Electronic Supplementary Material (ESI) for Chemical Communications

Anionic [4+3] heteroannulation of 2-azidoacrylates: A modular synthesis of 2-benzazepin-1-ones

Bidyut Kumar Dinda, Amit Kumar Jana and Dipakranjan Mal*
Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India
dmal@chem.iitkgp.ernet.in

Supporting Information

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1. General Remarks:

Melting points were determined in open-end capillary tubes and are uncorrected. Solvents were dried and distilled following the standard procedures. TLC was carried out on precoated plates (silica gel 60, GF254), and the spots were visualized with UV and fluorescent lights. Column chromatography was performed on silica gel (60–120 or 230–400 mesh). ^{1}H and ^{13}C NMR spectra for all the compounds were recorded at 200/400 and 50/100 MHz respectively. IR spectra were recorded on an FT-IR instrument using a KBr pellet.

2. General Procedure of Annulation:

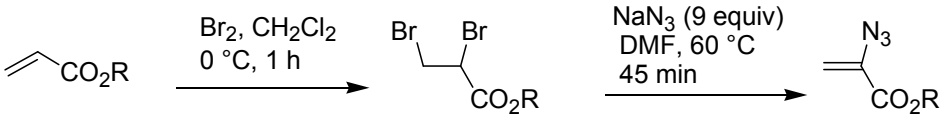
To a stirred solution of lithium hexamethyldisilazide (3.2 mmol) in THF (10 mL) at −78 °C under an inert atmosphere was added a solution of phthalide (1 mmol) in THF (5 mL). The resulting yellow solution was stirred at −78 °C for 30 min, after which a solution of a Michael acceptor (1.05 mmol) in THF (5 mL) was slowly added to the mixture. The cooling bath was removed after about 30 min and the reaction mixture was allowed to reach rt over a period of 15 min. Then it was allowed to stir at rt for further 6–7 h. After the completion of reaction (monitored by TLC) the mixture was quenched with 10% aq NH_4Cl (15 mL) and the resulting solution was concentrated under reduced pressure. The residue was extracted with ethyl acetate (3 × 50 mL) and the organic layer was washed with water (3 × 20 mL). Finally the resulting organic layer was washed with brine (2 × 20 mL). Organic layer was collected and dried (Na_2SO4), and concentrated. The residue was purified by column chromatography on silica gel to obtain a pure product.

3. General Procedure of Oxidation:

To a solution of benzazepinone (1 mmol) in dry chloroform (8 mL), active MnO_2 (5 mmol) was added and the mixture was allowed to stir at rt for 6–7 h. After completion of reaction (monitored by TLC) the mixture was filtered through a celite bed and concentrated in vacuum. The crude solid product was purified by column chromatography on silica gel to obtain a pure product.

4. Preparation of azidoacrylates: Azidoacrylates **1a** and **1b** were prepared by modification of the literature procedure.[1] Azidoacrylates **1d**,[2] **1e–1g**,[3] **1h**,[3,4] **1i**[3,5] and **1j**[6] were prepared according to the literature procedures.

4(i). General Procedure of the preparation of azidoacrylates 1a and 1b[1]:



23 R = Me
24 R = Et

25 R = Me
26 R = Et

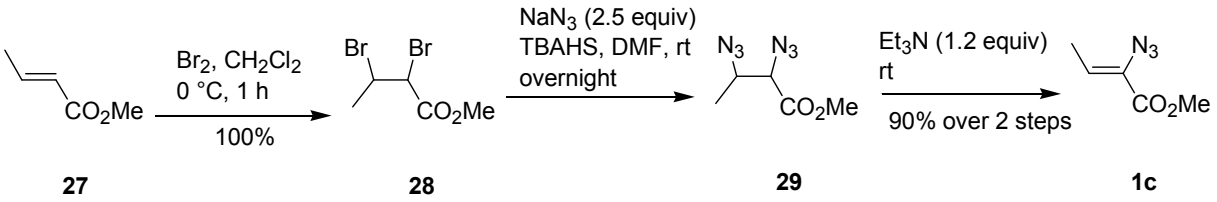
1a R = Me
1b R = Et

Scheme 1: Synthesis of azidoacrylates **1a** and **1b**

To a solution of methyl acrylate (**23**) or ethyl acrylate (**24**) (58.14 mmol in 25 mL DCM) 58.19 mmol of bromine in 3 mL DCM was added dropwise at 0 °C during 20 min under an inert atmosphere. The reaction mixture was allowed to stir at 0 °C for 1 h and then at rt for overnight. After completion of the reaction, the mixture was quenched with saturated aq $Na_2S_2O_3$ solution. Filtration of the mixture followed by extraction of the filtrate with DCM and water and then separation of the organic layer gave the dibromo compound in 90–95% yield.

The dibromo ester (**25** or **26**) (3.0 mmol) was dissolved in DMF and treated with 4.5 mmol of NaN_3 at 60 °C. After 20 min, an additional 3.0 mmol of the NaN_3 was added and the mixture was allowed to stir for further 25 min under the same temperature. After cooling, the reaction mixture at rt, it was extracted with ice cold *n*-pentane and water. Finally, the resulting organic layer was washed with brine. Organic layer was collected and dried (Na_2SO_4). Removal of the solvent under reduced pressure and at temperature below 25 °C gave the azidoacrylates in 80–85% yield.

4(ii). Preparation of methyl 2-azido-2-butenoate (1c):



Scheme 2: Synthesis of methyl 2-azido-2-butenoate (**1c**)

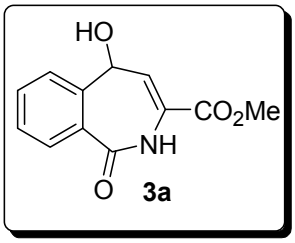
Dibrormo ester **28** was prepared by bromination of methyl crotonate (**27**) following the procedure 4(i). This was then reacted with sodium azide in the presence of tetrabutylammonium hydrogen sulphate (TBAHS). Treatment of diazido ester **29** with 1.2 equivalent of triethylamine in acetone at rt afforded the elimination product **1c**. The crude was extracted with ether and the organic layer was washed with water. Finally the resulting organic layer was washed with brine. Organic layer was collected and dried (Na_2SO4), and concentrated. Silica gel column chromatography of the residue with 10% ethylacetate-petroleum ether gave pure compound **1c**[7] in 90% overall yield for the last two steps.

5. Preparation of phthalides:

Phthalide **2a** is commercially available. Phthalide **2b**[8], **2c**[9], **2d**[10] and **2e**[11] were prepared according to literature procedure.

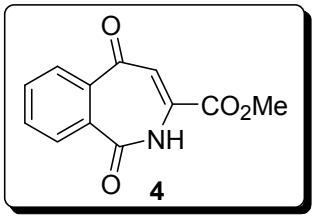
6. Spectrum Data of new compounds:

Methyl 5-hydroxy-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3a).



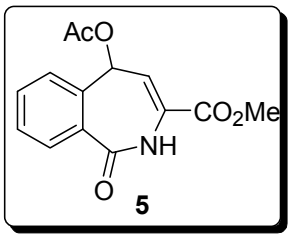
White solid. mp 121−124 °C. IR (KBr): $\tilde{\nu}$ = 1730, 1633, 1450, 1367, 1265, 1080, 760 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.95(brs, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.61–7.57 (m, 2H), 7.44–7.35 (m, 1H), 6.64 (d, *J* = 5.2 Hz, 1H), 5.37 (d, *J* = 5.2Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.5, 163.1, 143.6, 133.0 (CH), 130.9 (CH), 129.2, 128.8 (CH), 127.9 (CH), 125.3, 122.1 (CH), 68.1 (CH), 52.9 (CH_3). HRMS: Found: m/z 256.0584. Calcd for $C_{12}H_{11}NO_4$: $(M + Na)^+$ 256.0586.

Methyl 1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (4).



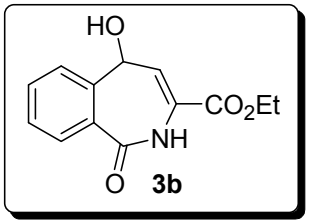
White solid. mp 176−178 °C. IR (KBr): $\tilde{\nu}$ = 1726, 1700, 1654, 1334, 1280, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.93 (brs, 1H), 8.55 (m, 1H), 8.28 (m, 1H), 7.80 (m, 2H), 6.89 (s, 1H), 4.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 165.3, 163.8, 137.0, 134.2 (CH), 133.6 (CH), 133.3 (CH), 131.8, 130.7 (CH), 129.9, 114.3 (CH), 54.5 (CH_3).

Methyl 5-acetoxy-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (5).



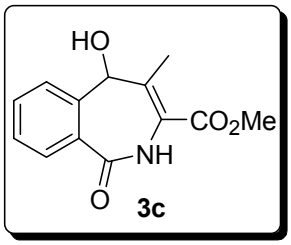
White solid, decomposes at high temperature. ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (brs, 1H), 8.00 (dd, *J* = 7.6Hz, 0.8Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 6.66 (dd, *J* = 6.2 Hz, 1.0 Hz, 1H), 6.29 (d, *J* = 6.0 Hz, 1H), 3.82 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 168.0, 163.3, 138.7, 133.2 (CH), 131.8 (CH), 130.3, 129.0 (CH), 127.6, 124.3 (CH), 122.8 (CH), 69.8 (CH), 53.3 (CH_3), 21.0 (CH_3).

Ethyl 5-hydroxy-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3b).



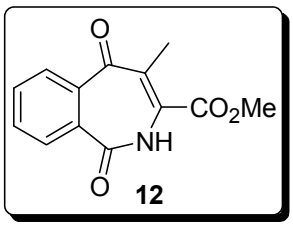
White solid. mp 105−108 °C. IR (KBr): $\tilde{\nu}$ = 1718, 1639, 1465, 1354, 1261, 1143, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.54 (m, 2H), 7.33 (m, 1H), 6.60 (d, *J* = 4.8 Hz, 1H), 5.05 (d, *J* = 4.8 Hz, 1H), 4.22 (q, *J* = 14.4 Hz, 7.2 Hz), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 162.8, 144.1, 133.2 (CH), 130.7 (CH), 130.0 (CH), 128.7, 127.9 (CH), 125.3, 122.3 (CH), 68.1 (CH), 62.4 (CH_2), 14.3 (CH_3).

Methyl 5-hydroxy-4-methyl-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3c).



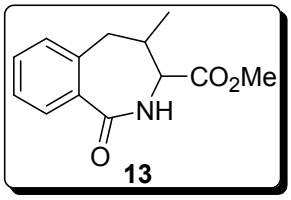
White solid. mp 162 °C. IR (KBr): $\tilde{\nu}$ = 1714, 1637, 1377, 1315, 1219 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.85 (brs, 1H), 7.58 (d, *J* = 4.4 Hz, 2H), 7.41–7.37 (m, 1H), 5.51 (s, 1H), 3.80 (s, 3H), 2.24 (s, 3H).

Methyl 4-methyl-1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (12).



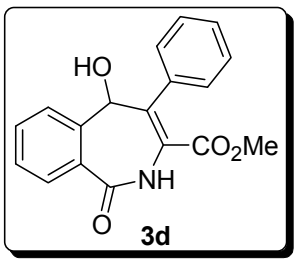
Colorless crystal. mp 152 °C. IR (KBr): $\tilde{\nu}$ = 1726, 1700, 1654, 1334, 1280, 1016, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (brs, 1H), 8.27 (m, 1H), 7.73 (m, 3H), 3.96 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.2, 165.9, 164.4, 139.3, 134.0 (CH), 133.0 (CH), 131.5 (CH), 129.3 (CH), 129.2, 129.1, 128.0, 53.8 (CH_3), 16.8 (CH_3).

Methyl 4-methyl-1-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*c*]azepine-3-carboxylate (13).



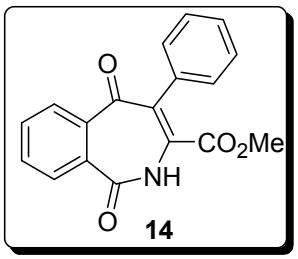
White solid. mp 110−112°C. IR (KBr): $\tilde{\nu}$ = 1730, 1629, 1450, 1240, 1150, 728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.66 (brs, 1H), 3.99 (t, *J* = 4.8 Hz, 1H), 3.76 (s, 3H), 2.80 (m, 1H), 2.59 (d, *J* = 11.2 Hz, 2H), 0.94 (d, *J* = 6.0 Hz, 3H). [Decoupling experiment by irradiation of the 'NH' proton revealed the coupling constant between $CHCO_2Me$ and $CHCH_3$ to be 4.0 Hz, which conformed to the cis stereochemistry of benzazepinone **15**]. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 171.2, 137.9, 134.5, 131.7 (CH), 129.1 (CH), 129.0 (CH), 127.6 (CH), 57.1 (CH), 52.8 (CH_3), 39.7 (CH), 39.2 (CH_2), 15.3 (CH_3). HRMS: Found: m/z 234.1124. Calcd for $C_{13}H_{16}NO_3$: $(M + H)^+$ 234.1130.

Methyl 5-hydroxy-1-oxo-4-phenyl-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3d).



Colorless crystal. mp 150−154 °C. IR (KBr): $\tilde{\nu}$ = 1708, 1654, 1260, 1204, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.58 (dd, *J* = 7.6 Hz, 7.2 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.38 (m, 4H), 7.00 (brs, 2H), 5.63 (s, 1H), 3.49 (s, 3H). HRMS: Found: m/z 310.1074. Calcd for $C_{18}H_{16}NO_4$: $(M + H)^+$ 310.1079.

Methyl 1,5-dioxo-4-phenyl-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (14).



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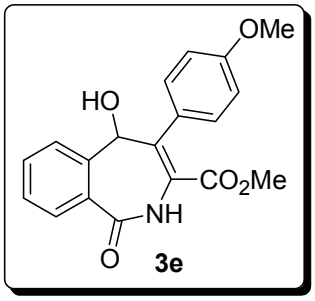
White solid. mp 194–195 °C. IR (KBr): $\tilde{\nu}$ = 1736, 1707, 1618, 1382, 1262, 1012, 760. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (brs1H), 8.37 (m, 1H), 7.78 (m, 3H), 7.36 (m, 3H), 7.24–7.21 (m, 2H), 3.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 166.0, 165.2, 140.0, 135.9, 134.3 (CH), 133.2, (CH), 131.9 (CH), 130.3, 129.6 (CH), 129.5 (CH), 129.1, 128.4 (CH), 128.3 (CH), 53.5 (CH_3).

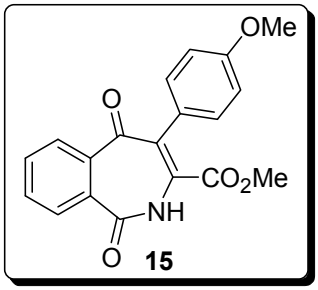
Methyl 5-hydroxy-4-(4-methoxy-phenyl)-1-oxo-2,5-dihydro-1H-benzo[c]azepine-3-carboxylate (3e).



