*Electronic Supplementary Information*

# Exploring ketyl and acyl radical cyclizations for the synthesis of γ-lactone-fused benzopyrans and benzofurans

Helen Santoso,[a,b] Myriam I. Casana[c] and Christopher D. Donner*[a,b]

[a] ARC Centre of Excellence for Free Radical Chemistry and Biotechnology, Australia
[b] School of Chemistry and Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne, Victoria, 3010, Australia
[c] ECPM, School of Chemistry, Polymers and Materials Science, The University of Strasbourg, 67000 Strasbourg, France

*cdonner@unimelb.edu.au

## *Contents*

## General experimental details

$^{1}H$ and $^{13}C$ NMR spectra were recorded using a Varian-500 spectrometer operating at 500 MHz and 125 MHz, respectively. Chemical shifts are given using residual $CHCl_3$ ($\delta$ = 7.26 for $^{1}H$ and 77.0 for $^{13}C$) as internal standard. Infrared (IR) spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer. Gas chromatography-mass spectrometry (GC-MS) spectra were recorded on an Agilent 7890A GC system using a HP-5MS column (30 m, i.d. 0.25 mm, film thickness 0.25 μm) and 5975C MS system (EI, 70 eV). GC heat program: $100_5 \rightarrow 250_5$, heating rate 5 °C $min^{-1}$. The retention time ($t_R$) and selected fragment ions as their mass/charge ratio (*m/z*) are reported. High resolution ESI mass spectra (HRMS) were recorded on a Thermo-Finnigan LTQ-FT ICR hybrid mass spectrometer. All moisture sensitive reactions were performed under a dry nitrogen or argon atmosphere in oven-dried or flame-dried glassware. Anhydrous tetrahydrofuran (THF) and dichloromethane were pre-dried over activated alumina under argon. Benzene was distilled from sodium/benzophenone ketyl prior to use. Thin layer chromatography was performed on pre-coated silica plates (Merck $60GF_{254}$) and compounds were visualized at 254 nm and 365 nm or stained with either phosphomolybdic acid or potassium permanganate solutions. Flash column chromatography was performed on silica gel (Kieselgel 60, 230-400 mesh) using the indicated solvent system; PE = petroleum ether. Melting points were measured in an open capillary automated melting point apparatus and are uncorrected.

**Experimental procedures**

**(*E*)-Ethyl 3-(2-(hydroxymethyl)benzyloxy)acrylate (10) and (2*E*,2'*E*)-diethyl 3,3'-(1,2-phenylenebis(methylene))bis(oxy)diacrylate (11)**

To a suspension of diol **9**[S1] (1.0 g, 7.24 mmol) in $CH_2Cl_2$ (25 mL) at 0 °C was added *N*-methyl morpholine (805 mg, 7.96 mmol) followed by the addition of ethyl propiolate (809 μL, 7.96 mmol) over 10 min and stirring was continued for a further 90 min. The solution was diluted with 0.5 M HCl, extracted with $CHCl_3$ (3 × 10 mL) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (gradient elution, EtOAc-PE, 1 : 3 to 1 : 1) gave diacrylate **11** (630 mg, 47%) as a colourless oil and monoacrylate **10** (770 mg, 45%) as a colourless solid.

**Spectroscopic data for monoacrylate 10.**

$R_f$ = 0.22 (EtOAc-PE, 1 : 2); m.p. 45-47 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3H), 2.80 (brs, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 4.65 (s, 2H), 4.97 (s, 2H), 5.32 (d, *J* = 12.6 Hz, 1H), 7.30-7.40 (m, 4H), 7.63 (d, *J* = 12.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.2, 59.8, 62.6, 70.6, 97.4, 127.9, 128.5, 128.9, 129.0, 133.1, 139.1, 161.8, 167.7; IR (neat): 3305, 2922, 1699, 1626, 1269, 1223, 1209, 1050, 1027, 963 cm$^{-1}$; GC-MS: *m/z* (%) = 121 ($[M - 115]^+$, 94), 120 (61), 119 (44), 93 (74), 91 (100), 77 (45): $t_R$ = 26.48 min; HRMS (ESI): calcd for $C_{13}H_{17}O_4$ $[M + H^+]$ 237.1121, found 237.1121.

**Spectroscopic data for diacrylate 11.**

$R_f$ = 0.48 (EtOAc-PE, 1 : 2); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 6H), 4.16 (q, *J* = 7.1 Hz, 4H), 4.92 (s, 4H), 5.32 (d, *J* = 12.6 Hz, 2H), 7.38-7.40 (m, 4H), 7.63 (d, *J* = 12.6 Hz, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.2, 59.8, 70.3, 97.7, 129.1, 129.4, 133.6, 161.4, 167.3; IR (neat): 2976, 1702, 1621, 1327, 1133 cm$^{-1}$; GC-MS: *m/z* (%) = 334 ($M^+$, 1), 173 (33), 145 (20), 117 (44), 105 (100), 104 (65): $t_R$ = 35.68 min; HRMS (ESI): calcd for $C_{18}H_{23}O_6$ $[M + H^+]$ 335.1489, found 335.1489.

**(*E*)-Ethyl 3-(2-formylbenzyloxy)acrylate (12)**

To a solution of alcohol **10** (250 mg, 1.06 mmol) in $CH_2Cl_2$ (5 mL) were added $PhI(OAc)_2$ (409 mg, 1.27 mmol) and TEMPO (17 mg, 0.11 mmol) and the mixture was stirred at r.t. for 3 h. After removal of the solvent *in vacuo* the remaining residue was purified by column chromatography (EtOAc-PE, 1 :

---

[S1] E. Zysman-Colman, N. Nevins, N. Eghbali, J. P. Snyder and D. N. Harpp, *J. Am. Chem. Soc.*, 2006, **128**, 291-304.

3) to give benzaldehyde **12** (242 mg, 98%) as a colourless solid. $R_f$ = 0.56 (EtOAc-PE, 1 : 1); m.p. 51-52 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H), 4.17 (q, *J* = 7.1 Hz, 2H), 5.37 (s, 2H), 5.38 (d, *J* = 12.5 Hz, 1H), 7.53-7.56 (m, 1H), 7.64-7.65 (m, 2H), 7.70 (d, *J* = 12.5 Hz, 1H), 7.86-7.87 (m, 1H), 10.10 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.3, 59.8, 70.2, 97.9, 127.4, 128.3, 132.9, 134.1, 134.5, 137.5, 161.7, 167.6, 193.0; IR (neat): 2990, 1705, 1690, 1627, 1603, 1575, 1327, 1142 cm$^{-1}$; GC-MS: *m/z* (%) = 234 ($M^+$, 1), 119 (100), 91 (75): $t_R$ = 25.01 min; HRMS (ESI): calcd for $C_{13}H_{15}O_4$ [M + $H^+$] 235.0965, found 235.0965.

**(4,5-Dimethoxy-1,2-phenylene)dimethanol (19)**[S2]

To 5,6-dimethoxyphthalide **18**[S3] (690 mg, 3.55 mmol) in THF (25 mL) at 0 °C was added $LiAlH_4$ (0.31 g, 8.04 mmol) in small portions over 15 min. Stirring was continued at 0 °C for 2.5 h followed by dropwise addition of saturated $NH_4Cl$ (4 mL) then 2 M HCl (2 mL). $CHCl_3$ (15 mL) was added and the mixture stirred for 15 min before addition of water (20 mL) and extraction with $CHCl_3$ (4 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give diol **19** (560 mg, 80%) as a colourless solid, m.p. 108-109 °C. $^1$H NMR (500 MHz, $CDCl_3$): δ = 2.97 (brs, 2H), 3.88 (s, 6H), 4.66 (s, 4H), 6.88 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 56.0, 63.9, 113.2, 132.0, 148.5; IR (neat): 3458, 3333, 2925, 1511, 1451, 1282, 1206, 1101 cm$^{-1}$.

**(*E*)-Ethyl 3-(2-(hydroxymethyl)-4,5-dimethoxybenzyloxy)acrylate (20) and (2*E*,2'*E*)-diethyl 3,3'-(4,5-dimethoxy-1,2-phenylene)bis(methylene)bis(oxy)diacrylate (21)**

To a suspension of diol **19** (545 mg, 2.75 mmol) in $CH_2Cl_2$ (15 mL) was added *N*-methyl morpholine (306 mg, 3.02 mmol) followed by the addition of ethyl propiolate (307 μL, 3.02 mmol) over 25 min and stirring was continued for a further 90 min. The solution was diluted with 0.2 M HCl (10 mL), extracted with $CH_2Cl_2$ (3 × 10 mL) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (gradient elution, EtOAc-PE, 3 : 7 to 1 : 1) gave diacrylate **21** (144 mg, 24%) as a colourless solid and monoacrylate **20** (457 mg, 56%) as a colourless oil.

**Spectroscopic data for monoacrylate 20.**

$R_f$ = 0.20 (EtOAc-PE, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.2 Hz, 3H), 2.25 (brs, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 4.13 (q, *J* = 7.2 Hz, 2H), 4.60 (s, 2H), 4.89 (s, 2H), 5.30 (d, *J* = 12.7 Hz, 1H),

---

[S2] M. A. A. Meziane, S. Royer and J. P. Bazureau, *Tetrahedron Lett*., 2001, **42**, 1017-1020.

[S3] A. K. Sinhababu and R. T. Borchardt, *J. Org. Chem*., 1983, **48**, 2356-2360.

6.84 (s, 1H), 6.94 (s, 1H), 7.63 (d, $J$ = 12.7 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.2, 55.9, 56.0, 59.8, 62.4, 70.4, 97.4, 112.2, 112.8, 125.2, 132.2, 148.3, 149.2, 161.6, 167.6; IR (neat): 3478, 2938, 1702, 1619, 1518, 1280, 1127, 1103 cm$^{-1}$; GC-MS: *m/z* (%) = 296 ($M^+$, 2), 181 (100), 153 (20): $t_R$ = 33.74 min; HRMS (ESI): calcd for $C_{15}H_{20}O_6Na$ [M + $Na^+$] 319.1152, found 319.1153.

**Spectroscopic data for diacrylate 21.**

$R_f$ = 0.43 (EtOAc-PE, 1 : 1); m.p. 105-106 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, $J$ = 7.1 Hz, 6H), 3.87 (s, 6H), 4.14 (q, $J$ = 7.1 Hz, 4H), 4.84 (s, 4H), 5.30 (d, $J$ = 12.6 Hz, 2H), 6.87 (s, 2H), 7.62 (d, $J$ = 12.6 Hz, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.2, 56.0, 59.8, 70.0, 97.6, 112.8, 126.2, 149.2, 161.4, 167.4; IR (neat): 2934, 1700, 1627, 1615, 1136, 1113 cm$^{-1}$; GC-MS: *m/z* (%) = 348 ([M – 46]$^+$, 1), 166 (25), 152 (100), 137 (30), 121 (28): $t_R$ = 35.40 min; HRMS (ESI): calcd for $C_{20}H_{26}O_8Na$ [M + $Na^+$] 417.1520, found 417.1520.

**(*E*)-Ethyl 3-(2-formyl-4,5-dimethoxybenzyloxy)acrylate (22)**

To a solution of alcohol **20** (400 mg, 1.35 mmol) in $CH_2Cl_2$ (5 mL) were added $PhI(OAc)_2$ (522 mg, 1.62 mmol) and TEMPO (21 mg, 0.13 mmol) and the mixture was stirred at r.t. for 2 h. After removal of the solvent *in vacuo* the remaining residue was purified by column chromatography (EtOAc-PE, 1 : 2) to give benzaldehyde **22** (360 mg, 91%) as a colourless solid, m.p. 105-108 °C. $R_f$ = 0.33 (EtOAc-PE, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, $J$ = 7.2 Hz, 3H), 3.96 (s, 3H), 3.98 (s, 3H), 4.18 (q, $J$ = 7.2 Hz, 2H), 5.31 (s, 2H), 5.39 (d, $J$ = 12.6 Hz, 1H), 7.07 (s, 1H), 7.35 (s, 1H), 7.70 (d, $J$ = 12.6 Hz, 1H), 10.02 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.1, 56.0, 56.1, 59.7, 69.4, 97.7, 110.5, 114.6, 126.1, 131.9, 148.5, 153.5, 161.3, 167.2, 190.4; IR (neat): 2968, 1698, 1627, 1594, 1516, 1275, 1209, 1189 cm$^{-1}$; GC-MS: *m/z* (%) = 294 ($M^+$, 2), 179 (100): $t_R$ = 32.88 min; HRMS (ESI): calcd for $C_{15}H_{19}O_6$ [M + $H^+$] 295.1176, found 295.1177.

**(*E*)-Ethyl 3-(6-(hydroxymethyl)-2,3-dimethoxybenzyloxy)acrylate (25), (*E*)-ethyl 3-(2-(hydroxymethyl)-3,4-dimethoxybenzyloxy)acrylate (26) and (2*E*,2'*E*)-diethyl 3,3'-(3,4-dimethoxy-1,2-phenylene)bis(methylene)bis(oxy)diacrylate (27)**

To a solution of diol **24**[S4] (630 mg, 3.17 mmol) in $CH_2Cl_2$ (15 mL) was added *N*-methyl morpholine (350 mg, 3.50 mmol) followed by the addition of ethyl propiolate (325 μL, 3.20 mmol) over 10 min and stirring was continued for a further 90 min. The solution was diluted with 0.2 M HCl (10 mL), extracted with $CH_2Cl_2$ (3 × 10 mL) and the combined organic extracts dried ($MgSO_4$), filtered and

[S4] D. C. Kim, W. H. Yoon, H. Choi and D. H. Kim, *J. Heterocyclic Chem*., 1993, **30**, 1431-1436.

concentrated *in vacuo*. Column chromatography (gradient elution, EtOAc-$CHCl_3$, 1 : 4 to 2 : 1) gave diacrylate **27** (260 mg, 21%) as a colourless oil and a mixture of isomeric monoacrylates **25** and **26** (560 mg, 60%) as a colourless oil. A small sample of the mixture of isomers **25** and **26** was further purified by column chromatography (EtOAc-PE, 1 : 2) to obtain a pure sample of isomer **26** for characterization.

**Spectroscopic data for monoacrylate 26.**

$R_f$ = 0.40 (EtOAc-PE, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3H), 2.35 (brs, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.69 (s, 2H), 4.92 (s, 2H), 5.32 (d, *J* = 12.7 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 1H), 7.05 (d, *J* = 8.6 Hz, 1H), 7.63 (d, *J* = 12.7 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.2, 55.7, 56.7, 59.8, 61.3, 71.0, 97.5, 111.6, 125.8, 126.4, 133.5, 148.0, 153.2, 161.5, 167.5; IR (neat): 3344, 2973, 1713, 1627, 1141 cm$^{-1}$; GC-MS: *m/z* (%) = 296 ($M^+$, 1), 181 (100), 166 (26), 151 (20): $t_R$ = 32.46 min; HRMS (ESI): calcd for $C_{15}H_{21}O_6$ [M + $H^+$] 297.1333, found 297.1333.

**Spectroscopic data for diacrylate 27.**

$R_f$ = 0.60 (EtOAc-PE, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.26-1.29 (m, 6H), 3.85 (s, 3H), 3.89 (s, 3H), 4.15-4.20 (m, 4H), 4.87 (s, 2H), 5.00 (s, 2H), 5.31 (d, *J* = 12.6 Hz, 1H), 5.36 (d, *J* = 12.7 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 12.6 Hz, 1H), 7.66 (d, *J* = 12.7 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.3, 55.8, 59.8, 59.9, 61.6, 64.2, 70.5, 97.4, 97.6, 112.8, 125.7, 127.4, 127.7, 148.6, 153.3, 161.6, 161.9, 167.5, 167.6; IR (neat): 2938, 1703, 1620, 1278, 1118, 1082 cm$^{-1}$; GC-MS: *m/z* (%) = 394 ($M^+$, 1), 233 (25), 205 (32), 165 (100), 150 (32): $t_R$ = 33.12 min; HRMS (ESI): calcd for $C_{20}H_{27}O_8$ [M + $H^+$] 395.1700, found 395.1700.

**(*E*)-Ethyl 3-(6-formyl-2,3-dimethoxybenzyloxy)acrylate (28) and (*E*)-ethyl 3-(2-formyl-3,4-dimethoxybenzyloxy)acrylate (29)**

To a solution of alcohols **25** and **26** (1:1 mixture, 200 mg, 0.67 mmol) in $CH_2Cl_2$ (4 mL) were added $PhI(OAc)_2$ (261 mg, 0.81 mmol) and TEMPO (26 mg, 0.17 mmol) and the mixture was stirred at r.t. for 3 h. After removal of the solvent *in vacuo* the remaining residue was purified by column chromatography (gradient elution, EtOAc-PE, 1 : 2 to 1 : 1) to give benzaldehyde **28** (83 mg) as a colourless oil and benzaldehyde **29** (96 mg) as a colourless solid in a combined 90% yield.

**Spectroscopic data for 28.**

$R_f$ = 0.19 (EtOAc-PE, 1 : 2); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H), 3.86 (s, 3H), 3.96 (s, 3H), 4.17 (q, *J* = 7.1 Hz, 2H), 5.37 (s, 2H), 5.38 (d, *J* = 12.4 Hz, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 7.65 (d, *J* = 8.6 Hz, 1H), 7.69 (d, *J* = 12.4 Hz, 1H), 10.00 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.3, 56.0, 59.8, 61.8, 62.5, 97.3, 112.2, 128.3, 129.7, 130.6, 148.7, 157.4, 162.1, 167.7, 190.6; IR

(neat): 2983, 1715, 1686, 1634, 1586, 1285, 1230, 1144, 1078 $cm^{-1}$; GC-MS: *m/z* (%) = 294 ($M^+$, 1), 179 (100): $t_R$ = 32.55 min; HRMS (ESI): calcd for $C_{15}H_{19}O_6$ [M + $H^+$] 295.1176, found 295.1177.

**Spectroscopic data for 29.**

$R_f$ = 0.32 (EtOAc-PE, 1 : 2); m.p. 78-81 °C (EtOAc-PE); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H), 3.92 (s, 3H), 3.98 (s, 3H), 4.16 (q, *J* = 7.1 Hz, 2H), 5.23 (s, 2H), 5.34 (d, *J* = 12.7 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 1H), 7.67 (d, *J* = 12.7 Hz, 1H), 10.53 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.3, 56.0, 59.8, 62.4, 70.5, 97.4, 117.4, 122.8, 126.7, 129.2, 152.4, 153.9, 162.1, 167.8, 192.2; IR (neat): 2901, 1702, 1683, 1625, 1574, 1494, 1310, 1236, 1135, 1043 $cm^{-1}$; GC-MS: *m/z* (%) = 294 ($M^+$, 1), 179 (100), 136 (20): $t_R$ = 32.20 min; HRMS (ESI): calcd for $C_{15}H_{19}O_6$ [M + $H^+$] 295.1176, found 295.1177.

**General procedure for radical cyclization of benzaldehydes 13, 22, 28 and 29**

A solution of benzaldehyde (50 mg, 0.170 mmol), $Bu_3SnH$ (74 mg, 0.255 mmol) and AIBN (3 mg, 0.017 mmol) in benzene (13 mL) was flushed with argon for 30 min after which the solution was heated at reflux for 5 h during which further portions of AIBN (3 mg) were added after 1.5 h and 3 h of heating. After cooling and removal of the solvent *in vacuo* the remaining residue was filtered through a short column of 10% KF/silica (EtOAc-hexane, 1 : 1) to remove tin-containing material and fractions having $R_f$ 0.2-0.5 were combined to give 40-47 mg of recovered product mixture. Integration of the resultant $^1$H NMR spectra allowed the product ratio (*cis*:*trans*:reduction) to be determined (see Table 1).

**Ethyl 2-(5,8-dimethoxy-4-oxoisochroman-3-yl)acetate (37)**

A solution of benzaldehyde **13** (48 mg, 0.16 mmol) in toluene (2 mL) with ACCN (12 mg, 0.05 mmol) and *tert*-dodecanethiol (10 mg, 0.05 mmol) was flushed with argon for 45 min then heated at reflux for 22 h. After removal of the solvent *in vacuo*, purification by column chromatography (EtOAc-PE, 1 : 3) gave recovered benzaldehyde **13** (23 mg, 48%) and benzopyran **37** (11 mg, 23% [44% based on recovered **13**]) as a colourless oil. $R_f$ = 0.36 (EtOAc-PE, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.1 Hz, 3H), 2.79 (dd, *J* = 16.4, 7.6 Hz, 1H), 3.10 (dd, *J* = 16.4, 4.3 Hz, 1H), 3.81 (s, 3H), 3.89 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.48-4.51 (m, 1H), 4.71 (d, *J* = 16.2 Hz, 1H), 5.12 (d, *J* = 16.2 Hz, 1H), 6.86 (d, *J* = 9.1 Hz, 1H), 7.04 (d, *J* = 9.1 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 14.1, 36.2, 56.0, 56.3, 60.8, 63.5, 78.8, 111.0, 116.7, 119.0, 132.2, 148.1, 154.1, 170.9, 192.9; IR (neat): 2938, 1736, 1691, 1483, 1267, 1175 $cm^{-1}$; GC-MS: *m/z* (%) = 294 ($M^+$, 60), 249 (45), 206 (90), 178 (70), 163 (100),

148 (41), 120 (71): $t_R$ = 31.92 min; HRMS (ESI): calcd for $C_{15}H_{18}O_6Na$ [M + $Na^+$] 317.0996, found 317.0995.

**(*E*)-Methyl 4-(2-formylphenoxy)but-2-enoate (40)**[S5]

To a mixture of salicylaldehyde **38** (5.0 g, 41.0 mmol) and $K_2CO_3$ (8.5 g, 61.5 mmol) in DMF (5 mL) was added methyl-4-bromobut-2-enoate (11.0 g, 61.5 mmol) and the reaction mixture was allowed to stir at r.t. for 16 h. The mixture was filtered through celite using EtOAc (50 mL) to rinse the solid residue. The filtrate was then washed with water (3 × 30 mL) and the organic layer dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (EtOAc-PE, 1 : 2) gave ether **40** (5.49 g, 61%) as a pale yellow solid. $R_f$ = 0.52 (EtOAc-PE, 1 : 1); m.p. 70-71 °C (lit.[S5] m.p. 72-73 °C); $^1$H NMR (500 MHz, $CDCl_3$): δ = 3.78 (s, 3H), 4.84 (dd, *J* = 4.1, 2.1 Hz, 2H), 6.23 (dt, *J* = 15.8, 2.1 Hz, 1H), 6.93-6.95 (m, 1H), 7.06-7.09 (m, 1H), 7.12 (dt, *J* = 15.8, 4.1 Hz, 1H), 7.53-7.56 (m, 1H), 7.86-7.88 (m, 1H), 10.55 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 51.7, 66.8, 112.5, 121.4, 122.1, 125.1, 128.8, 135.8, 141.4, 160.1, 166.2, 189.2; IR (neat): 2953, 1716, 1682, 1662, 1596, 1303, 1239, 1166 $cm^{-1}$; GC-MS: *m/z* (%) = 220 ($M^+$, 1), 202 (27), 188 (100), 161 (81), 121 (94), 99 (74), 71 (56): $t_R$ = 23.60 min.

The spectroscopic data ($^1$H and $^{13}$C NMR) were consistent with reported values.[S5]

**(*E*)-Methyl 4-(2-formyl-3,6-dimethoxyphenoxy)but-2-enoate (41)**

To a mixture of phenol **39**[S6] (1.30 g, 7.14 mmol) and $K_2CO_3$ (1.48 g, 10.7 mmol) in DMF (5 mL) was added methyl-4-bromobut-2-enoate (1.92 g, 10.7 mmol) and the reaction mixture was allowed to stir at r.t. for 20 h. The mixture was filtered through celite using EtOAc (50 mL) to rinse the solid residue. The filtrate was then washed with water (3 × 20 mL) and the organic layer dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (EtOAc-PE, 1 : 1) gave ether **41** (1.59 g, 80%) as a pale yellow solid. $R_f$ = 0.36 (EtOAc-PE, 1 : 1); m.p. 87-88 °C ($CH_2Cl_2$-hexane); $^1$H NMR (500 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.82 (s, 3H), 3.85 (s, 3H), 4.75-4.76 (m, 2H), 6.24 (dt, *J* = 15.7, 2.0 Hz, 1H), 6.67 (d, *J* = 9.2 Hz, 1H), 7.08 (dt, *J* = 15.7, 4.6 Hz, 1H), 7.09 (d, *J* = 9.2 Hz, 1H), 10.45 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 51.6, 56.3, 56.8, 72.5, 106.9, 119.1, 119.9, 121.6, 143.0, 146.7, 149.8, 155.1, 166.6, 189.4; IR (neat): 2956, 1717, 1685, 1487, 1436, 1261, 1197, 1169, 1100 $cm^{-1}$; GC-MS:

---

[S5] E. Ciganek, *Synthesis*, 1995, 1311-1314.

[S6] U. Wriede, M. Fernandez, K. F. West, D. Harcourt and H. W. Moore, *J. Org. Chem.*, 1987, **52**, 4485-4489.

*m/z* (%) = 280 ($M^+$, 63), 221 (26), 205 (36), 181 (100), 166 (57), 151 (24), 123 (32), 99 (33): $t_R$ = 30.36 min; HRMS (ESI): calcd for $C_{14}H_{17}O_6$ [M + $H^+$] 281.1020, found 281.1020.

**Methyl 2-(4-oxochroman-3-yl)acetate (42)**[S5]

A solution of benzaldehyde **40** (200 mg, 0.91 mmol) in chlorobenzene (10 mL) with ACCN (335 mg, 1.37 mmol) and *tert*-dodecanethiol (553 mg, 2.73 mmol) was flushed with argon for 30 min then heated at 100 °C for 20 h. After removal of the solvent *in vacuo*, purification by column chromatography (EtOAc-PE, 1 : 2) gave benzopyran **42** (136 mg, 68% [92% based on recovered **40**]) and recovered benzaldehyde **40** (52 mg, 26%).

**Spectroscopic data for 42.**

$R_f$ = 0.63 (EtOAc-PE, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 2.44 (dd, *J* = 17.0, 8.1 Hz, 1H), 2.95 (dd, *J* = 17.0, 5.0 Hz, 1H), 3.31-3.37 (m, 1H), 3.74 (s, 3H), 4.30 (dd, *J* = 12.0, 11.2 Hz, 1H), 4.60 (dd, *J* = 11.2, 5.3 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 30.1, 42.5, 52.0, 70.2, 117.8, 120.4, 121.5, 127.3, 136.0, 161.7, 171.8, 192.5; IR (neat): 2951, 1734, 1688, 1604, 1480, 1457, 1166 $cm^{-1}$; GC-MS: *m/z* (%) = 220 ($M^+$, 2), 189 (17), 147 (100), 120 (58), 92 (33): $t_R$ = 21.20 min.

The spectroscopic data ($^1$H and $^{13}$C NMR) were consistent with reported values.[S5]

**Methyl 2-(5,8-dimethoxy-4-oxochroman-3-yl)acetate (43)**

A solution of benzaldehyde **41** (140 mg, 0.50 mmol) in chlorobenzene (2 mL) with ACCN (183 mg, 0.75 mmol) and *tert*-dodecanethiol (303 mg, 1.50 mmol) was flushed with argon for 45 min then heated at 100 °C for 18 h. After removal of the solvent *in vacuo*, purification by column chromatography (EtOAc-PE, 1 : 1) gave benzopyran **43** (90 mg, 64%) as a colourless solid. $R_f$ = 0.17 (EtOAc-PE, 1 : 1); m.p. 95-96 °C ($CH_2Cl_2$-hexane); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.37 (dd, *J* = 17.0, 8.0 Hz, 1H), 2.84 (dd, *J* = 17.0, 5.4 Hz, 1H), 3.25-3.28 (m, 1H), 3.66 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 4.29 (dd, *J* = 11.7, 11.1 Hz, 1H), 4.61 (dd, *J* = 11.1, 5.2 Hz, 1H), 6.39 (d, *J* = 9.2 Hz, 1H), 6.97 (d, *J* = 9.2 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 30.0, 43.0, 51.8, 56.0, 56.6, 70.1, 102.5, 111.4, 117.9, 142.2, 152.5, 154.1, 171.7, 191.0; IR (neat): 2947, 1727, 1682, 1487, 1247, 1186, 1110, 1086 $cm^{-1}$; GC-MS: *m/z* (%) = 280 ($M^+$, 100), 249 (29), 180 (48), 137 (57), 122 (24), 99 (59): $t_R$ = 30.43 min; HRMS (ESI): calcd for $C_{14}H_{16}O_6Na$ [M + $Na^+$] 303.0839, found 303.0838.

**(3a*S**,9b*S**)-3a,4-Dihydro-3*H*-furo[3,2-*c*]chromen-2(9b*H*)-one (44)**[S7]

To ketone **42** (30 mg, 0.14 mmol) in $CH_2Cl_2$ (1.0 mL) and MeOH (0.7 mL) was added $CeCl_3.7H_2O$ (102 mg, 0.27 mmol). The solution was cooled to –78 °C and $NaBH_4$ (8 mg, 0.20 mmol) was added. After stirring for 45 min, 0.2 M HCl (5 mL) was added and the mixture extracted with $CHCl_3$ (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residual crude alcohol was dissolved in $CHCl_3$ (1 mL) and *p*-TsOH.$H_2O$ (1 mg) was added. After stirring at r.t. for 90 min the solvent was removed *in vacuo* and column chromatography (EtOAc-PE, 1 : 3) gave lactone **44** (18 mg, 69%) as a colourless oil. $R_f$ = 0.26 (EtOAc-PE, 1 : 2); $^1$H NMR (500 MHz, $CDCl_3$): δ = 2.46 (dd, *J* = 17.8, 4.3 Hz, 1H), 2.86 (dd, *J* = 17.8, 8.4 Hz, 1H), 2.98-3.05 (m, 1H), 3.83 (dd, *J* = 11.5, 9.4 Hz, 1H), 4.21 (dd, *J* = 11.5, 4.4 Hz, 1H), 5.48 (d, *J* = 6.2 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 7.01-7.04 (m, 1H), 7.26-7.30 (m, 1H), 7.41 (d, *J* = 7.2 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 31.1, 33.6, 64.8, 74.2, 117.4, 118.5, 121.9, 130.7, 131.4, 155.1, 175.3; IR (neat): 2856, 1779, 1748, 1489, 1466, 1454, 1223, 1196, 1173, 1156, 1044 cm$^{-1}$; GC-MS: *m/z* (%) = 190 ($M^+$, 88), 145 (75), 131 (100): $t_R$ = 21.79 min.

The spectroscopic data ($^1$H and $^{13}$C NMR) were consistent with reported values.[S7,S8]

**(3a*S**,9b*S**)-6,9-Dimethoxy-3a,4-dihydro-3*H*-furo[3,2-*c*]chromen-2(9b*H*)-one (45)**

To ketone **43** (115 mg, 0.41 mmol) in $CH_2Cl_2$ (3.5 mL) and MeOH (2.5 mL) was added $CeCl_3.7H_2O$ (306 mg, 0.82 mmol). The solution was cooled to –78 °C and $NaBH_4$ (23 mg, 0.62 mmol) was added. After stirring for 45 min, 0.2 M HCl (5 mL) was added and the mixture extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residual crude alcohol was dissolved in $CHCl_3$ (4 mL) and *p*-TsOH.$H_2O$ (5 mg) was added. After stirring at r.t. for 90 min the solvent was removed *in vacuo* and column chromatography (graded solvent, EtOAc-PE, 1 : 1 to 2 : 1) gave lactone **45** (86 mg, 84%) as a colourless solid. $R_f$ = 0.40 (EtOAc-PE, 2 : 1); m.p. 116-117 °C; $^1$H NMR (500 MHz, $CDCl_3$) δ 2.37-2.40 (m, 1H), 2.86-2.92 (m, 2H), 3.75-3.79 (m, 1H), 3.82 (s, 3H), 3.83 (s, 3H), 4.28 (dd, *J* = 11.3, 4.2 Hz, 1H), 5.60 (d, *J* = 5.1 Hz, 1H), 6.42 (d, *J* = 8.9 Hz, 1H), 6.84 (d, *J* = 8.9 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 31.3, 32.7, 55.9, 56.5, 64.9, 70.8, 101.8, 108.8, 112.7, 142.6, 145.8, 153.3, 175.3; IR (neat): 2941, 1770, 1493, 1251, 1159, 1100, 1080 cm$^{-1}$; GC-MS: *m/z* (%) = 250 ($M^+$, 100), 235 (58), 191 (28): $t_R$ = 30.77 min; HRMS (ESI): calcd for $C_{13}H_{15}O_5$ [M + $H^+$] 251.0914, found 251.0913.

