $C_{35}H_{32}ClN_2O_{9.50}$, *Mr* = 668.08, Triclinic, *a* = 10.1026(11) Å, *b* = 12.2338(13) Å, *c* = 13.8484(14) Å, *U* = 1635.5(3) $Å^3$, *T* = 298(2) K, space group P-1, *Z* = 2, 10324 reflections measured, 5773 unique (R_{int} = 0.1081) which were used in all calculation. The final *wR(F_2) was* 0.4274 (all data)

Crystal data for **5i**: $C_{31}H_{28}N_2O_6$, *Mr* = 524.55, Monoclinic, *a* = 16.7024(15) Å, *b* = 8.0751(7) Å, *c* = 19.7821(17) Å, *U* = 2664.9(4) $Å^3$, *T* = 298(2) K, space group P2(1)/c, *Z* = 4, 13014 reflections measured, 4692 unique (R_{int} = 0.0811) which were used in all calculation. The final *wR(F_2)* was 0.1191 (all data)

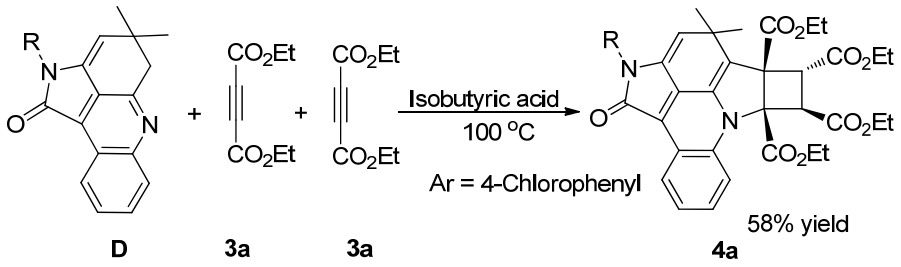
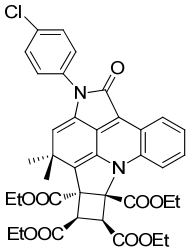


Fig 3 the supporting reaction for the proposed mechanism

General procedure for the synthesis of hexacyclic fused acridines 4a

Example for the synthesis of 4a: **Tetraethyl 6-(4-chlorophenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a -hexahydro-5H-cyclobuta [4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate**

Microwave Heating: Indoline-2,3-dione (**1a**, 1.0 mmol, 0.15 g, 1.0 equiv.) was introduced in a 10-mL Initiator^{TM} reaction vial, 3-((4-chlorophenyl)amino)-5,5-dimethylcyclohex-2-enone (**2a**, 1.0 mmol, 0.25 g, 1.0 equiv.) and isobutyric acid (1.5 mL) were then successively added, followed by diethyl but-2-ynedioate (**3a**, 2.2 mmol, 0.38g, 2.2 equiv.). Subsequently, the reaction vial was capped and then pre-stirring for 20 second. The mixture was irradiated (Time: 20 min, Temperature: 100 ^{o}C; Absorption Level: High; Fixed Hold Time) until TLC (petroleum ether: acetone 3:1) revealed that conversion of the starting material **1a** was completed. The reaction mixture was then cooled to room temperature and then diluted with cold water (40 ml). The resulting suspension was neutralized with 10% NaOH solution and then extracted by acetic ester. Next, the organic phase was concentrated by vacuum distillation and was purified by flash column chromatography (silica gel, mixtures of *n*-hexane / acetic ester, 6:1, v/v) to afford the desired pure products **4a** as pale red solid (Mp: 201.1-202.8 ^{o}C).



IR (KBr, v, cm^{-1}): 3445, 3205, 1750, 1706, 1699, 1453, 1275, 1208, 812;

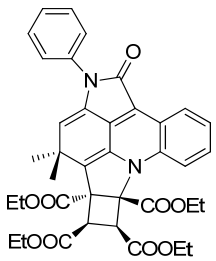
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.87(d, *J* = 7.6 Hz, 1H, ArH), 7.53 (s, 4H, ArH), 7.18 (s, 2H, ArH), 6.93 (s, 1H, ArH), 5.63 (s, 1H, CH), 4.39–4.29 (m, 2H, CH), 4.29–4.15 (m, 8H, CH_2), 1.38–1.30 (m, 15H, CH_3), 1.21 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.2, 170.1, 169.5, 166.7, 141.6, 139.1, 134.0, 132.3, 131.4, 129.4, 129.1, 126.7, 125.3, 122.6, 121.0, 119.5, 116.8, 114.9, 105.2, 77.9, 68.6, 62.2, 62.1, 61.6, 61.3, 49.5, 46.0, 43.1, 29.7, 28.5, 14.1, 14.0, 14.0, 13.9.

HRMS (ESI) *m/z*: calcd for $C_{38}H_{36}ClN_2O_9$: 699.2109 $[M-H]^-$; found: 699.2109

Tetraethyl 8,8-dimethyl-5-oxo-6-phenyl-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo [3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4b)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 203.1-204.7 ^{o}C).



IR (KBr, v, cm^{-1}): 3439, 2980, 1759, 1733, 1699, 1598, 1449, 1251, 1230, 821;

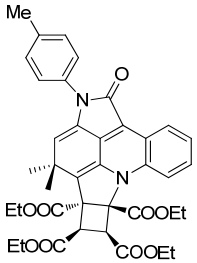
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) :7.87 (d, *J* = 8.0 Hz, 1H, ArH), 7.53 (d, *J* = 4.0 Hz, 4H, ArH), 7.39 (s, 1H, ArH), 7.18 (s, 2H, ArH), 6.93 (s, 1H, ArH), 5.62 (s, 1H, CH), 4.40–4.33 (m, 2H, CH), 4.33–4.12 (m, 8H, CH_2), 1.38–1.30 (m, 15H, CH_3), 1.20 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.3, 170.0, 169.6, 166.8, 166.7, 141.7, 139.1, 135.4, 132.6, 131.7, 129.3, 128.9, 126.8, 125.5, 125.3, 122.6, 121.0, 119.6, 116.9, 114.9, 105.0, 78.0, 68.7, 62.2, 62.1, 61.6, 61.3, 49.5, 46.0, 43.0, 29.7, 28.5, 14.1, 14.0, 14.0, 13.9.

HRMS (ESI) *m/z*: calcd for $C_{38}H_{37}N_2O_9$: 665.2499 $[M-H]^-$; found: 665.2492

Tetraethyl 8,8-dimethyl-5-oxo-6-(p-tolyl)-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo [3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4c)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 203-204 ^oC).



IR (KBr, v, cm^{-1}): 3444, 2980, 1760, 1737, 1700, 1598, 1291, 821;

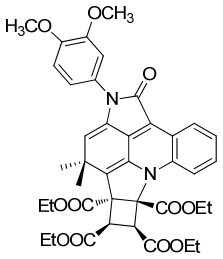
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.86 (d, *J* = 7.2 Hz, 1H, ArH), 7.38 (d, *J* = 8.8Hz, 2H, ArH), 7.33(d, *J* = 8.4 Hz, 2H, ArH), 7.18 (s, 2H, ArH), 6.92 (s, 1H, ArH), 5.58 (s, 1H, CH), 4.41–4.40 (m, 2H, CH), 4.27–4.25 (m, 8H, CH_2), 2.43 (s, 3H, CH_3), 1.38–1.29 (m, 15H), 1.19 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.3, 170.1, 169.6, 167.1, 166.8, 141.7, 139.1, 136.7, 132.7, 132.5, 131.9, 129.8, 128.9, 125.5, 125.3, 122.6, 121.0, 119.7, 116.9, 114.8, 104.9, 78.0, 68.7, 62.2, 62.1, 61.6, 61.3, 49.5, 46.0, 43.0, 29.6, 28.5, 21.1, 14.1, 14.0, 13.9, 13.9.

HRMS (ESI) *m/z*: calcd for $C_{39}H_{39}N_2O_9$: 679.2656 $[M-H]^-$; found: 679.2624.

Tetraethyl 6-(3,4-dimethoxyphenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4d)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 186.7-187.4 ^oC).



IR (KBr, v, cm^{-1}): 3585, 2982, 1758, 1734, 1700,1516, 1248, 1203, 1027, 808;

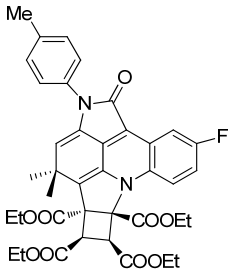
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.86 (d, *J* = 7.6 Hz, 1H, ArH), 7.18 (s, 2H, ArH), 7.01–6.95 (m, 2H, ArH), 6.93 (s, 1H, ArH), 6.91 (s, 1H, ArH), 5.59 (s, 1H, CH), 4.41–4.39 (m, 2H, CH), 4.27–4.25 (m, 8H, CH_2), 3.91 (s,*3*H, CH_3O), 3.90 (s,*3*H, CH_3O), 1.38–1.30 (m, 15H, CH_3), 1.20 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.3, 170.1, 169.6, 167.2, 166.7, 149.4, 148.0, 141.7, 139.1, 138.5, 132.5, 132.2, 128.3, 125.6, 125.3, 123.7, 122.5, 121.0, 119.7, 118.1, 116.8, 114.8, 112.3, 111.3, 109.9, 104.9, 78.0, 68.7, 62.1, 61.3, 56.1, 49.5, 46.0, 43.0, 29.7, 28.5, 14.1, 14.0, 13.9.

HRMS (ESI) *m/z*: calcd for $C_{40}H_{41}N_2O_{11}$; 725.2710 $[M-H]^-$; found:725.2709.

Tetraethyl 3-fluoro-6-(4-methoxyphenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate(4e)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 197-199 ^{o}C).



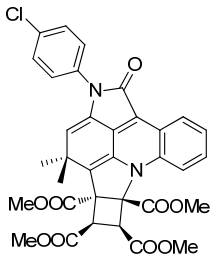
IR (KBr, v, cm^{-1}):3445, 2981, 1759, 1737, 1699, 1518, 1447, 1203, 807;

^{1}H NMR (400 MHz, CD_3COOD) (δ, ppm) : 7.57 (dd, *J* = 8.8, 2.8 Hz, 1H, ArH), 7.36 (d, *J* = 11.2 Hz, 4H, ArH), 7.16 (dd, *J* = 9.2, 4.6 Hz, 1H, ArH), 7.00–6.82 (m, 1H, ArH), 5.63 (s, 1H, CH), 4.41 (s, 2H, CH), 4.28–4.22 (m, 8H, CH_2), 2.43 (s, 3H, CH_3), 1.38–1.29 (m, 16H, CH_3), 1.19 (s, 3H, CH_3);

HRMS (ESI) *m/z*: calc. for $C_{39}H_{39}FN_2O_9$:697.2561[M-H]$^{-}$; found:697.2567.

Tetraethyl 6-(4-chlorophenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4f)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 231.2-232.5 ^{o}C).



IR (KBr, v, cm^{-1}): 3445, 2948, 1763, 1738, 1703, 1600, 1294, 834;

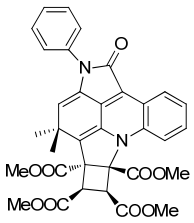
^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm) 7.69 (d, *J* = 7.6 Hz, 1H, ArH), 7.59 (d, *J* = 8.4 Hz, 2H, ArH), 7.48 (d, *J* = 8.4 Hz, 2H, ArH), 7.13 (t, *J* = 7.6 Hz, 1H, ArH), 6.94 (d, *J* = 7.6 Hz, 1H, ArH), 6.88 (t, *J* = 7.6 Hz, 1H, ArH), 5.75 (s, 1H, CH), 4.24 (d, *J* = 4.0 Hz, 2H, CH), 3.73 (s, 3H, CH_3), 3.70 (s, 3H, CH_3), 3.68 (s, 6H, CH_3), 1.13 (s, 3H, CH_3), 1.04 (s, 3H, CH_3) ;

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.5, 170.3, 169.9, 167.6, 166.6, 141.7, 138.9, 133.9, 132.5, 132.4, 131.4, 129.4, 126.7, 125.4, 122.5, 121.2, 119.4, 116.9, 114.5, 104.8, 68.8, 52.9, 52.7, 52.6, 52.4, 49.1, 45.9, 43.1, 29.3, 28.6.

HRMS (ESI) *m/z*: calcd for $C_{34}H_{28}ClN_2O_9$: 643.1483 [M-H]$^{-}$; found: 643.1448.

Tetramethyl 8,8-dimethyl-5-oxo-6-phenyl-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5] pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4g)

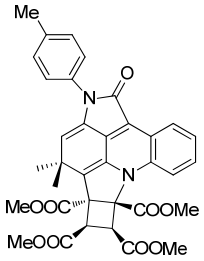
The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 256.8-258.1 ^{o}C).



IR (KBr, v, cm^{-1}): 3481, 2955, 1767, 1736, 1699, 1598, 1453, 1270, 807;
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.82 (d, *J* = 7.6 Hz, 1H, ArH), 7.60 (s, 4H, ArH), 7.39 (dd, *J* = 6.8, 4.4 Hz, 1H, ArH), 7.09 (t, *J* = 8.0 Hz, 1H, ArH), 6.89 (t, *J* = 7.6 Hz, 1H, ArH), 6.28 (d, *J* = 8.4 Hz, 1H, ArH), 5.72 (s, 1H, CH), 4.97 (d, *J* = 9.6 Hz, 1H, CH), 4.17 (d, *J* = 9.6 Hz, 1H, CH), 3.86 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.50 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.31 (s, 3H, CH_3);
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 171.4, 167.4, 166.4, 143.0, 139.1, 136.2, 134.6, 133.0, 131.2, 129.5, 129.4, 127.3, 126.3, 124.5, 123.0, 121.4, 120.8, 119.9, 117.5, 113.8, 113.8, 52.8, 52.43, 52.1, 49.7, 43.6, 31.6, 31.2.
HRMS (ESI) *m/z*: calcd for $C_{34}H_{29}N_2O_9$: 609.1077 $[M-H]^-$; found: 609.1077.

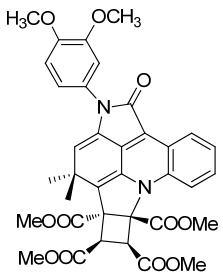
Tetramethyl 8,8-dimethyl-5-oxo-6-(p-tolyl)-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5] pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4h)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 238.9-240 ^oC).



IR(KBr,v,cm^{-1}):3456, 2952, 1764, 1738, 1699, 1439, 1205, 807;
^{1}H NMR (400 MHz, CD_3COOD) (δ, ppm) : 7.69 (d, *J* = 7.2 Hz, 1H,ArH), 7.32 (s, 4H,ArH), 7.16 (t, *J* = 7.2 Hz, 1H, ArH), 6.96 (s, 2H, ArH), 5.64 (s, 1H, CH), 4.23 (s, 2H, CH), 3.73 (s, 3H, CH_3), 3.70 (s, 3H, CH_3), 3.68 (s, 6H, CH_3), 2.36 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.03 (s, 3H, CH_3);
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.6, 170.3, 170.0, 167.6, 166.9, 141.8, 138.9, 136.8, 129.9, 129.2, 125.5, 125.4, 122. 4, 121.1, 119.6, 117.0, 114.4, 104.6, 78.1, 68.9, 52.9, 52.7, 52.5, 52.3, 49.1, 45.8, 43. 0, 29.3, 28.6, 21.1.
HRMS (ESI) *m/z*: calcd for $C_{35}H_{31}N_2O_9$:623.203 $[M-H]^-$; found:623.2005.

Tetramethyl 6-(3,4-dimethoxyphenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4i)



The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 234.8-235.2 ^{o}C).

IR (KBr, v, cm^{-1}): 3454, 2960, 1769, 1737, 1700, 1598, 1517, 1243, 815;

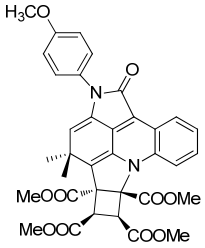
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.86 (d, *J* = 7.2 Hz, 1H, ArH), 7.19 (t, *J* = 7.6 Hz, 1H, ArH), 7.13–7.09 (m, 2H, ArH), 7.05 (d, *J* = 8.4 Hz, 1H, ArH), 7.01 (d, *J* = 8.4 Hz, 1H, ArH), 6.93 (s, 1H, ArH), 5.58 (s, 1H, CH), 4.46 (s, 1H, CH), 4.42 (s, 1H, CH), 3.91 (s, 3H, CH_3O), 3.90 (s, 3H, CH_3O), 3.85 (s, 3H, CH_3O), 3.81 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.16 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.6, 170.3, 169.9, 167.6, 167.1, 149.4, 148.1, 141.8, 139.0, 132.2, 132.2, 129.2, 128.3, 125.4, 122.3, 121.1, 119.6, 118.0, 117.0, 114.4, 111.3, 109.9, 104.5, 78.2, 68.9, 56.1, 52.3, 49.1, 45.9, 43.0, 28.6.

HRMS (ESI) *m/z*: calcd for $C_{36}H_{33}N_2O_{11}$: 669.2084 [M-H]$^{-}$; found: 669.2062.

Tetramethyl 6-(4-methoxyphenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta [4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4j)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 234.6-236 ^{o}C).



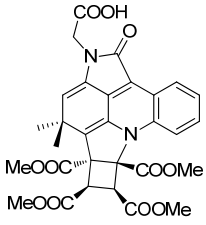
IR (KBr, v, cm^{-1}): 3753, 2951, 1764, 1738, 1698, 1516, 1252, 807;

^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.68 (d, *J* = 8 Hz, 1H, ArH), 7.33 (d, *J* = 8.8 Hz, 2H, ArH), 7.17 (t, *J* = 8.0 Hz, 1H, ArH), 7.07 (d, *J* = 8.8Hz, 2H, ArH), 6.94 (d, *J* = 8.0Hz, 1H, ArH), 6.89 (t, *J* = 7.2 Hz, 1H, ArH), 5.59 (s, 1H, CH), 4.23 (s, 2H, CH), 3.80 (s, 3H,CH_3O), 3.80 (s, 3H, CH_3), 3.73 (s, 3H, CH_3), 3.71 (s, 3H, CH_3), 3.68 (s, 6H, CH_3), 1.09 (s, 3H, CH_3), 1.03 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.6, 170.3, 170.0, 167.7, 167.1, 158.41, 141.8, 139.0, 132.2, 132.2, 129.2, 128.0, 127.1, 125.4, 122.1, 121.1, 119.7, 117.0, 114.6, 114.4, 104.5, 78.2, 68.9, 55.5, 52.9, 52.7, 52.5, 52.3, 49.1, 45.9, 43.0, 29.3, 28.6.

HRMS (ESI) *m/z*: calcd for $C_{35}H_{31}N_2O_{10}$: 639.1979 [M-H]$^{-}$; found: 639.1978.

Tetramethyl 2-(8b,9,10,10a-tetrakis(methoxycarbonyl)-8,8-dimethyl-5-oxo-8b,9,10,10a- tetrahydro -5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridin-6(8H)-yl)acetic acid (4k)

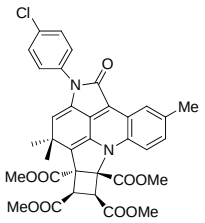


The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 221.-221.8 ^{o}C).

IR (KBr, v, cm^{-1}): 3447, 2956, 1756, 1738, 1681, 1599, 1260, 807;
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.79 (d, *J* = 7.6 Hz, 1H, ArH), 7.17 (s, 1H, ArH), 7.09 (d, *J* = 7.6 Hz, 1H, ArH), 6.91 (s, 1H, ArH), 5.56 (s, 1H, CH), 4.58 (d, *J* = 4.0 Hz, 2H, CH), 4.46 (d, *J* = 10.0 Hz, 1H, CH_2), 4.40 (d, *J* = 10.0 Hz, 1H, CH_2), 3.83 (s, 3H, CH_3), 3.81 (s, 3H CH_3,), 3.79 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.16 (s, 3H, CH_3);
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 170.6, 170.2, 170.0, 167.6, 166.4, 138.8, 131.2, 129.3, 125.4, 121.4, 121.1, 119.42, 117.1, 114.5, 104.55, 78.1, 69.0, 52.9, 52.7, 52.5, 52.3, 49.1, 45.8, 43.0, 41.1, 29.1, 28.6.
HRMS (ESI) *m/z*: calcd for $C_{30}H_{27}N_2O_{11}$: 591.1615 $[M-H]^-$; found: 591.1622.

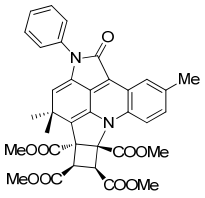
Tetramethyl 6-(4-chlorophenyl)-3,8,8-trimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta [4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4l)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 90 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 211.3-213.4 ^oC).



IR (KBr, v, cm^{-1}): 3448, 2954, 1737, 1707, 1699, 1494, 1278, 799;
^{1}H NMR (400 MHz , CD_3COOD) (δ,ppm) : 7.65 (d, *J* = 1.2 Hz, 1H, ArH), 7.54 (d, *J* = 1.6 Hz, 4H, ArH), 6.92 (d, *J* = 7.2 Hz, 1H, ArH), 6.20 (d, *J* = 8.4 Hz, 1H, ArH), 5.72 (s, 1H, CH), 4.95 (d, *J* = 9.6 Hz, 1H, CH), 4.14 (d, *J* = 9.6 Hz, 1H, CH), 3.85 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.51 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.31 (s, 3H, CH_3);
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 169.8, 169.2, 168.2, 167.4, 166.7, 140.5, 137.3, 134.1, 133.0, 132.2, 131.4, 130.3, 129.4, 129.3, 126.6, 126.1, 122.8, 119.2, 116.0, 111.6, 109.9, 70.0, 53.4, 46.1, 43.2, 29.6, 28.9, 20.5.
HRMS (ESI) *m/z*: calcd for $C_{35}H_{30}ClN_2O_9$:657.1640 $[M-H]^-$; found:657.1626.

Tetramethyl 3,8,8-trimethyl-5-oxo-6-phenyl-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5] pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4m)



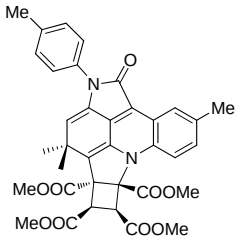
The title compound was prepared following the general procedure (Microwave Heating, Temperature: 90 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 233.2-233.9 ^oC).
IR (KBr, v, cm^{-1}): 3460, 2953, 1769, 1738, 1700, 1573, 1269, 1206, 1037, 808;
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.71 (s, 1H, ArH), 7.53 (d, *J* = 6.0 Hz, 4H, ArH), 7.40 (dd, *J* = 7.2, 4.8 Hz, 1H, ArH), 7.02 (s, 2H, ArH), 5.60 (s, 1H, CH), 4.46 (d, *J* = 9.6 Hz, 1H, CH), 4.39 (d, *J* = 6.8 Hz, 1H, CH), 3.85 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.16 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 170.7, 170.3, 170.0, 167.8, 166.9, 141.9, 136.7, 135.4, 132.4, 131.7, 130.5, 129.9, 129.2, 126.8, 125.8, 125.5, 122.5, 119.4, 117.0, 114.2, 104.2, 78.1, 69.0, 52.9, 52.6, 52.5, 52.3, 49.2, 45.8, 43.0, 29.3, 28.7, 20.5.

HRMS (ESI) *m/z*: calcd for $C_{36}H_{34}N_2O_9$: 623.2030 $[M-H]^-$; found: 623.2049.

Tetramethyl 3,8,8-trimethyl-5-oxo-6-(p-tolyl)-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5] pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4n)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 90 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 203.1-204.7 ^oC).



IR (KBr, v, cm^{-1}): 3564, 3127, 1744, 1704, 1699, 1400, 1233, 805;

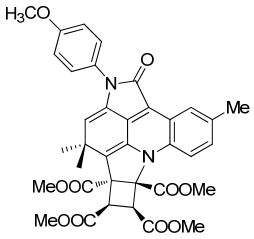
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.65 (s, 1H, ArH), 7.39 (d, *J* = 8.9, 2H, ArH), 7.34 (d, *J* = 8.4, 2H, ArH), 6.91 (d, *J* = 8.4 Hz, 1H, ArH), 6.19 (d, *J* = 8.0 Hz, 1H, ArH), 5.67 (s, 1H, CH), 4.95 (d, *J* = 9.6 Hz, 1H, CH), 4.15 (d, *J* = 9.6 Hz, 1H, CH), 3.85 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.51 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 1.29 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 169.9,169.2, 168.3, 167.4, 167.0, 140.6, 137.3, 136.6, 132.8, 132.8, 131.8, 130.2, 129.9, 129.0, 126.1, 125.4, 122.5, 119.4, 116.1, 111.6, 109.6, 77.1, 70.0, 53.4, 52.7, 52.4, 52.3, 48.1, 46.1, 43.1, 29.6, 28.8, 21.1, 20.5.

HRMS (ESI) *m/z*: calcd for $C_{36}H_{33}N_2O_9$: 639.2186 $[M-H]^-$; found: 639.2186.

Tetramethyl 6-(4-methoxyphenyl)-3,8,8-trimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4o)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 90 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 189.1-189.7 ^oC).



IR (KBr, v, cm^{-1}): 3445, 3114, 2926, 1772, 1748, 1689, 1294, 1211, 809;

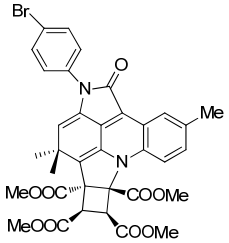
^{1}H NMR (400 MHz, Acetic) (δ ppm): 7.64 (s, 1H,ArH), 7.42 (d, *J* = 8.8 Hz, 2H, ArH), 7.08 (d, *J* = 8.8 Hz, 2H, ArH), 6.91 (d, *J* = 7.6 Hz, 1H, ArH), 6.19 (d, *J* = 8.4 Hz, 1H, ArH), 5.63 (s, 1H, CH), 4.95 (d, *J* = 9.6 Hz, 1H, CH), 4.15 (d, *J* = 9.6 Hz, 1H, CH), 3.89 (s, 3H, OCH_3), 3.85 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.51 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 1.29 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 169.9, 169.2, 168.3, 167.4, 167.2, 158.3, 140.6, 137.3, 132.7, 132.1, 130.2, 129.1, 128.1, 127.0, 126.1, 122.4, 119.5, 116.1, 114.6, 111.6, 109.6, 77.1, 70.0, 55.5, 52.7, 52.4, 52.3, 48.1, 46.1, 43.1, 29.6, 28.8, 20.5.

HRMS (ESI) m/z: calcd for $C_{36}H_{32}N_2O_{10}$:653.2135 $[M-H]^-$; found: 653.2122.

Tetramethyl 6-(4-bromophenyl)-3,8,8-trimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H- cyclobuta [4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4p)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 90 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 215.1-216.4 ^{o}C).



IR (KBr, v, cm^{-1}): 3445, 2954, 1750, 1737, 1707, 1492, 1277, 830;

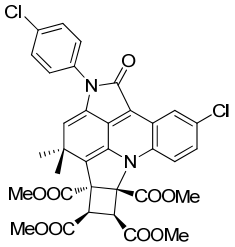
^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.69 (d, *J* = 8.8 Hz, 2H, ArH), 7.64 (d, *J* = 1.6 Hz, 1H, ArH), 7.48 (s, 1H, ArH), 7.46 (s, 1H, ArH), 6.92 (d, *J* = 5.6 Hz, 1H, ArH), 6.20 (d, *J* = 8.4 Hz, 1H, ArH), 5.73 (s, 1H, CH), 4.95 (d, *J* = 9.6 Hz, 1H, CH), 4.14 (d, *J* = 9.6 Hz, 1H, CH), 3.85 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.51 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.31 (s, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 169.8, 169.2, 168.2, 167.4, 166.7, 140.4, 137.3, 134.6, 133.0, 132.4, 131.3, 130.2, 129.3, 126.9, 126.1, 122.9, 120.1, 119.2, 116.0, 111.6, 109.9, 70.0, 53.4, 52.7, 52.4, 52.3, 48.1, 46.1, 43.2, 29.6, 28.9, 20.4.

HRMS (ESI) *m/z*: calcd for $C_{35}H_{30}BrN_2O_9$: 701.1135 [M-H]$^{-}$; found: 701.1118.

Tetramethyl 3-chloro-6-(4-chlorophenyl)-8,8-dimethyl-5-oxo-6,8,8b,9,10,10a-hexahydro-5H-cyclobuta[4,5]pyrrolo[3,2,1-de]pyrrolo[4,3,2-mn]acridine-8b,9,10,10a-tetracarboxylate (4q)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 100 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 6:1, v/v) (Mp: 186.3-186.7 ^{o}C).



IR (KBr, v, cm^{-1}): 3448, 2954, 1737, 1706, 1700, 1279, 800;

^{1}H NMR (400 MHz, CD_3COOD) (δ,ppm) : 7.73 (d, *J* = 2.4 Hz, 1H, ArH), 7.53 (d, *J* = 2.8 Hz, 4H, ArH), 7.09 (dd, *J* = 8.8, 2.3 Hz, 1H, ArH), 6.25 (d, *J* = 8.8 Hz, 1H, ArH), 5.78 (s, 1H, CH), 4.96 (d, *J* = 9.6 Hz, 1H, CH), 4.14 (d, *J* = 9.6 Hz, 1H, CH), 3.87 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 3.53 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.31 (s, 3H, CH_3);

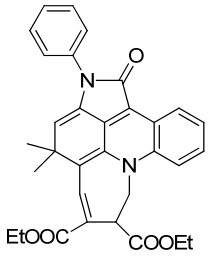
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 169.6, 169.0, 167.9, 167.0, 166.1, 139.9, 138.2, 133.8, 132.5, 131.2, 129.5, 128.2, 126.6, 125.3, 123.5, 120.8, 115.1, 112.7, 111.5, 76.9, 69.8, 53.6, 52.8, 52.5, 52.4, 48.0, 46.0, 43.4, 29.4, 28.7.

HRMS (ESI) *m/z*: calcd for $C_{34}H_{27}Cl_2N_2O_9$: 677.1094 [M-H]$^{-}$; found: 677.1093.

General procedure for the synthesis of pentacyclic fused acridines 5a

Example for the synthesis of 5a: **Diethyl 4,4-dimethyl-1-oxo-2-phenyl-2,4,7,8-tetrahydro-1H-azepino [3,2,1-de]pyrrolo [4,3,2-mn]acridine-6,7-dicarboxylate**

Microwave Heating: Indoline-2,3-dione (**1a**, 1.0 mmol, 0.15 g, 1.0 equiv.) was introduced in a 10-mL Initiator^{TM} reaction vial, 5,5-dimethyl-3-(phenylamino)cyclohex-2-enone (**2b**, 1.0 mmol, 0.22 g, 1.0 equiv.) and isobutyric acid (1.5 mL) were then successively added, followed by ethyl propiolate (**3c**, 2.2 mmol, 0.22g, 2.2 equiv.). Subsequently, the reaction vial was capped and then pre-stirring for 20 second. The mixture was irradiated (Time: 20 min, Temperature: 140 ^{o}C; Absorption Level: High; Fixed Hold Time) until TLC (petroleum ether: acetone 3:1) revealed that conversion of the starting material **1a** was completed. The reaction mixture was then cooled to room temperature and then diluted with cold water (40 ml). The resulting suspension was neutralized with 10% NaOH solution and then extracted by acetic ester. Next, the organic phase was concentrated by vacuum distillation and was purified by flash column chromatography (silica gel, mixtures of *n*-hexane / acetic ester, 8:1, v/v) to afford the desired pure products **5a** as pale red solid (Mp: 201.3-201.9 ^{o}C).



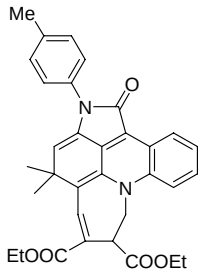
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.71 (d, J = 7.6 Hz ,1H, ArH), 8.36 (s, 1H, ArH), 8.02–7.97 (m, 4H, ArH), 7.85 (s, 3H, ArH), 7.75–7.44 (m, 1H, ArH), 6.34 (s, 1H, CH), 5.38 (s, 1H, CH), 5.19 (s, 1H, CH), 4.79–4.70 (m, 2H, CH_2), 4.62–4.50 (m, 2H, CH_2), 3.99 (s, 1H, CH), 2.01 (s, 3H, CH_3), 1.98 (s, 3H，CH_3), 1.80 (t, J = 7.2 Hz, 3H, CH_3), 1.63 (t, J = 7.2 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 152.9, 149.0, 146.5, 144.3, 142.8, 141.1, 139.3, 139.1, 137.4, 136.4, 134.1, 134.1, 132.9, 132.5, 131.0, 129.5, 127.2, 124.1, 123.9, 71.4, 71.1, 70.6, 67.3, 59.7, 53.4, 40.2, 39.9, 39.6, 26.6, 23.4, 23.2.

HRMS (ESI) *m/z*: calcd for $C_{32}H_{29}N_2O_5$:521.2076 $[M-H]^-$; found: 521.2054.

Diethyl 4,4-dimethyl-1-oxo-2-(p-tolyl)-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de]pyrrolo [4,3,2-mn]acridine-6,7-dicarboxylate (5b)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 189.4-190.1 ^{o}C).