3e

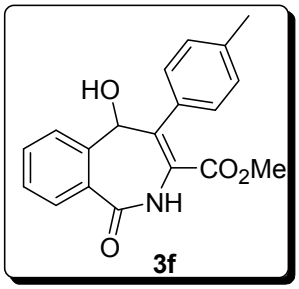
White solid. mp 144−146 °C. IR (KBr): $\tilde{\nu}$ = 1708, 1654, 1248, 1178, 1034, 752 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (brs, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.2 Hz, 1H), 6.91 (m, 4H), 5.67 (d, *J* = 4.4 Hz, 1H), 3.83 (s, 3H), 3.54 (s, 3H), 2.22 (d, *J* = 5.2 Hz, 1H, −OH proton, D_2O exchangeable).

Methyl 4-(4-methoxy-phenyl)-1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (15).



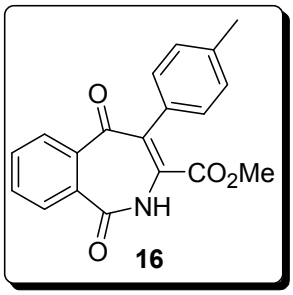
White solid. mp 212−214 °C. IR (KBr): $\tilde{\nu}$ = 1740, 1719, 1628, 1384, 1250, 928, 554 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.42 (brs, 1H), 8.35 (m, 1H), 7.77 (m, 3H), 7.16 (d, *J* = 8.2 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 2H), 3.83 (s, 3H), 3.56 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.9, 165.9, 165.4, 159.8, 140.1, 134.3 (CH), 133.2 (CH), 131.8 (CH), 130.8 (CH), 130.2, 129.8, 129.5 (CH), 129.1, 127.9, 113.8 (CH), 55.5 (CH_3), 53.6 (CH_3).

Methyl 5-hydroxy-1-oxo-4-p-tolyl-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3f).



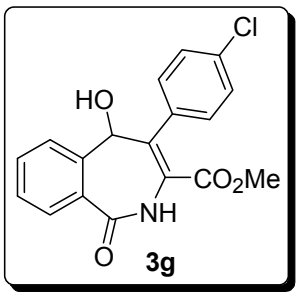
White solid. mp 136 °C. IR (KBr): $\tilde{\nu}$ = 1709, 1640, 1262, 1044, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.56 (m, 1H), 7.43−7.37 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.89 (brs, 2H), 5.58 (s, 1H), 3.51 (s, 3H), 2.37 (s, 3H).

Methyl 1,5-dioxo-4-p-tolyl-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (16).



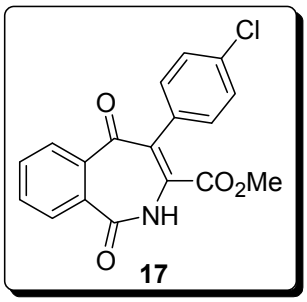
White solid. mp 220−222 °C. IR (KBr): $\tilde{\nu}$ = 1735, 1710, 1664, 1364, 1280, 950, 742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 (brs, 1H), 8.35 (m, 1H), 7.76 (m, 3H), 7.17 (d, *J* = 7.6 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.55 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.7, 166.0, 165.2, 140.3, 138.3, 134.2 (CH), 133.1 (CH), 132.8, 131.8 (CH), 130.5, 129.9, 129.5 (CH), 129.4 (CH), 129.1 (CH), 53.5 (CH_3), 21.5 (CH_3) [N.B. one quaternary C is missing].

Methyl 4-(4-chloro-phenyl)-5-hydroxy-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3g).



Colorless crystal. mp 168 °C. IR (KBr): $\tilde{\nu}$ = 1736, 1630, 1258, 1090, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 6.4 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.94 (brs, 2H), 5.56 (s, 1H), 3.52 (s, 3H), 2.74 (brs, 1H, -OH proton).

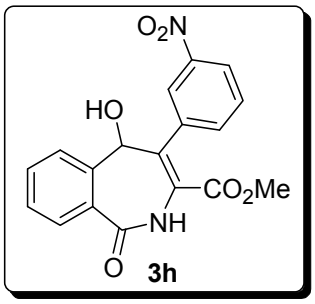
Methyl 4-(4-chloro-phenyl)-1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (17).



White solid. mp 218 °C. IR (KBr): $\tilde{\nu}$ = 1742, 1705, 1620, 1218, 1020, 772 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.37 (d, *J* = 7.2 Hz, 1H), 7.78 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 3.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.8, 165.9, 164.9, 139.7, 134.6, 134.4 (CH), 134.3, 133.4 (CH), 132.0 (CH), 131.0 (CH), 130.4, 129.7 (CH), 129.1,

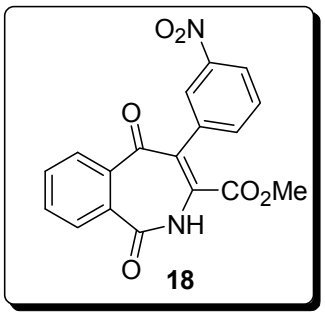
128.8, 128.6 (CH), 53.7 (CH_3). HRMS: Found: m/z 342.0539. Calcd for $C_{18}H_{13}ClNO_4$: $(M + H)^+$ 342.0533.

Methyl 5-hydroxy-4-(3-nitro-phenyl)-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3h).



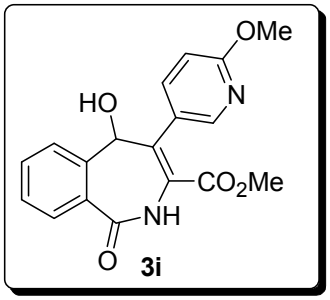
Brown solid. mp 138−140 °C. IR (KBr): $\tilde{\nu}$ = 1737, 1639, 1527, 1346, 1199, 1113, 1005, 750, 557 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 8.0 Hz, 1H), 8.10 (s, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.93 (brs, 1H), 7.63 (m, 1H), 7.55–7.48 (m, 3H), 7.39 (d, *J* = 8.0 Hz, 1H), 5.76 (s, 1H), 3.54 (s, 3H).

Methyl 4-(3-nitro-phenyl)-1,5-dioxo-2,5-dihydro-1H-benzo[c]azepine-3-carboxylate (18).



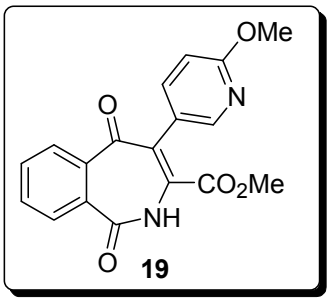
White solid. mp 224 °C. IR (KBr): $\tilde{\nu}$ = 1744, 1716, 1618, 1400, 1022, 722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.72 (s, 1H), 8.40 (d, *J* = 7.2 Hz, 1H), 8.24 (d, *J* = 7.2 Hz, 1H), 8.10 (s, 1H), 7.81 (m, 3H), 7.57 (m, 2H), 3.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 165.7, 164.1, 148.1, 139.2, 137.6, 136.0 (CH), 134.6 (CH), 133.7 (CH), 132.3 (CH), 131.0, 130.6 (CH), 129.1 (CH), 127.2, 124.8 (CH), 123.2 (CH), 54.0 (CH_3) [N.B. one quaternary C is missing].

Methyl 5-Hydroxy-4-(6-methoxy-pyridin-3-yl)-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3i).



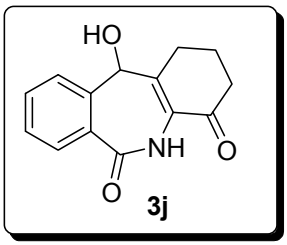
Yellow solid. mp 123−124°C. IR (KBr): $\tilde{\nu}$ = 1716, 1653, 1315, 1284, 1022, 668 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.95 (d, *J* = 7.2 Hz, 1H), 7.84 (s, 1H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.45–7.39 (m, 3H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.66 (s, 1H), 3.99 (s, 3H), 3.58 (s, 3H).

Methyl 4-(6-methoxy-pyridin-3-yl)-1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (19).



White solid. mp 190−193°C. IR (KBr): $\tilde{\nu}$ = 1740, 1707, 1636, 1440, 722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.72 (s, 1H), 8.36 (d, *J* = 7.6 Hz, 1H), 7.96 (s, 1H), 7.78 (m, 3H), 7.55 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 3.96 (s, 3H), 3.62 (s, 3H). ^{13}C NMR (100 MHz, d_6-Acetone): δ 191.2, 166.7, 165.3, 164.6, 148.1 (CH), 141.8 (CH), 140.0, 135.6, 134.9 (CH), 133.9 (CH), 132.7 (CH), 130.6 (CH), 130.5, 125.9, 110.7 (CH), 79.3, 53.7 (CH_3), 53.5 (CH_3).

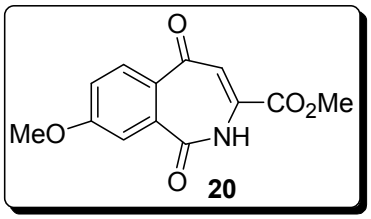
11-hydroxy-2,3,5,11-tetrahydro-1*H*-dibenzo[*b*,*e*]azepine-4,6-dione (3j).



3j

Colorless crystal. mp >250 °C. IR (KBr): $\tilde{\nu}$ = 1717, 1636, 1362, 1118, 750 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (brs, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 4.0 Hz, 2H), 7.40 (t, *J* = 4.0 Hz, 1H), 5.33 (s, 1H), 2.65 (s, 2H), 2.51–2.42 (m, 2H), 2.04−2.02 (m, 1H), 1.79−1.7 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 168.9, 148.7, 143.2, 133.1 (CH), 130.5 (CH), 128.8, 128.0 (CH), 127.4, 122.4 (CH), 69.5 (CH), 36.35 (CH_2), 23.72 (CH_2), 21.4 (CH_2).

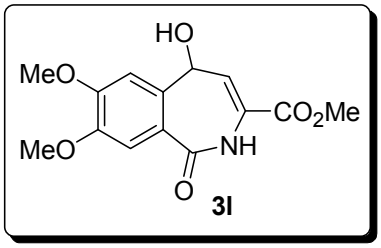
Methyl 8-methoxy-1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (20).



20

White solid. mp 179−182 °C. IR (KBr): $\tilde{\nu}$ = 1727, 1707, 1608, 1448, 1243, 1150, 725 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.95 (brs, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.01 (d, *J* = 2.8 Hz, 1H), 7.30 (dd, *J* = 9.0 Hz, 2.6, 1H), 6.89 (s, 1H), 3.99 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.0, 165.1, 164.1, 163.9, 133.7 (CH), 132.1, 130.7, 130.4, 121.8 (CH), 115.9 (CH), 115.0 (CH), 56.1 (CH_3), 54.7 (CH_3).

Methyl 5-hydroxy-7,8-dimethoxy-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (3l).

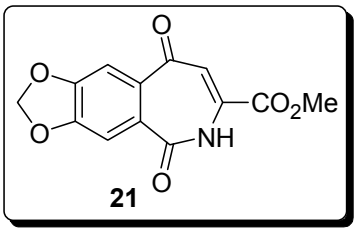


3l

White crystalline solid. mp 120−122 °C. IR (KBr): $\tilde{\nu}$ = 1718, 1636, 1266, 1130, 766 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (brs, 1H), 7.46 (s, 1H), 7.10 (s, 1H), 6.67 (d, *J* = 5.2 Hz, 1H),

5.46 (d, *J* = 4.8 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 163.5, 153.2, 148.5, 137.1, 128.3 (CH), 125.7, 120.9, 113.4 (CH), 105.0 (CH), 68.1 (CH), 56.4 (2 X CH_3), 53.2 (CH_3).

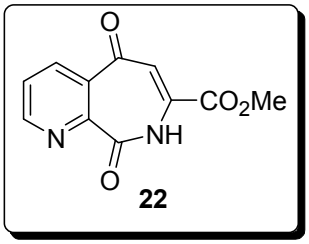
Methyl 5,9-dioxo-6,9-dihydro-5*H*-1,3-dioxa-6-aza-cyclohepta[*f*]indene-7-carboxylate (21).



21

White solid. mp >250 °C. IR (KBr): $\tilde{\nu}$ = 1726, 1705, 1629, 1400, 1330, 772 cm^{-1}. ^{1}H NMR (400 MHz, d_6-DMSO) δ 10.14 (brs, 1H), 7.80 (s, 1H), 7.56 (s, 1H), 6.53 (s, 1H), 6.34 (s, 2H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, d^6-DMSO): δ 184.7, 164.2, 163.4, 152.5, 152.1, 134.0, 132.8, 127.2, 112.8 (CH), 110.4 (CH), 107.7 (CH), 103.5 (CH_2), 54.0 (CH_3).

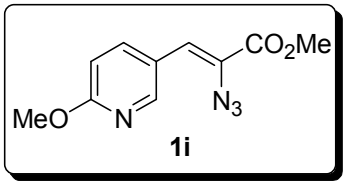
Methyl 5,9-dioxo-8,9-dihydro-5*H*-pyrido[2,3-*c*]azepine-7-carboxylate (22).



22

White solid. mp 192 °C. IR (KBr): $\tilde{\nu}$ = 1733, 1707, 1634, 1448, 1150, 1030, 728 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (brs, 1H), 9.02 (s, 1H), 8.87 (d, *J* = 8.0 Hz, 1H), 7.75 (brs, 1H), 7.03 (s, 1H), 4.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.6, 164.0, 163.7, 155.3 (CH), 151.3, 142.2 (CH), 131.3, 127.5 (CH), 114.1 (CH), 54.9 (CH_3) [N.B. one quaternary C is missing].

Methyl 2-azido-3-(6-methoxy-pyridin-3-yl)-acrylate (1i).



1i

Yellow solid. mp 78−80 °C. IR (KBr): $\tilde{\nu}$ = 2127, 1710, 1631, 1438, 1256, 1025, 772 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.0 Hz, 1H), 8.26 (dd, *J* = 8.8 Hz, 2.0 Hz, 1H), 6.82 (s, 1H), 6.76 (d, *J* = 9.2 Hz, 1H), 4.02 (s, 3H), 3.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.4, 164.0, 150.2 (CH), 139.7 (CH), 124.9, 123.2, 122.3 (CH), 111.0 (CH), 53.9 (CH_3), 53.1 (CH_3).