---

[S7] Y. Ozaki, K. Mochida and S.-W. Kim, *Chem. Pharm. Bull.*, 1987, **35**, 1790-1795.

[S8] J. Bentley, P. A. Nilsson and A. F. Parsons, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1461-1469.

**(3a*S**,9b*S**)-3a,4-Dihydro-3*H*-furo[3,2-*c*]chromen-2(9b*H*)-one (44)**[S7] **and methyl 2-((3*R**,4*S**)-4-hydroxychroman-3-yl)acetate (46)**[S8]

To benzaldehyde **40** (200 mg, 0.91 mmol) in benzene (20 mL) were added $Bu_3SnH$ (397 mg, 1.36 mmol ) and AIBN (15 mg, 0.09 mmol). The solution was flushed with argon for 30 min then heated at reflux for 2 h. The mixture was cooled to r.t., concentrated *in vacuo* and the resulting oil purified by column chromatography (EtOAc-hexane, 1 : 1 in 5% KF/silica) to yield an inseparable 1.4:1 mixture of lactone **44** and alcohol **46** as a colourless oil (170 mg) in a combined 92% yield.

**Spectroscopic data for alcohol 46.**

$R_f$ = 0.28 (EtOAc-hexane, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$) δ = 2.11-2.12 (m, 1H), 2.37-2.38 (m, 2H), 2.47-2.50 (m, 1H), 3.70 (s, 3H), 4.08 (dd, *J* = 11.3, 5.1 Hz, 1H), 4.33 (dd, *J* = 11.3, 2.7 Hz, 1H), 4.51 (t, *J* = 5.1 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 6.93-6.96 (m, 1H), 7.20-7.23 (m, 1H), 7.34 (d, *J* = 7.7 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ = 33.1, 36.6, 51.9, 65.5, 67.8, 116.9, 121.0, 123.0, 129.7, 129.8, 154.0, 172.6; GC-MS: *m/z* (%) = 190 ($M^+$, 96), 145 (78), 131 (100): $t_R$ = 24.32 min.

The spectroscopic data for **46** ($^1$H and $^{13}$C NMR) were consistent with reported values.[S8]

The spectroscopic data for lactone **44** were identical to those described above.

**(3a*S**,9b*S**)-6,9-Dimethoxy-3a,4-dihydro-3*H*-furo[3,2-*c*]chromen-2(9b*H*)-one (45) and methyl 2-((3*R**,4*S**)-4-hydroxy-5,8-dimethoxychroman-3-yl)acetate (47)**

To benzaldehyde **41** (110 mg, 0.392 mmol) in benzene (7.5 mL) were added $Bu_3SnH$ (160 mg, 0.549 mmol ) and AIBN (6.4 mg, 0.039 mmol). The solution was flushed with argon for 30 min then heated at reflux for 2 h. The mixture was cooled to r.t., concentrated *in vacuo* and the resulting oil purified by column chromatography (EtOAc-hexane, 1 : 1 in 10% KF/silica) to give alcohol **47** (44 mg, 40%) as a colourless oil and lactone **45** (38 mg, 39%) as a colourless solid.

**Spectroscopic data for alcohol 47.**

$R_f$ = 0.20 (EtOAc-hexane, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$) δ = 2.30 (dd, *J* = 16.6, 6.9 Hz, 1H), 2.40 (dd, *J* = 16.6, 8.0 Hz, 1H), 2.52-2.56 (m, 1H), 2.88 (s, 1H), 3.68 (s, 3H), 3.82 (s, 6H), 4.23 (dd, *J* = 11.0, 3.5 Hz, 1H), 4.27 (dd, *J* = 11.0, 2.0 Hz, 1H), 4.68 (s, 1H), 6.37 (d, *J* = 8.8 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ = 32.8, 35.2, 51.7, 55.5, 56.3, 63.1, 65.5, 100.8, 110.7, 113.2, 142.8, 144.3, 152.4, 172.4; HRMS (ESI): calcd for $C_{14}H_{18}O_6Na$ [M + $Na^+$] 305.0996, found 305.0996.

The spectroscopic data for lactone **45** were identical to those described above.

**(*E*)-Ethyl 3-(2-formylphenoxy)acrylate (48)**[S9]

To a solution of salicylaldehyde **38** (1.0 g, 8.19 mmol) in MeCN (5 mL) at 0 °C was added *N*-methyl morpholine (40 mg, 0.41 mmol) followed by the dropwise addition of ethyl propiolate (0.92 mL, 9.00 mmol). Stirring was continued at 0 °C for 1 h then at r.t. for 2 h. After removal of the solvent *in vacuo*, column chromatography (gradient elution, EtOAc-PE, 1 : 9 to 1 : 4) gave acrylate **48** (1.47 g, 82%) as a pale yellow oil. $R_f$ = 0.25 (EtOAc-PE, 1 : 9); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.2 Hz, 3H), 4.21 (q, *J* = 7.2 Hz, 2H), 5.63 (d, *J* = 12.3 Hz, 1H), 7.16 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.30-7.34 (m, 1H), 7.63-7.67 (m, 1H), 7.84 (d, *J* = 12.3 Hz, 1H), 7.93 (dd, *J* = 7.7, 1.8 Hz, 1H), 10.37 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.3, 60.4, 104.2, 118.3, 125.4, 126.5, 129.0, 136.0, 157.6, 158.0, 166.5, 188.1; IR (neat): 2982, 1708, 1693, 1601, 1218, 1116 cm$^{-1}$; GC-MS: *m/z* (%) = 220 ($M^+$, 1), 147 (100), 121 (27): $t_R$ = 22.46 min.

The spectroscopic data ($^1$H and $^{13}$C NMR) were consistent with reported values.[S9]

**(*E*)-Ethyl 3-(2-formyl-3,6-dimethoxyphenoxy)acrylate (49)**

To a solution of phenol **39**[S6] (1.0 g, 5.49 mmol) in $CH_2Cl_2$ (20 mL) was added *N*-methyl morpholine (0.67 g, 6.59 mmol) followed by the addition of ethyl propiolate (0.61 mL, 6.04 mmol) over 5 min and stirring was continued for a further 6 h. The solution was diluted with 0.2 M HCl (20 mL), extracted with $CH_2Cl_2$ (3 × 10 mL) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (gradient elution, $CHCl_3$-PE, 3 : 1 to $CHCl_3$) gave acrylate **49** (1.38 g, 90%) as a yellow solid. $R_f$ = 0.30 (EtOAc-PE, 1 : 1); m.p. 84-85 °C; $^1$H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, *J* = 7.1 Hz, 3H), 3.77 (s, 3H), 3.84 (s, 3H), 4.10 (q, *J* = 7.1 Hz, 2H), 5.17 (d, *J* = 12.2 Hz, 1H), 6.80 (d, *J* = 9.1 Hz, 1H), 7.14 (d, *J* = 9.1 Hz, 1H), 7.63 (d, *J* = 12.2 Hz, 1H), 10.31 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 14.1, 56.3, 56.8, 59.8, 100.0, 109.1, 118.2, 119.3, 144.0, 145.2, 155.4, 161.1, 166.9, 187.8; IR (neat): 2979, 1695, 1647, 1489, 1268, 1122 cm$^{-1}$; GC-MS: *m/z* (%) = 280 ($M^+$, 1), 207 (100), 192 (20): $t_R$ = 30.23 min; HRMS (ESI): calcd for $C_{14}H_{16}O_6Na$ [M + $Na^+$] 303.0839, found 303.0839.

***cis*-Benzofuran (50)**[S10] **and *trans*-benzofuran (53)**

A solution of benzaldehyde **48** (250 mg, 1.14 mmol), $Bu_3SnH$ (430 mg, 1.48 mmol) and AIBN (19 mg, 0.11 mmol) in benzene (25 mL) was flushed with argon for 30 min after which the solution was heated

---

[S9] S.-L. Cui, J. Wang, X.-F. Lin and Y.-G. Wang, *J. Org. Chem*., 2007, **72**, 7779-7782.

[S10] A. Kasahara, T. Izumi, A. Suzuki and T. Takeda, *Bull. Chem. Soc. Jpn*., 1976, **49**, 3711-3712.

at reflux for 3 h. After cooling and removal of the solvent *in vacuo* the remaining residue was purified by column chromatography (EtOAc-hexane, 1 : 1 in 10% KF/silica) to give an inseparable mixture of lactone **50** and alcohol **52** as a colourless oil (193 mg) in a combined 86% yield (**50**:**52** 34:66), $R_f$ = 0.25 (EtOAc-hexane, 1 : 2). To allow characterization of the cyclization products a small ammount of the mixture was acetylated as follows. To a mixture of lactone **50** and alcohol **52** (75 mg) in $CH_2Cl_2$ (0.5 mL) were added pyridine (53 mg, 0.68 mmol), DMAP (4 mg, 0.03 mmol) and acetic anhydride (103 mg, 1.01 mmol). After stirring for 90 min the mixture was diluted with 1 M HCl (5 mL) and stirred vigorously for 10 min. After extracting with $CHCl_3$ (3 × 5 mL) the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (EtOAc-hexane, 1 : 2) gave acetate **53** (58 mg) as a colourless oil and recovered lactone **50** (22 mg) as a colourless solid.

**Spectroscopic data for acetate 53.**

$R_f$ = 0.40 (EtOAc-hexane, 1 : 2); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3H), 2.09 (s, 3H), 2.72 (dd, *J* = 16.1, 8.2 Hz, 1H), 2.81 (dd, *J* = 16.1, 5.3 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 5.00-5.03 (m, 1H), 6.05 (d, *J* = 2.4 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.94 (m, 1H), 7.29 (m, 1H), 7.40 (d, *J* = 7.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.1, 21.0, 38.1, 60.9, 78.3, 83.9, 110.8, 121.2, 123.5, 126.9, 131.4, 160.2, 169.8, 170.9; IR (neat): 2982, 1731, 1226, 1175, 1016 cm$^{-1}$; GC-MS: *m/z* (%) = 264 ($M^+$, 7), 221 (8), 204 (33), 134 (40), 131 (100): $t_R$ = 24.29 min; HRMS (ESI): calcd for $C_{14}H_{16}O_5Na$ [M + $Na^+$] 287.0890, found 287.0891.

**Spectroscopic data for lactone 50.**

$R_f$ = 0.25 (EtOAc-hexane, 1 : 2); m.p. 107-108 °C (lit.[S10] m.p. 111-112 °C); $^1$H NMR (500 MHz, $CDCl_3$): δ = 2.99 (dd, *J* = 19.1, 2.0 Hz, 1H), 3.05 (dd, *J* = 19.1, 6.6 Hz, 1H), 5.35-5.38 (m, 1H), 5.98 (d, *J* = 5.8 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.98-7.01 (m, 1H), 7.32-7.35 (m, 1H), 7.47 (d, *J* = 7.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 35.4, 80.9, 83.6, 110.7, 121.7, 123.0, 126.8, 132.1, 160.7, 174.6; IR (neat): 3052, 1752, 1174, 1004 cm$^{-1}$.

Spectroscopic data for **50** ($^1$H NMR) were consistent with reported values.[S10]

***cis*-Dimethoxybenzofuran (51) and *trans*-dimethoxybenzofuran (54)**

A solution of benzaldehyde **49** (250 mg, 0.89 mmol), $Bu_3SnH$ (338 mg, 1.16 mmol) and AIBN (15 mg, 0.09 mmol) in benzene (23 mL) was flushed with argon for 30 min after which the solution was heated at reflux for 2 h. After cooling and removal of the solvent *in vacuo* the remaining residue was filtered through a short column of 10% KF/silica (EtOAc-$CHCl_3$, 1 : 9). The fractions containing material between $R_f$ 0.15-0.40 were combined and subjected to further chromatography (EtOAc-$CHCl_3$, 1 : 9 to

1 : 4 in silica) to give lactone **51** (150 mg, 71%) as a colourless solid and alcohol **54** (64 mg, 25%) as a colourless oil.

**Spectroscopic data for lactone 51.**

$R_f$ = 0.38 (EtOAc-$CHCl_3$, 1 : 9); m.p. 181-181 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ = 3.01-3.09 (m, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 5.40-5.43 (m, 1H), 6.09 (d, *J* = 6.1 Hz, 1H), 6.39 (d, *J* = 8.8 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 35.2, 55.9, 56.7, 82.1, 82.4, 103.4, 112.6, 115.9, 139.0, 150.6, 151.5, 174.4; IR (neat): 2955, 1759, 1508, 1259, 1152, 1085, 1042 cm$^{-1}$; GC-MS: *m/z* (%) = 236 ($M^+$, 100), 221 (44), 191 (25), 177 (37): $t_R$ = 29.75 min; HRMS (ESI): calcd for $C_{12}H_{12}O_5Na$ [M + $Na^+$] 259.0577, found 259.0582.

**Spectroscopic data for alcohol 54.**

$R_f$ = 0.18 (EtOAc-$CHCl_3$, 1 : 9); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.2 Hz, 3H), 2.53 (brs, 1H), 2.68 (dd, *J* = 16.2, 8.0 Hz, 1H), 2.87 (dd, *J* = 16.2, 6.1 Hz, 1H), 3.83 (s, 6H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.97-5.00 (m, 1H), 5.36-5.37 (m, 1H), 6.34 (d, *J* = 8.8 Hz, 1H), 6.79 (d, *J* = 8.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.1, 38.1, 55.6, 56.7, 60.9, 75.9, 87.4, 102.4, 114.6, 116.1, 139.4, 149.3, 151.2, 170.1; IR (neat): 3491, 2936, 1730, 1506, 1259, 1081, 1020 cm$^{-1}$; GC-MS: *m/z* (%) = 264 ([M – 18]$^+$, 100), 249 (75), 191 (55), 176 (34), 161 (24): $t_R$ = 28.71 min; HRMS (ESI): calcd for $C_{14}H_{18}O_6Na$ [M + $Na^+$] 305.0996, found 305.0996.

**Ethyl 2-(3-oxo-2,3-dihydrobenzofuran-2-yl)acetate (55)**

A solution of benzaldehyde **48** (72 mg, 0.33 mmol) in chlorobenzene (1.5 mL) with ACCN (120 mg, 0.49 mmol) and *tert*-dodecanethiol (199 mg, 0.98 mmol) was flushed with argon for 45 min then heated at 100 °C for 18 h. After removal of the solvent *in vacuo*, column chromatography (EtOAc-hexane, 1 : 4) gave an inseparable mixture of starting aldehyde **48** and ketone **55** (63:37) as a colourless oil (54 mg) in a combined 75% yield.

**Ethyl 2-(4,7-dimethoxy-3-oxo-2,3-dihydrobenzofuran-2-yl)acetate (56) and ethyl 2-(3-hydroxy-4,7-dimethoxybenzofuran-2-yl)acetate (57)**

A solution of benzaldehyde **49** (100 mg, 0.36 mmol) in chlorobenzene (1.5 mL) with ACCN (131 mg, 0.54 mmol) and *tert*-dodecanethiol (217 mg, 1.07 mmol) was flushed with argon for 45 min then heated at 100 °C for 18 h. After removal of the solvent *in vacuo*, column chromatography (EtOAc-hexane, 1 : 1) gave ketone **56** (47 mg, 47%) as a pale yellow solid and enol **57** (11 mg, 11%) as a colourless oil.

**Spectroscopic data for ketone 56.**

$R_f$ = 0.22 (EtOAc-hexane, 1 : 1); m.p. 146-147 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.2 Hz, 3H), 2.88 (dd, *J* = 17.1, 7.1 Hz, 1H), 3.08 (dd, *J* = 17.1, 3.8 Hz, 1H), 3.88 (s, 3H), 3.90 (s, 3H), 4.10-4.17 (m, 2H), 4.89 (dd, *J* = 7.1, 3.8 Hz, 1H), 6.37 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.0, 36.0, 56.1, 56.9, 61.1, 81.6, 102.4, 111.5, 121.1, 140.0, 151.5, 162.8, 169.0, 197.7; IR (neat): 2942, 1731, 1701, 1604, 1514, 1268, 1242, 1180 cm$^{-1}$; HRMS (ESI): calcd for $C_{14}H_{16}O_6Na$ [M + Na$^+$] 303.0839, found 303.0840.

**Spectroscopic data for enol 57.**

$R_f$ = 0.12 (EtOAc-hexane, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3H), 2.76 (d, *J* = 16.9 Hz, 1H), 3.06 (d, *J* = 16.9 Hz, 1H), 3.87 (s, 3H), 3.90 (s, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 6.13 (brs, 1H), 6.38 (d, *J* = 8.8 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 13.9, 38.1, 56.1, 57.0, 61.7, 102.1, 102.9, 109.0, 122.9, 139.6, 152.4, 160.3, 170.8, 193.3; IR (neat): 3353, 2935, 1723, 1600, 1513, 1265, 1072 cm$^{-1}$; HRMS (ESI): calcd for $C_{14}H_{16}O_6Na$ [M + Na$^+$] 303.0839, found 303.0840.

**(3a*R**,9b*R**)-3,3a-Dihydro-5*H*-furo[3,2-*c*]isochromene-2,6,9(9b*H*)-trione (5)**

To benzopyran **15**[S11] (11 mg, 0.044 mmol) in MeCN (0.5 mL) and acetone (0.2 mL) was added cerium(IV) ammonium nitrate (60 mg, 0.109 mmol) in water (0.2 mL) and the solution stirred at r.t. for 30 min. After dilution with water and extraction with $CHCl_3$ (3 × 5 mL), the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (EtOAc-$CHCl_3$, 1 : 1) gave benzoquinone **5** (9 mg, 93%) as a yellow oil. $R_f$ = 0.36 (EtOAc-$CHCl_3$, 1 : 1); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.72 (d, *J* = 17.8 Hz, 1H), 2.92 (dd, *J* = 17.8, 4.9 Hz, 1H), 4.32 (dd, *J* = 18.8, 2.0 Hz, 1H), 4.35 (dd, *J* = 4.9, 2.9 Hz, 1H), 4.76 (d, *J* = 18.8 Hz, 1H), 5.09-5.10 (m, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 6.88 (d, *J* = 10.3 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 36.8, 61.2, 68.6, 72.4, 132.9, 136.3, 136.8, 143.7, 173.6, 184.0, 185.1; IR (neat): 2923, 1748, 1658, 1200, 1154, 1057 cm$^{-1}$; GC-MS: *m/z* (%) = 176 ([M – 44]$^+$, 100), 175 (65), 147 (28), 91 (20): $t_R$ = 17.98 min; HRMS (ESI): calcd for $C_{11}H_9O_5$ [M + H$^+$] 221.0445, found 221.0443.

**(3a*S**,9b*S**)-3a,4-Dihydro-3*H*-furo[3,2-*c*]chromene-2,6,9(9b*H*)-trione (58)**

To benzopyran **45** (15 mg, 0.060 mmol) in MeCN (0.5 mL) and water (0.25 mL) was added phenyliodine bis(trifluoroacetate) (51 mg, 0.119 mmol) and the solution stirred at r.t. for 1 h. Dilute

---

[S11] C. D. Donner, *Synthesis*, 2010, 415-420.

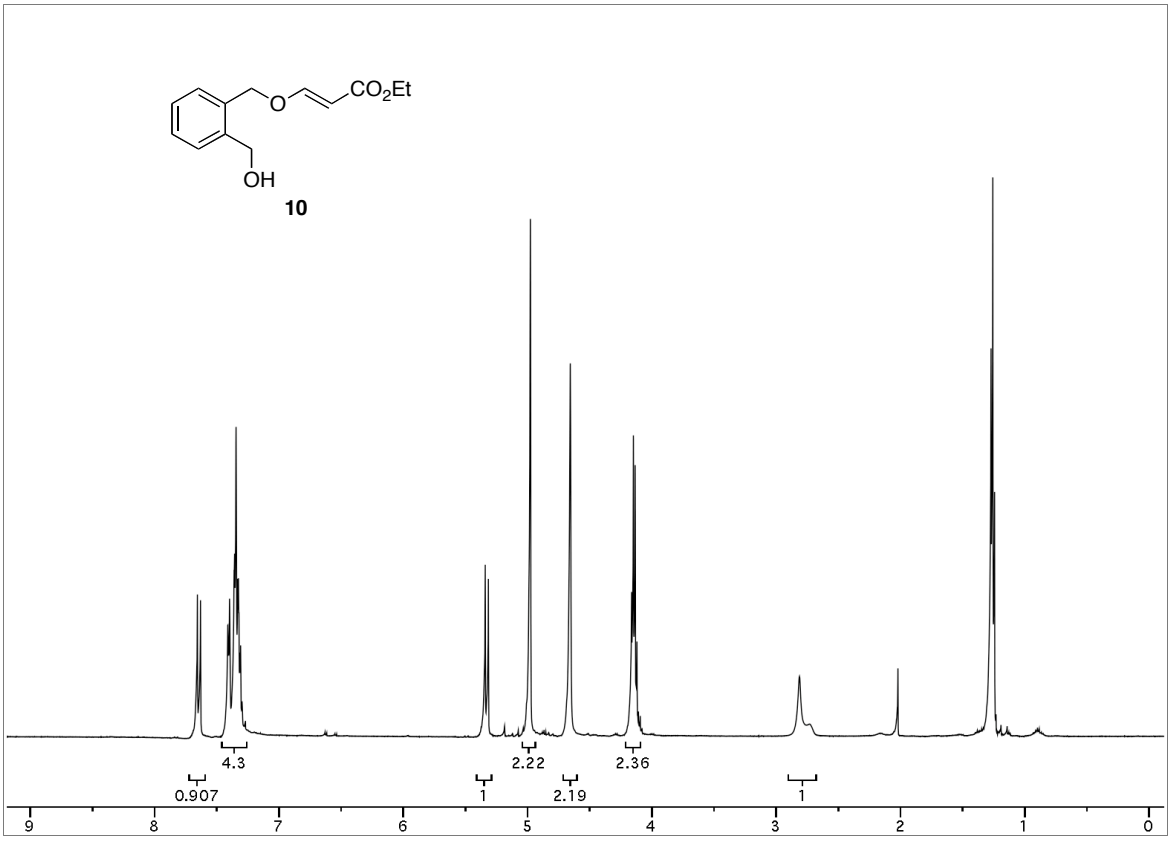
$NaHCO_3$ (5 mL) was added and the mixture extracted with $CHCl_3$ (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (EtOAc-$CHCl_3$-MeCN, 2 : 1 : 1) gave benzoquinone **58** (10 mg, 76%) as a yellow solid. $R_f$ = 0.26 (EtOAc-$CHCl_3$, 2 : 1); m.p. 180-185 °C (decomp.); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.35 (d, *J* = 16.2 Hz, 1H), 2.89-2.97 (m, 2H), 3.78-3.83 (m, 1H), 4.48 (dd, *J* = 11.7, 4.8 Hz, 1H), 5.39 (d, *J* = 4.9 Hz, 1H), 6.79 (d, *J* = 10.2 Hz, 1H), 6.83 (d, *J* = 10.2 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 30.9, 31.8, 65.9, 67.6, 115.2, 134.5, 137.4, 155.3, 173.6, 180.5, 184.7; IR (neat): 2933, 1773, 1682, 1647, 1593, 1416, 1197, 1162 cm$^{-1}$; HRMS (ESI): calcd for $C_{11}H_9O_5$ [M + H$^+$] 221.0445, found 221.0445.

**Pyranonaphthoquinone (59)**

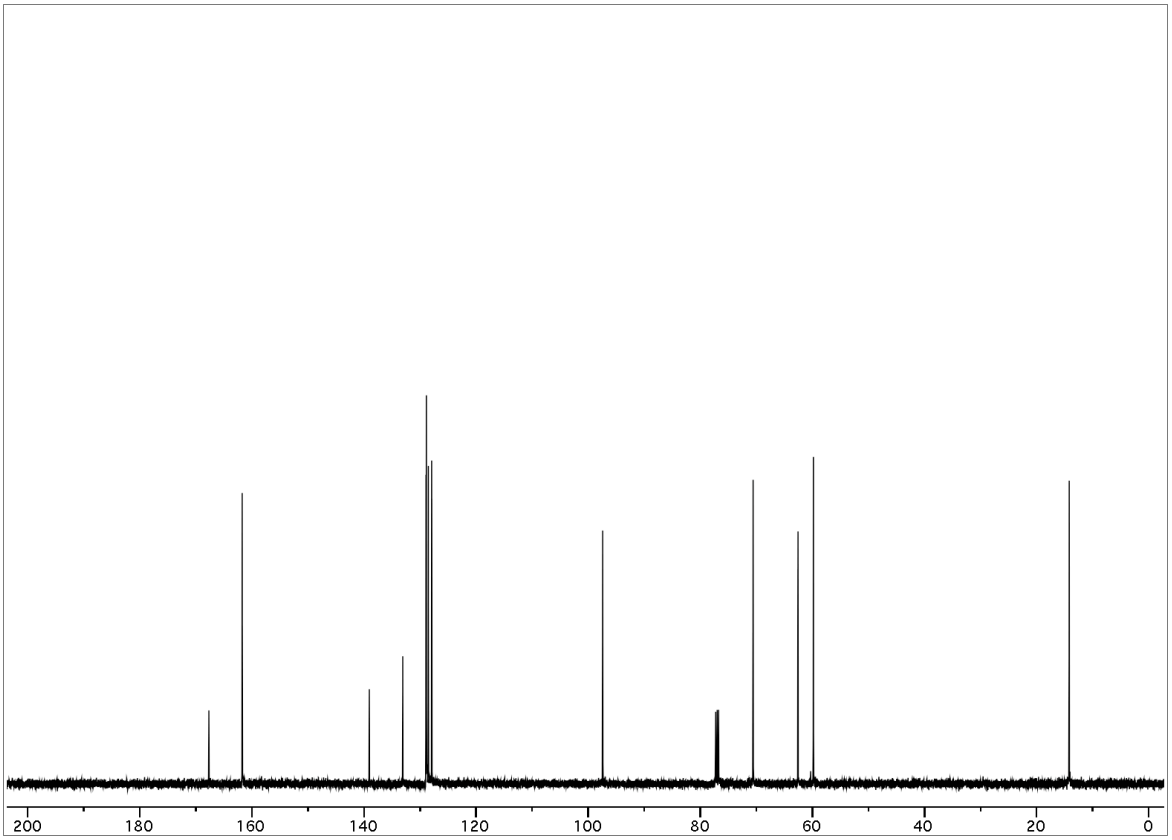
To a solution of benzoquinone **58** (11 mg, 0.054 mmol) in $CH_2Cl_2$ (2 mL) under nitrogen was added 1,3-dimethoxy-1-trimethylsiloxybuta-1,3-diene (22 mg, 0.109 mmol). The mixture was stirred at r.t. for 90 min, then silica gel (0.25 g) was added and the suspension was stirred vigorously for a further 1 h open to air. The mixture was concentrated *in vacuo* and the residual solid was purified by column chromatography (gradient elution, EtOAc-$CHCl_3$, 2 : 1 to EtOAc) to give naphthoquinone **59** (9 mg, 55%) as a yellow solid. $R_f$ = 0.24 (EtOAc); m.p. 225-230 °C ($CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.36 (d, *J* = 16.0 Hz, 1H), 2.88-2.96 (m, 2H), 3.80-3.84 (m, 1H), 3.96 (s, 3H), 3.97 (s, 3H), 4.51 (dd, *J* = 11.6, 4.9 Hz, 1H), 5.53 (d, *J* = 5.3 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 7.33 (d, *J* = 2.5 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 31.1, 31.8, 56.1, 56.5, 66.0, 68.5, 103.7, 103.9, 113.2, 114.7, 136.0, 158.2, 162.6, 165.6, 174.0, 175.8, 182.5; IR (neat): 2949, 1767, 1665, 1631, 1595, 1336, 1236, 1217, 1160 cm$^{-1}$; HRMS (ESI): calcd for $C_{17}H_{15}O_7$ [M + H$^+$] 331.0812, found 331.0813.

**Furanobenzoquinone (60)**

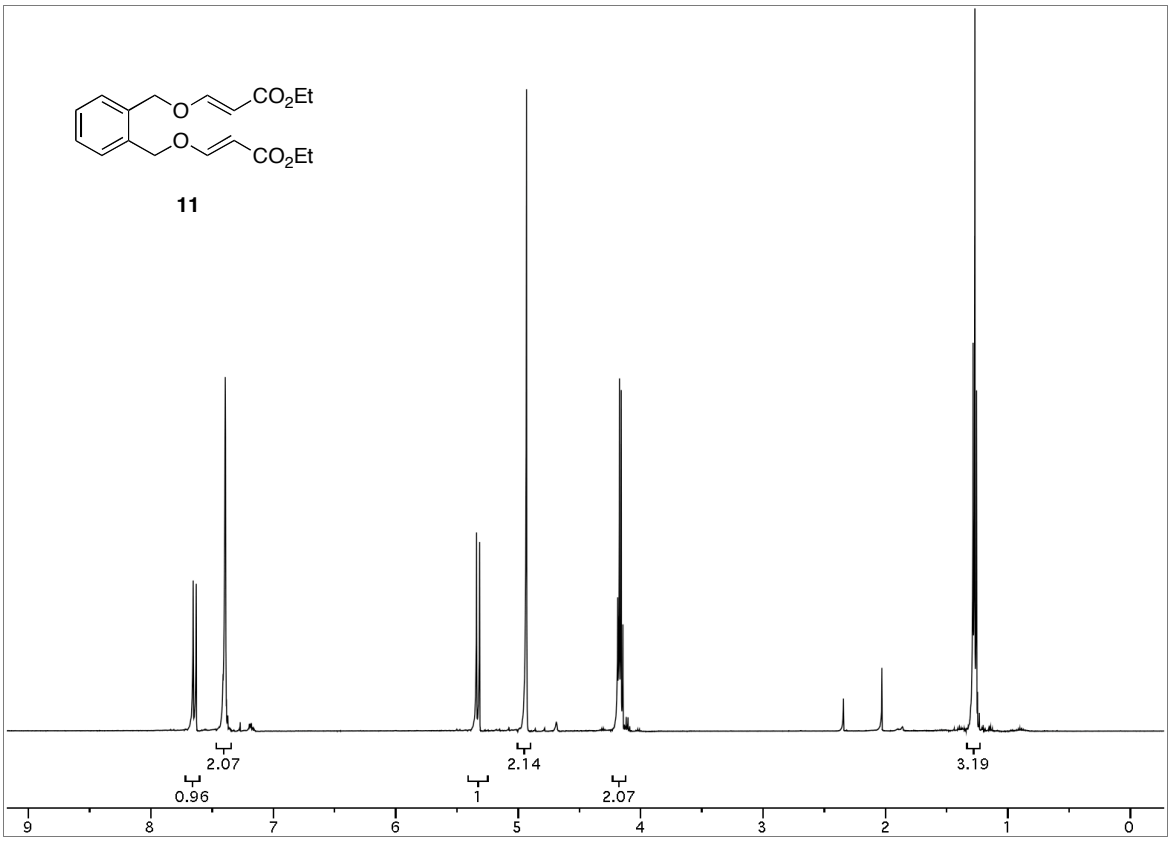
To benzofuran **51** (22 mg, 0.093 mmol) in MeCN (1.5 mL) and water (0.5 mL) was added phenyliodine bis(trifluoroacetate) (80 mg, 0.186 mmol) and the solution stirred at r.t. for 2 h. The mixture was diluted with water and extracted with $CHCl_3$ (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Column chromatography (EtOAc-$CHCl_3$-MeCN, 1 : 4 : 1) gave benzoquinone **60** (12 mg, 63%) as a yellow solid. $R_f$ = 0.38 (EtOAc-$CHCl_3$-MeCN, 1 : 4 : 1); m.p. 120-130 °C (decomp.); $^1$H NMR (500 MHz, $d_6$-acetone): δ = 2.95 (dd, *J* = 19.2, 1.0 Hz, 1H), 3.28 (dd, *J* = 19.2, 7.7 Hz, 1H), 5.75-5.78 (m, 1H), 6.10 (d, *J* = 6.6 Hz, 1H), 6.76 (d, *J* = 10.3 Hz, 1H), 6.78 (d, *J* = 10.3 Hz, 1H); $^{13}$C NMR (125 MHz, $d_6$-acetone): δ = 34.5, 82.1, 85.9, 119.6, 135.4, 138.4, 162.2, 174.7, 180.3, 183.9; IR (neat): 2953, 1778, 1687, 1646, 1175, 1138, 1049 cm$^{-1}$; HRMS (ESI): calcd for $C_{10}H_6O_5Na$ [M + Na$^+$] 229.0107, found 229.0108.