IR (KBr, v, cm^{-1}): 3411, 2978, 2903, 1746, 1687, 1646, 1601, 1513, 1395, 1077, 758;

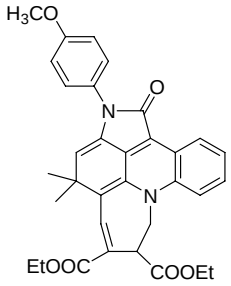
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.27 (d, J = 7.2 Hz, 1H,ArH), 7.92 (s, 1H, ArH), 7.53 – 7.29 (m, 6H, ArH), 7.19 (s, 1H, ArH), 5.86 (s, 1H, CH), 4.94 (s, 1H, CH), 4.74 (s, 1H, CH), 4.32 – 4.28 (m, 2H, CH), 4.16 – 4.08 (m, 2H,CH), 3.55 (s, 1H,CH), 2.45 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 1.36 (t, J = 6.8 Hz, 3H, CH_3), 1.18 (t, J = 6.8 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ, ppm): 170.9, 167.0, 166.5, 143.1, 138.9, 137.2, 136.0, 132.9, 132.0, 131.4, 130.0, 129.3, 126.2, 124.5, 122.9, 121.3, 119.9, 117.4, 114.0, 113.8, 61.3, 60.7, 52.8, 49.8, 43.6, 31.5, 31.2, 21.2, 14.4, 14.1.;

HRMS (ESI) *m/z*: calcd for $C_{33}H_{31}N_2O_5$:535.2233 $[M-H]^-$; found:535.2206.

2-(4-Methoxyphenyl)-4,4-dimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de]pyrrolo[4,3,2-mn]acridine -6,7-dicarboxylate (5c)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 209.8-210.6 ^{o}C).



IR(KBr, v, cm^{-1}): 3419, 2955, 1743, 1695, 1680, 1499, 1253, 1055, 764;

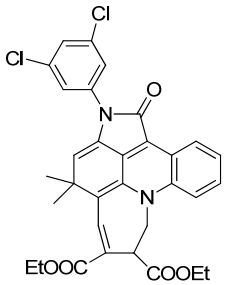
^{1}H NMR (400 MHz, $CDCl_3$) (δ,ppm): 8.26 (d, *J* = 7.2 Hz, 1H, ArH), 7.81 (s, 1H, ArH), 7.34–7.26 (m, 4H, ArH), 7.10 (s, 1H, ArH), 7.03 (d, *J* = 7.6 Hz, 2H, ArH), 5.61 (s, 1H, CH), 4.78 (s, 1H, CH), 4.64 (s, 1H, CH), 4.34 –4.18 (m, 2H, CH_2), 4.17 –3.98 (m, 2H, CH_2), 3.86 (s, 3H, CH_3), 3.46 (s, 1H, CH), 1.50 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.33 (t, *J* = 6.4 Hz, 3H, CH_3), 1.17 (t, *J* = 6.4 Hz, 3H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm) 170.8, 167.0, 166.6, 158.7, 143.1, 138.9, 136.0, 132.9, 131.7, 129.3, 127.7, 127.2, 124.5, 122.9, 121.3, 121.2, 119.9, 117.4, 114.6, 114.0, 113.8, 61.3, 60.7, 52.8, 49.8, 43.5, 31.5, 31.2, 30.9, 14.4, 14.1.

HRMS (ESI) *m/z*: calcd for $C_{33}H_{31}N_2O_6$: 551.2182 $[M-H]^-$; found:551.2157.

Diethyl 2-(3,5-dichlorophenyl)-4,4-dimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de] pyrrolo[4,3,2-mn]acridine-6,7-dicarboxylate(5d)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 196.7-197.4 ^{o}C).

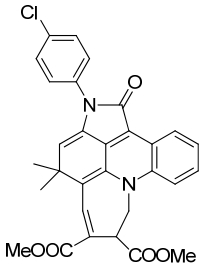


IR(KBr, v, cm^{-1}):3441, 3119, 2947, 1737, 1729, 1679, 1498, 1235, 817;

^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.25 (d, J = 7.4 Hz, 1H, ArH), 7.92 (s, 1H, ArH), 7.57 (d, J = 1.8 Hz, 2H, ArH), 7.51 (t, J = 1.7 Hz, 1H, ArH), 7.41 (s, 2H, ArH), 7.19 (t, J = 7.0 Hz, 1H, ArH), 6.01 (s, 1H, CH), 4.93 (s, 1H, CH), 4.74 (s, 1H, CH), 4.49 – 4.25 (m, 2H, CH_2), 4.13 (qt, J = 18.1, 7.2 Hz, 2H, CH_2), 3.56 (s, 1H, CH), 1.59 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.20 (s, 3H, CH_3).
^{13}C NMR (100 MHz, DMSO) (δ ppm): 165.5, 161.6, 160.6, 137.9, 133.2, 130.4, 130.3, 128.2, 125.1, 124.4, 122.0, 119.3, 119.2, 117.8, 116.9, 116.5, 114.2, 111.7, 109.0, 108.8, 56.1, 55.6, 44.5, 38.5, 26.3, 25.9, 9.2, 8.8.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{27}Cl_2N_2O_5$: 589.1295 $[M-H]^-$; found:589.1267.

Dimethyl 2-(4-chlorophenyl)-4,4-dimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de] pyrrolo[4,3,2-mn]acridine-6,7-dicarboxylate (5e)

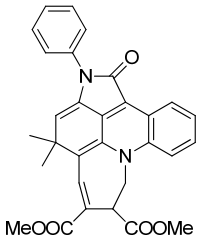
The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 205.1-206.7 ^{o}C).



IR (KBr, v, cm^{-1}): 3420, 2956, 1736, 1722, 1699, 1680, 1433, 1211, 1043, 766;
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.22 (d, J = 7.6 Hz, 1H, ArH), 7.87 (s, 1H, ArH), 7.53 (d, J = 8.8 Hz, 2H, ArH), 7.49 (d, J = 8.8 Hz, 2H, ArH), 7.34 (m, 2H, ArH), 7.15 (t, J = 8.8 Hz, J = 8.8 Hz, 1H, ArH), 5.86 (s, 1H, CH), 4.88 (s, 1H, CH), 4.73 (s, 1H, CH), 3.80 (s, 3H, OCH_3), 3.61 (s, 3H, CH_3), 3.49 (s, 1H, CH), 1.53 (s, 3H, CH_3), 1.50 (s, 3H, CH_3);
^{13}C NMR (100 MHz, CDCl3) (δ ppm): 171.3, 167.4, 166.2, 143.0, 138.9, 136.1, 133.2, 133.1, 132.9, 130.9, 129.6, 129.5, 127.4, 124.5, 123.0, 121.1, 119.7, 117.3, 113.9, 113.8, 52.8, 52.4, 52.1, 49.7, 43.6, 31.6, 31.2, 30.9.
HRMS (ESI) *m/z*: calcd for $C_{30}H_{24}ClN_2O_5$: 527.1374 $[M-H]^-$; found:527.1343.

Dimethyl 4,4-dimethyl-1-oxo-2-phenyl-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de]pyrrolo [4,3,2-mn]acridine-6,7-dicarboxylate (5f)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 219.1-220.8 ^{o}C).

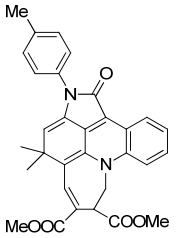


IR(KBr, v, cm^{-1}): 3444, 2908, 1743, 1695, 1680, 1499, 1252, 1055, 746;
^{1}H NMR (400 MHz, $CDCl_3$) (δ ppm): 8.28 (d, J = 7.6 Hz, 1H, ArH), 7.81 (s, 1H, ArH), 7.52 (d, J = 6.8 Hz, 2H, ArH), 7.45 – 7.29 (m, 4H, ArH), 7.13 (d, J = 7.2 Hz, 1H, ArH), 5.70 (s, 1H, CH), 4.80 (s, 1H, CH), 4.69 (s, 1H, CH), 3.80 (s, 3H, CH_3), 3.62 (s, 3H, CH_3), 3.47 (s, 1H, CH), 1.52 (s, 3H, CH_3), 1.47 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 171.4, 167.4, 166.4, 143.0, 139.1, 136.2, 134.6, 133.0, 131.2, 129.5, 129.4, 127.2, 126.3, 124.5, 123.0, 121.4, 120.8, 119.9, 117.5, 113.8, 113.8, 52.8, 52.4, 52.1, 49.7, 43.6, 31.6, 31.2, 30.9.
HRMS (ESI) *m/z*: calcd for $C_{30}H_{25}N_2O_5$:493.1763 $[M-H]^-$; found:493.1738.

dimethyl 4,4-dimethyl-1-oxo-2-(p-tolyl)-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de]pyrrolo [4,3,2-mn]acridine-6,7-dicarboxylate (5g)

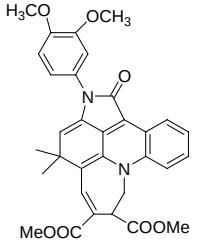
The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 196.6-197.3 ^oC).



IR(KBr, v, cm^{-1}): 3430, 2950, 1746, 1721, 1730, 1601, 1395, 1077, 758;
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.27 (dd, *J* = 1.2 Hz, *J* = 7.6 Hz, 1H, ArH), 7.92 (s, 1H, ArH), 7.44 – 7.36 (m, 6H, ArH), 7.18 (t, *J* = 7.2 Hz, 1H, ArH), 5.86 (s, 1H, CH), 4.86 (s, 1H, CH), 4.79 (s, 1H, CH), 3.85 (s, 3H, CH_3), 3.65 (s, 3H, CH_3), 3.47 (s, 1H,CH), 2.45 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 1.53 (s, 3H, CH_3).
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 171.4, 167.4, 166.5, 143.0, 139.1, 137.2, 136.3, 132.9, 131.9, 131.4, 130.0, 129.5, 126.2, 124.5, 123.0, 121.3, 120.7, 120.0, 117.5, 113.8, 113.7, 52.7, 52.4, 52.1, 49.7, 43.6, 31.6, 31.2, 30.9, 21.2.
HRMS (ESI) *m/z*: calcd for $C_{31}H_{27}N_2O_5$: 507.1920 $[M-H]^-$; found:507.1889.

Dimethyl 2-(3,4-dimethoxyphenyl)-4,4-dimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de] pyrrolo[4,3,2-mn]acridine-6,7-dicarboxylate (5h)

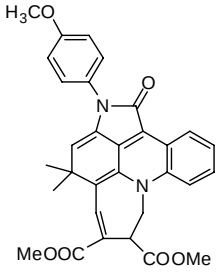
The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 196.6-197.3 ^oC).



IR(KBr, v, cm^{-1}): 3430, 2949, 1738, 1687, 1655, 1515, 1238, 1165, 758;
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.26 (dd, *J* = 7.7, 1.2Hz, 1H, ArH), 7.92 (s, 1H, ArH), 7.44–7.36 (m, 2H, ArH), 7.18 (t, *J* = 7.2 Hz, 1H, ArH), 7.10 – 7.02 (m, 3H, ArH), 5.88 (s, 1H, CH), 4.93 (s, 1H, CH_2), 4.72 (s, 1H, CH_2), 3.93 (s, 3H, CH_3), 3.91 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 3.65 (s, 3H, CH_3), 3.51 (s, 1H, CH), 1.56 (s, 3H, CH_3), 1.54 (s, 3H, CH_3).
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 166.1, 162.2, 161.4, 144.1, 143.1, 137.8, 133.8, 131.0, 127.6, 126.37, 124.3, 122.2, 119.3, 117.8, 116.1, 115.5, 114.7, 113.5, 112.2, 108.6, 108.5, 106.1, 105.1, 50.9, 47.5, 47.1, 46.8, 44.5, 38.3, 26.3, 25.9, 25.7.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{29}N_2O_7$: 553.1957 $[M-H]^-$; found:553.1917.

Dimethyl 2-(4-methoxyphenyl)-4,4-dimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de] pyrrolo[4,3,2-mn]acridine-6,7-dicarboxylate (5i)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 192.6-193.3 ^{o}C).



IR (KBr, v, cm^{-1}): 3440, 2951, 1743, 1695, 1680, 1499, 1429, 1425, 764;

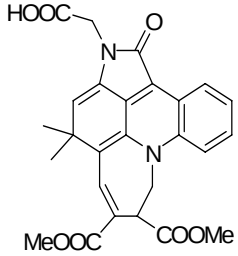
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.27 (d, *J* = 6.8 Hz, 1H, ArH), 7.92 (s, 1H,ArH), 7.44 (M, 4H, ArH), 7.19 (t, *J* = 7.3 Hz, 1H, ArH), 7.11 (d, *J* = 8.9 Hz, 2H, ArH), 5.83 (s, 1H, CH), 4.95 (s, 1H, CH), 4.78 (s, 1H, CH), 3.90 (s, 3H, CH), 3.85 (s, 3H, CH), 3.66 (s, 3H, CH_3), 3.56 (s, 1H, CH), 1.55 (d, *J* = 7.3 Hz, 3H, , CH_3), 1.54 (s, 3H, CH_3).

^{13}C NMR (100 MHz, CDCl3) δ 170.9, 167.0, 166.7, 158.7, 143.1, 138.9, 136.0, 132.9, 131.7, 129.3, 127.7, 127.2, 124.5, 122.9, 121.3, 121.2, 119.9, 117.4, 114.7, 114.0, 113.8, 61.3, 60.7, 55.6, 52.8, 49.8, 43.5, 31.5, 31.2, 30.9.

HRMS (ESI) *m/z*: calcd for $C_{31}H_{27}N_2O_6$:523.1869 $[M-H]^-$; found:523.1860.

2-(6,7-Bis(methoxycarbonyl)-4,4-dimethyl-1-oxo-7,8-dihydro-1H-azepino[3,2,1-de]pyrrolo[4,3,2-mn]acridin -2(4H)-yl)acetic acid (5j)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 171.8-172.3 ^{o}C).



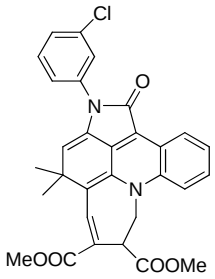
IR(KBr, v, cm^{-1}): 3122, 2931, 1740, 1704, 1680, 1398, 1229, 1044, 757;

^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.64 (d, *J* = 6.8 Hz, 1H,ArH), 8.35 (s, 1H, ArH), 7.87 – 7.78 (m, 2H, ArH), 7.62 (t, *J* = 7.2 Hz, 1H, ArH), 6.35 (s, 1H, CH), 5.35 (s, 1H, CH), 5.21 (s, 1H, CH), 5.14 (d, *J* = 9.2 Hz, 2H, CH_2), 4.28 (s, 3H, CH_3), 4.08 (s, 3H, CH_3), 3.98 (s, 1H, CH), 2.00 (s, 3H, CH_3), 1.98 (s, 3H, CH_3).

HRMS (ESI) *m/z*: calcd for $C_{26}H_{23}N_2O_7$:521.2076 $[M-H]^-$; found:521.2054.

Dimethyl 2-(3-chlorophenyl)-4,4-dimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de] pyrrolo[4,3,2-mn]acridine-6,7-dicarboxylate(5k)

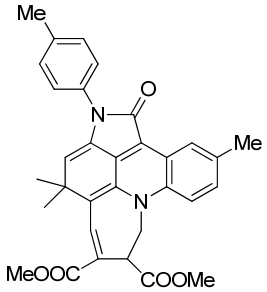
The title compound was prepared following the general procedure (Microwave Heating, Temperature: 140 ^{o}C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 198.2-198.7 ^{o}C).



IR (KBr, v, cm^{-1}): 3447, 3100, 2990, 1747, 1722, 1703, 1600, 1513, 1212, 1049, 768;
^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.34 – 8.14 (m, 1H, ArH), 7.87 (s, 1H, ArH), 7.57 (d, *J* = 1.8 Hz, 1H, ArH), 7.53 – 7.26 (m, 5H, ArH), 7.15 (t, *J* = 7.4 Hz, 1H, ArH), 5.90 (s, 1H,CH), 4.88 (s, 1H,CH), 4.73 (s, 1H,CH), 3.80 (s, 3H, CH_3), 3.61 (s, 3H, CH_3), 3.50 (d, *J* = 13.3 Hz, 1H, CH), 1.53 (s, 3H, CH_3), 1.50 (s, 3H, CH_3);
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 171.3, 167.4, 166.1, 143.1, 138.9, 136.0, 135.8, 134.9, 133.2, 130.3, 129.7, 127.4, 126.4, 124.5, 124.3, 123.1, 121.5, 121.2, 119.7, 117.3, 114.0, 113.8, 52.8, 52.4, 52.1, 49.7, 43.6, 31.6, 31.2.
HRMS (ESI) *m/z*: calcd for $C_{30}H_{24}ClN_2O_5$: 527.1374 $[M-H]^-$; found:527.1367.

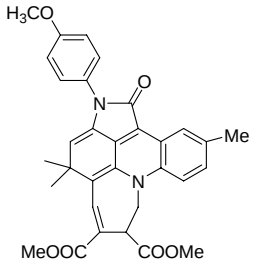
Dimethyl 4,4,12-trimethyl-1-oxo-2-(p-tolyl)-2,4,7,8-tetrahydro-1H-azepino[3,2,1-de]pyrrolo [4,3,2-mn]acridine-6,7-dicarboxylate (5l)

The title compound was prepared following the general procedure (Microwave Heating, Temperature: 130 ^oC) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 169.7-171.4 ^oC).



IR (KBr, v, cm^{-1}): 3411, 3131, 2988, 1722, 1687, 1675, 1531, 1231, 1055, 766;
^{1}H NMR (400 MHz, $CDCl_3$) (δ ppm): 8.10 (s, 1H, ArH), 7.81 (s, 1H, ArH), 7.31 (s, 4H, ArH), 7.18 (d, *J* = 8.0 Hz, 2H, ArH), 7.13 (d, *J* = 8.0 Hz, 2H, ArH), 5.66 (s, 1H, CH), 4.77 (s, 1H, CH), 4.68 (s, 1H, CH), 3.79 (s, 3H, CH_3), 3.61 (s, 3H, CH_3), 3.42 (s, 1H, CH_3), 2.42 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.45 (s, 3H, CH_3);
^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm) 171.4, 167.5, 166.5, 140.9, 139.2, 137.2, 136.4, 132.8, 132.7, 132.0, 131.4, 130.4, 129.9, 126.1, 124.6, 121.3, 120.1, 119.8, 117.5, 113.7, 113.2, 52.7, 52.4, 52.0, 49.8, 43.5, 31.6, 31.2, 30.9, 21.2, 20.6.
HRMS (ESI) *m/z*: calcd for $C_{32}H_{29}N_2O_5$: 521.2076 $[M-H]^-$; found:521.2050.

Dimethyl 2-(4-methoxyphenyl)-4,4,12-trimethyl-1-oxo-2,4,7,8-tetrahydro-1H-azepino [3,2,1-de]pyrrolo[4,3,2-mn]acridine-6,7-dicarboxylate (5m)



The title compound was prepared following the general procedure (Microwave Heating, Temperature: 130 °C) and was obtained as a pale red solid after purification by silica gel column chromatography (*n*-hexane / acetic ester, 8:1, v/v) (Mp: 178.9-180.0 °C).

Pale red solid; mp:°C;

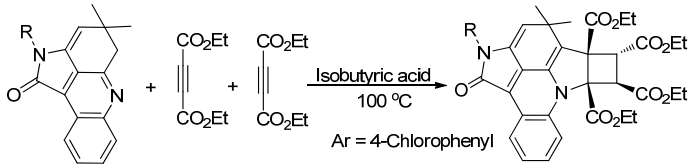
IR (KBr, v, cm^{-1}):3441, 3121, 2948, 1740, 1711, 1673, 1497, 1234, 810;

^{1}H NMR (400 MHz, CD_3COOD) (δ ppm): 8.10 (s, 1H, ArH), 7.92 (s, 1H, ArH), 7.44 (d, *J* = 8.0 Hz, 2H, ArH), 7.29 (d, *J* = 9.6 Hz, 1H, ArH), 7.25 (d, *J* =8.0 Hz, 1H, ArH), 7.11 (d, *J* = 4.4 Hz, 2H, ArH), 5.82 (s, 1H, CH), 4.93 (s, 1H, CH), 4.78 (s, 1H, CH), 3.90 (s, 3H, CH_3), 3.84 (s, 3H, CH_3), 3.65 (s, 3H, CH_3), 3.51 (s, 1H,CH), 2.39 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.52 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 171.4, 167.5, 166.7, 158.7, 140.9, 139.2, 136.4, 132.7, 130.4, 127.7, 124.6, 121.1, 117.5, 114.6, 113.7, 113.2, 55.6, 52.7, 52.4, 52.0, 49.8, 43.5, 31.6, 31.2, 20.6.

HRMS (ESI) *m/z*: calcd for $C_{32}H_{29}N_2O_6$:537.2026 $[M-H]^-$; found:537.2004.

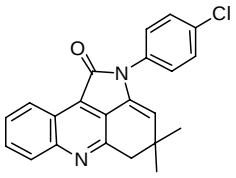
The supporting reaction for the proposed mechanism



D **3a** **3a** **4a**

Microwave Heating: 2-(4-Chlorophenyl)-4,4-dimethyl-4,5-dihydropyrrolo[2,3,4-*kl*]acridin-1(2H)-one (**D**, 1.0 mmol, 0.36 g, 1.0 equiv.) and isobutyric acid (1.5 mL) was introduced in a 10-mL Initiator^{TM} reaction vial, and diethyl but-2-ynedioate (**3a**, 2.2 mmol, 0.38g, 2.2 equiv.) were then successively added. the reaction vial was capped and then pre-stirring for 20 second. The mixture was irradiated (Time: 20 min, Temperature: 100 °C; Absorption Level: High; Fixed Hold Time) until TLC (petroleum ether: acetone 3:1) revealed that conversion of the starting material **D** was completed. The work-up was the same to that described above. The reaction gave final prodcut **4a** in 58% chemical yield.

2-(4-Chlorophenyl)-4,4-dimethyl-4,5-dihydropyrrolo[2,3,4-*kl*]acridin-1(2H)-one D



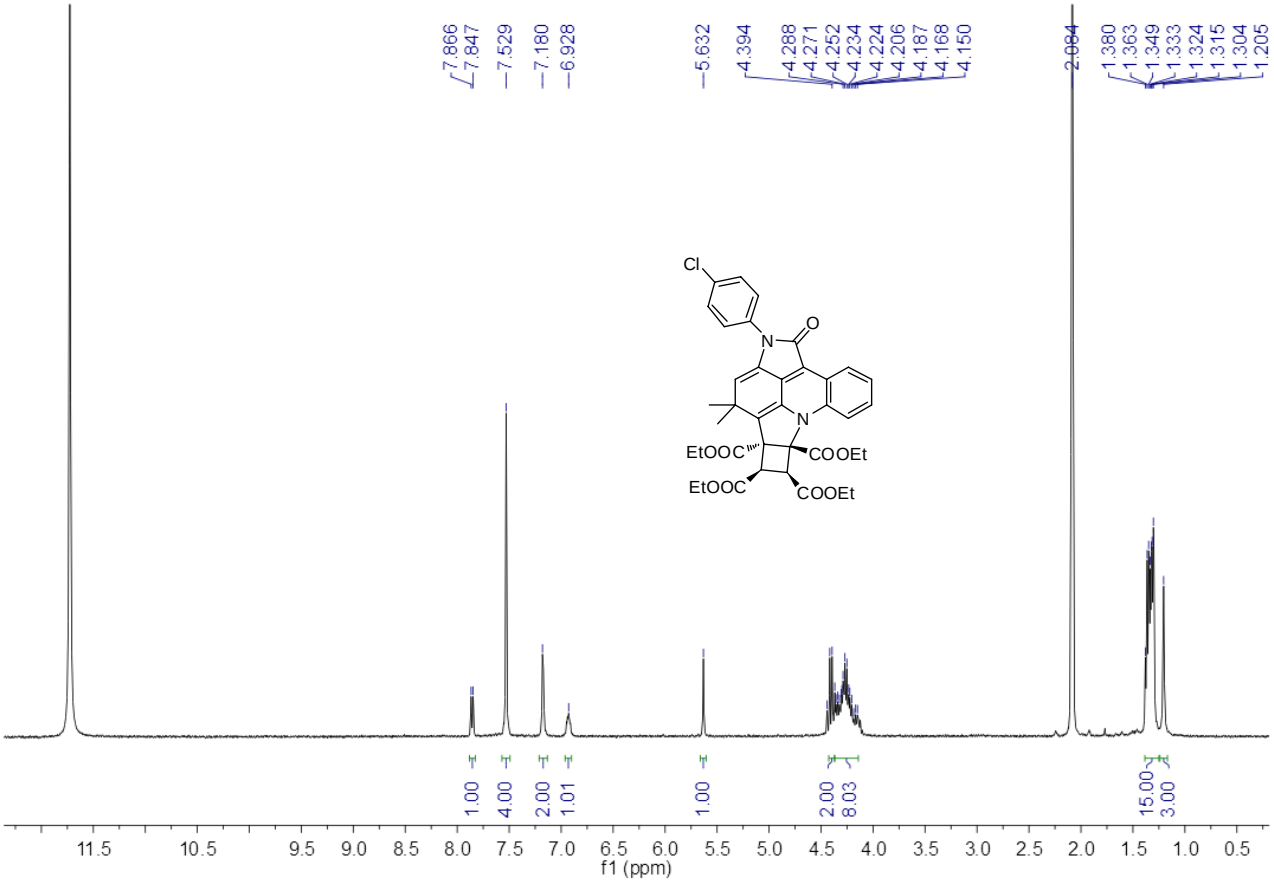
Yellow green solid , mp: 183-184 °C;

IR (KBr, v, cm^{-1}): 2958, 1699, 1651, 1496, 1467, 1411, 1404, 1377, 1346, 1298, 1147, 1117, 1093, 1018, 831, 825, 775;

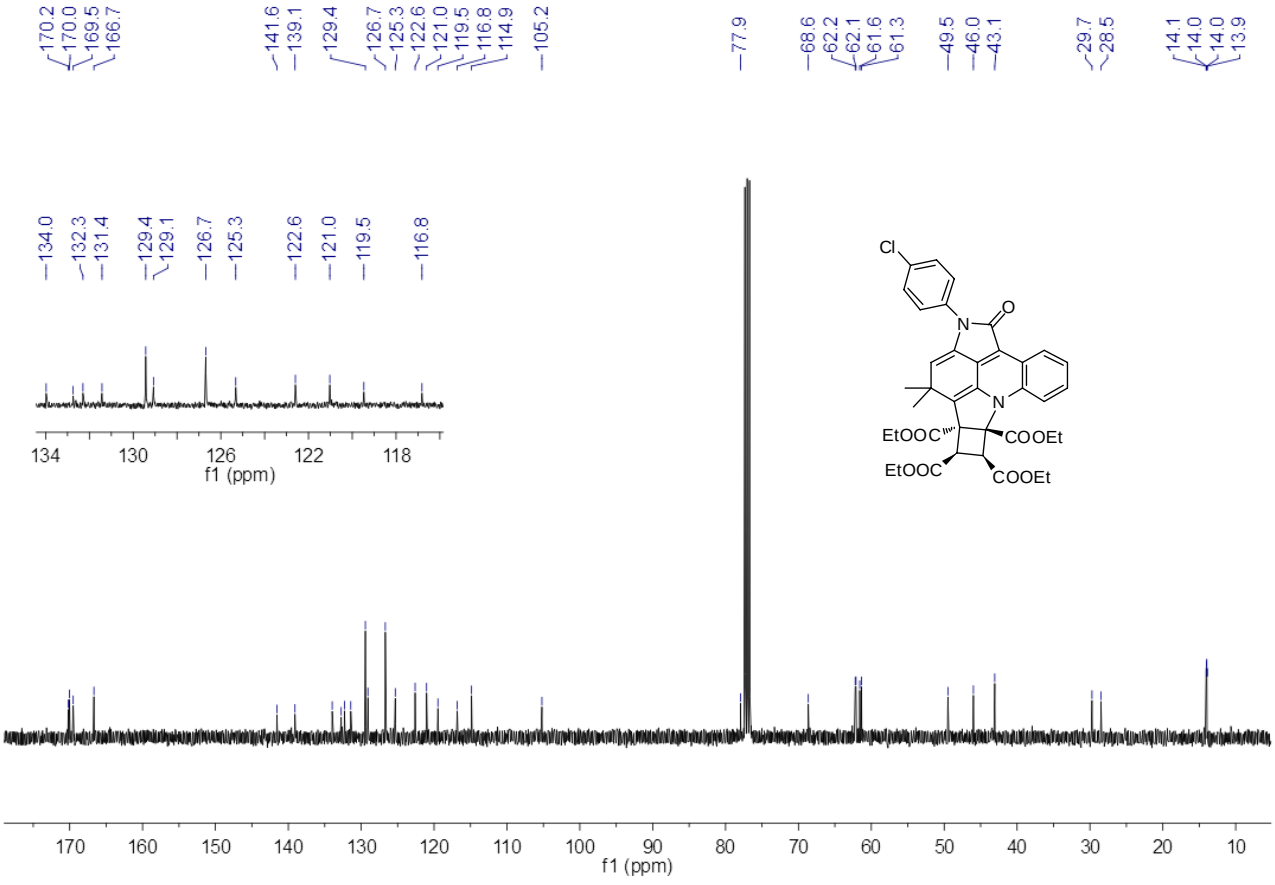
^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.53 (d, *J* = 6.8Hz, 1H, ArH), 8.14 (d, *J* = 7.6Hz, 1H, ArH), 7.81-7.59 (m, 6H, ArH), 5.80 (s, 2H, CH), 3.16 (s, 2H, CH_2), 1.28 (s, 6H, CH_3);

HRMS (ESI): m/z calcd for: $C_{22}H_{18}ClN_2O$, 361.1108, found: 361.1093.