7. References:

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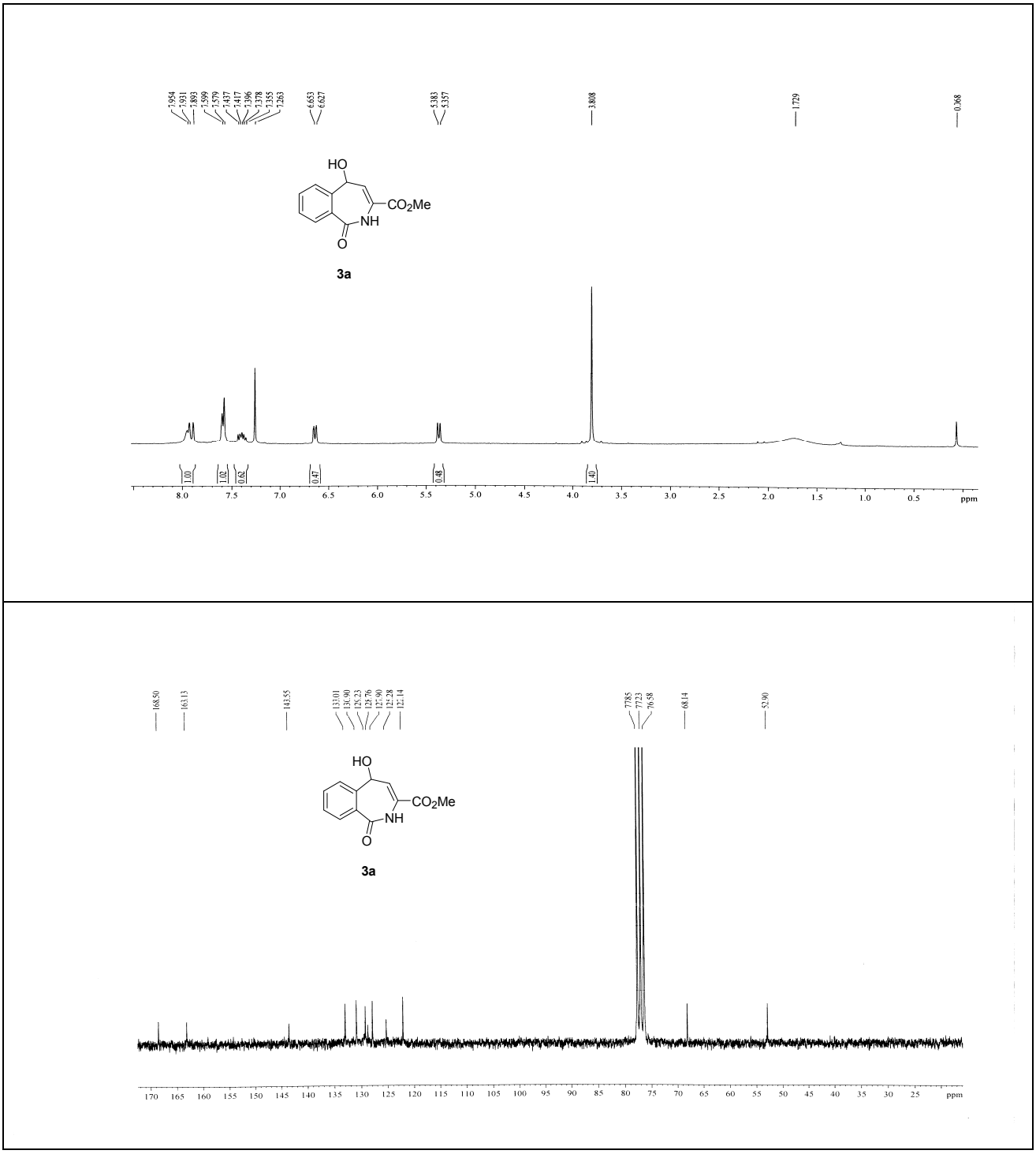
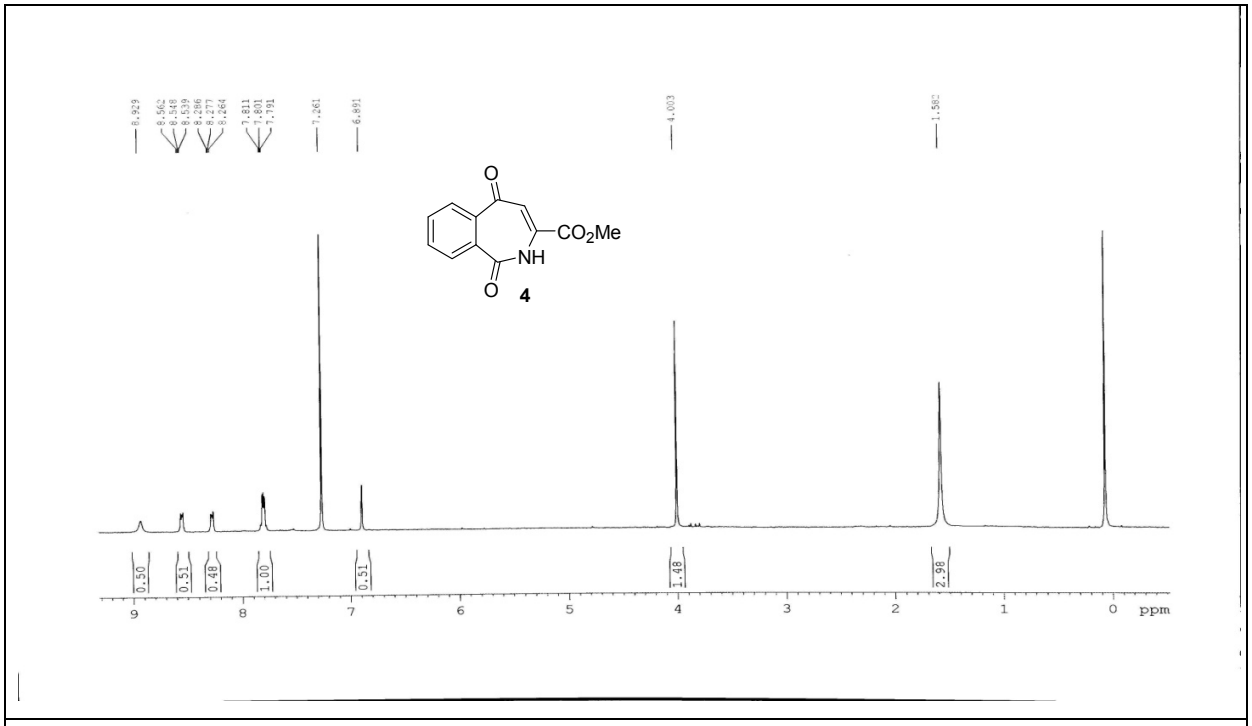
8. NMR Spectra of the new compounds:

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7.811
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7.791
7.261
6.891
4.603
1.582
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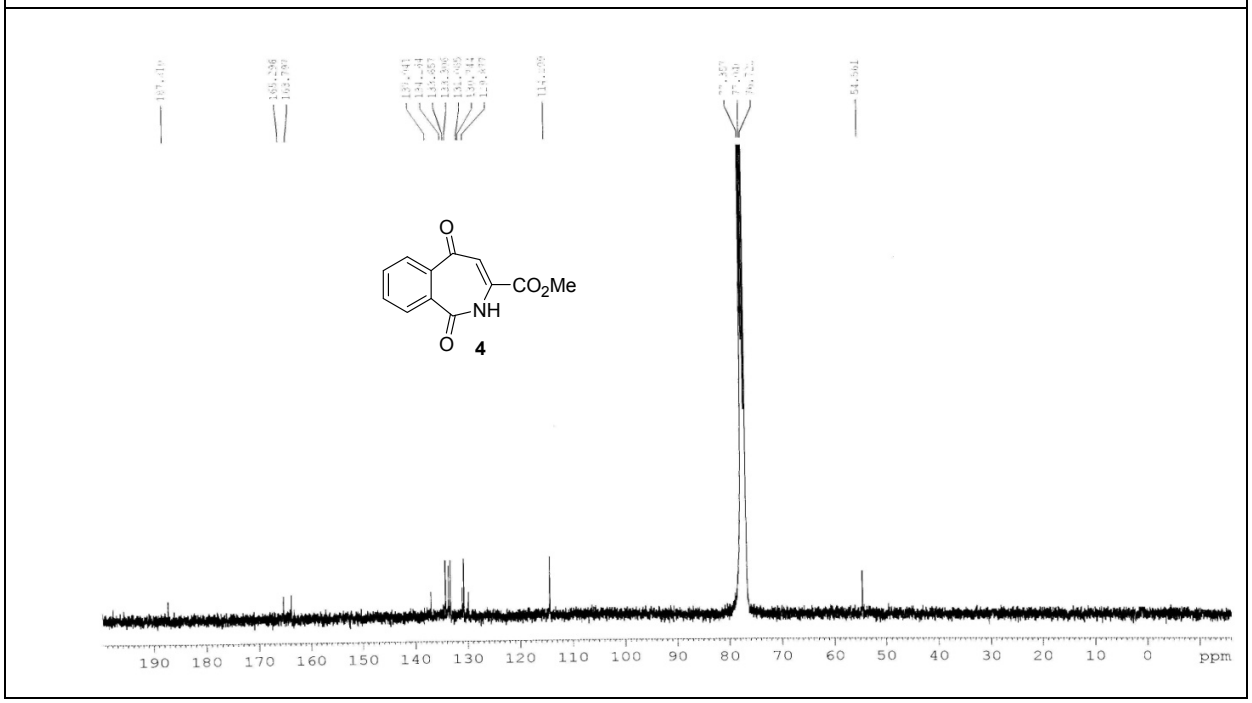
CO2Me
NH
O
4
0.50
0.51
0.48
1.00
0.51
1.48
2.98
9
8
7
6
5
4
3
2
1
0
ppm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100
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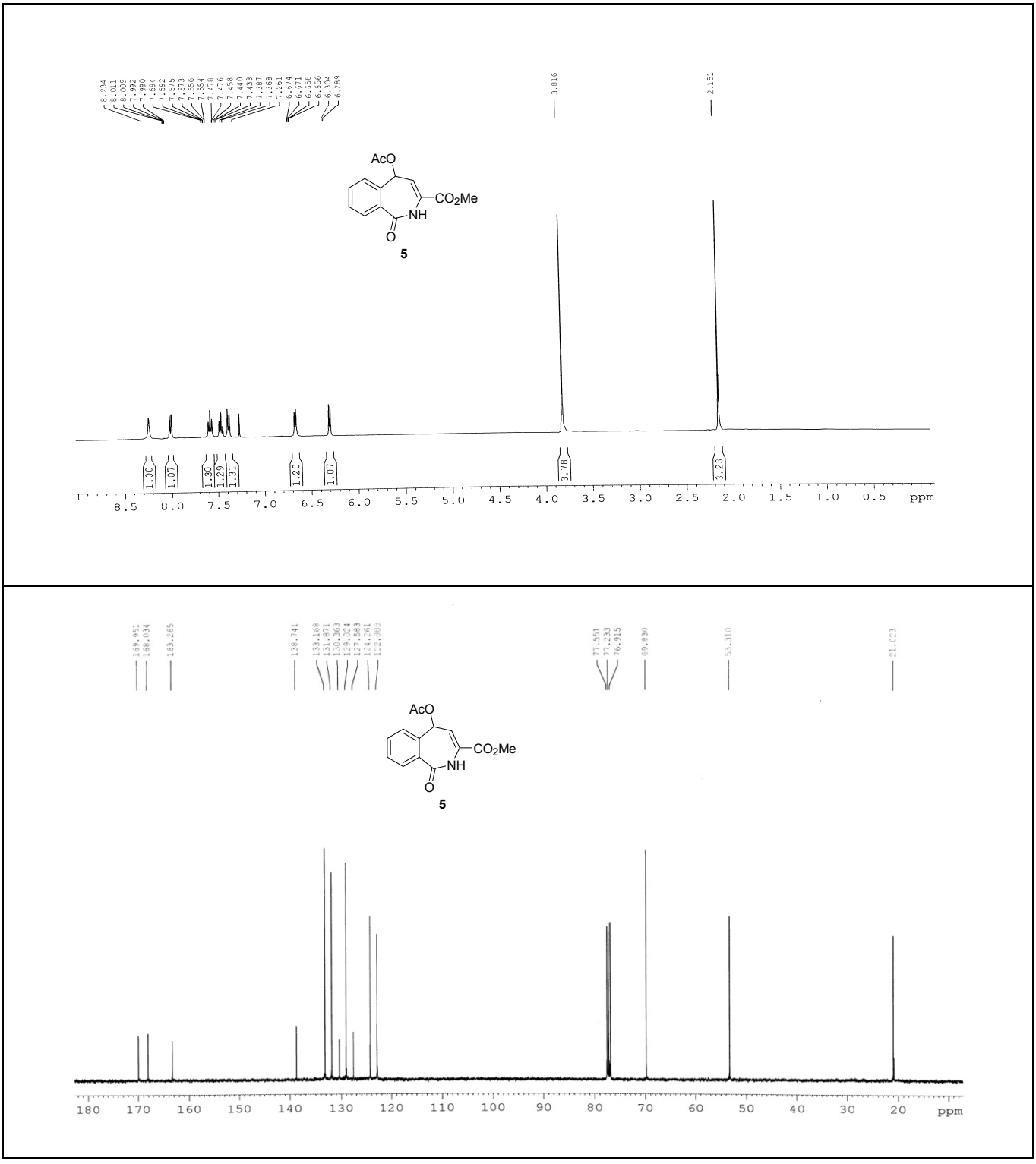
10
0
ppm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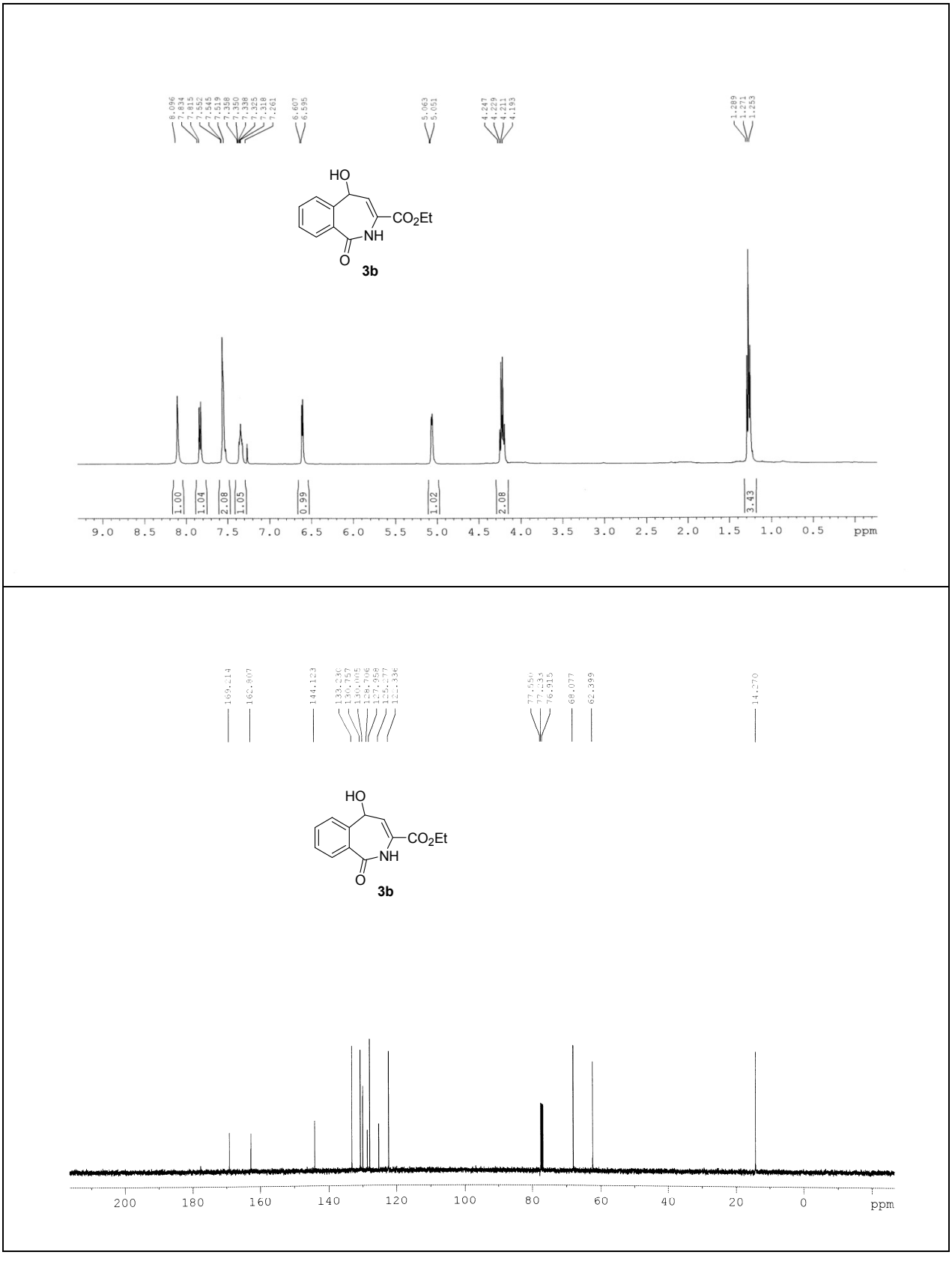
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ppm
HO
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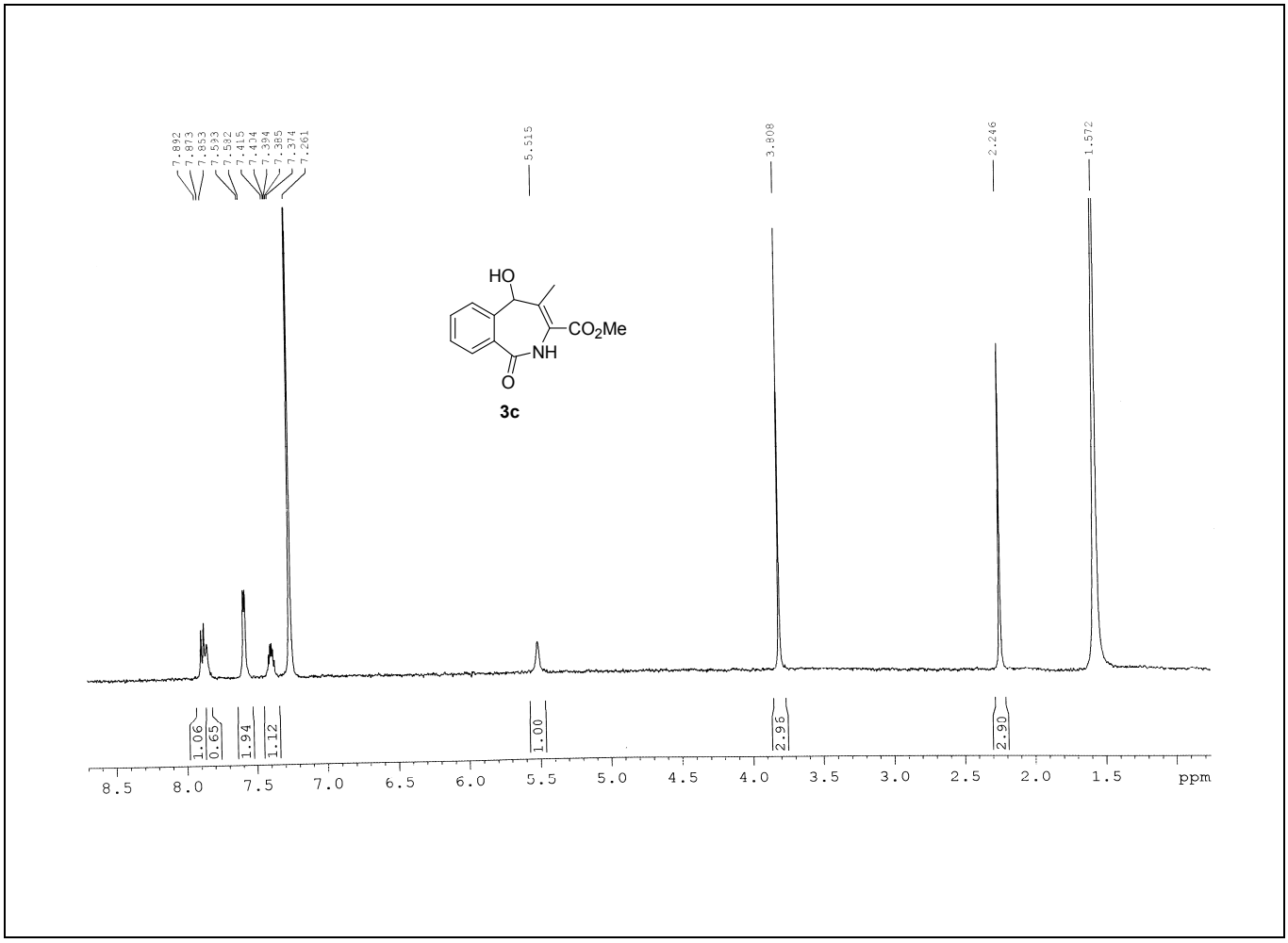
3b
ppm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7.394
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7.374
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2.246
1.572
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CO2Me
NH