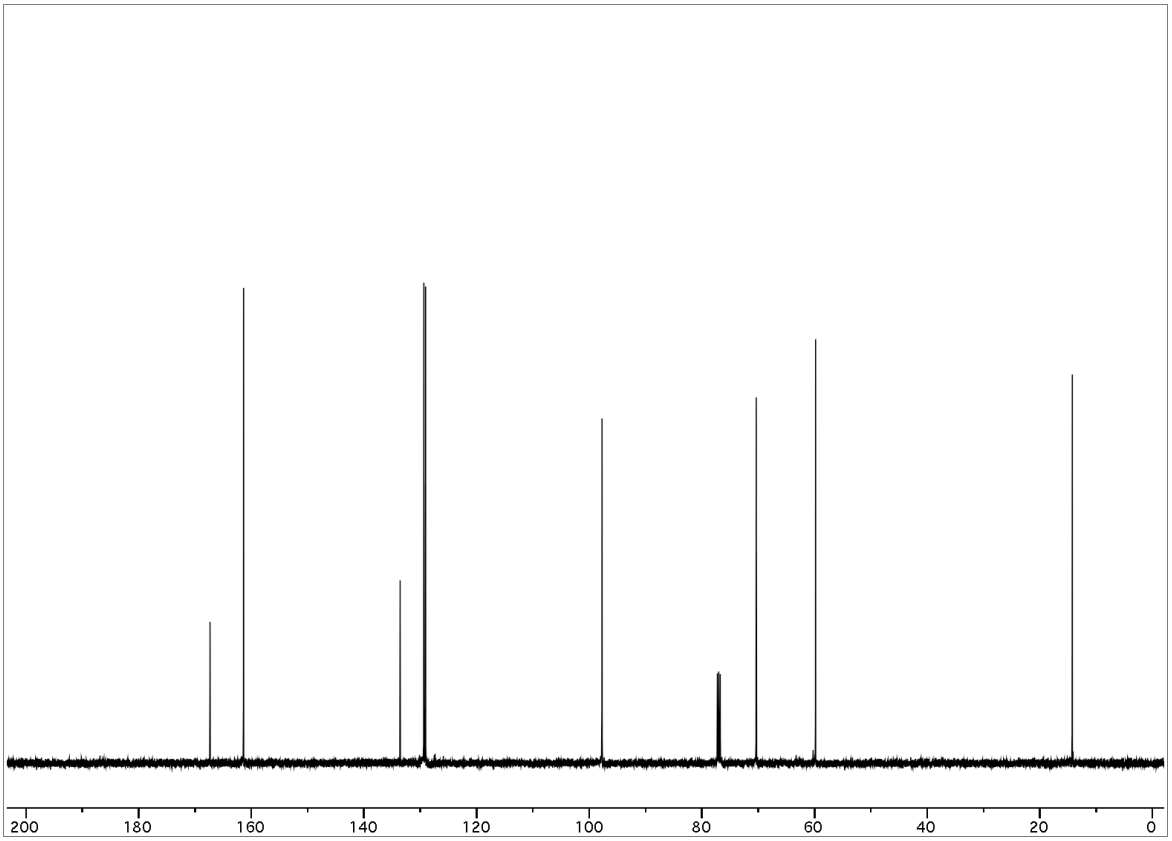

$^{1}$H NMR (500 MHz) spectrum of **10** in $CDCl_3$.



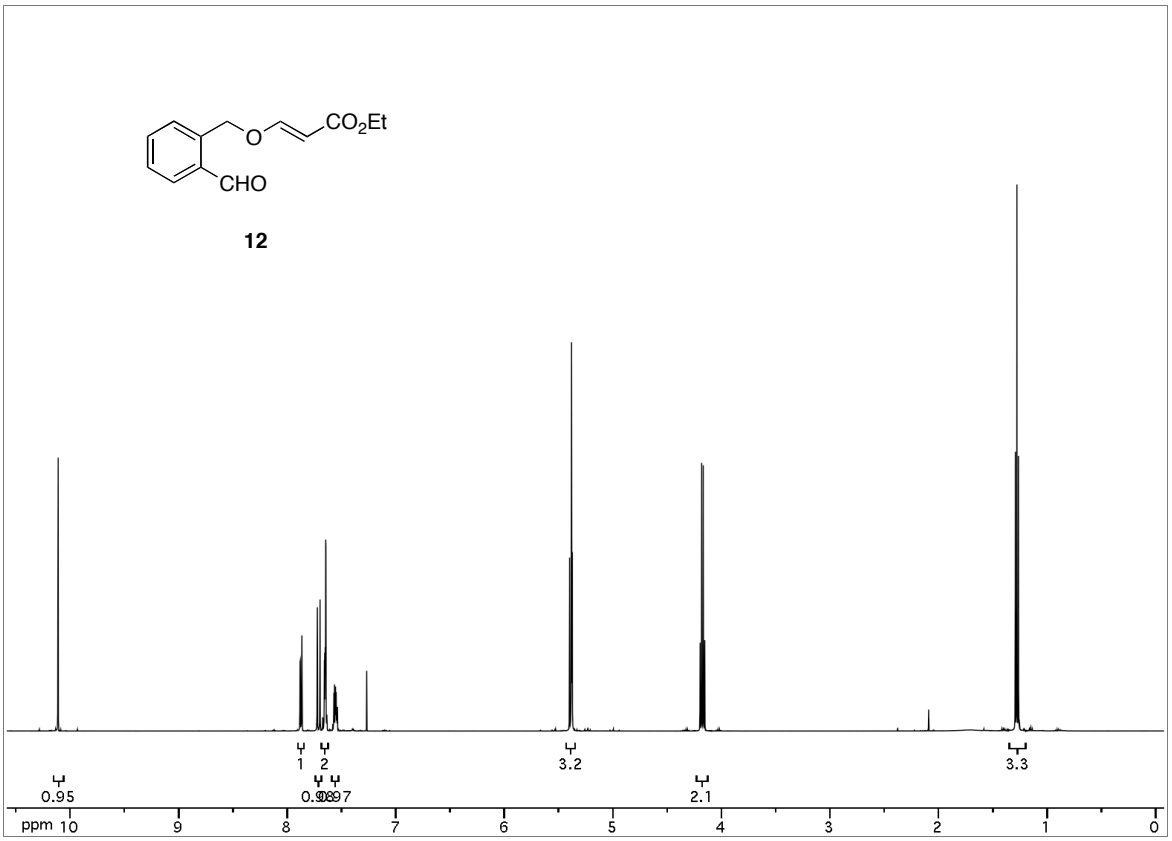

$^{13}$C NMR (125 MHz) spectrum of **10** in $CDCl_3$.



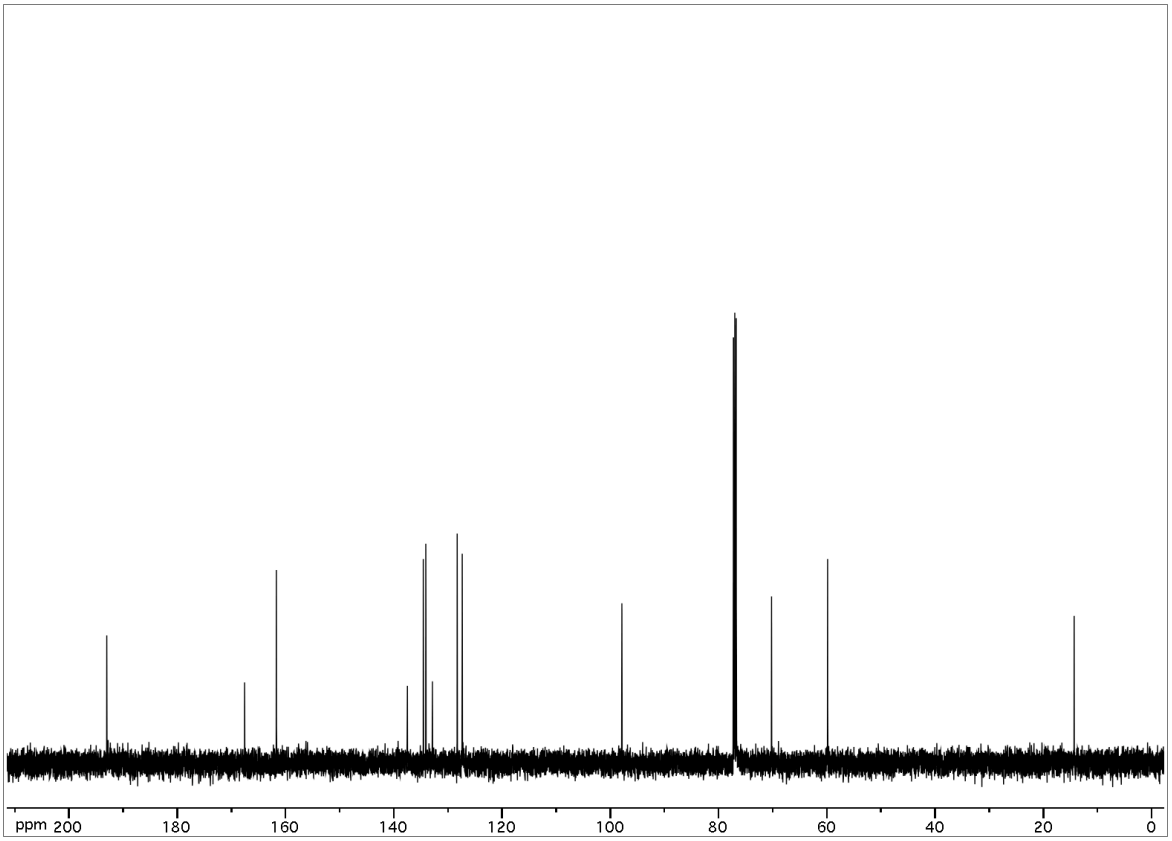

$^{1}$H NMR (500 MHz) spectrum of **11** in $CDCl_3$.



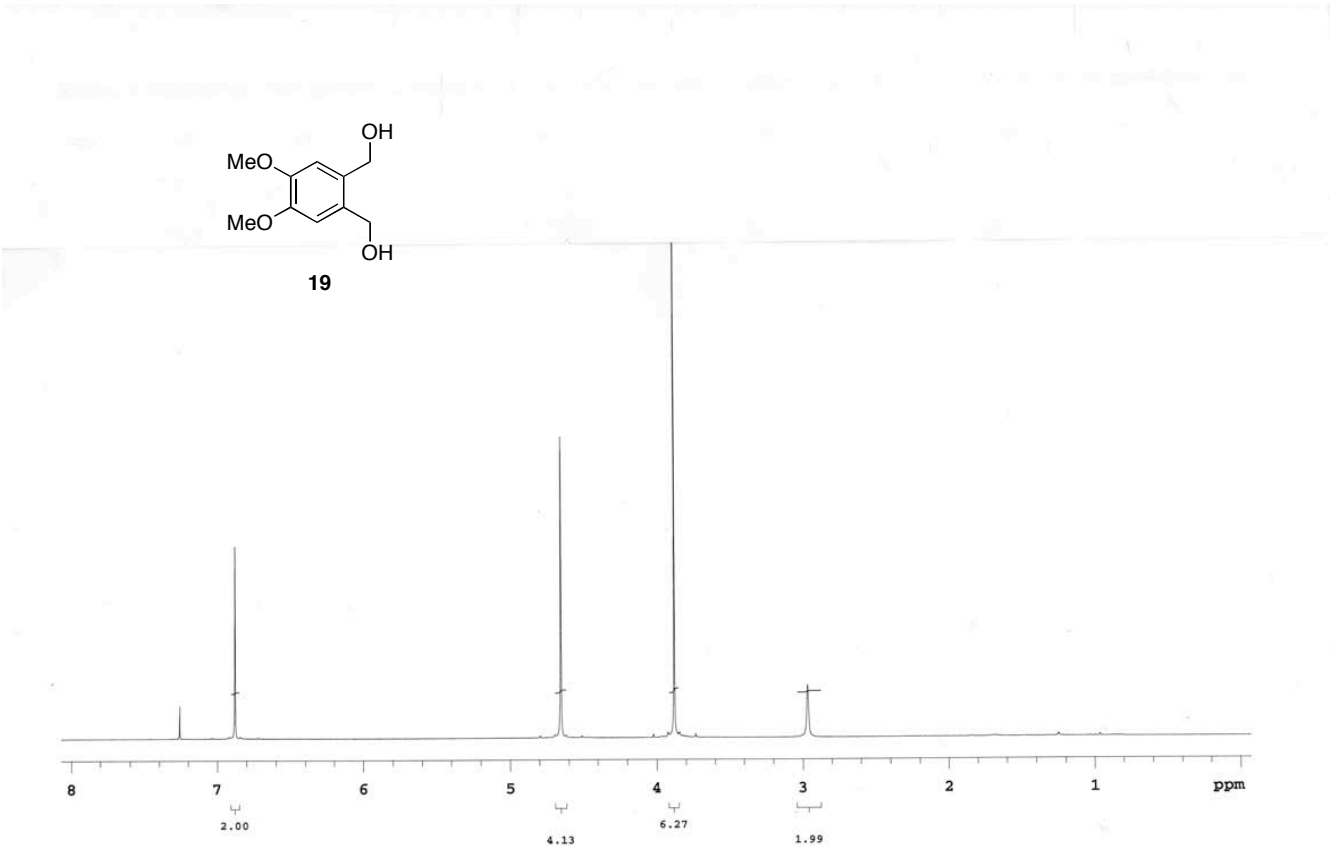

$^{13}$C NMR (125 MHz) spectrum of **11** in $CDCl_3$.



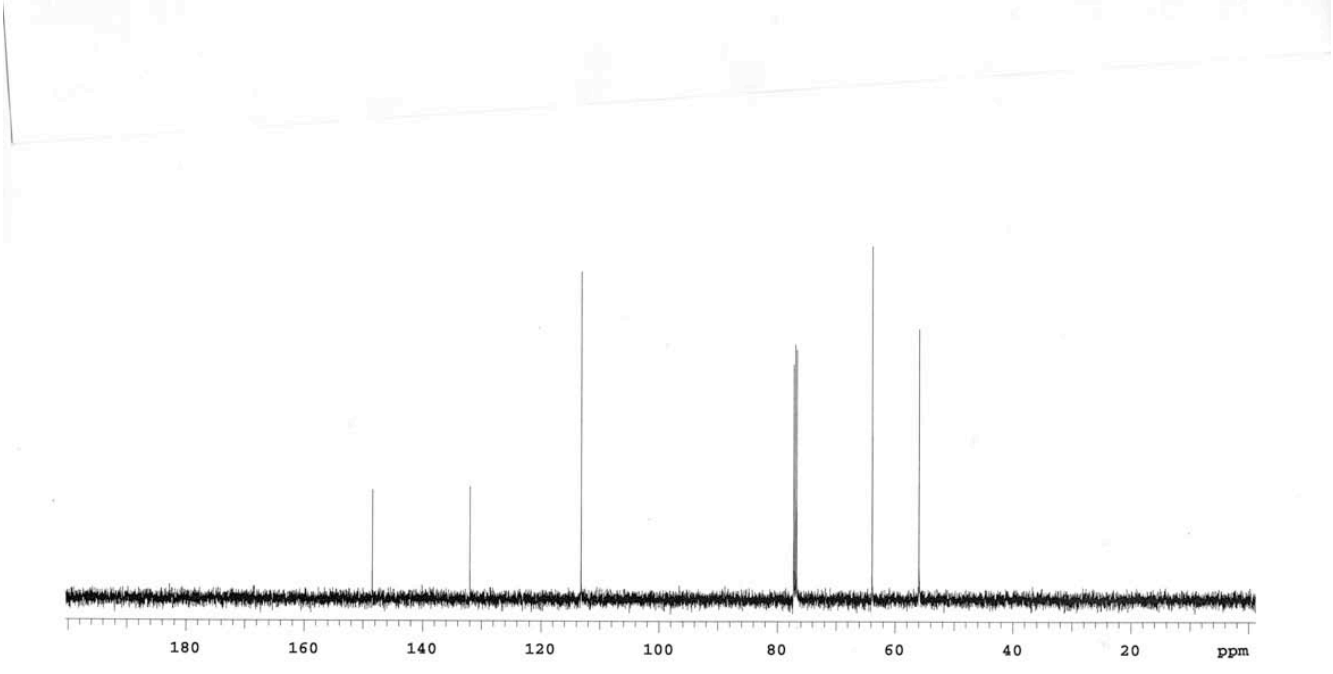

$^{1}$H NMR (500 MHz) spectrum of **12** in $CDCl_3$.



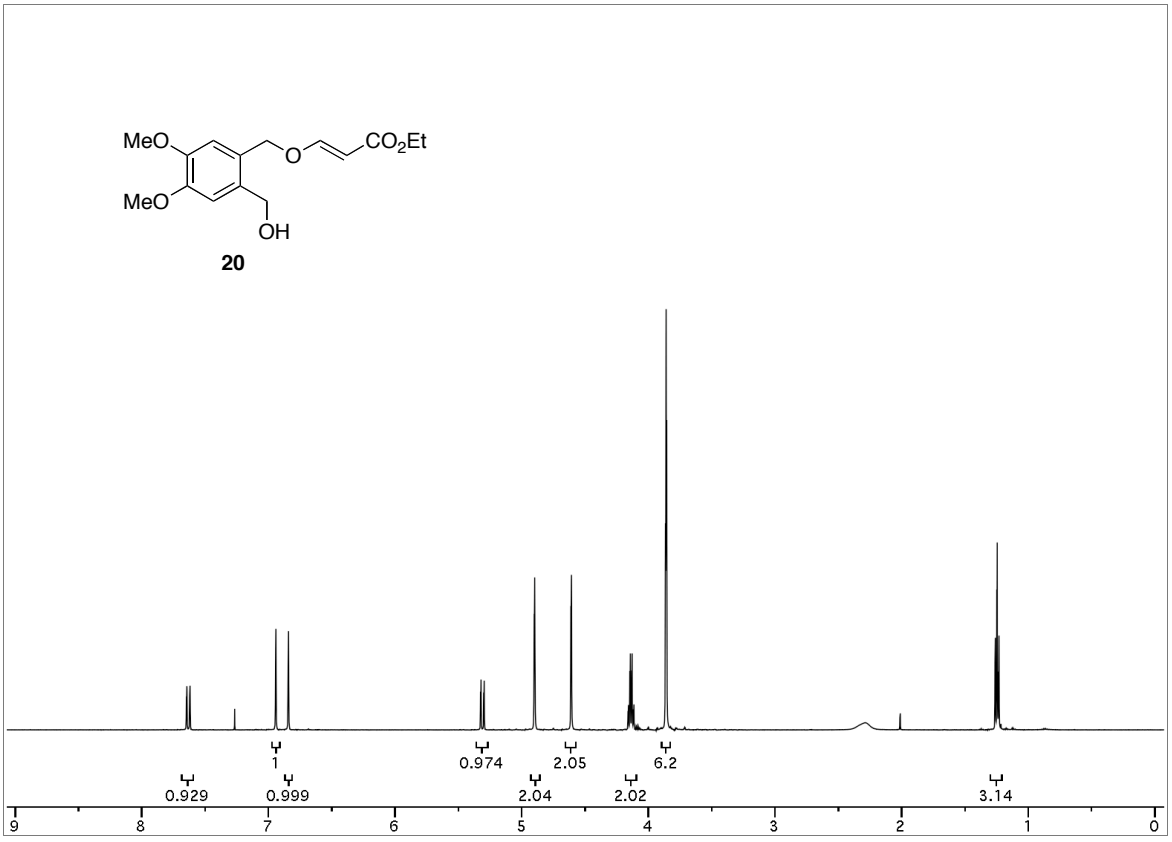

$^{13}$C NMR (125 MHz) spectrum of **12** in $CDCl_3$.



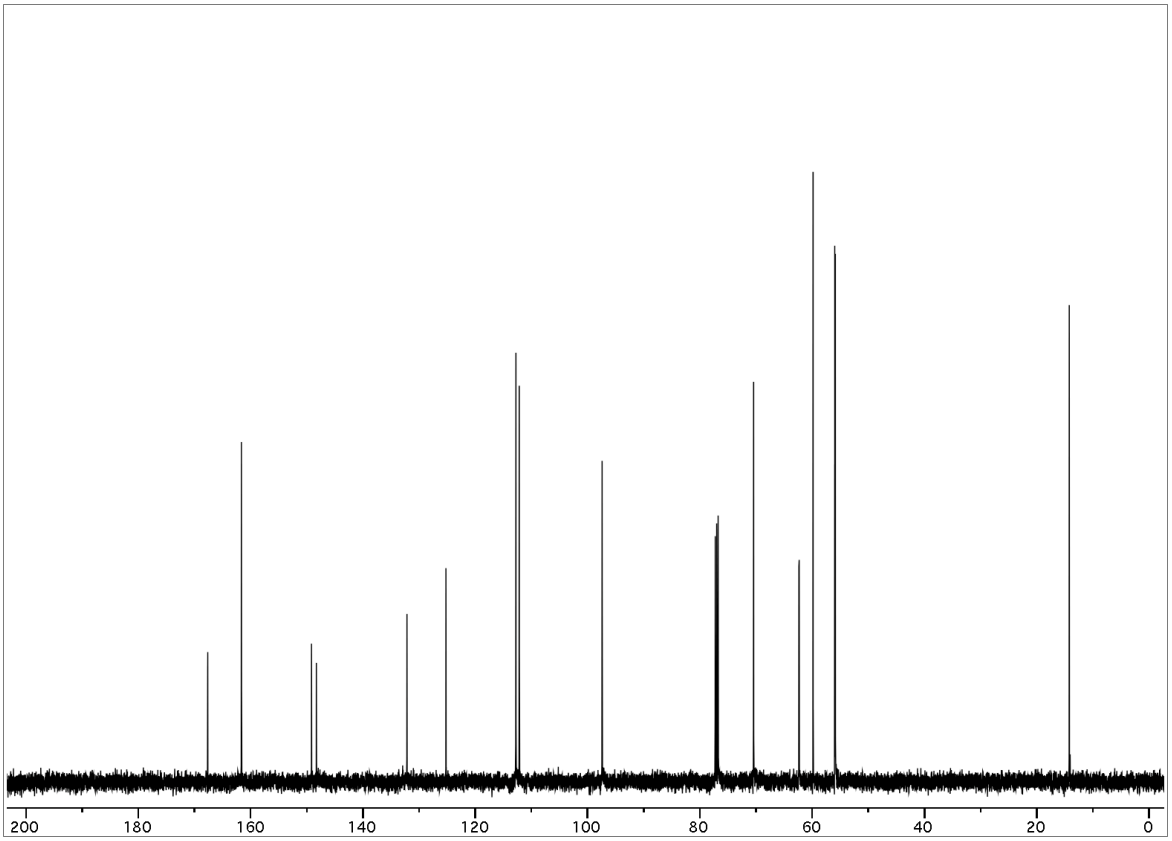

$^{1}$H NMR (500 MHz) spectrum of **19** in $CDCl_3$.



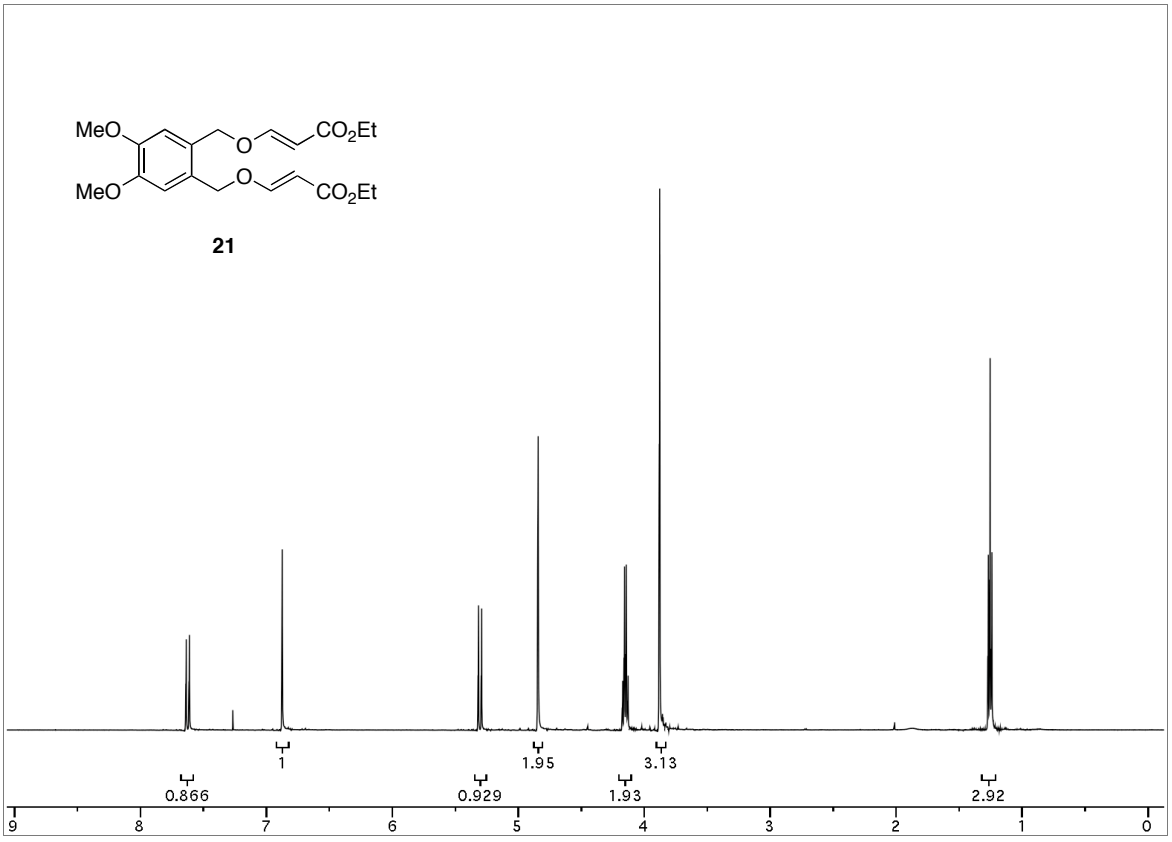

$^{13}$C NMR (125 MHz) spectrum of **19** in $CDCl_3$.



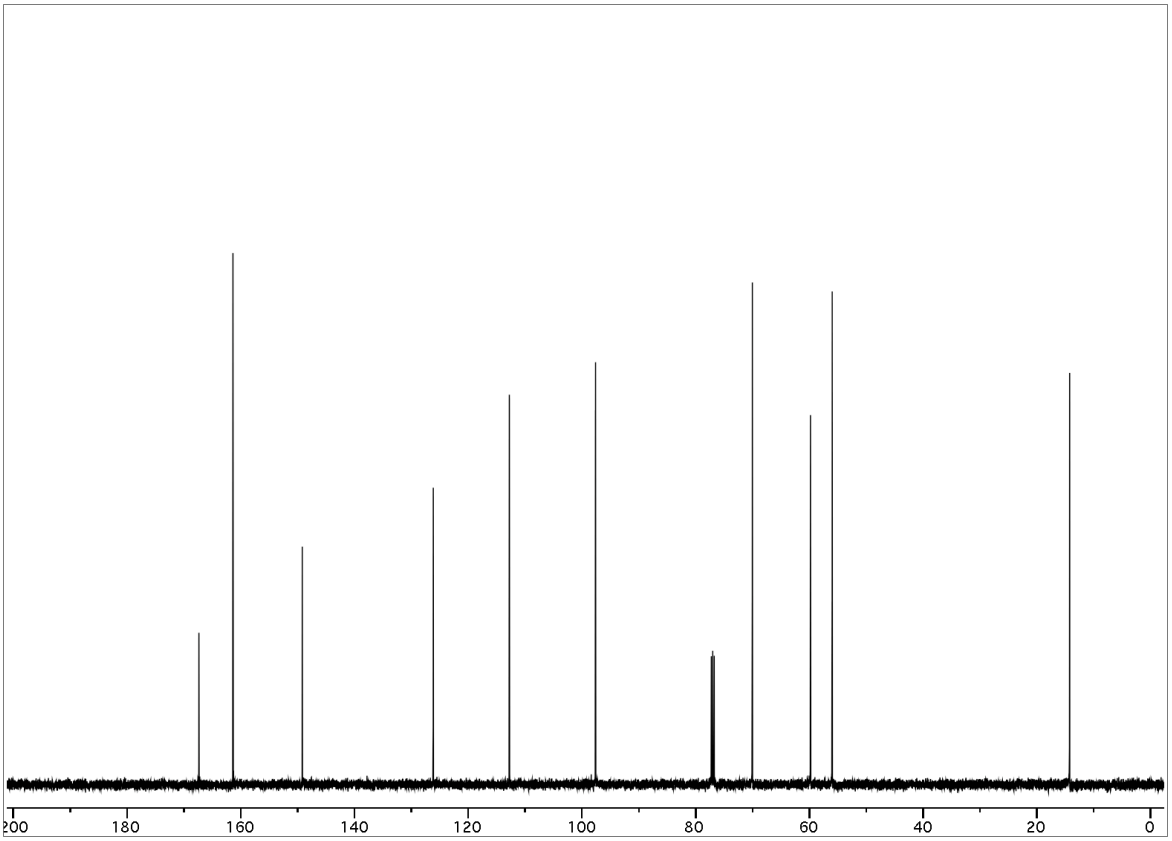

$^{1}$H NMR (500 MHz) spectrum of **20** in $CDCl_3$.