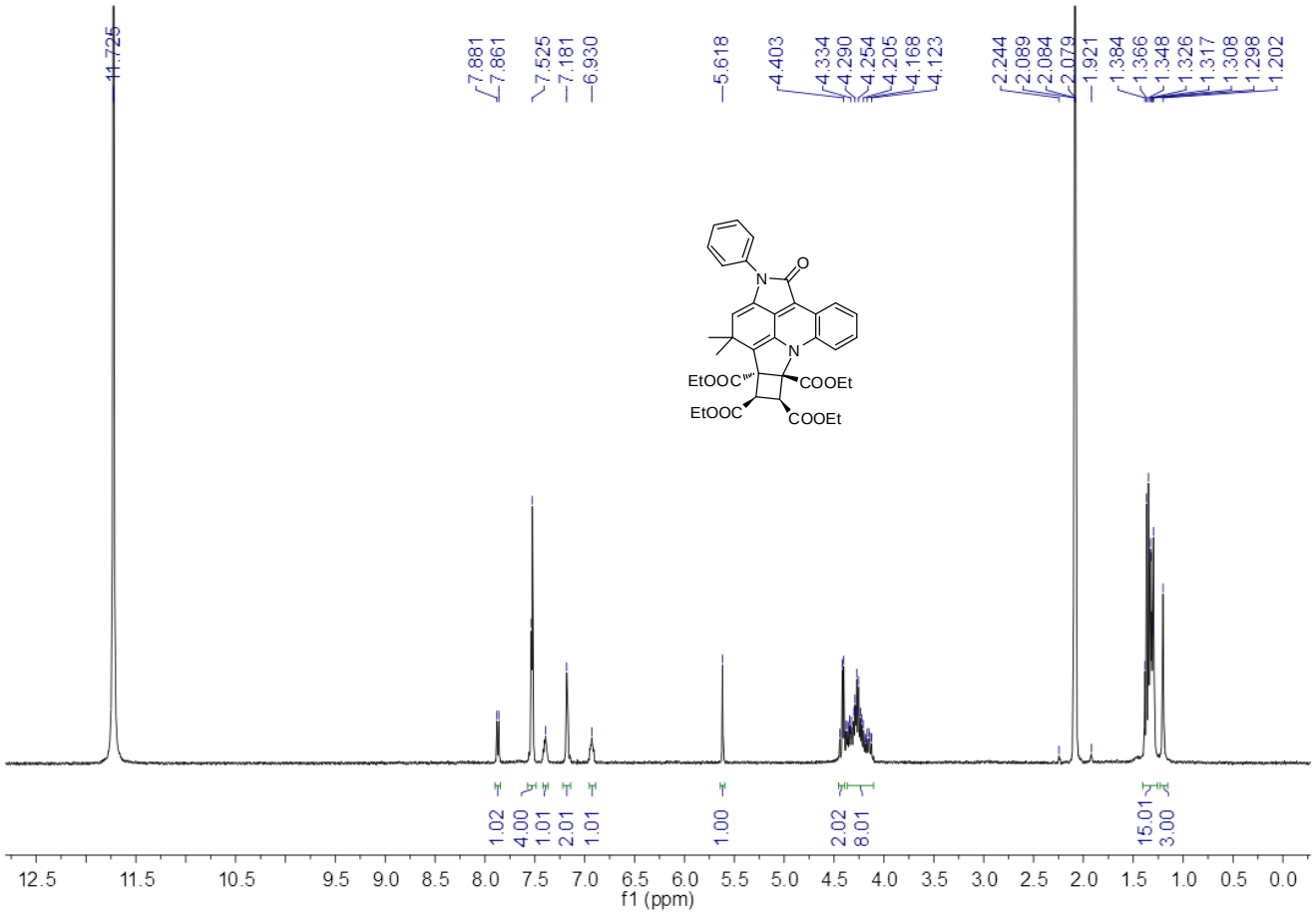
Copies of Spectra for Products 4, 5 and intermediate D