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3c
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0.65
1.94
1.12
1.00
2.96
2.90
8.5
8.0
7.5
7.0
6.5
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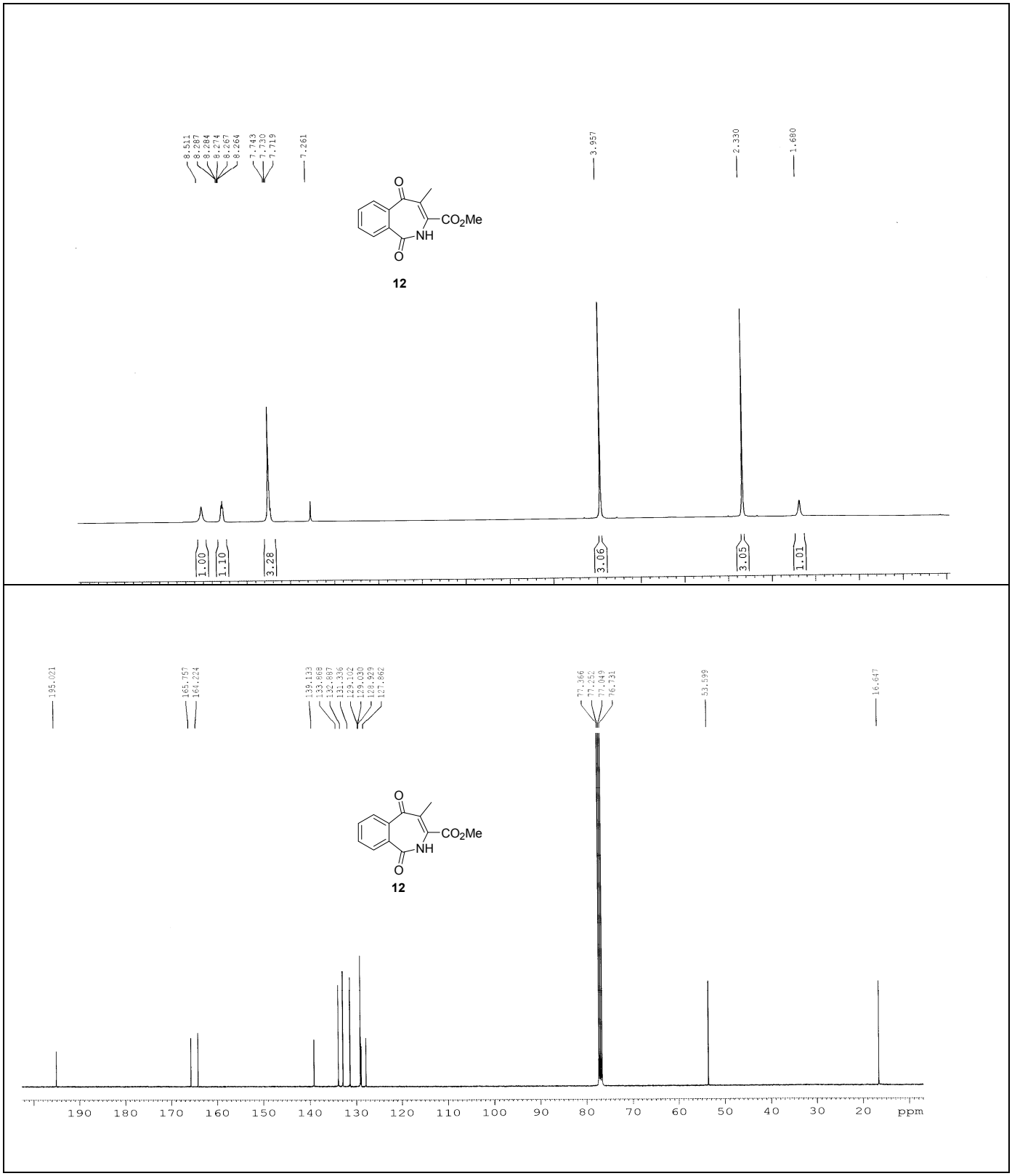
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm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O
12
1.00
1.10
3.28
3.06
3.05
1.01
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164.224
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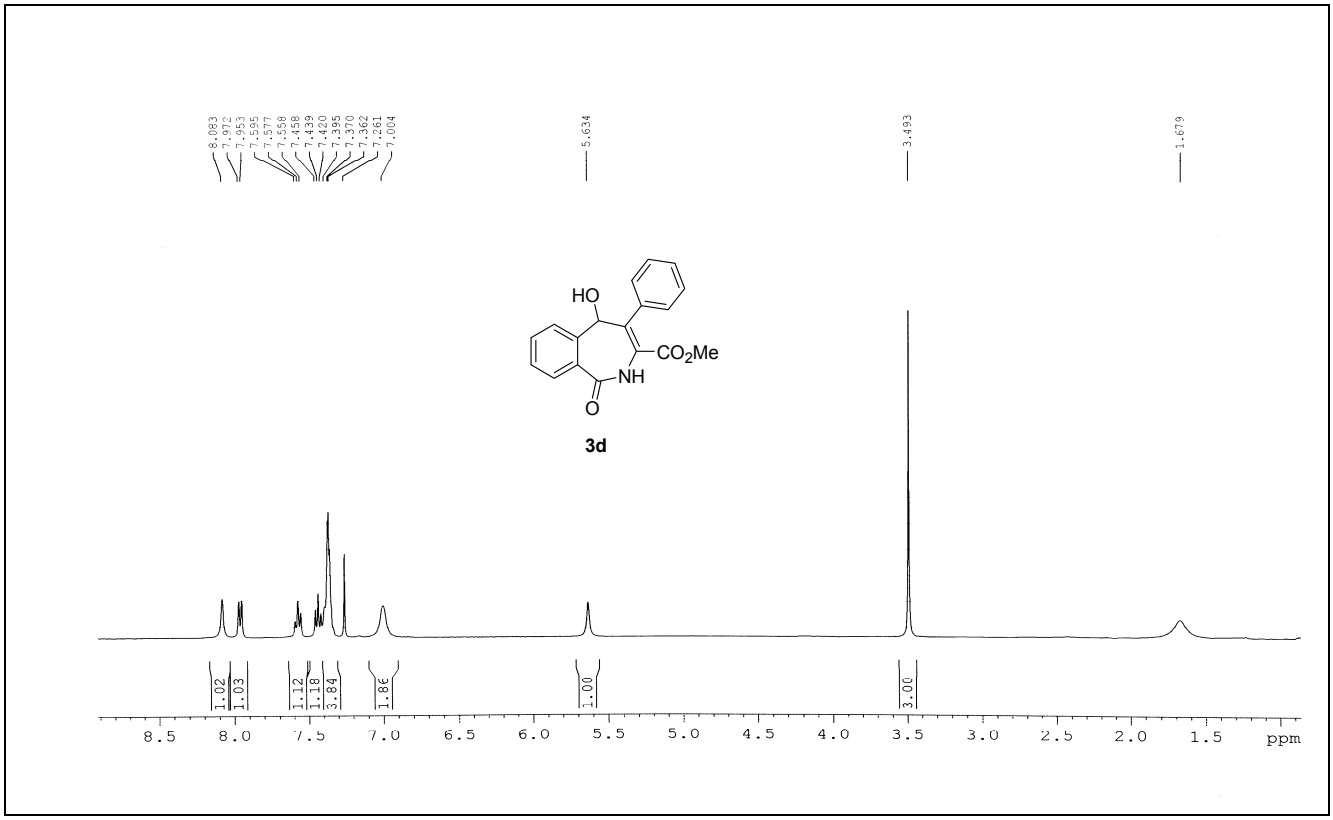
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NH
O
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1.12
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8.0
7.5
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3.0
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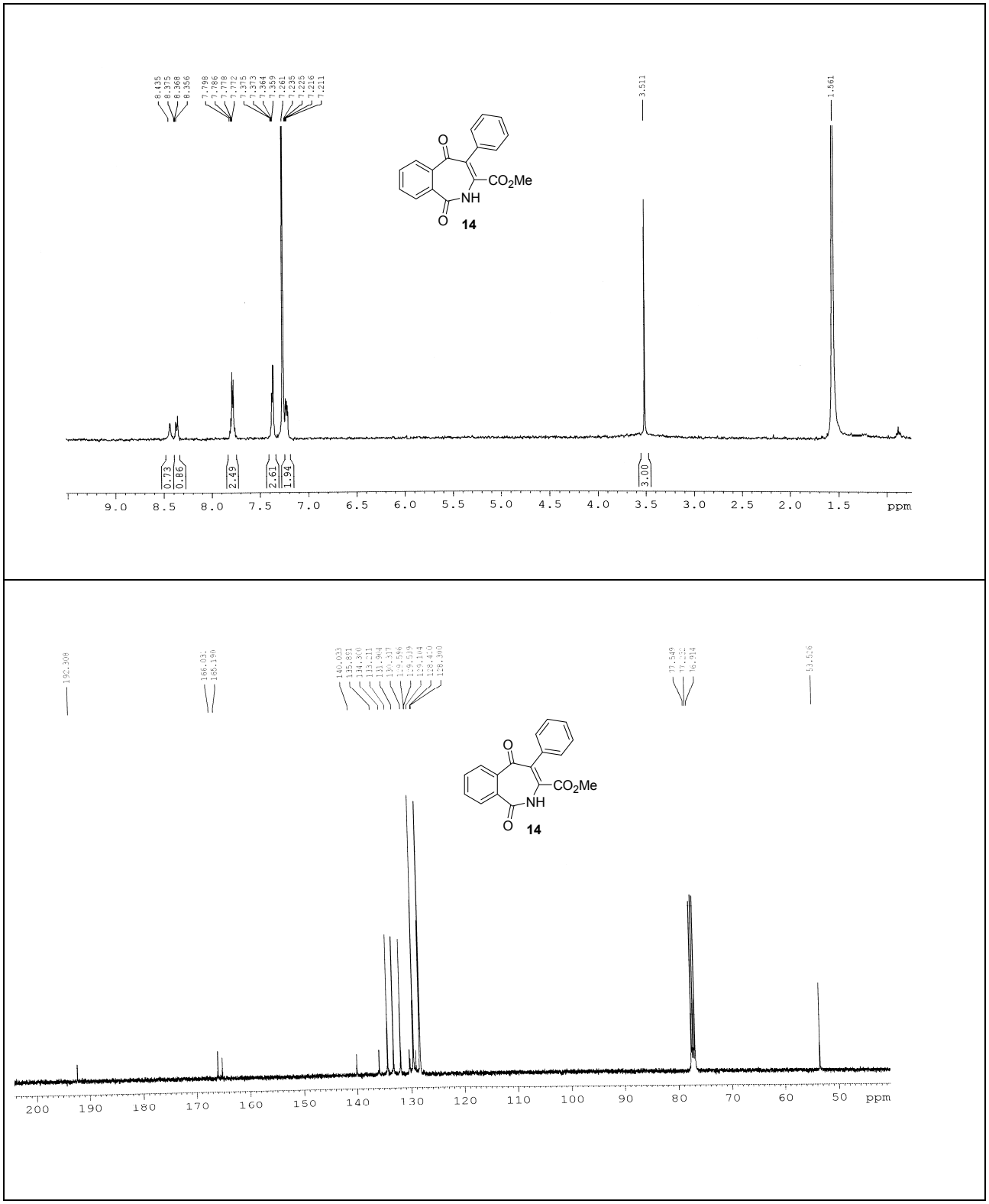
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7.235
7.225
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7.211