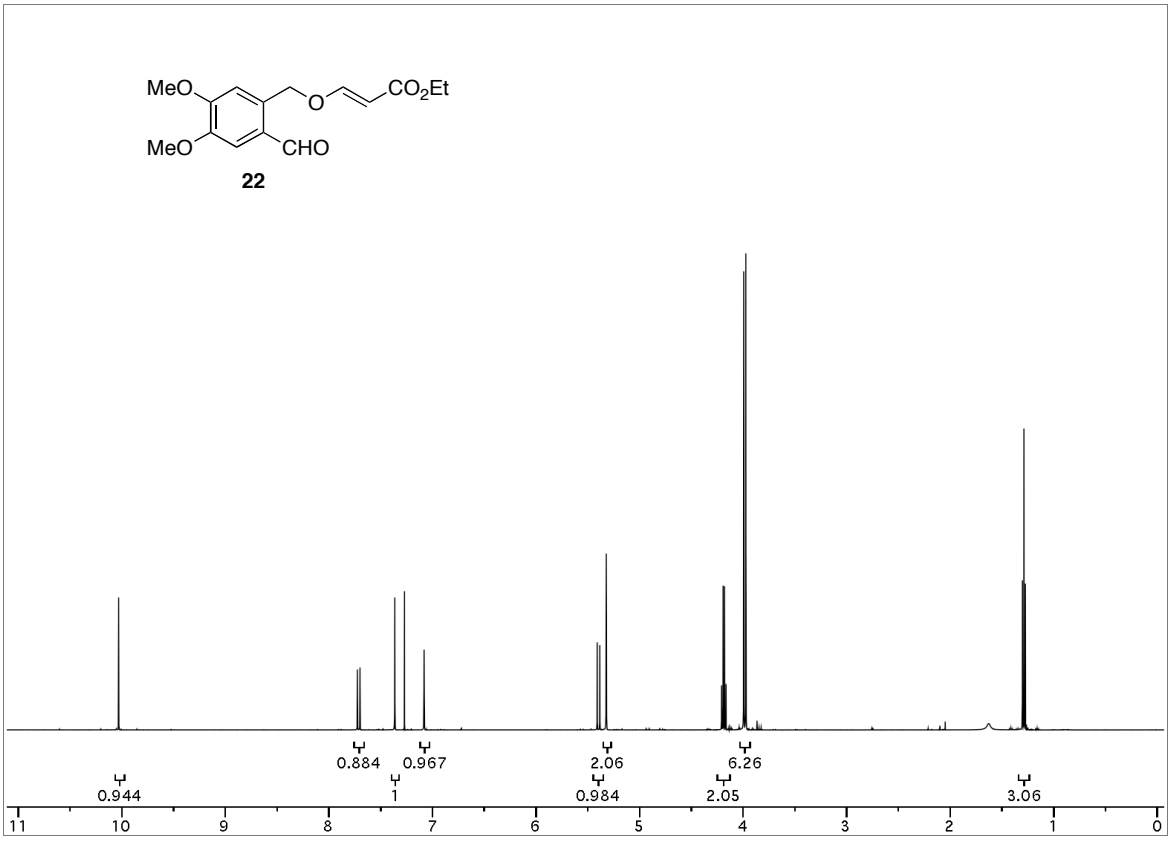

$^{13}$C NMR (125 MHz) spectrum of **20** in $CDCl_3$.



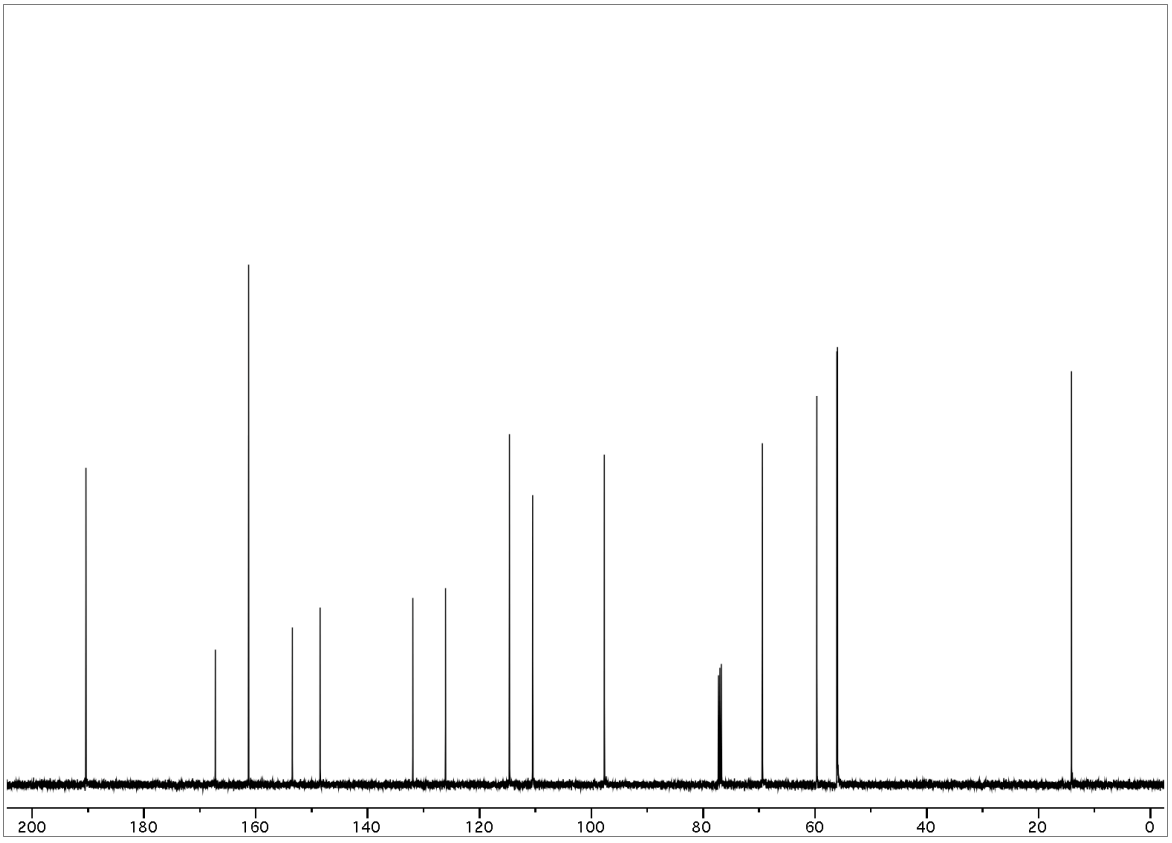

$^{1}$H NMR (500 MHz) spectrum of **21** in $CDCl_3$.



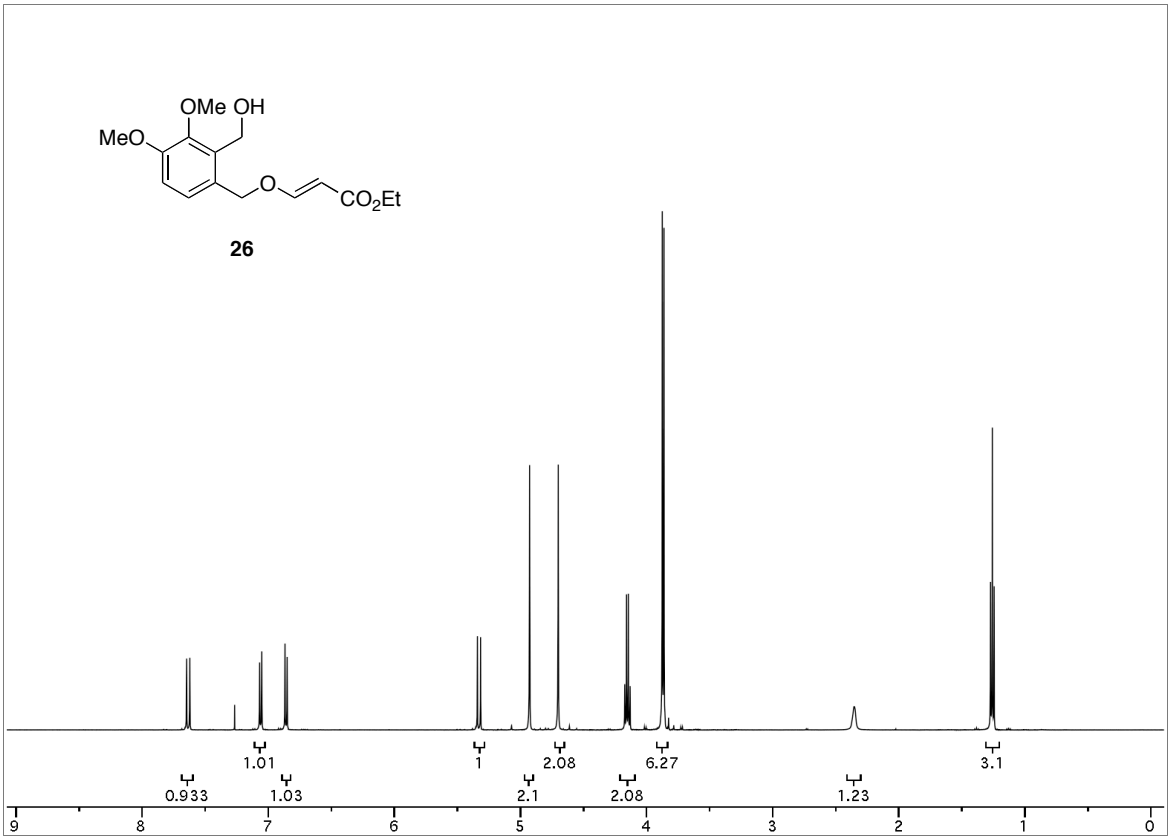

$^{13}$C NMR (125 MHz) spectrum of **21** in $CDCl_3$.



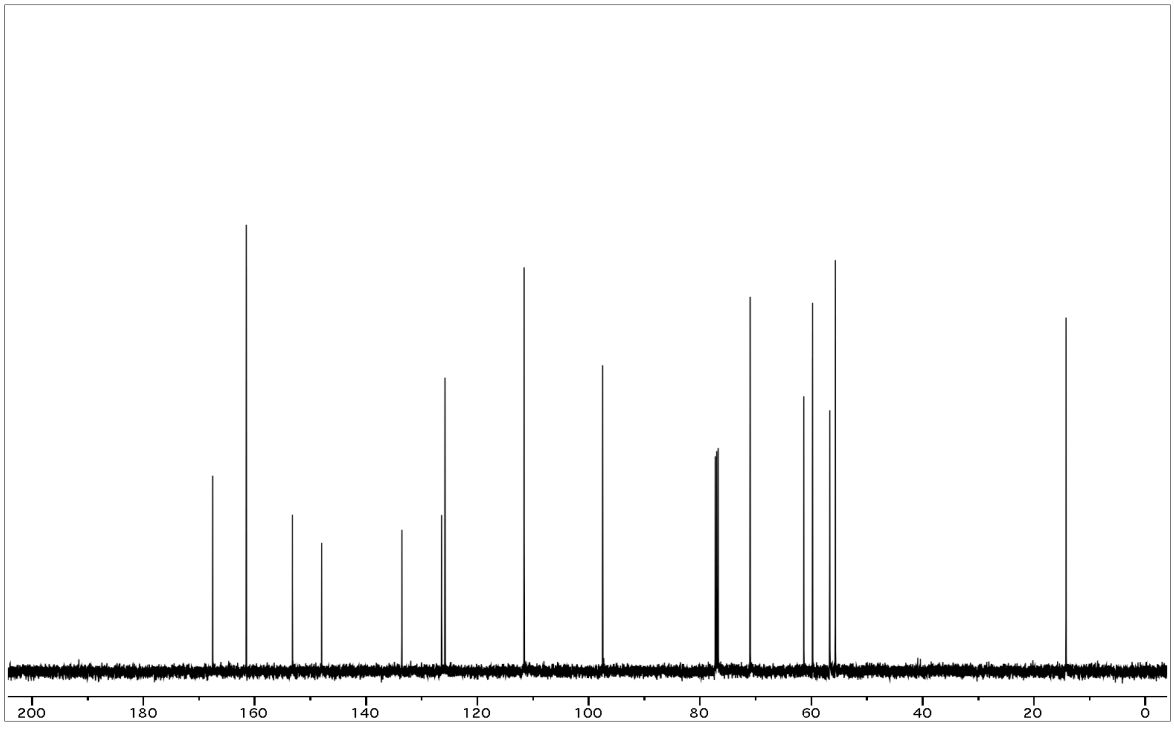

$^{1}$H NMR (500 MHz) spectrum of **22** in $CDCl_3$.



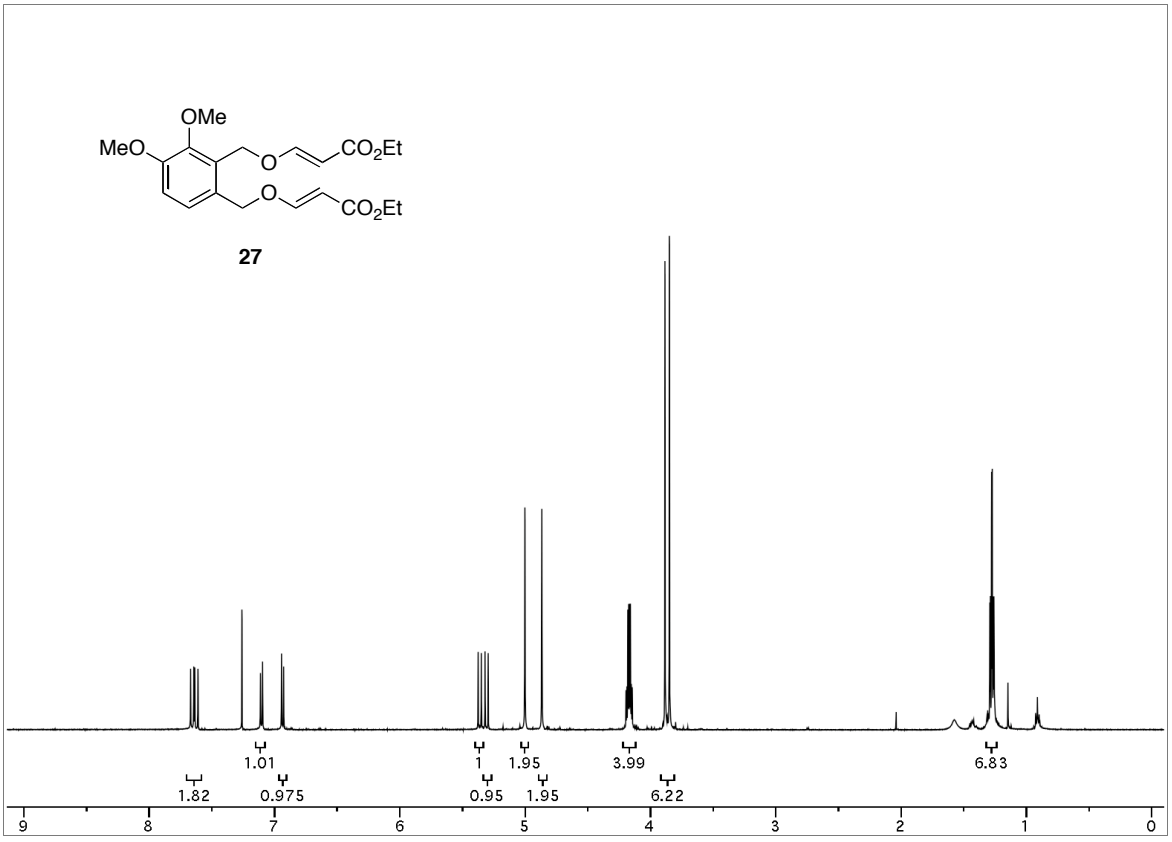

$^{13}$C NMR (125 MHz) spectrum of **22** in $CDCl_3$.



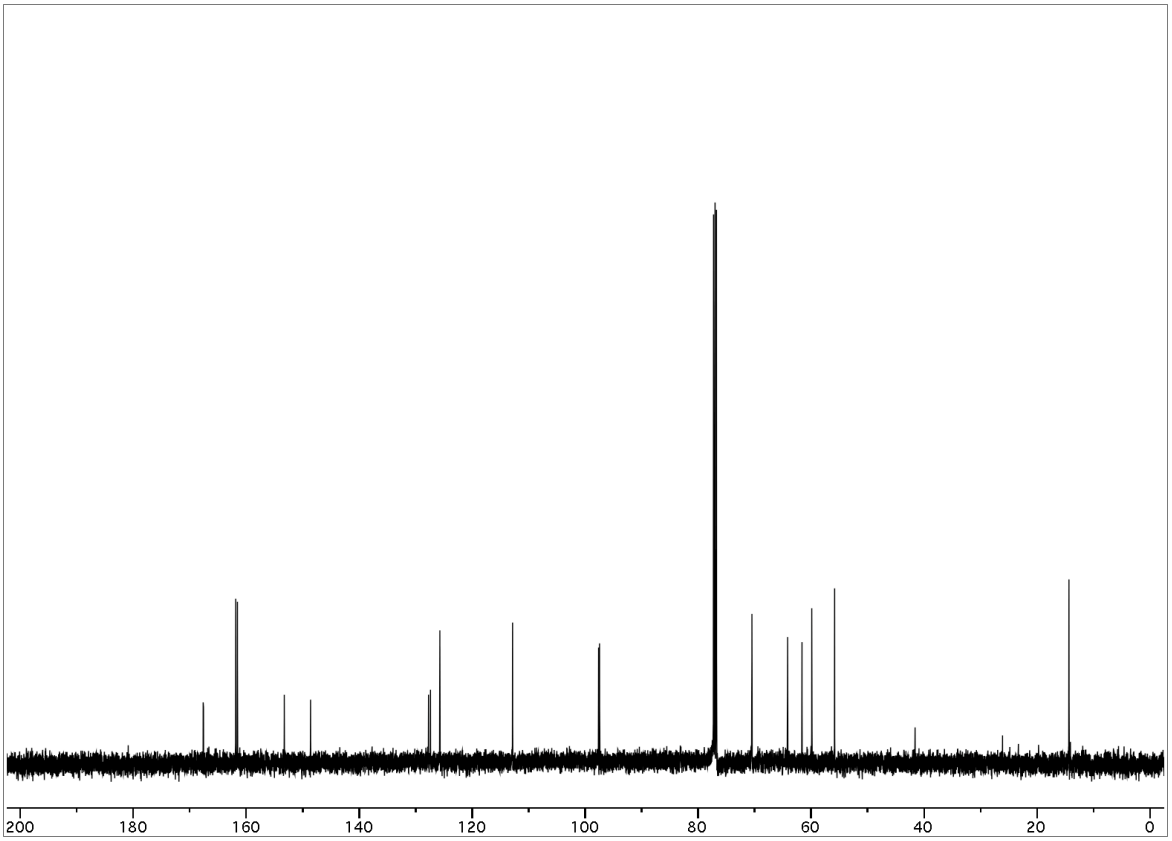

$^{1}$H NMR (500 MHz) spectrum of **26** in $CDCl_3$.



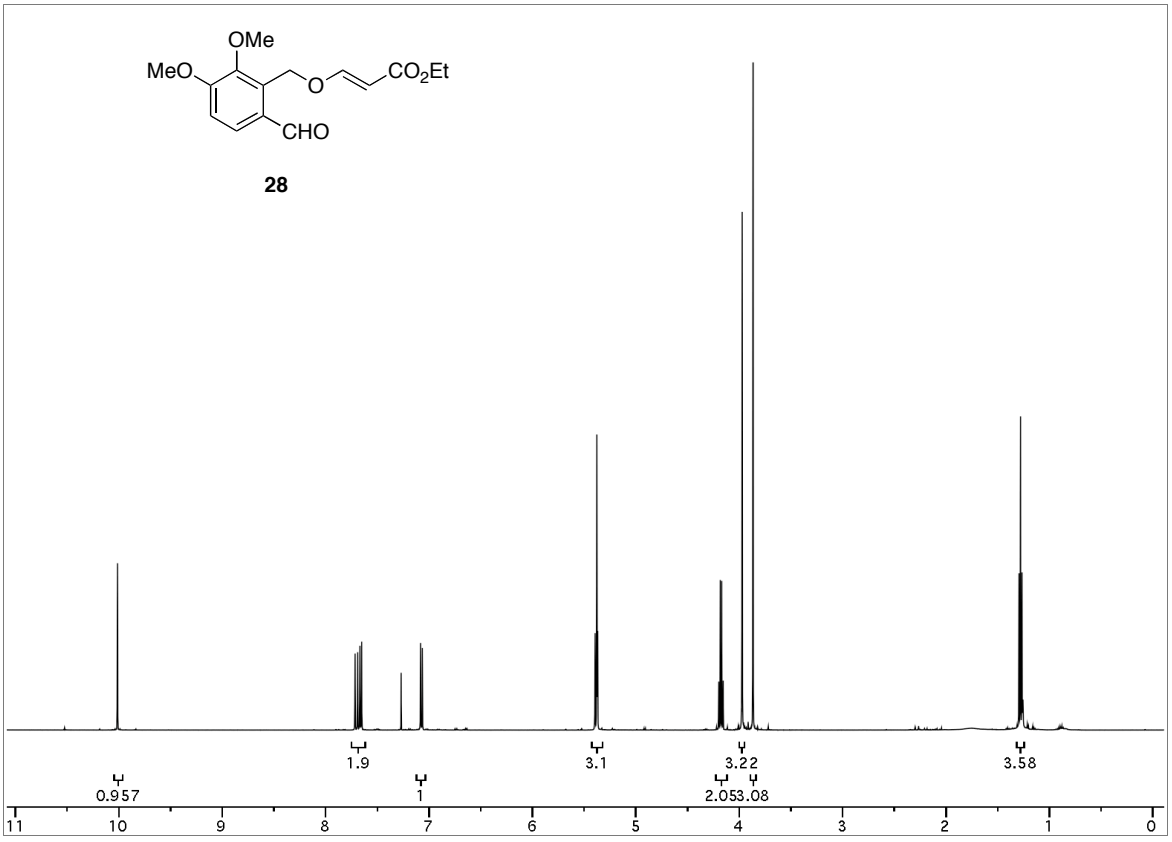

$^{13}$C NMR (125 MHz) spectrum of **26** in $CDCl_3$.



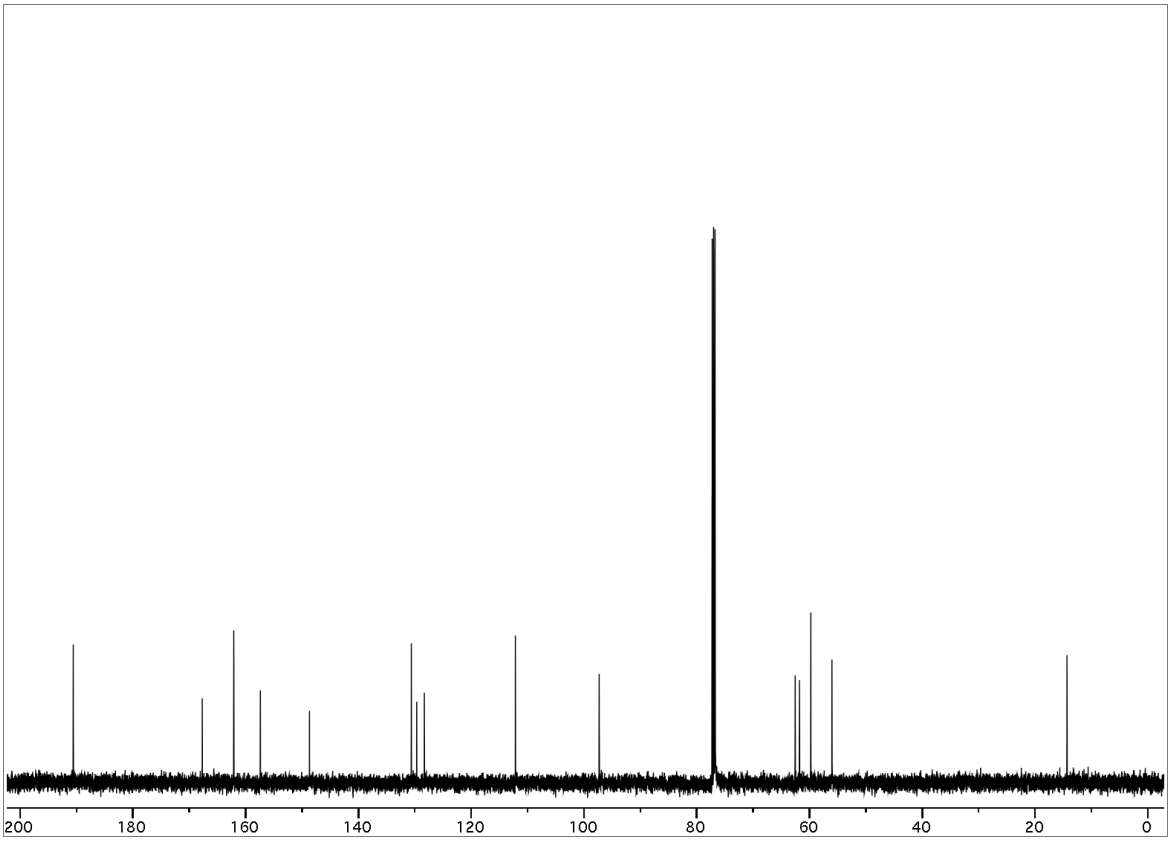

$^{1}$H NMR (500 MHz) spectrum of **27** in $CDCl_3$.



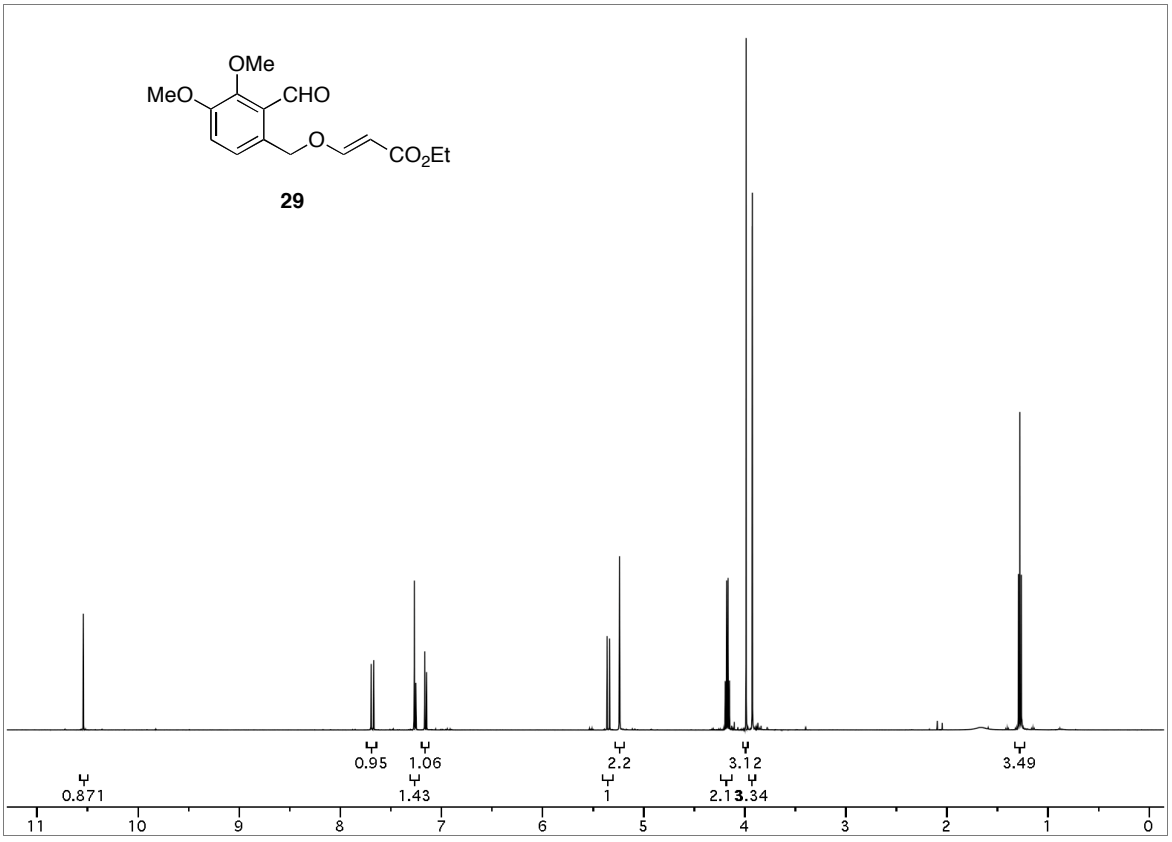

$^{13}$C NMR (125 MHz) spectrum of **27** in $CDCl_3$.



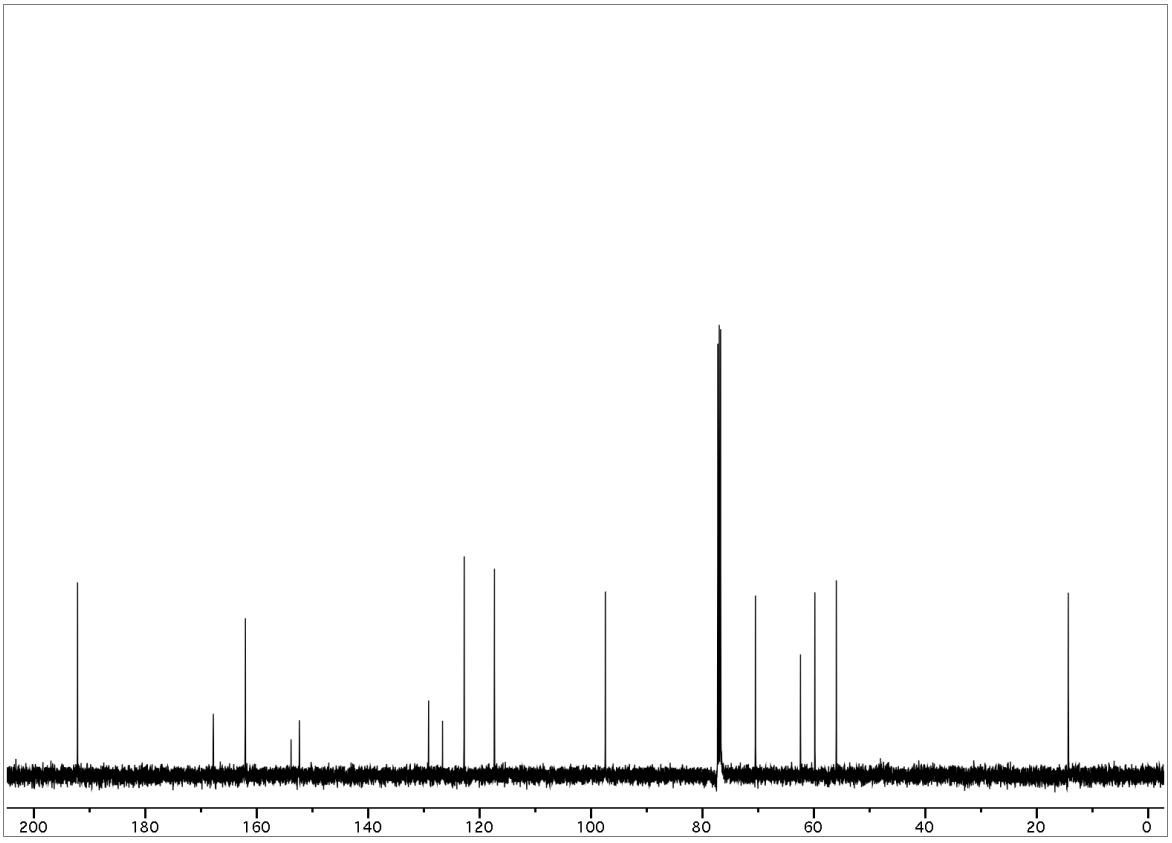

$^{1}$H NMR (500 MHz) spectrum of **28** in $CDCl_3$.



