Supporting Information

Combination iminium, enamine and copper(I) cascade catalysis: A carboannulation for the synthesis of cyclopentenes

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1. General Experimental

All reactions were performed under an atmosphere of dry nitrogen unless otherwise stated. All glass apparatus was oven dried and cooled under vacuum before use.

1) Solvents and Reagents

Bulk solutions were evaporated under reduced pressure using a Büchi rotary evaporator. Reagents used were obtained from commercial suppliers or redistilled. Petroleum ether refers to distilled light petroleum of fraction (40-65 °C). Anhydrous methanol was distilled over Mg. Pyrrolidine was distilled over KOH. Anhydrous NMP was purchased from Aldrich.

2) Chromatography

Flash column chromatography was carried out using Merck Kiesegal 60 silica gel (230-400 mesh). Thin-layer chromatography (TLC) was carried out using Merck Kiesegal 60 F_{254} (230-400 mesh) fluorescent treated silica which were visualised under UV light (250nm) or by staining with aqueous potassium permanganate solutions as appropriate.

3) Spectra

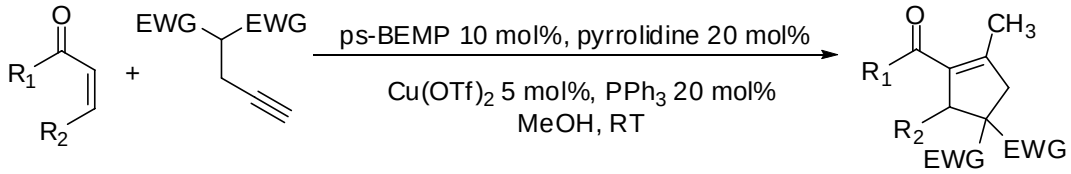
All ^{1}H and^{13}C NMR spectra were recorded using Bruker 500 MHz or Bruker 400 MHz spectrometers and use ppm for measurement against a TMS internal standard. Chemical shifts (δ) are given in parts per million (ppm), and coupling constants (J) are given in Hertz (Hz). DEPT135 and two-dimensional (COSY, HMQC) NMR spectroscopy were used where appropriate to assist the assignment of signals in the ^{1}H and ^{13}C NMR spectra. Low resolution mass spectrometry (EI, CI) was recorded on a Fissions VG Trio 2000 quadropole mass spectrometer. High resolution mass spectra (accurate mass) were recorded on a Thermo Finnigan Mat 95XP mass spectrometer. Infrared spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer from a thin film deposited onto a sodium chloride plate, or by mean of KBr disk.

4) General procedures for synthesis of starting materials

Dimethyl propargylmalonate (**12**), methyl 2-(phenylsulfonyl)pent-4-ynoate (used as starting material for synthesis of **27**, **28** and **29**) and ethyl 2-(phenylsulfonyl)pent-4-ynoate (for **26**) were all synthesized by treating dimethylmalonate or the 2-(phenylsulfonyl)pent-4-ynoate with NaH and performing the nucleophilic addition of the obtained anions to propargyl chloride in presence of KI.[S1] Dimethyl 2-(3-phenylprop-2-ynyl)malonate (**30**, starting material for **31**) was obtained by a Sonogashira coupling[S2] of **12** with iodobenzene. Methyl substituted cycloxenones (starting materials for synthesis of **17**, **18** and **19**) were synthesized by *t*-BuOK-catalyzed annulation of appropriate β-ketoesters with conjugated enones or enals.[S3]

2. Practical experimental

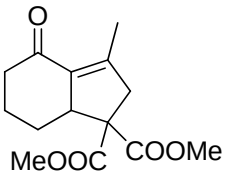
2.1. General procedure for one-pot reactions.