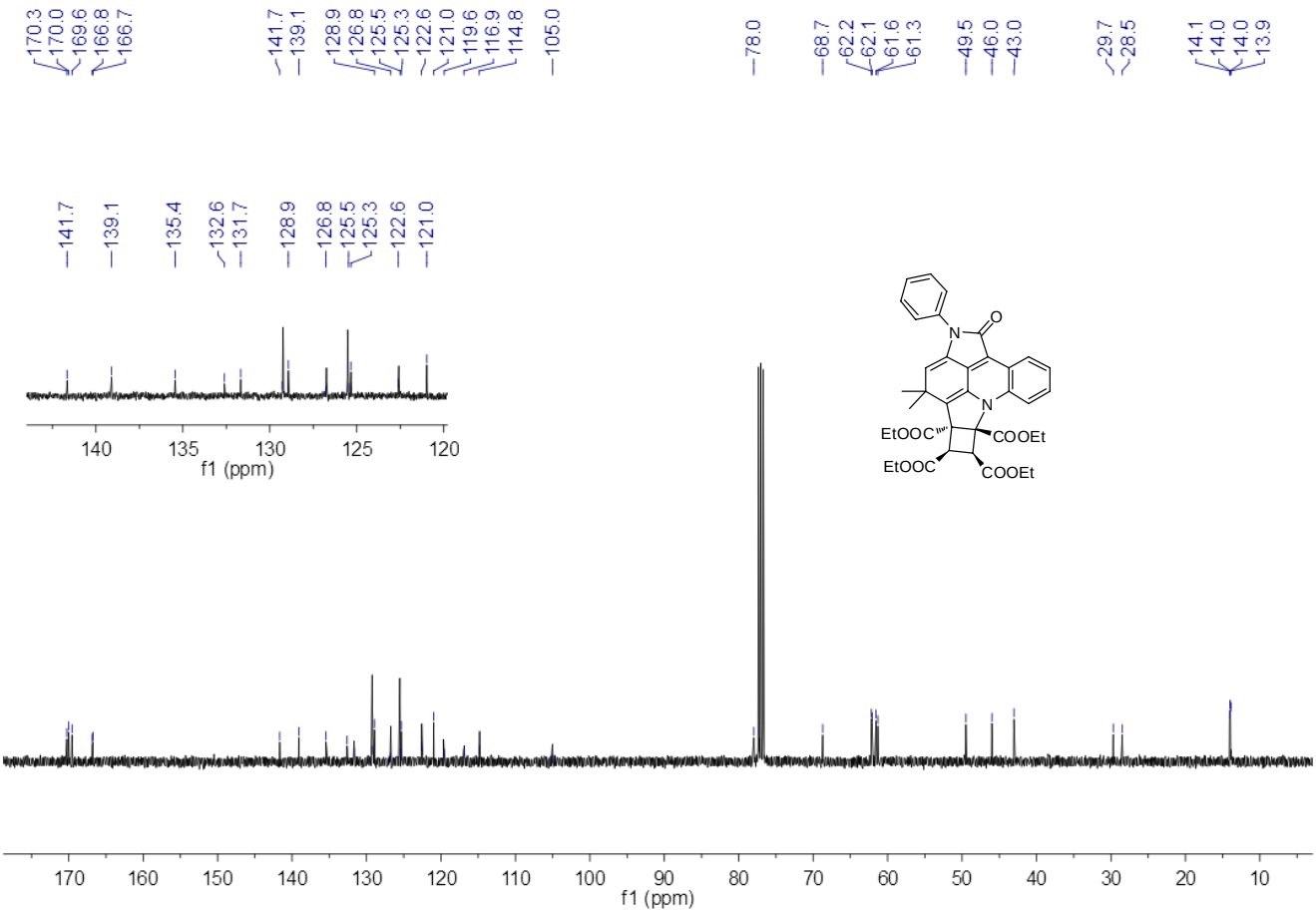
^{1}H NMR Spectrum of Compound 4a



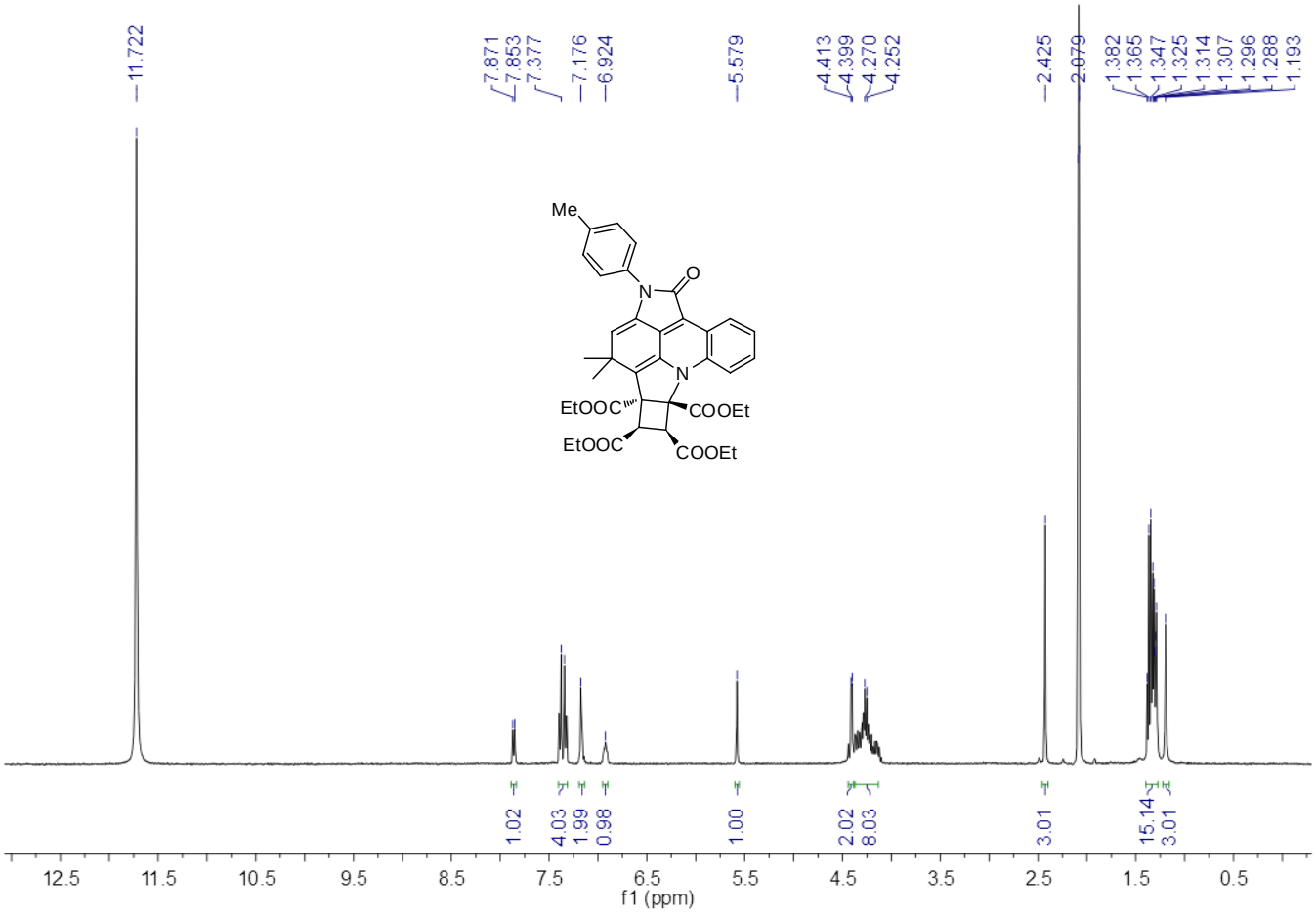
^{13}C NMR Spectrum of Compound 4a



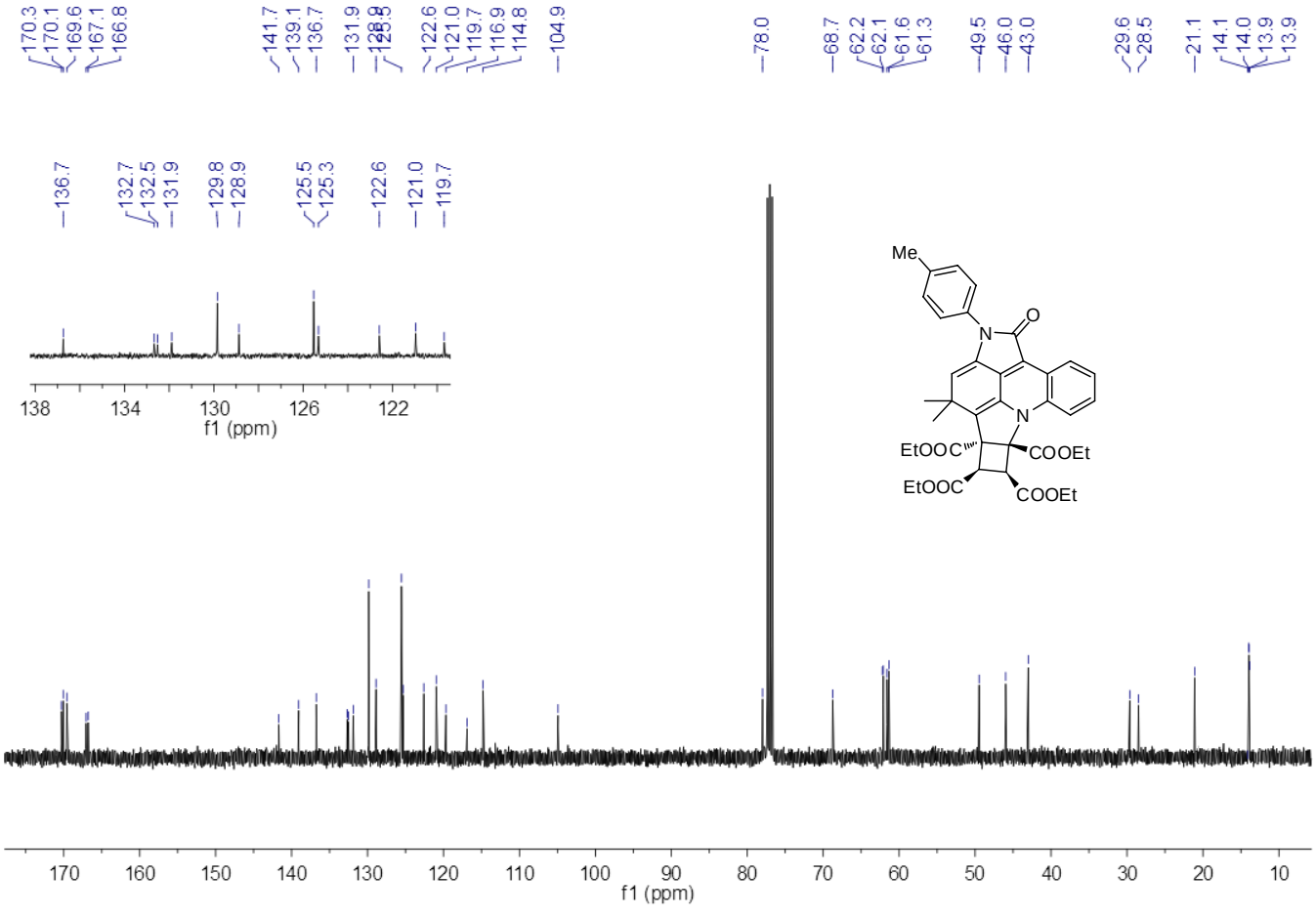
^{1}H NMR Spectrum of Compound 4b



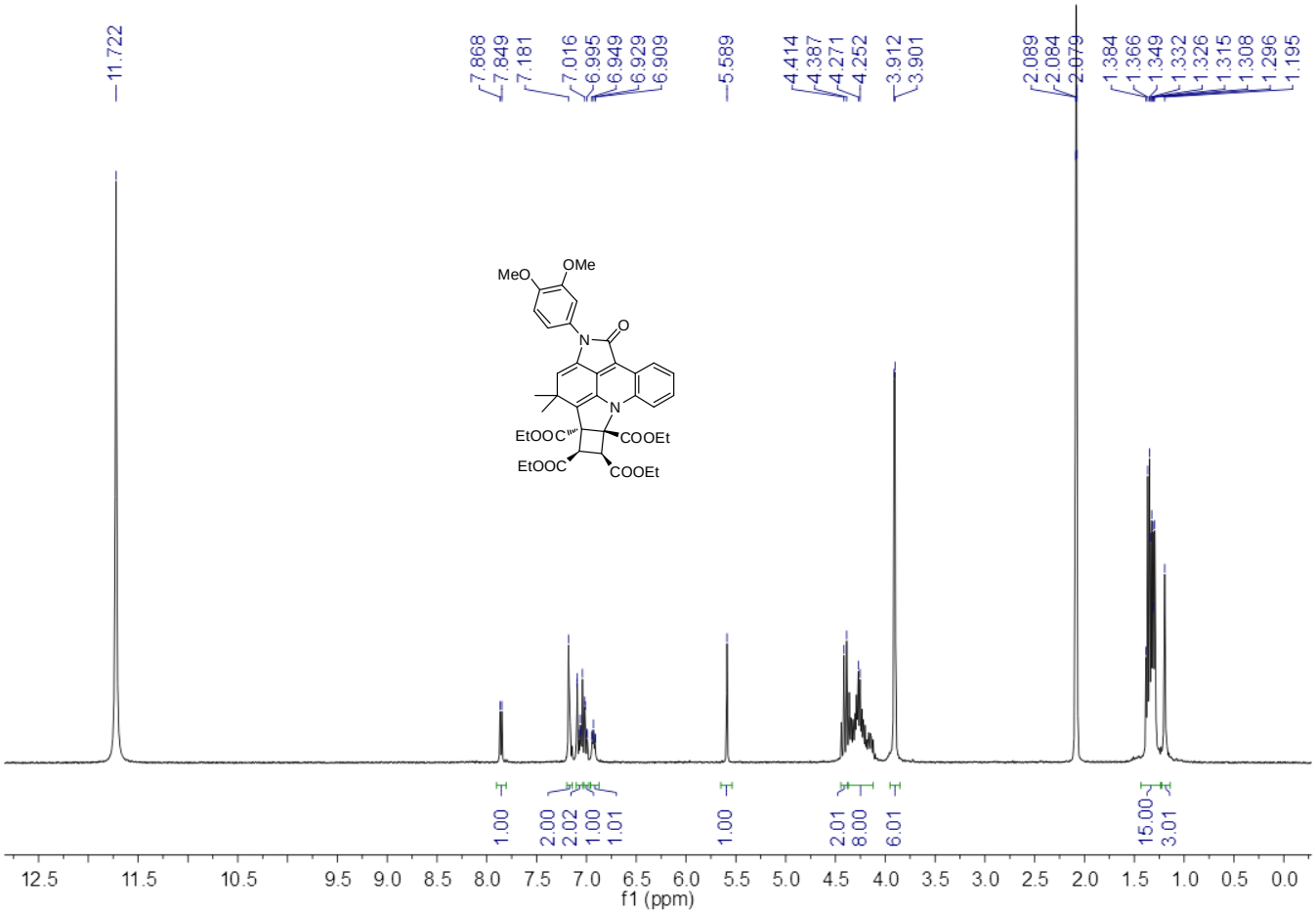
^{13}C NMR Spectrum of Compound 4b



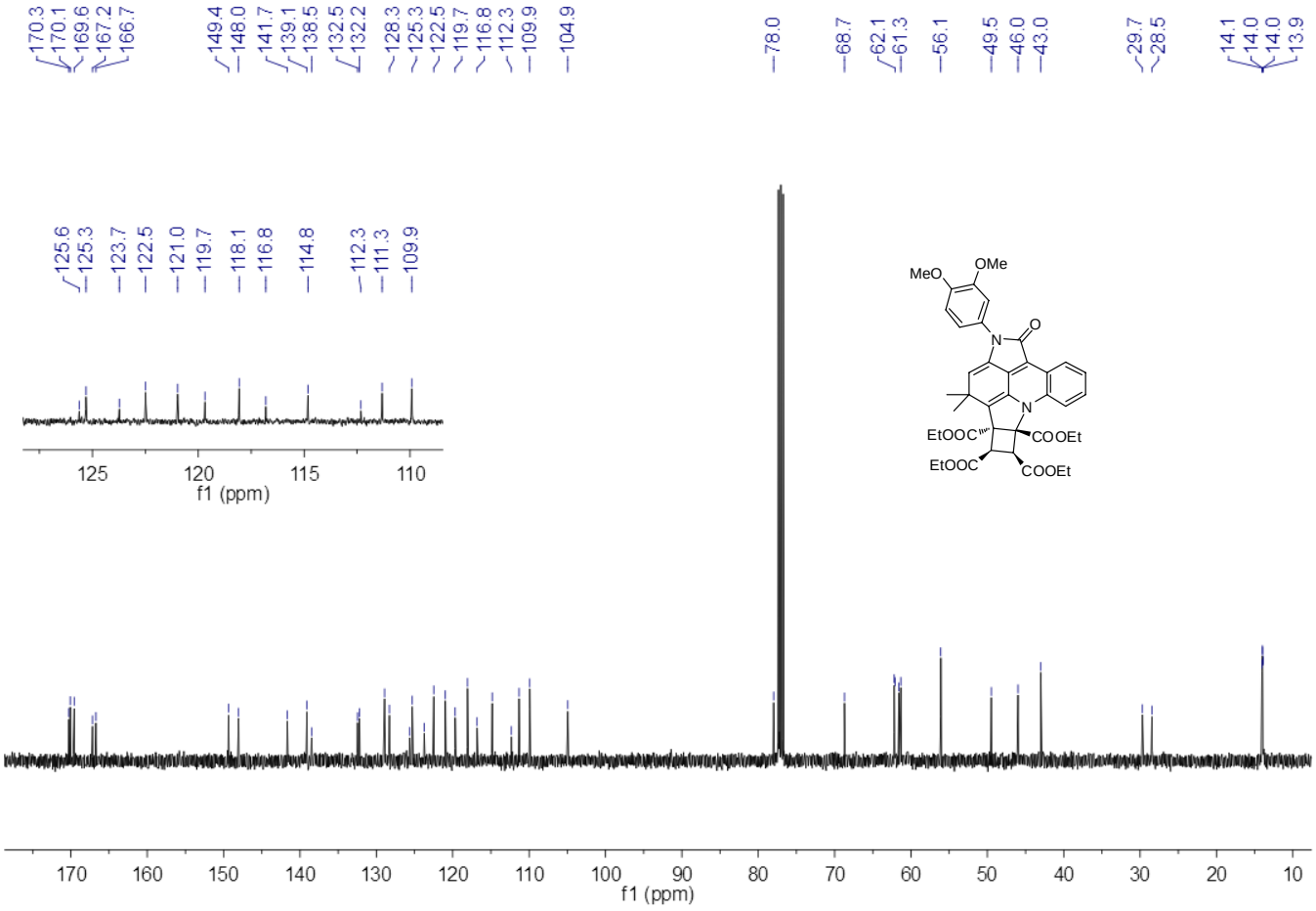
^{1}H NMR Spectrum of Compound 4c



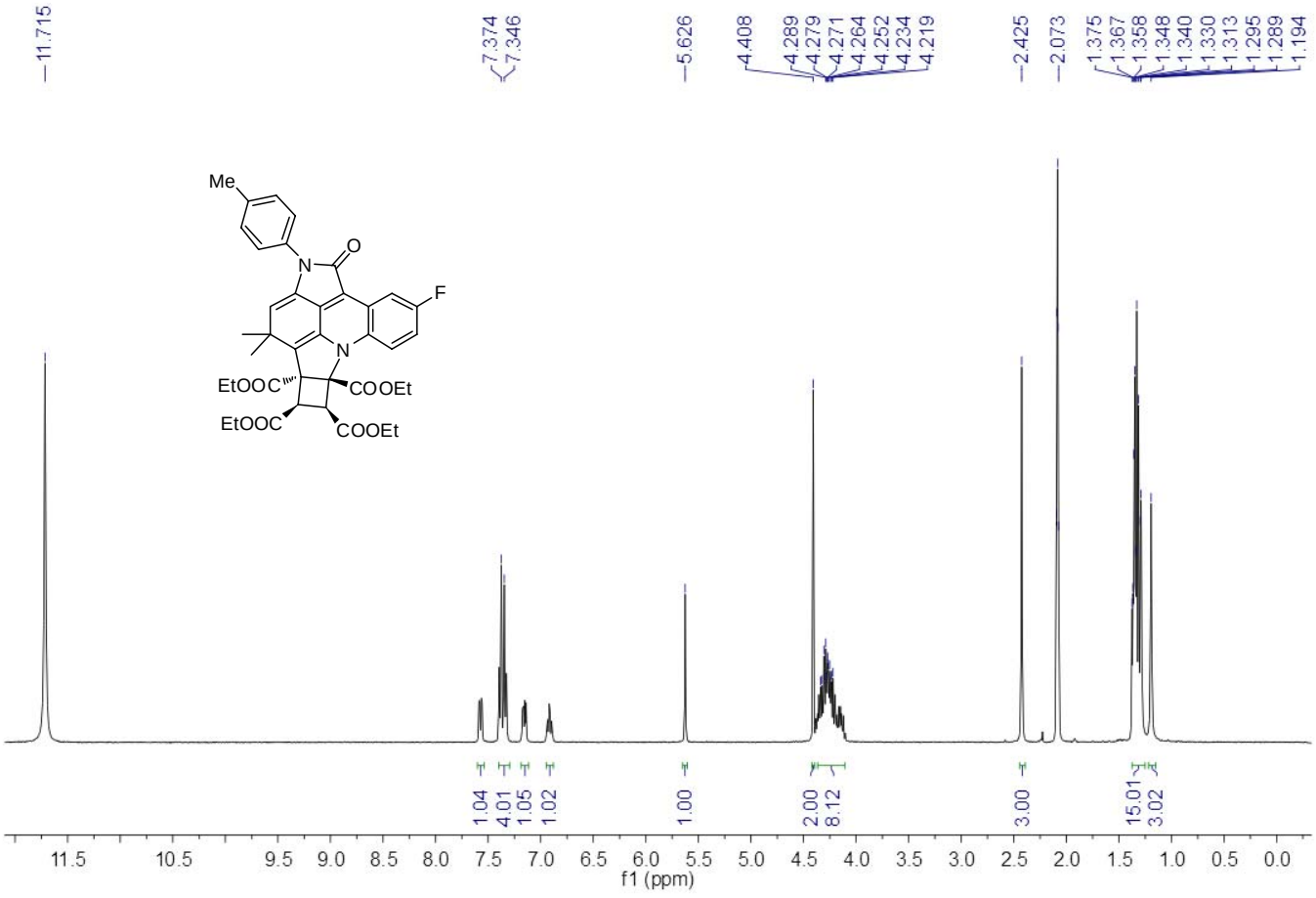
^{13}C NMR Spectrum of Compound 4c



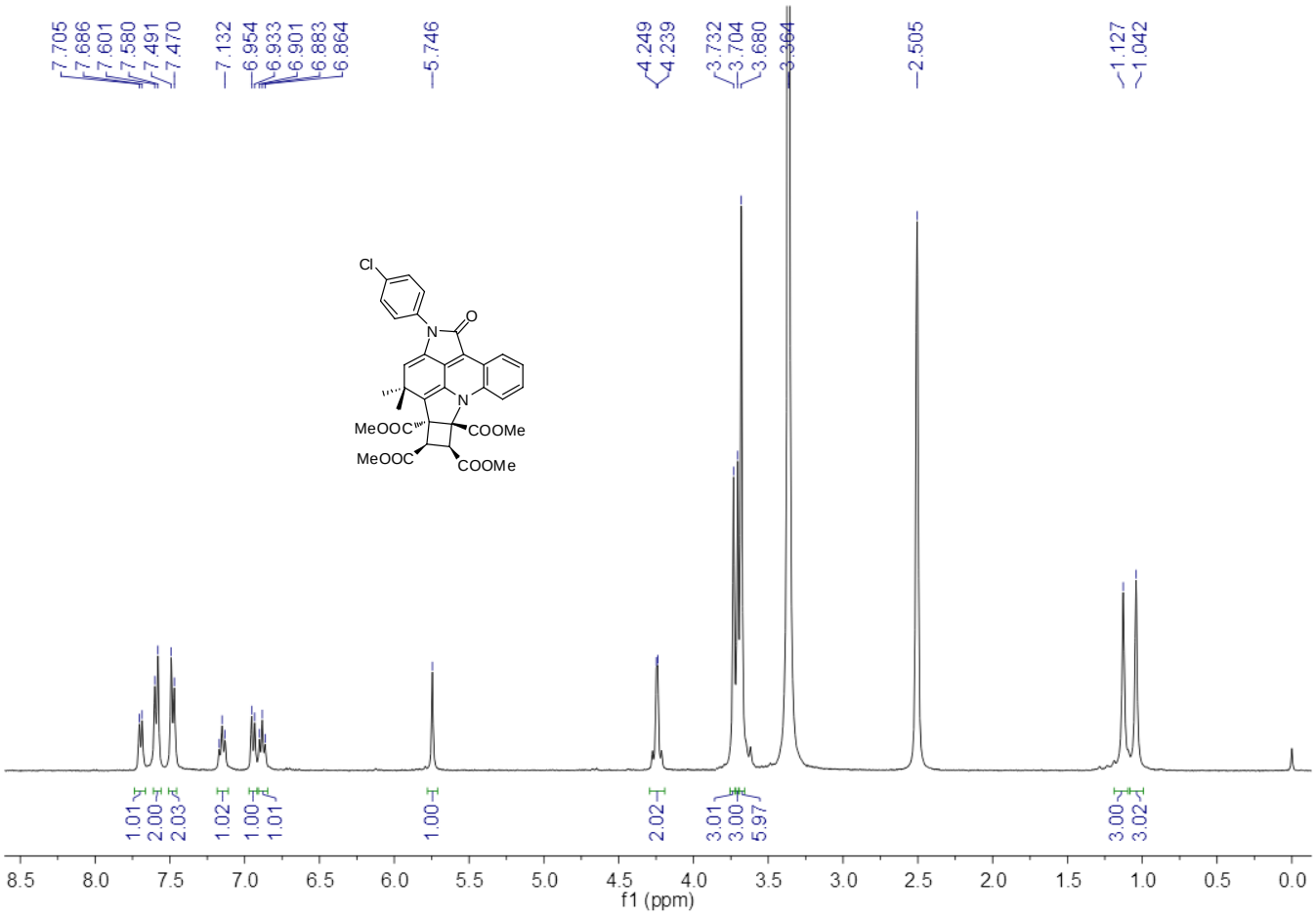
^{1}H NMR Spectrum of Compound 4d



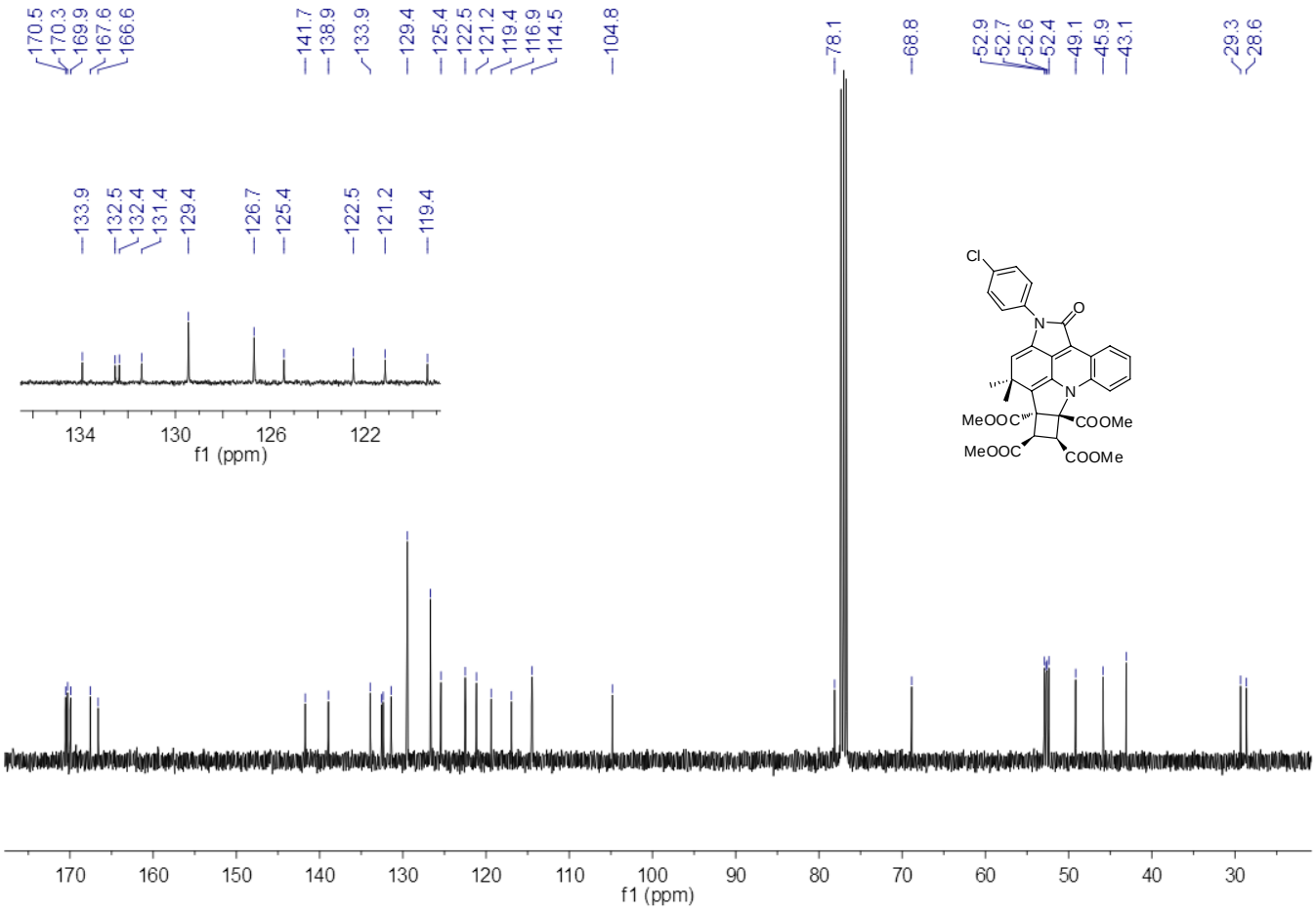
^{13}C NMR Spectrum of Compound 4d



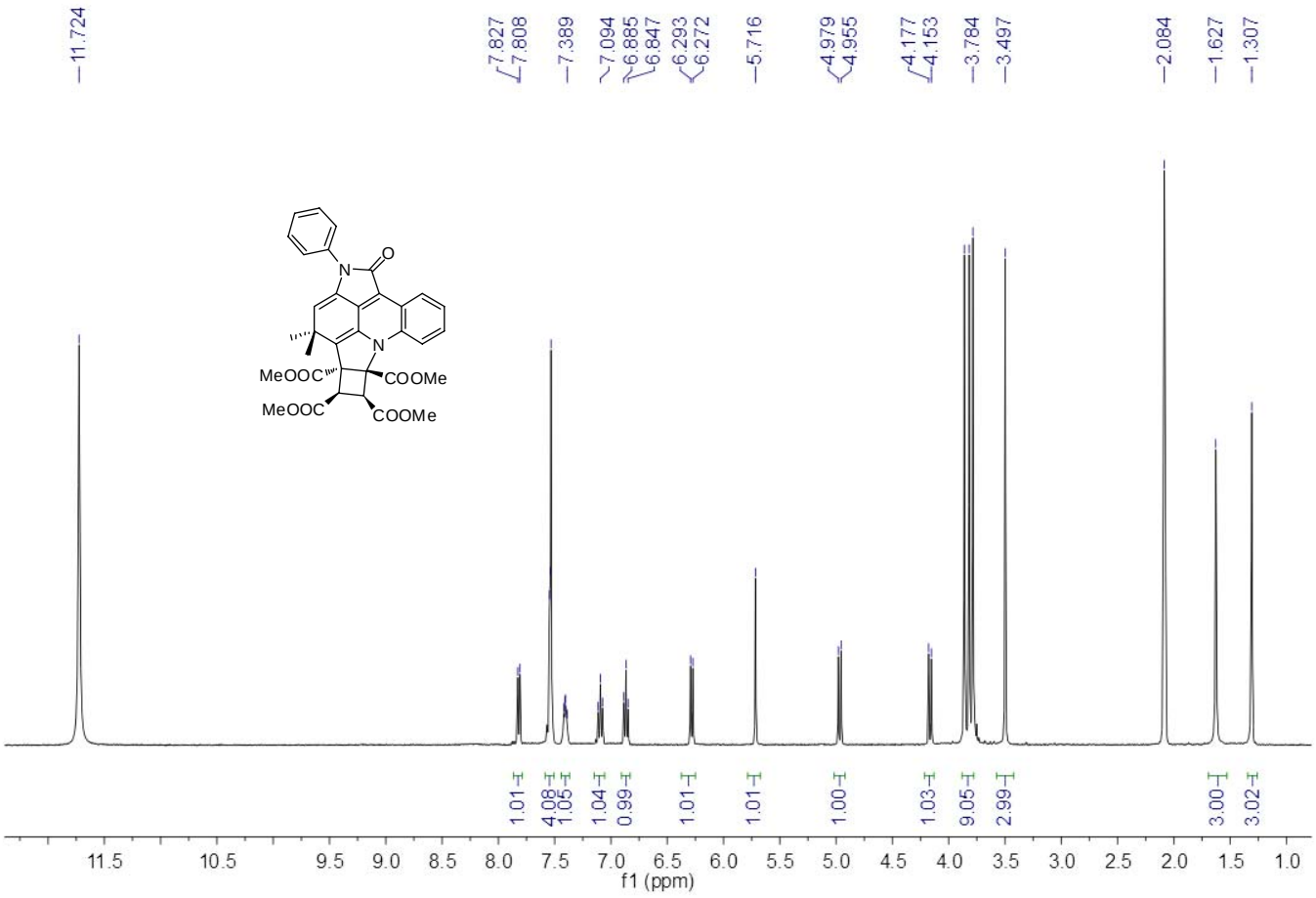
^{1}H NMR Spectrum of Compound 4e



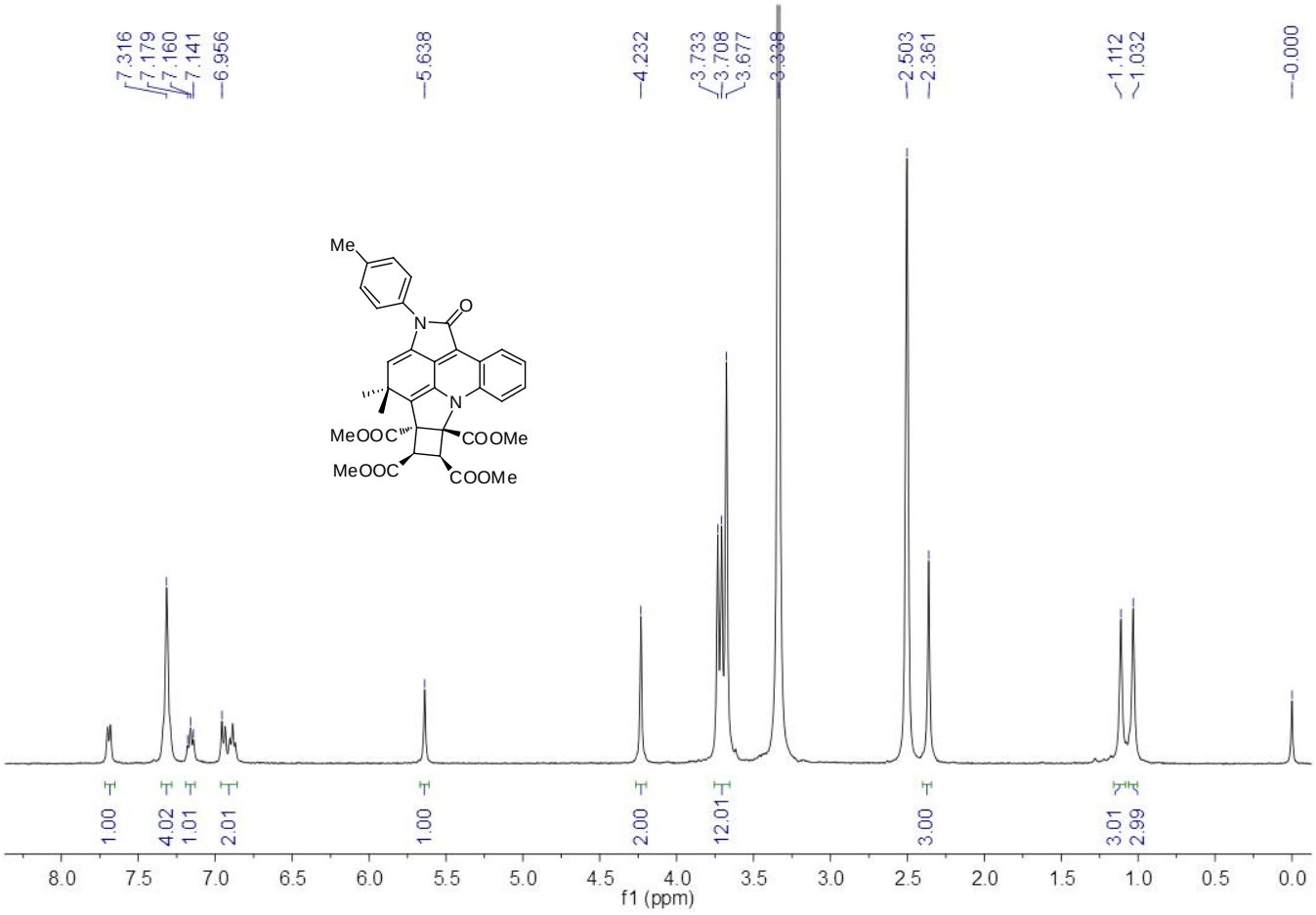
^{1}H NMR Spectrum of Compound 4f



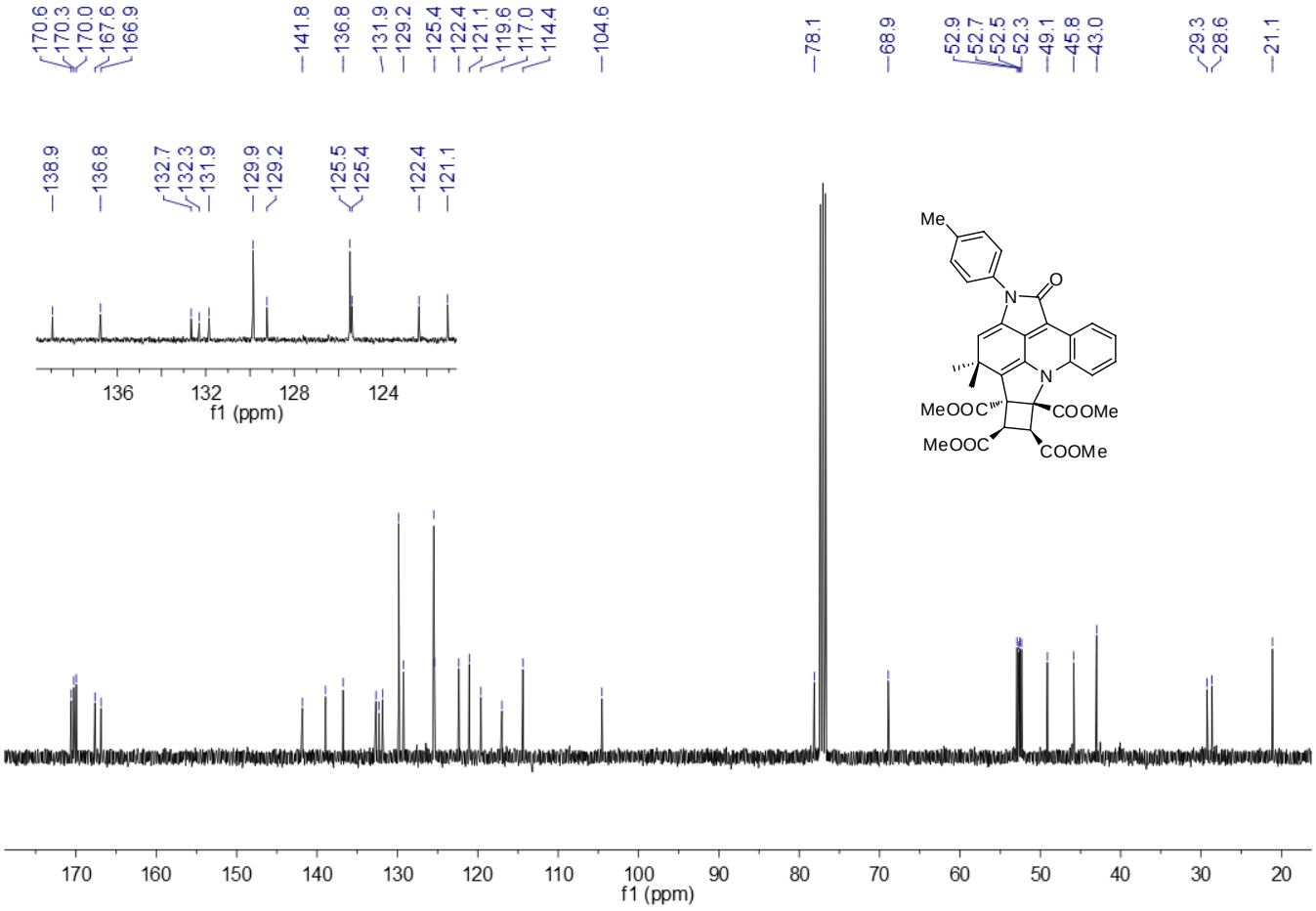
^{13}C NMR Spectrum of Compound 4f