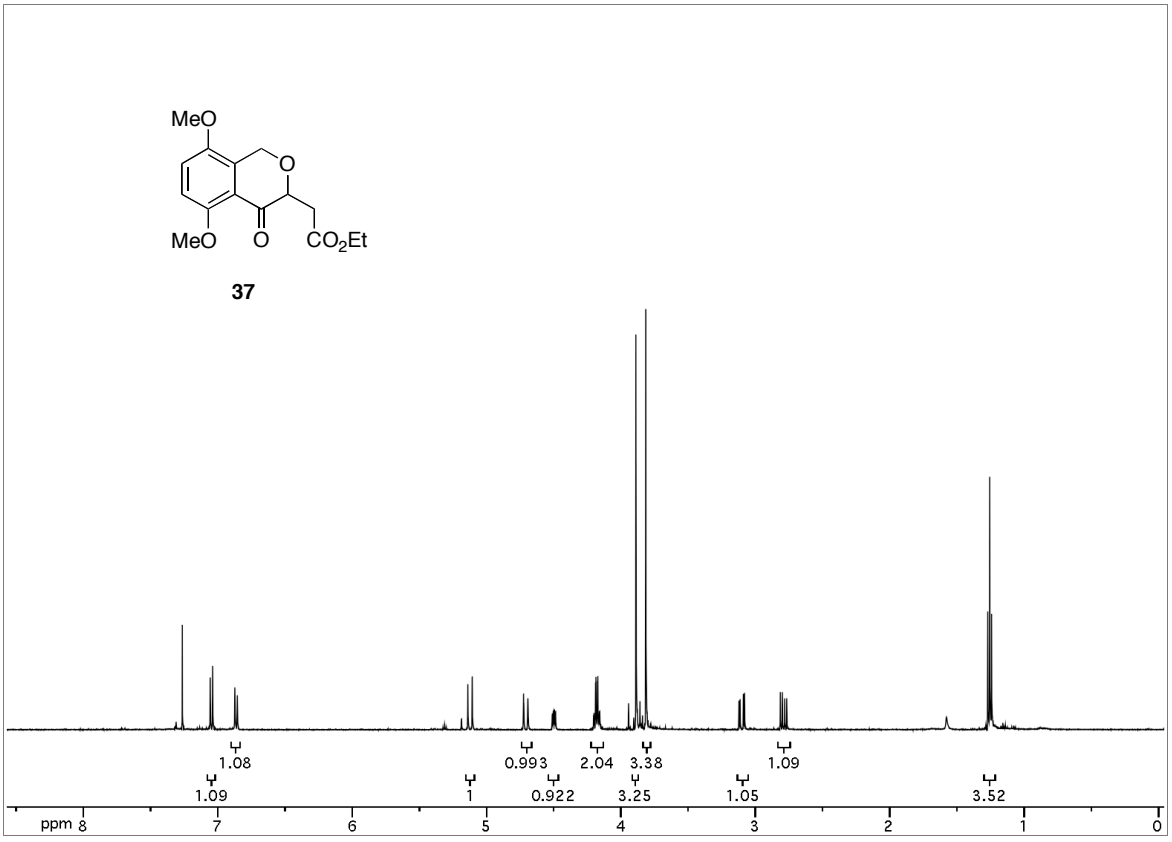

$^{13}$C NMR (125 MHz) spectrum of **28** in $CDCl_3$.



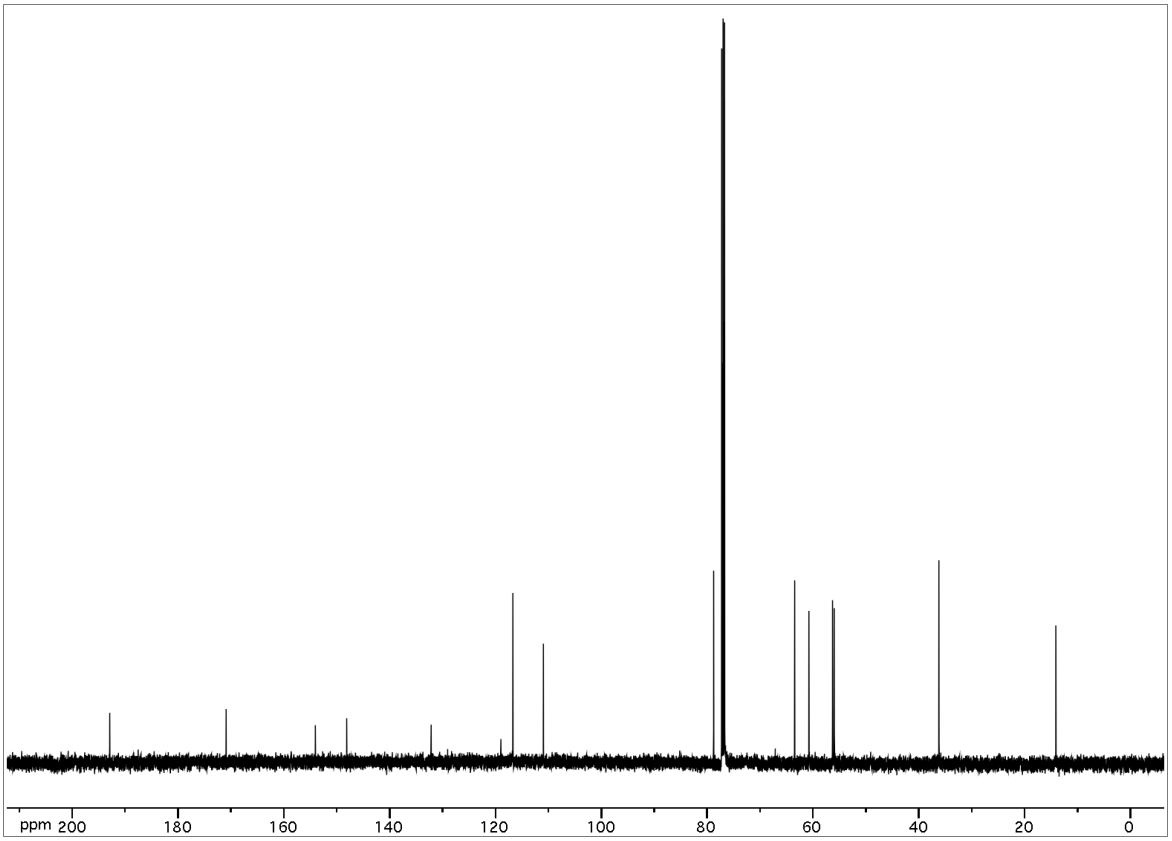

$^{1}$H NMR (500 MHz) spectrum of **29** in $CDCl_3$.



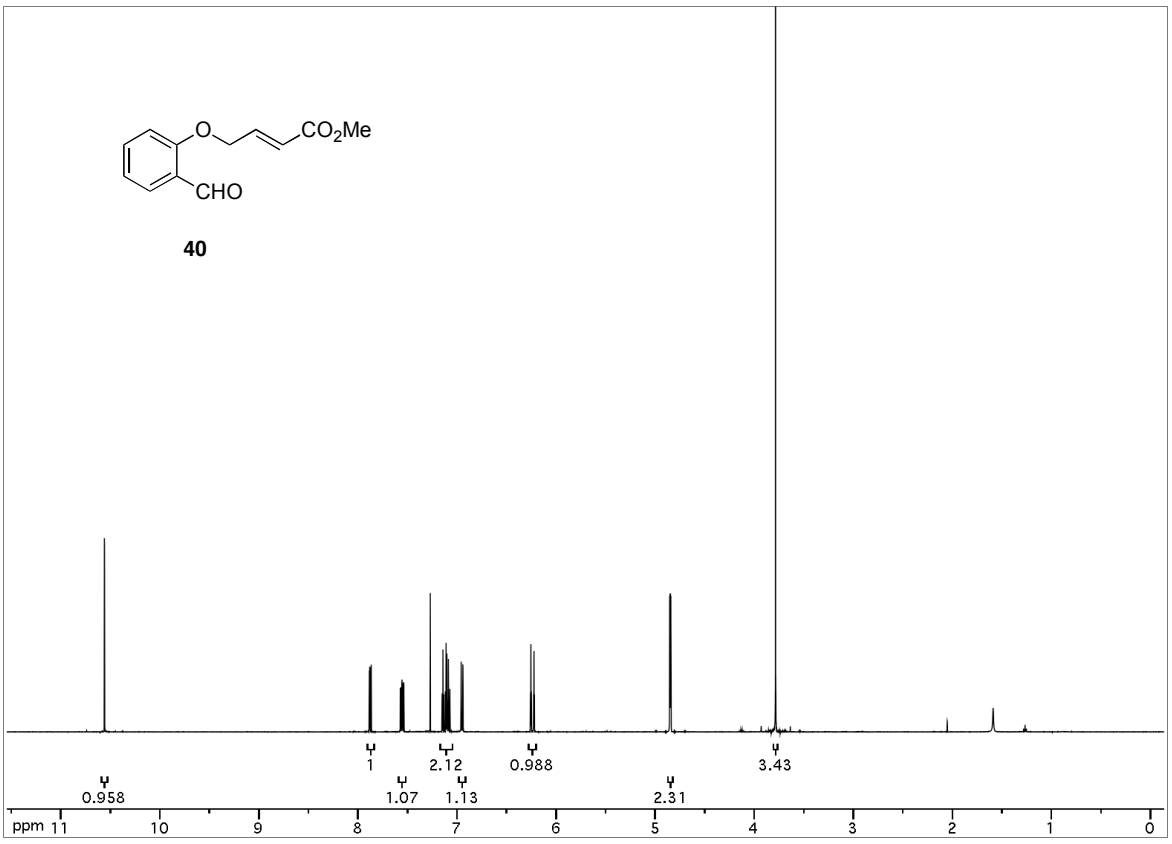

$^{13}$C NMR (125 MHz) spectrum of **29** in $CDCl_3$.



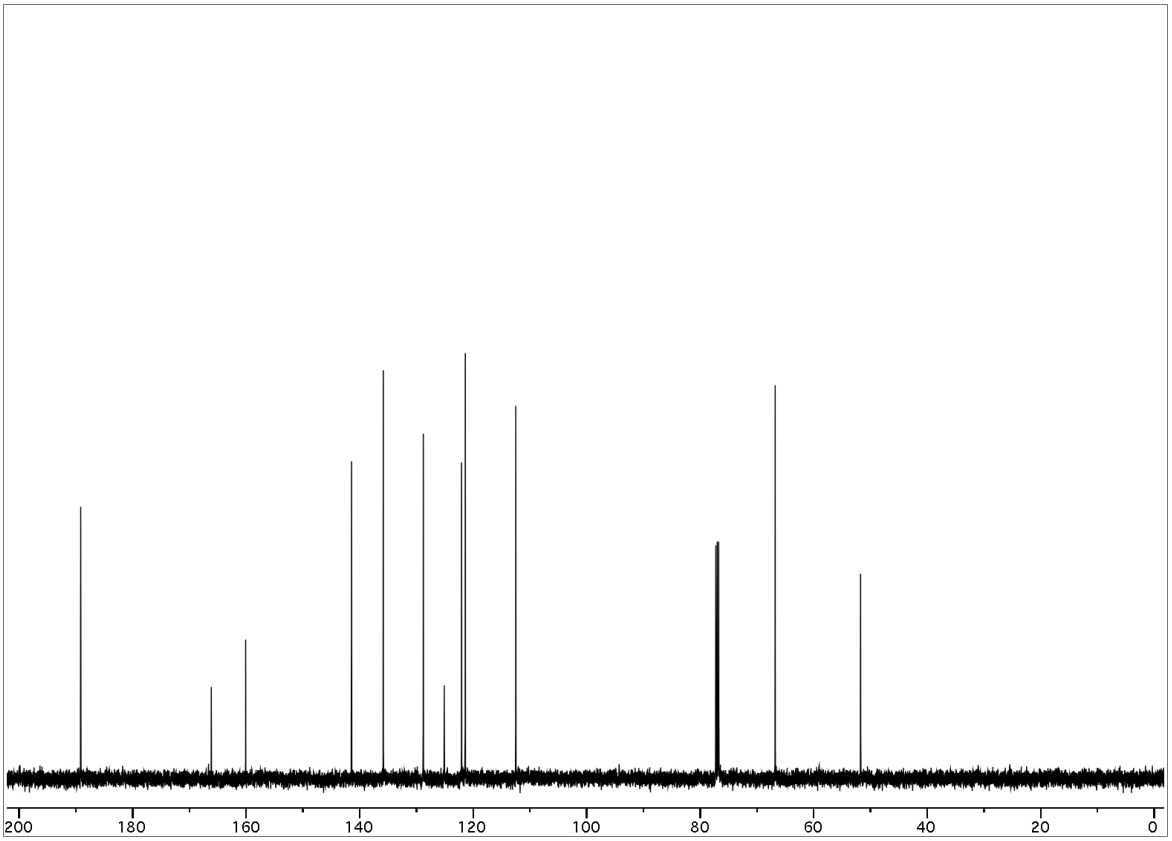

$^{1}$H NMR (500 MHz) spectrum of **37** in $CDCl_3$.



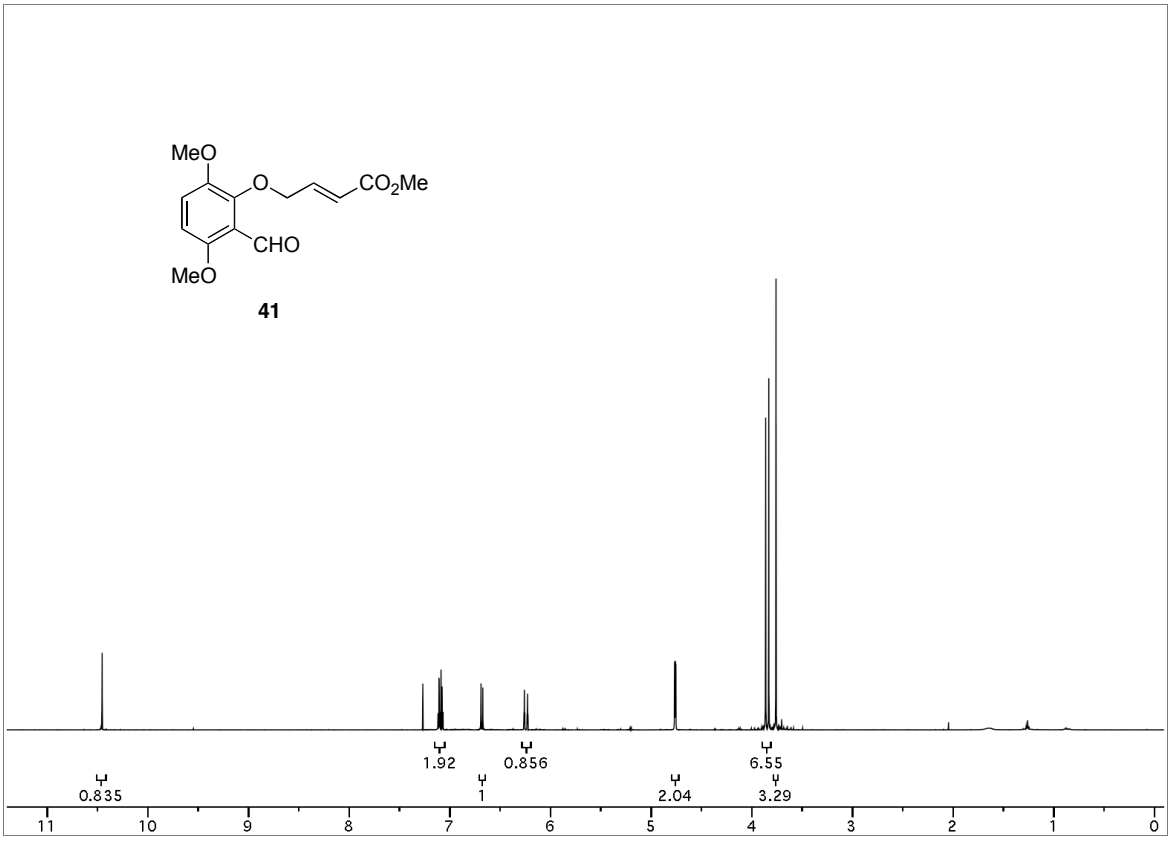

$^{13}$C NMR (125 MHz) spectrum of **37** in $CDCl_3$.



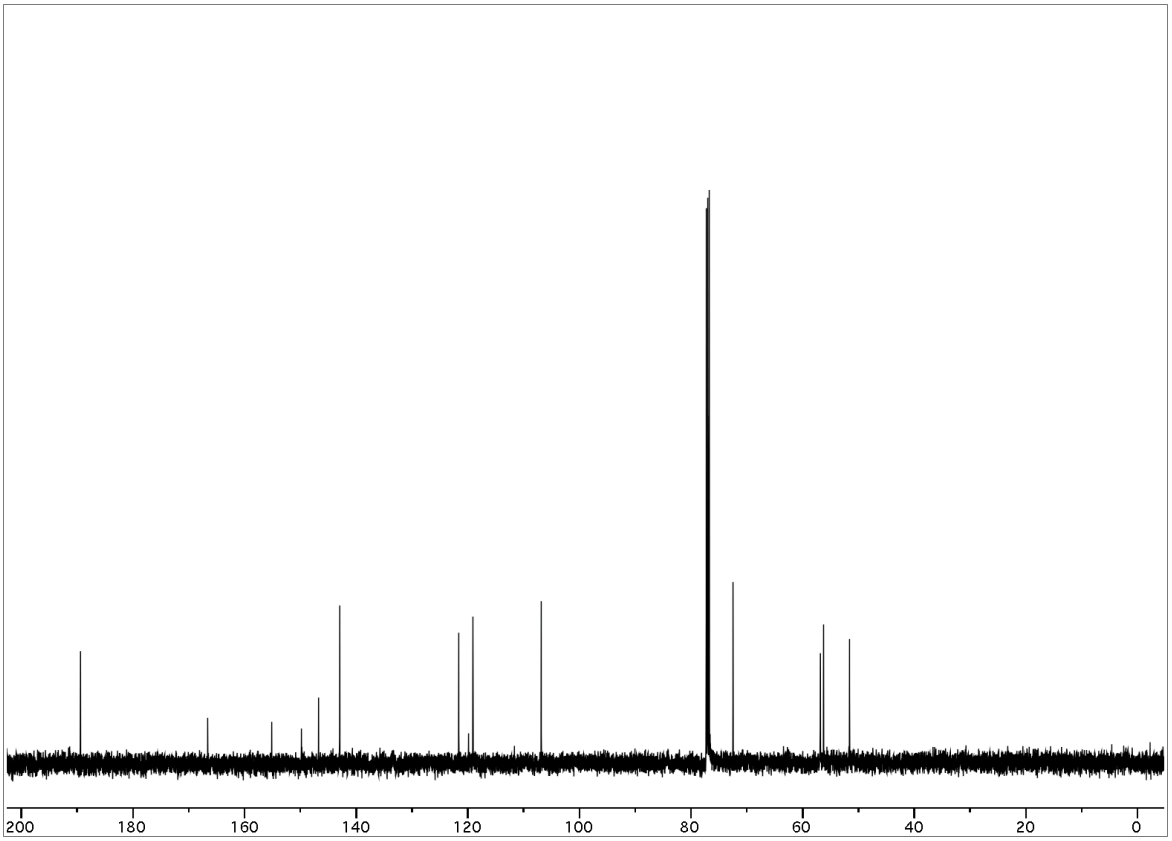

$^{1}$H NMR (500 MHz) spectrum of **40** in $CDCl_3$.



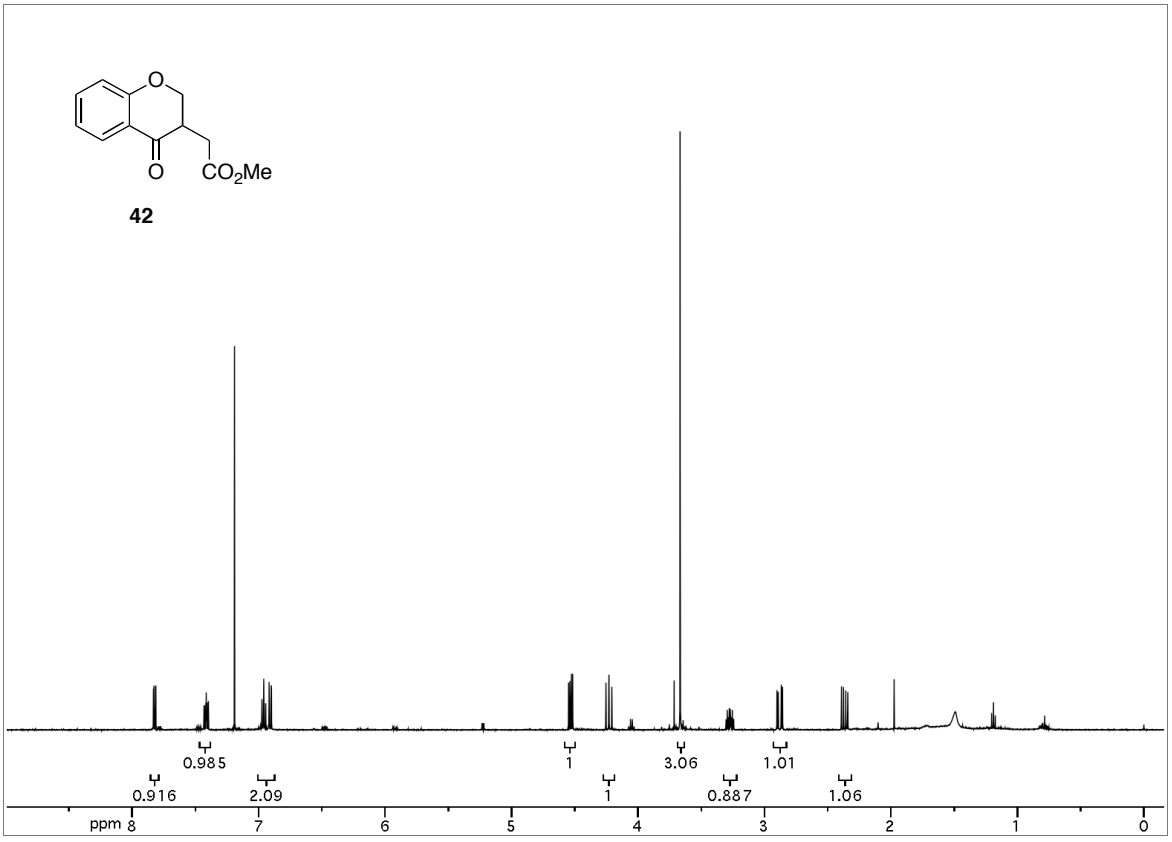

$^{13}$C NMR (125 MHz) spectrum of **40** in $CDCl_3$.



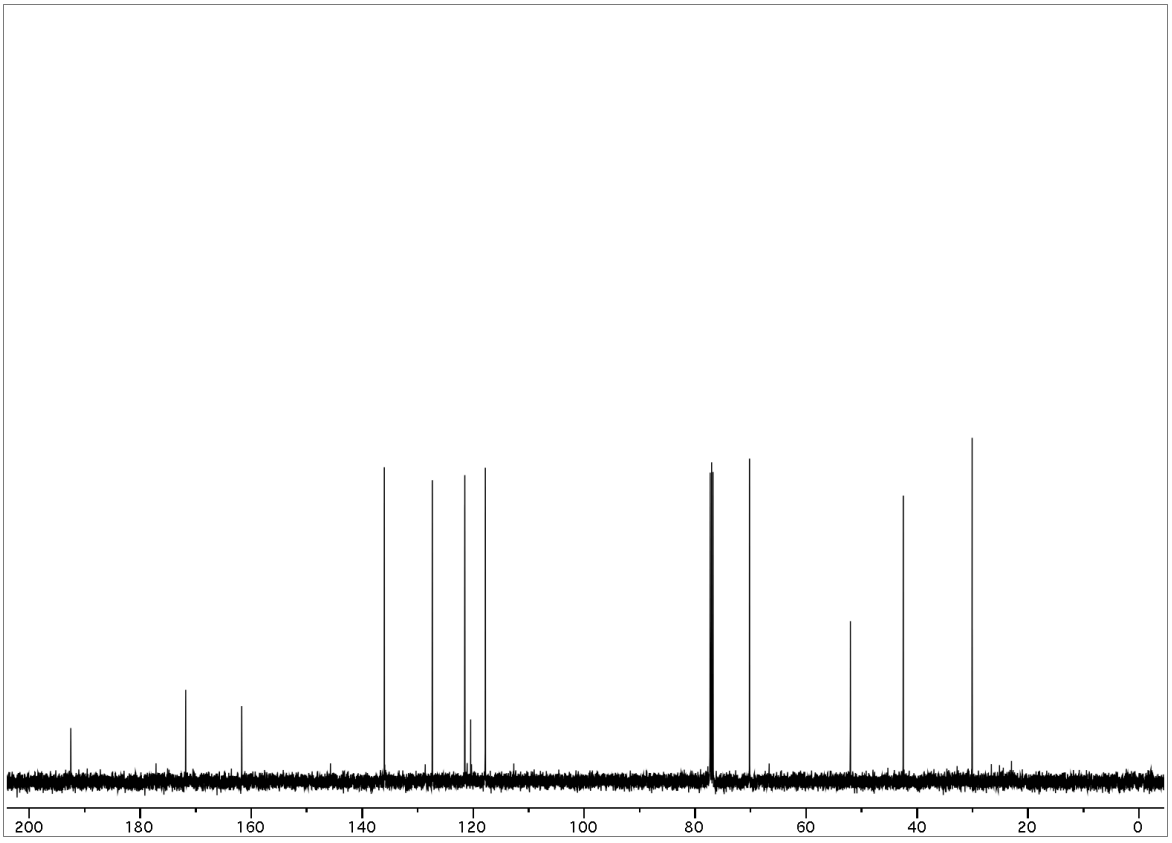

$^{1}$H NMR (500 MHz) spectrum of **41** in $CDCl_3$.



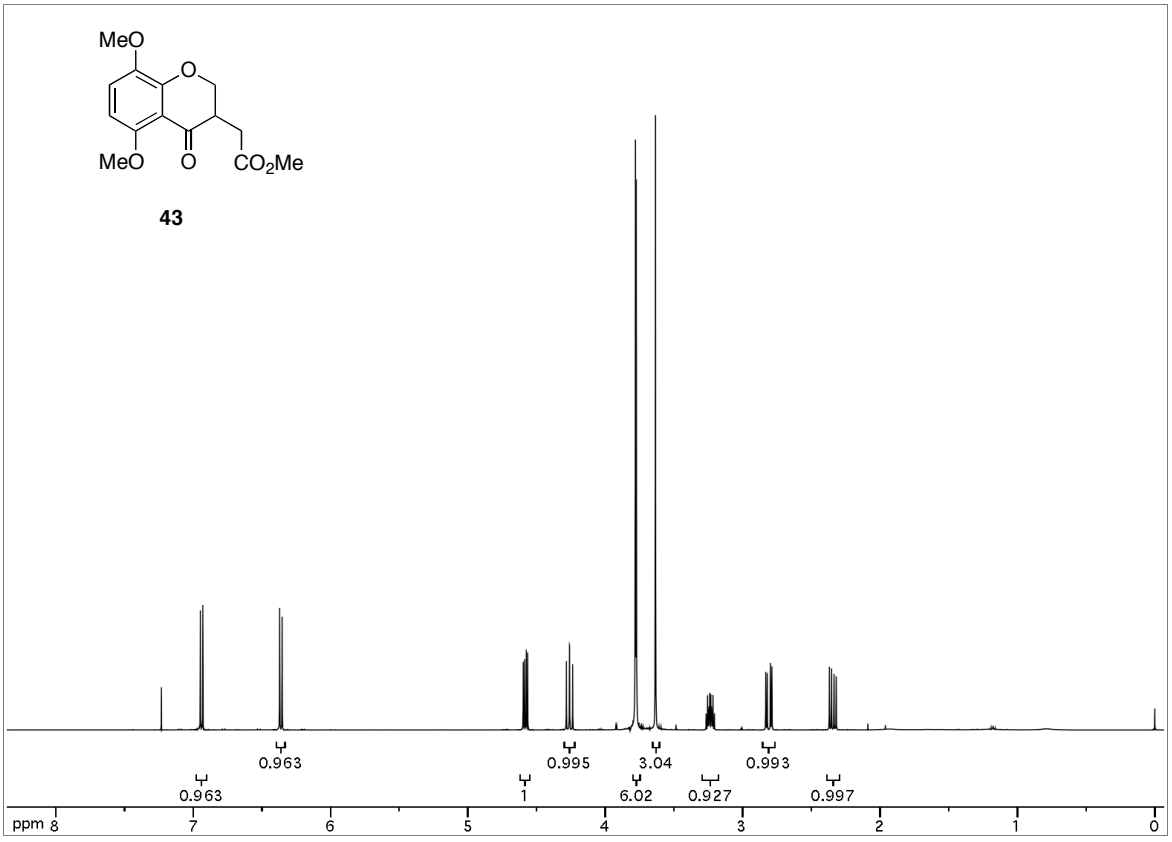

$^{13}$C NMR (125 MHz) spectrum of **41** in $CDCl_3$.



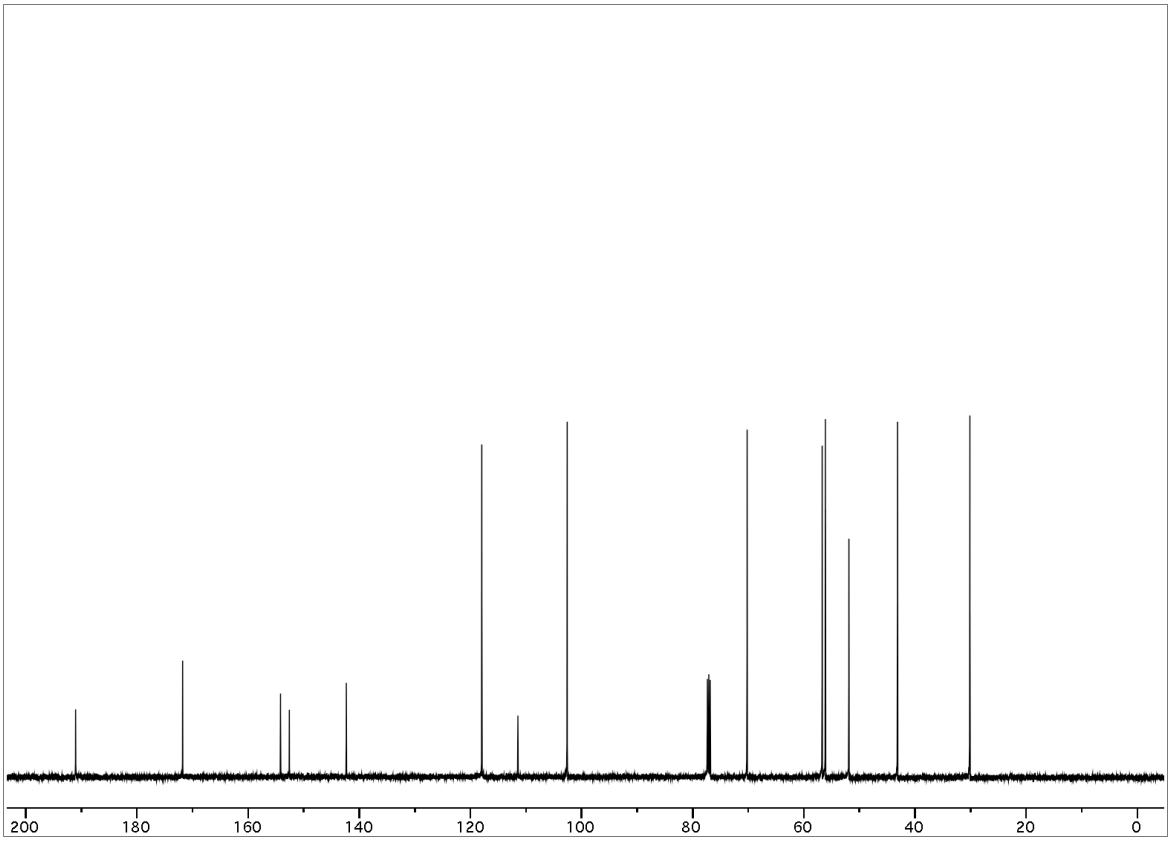

$^{1}$H NMR (500 MHz) spectrum of **42** in $CDCl_3$.