To a solution of the nucleophile (0.62 mmol), $Cu(OTf)_2$ (7.4 mg, 0.020 mmol) and PPh_3 (22 mg, 0.082 mmol) in anhydrous MeOH (1 mL) ps-BEMP (19 mg, 0.041 mmol) was suspended, then the conjugated ketone (0.41 mmol) and pyrrolidine (7 μL, 0.082 mmol) were added; the mixture was stirred at RT till complete conversion of the ketone by TLC, then diluted with CH_2Cl_2 and filtered to eliminate ps-BEMP. Solvents were evaporated and the obtained crude was purified by chromatography.

2.2. Synthesis and characterization of compounds 16-29 and 31

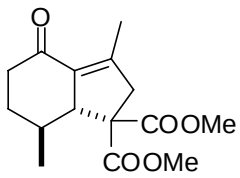
2.2.1. Compound **16**



5,5-Dicarboxymethyl-7-methyl-1-oxo-bicyclo[4.3.0]non-7-ene (**16**). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and cyclohexenone (40 μL); the

mixture was stirred at RT for 3h and the obtained crude was purified by chromatography (AcOEt/petroleum ether 1:10, R_f 0.29 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (93 mg, 85%): mp 97-98 ^{0}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.73 (s, 3H), 3.70 (dd, *J* = 5.0, 2.5 Hz, 1H), 3.09 (d, *J* = 18.0 Hz, 1H), 2.77 (d, *J* = 18.0 Hz, 1H), 2.45 (ddd, *J* = 17.5, 2.0, 2.0 Hz, 1H), 2.22-2.12 (m, 2H), 2.09 (s, 3H), 2.04-2.01 (m, 1H), 1.77 (dddd, *J* = 25.0, 13.5, 3.0, 3.0 Hz, 1H), 1.16 (dddd, *J* = 25.0, 12.5, 12.5, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.2, 171.7, 170.7, 149.5, 131.9, 61.9, 52.7, 52.3, 51.9, 46.0, 40.6, 27.5, 23.4, 15.7; IR ν_{max} (film)/cm^{-1} 3455, 2992, 2953, 2935, 2865, 1732, 1677, 1619, 1437, 1272, 1264, 1251, 1228, 1178, 1160, 1095, 1083, 1060, 1044, 952, 936; MS (ES+) m/z (rel. intensity %) 267 ($M+H^+$, 25), 289 ($M+Na^+$, 100); HRMS (ES) calcd. $C_{14}H_{18}O_5Na$ ($M+Na^+$) 289.1046, found 289.1046.

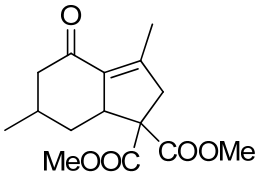
2.2.2. Compound **17**



5,5-Dicarboxymethyl-4,7-dimethyl-1-oxo-bicyclo[4.3.0]non-7-ene (**17**). The general procedure was followed, using 4-methylcyclohexenone (46 mg) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT 18h; crude NMR showed the dr of product was 20:1. Purification was accomplished by chromatography (Et_2O/petroleum ether 5:1, R_f 0.48 in AcOEt/petroleum ether 1:2), affording the major diastereomer as a white solid (77 mg, 66%): mp 84-85 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.68 (s, 3H), 3.46-3.40 (m, 1H), 2.95 (d, *J* = 17.8 Hz, 1H), 2.68 (d, *J* = 17.8 Hz, 1H), 2.35 (d, *J* = 17.4 Hz, 1H), 2.26-2.15 (m, 1H), 2.05 (s, 3H), 1.86-1.80 (m, 1H), 1.56-1.45 (m, 2H), 1.04 (d, *J* = 5.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.2, 172.0, 171.0, 150.4, 131.2, 62.7, 57.7, 52.7, 57.2, 47.4, 40.5, 33.9, 32.9, 20.1, 15.9; IR ν_{max} (KBr)/cm^{-1} 2996, 2971, 2952, 2930, 2854, 1748, 1729, 1678, 1618, 1436, 1374, 1338, 1314, 1274, 1254, 1219, 1201, 1173, 1098, 1081, 1065, 1052, 999, 961, 940, 853, 807, 748, 722, 675, 623, 610; MS (CI) m/z (rel. intensity %)

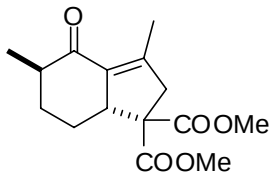
281 ($M+H^+$, 99), 298 ($M+NH_4^+$, 39); HRMS (CI) calcd. $C_{15}H_{24}NO_5$ ($M+NH_4^+$) 298.1649, found 298.1645.