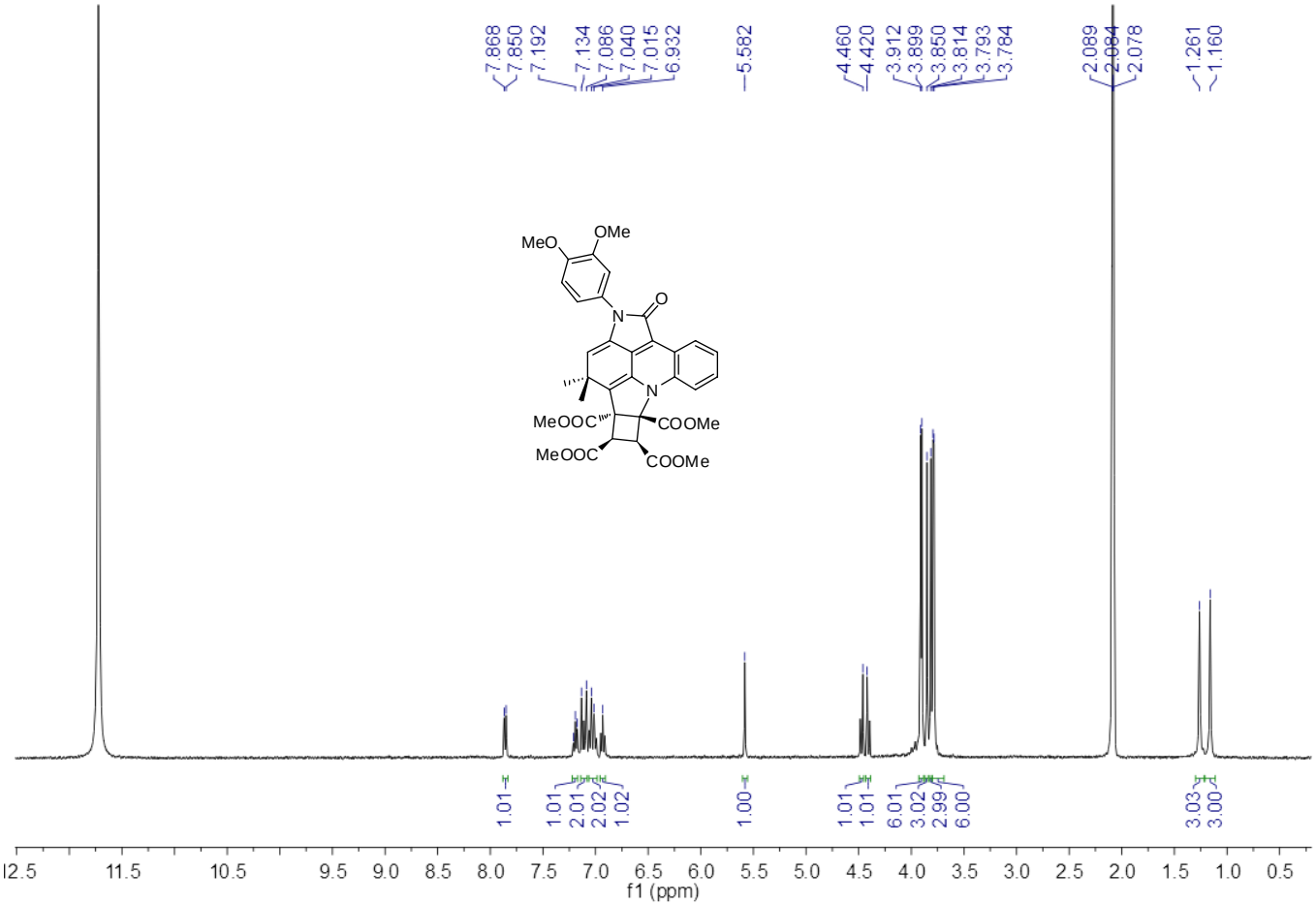
^{1}H NMR Spectrum of Compound 4g



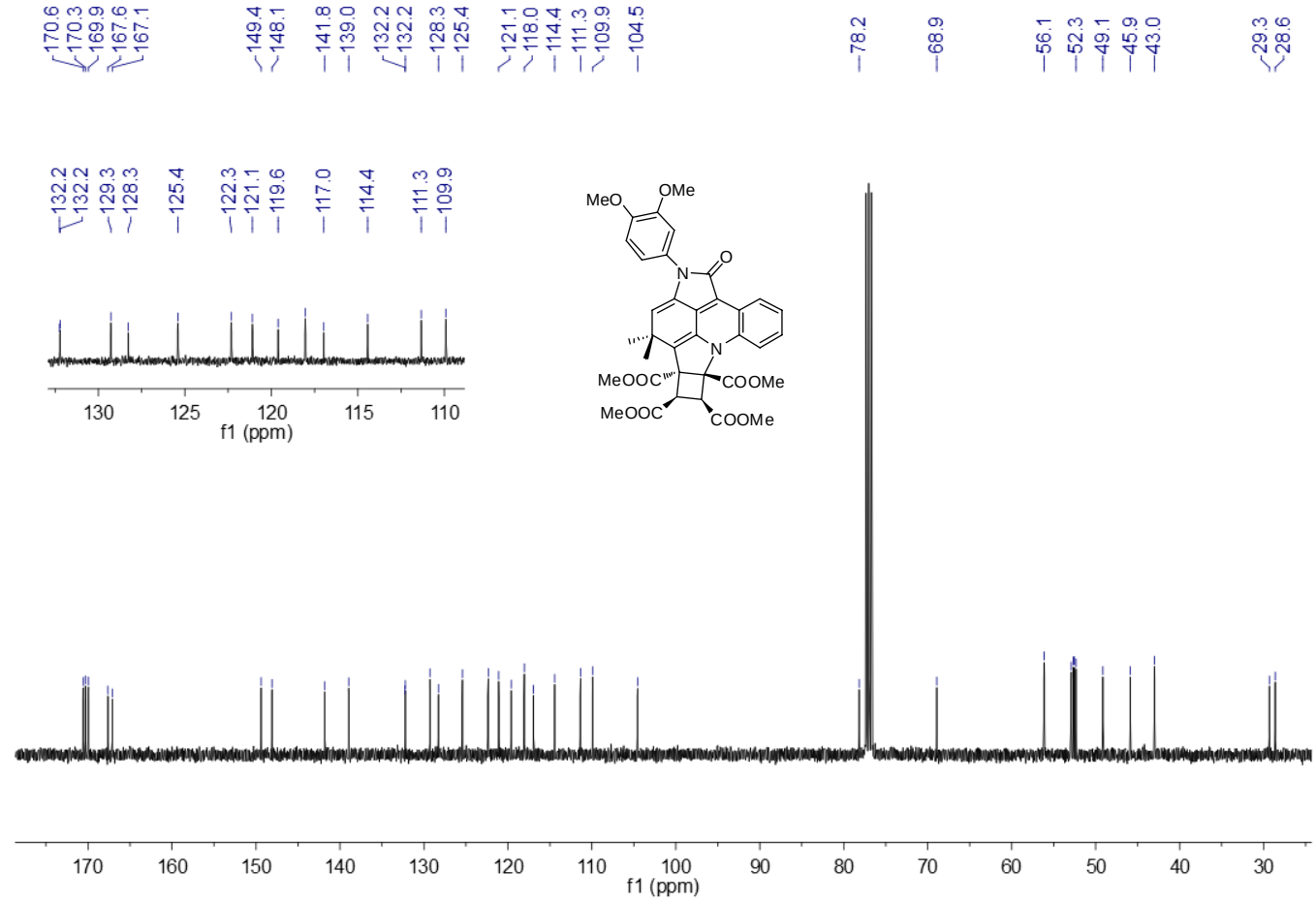
^{1}H NMR Spectrum of Compound 4h



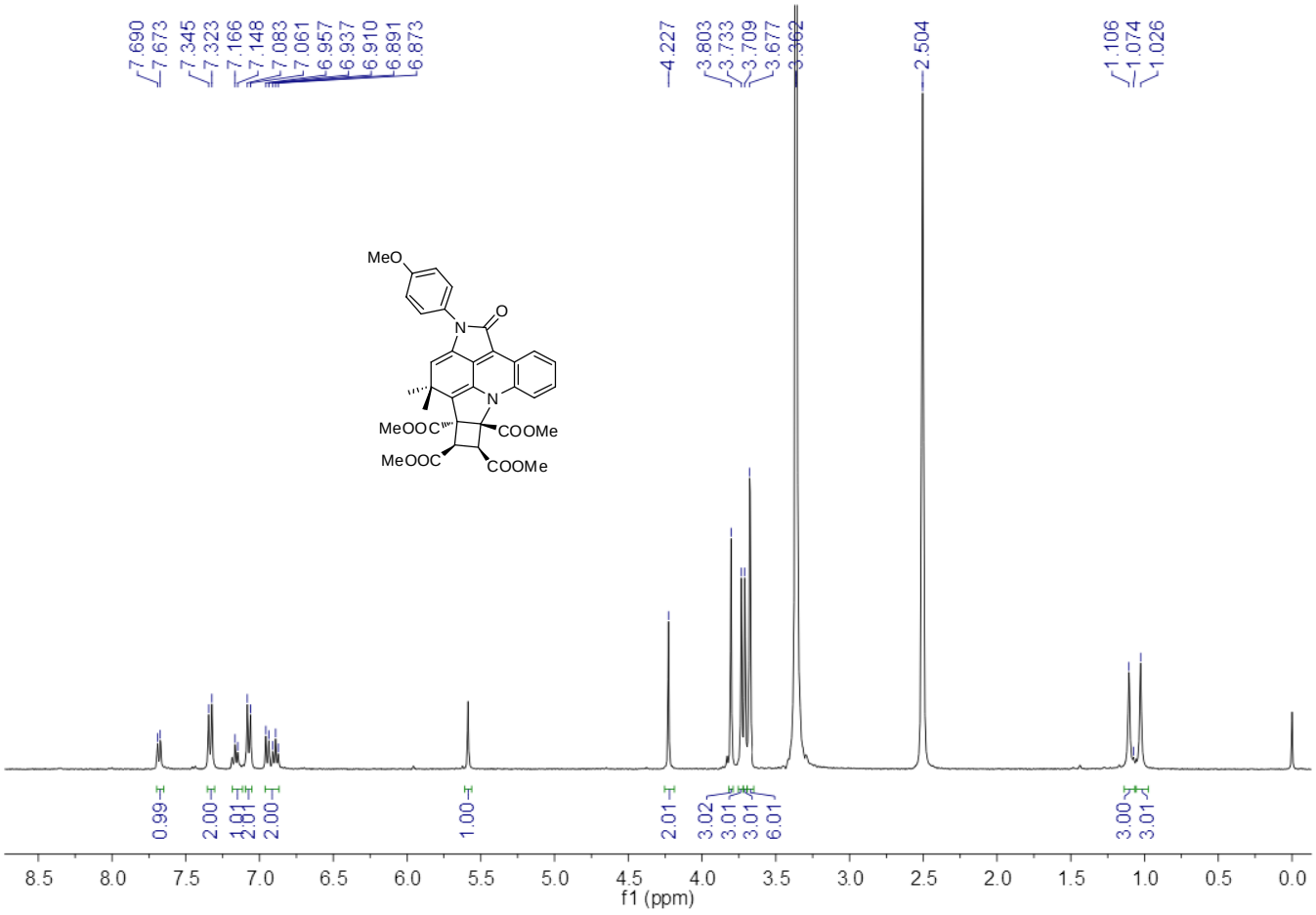
^{13}C NMR Spectrum of Compound 4h



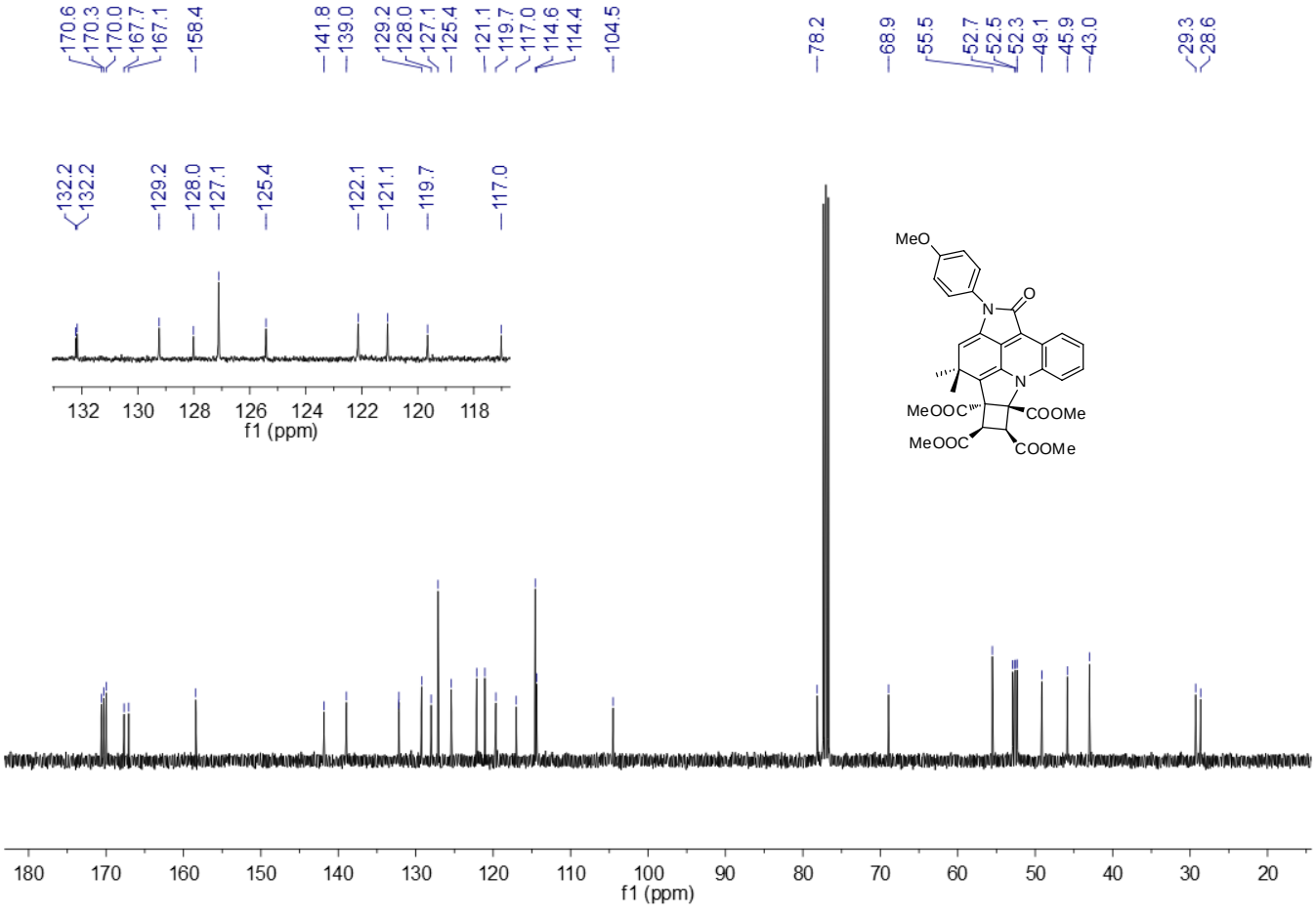
^{1}H NMR Spectrum of Compound 4i



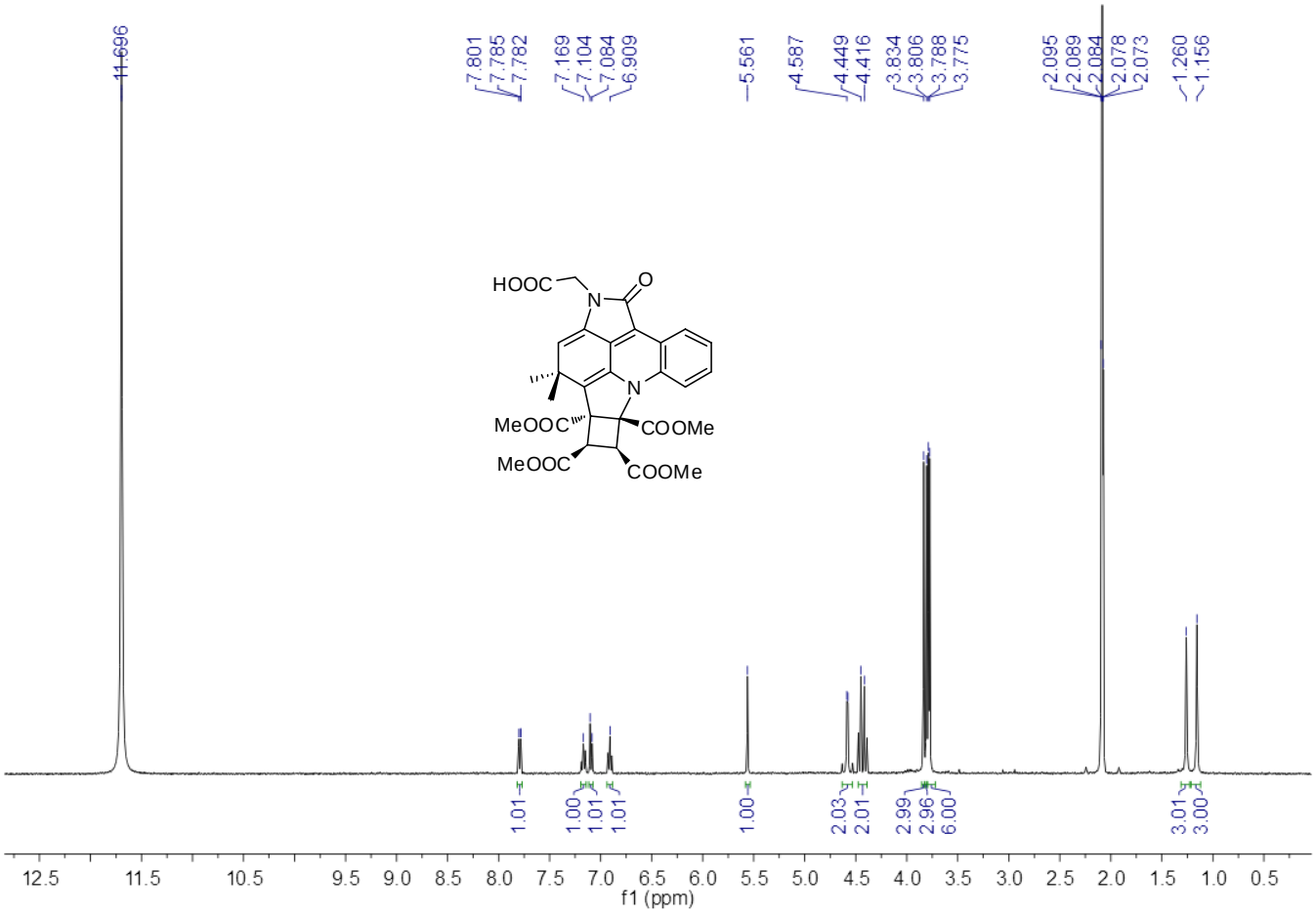
^{13}C NMR Spectrum of Compound 4i



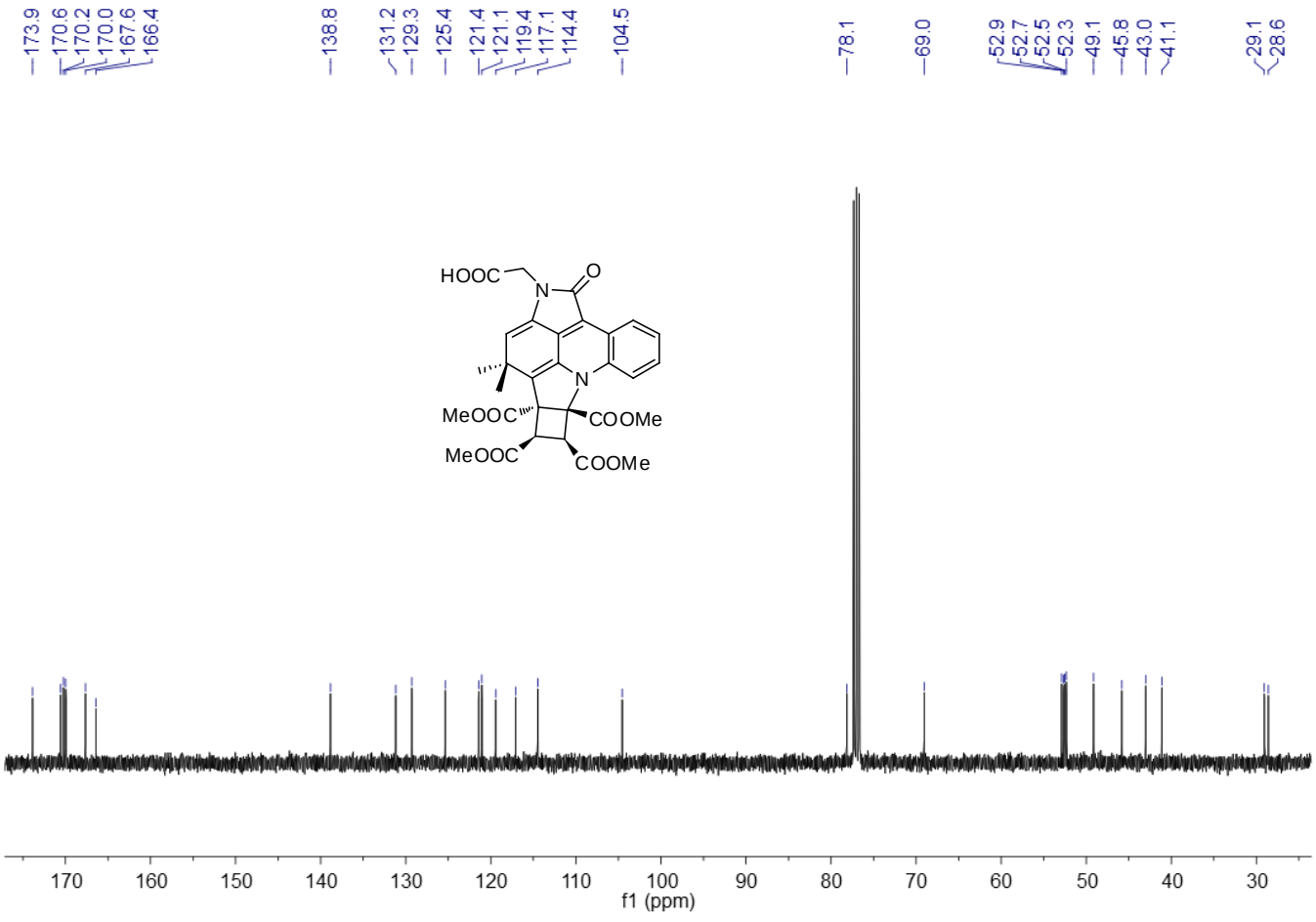
^{1}H NMR Spectrum of Compound 4j



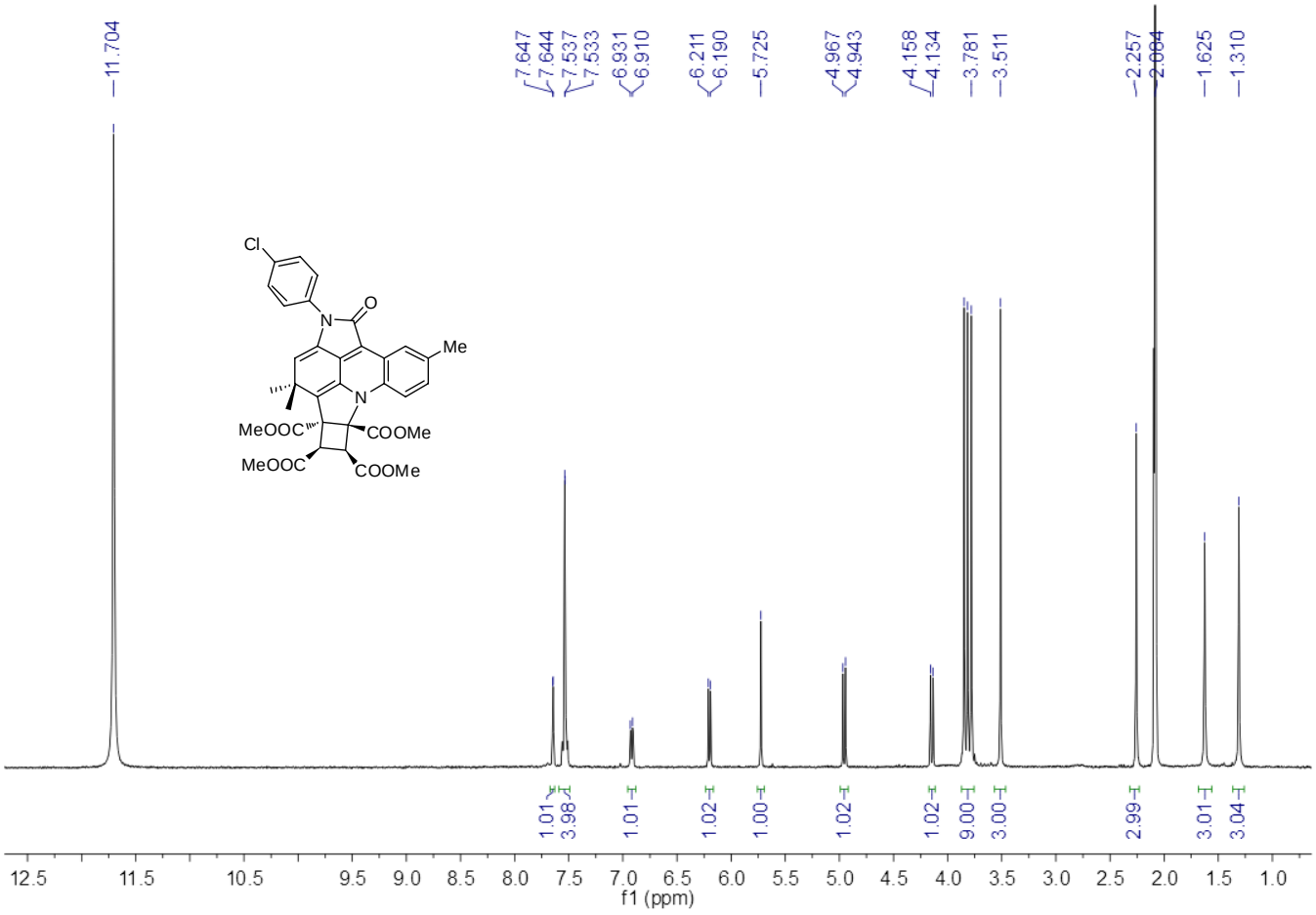
^{13}C NMR Spectrum of Compound 4j



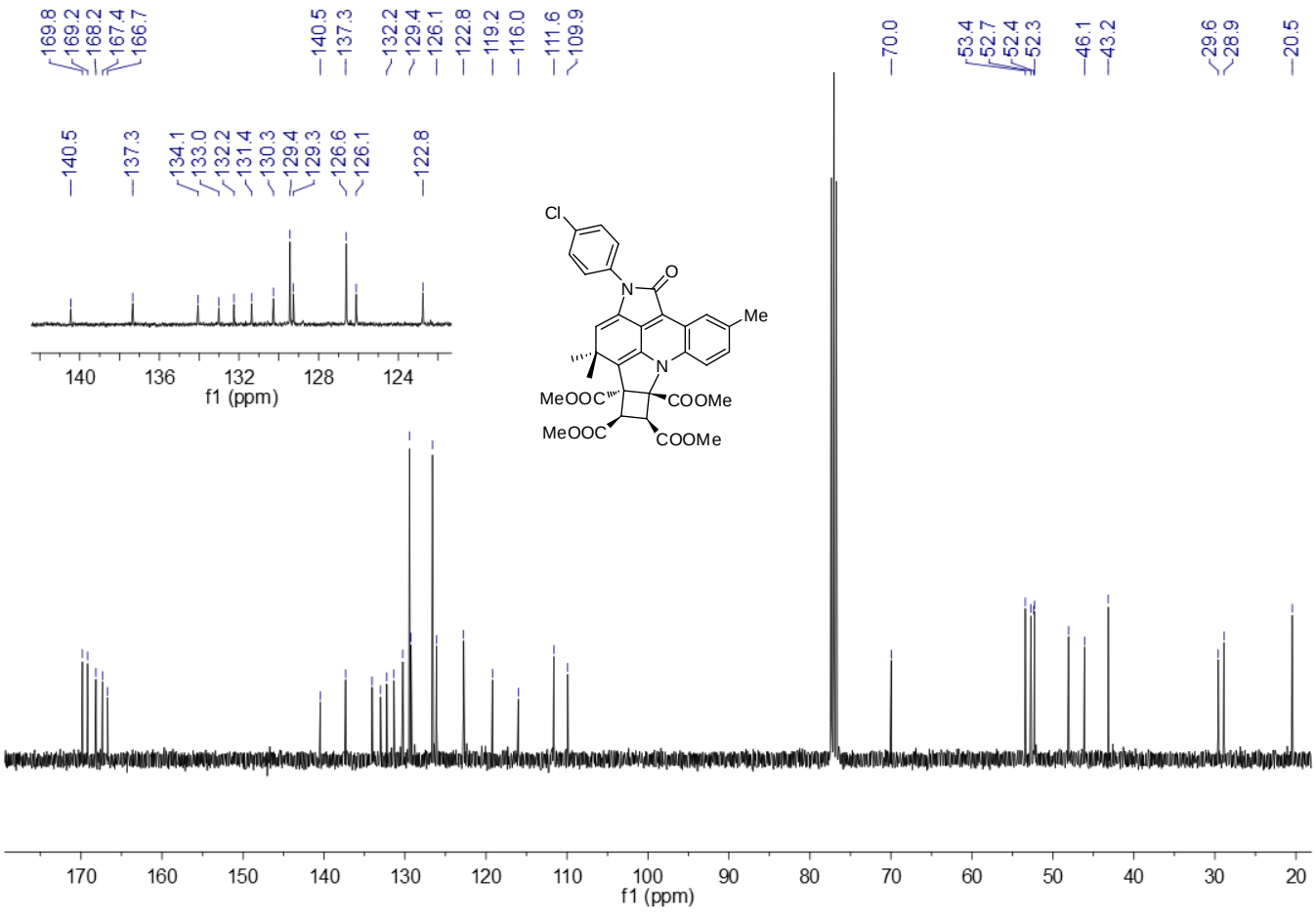
^{1}H NMR Spectrum of Compound 4k



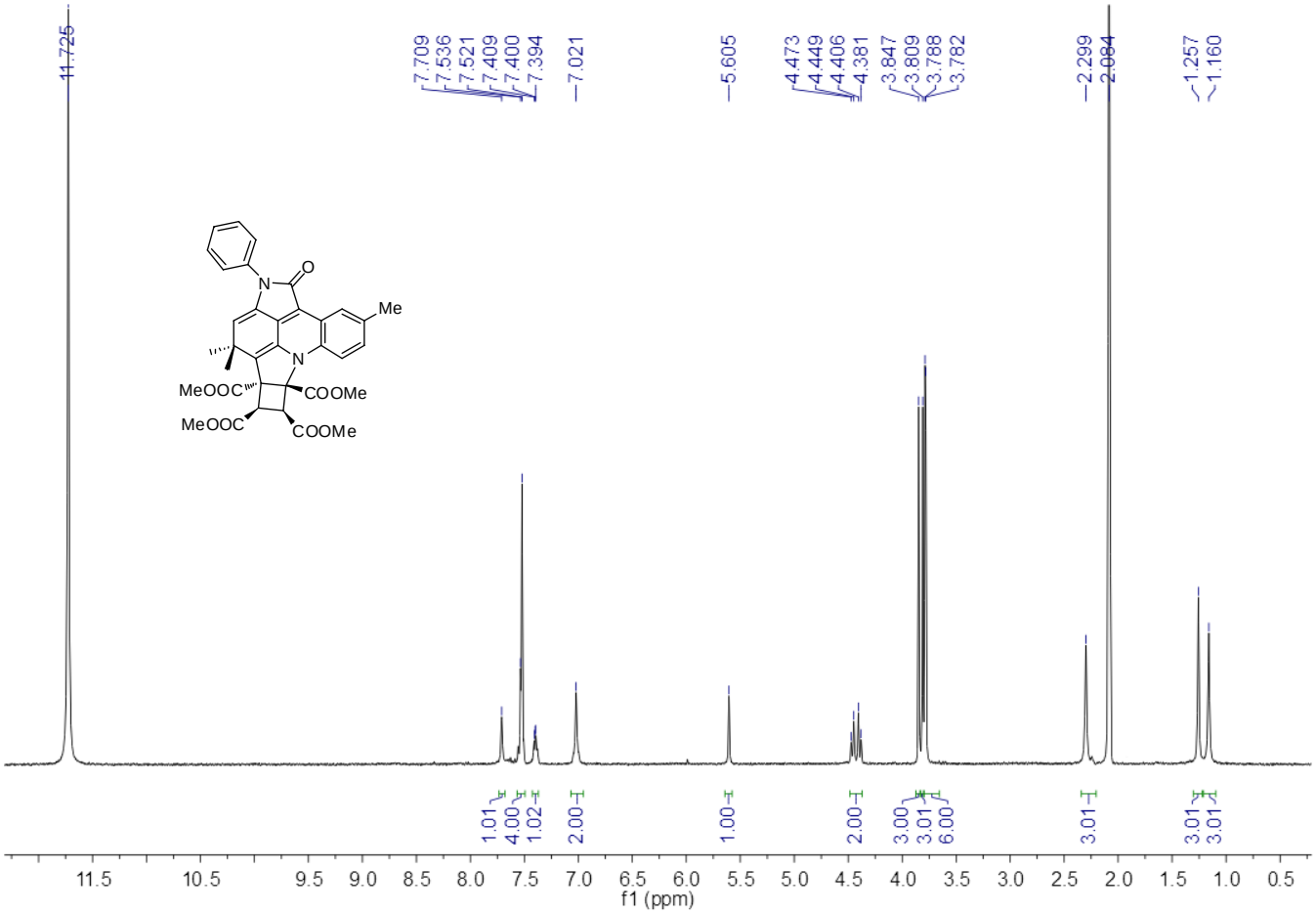
^{13}C NMR Spectrum of Compound 4k



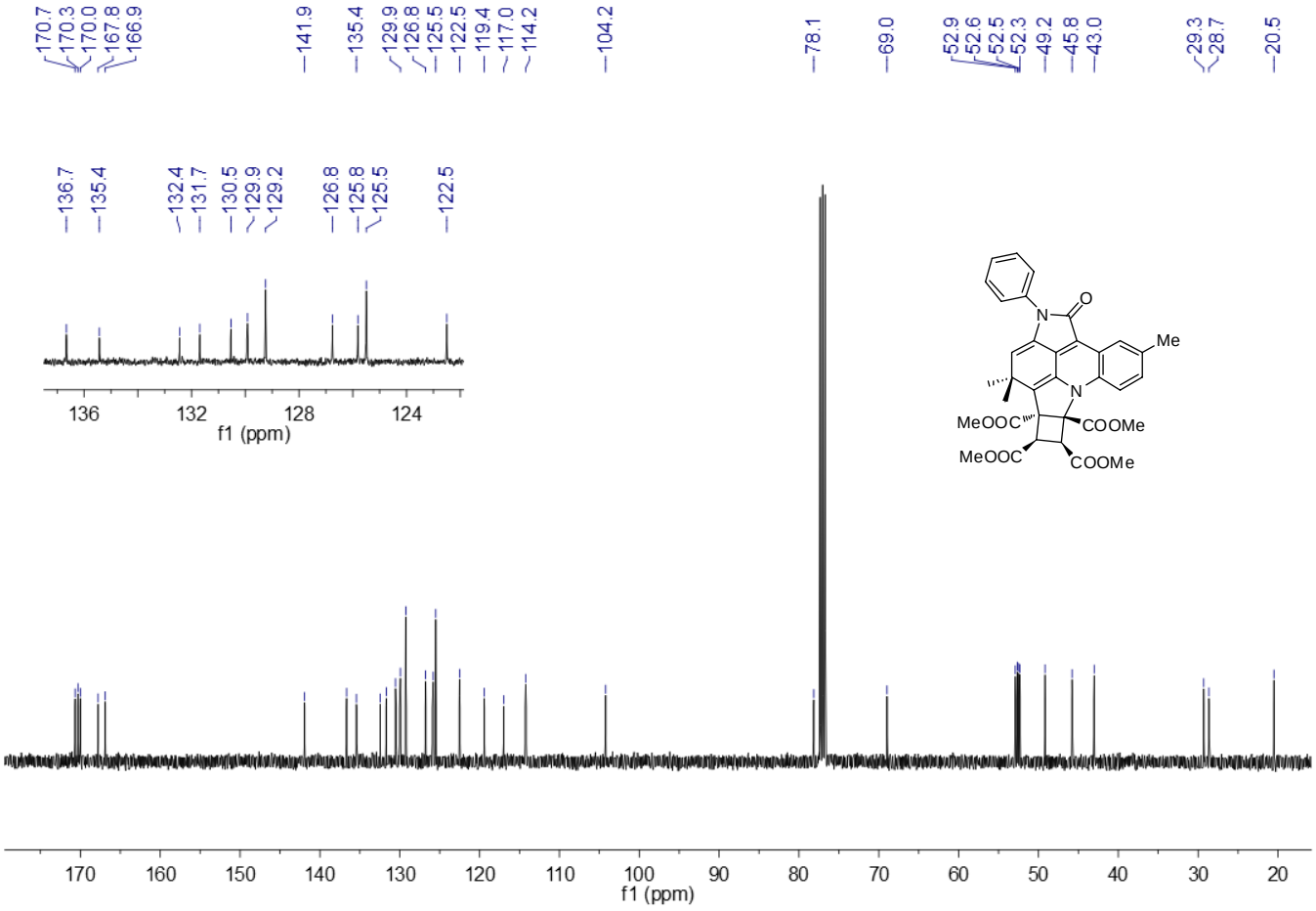
^{1}H NMR Spectrum of Compound 4l



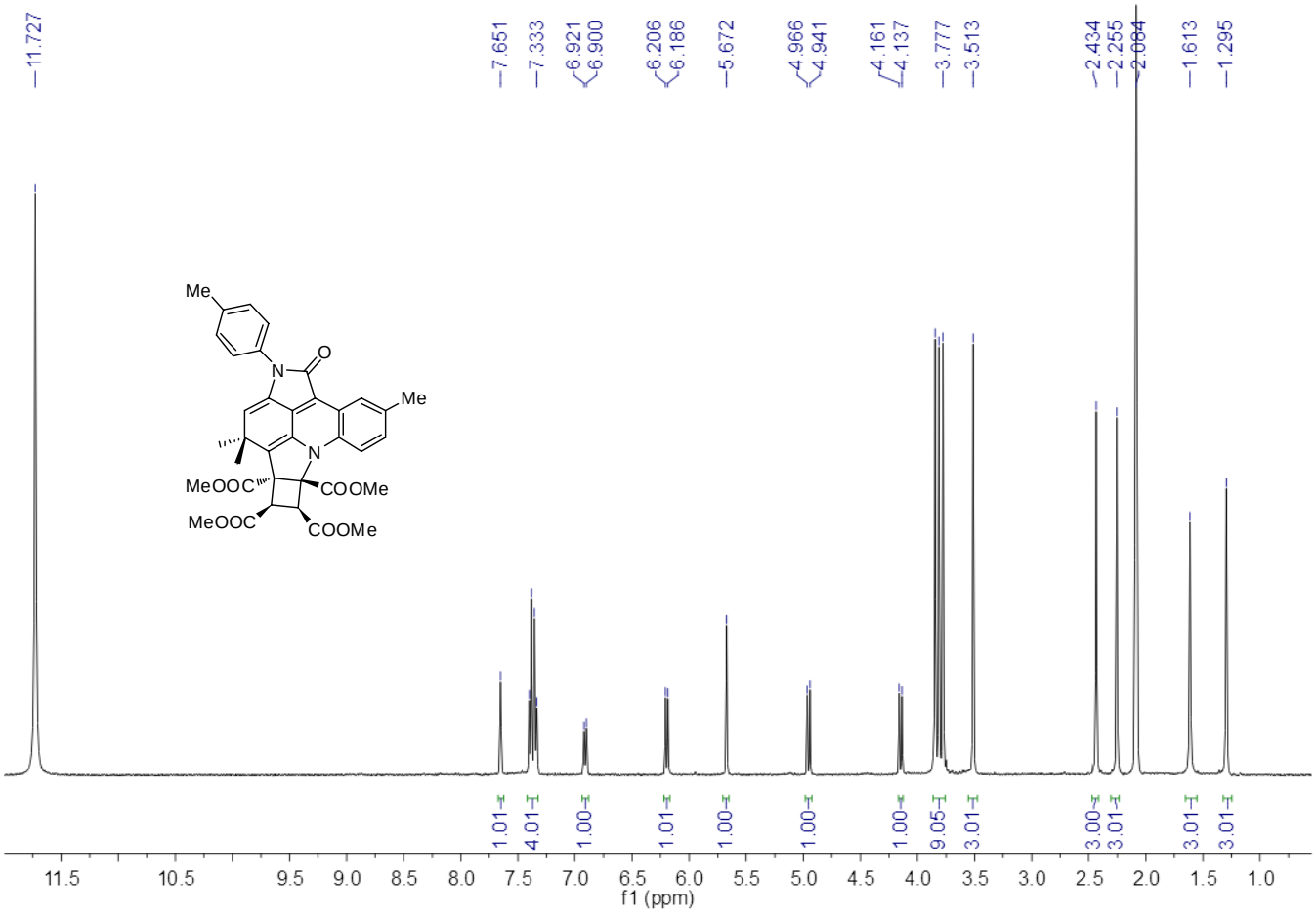