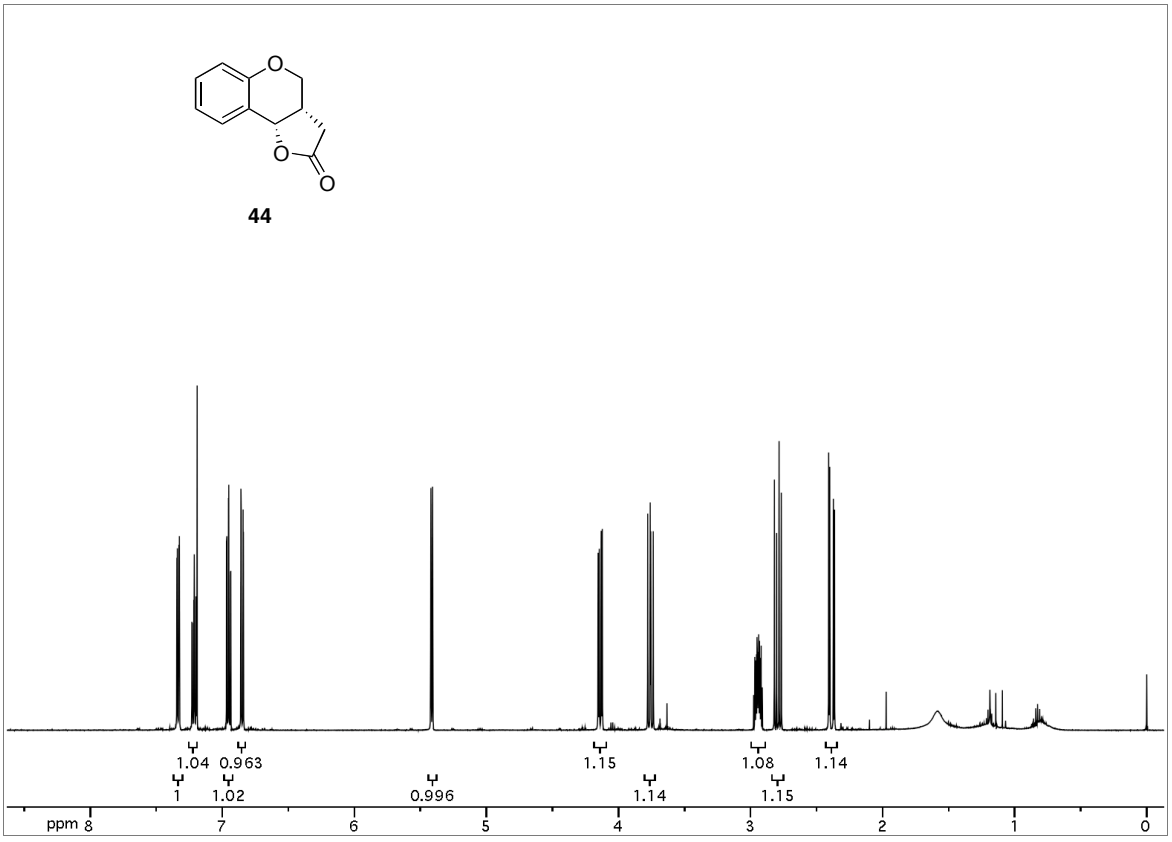

$^{13}$C NMR (125 MHz) spectrum of **42** in $CDCl_3$.



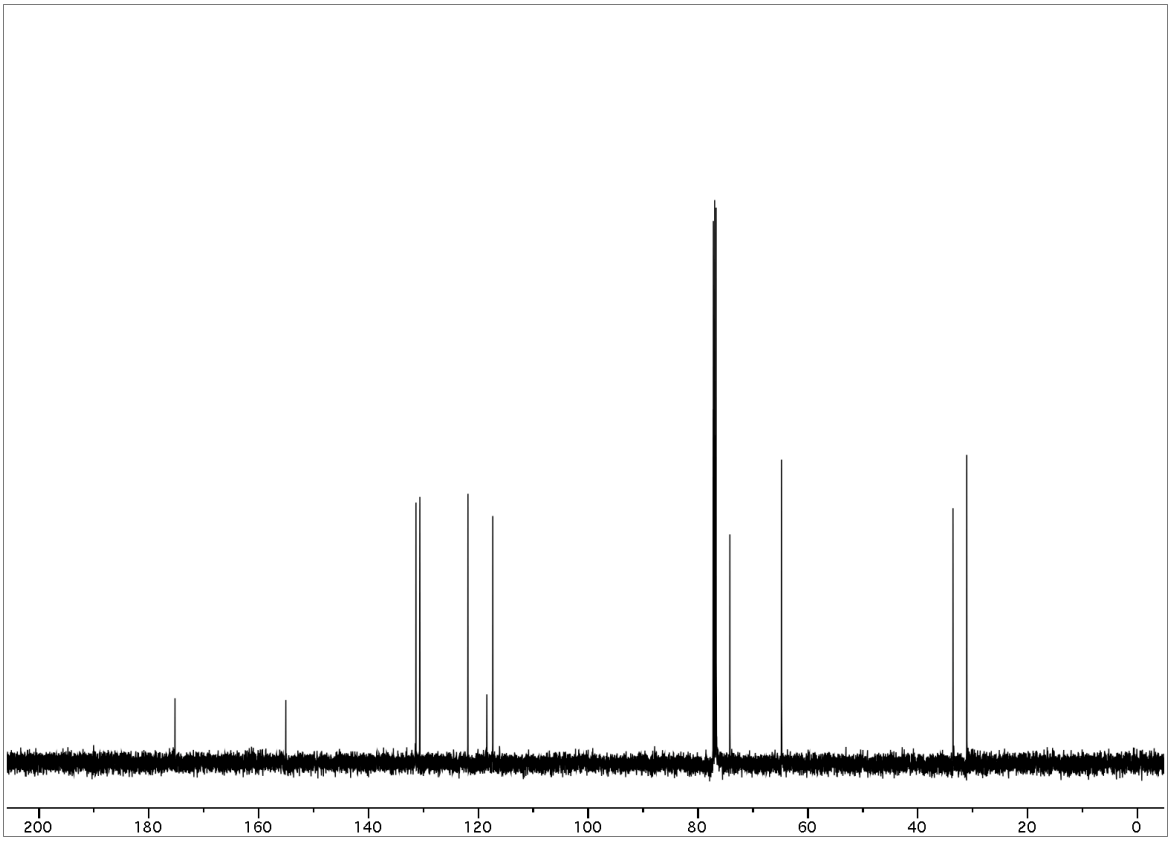

$^{1}$H NMR (500 MHz) spectrum of **43** in $CDCl_3$.



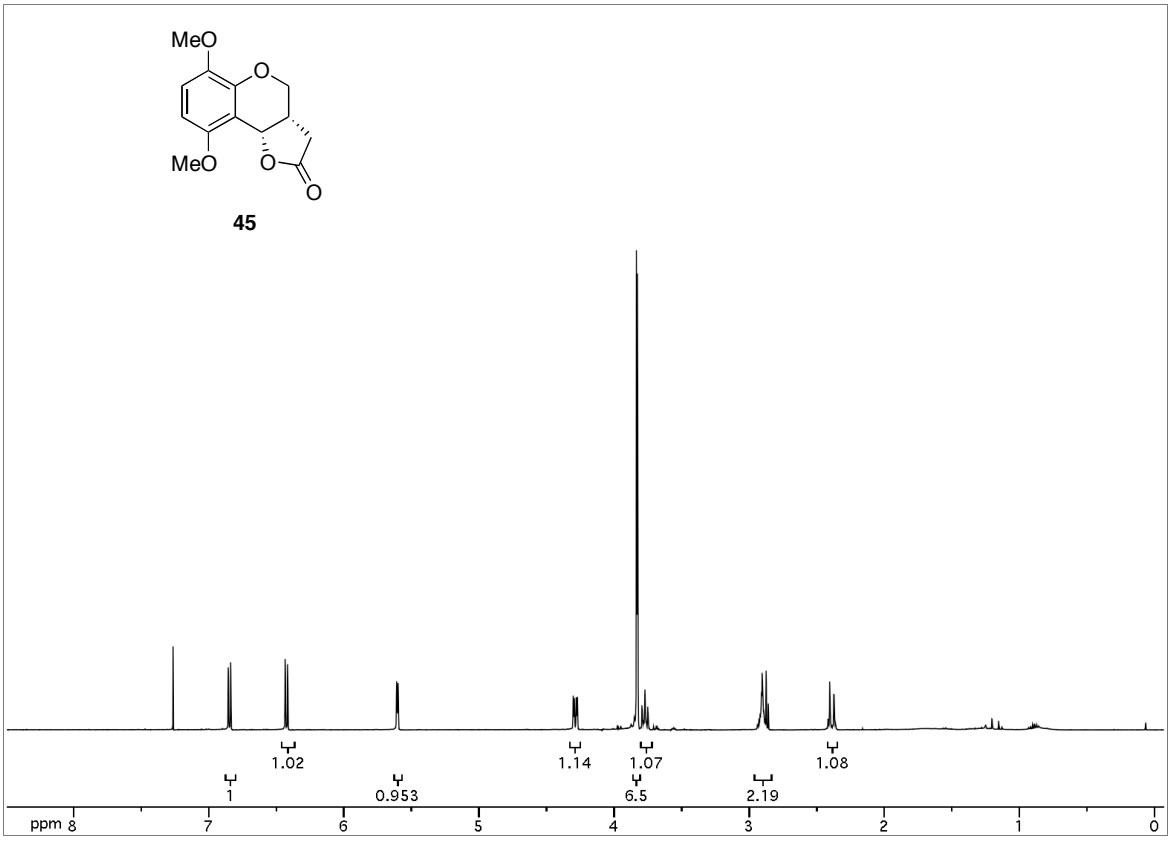

$^{13}$C NMR (125 MHz) spectrum of **43** in $CDCl_3$.



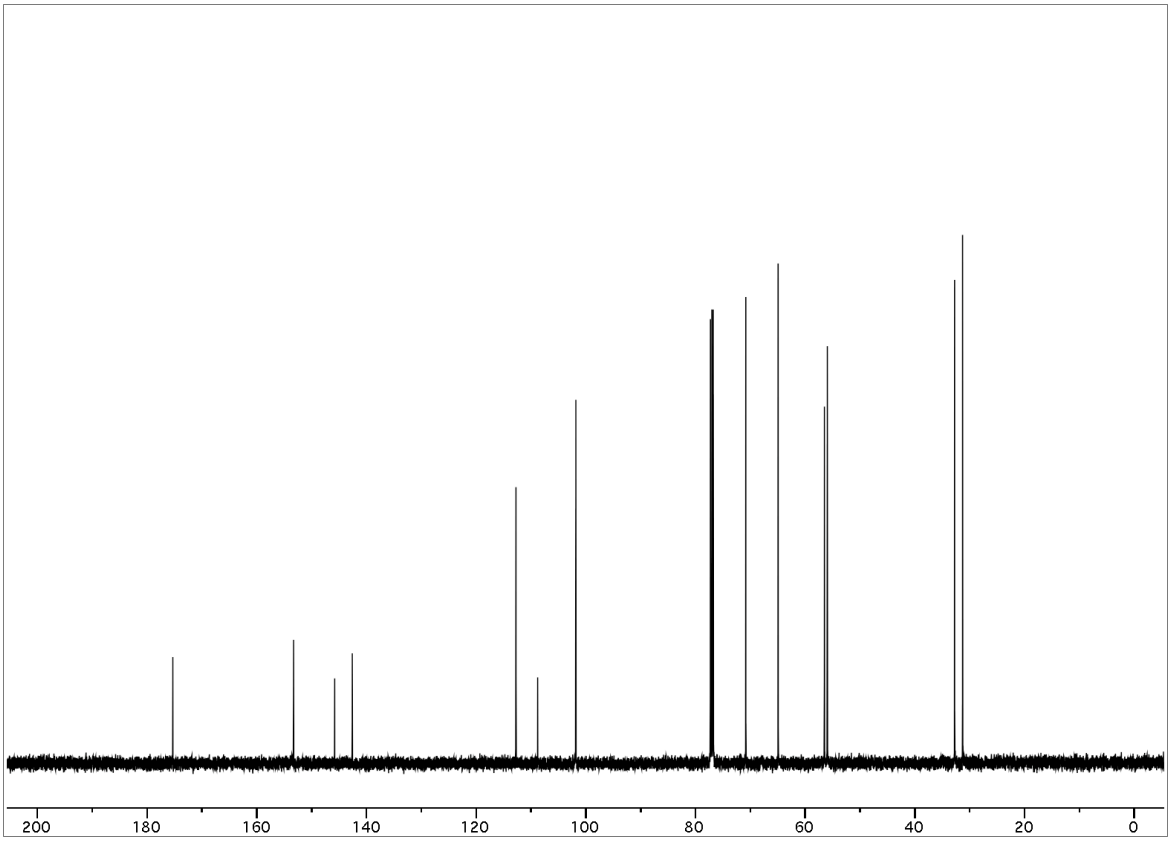

$^{1}$H NMR (500 MHz) spectrum of **44** in $CDCl_3$.



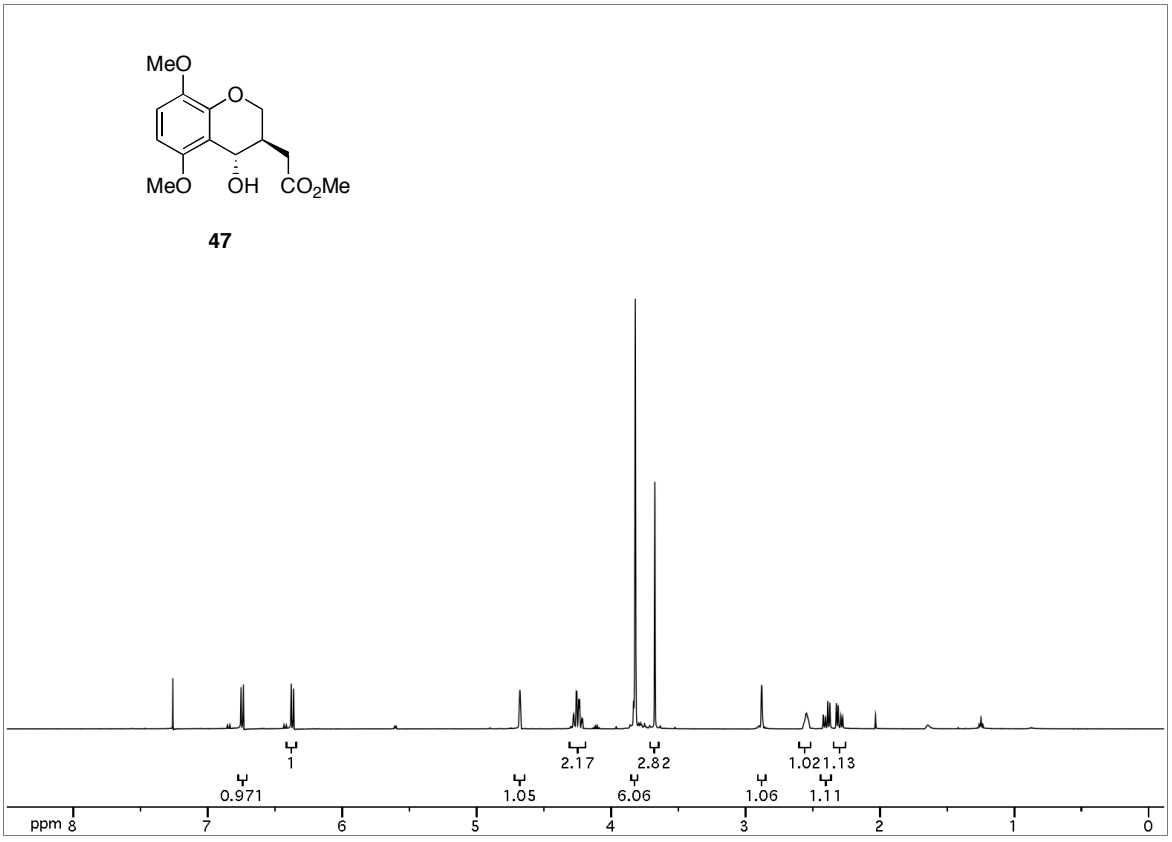

$^{13}$C NMR (125 MHz) spectrum of **44** in $CDCl_3$.



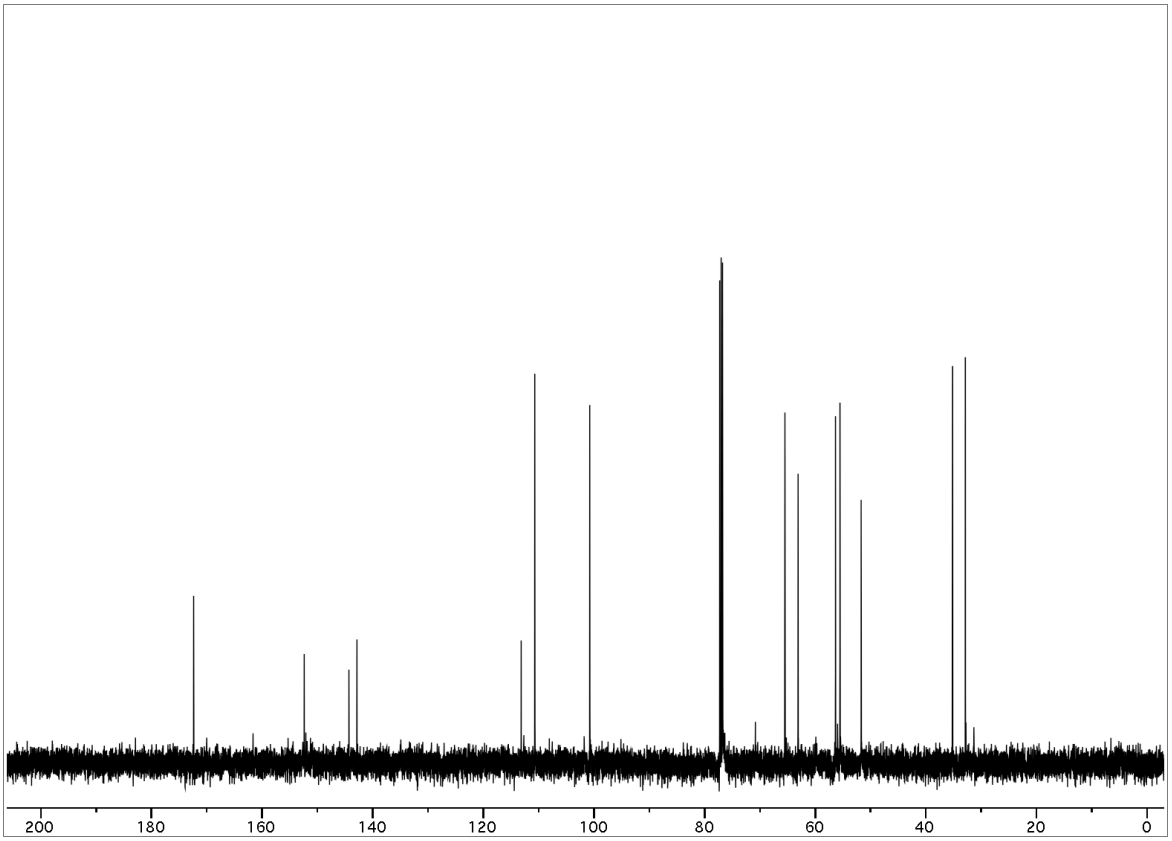

$^{1}$H NMR (500 MHz) spectrum of **45** in $CDCl_3$.



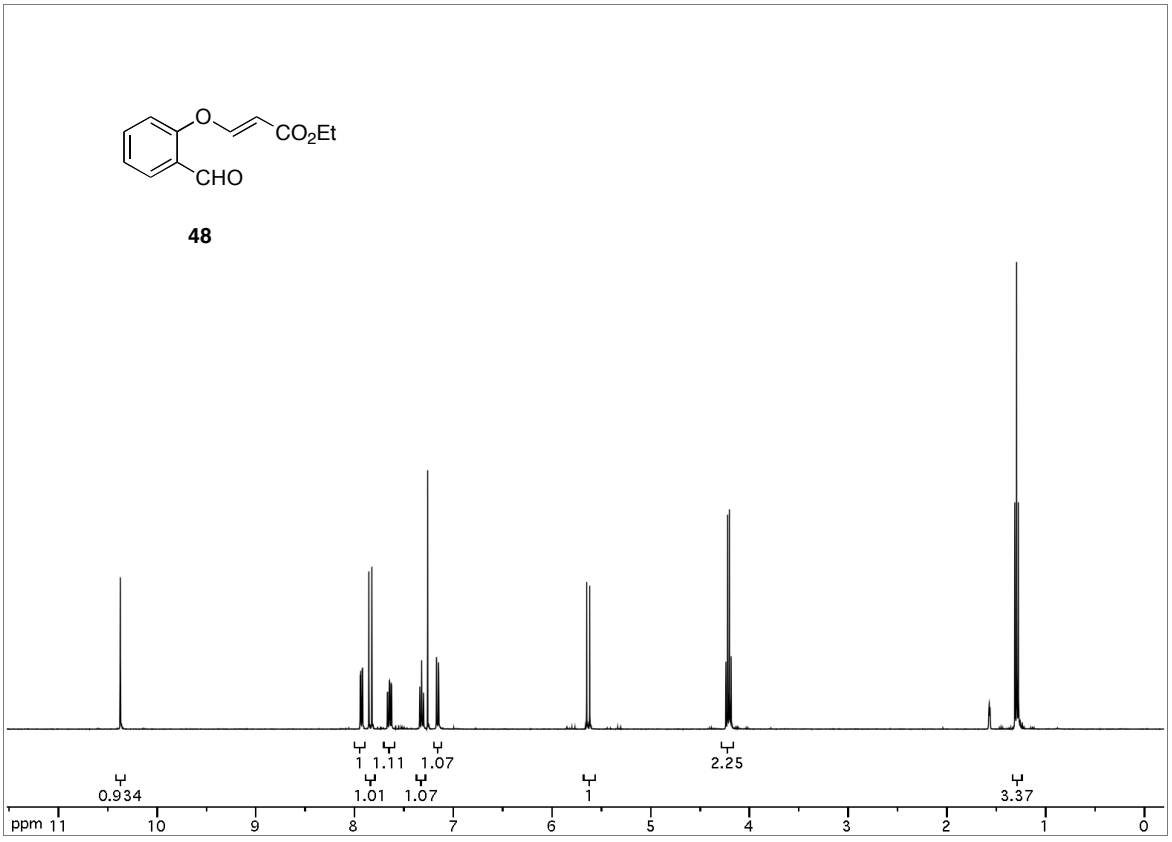

$^{13}$C NMR (125 MHz) spectrum of **45** in $CDCl_3$.



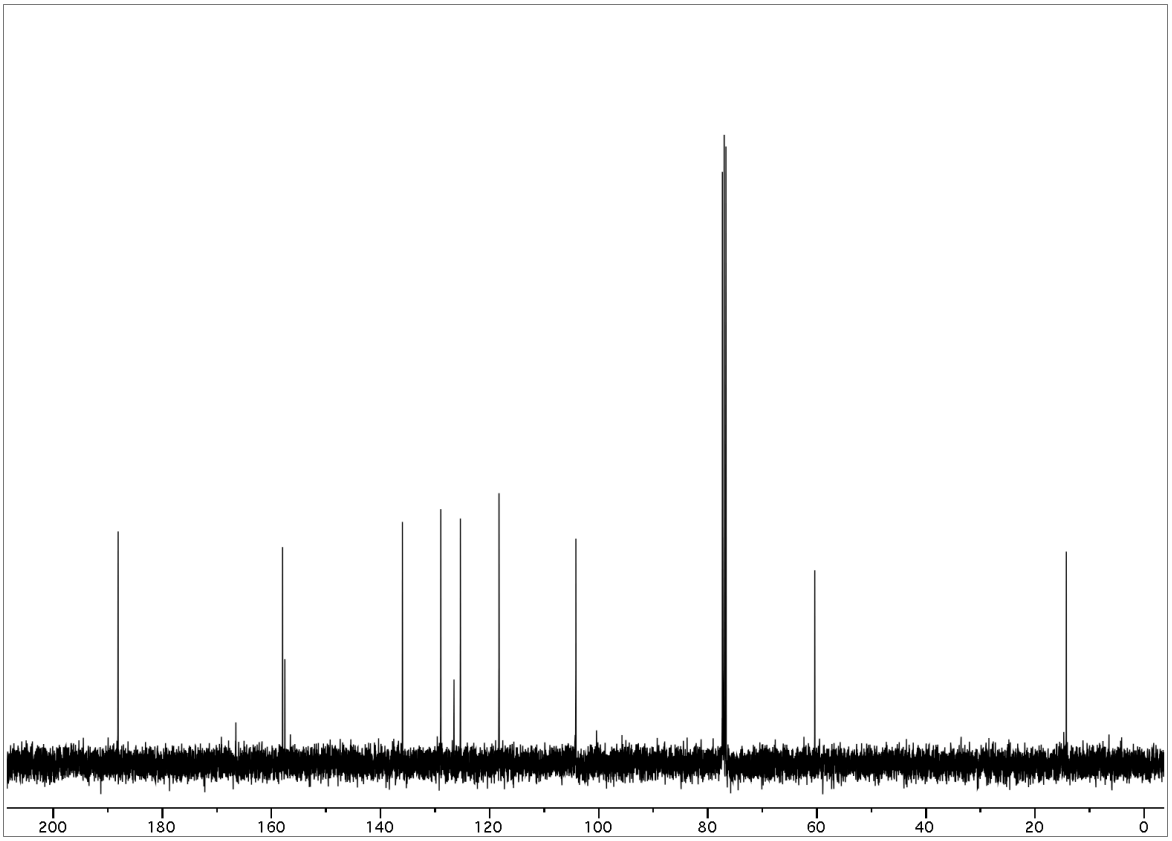

$^{1}$H NMR (500 MHz) spectrum of **47** in $CDCl_3$.



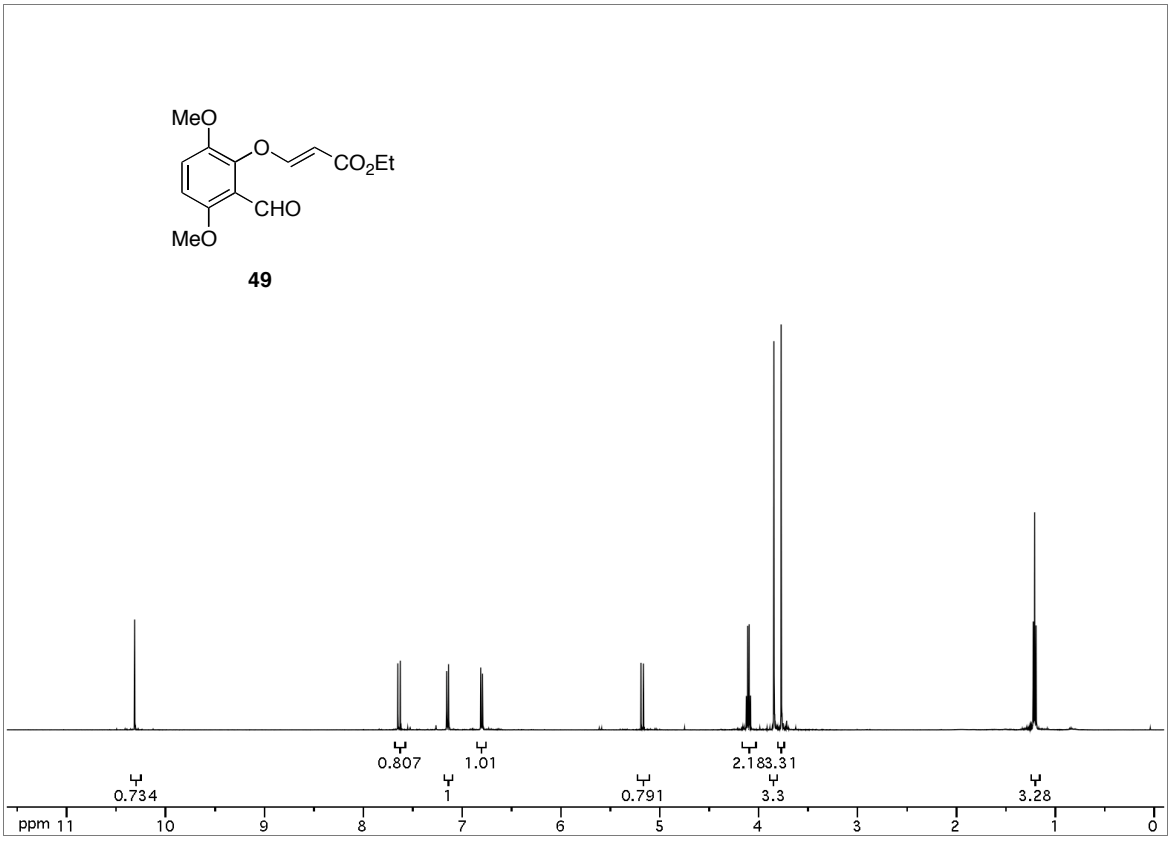

$^{13}$C NMR (125 MHz) spectrum of **47** in $CDCl_3$.



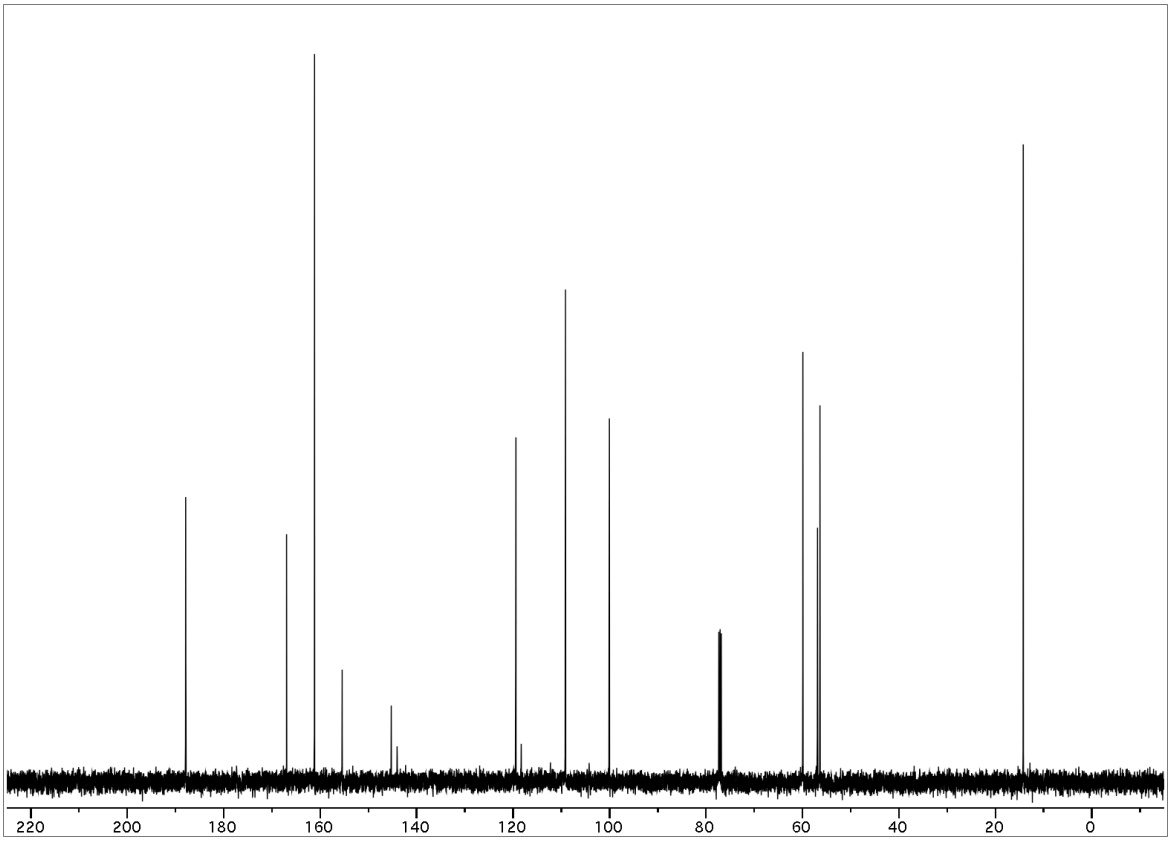

$^{1}$H NMR (500 MHz) spectrum of **48** in $CDCl_3$.