3.511
1.561
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CO2Me
NH
O
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0.86
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2.61
1.94
3.00
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192.308
166.031
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129.539
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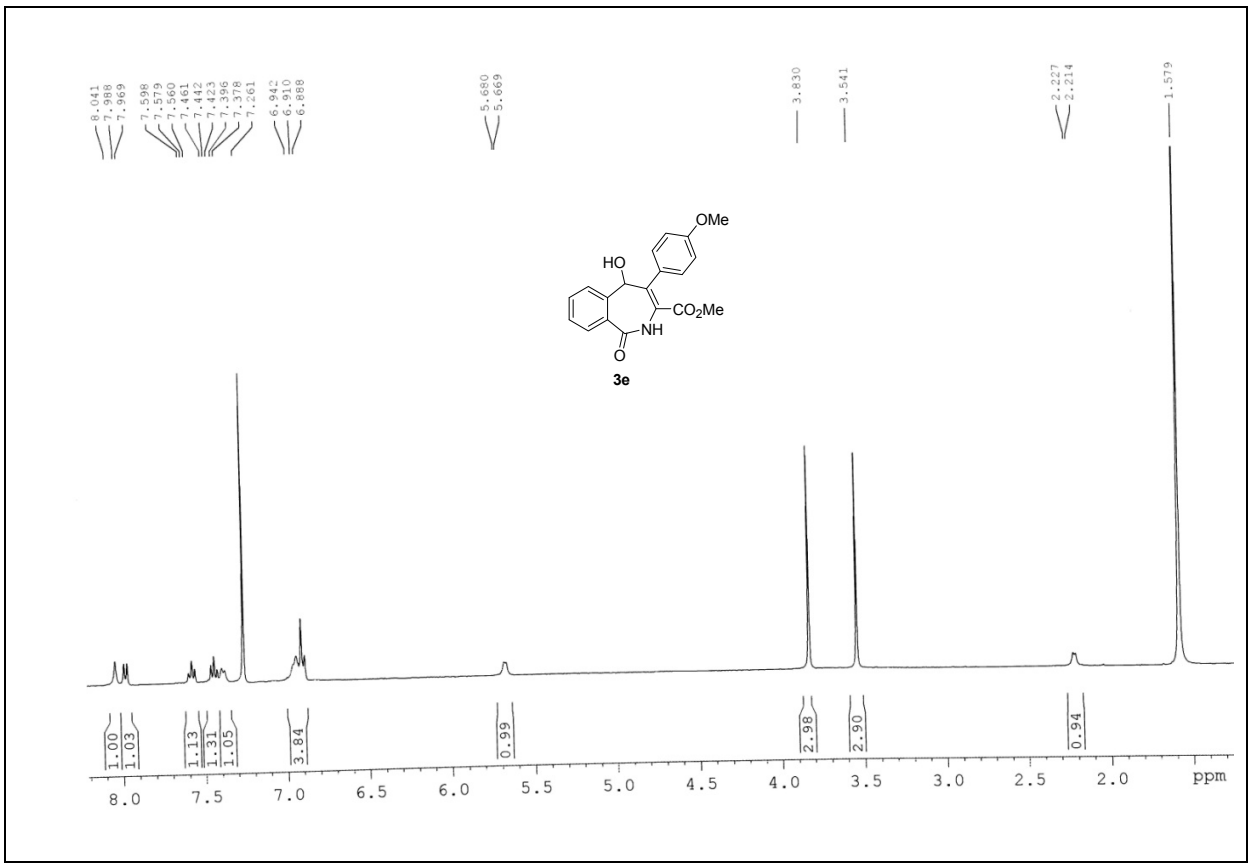
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1.13
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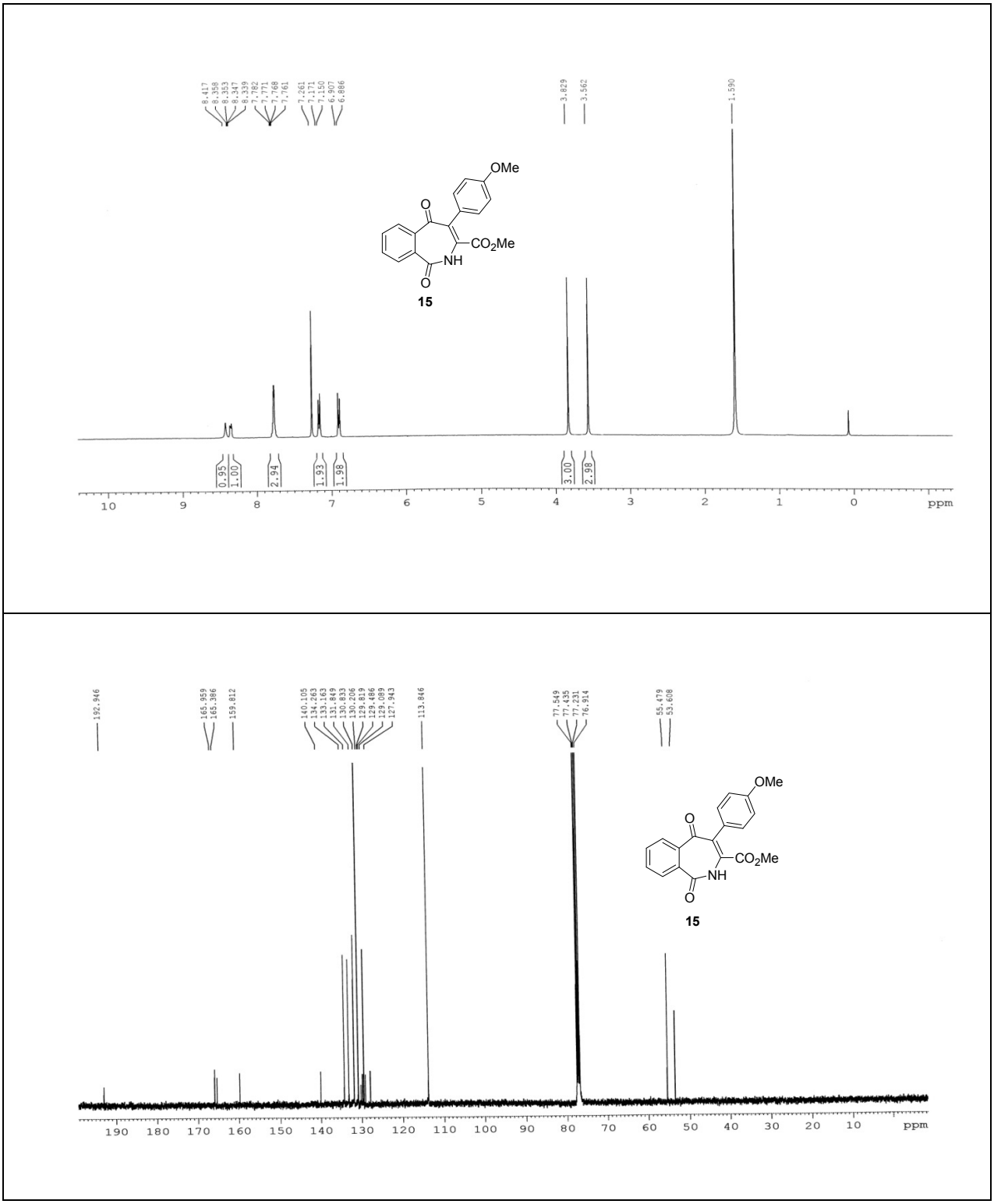
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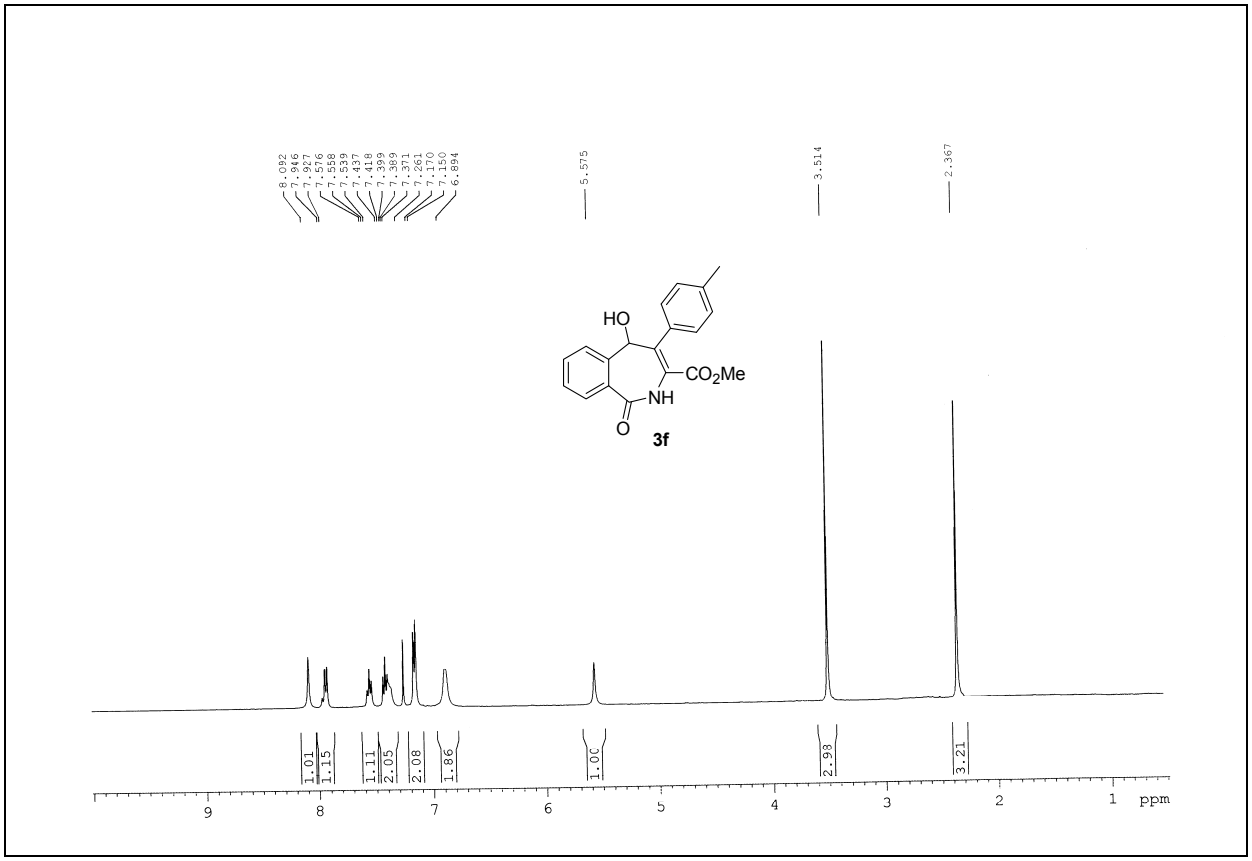
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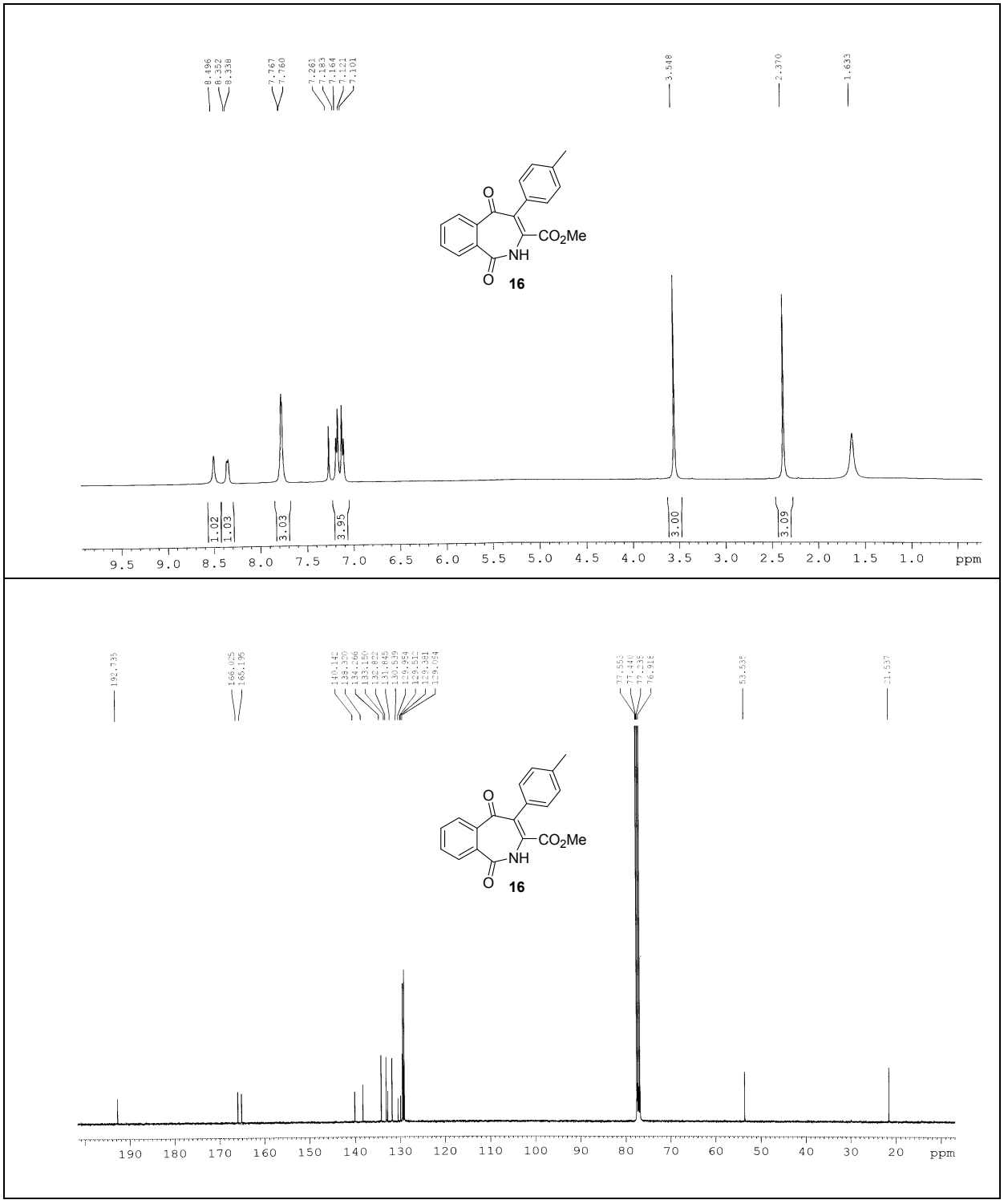
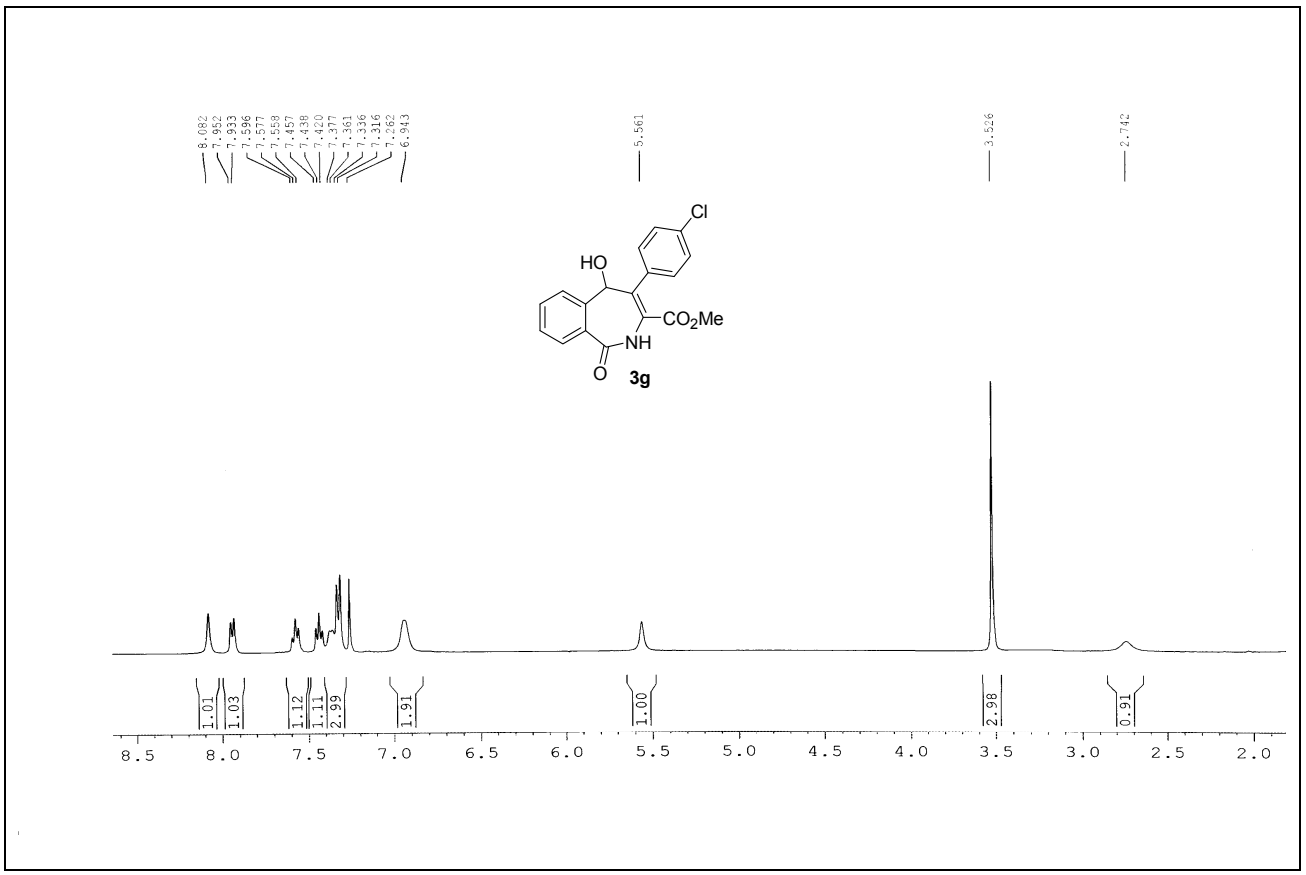
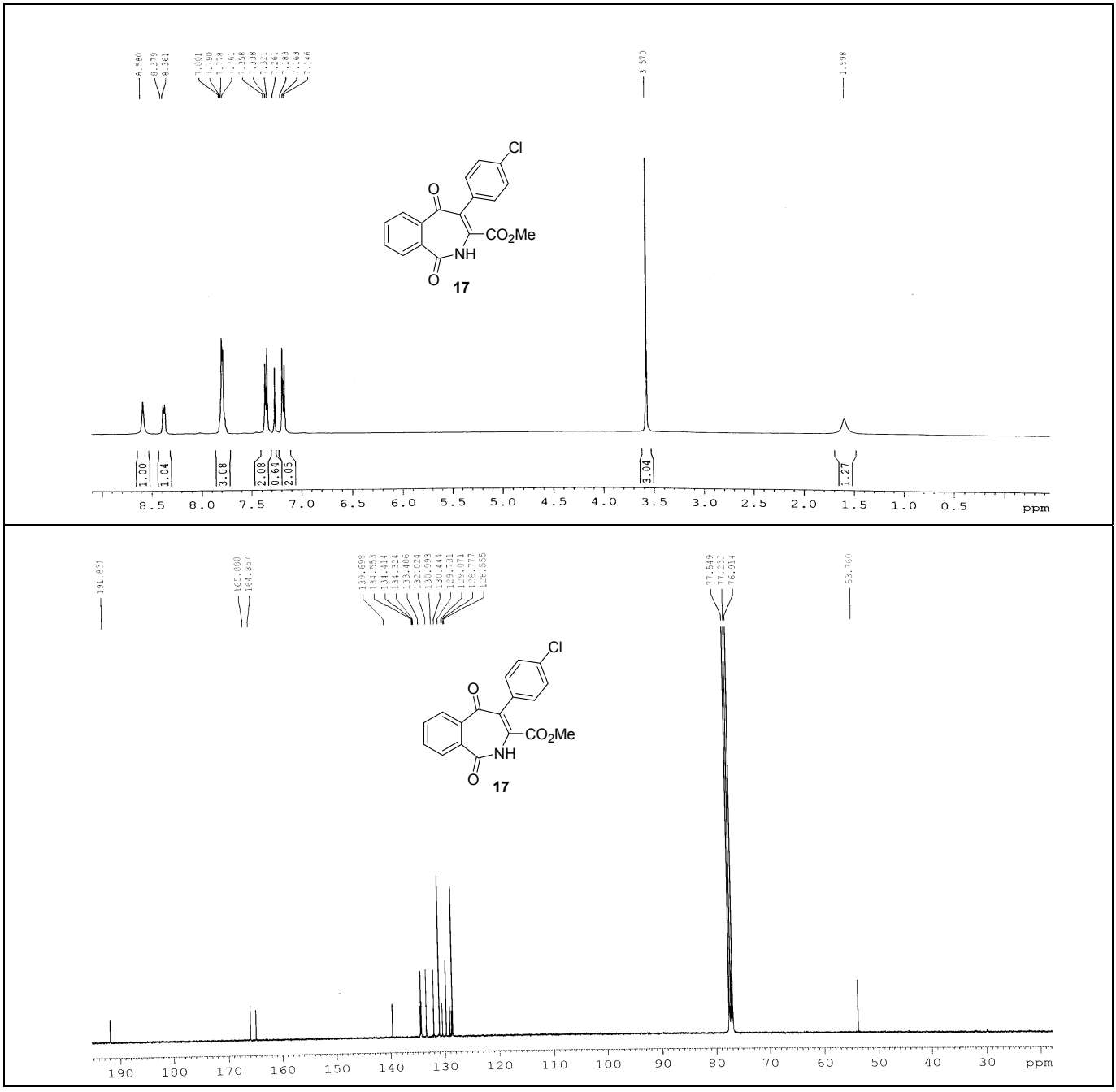
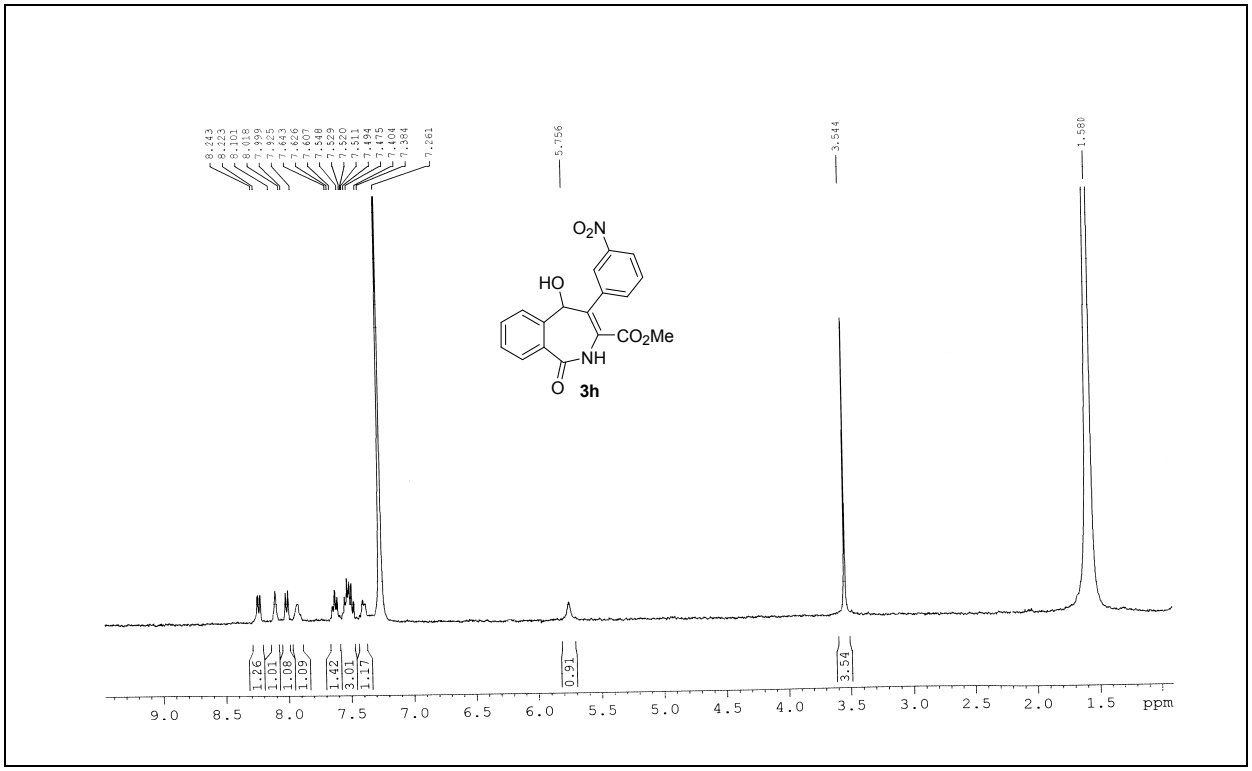
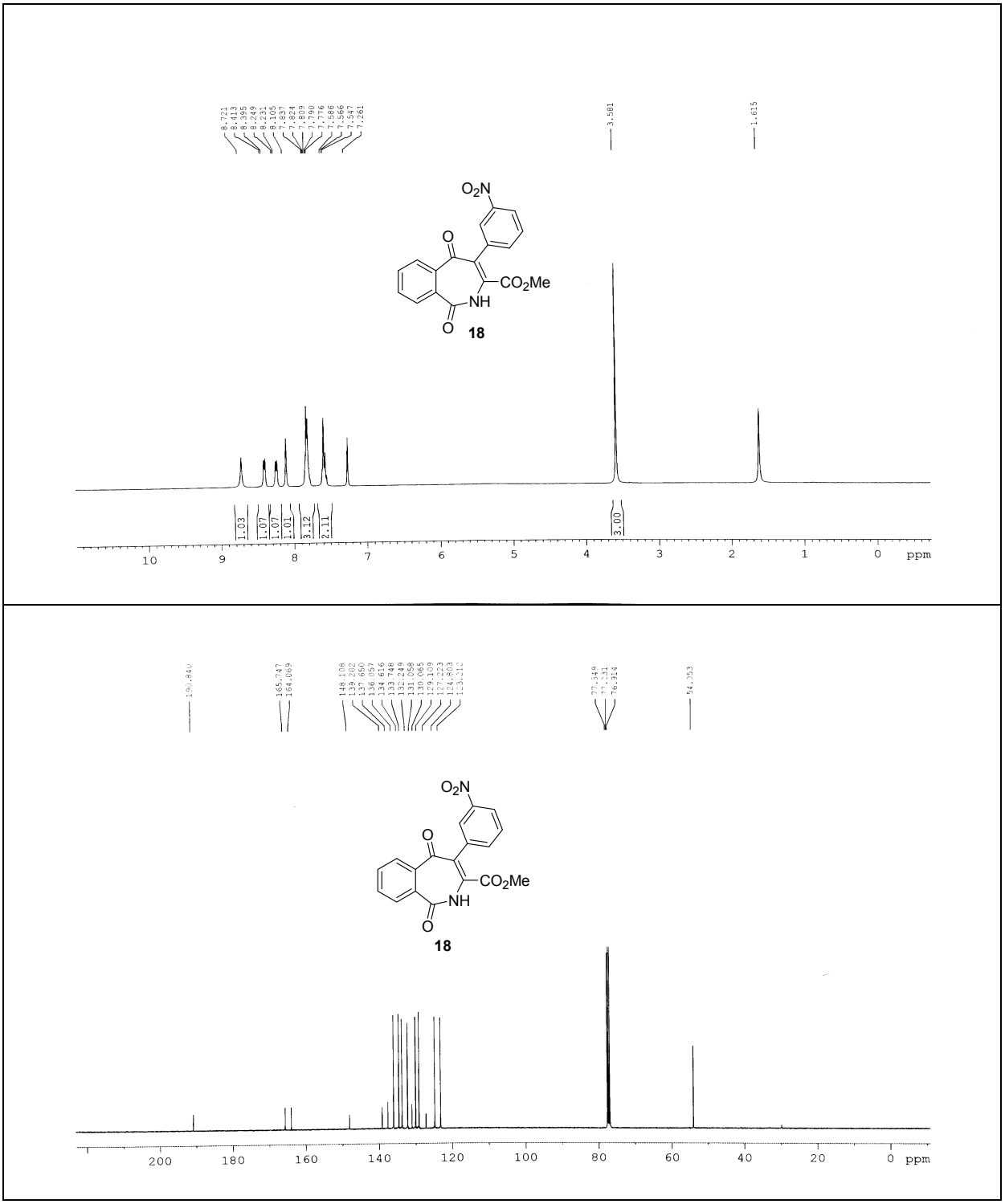
2.05
2.08
1.86
1.00
2.93
3.21
9
8
7
6
5
4
3
2
1
ppm