2.2.3. Compound **18**



5,5-Dicarboxymethyl-3,7-dimethyl-1-oxo-bicyclo[4.3.0]non-7-ene (**18**). The general procedure was followed, using 3-methylcyclohexenone (46 mg) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT for 16h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:10, R_f 0.41 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (87 mg, 74%) with a diasteromeric ratio 2:1: mp 58-60 ^{0}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87-3.83 (m, 1H, major), 3.69 (s, 4H of minor and 3H of major), 3.67 (s, 3H, of minor), 3.66 (s, 3H of major), 3.02 (d, *J* = 18.2 Hz, 1H of major and 1H of minor), 2.74 (d, *J* = 18.1 Hz, 1H of major and 1H minor), 2.38 (d, *J* = 17.0 Hz, 1H of minor), 2.30 (dd, *J* = 5.3 Hz, *J* = 16.3 Hz, 1H of major), 2.27-2.23 (m, 1H of major),2.16-2.12 (m, 1H of major), 2.02 (s, 3H of major and 3H of minor), 2.00-1.98 (m, 1H of minor), 1.97-1.78 (m, 1H of major and 2H of minor), 1.38 (dt, *J* = 4.3 Hz, *J* = 12.5 Hz, 1H of major), 1.00 (d, *J* = 7.1 Hz, 3H of major), 0.95 (d, *J* = 6.5 Hz, 3H of minor), 0.87-0.80 (m, 1H of minor); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 197.3, 170.2, 170.2, 169.4, 169.2, 147.9, 147.7, 130.2, 129.7, 60.7, 60.4, 51.3, 51.2, 50.8, 50.8, 49.9, 47.7, 46.1, 45.4, 44.8, 44.6, 34.5, 31.4, 29.3, 26.8, 20.5, 18.0, 14.1, 14.1; IR ν_{max} (film)/cm $^{-1}$ 2954, 1733, 1683, 1628, 1435, 1378, 1266, 1222, 1198, 1170, 1088, 1060, 953; MS (ES+) m/z (rel. intensity %) 303 ($M+Na^+$, 100); HRMS (ES) calcd. $C_{15}H_{20}O_5Na$ ($M+Na^+$) 303.1203, found 303.1196.

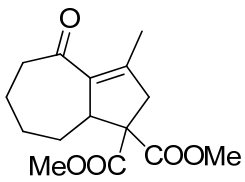
2.2.4. Compound **19**



5,5-Dicarboxymethyl-2,7-dimethyl-1-oxo-bicyclo[4.3.0]non-7-ene (**19**). The general procedure was followed, using 3-methylcyclohexenone (46 mg) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:10, R_f 0.33 and 0.37 in AcOEt/petroleum ether 1:3), affording the pure product as a colorless oil (99 mg, 84%) with a diasteromeric ratio 3:1. Major diastereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77-3.75 (m, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.10 (d, *J* = 18.0 Hz, 1H), 2.77 (d, *J* = 18.0 Hz, 1H), 2.19-2.13 (m, 1H), 2.12-2.05 (m, 2H), 2.03 (s, 3H), 160-1.52 (m, 1H), 1.32-1.20 (m, 1H), 1.11 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 171.7, 170.8, 147.6, 132.2, 61.8, 52.8, 52.7, 52.3, 46.2, 45.0, 32.6, 27.9, 15.4, 14.9; IR ν_{max} (film)/cm^{-1} 2954, 2867, 1731, 1683, 1631, 1435, 1375, 1327, 1269, 1221, 1200, 1173, 1094, 1060, 956, 899, 844, 806, 734; MS (EI) m/z (rel. intensity %) 280 (M^+, 37); HRMS (EI) calcd. $C_{15}H_{20}O_5$ (M^+) 280.1311, found 280.1320.