^{13}C NMR Spectrum of Compound 4l



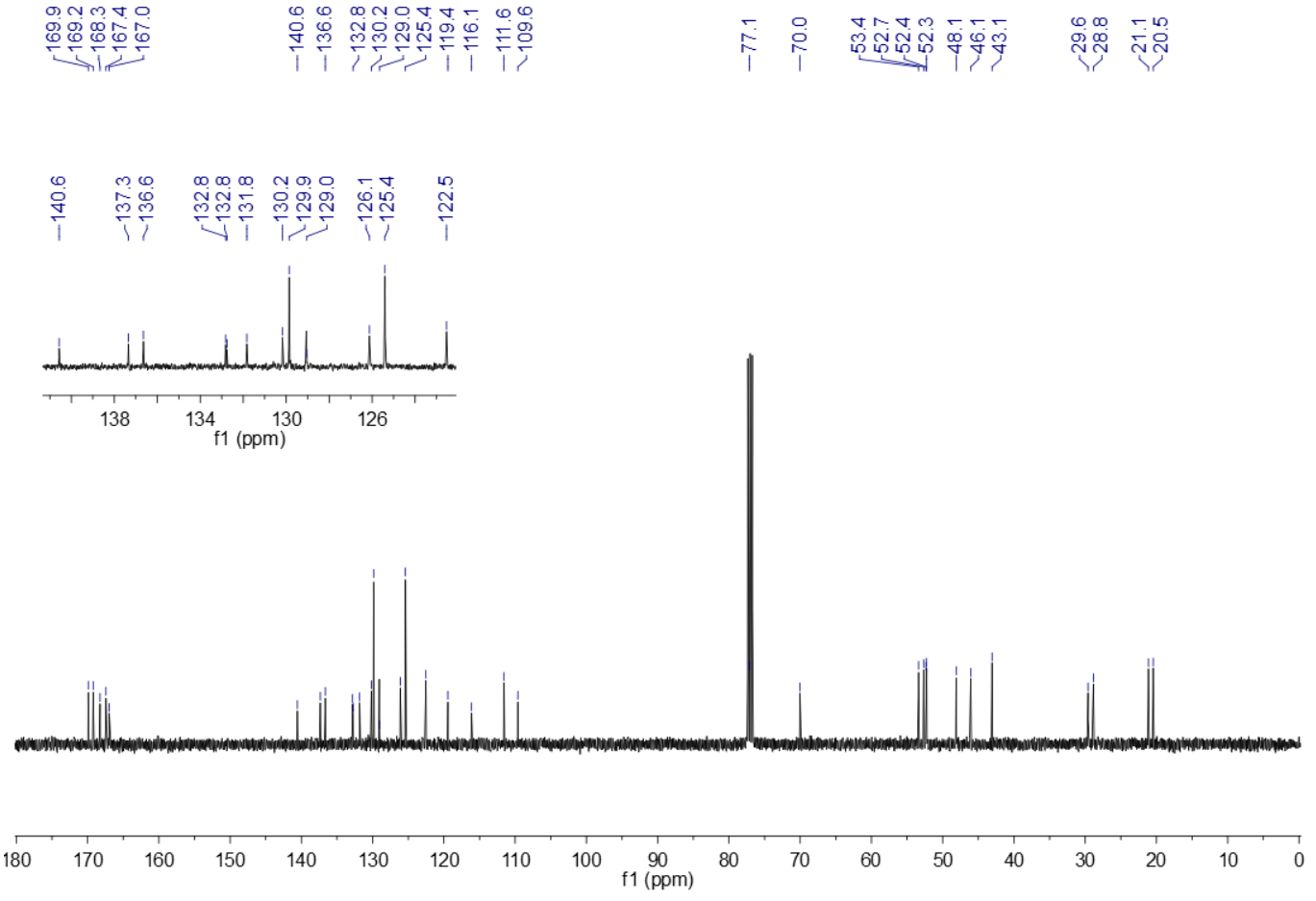
^{1}H NMR Spectrum of Compound 4m



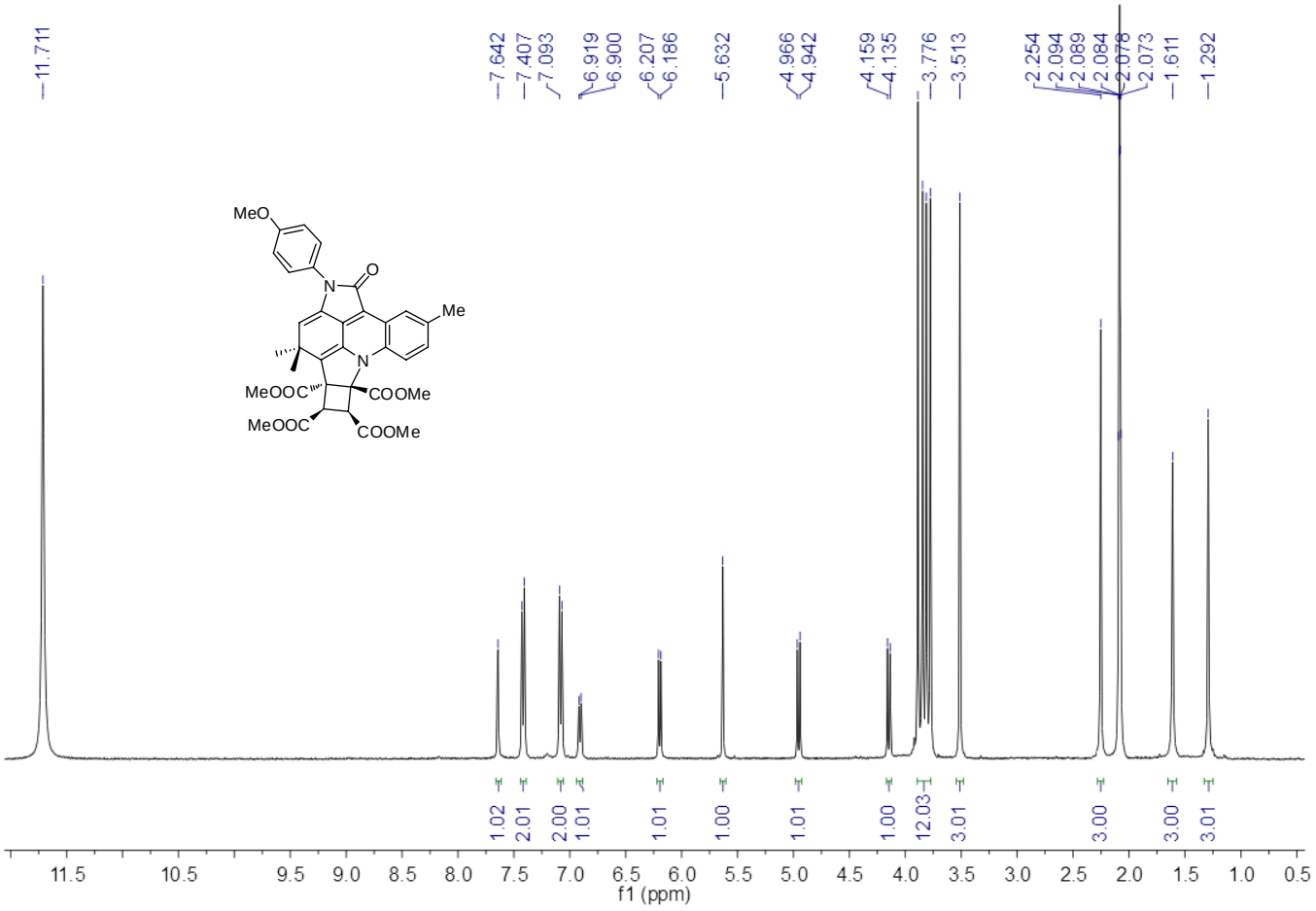
^{13}C NMR Spectrum of Compound 4m



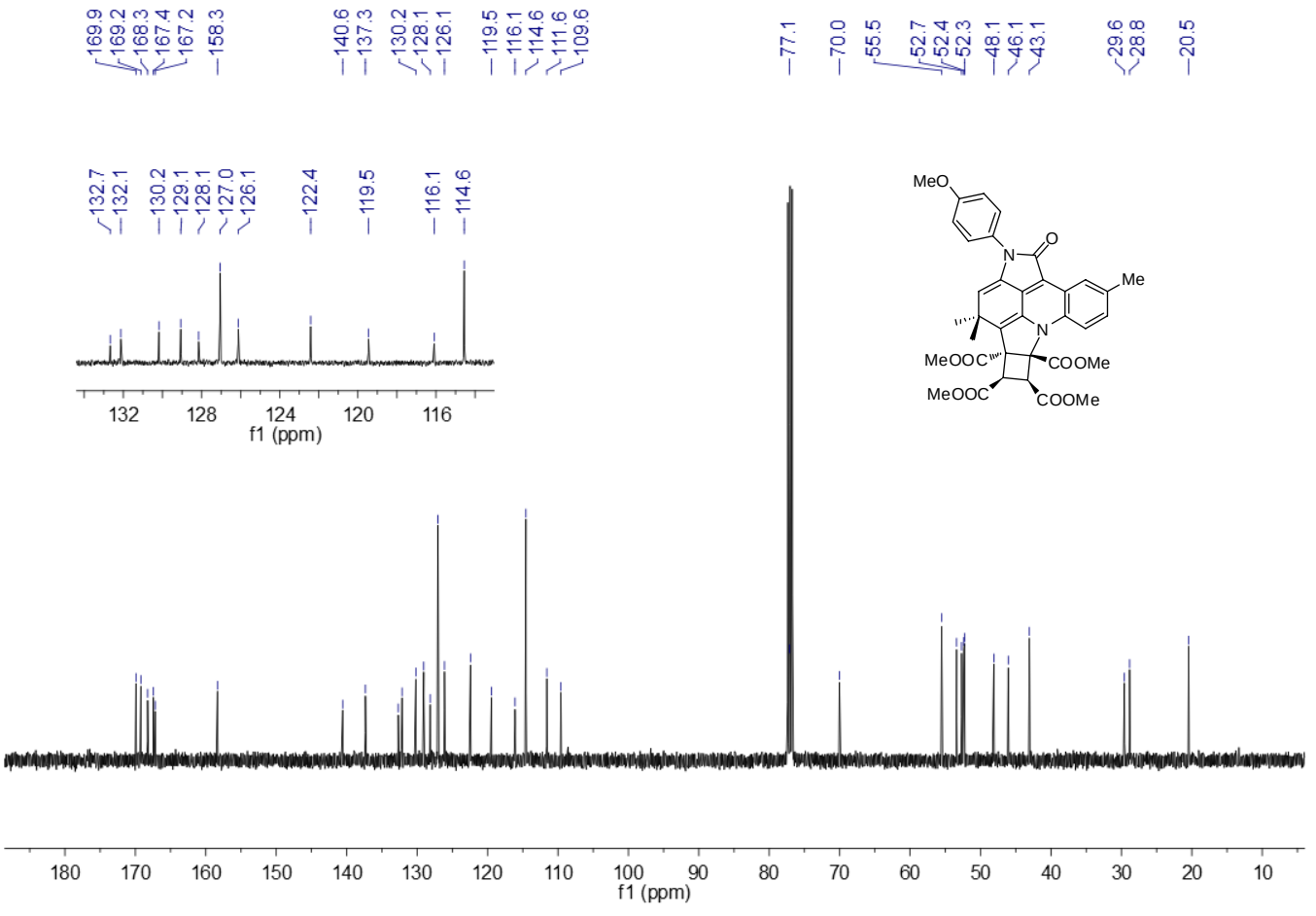
^{1}H NMR Spectrum of Compound 4n



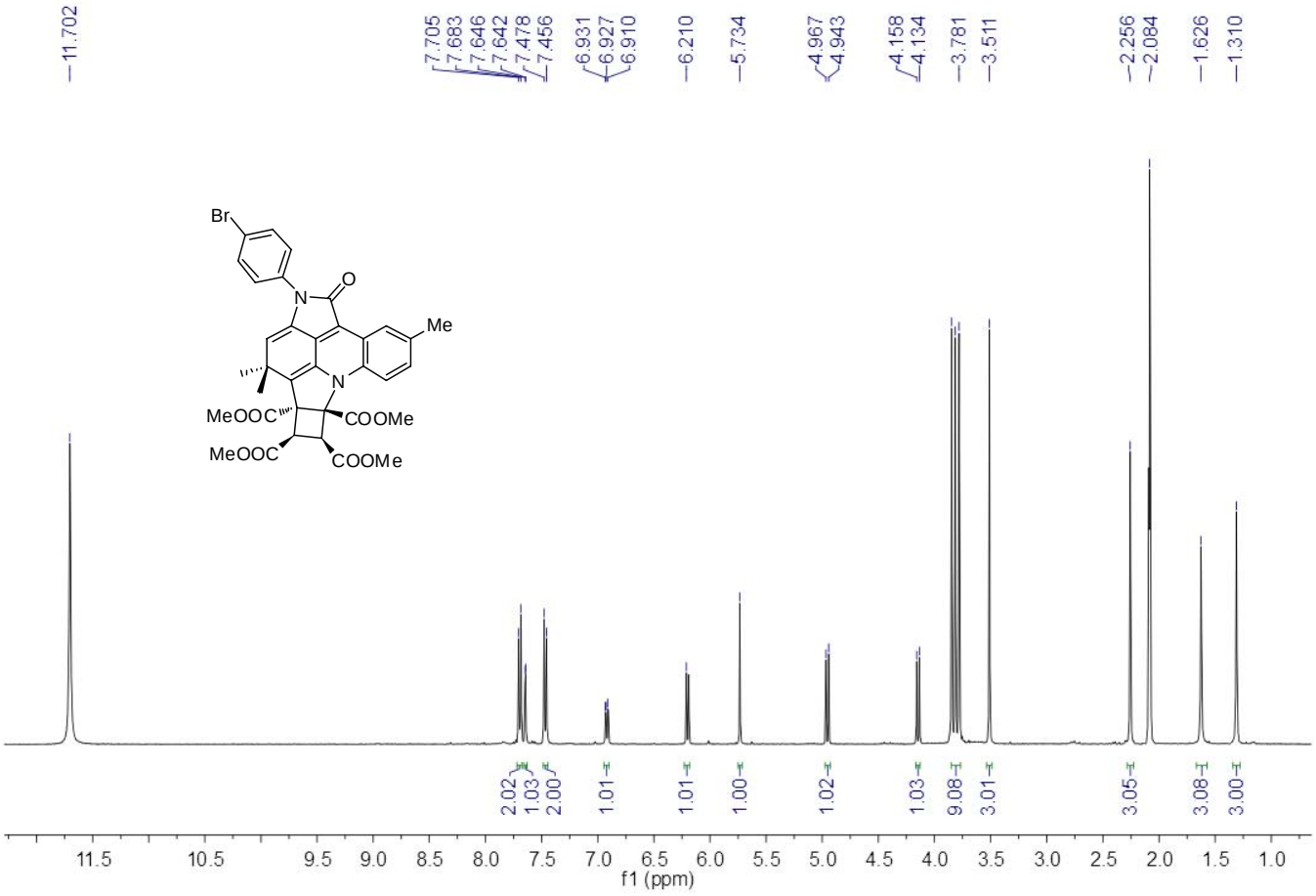
^{13}C NMR Spectrum of Compound 4n



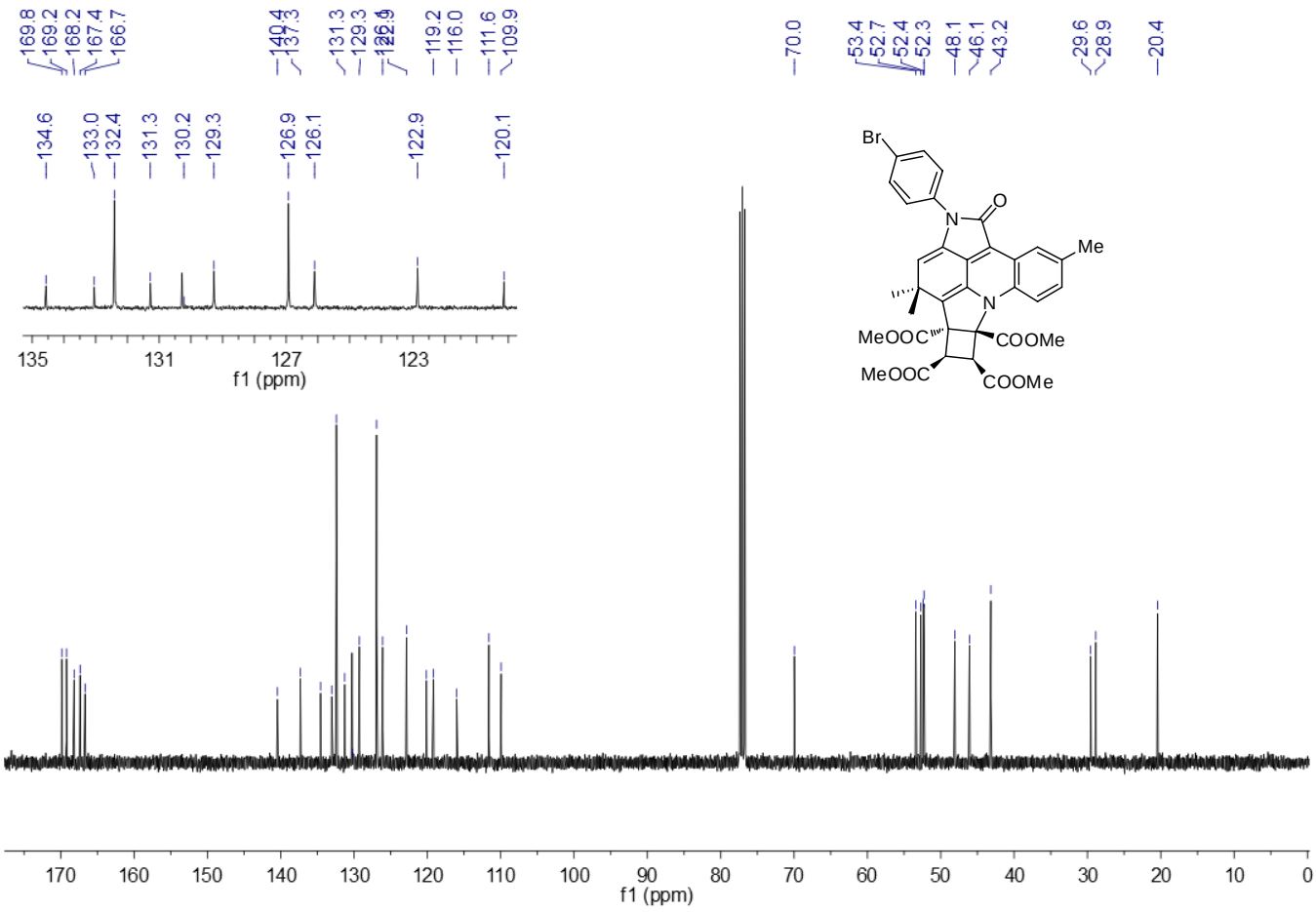
^{1}H NMR Spectrum of Compound 4o



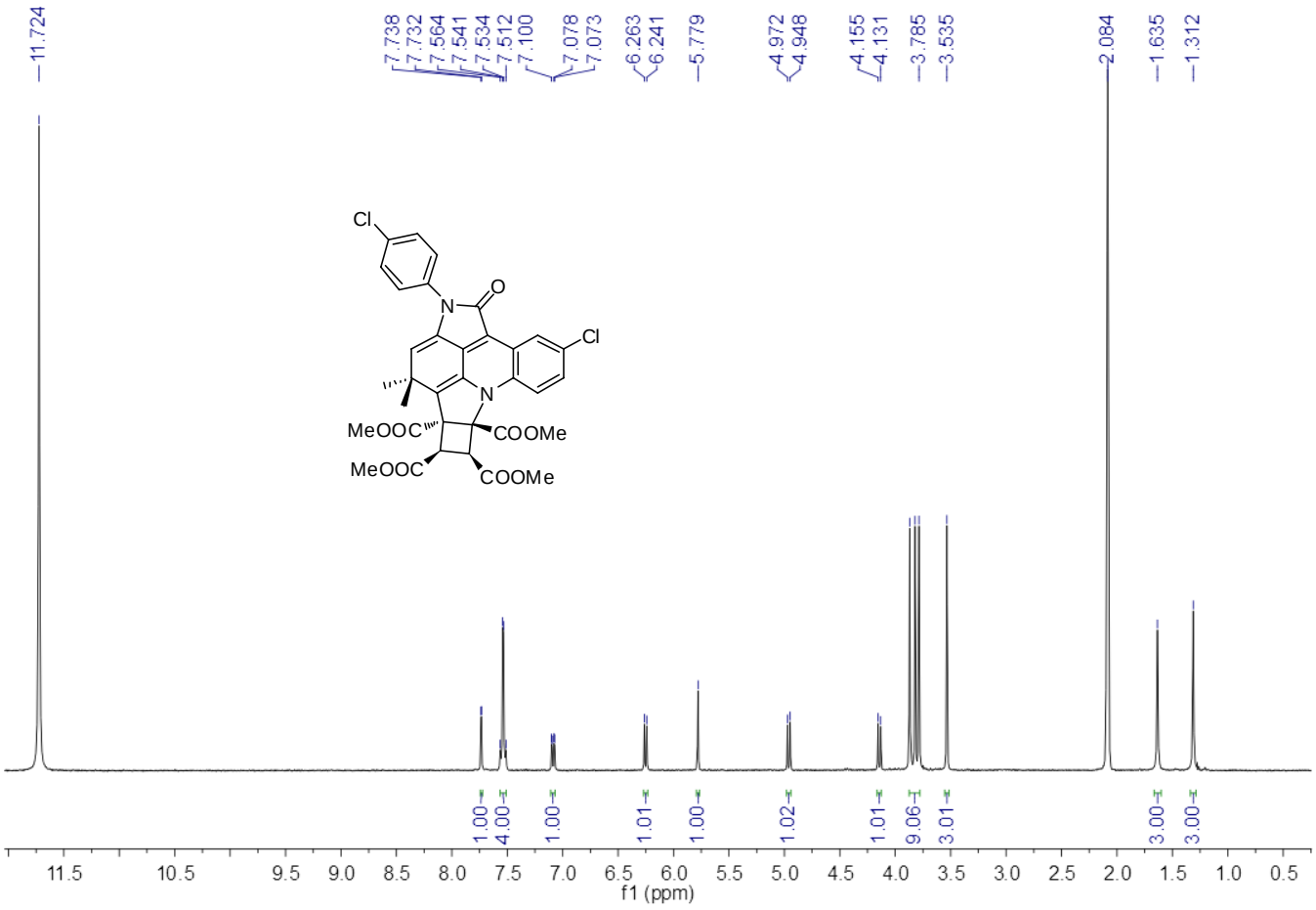
^{13}C NMR Spectrum of Compound 4o



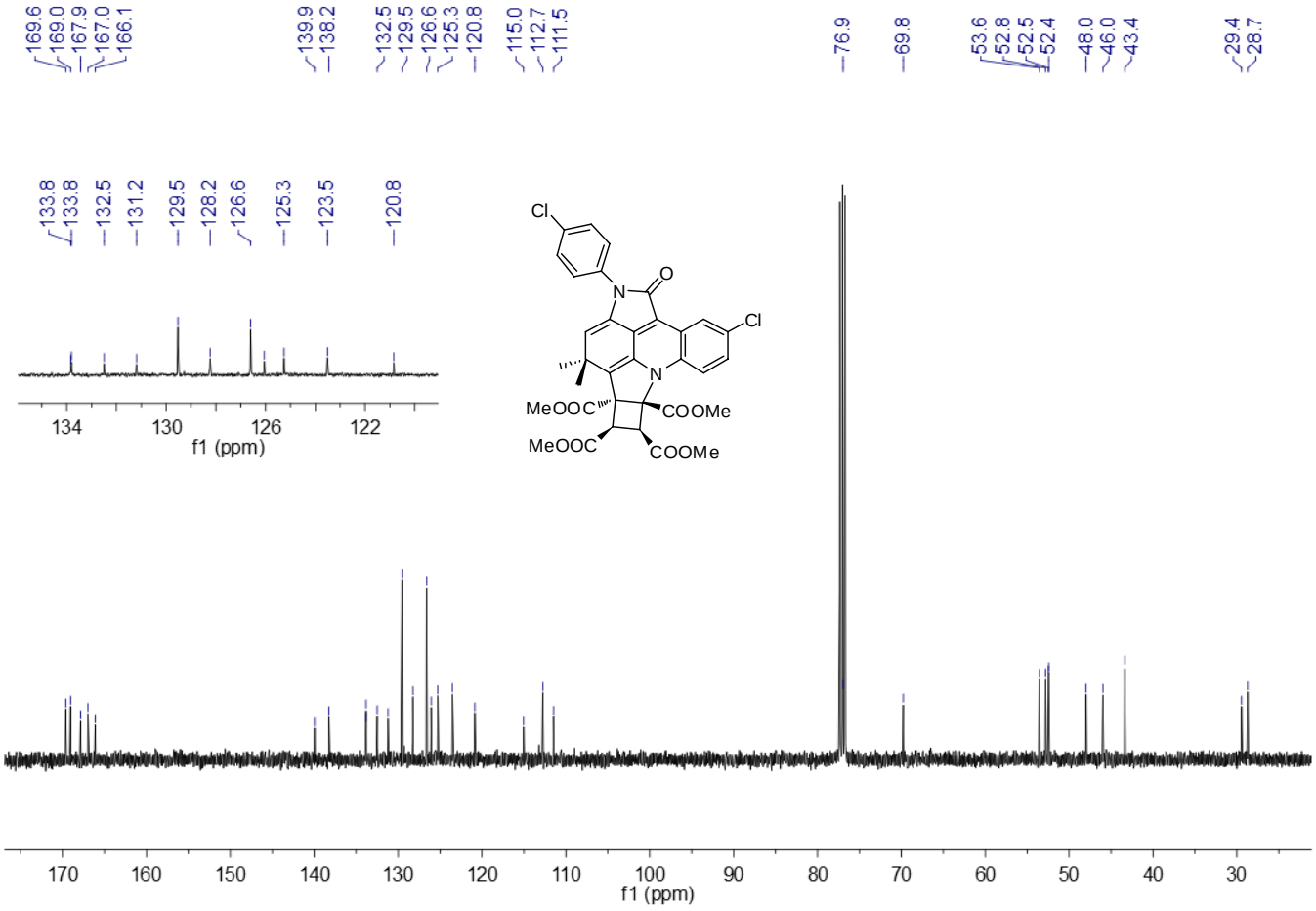
^{1}H NMR Spectrum of Compound 4p



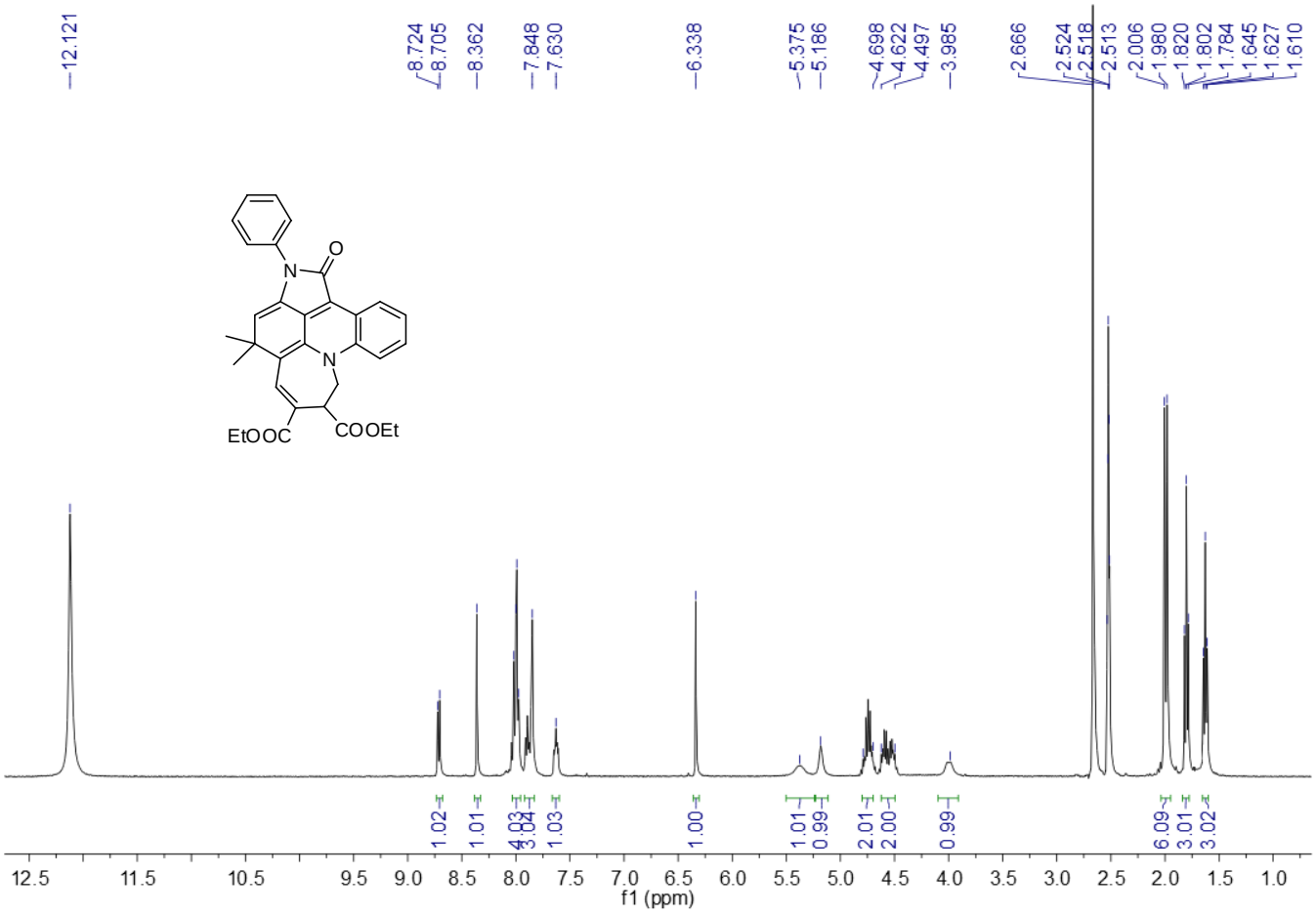
^{13}C NMR Spectrum of Compound 4p



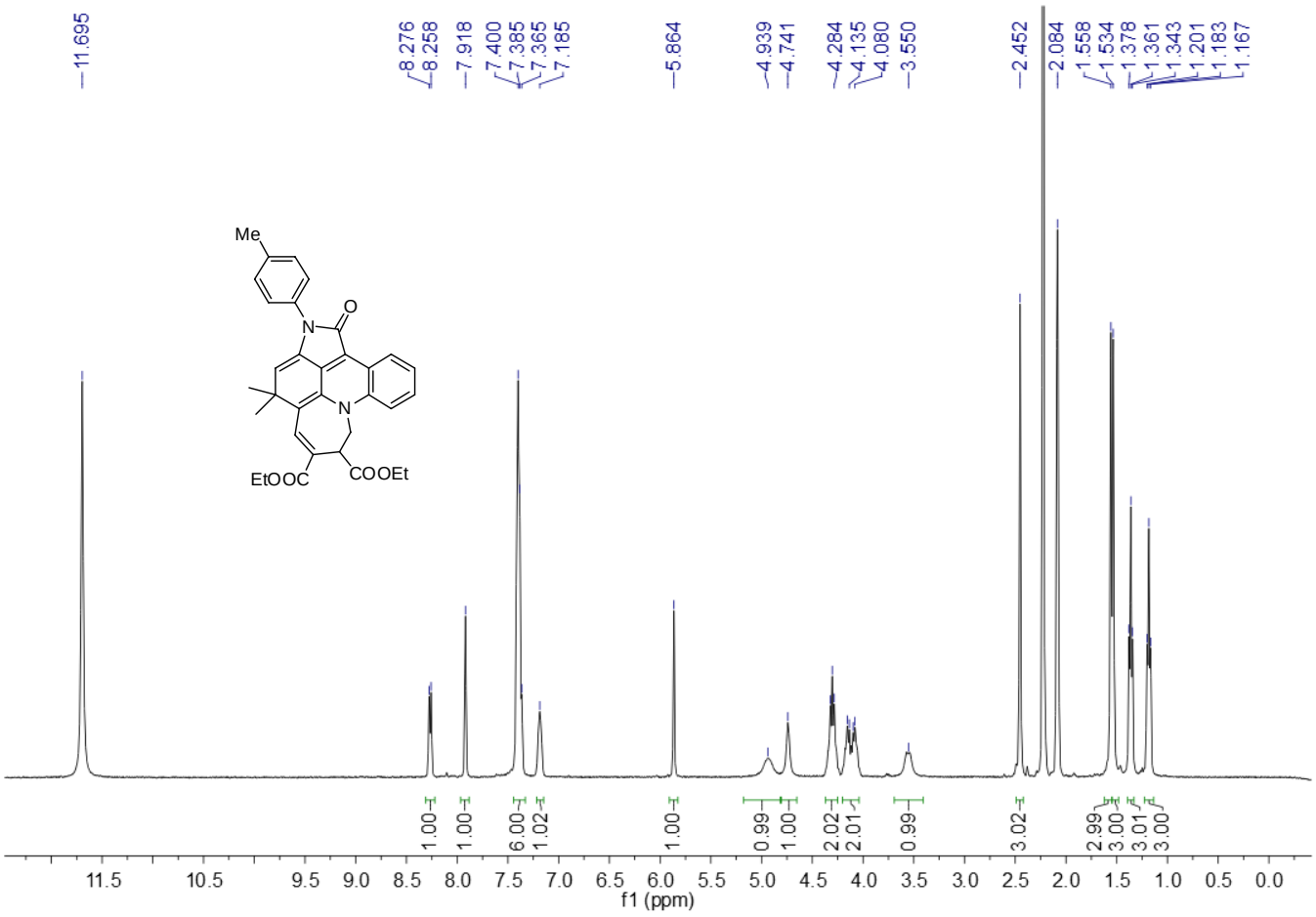
^{1}H NMR Spectrum of Compound 4q



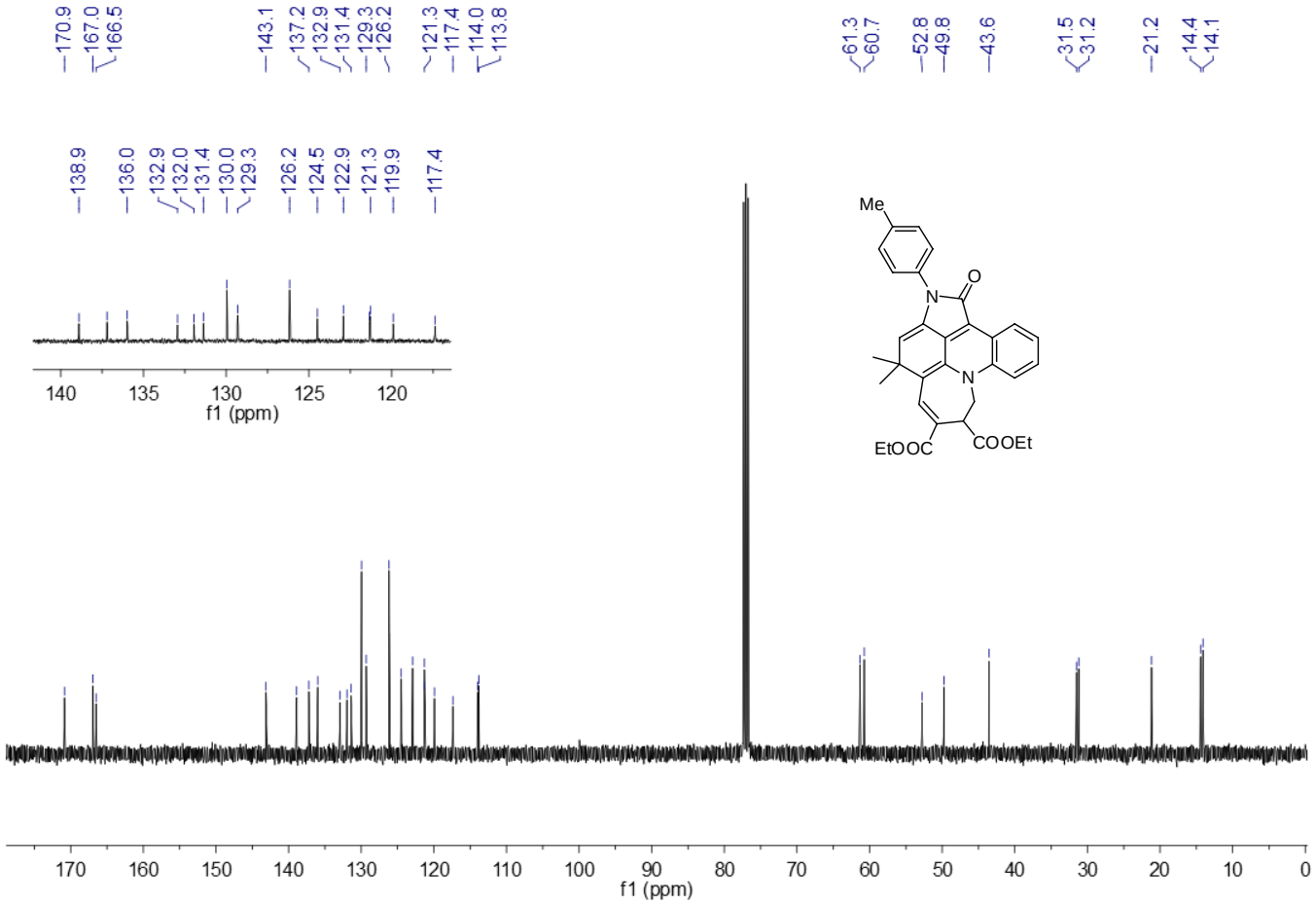
^{13}C NMR Spectrum of Compound 4q



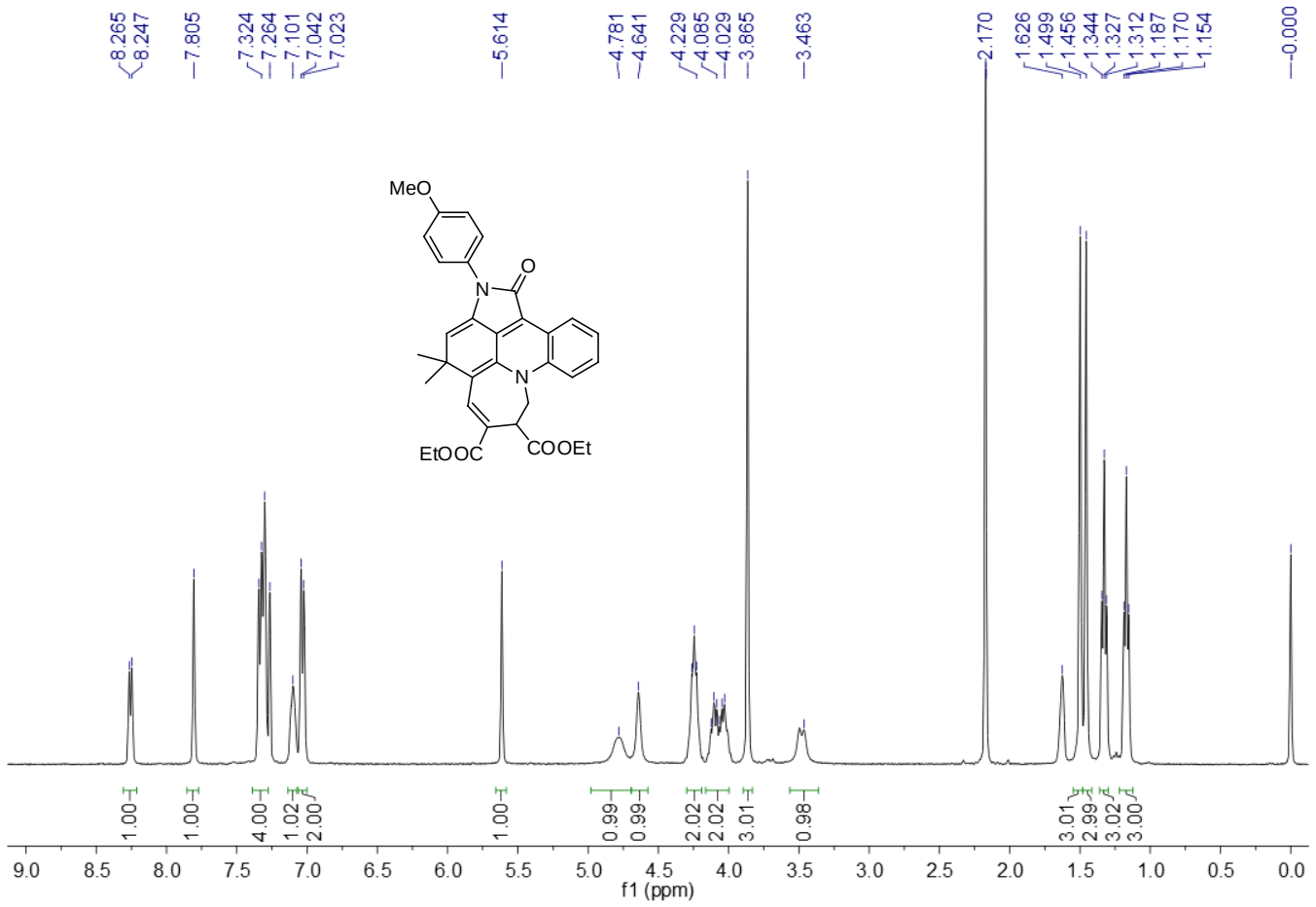