8.496
8.352
8.338
7.767
7.760
7.261
7.183
7.164
7.121
7.101
3.548
2.370
1.633
O
CO2Me
NH
O
16
1.02
1.03
3.03
3.95
3.00
3.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
192.735
166.025
165.195
140.142
138.320
134.266
133.150
132.822
131.845
130.939
129.954
129.511
129.381
129.054
77.556
77.440
77.238
76.919
53.638
21.537
O
CO2Me
NH
O
16
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


8.082
7.952
7.933
7.596
7.577
7.558
7.457
7.438
7.420
7.377
7.361
7.336
7.316
7.262
6.943
5.561
3.526
2.742
Cl
HO
CO2Me
NH
O
3g
1.01
1.03
1.12
1.11
2.99
1.91
1.00
2.98
0.91
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0


Cl
O
CO2Me
NH
O
17
ppm
Cl
O
CO2Me
NH
O
17
ppm


8.243
8.223
8.101
8.018
7.999
7.925
7.843
7.826
7.807
7.548
7.529
7.520
7.511
7.494
7.475
7.404
7.384
7.261
5.756
3.544
1.580
O2N
HO
CO2Me
NH
O
3h
1.26
1.01
1.08
1.09
1.42
3.01
1.17
0.91
3.54
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm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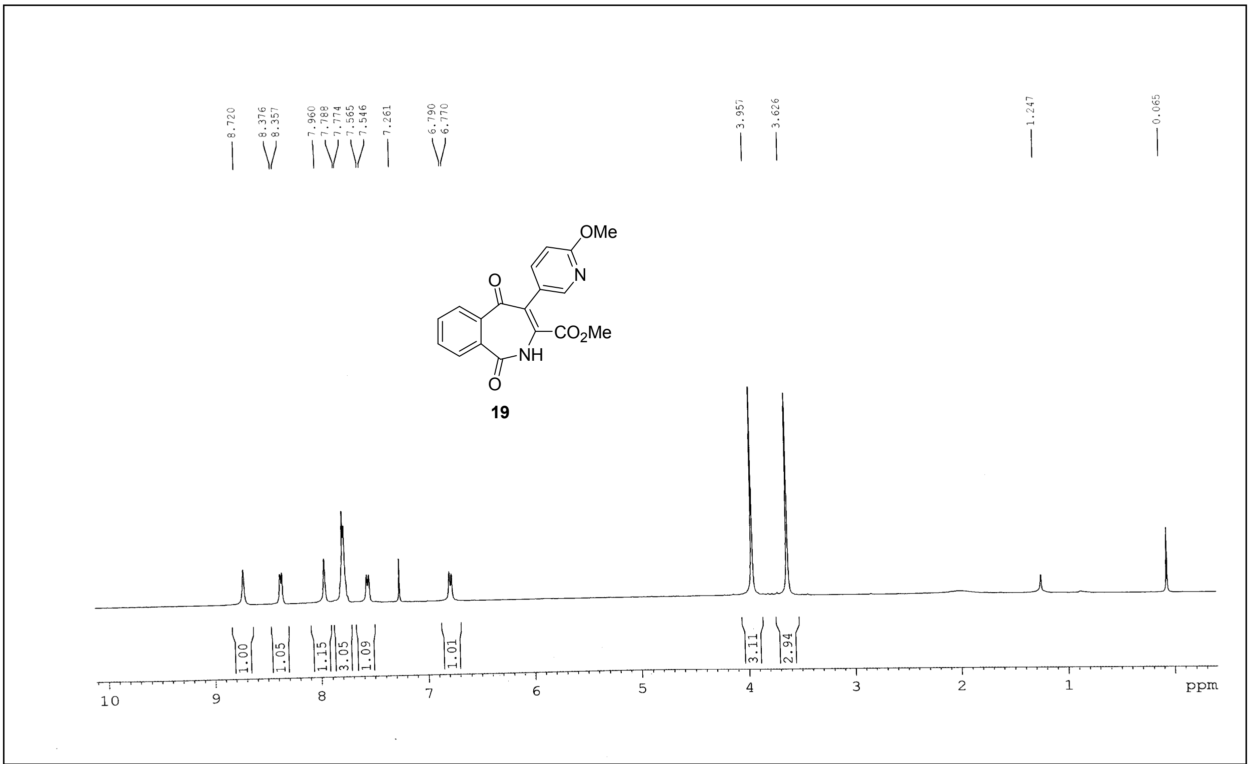
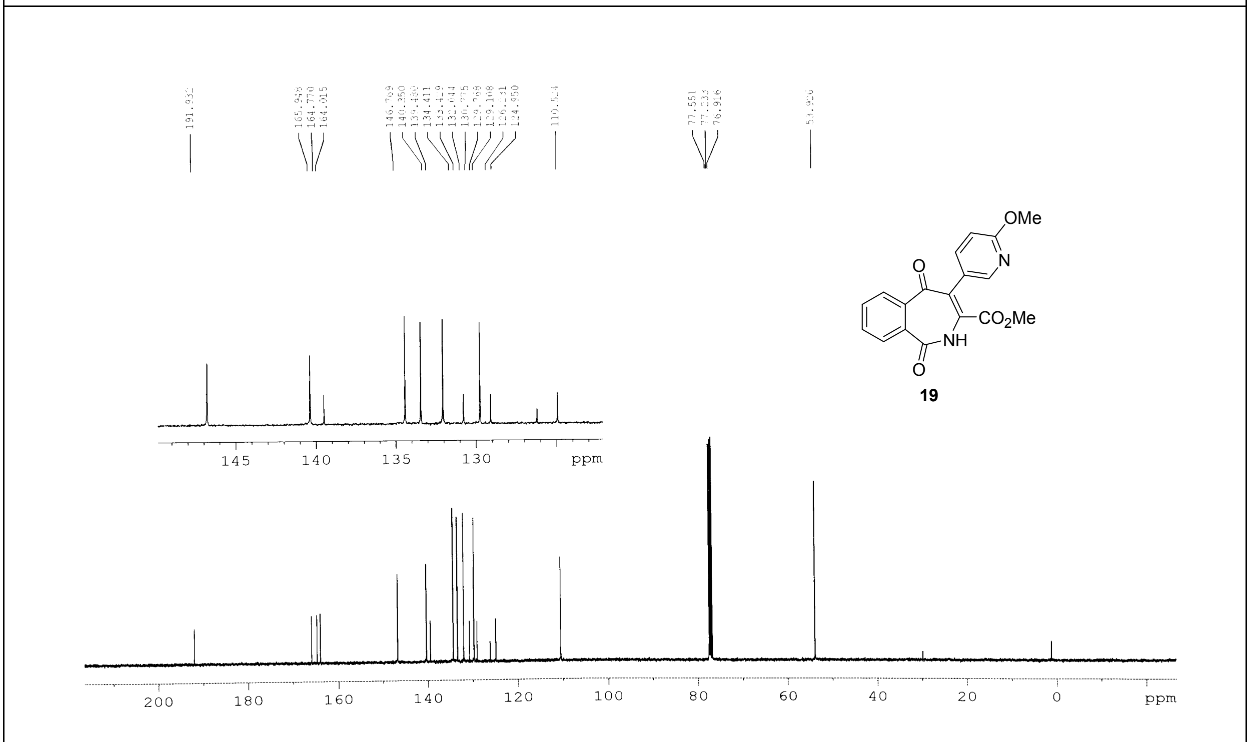
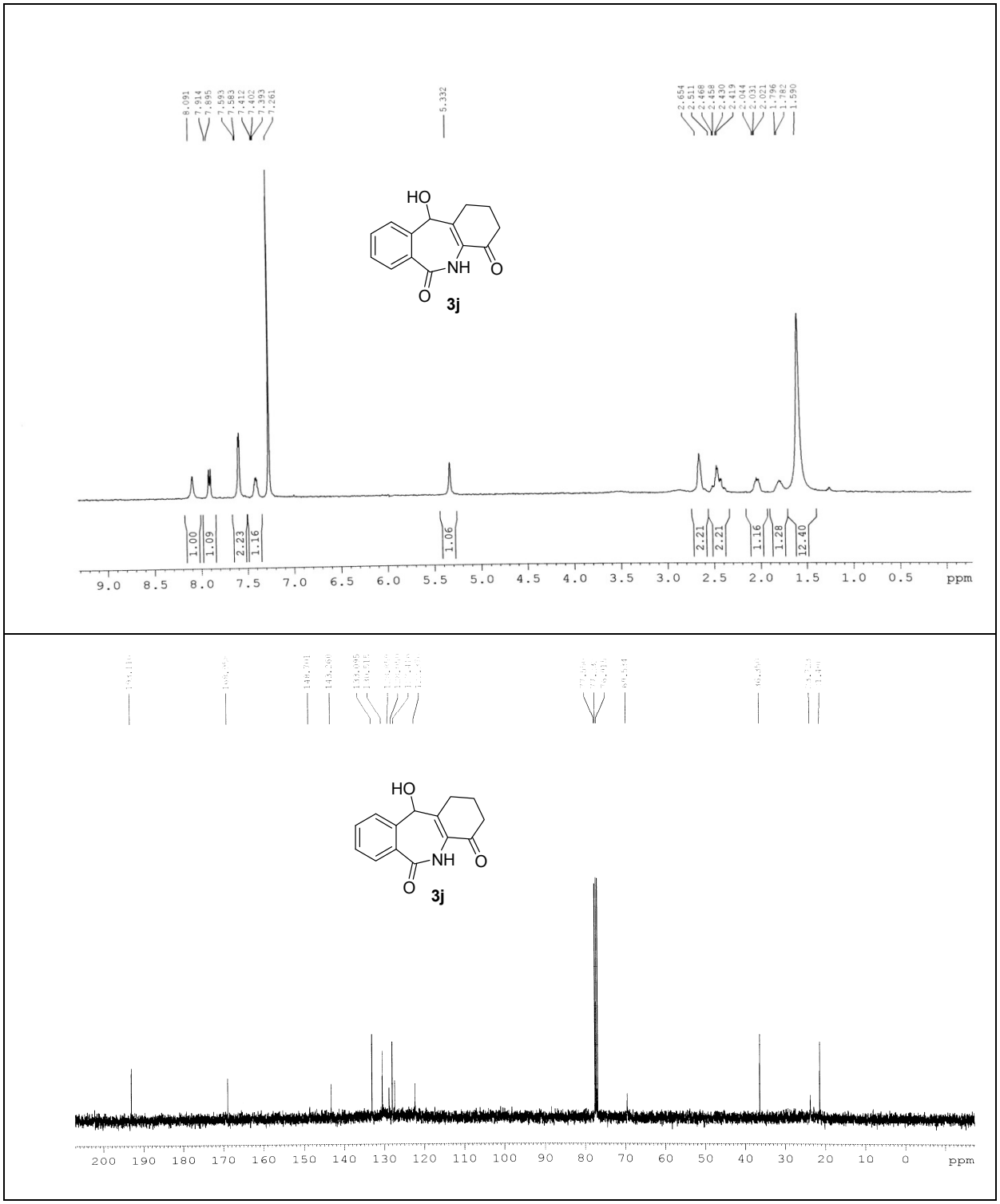
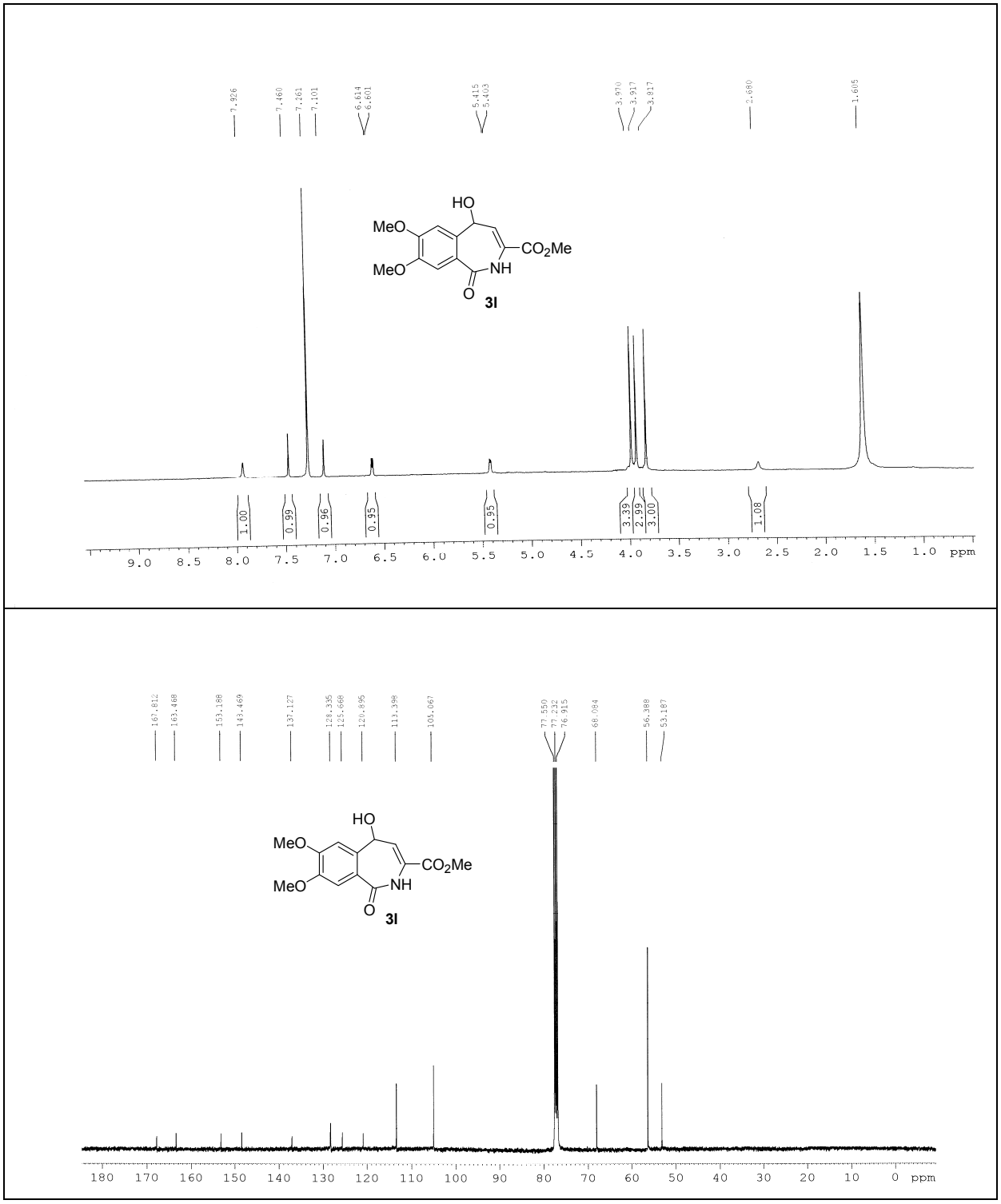
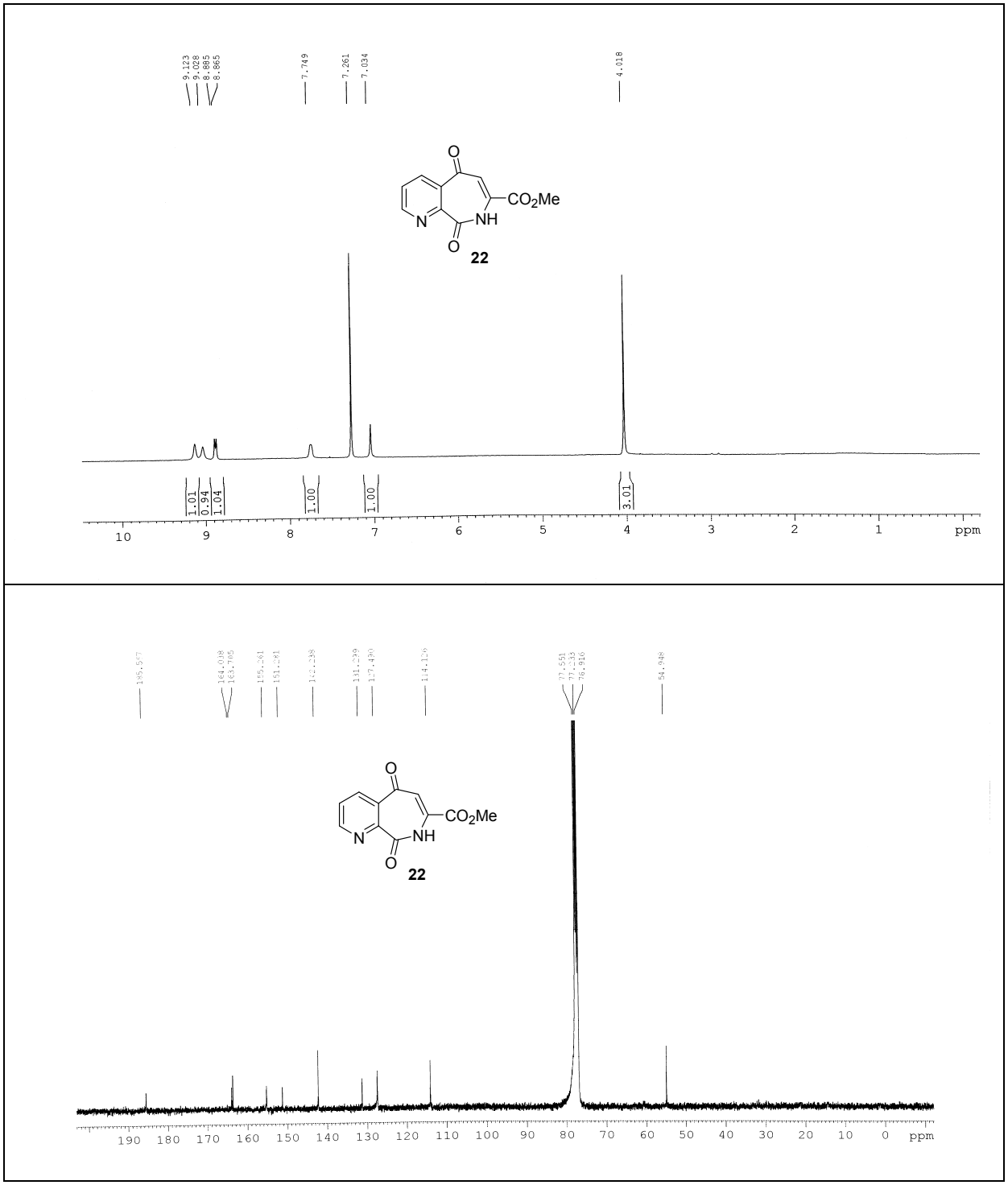
8.413
8.395
8.249
8.231
8.105
7.837
7.804
7.789
7.790
7.776
7.586
7.566
7.547
7.261
3.581
1.615
O2N
O
CO2Me
NH
O
18
1.03
1.07
1.07
1.01
3.12
2.11
3.00
10
9
8
7
6
5
4
3
2
1
0
ppm
160.840
165.747
164.069
148.108
139.202
137.650
136.057
134.456
133.748
132.249
131.058
130.065
129.109
127.223
124.803
123.212
77.249
77.131
76.314
54.353
O2N
O
CO2Me
NH
O
18
200
180
160
140
120
100
80
60
40
20
0
ppm