Minor distereoisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78-3.77 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.15 (d, *J* = 16.5 Hz, 1H), 2.81 (d, *J* = 16.5 Hz, 1H), 2.52-2.47 (m, 1H), 2.08 (s, 3H), 2.04-1.98 (m, 2H), 1.71-1.65 (m, 1H), 1.43-1.29 (m, 1H), 1.08 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 202.7, 171.8, 170.7, 150.0, 131.2, 61.8, 52.8, 52.3, 51.2, 46.3, 42.6, 29.5, 22.5, 17.2, 15.6; IR ν_{max} (film)/cm^{-1} 2954, 2871, 1734, 1682, 1629, 1435, 1374, 1326, 1268, 1173, 1121, 1092, 1059, 993, 955, 902, 846.

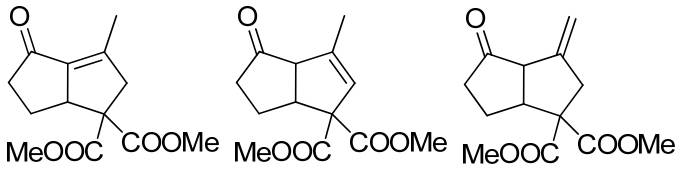
2.2.5. Compound **20**



6,6-Dicarboxymethyl-8-methyl-1-oxo-bicyclo[5.3.0]dec-8-ene (**20**). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and cycloheptenone (45 μL); the

mixture was stirred at RT for 72h and the obtained crude was purified by chromatography (Et_2O/petroleum ether 1:5, R_f 0.24 in AcOEt/petroleum ether 1:2), affording the pure product as a colorless oil (78 mg, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 3H), 3.68-3.66 (m, 1H), 3.66 (s, 3H), 3.26 (d, *J* = 18.7 Hz, 1H), 2.76 (d, *J* = 18.7 Hz, 1H), 2.54-2.41 (m, 2H), 2.00 (s, 3H), 1.98-1.93 (m, 1H), 1.89-1.82 (m, 1H), 1.70 (d, *J* = 13.0 Hz, 1H), 1.59-1.47 (m, 1H), 1.39-1.28 (m, 1H), 1.19 (qd, *J* = 12.6 Hz, *J* = 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6, 171.9, 170.3, 150.9, 137.2, 62.8, 53.0, 52.6, 51.7, 45.4, 45.3, 31.8, 30.4, 24.6, 16.3; IR ν_{max} (film)/cm $^{-1}$ 2999, 2928, 2854, 1737, 1676, 1619, 1436, 1376, 1316, 1257, 1177, 1163, 1082, 1003, 964, 896, 860, 819, 724, 693; MS (EI) m/z (rel. intensity %) 280 (M^+, 6), 249 (M-OMe^+, 21); HRMS (EI) calcd. $C_{14}H_{17}O_4$ (M-OMe^+) 249.1127, found 249.1124.

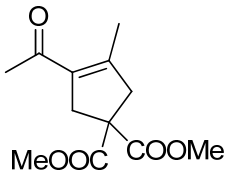
2.2.6. Compound **21**



4,4-Dicarboxymethyl-6-methyl-1-oxo-bicyclo[3.3.0]octene (**21a-c**, mixture of isomers). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and cyclohexenone (35 μL); the mixture was stirred at RT for 2d and the obtained crude was purified by chromatography (AcOEt/petroleum ether 1:10, R_f 0.30 and 0.27 in AcOEt/petroleum ether 1:2), affording pure isomer **21a** and a mixture of **21b** with traces of **21c** both as colorless oils (89 mg, 86%). Compound **21a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.15-4.10 (m, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.34 (d, *J* = 18.0 Hz, 1H), 3.03 (d, *J* = 18.0 Hz, 1H), 2.45-2.42 (m, 2H), 2.16-2.11 (m, 1H), 1.98 (s, 3H), 1.30-1.22 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 171.5, 170.2, 146.2, 137.1, 62.6, 54.0, 52.9, 52.5, 50.7, 43.8, 26.1, 14.6; IR ν_{max} (film)/cm^{-1} 3464, 2956, 1734, 1665, 1435, 1376, 1264, 1175, 1138, 1083, 1018, 952, 867; MS (CI) m/z (rel. intensity %) 253 (M+H^+, 90), 270 (M+NH_4^+, 100); HRMS (ES) calcd. $C_{13}H_{20}NO_5$ (M+NH_4^+) 270.1336, found 270.1330. Compound **21b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.48 (dd, *J* = 1.5 Hz, *J* = 2.5 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 3.59 (td, *J* =