^{1}H NMR Spectrum of Compound 5a



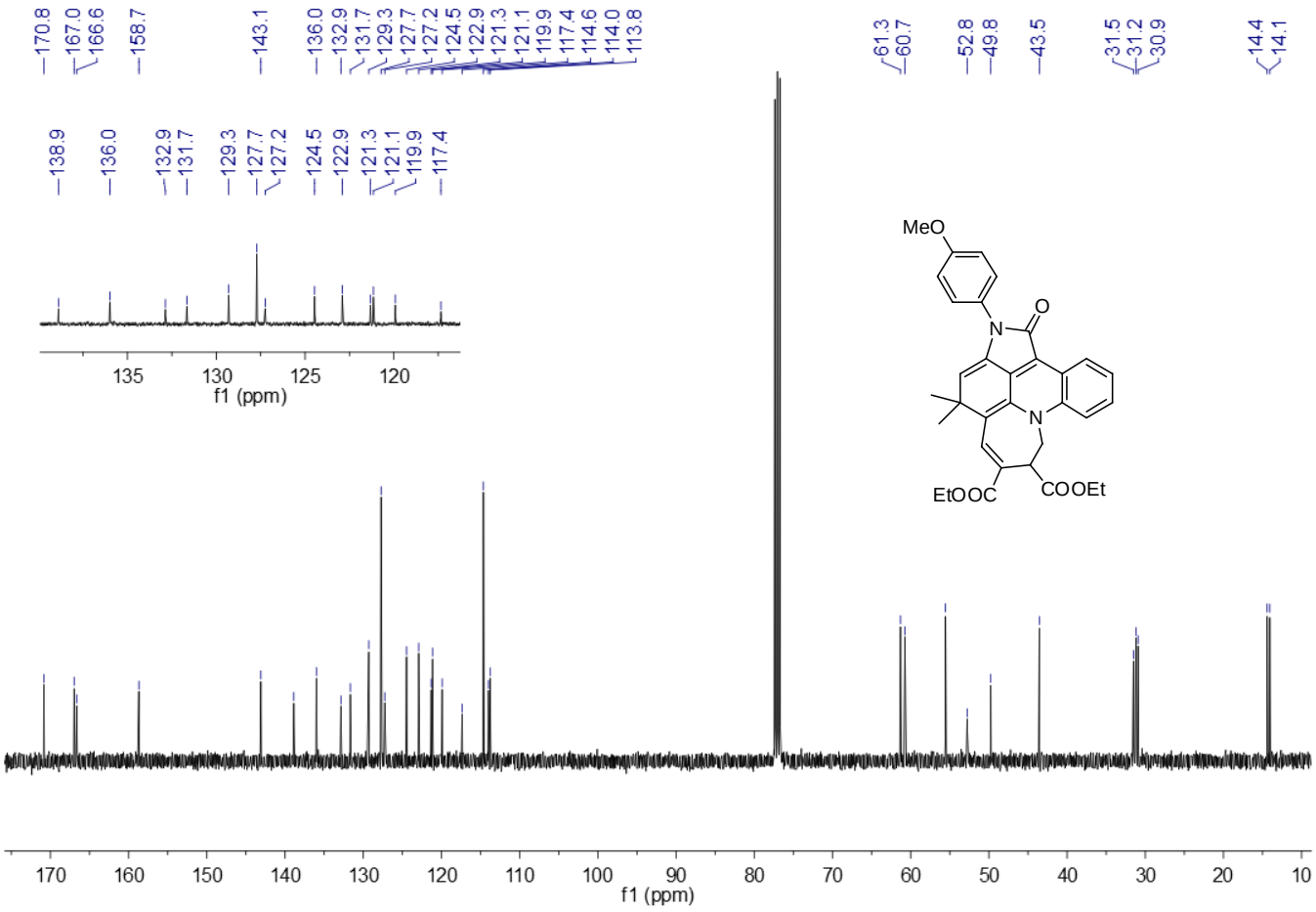
^{1}H NMR Spectrum of Compound 5b



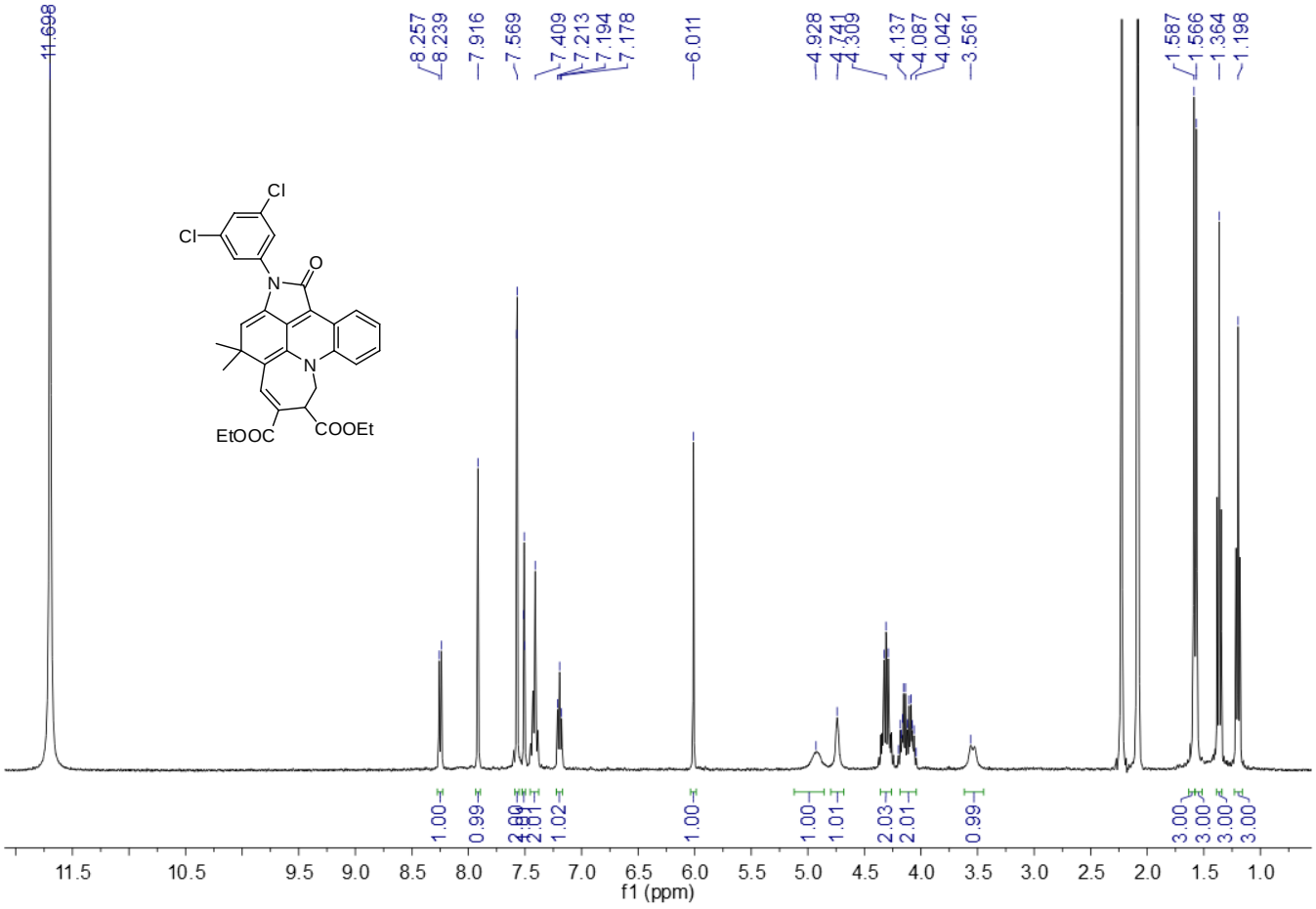
^{13}C NMR Spectrum of Compound 5b



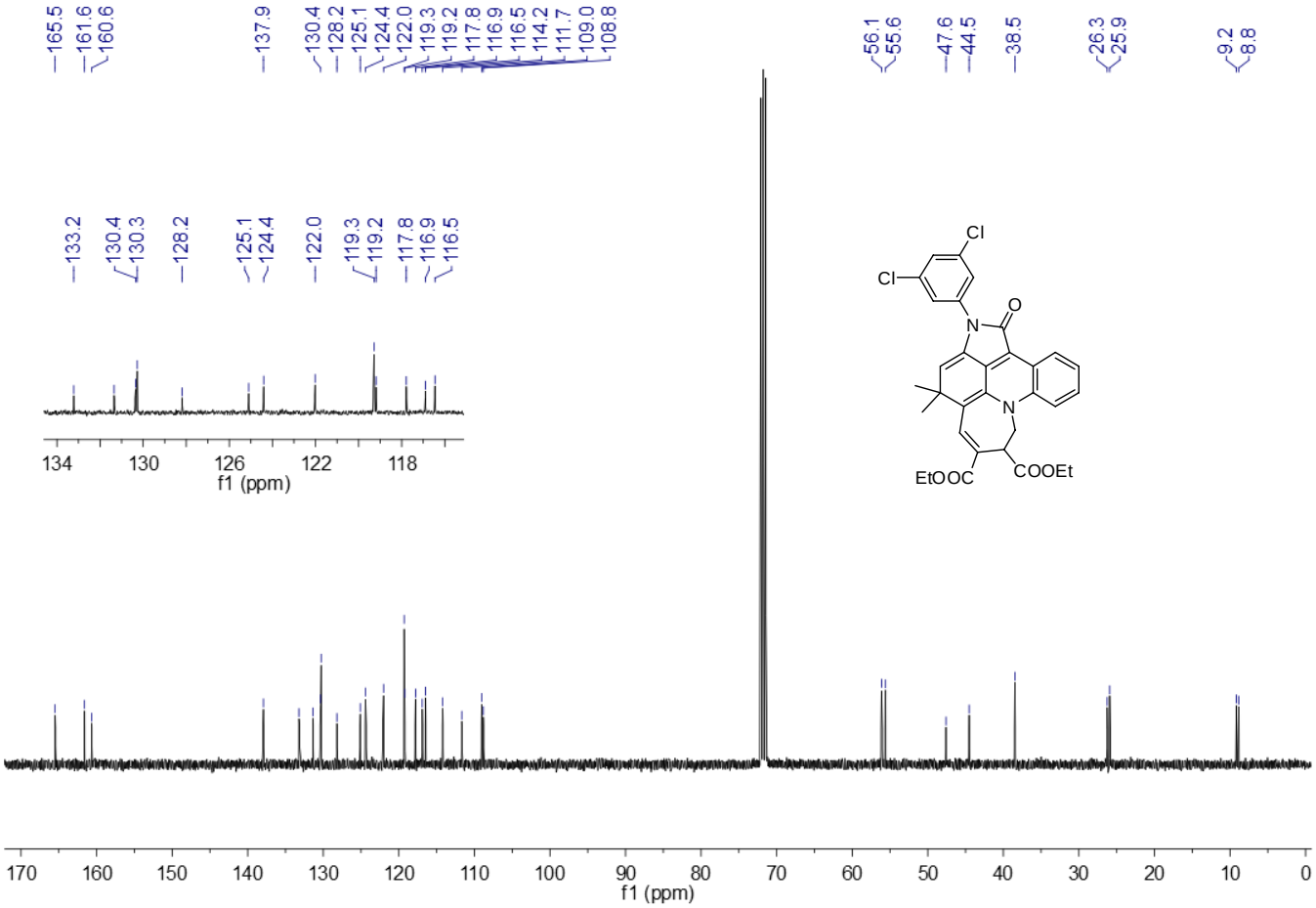
^{1}H NMR Spectrum of Compound 5c



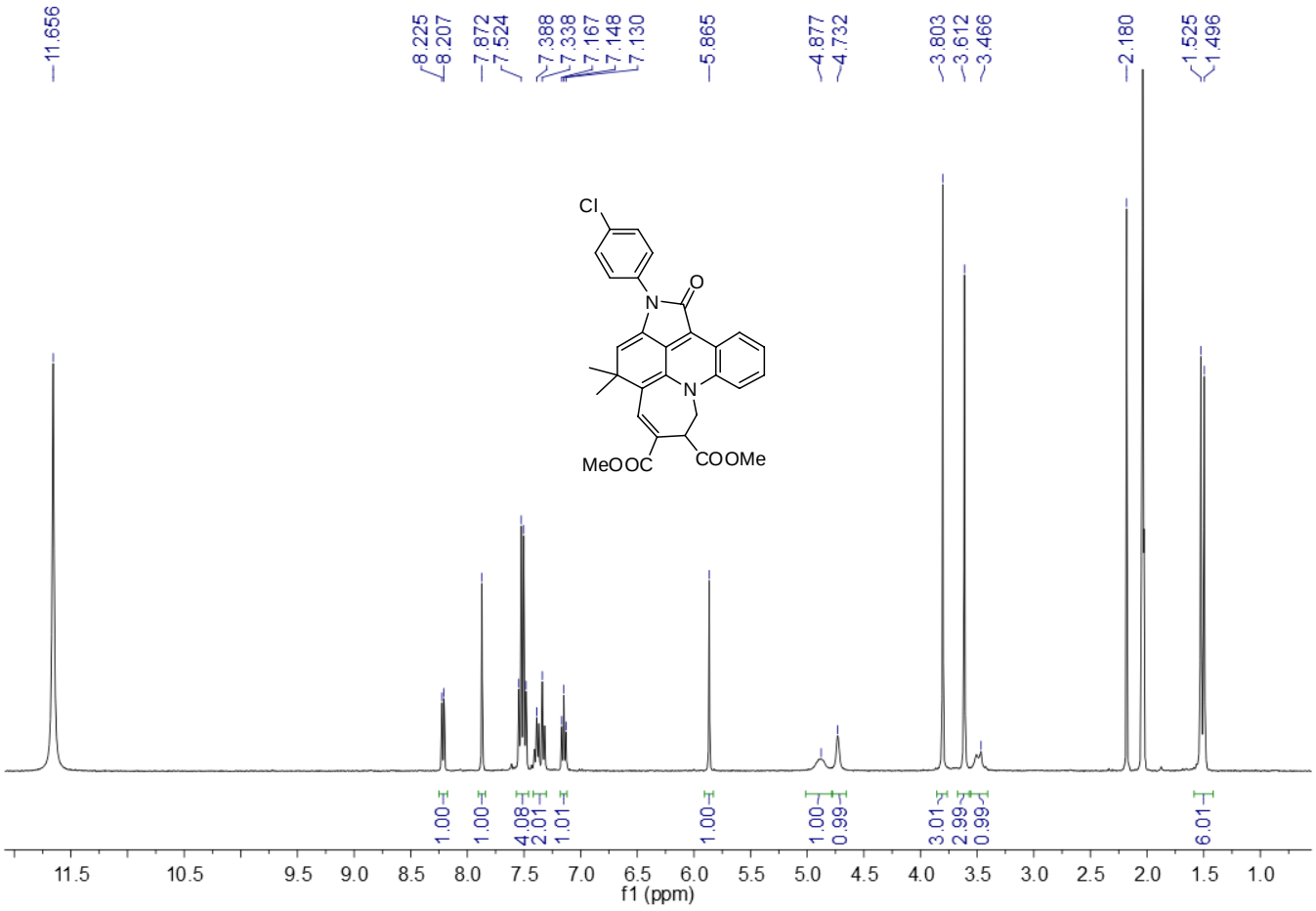
^{13}C NMR Spectrum of Compound 5c



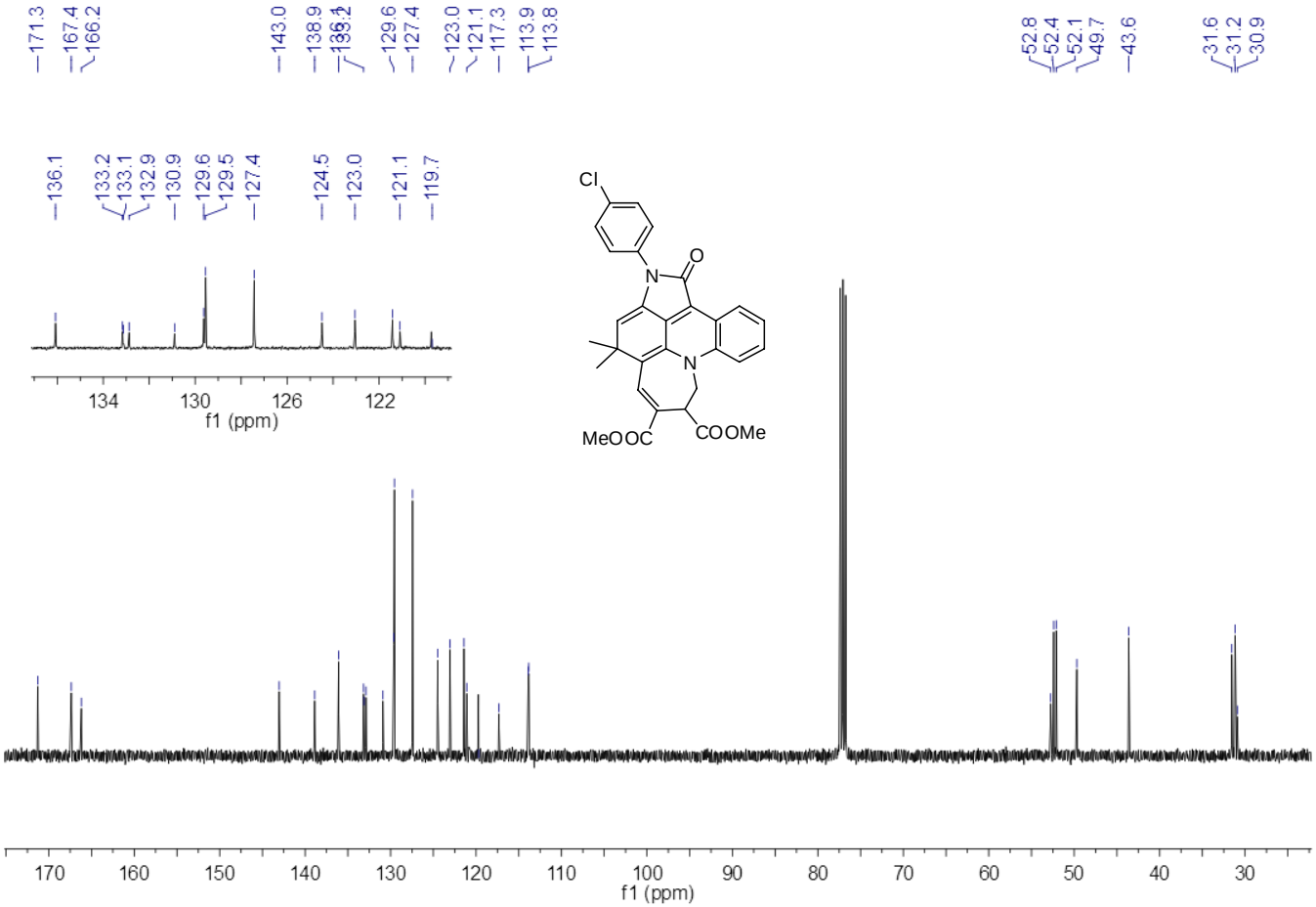
^{1}H NMR Spectrum of Compound 5d



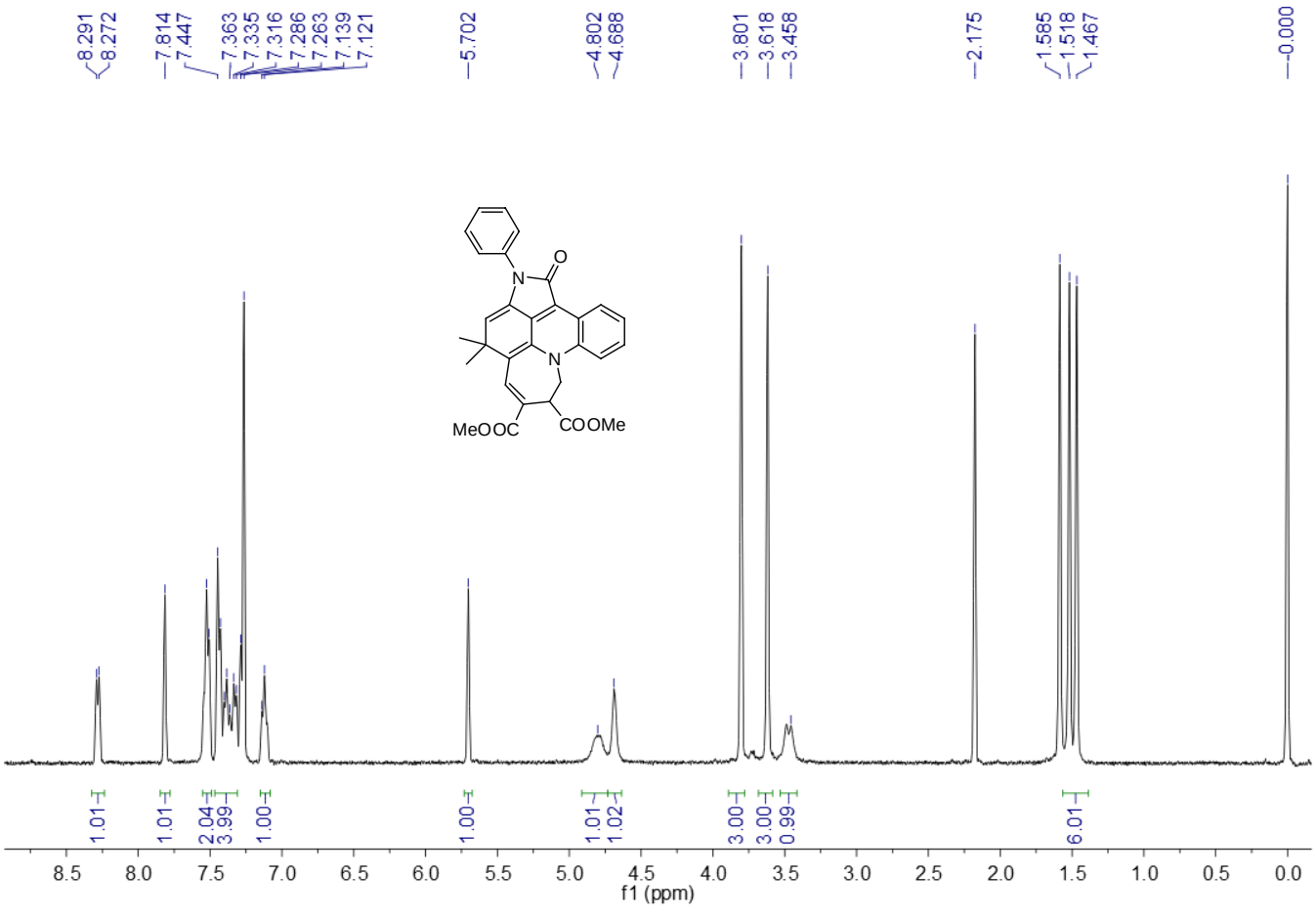
^{13}C NMR Spectrum of Compound 5d



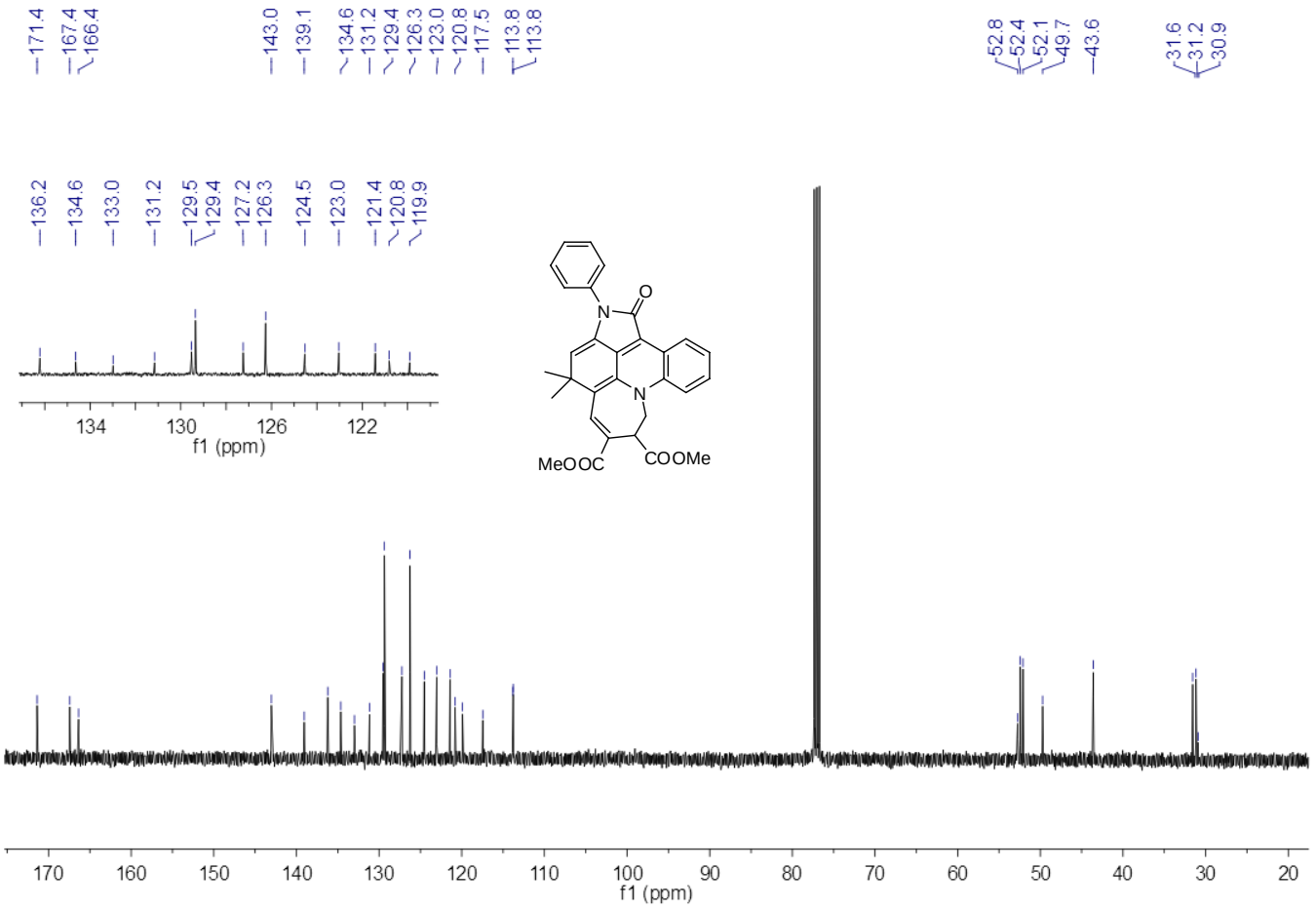
^{1}H NMR Spectrum of Compound 5e



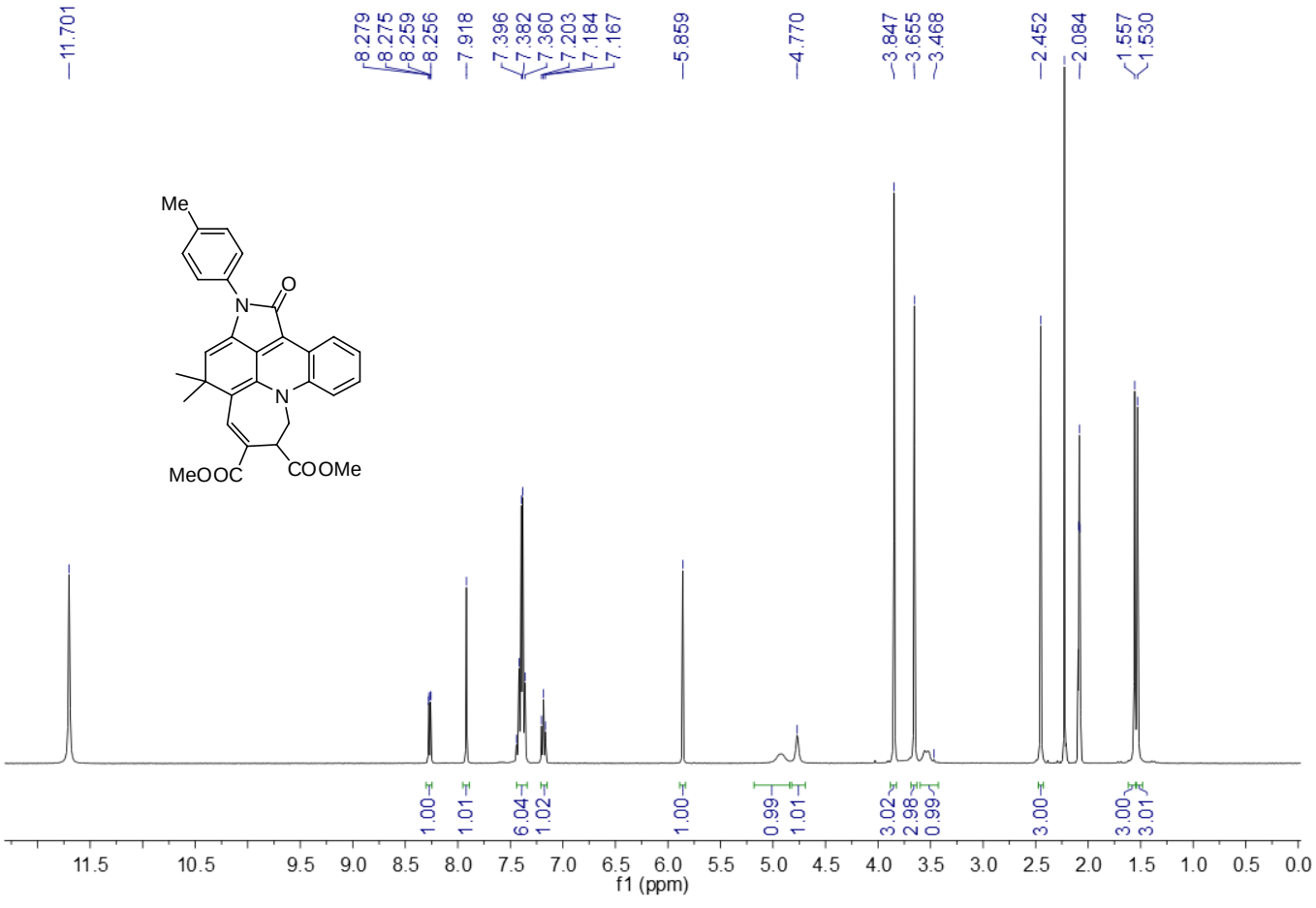
^{13}C NMR Spectrum of Compound 5e



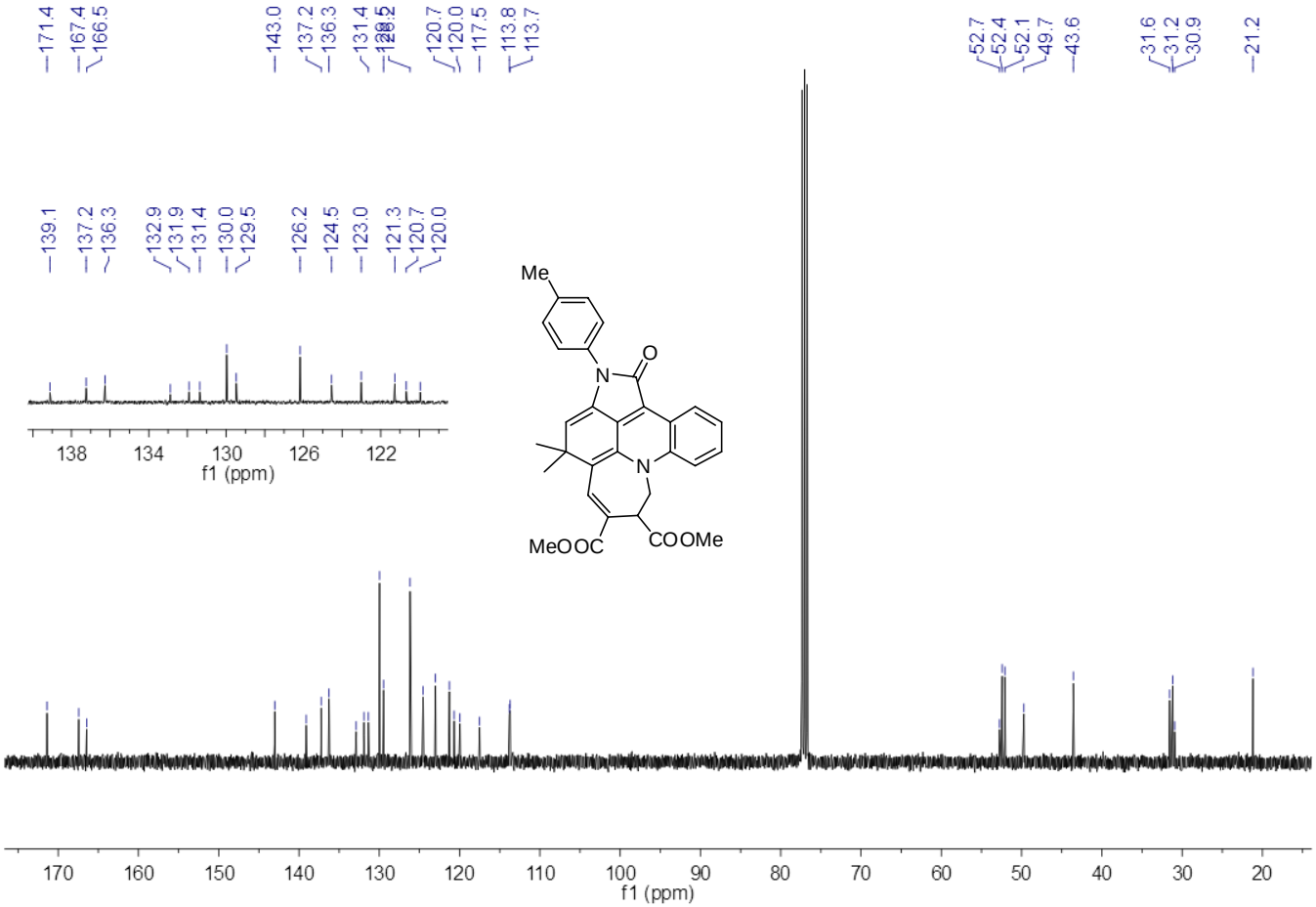
^{1}H NMR Spectrum of Compound 5f



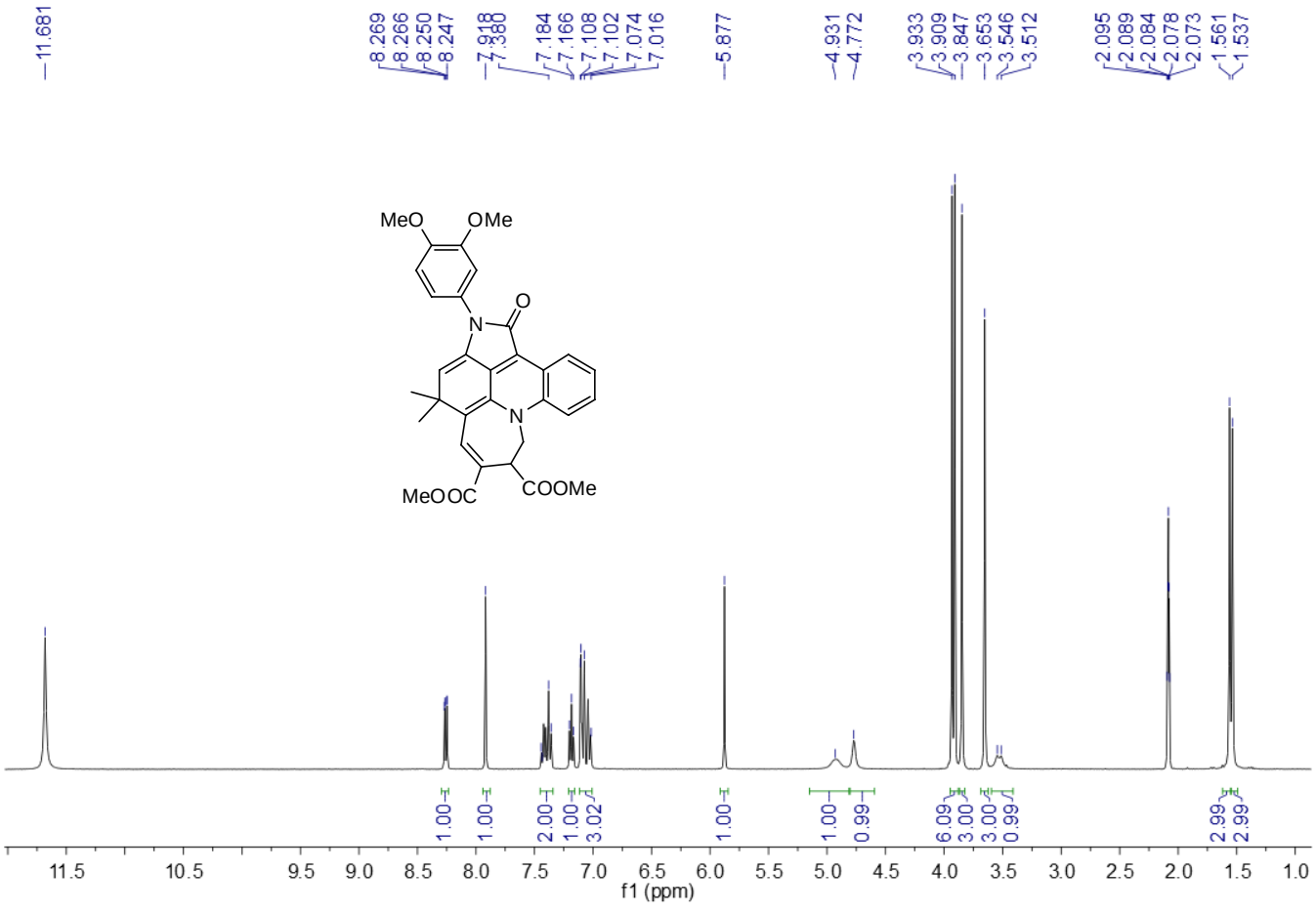
^{13}C NMR Spectrum of Compound 5f



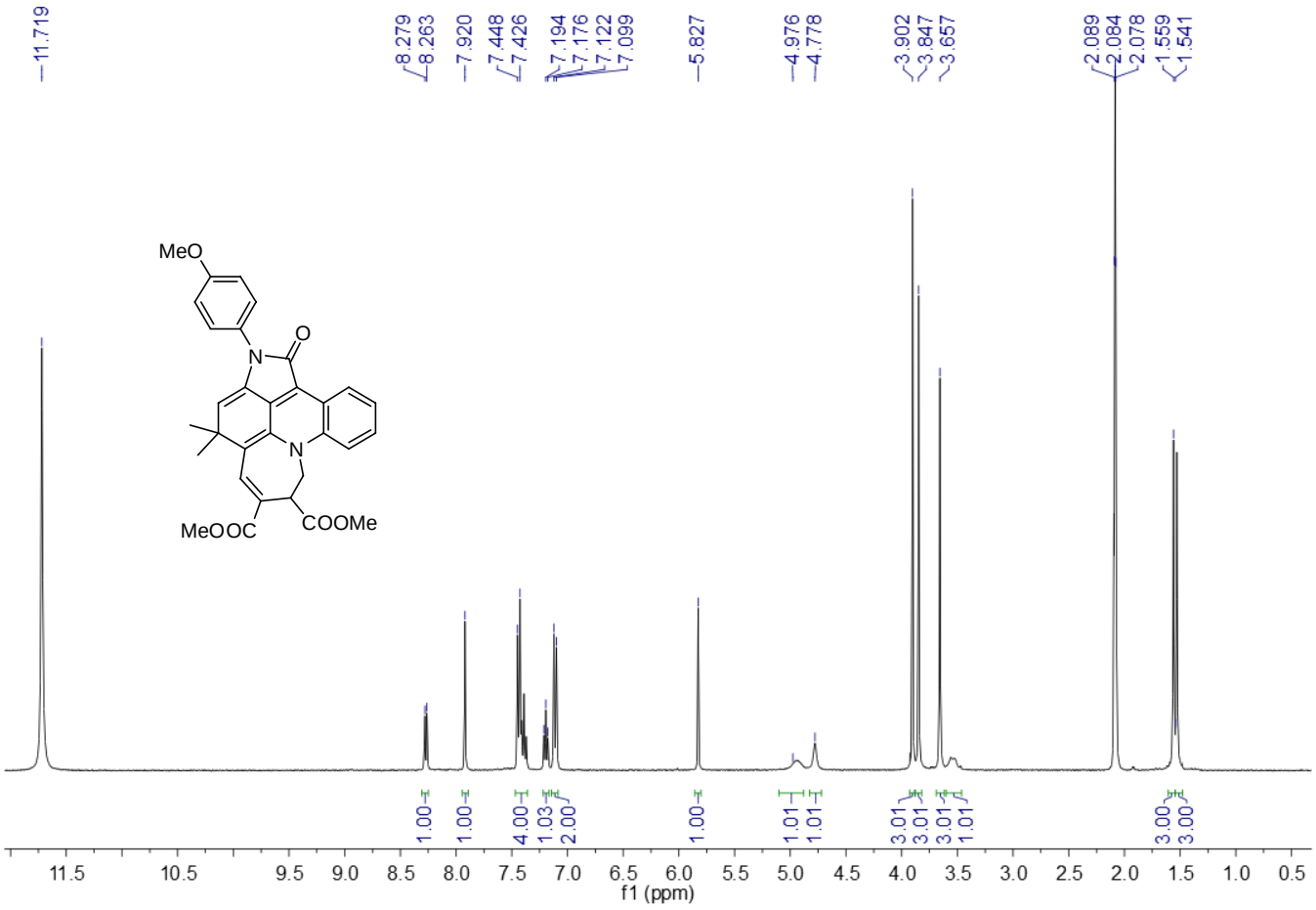