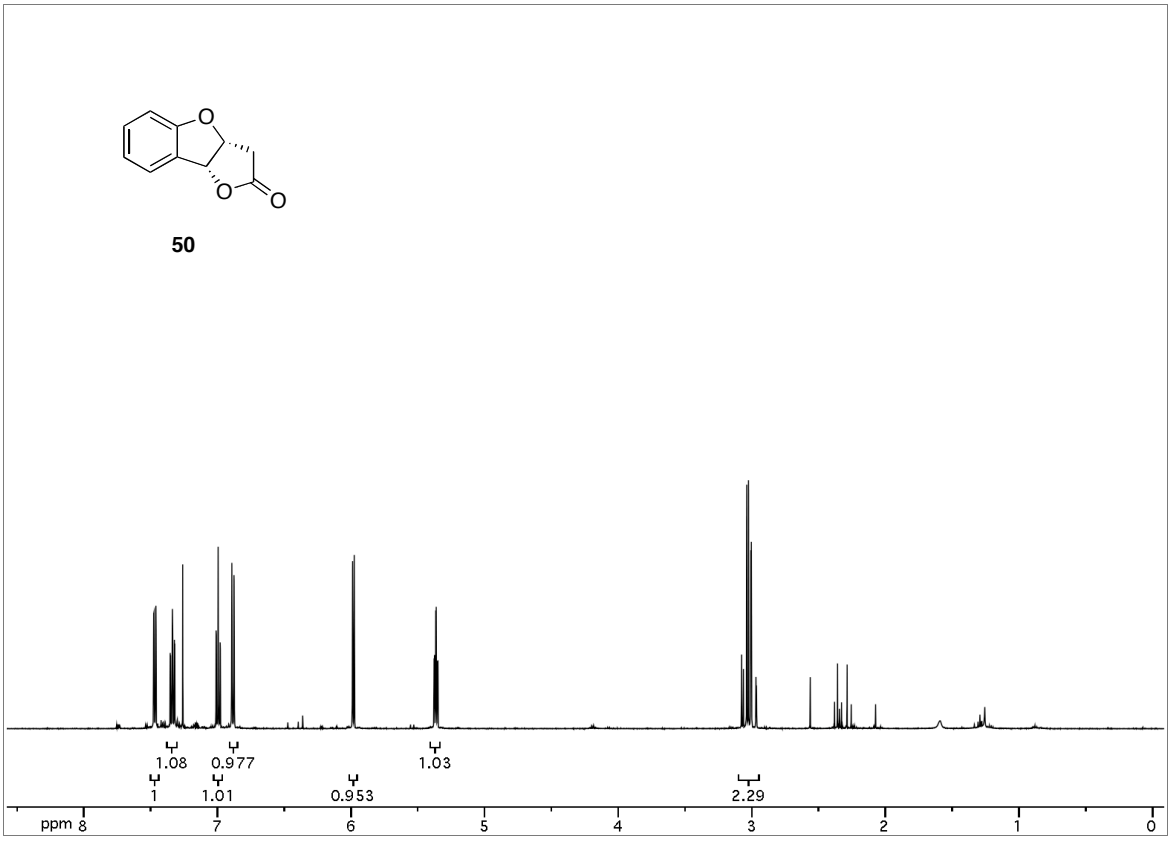

$^{13}$C NMR (125 MHz) spectrum of **48** in $CDCl_3$.



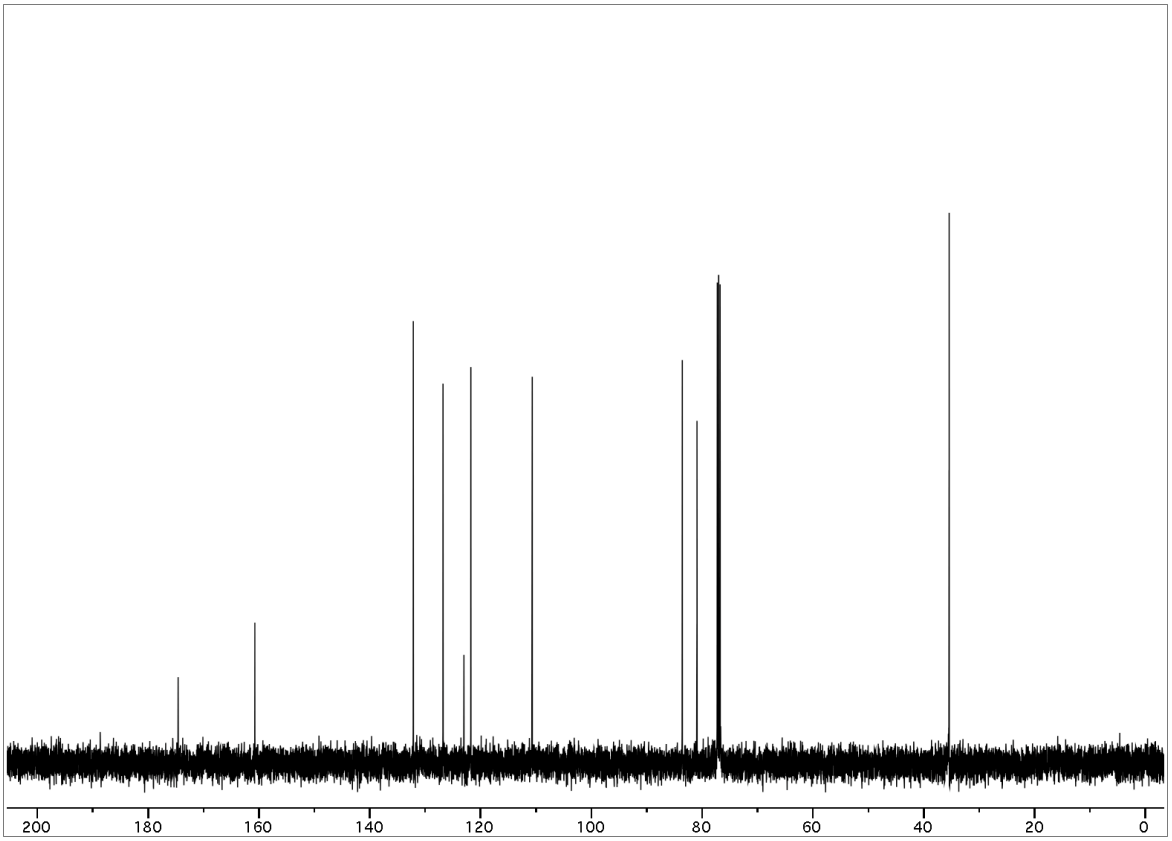

$^{1}$H NMR (500 MHz) spectrum of **49** in $CDCl_3$.



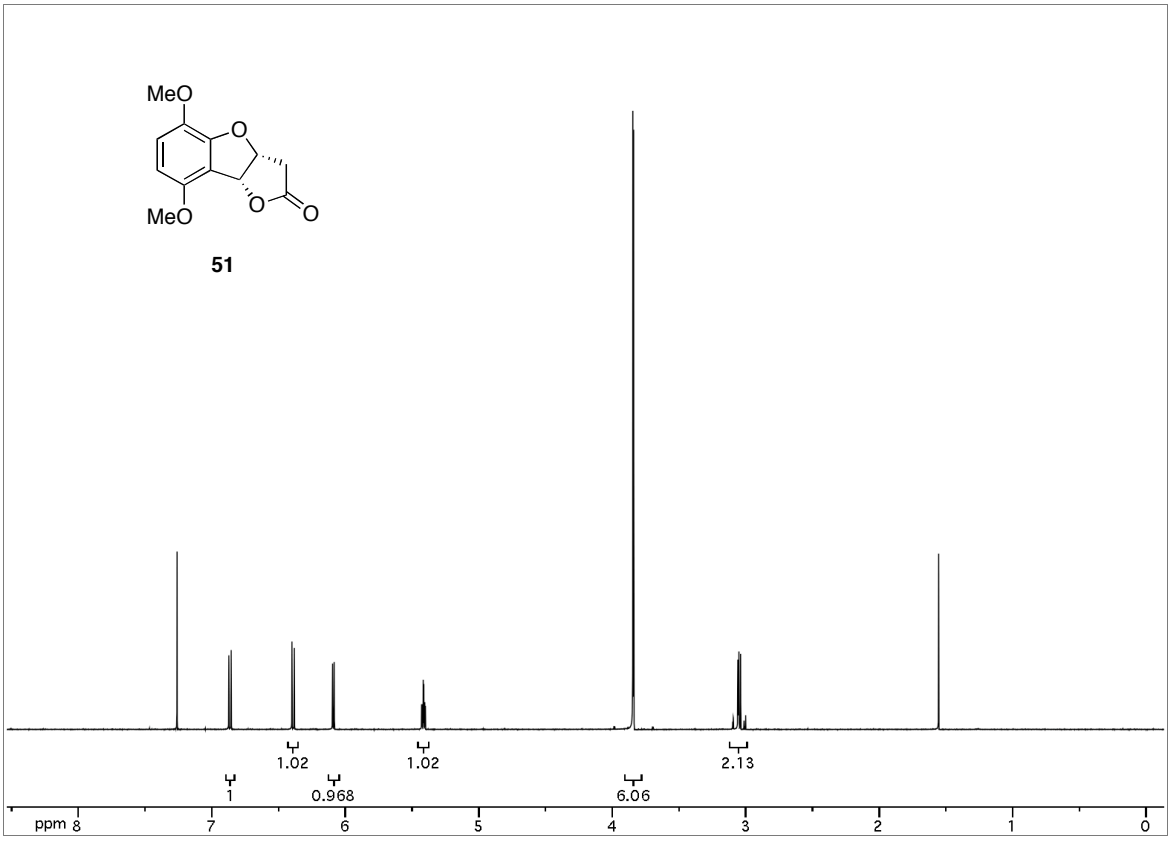

$^{13}$C NMR (125 MHz) spectrum of **49** in $CDCl_3$.



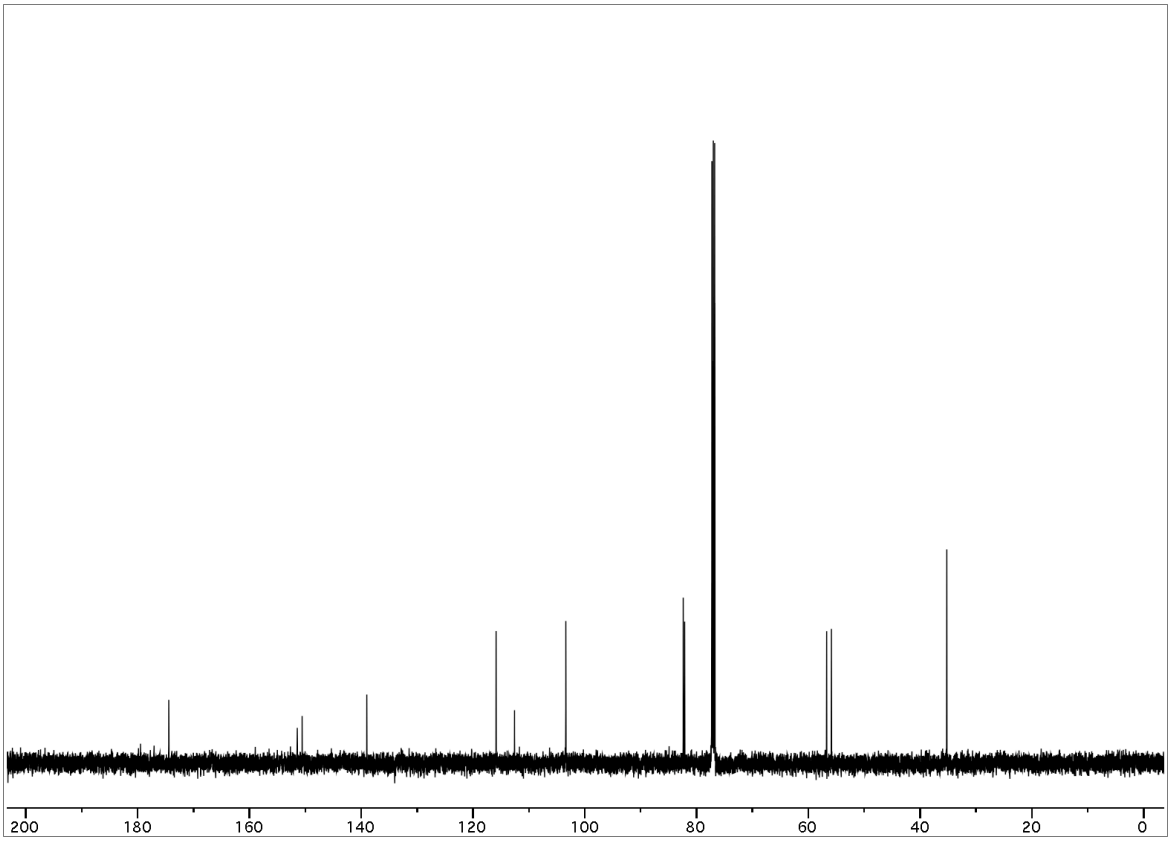

$^{1}$H NMR (500 MHz) spectrum of **50** in $CDCl_3$.



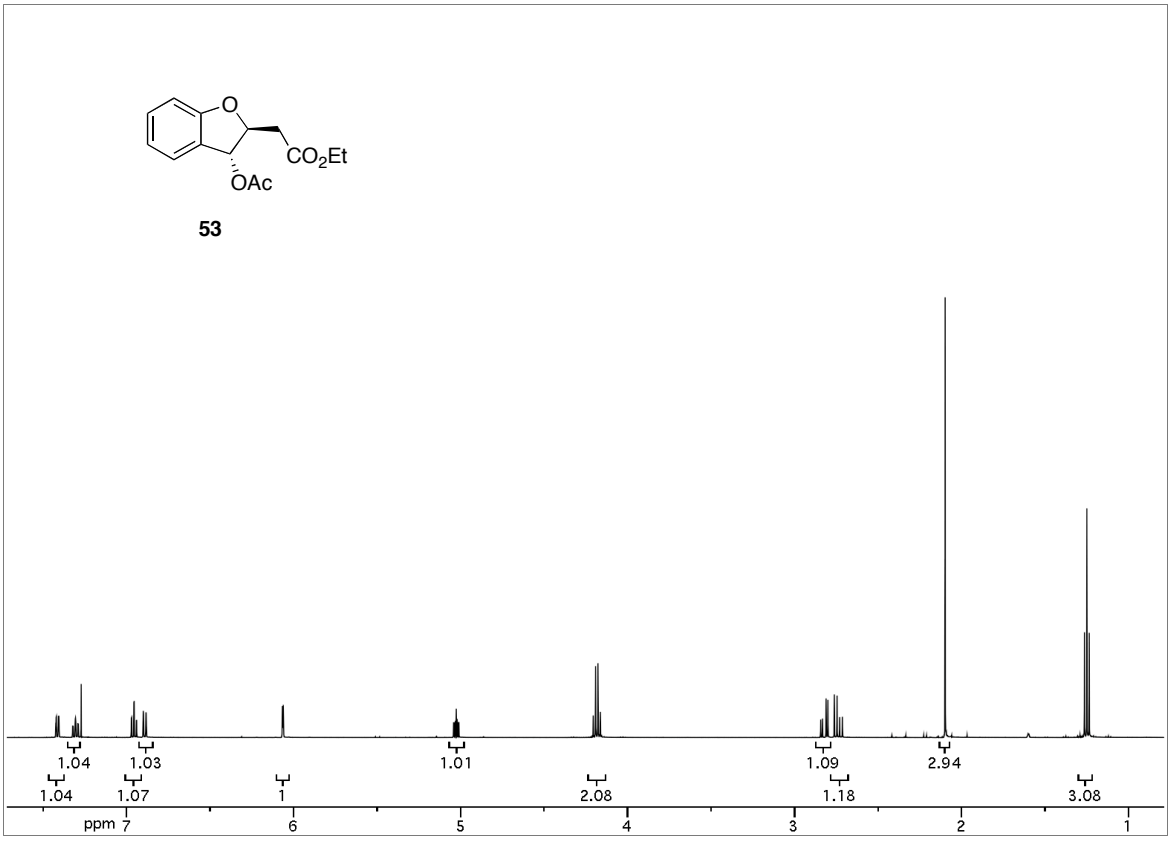

$^{13}$C NMR (125 MHz) spectrum of **50** in $CDCl_3$.



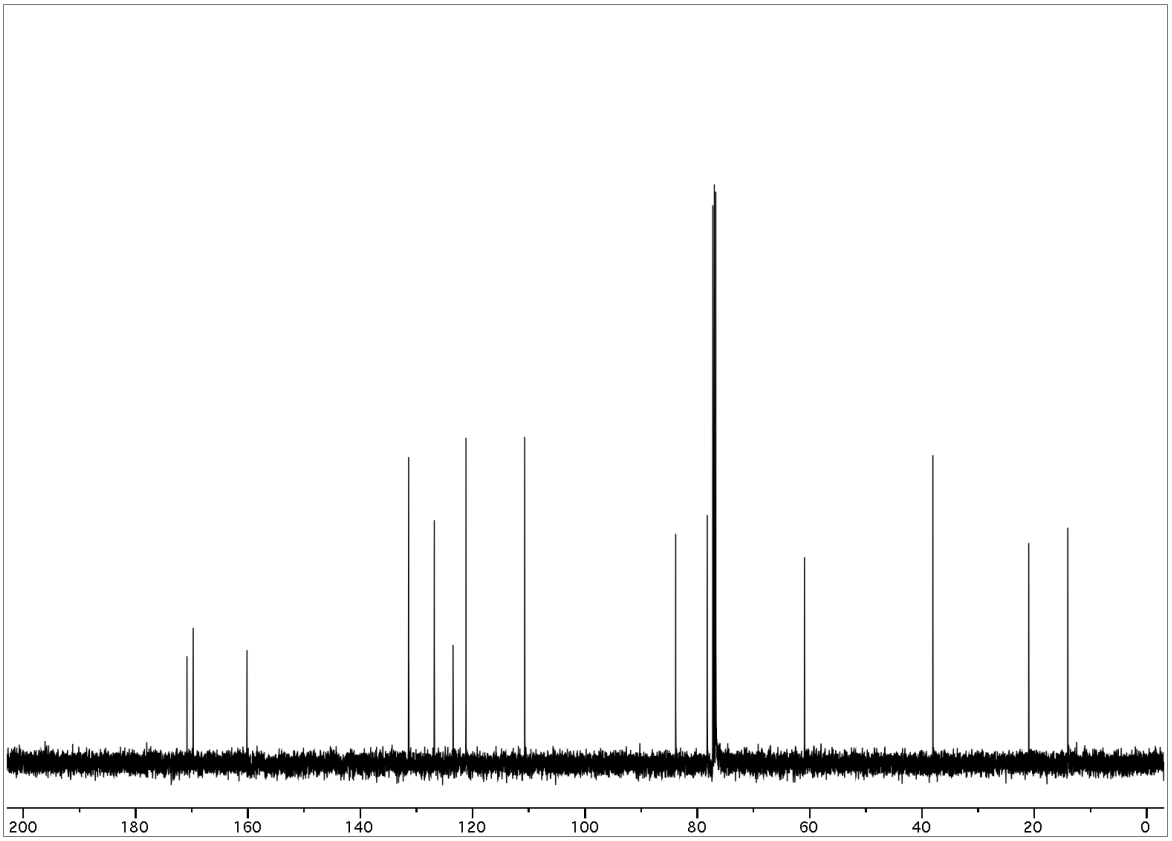

$^{1}$H NMR (500 MHz) spectrum of **51** in $CDCl_3$.



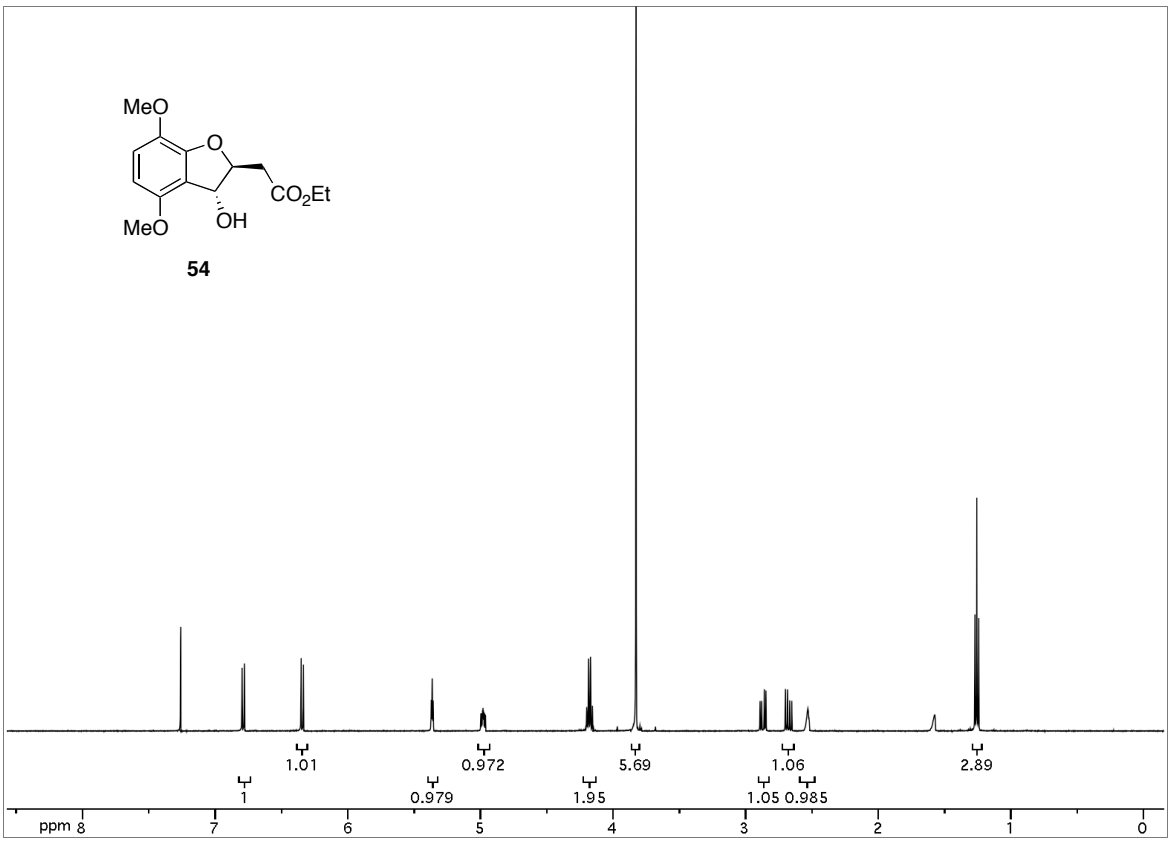

$^{13}$C NMR (125 MHz) spectrum of **51** in $CDCl_3$.



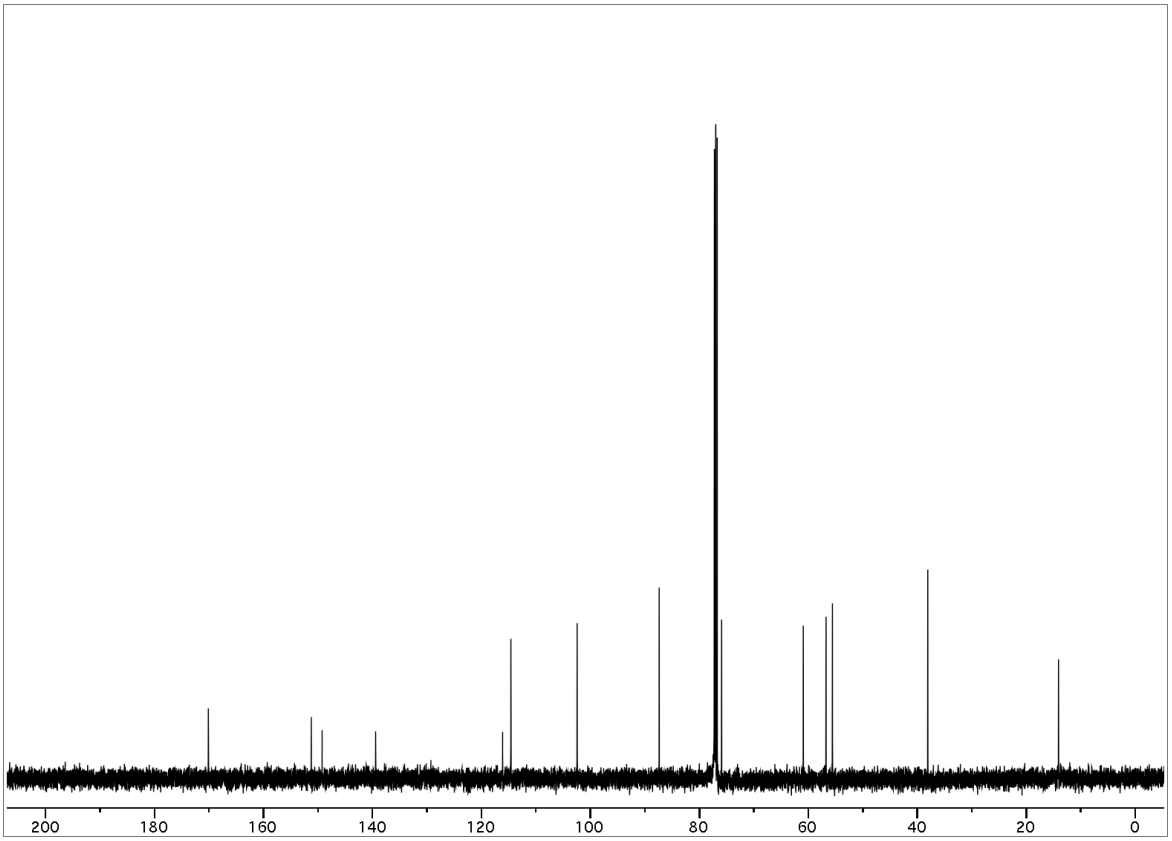

$^{1}$H NMR (500 MHz) spectrum of **53** in $CDCl_3$.



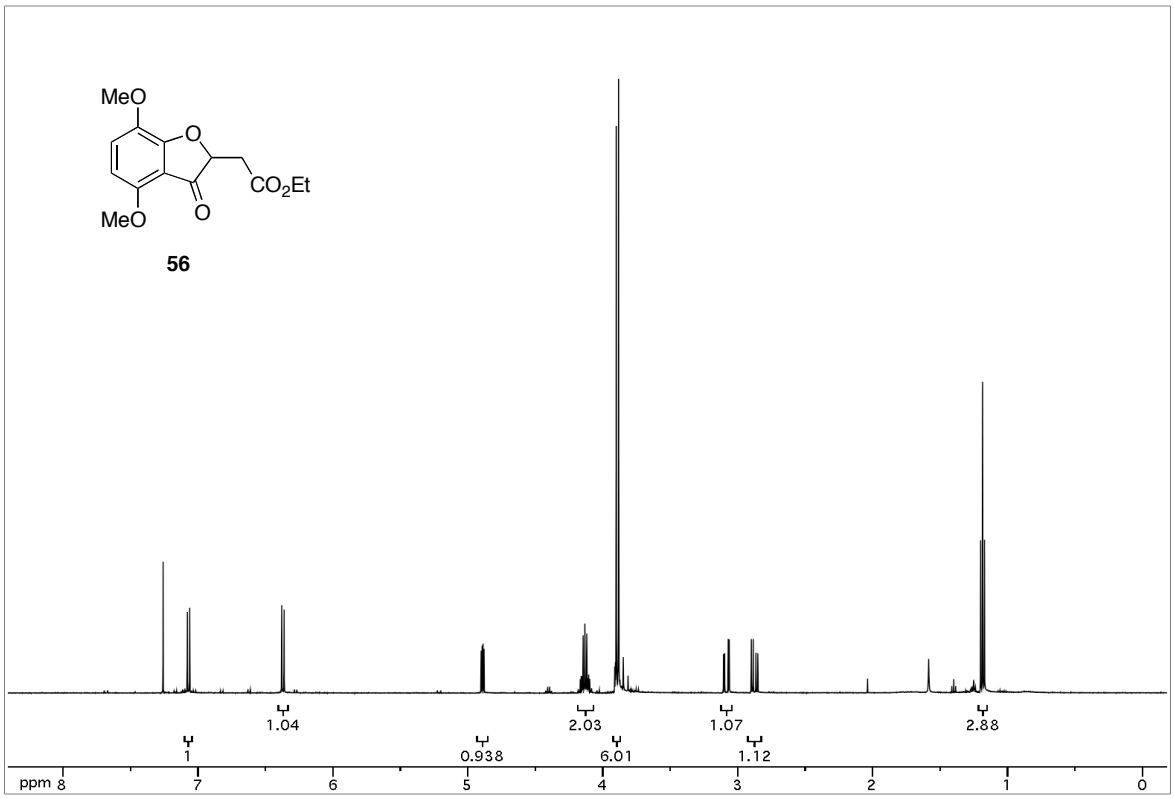

$^{13}$C NMR (125 MHz) spectrum of **53** in $CDCl_3$.



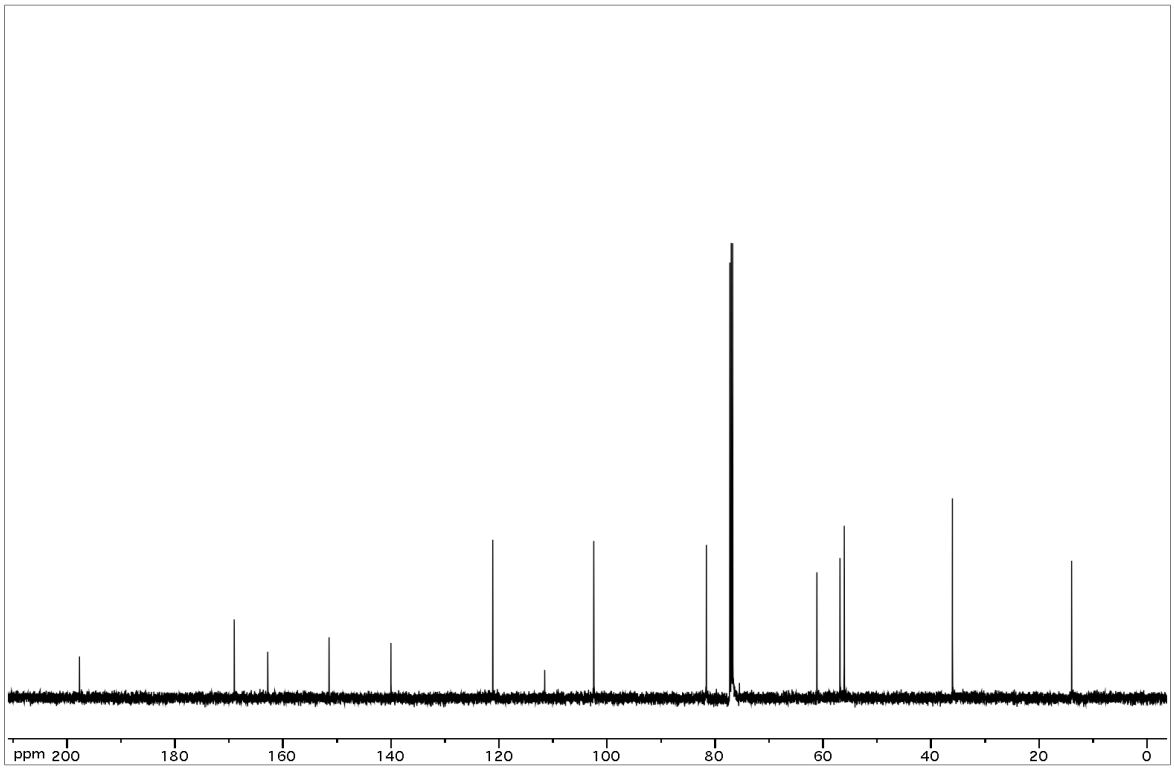

$^{1}$H NMR (500 MHz) spectrum of **54** in $CDCl_3$.