8.720
8.376
8.357
7.960
7.788
7.774
7.565
7.546
7.261
6.790
6.770
3.957
3.626
1.247
0.065
OMe
N
O
CO2Me
NH
O
19
1.00
1.05
1.15
3.05
1.09
1.01
3.11
2.94
10
9
8
7
6
5
4
3
2
1
ppm


OMe
N
O
CO2Me
NH
O
19
145
140
135
130
ppm
200
180
160
140
120
100
80
60
40
20
0
ppm


HO
NH
O
O
3j
ppm
HO
NH
O
O
3j
ppm


7.926
7.460
7.261
7.101
6.614
6.601
5.415
5.403
3.970
3.917
3.817
2.680
1.605
HO
MeO
MeO
CO2Me
NH
O
3l
1.00
0.99
0.96
0.95
0.95
3.39
2.99
3.00
1.08
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
167.812
163.468
153.188
143.469
137.127
128.335
125.668
120.895
113.398
105.067
77.550
77.232
76.915
68.084
56.388
53.187
HO
MeO
MeO
CO2Me
NH
O
3l
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


9.123
9.028
8.885
8.865
7.749
7.261
7.034
4.018
O
CO2Me
N
NH
O
22
1.01
0.94
1.04
1.00
1.00
3.01
10
9
8
7
6
5
4
3
2
1
ppm
195.577
164.038
163.705
155.261
151.241
142.238
141.239
139.490
114.126
77.551
77.233
76.916
54.948
O
CO2Me
N
NH
O
22
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

9. X-ray crystal structure:

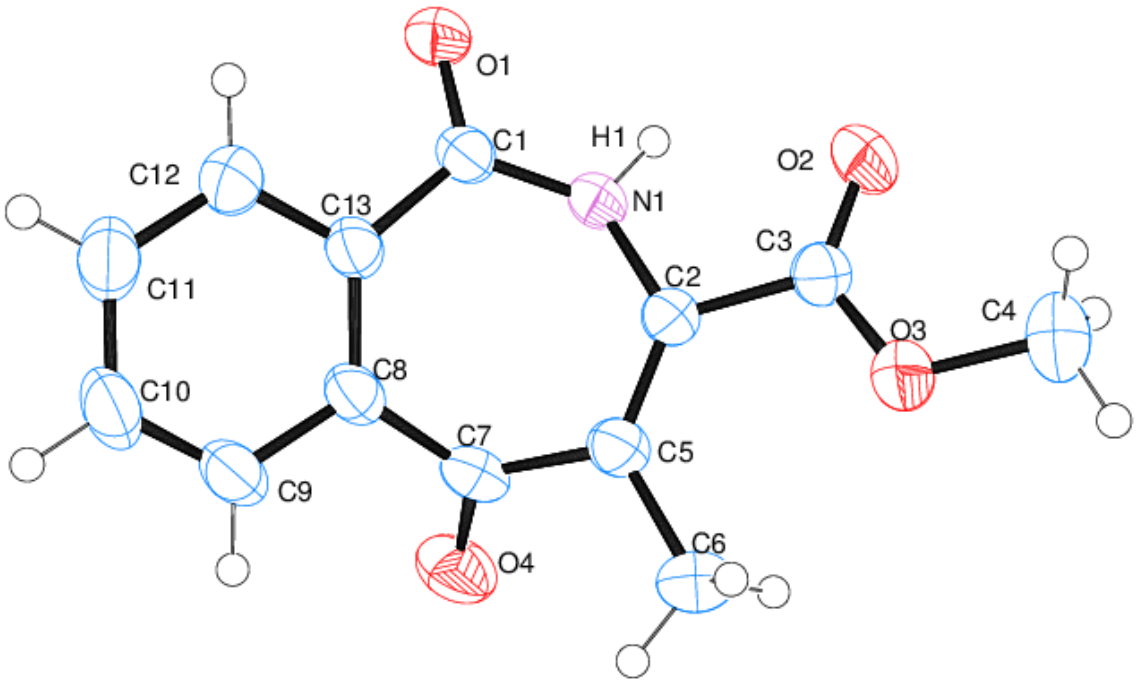


Figure 1. ORTEP projection of the Methyl 4-methyl-1,5-dioxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (**12**)

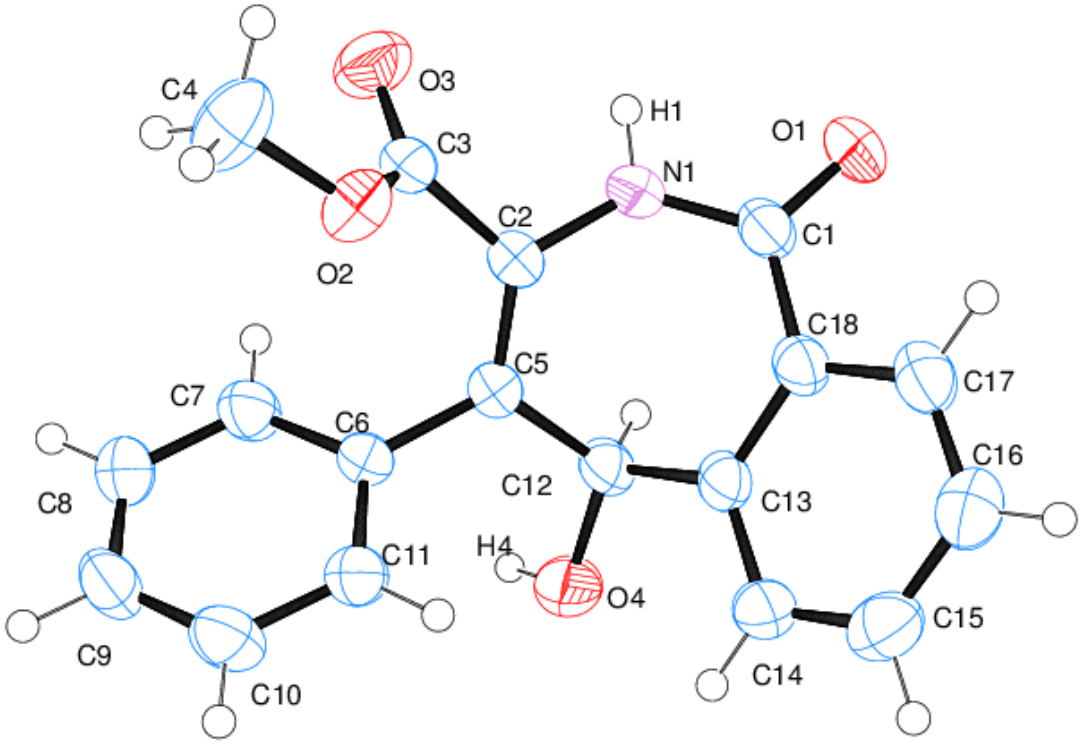


Figure 2. ORTEP projection of the Methyl 5-hydroxy-1-oxo-4-phenyl-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (**3d**)

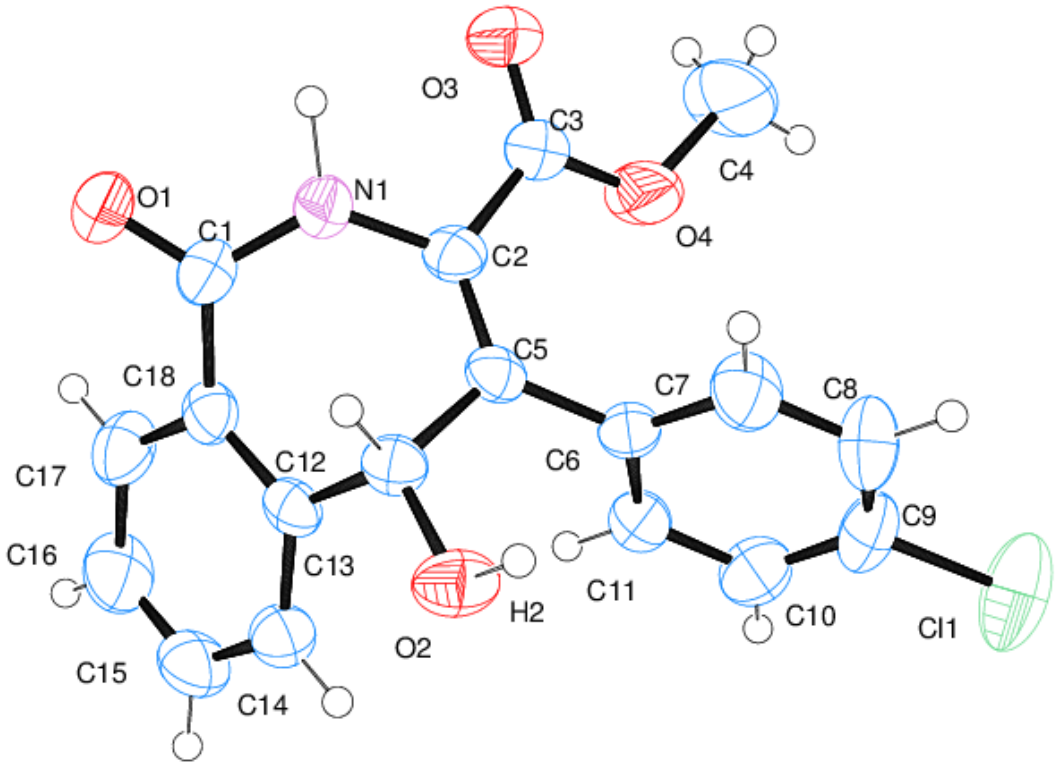


Figure 3. ORTEP projection of the methyl 4-(4-chloro-phenyl)-5-hydroxy-1-oxo-2,5-dihydro-1*H*-benzo[*c*]azepine-3-carboxylate (**3g**)