^{1}H NMR Spectrum of Compound 5g



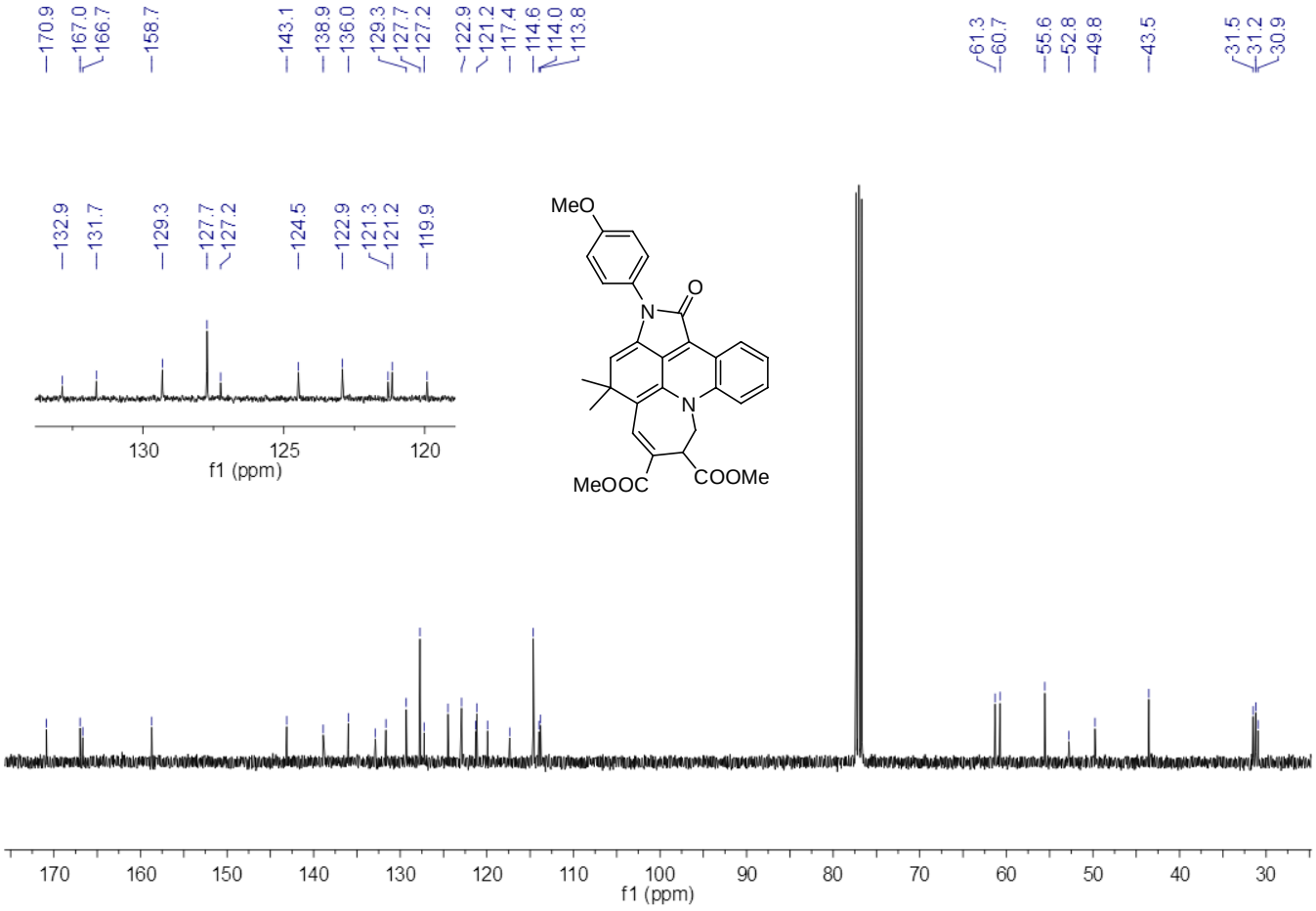
^{13}C NMR Spectrum of Compound 5g



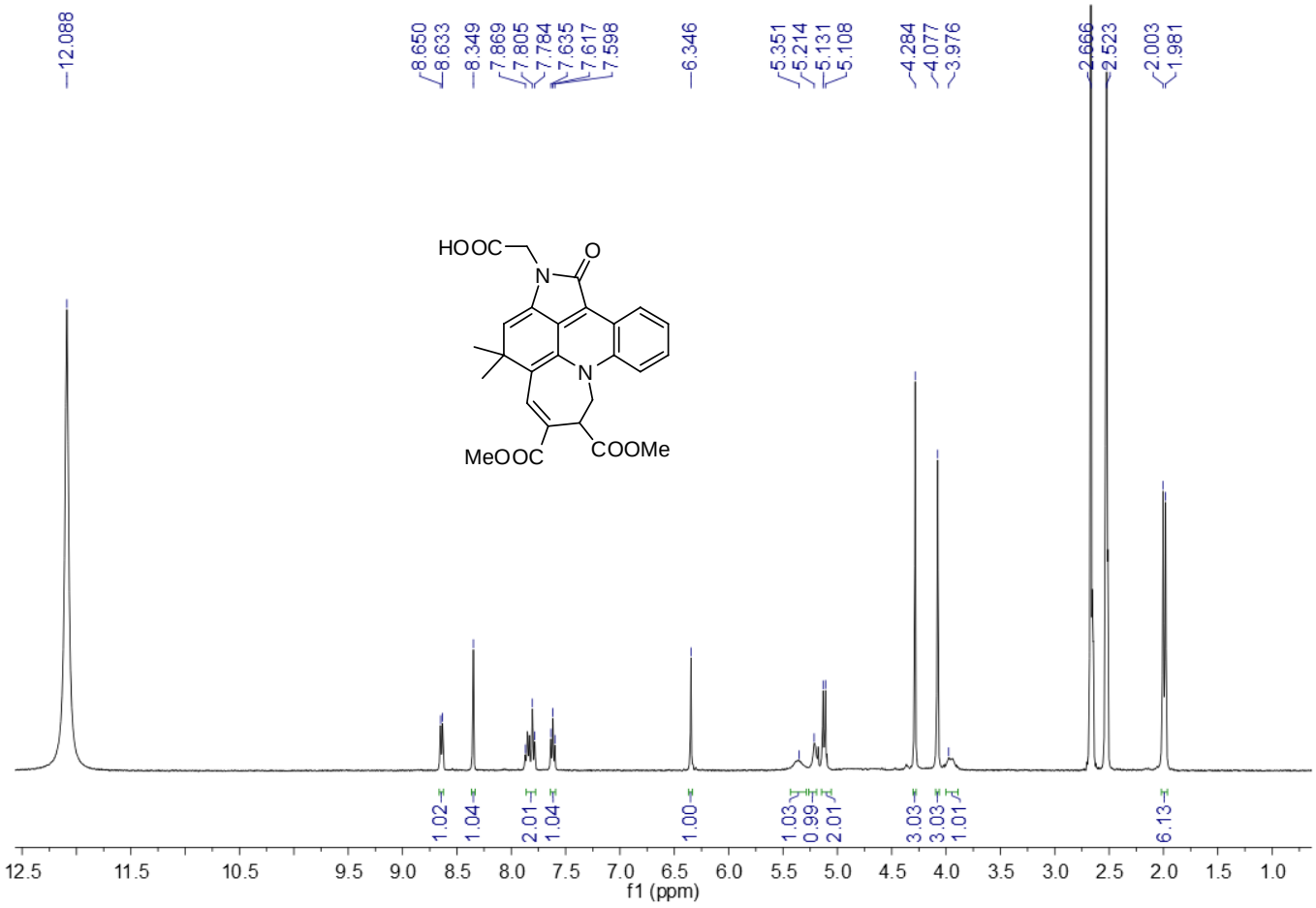
^{1}H NMR Spectrum of Compound 5h



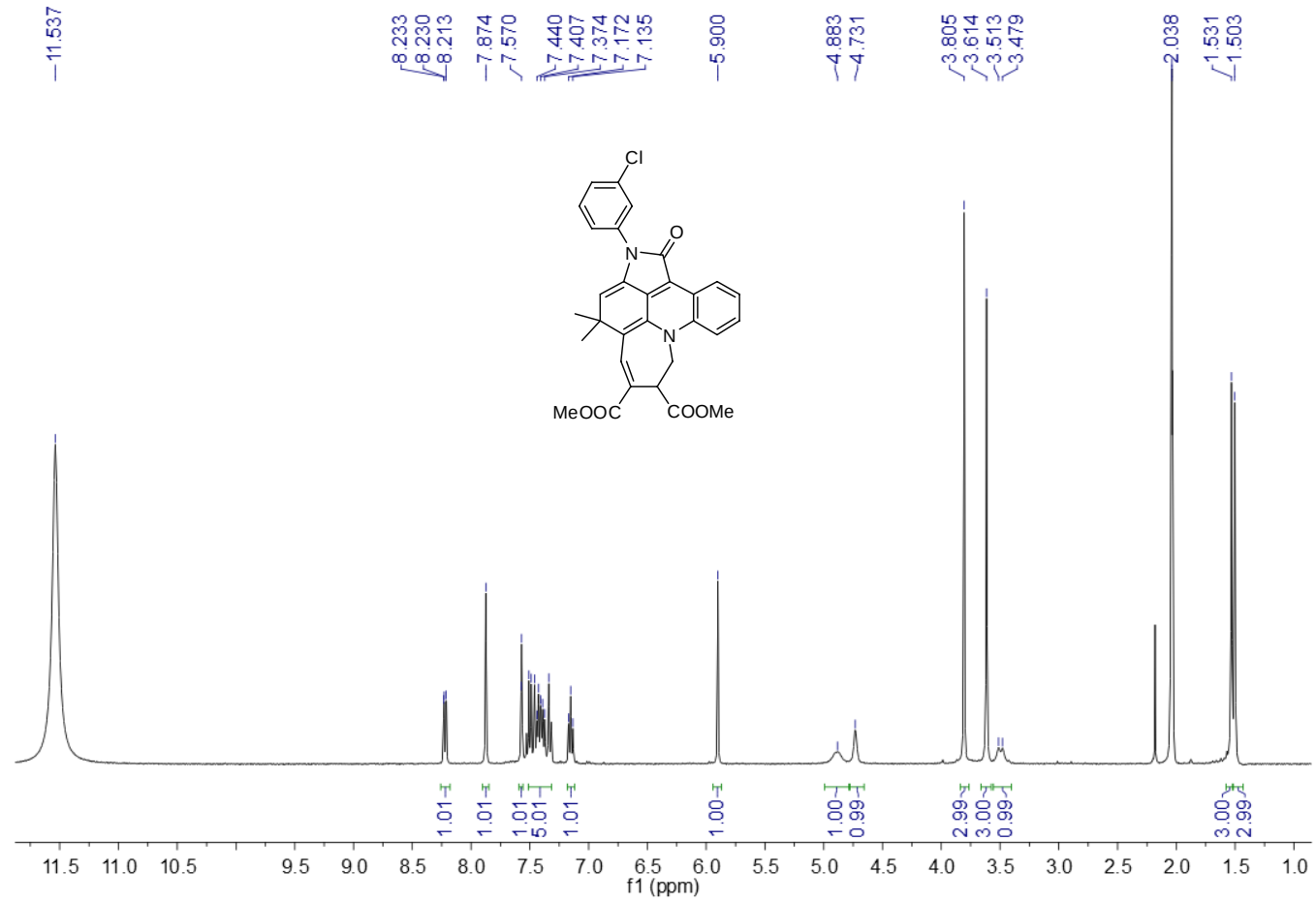
^{1}H NMR Spectrum of Compound 5i



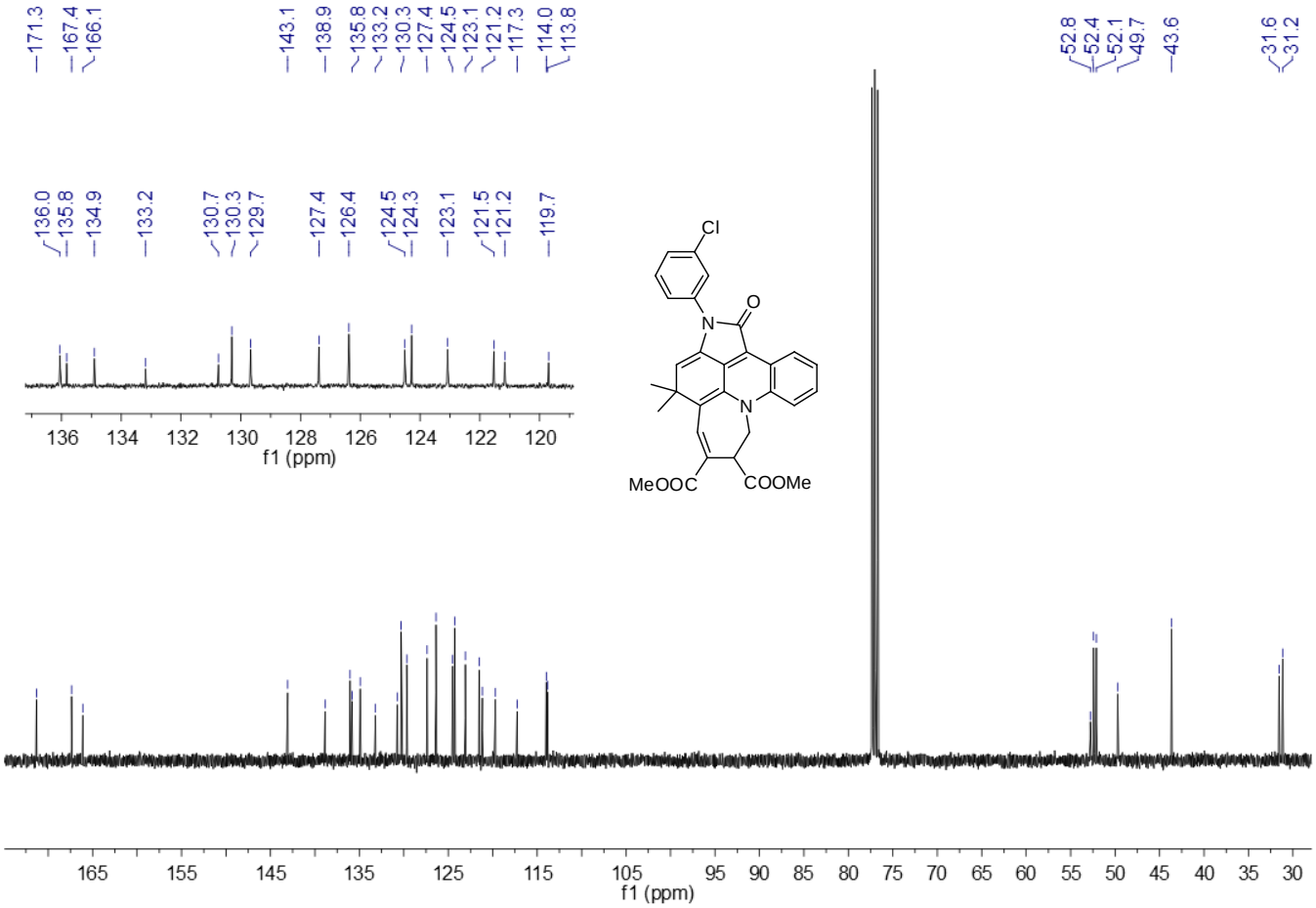
^{13}C NMR Spectrum of Compound 5i



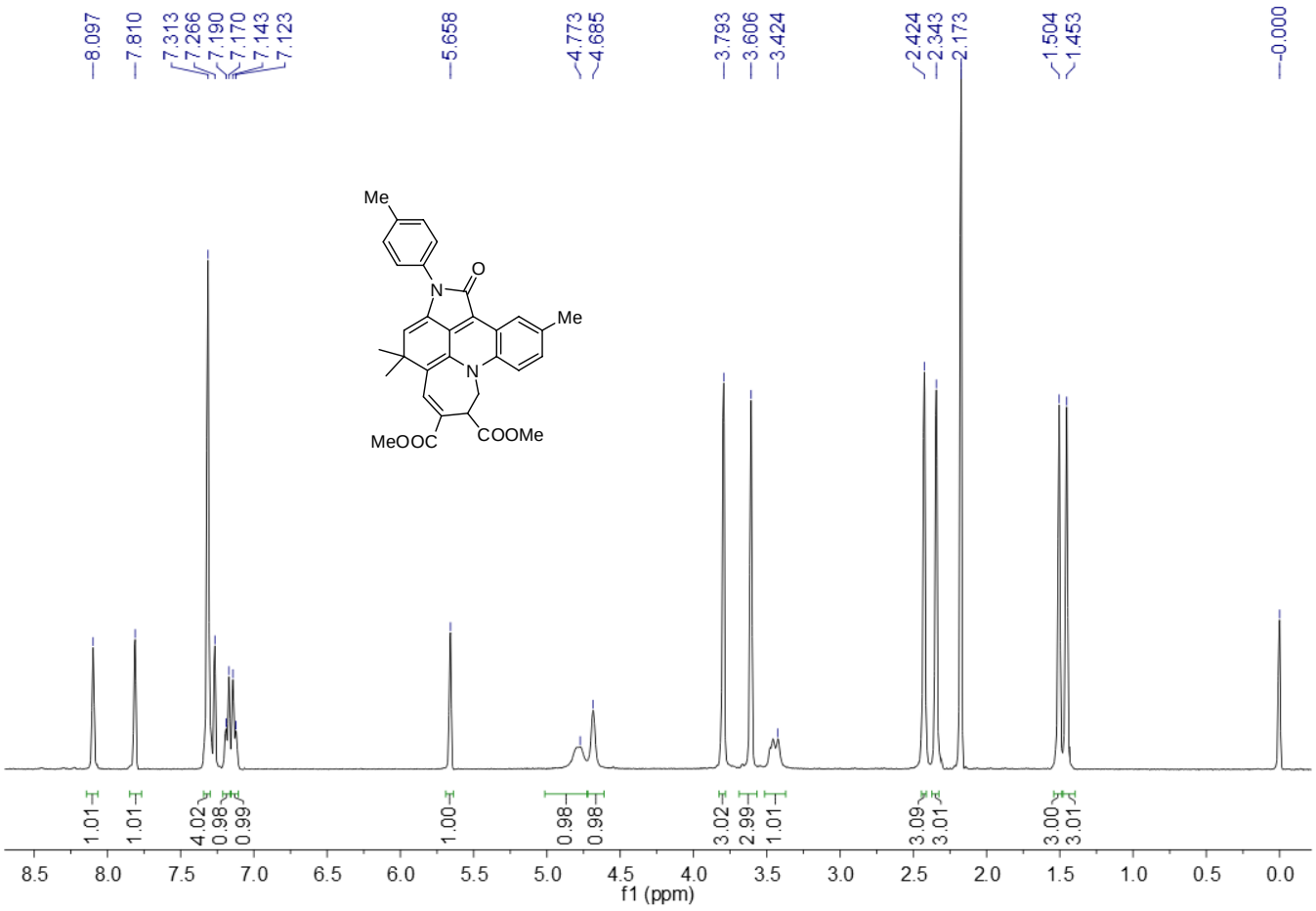
^{1}H NMR Spectrum of Compound 5j



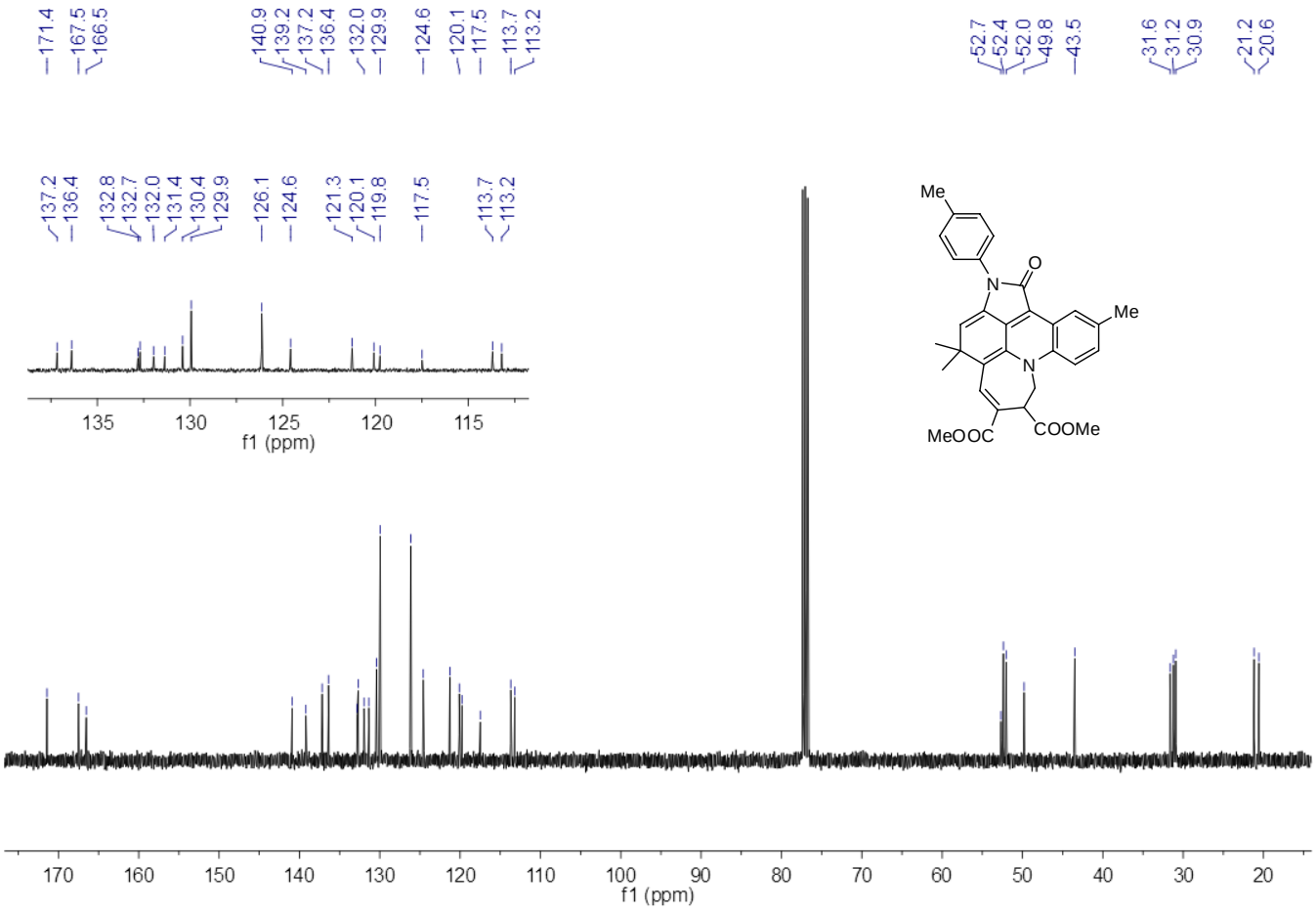
^{1}H NMR Spectrum of Compound 5k



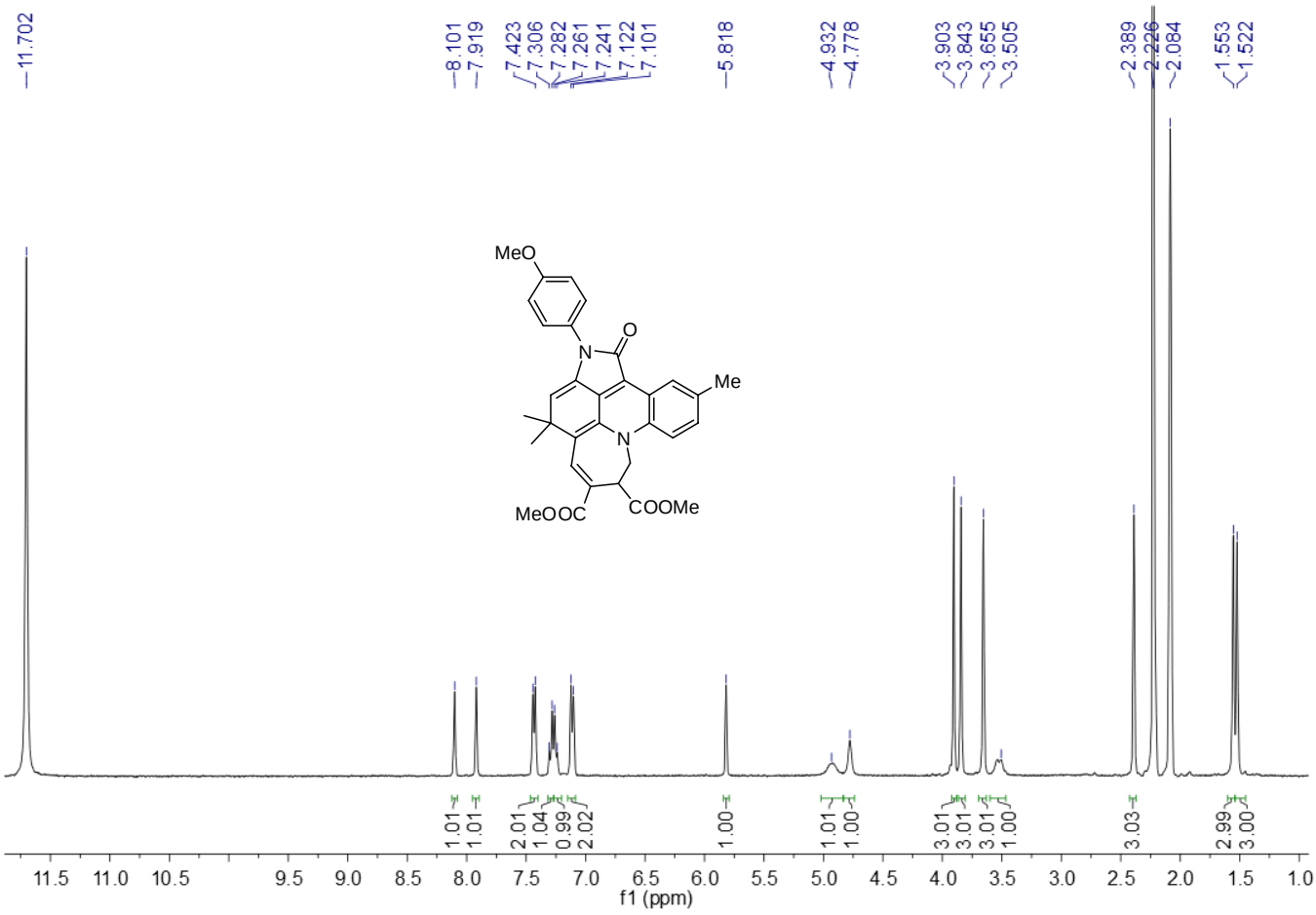
^{13}C NMR Spectrum of Compound 5k



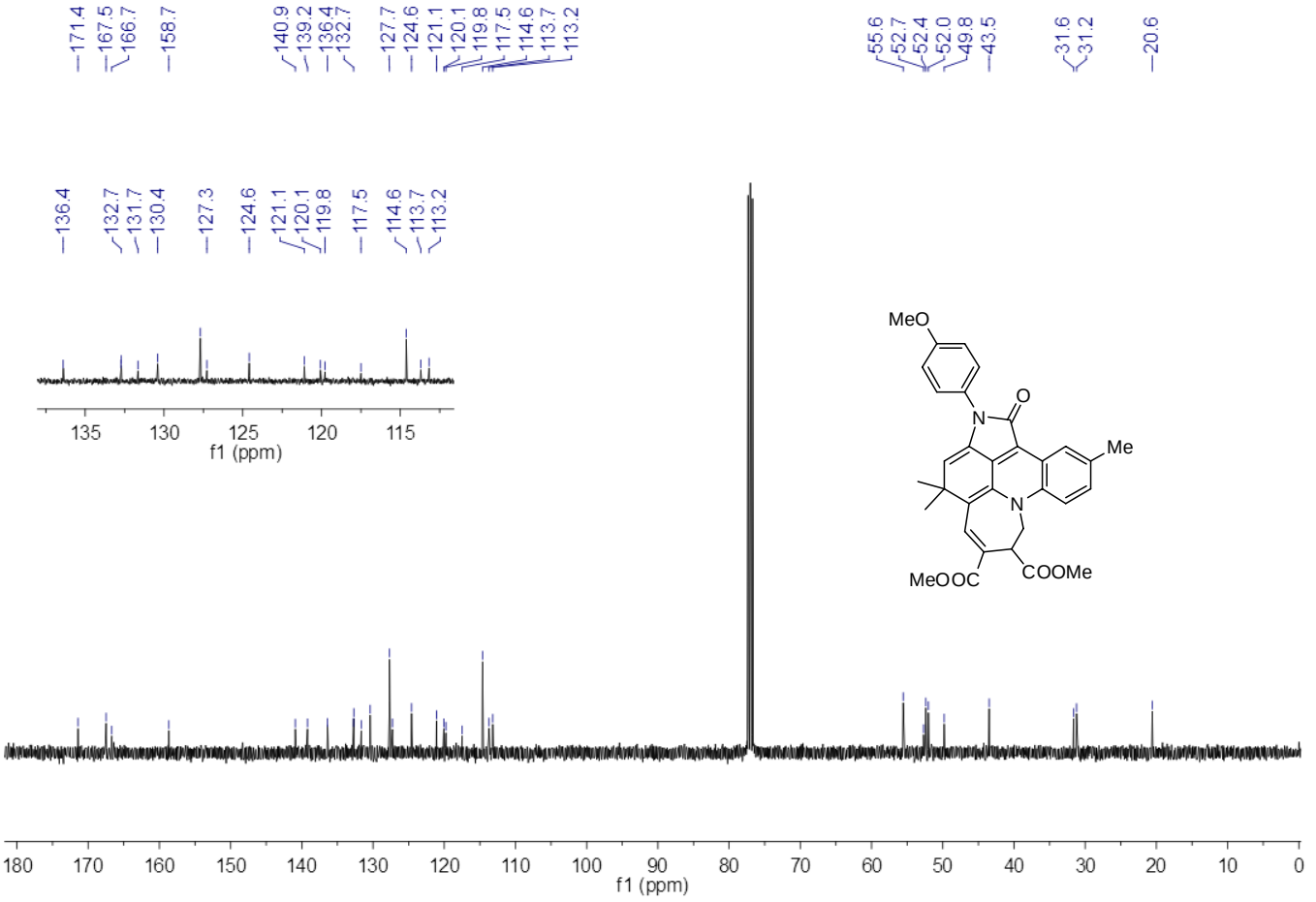
^{1}H NMR Spectrum of Compound 5l



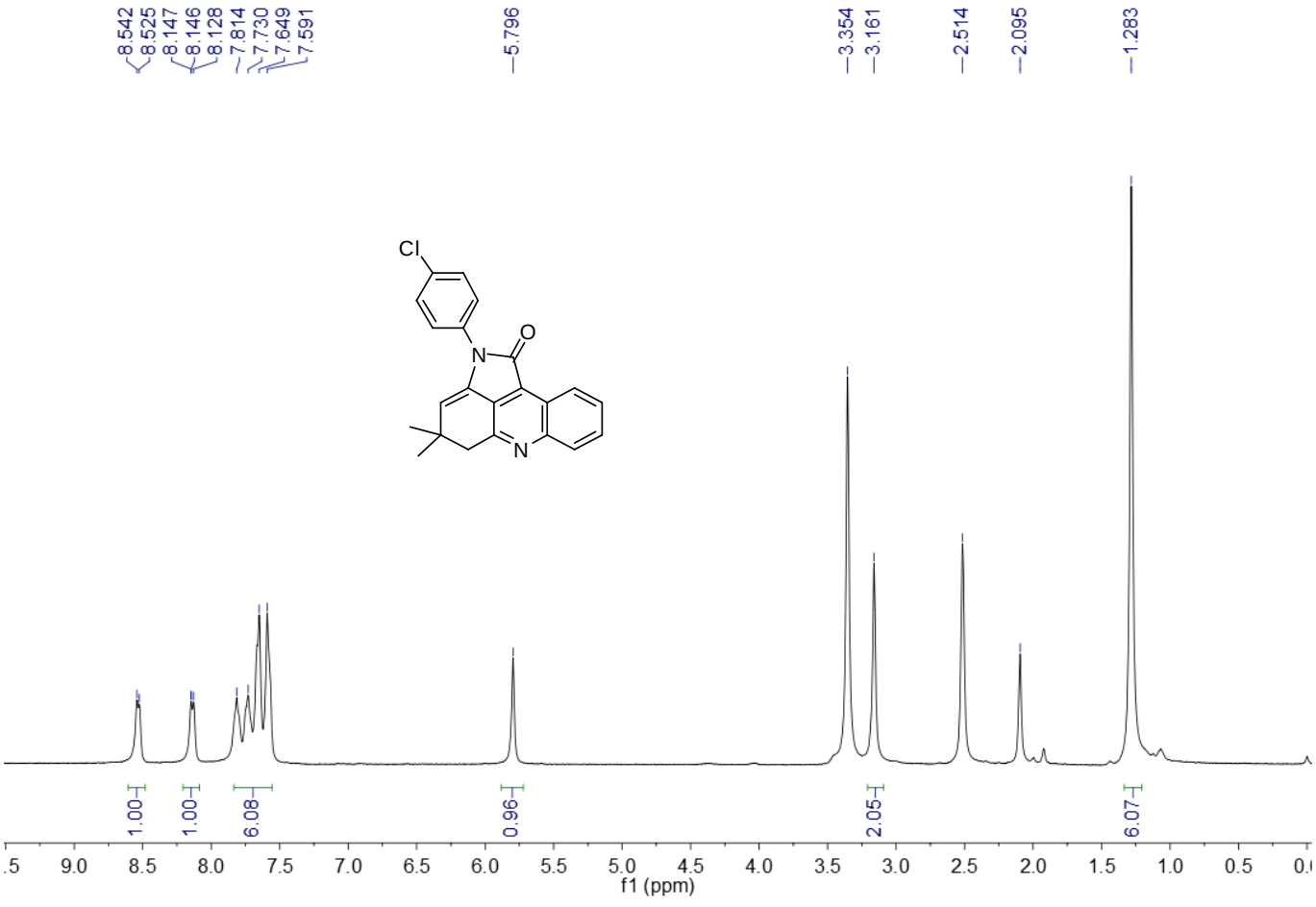
^{13}C NMR Spectrum of Compound 5l



^{1}H NMR Spectrum of Compound 5m



^{13}C NMR Spectrum of Compound 5m



^{1}H NMR Spectrum of Compound D