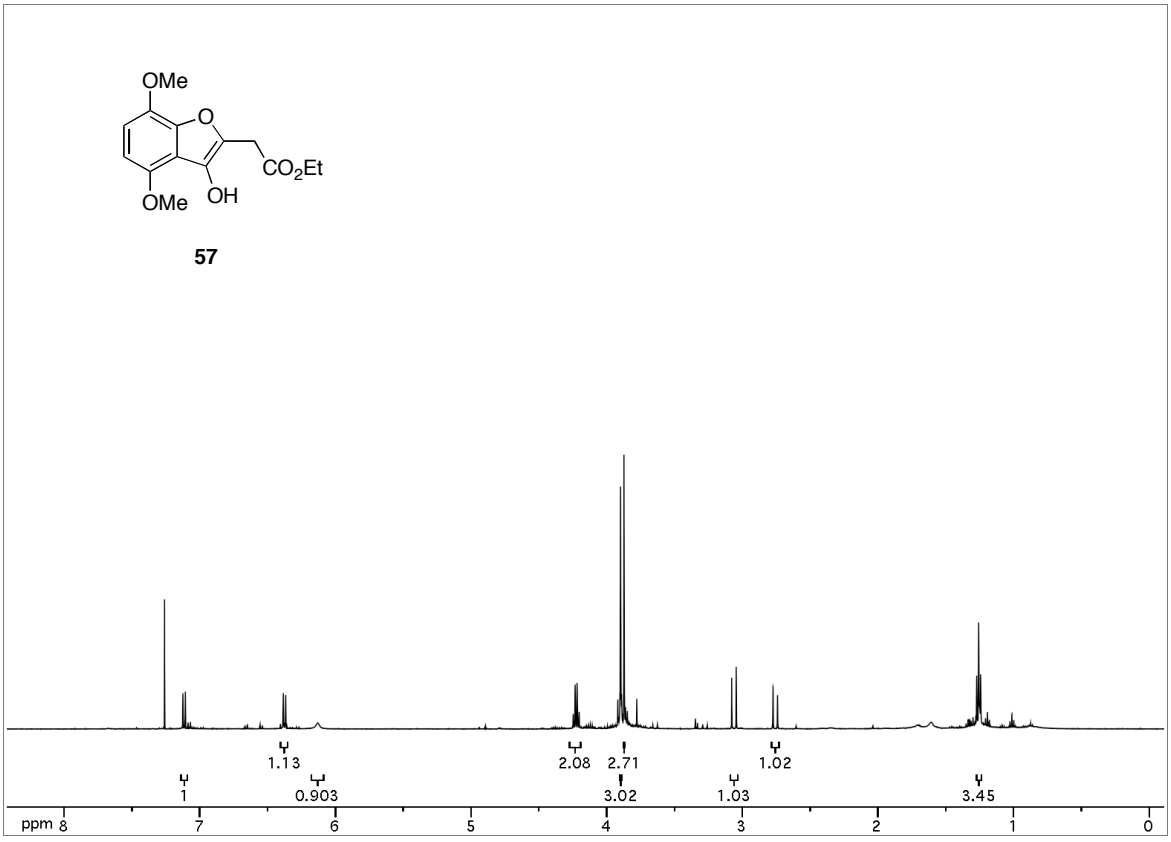

$^{13}$C NMR (125 MHz) spectrum of **54** in $CDCl_3$.



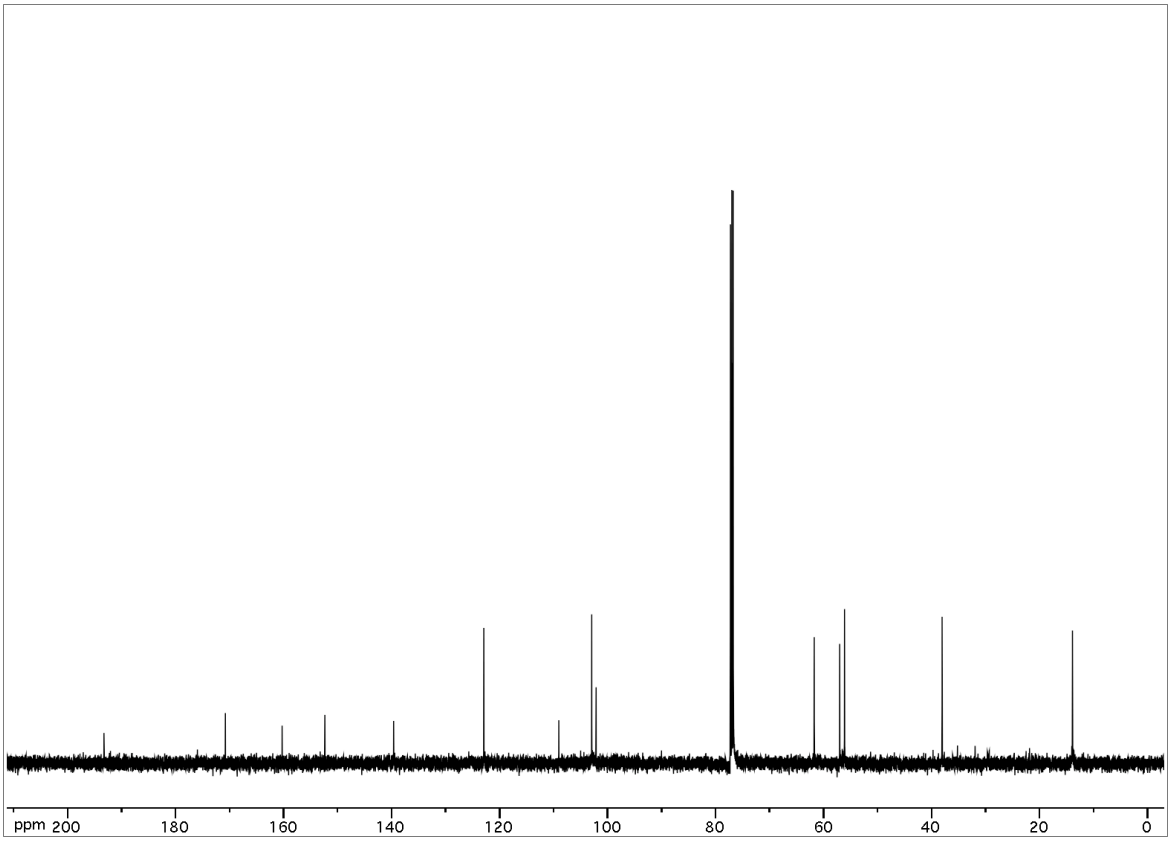

$^{1}$H NMR (500 MHz) spectrum of **56** in $CDCl_3$.



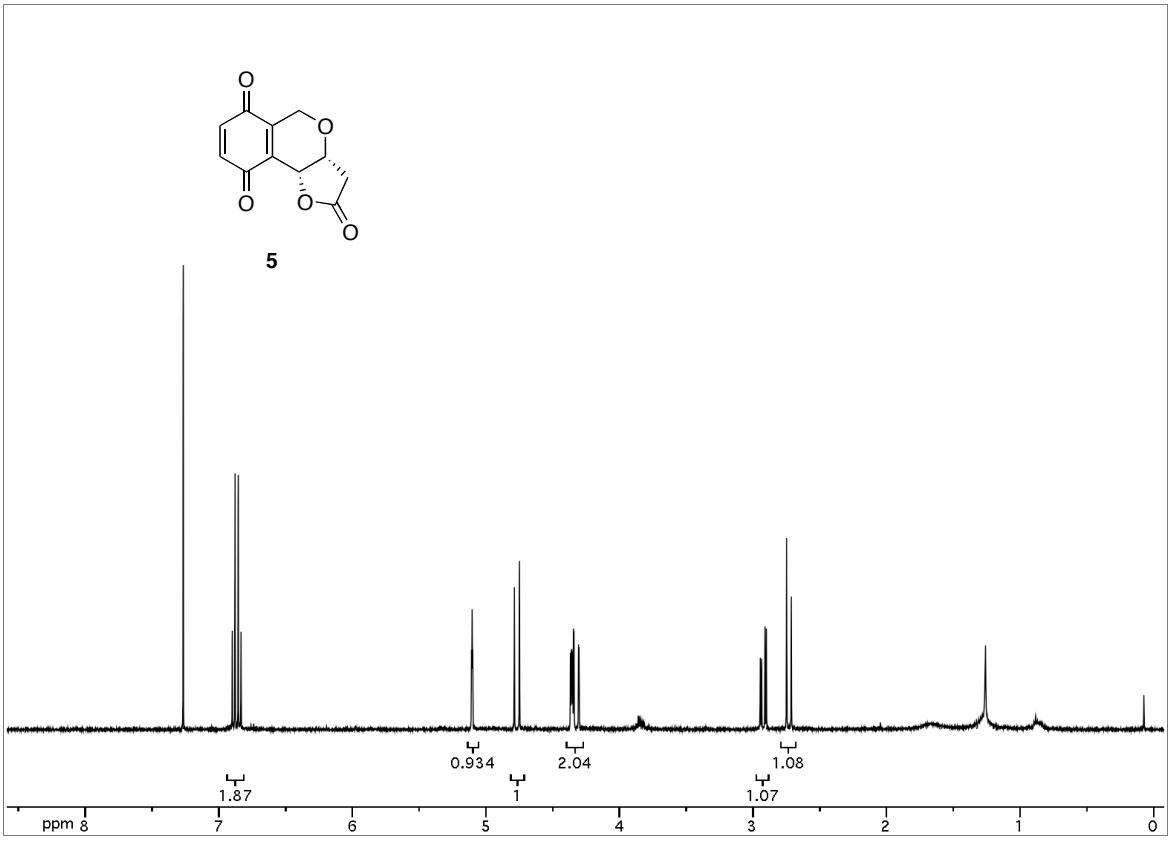

$^{13}$C NMR (125 MHz) spectrum of **56** in $CDCl_3$.



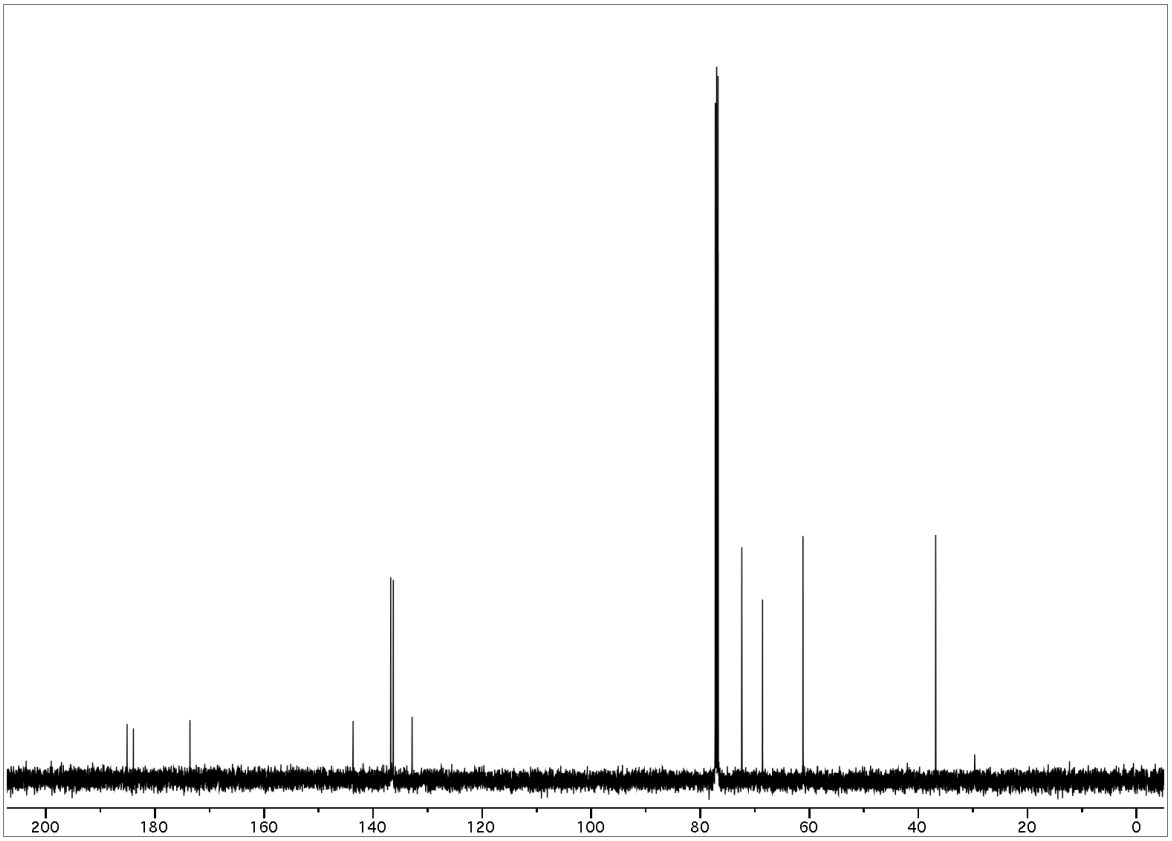

$^{1}$H NMR (500 MHz) spectrum of **57** in $CDCl_3$.



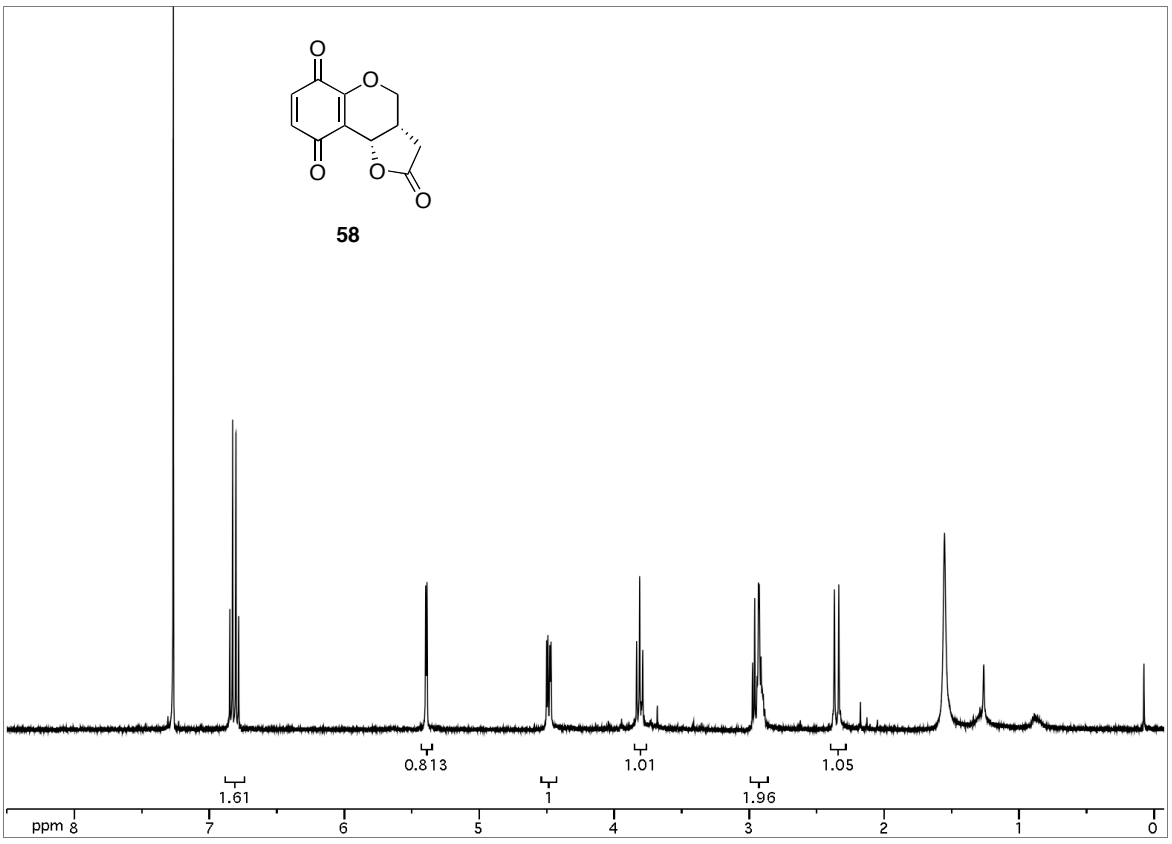

$^{13}$C NMR (125 MHz) spectrum of **57** in $CDCl_3$.



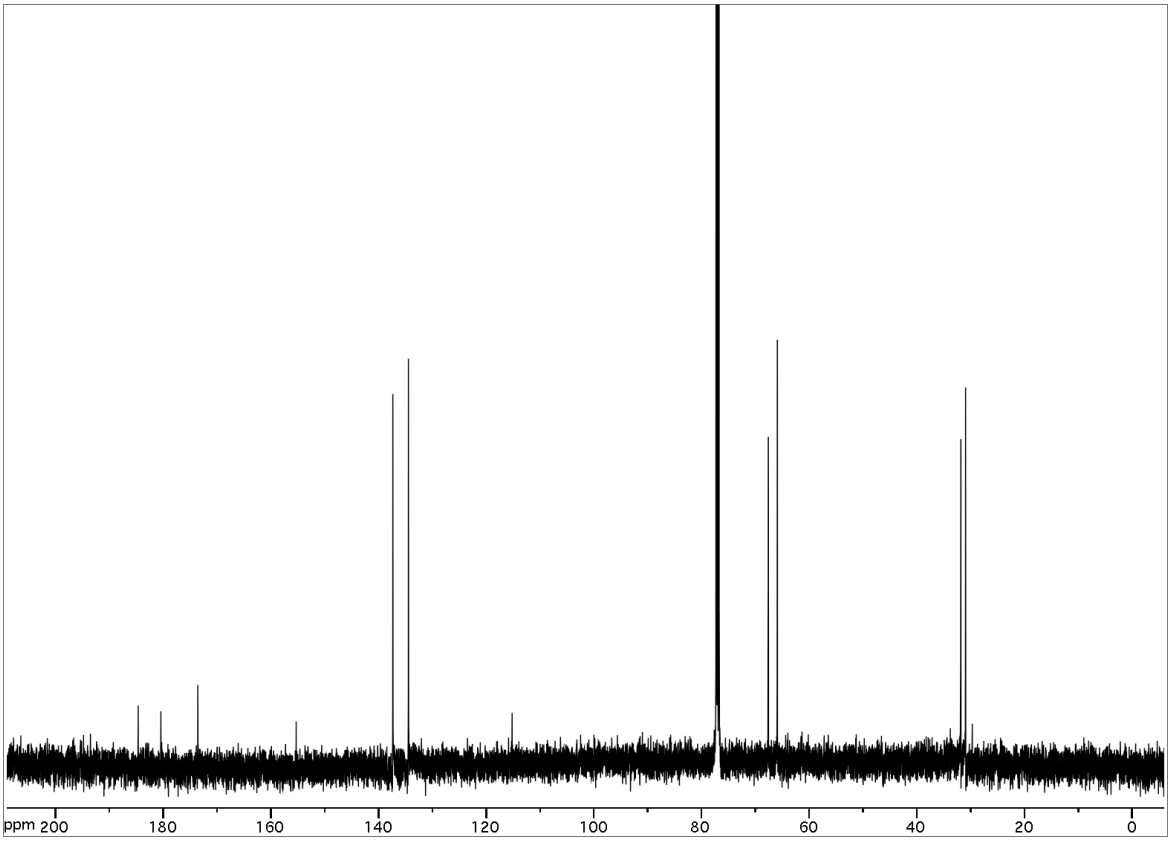

$^{1}$H NMR (500 MHz) spectrum of **5** in $CDCl_3$.



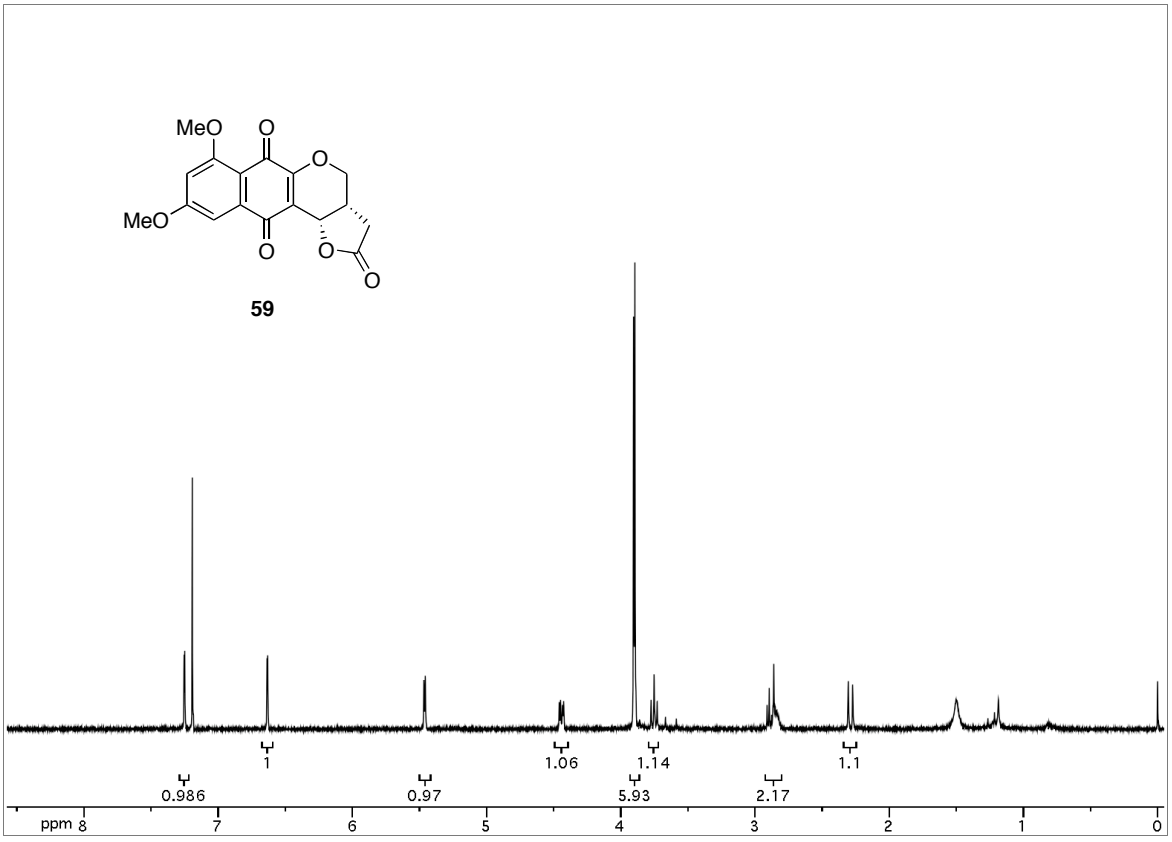

$^{13}$C NMR (125 MHz) spectrum of **5** in $CDCl_3$.



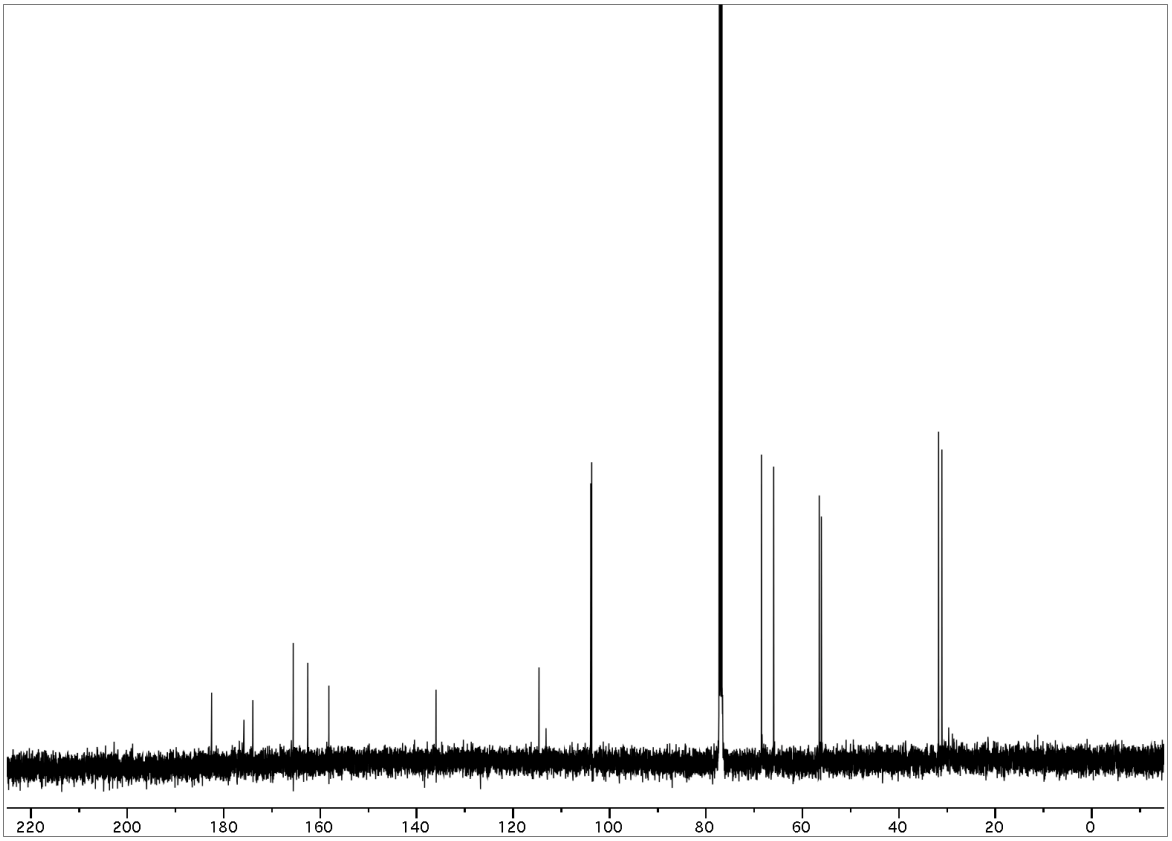

$^{1}$H NMR (500 MHz) spectrum of **58** in $CDCl_3$.



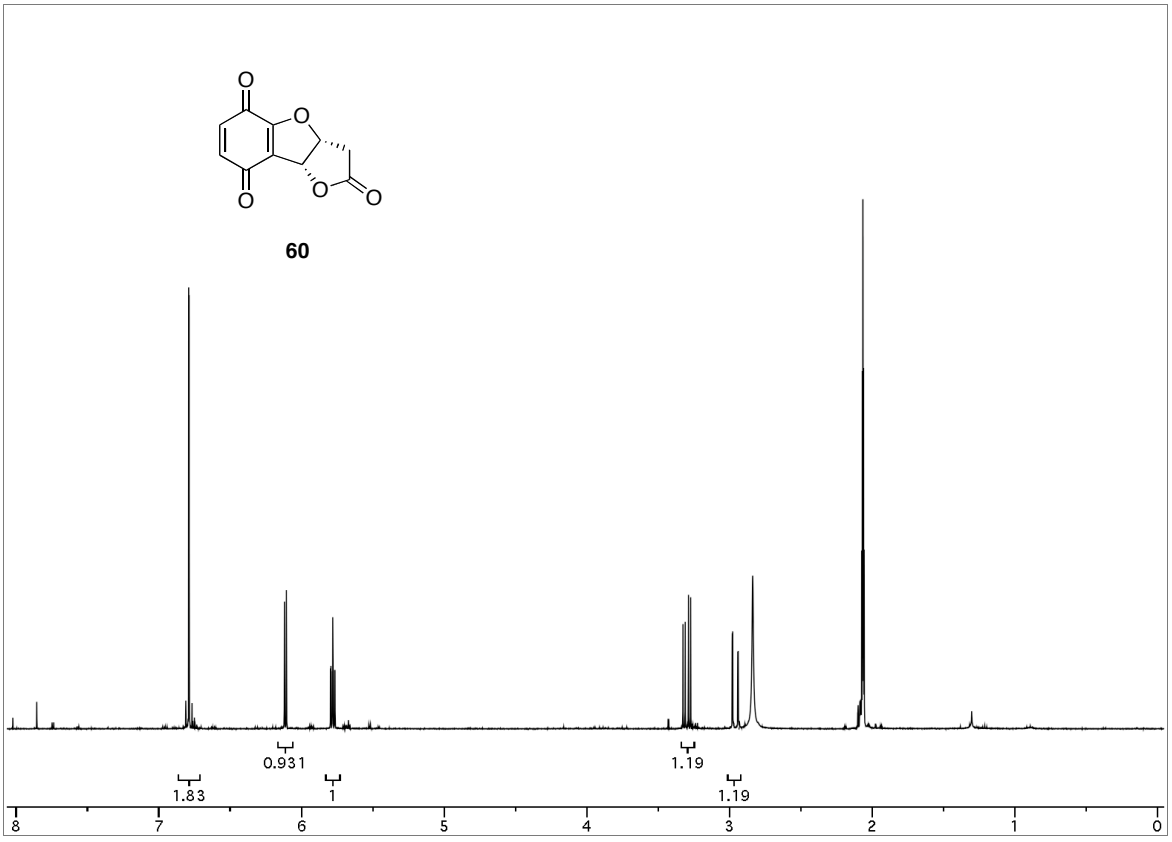

$^{13}$C NMR (125 MHz) spectrum of **58** in $CDCl_3$.



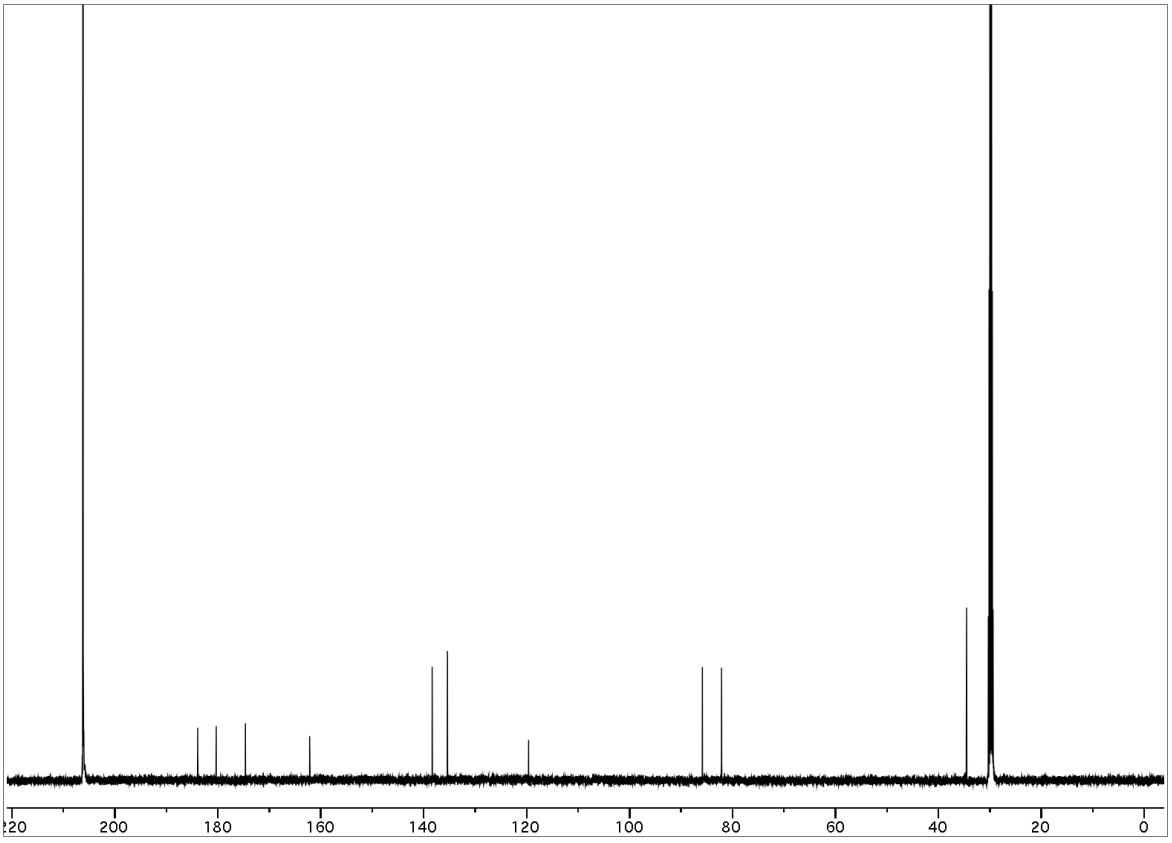

$^{1}$H NMR (500 MHz) spectrum of **59** in $CDCl_3$.




$^{13}$C NMR (125 MHz) spectrum of **59** in $CDCl_3$.




$^{1}$H NMR (500 MHz) spectrum of **60** in $d_6$-acetone.




$^{13}$C NMR (125 MHz) spectrum of **60** in $d_6$-acetone.