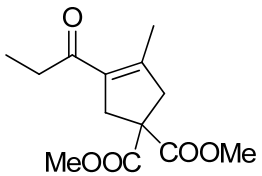
7.5 Hz, *J* = 10.0 Hz, 1H), 3.27 (d, *J* = 7.0 Hz, 1H), 2.25-2.13 (m, 2H), 2.00 (ddt, *J* = 3.5 Hz, *J* = 7.0 Hz, *J* = 7.5 Hz, 1H), 1.75 (t, *J* = 1.5 Hz, 3H), 1.51-1.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 215.2, 170.6, 170.1, 142.3, 124.2, 69.2, 61.3, 52.9, 52.5, 44.9, 38.5, 23.9, 14.7; IR: ν_{max} (film)/cm^{-1} 3463, 2955, 2917, 2847, 1739, 1729, 1648, 1435, 1410, 1382, 1275, 1221, 1176, 1117, 1066, 1028, 1025, 856, 837; MS (CI) m/z (rel. intensity %) 253 ($M+H^+$, 40), 270 ($M+NH_4^+$, 100); HRMS (ES) calcd. $C_{13}H_{20}NO_5$ ($M+NH_4^+$) 270.1336, found 270.1329.

2.2.7. Compound **22**



3-Acetyl-1,1-dicarboxymethyl-4-methyl-cyclopent-3-ene (**22**). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and methyl vinyl ketone (35 μL) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:10, R_f 0.30 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish oil (71 mg, 71%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (s, 6H), 3.32 (d, *J* = 2.0 Hz, 2H), 3.17 (s, 2H), 2.25 (s, 3H), 2.07 (t, *J* = 2.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 171.9 (2C), 149.9, 132.6, 56.4, 53.0 (2C), 47.8, 41.9, 30.4, 16.3; IR ν_{max} (film)/cm^{-1} 3002, 2956, 1735, 1684, 1655, 1621, 1435, 1362, 1269, 1254, 1201, 1168, 1073; MS (CI) m/z (rel. intensity %) 241 ($M+H^+$, 77), 258 ($M+NH_4^+$, 98); HRMS (CI) calcd. $C_{12}H_{20}NO_5$ ($M+NH_4^+$) 258.1336, found 258.1333.

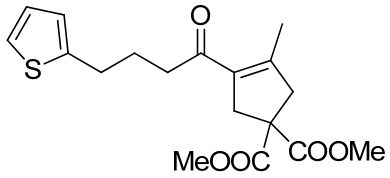
2.2.8. Compound **23**



1,1-Dicarboxymethyl-4-methyl-3-propionyl-cyclopent-3-ene (**23**). The general procedure was followed, using ethyl vinyl ketone (40 μL) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT for 84h; purification was accomplished by chromatography

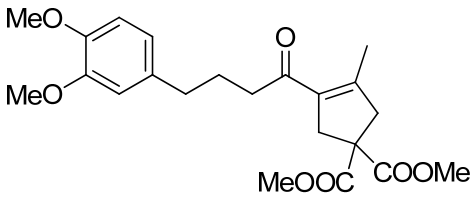
(Et_2O/petroleum ether 1:5, R_f 0.33 in AcOEt/petroleum ether 1:2), affording the pure product as a colorless oil (96 mg, 94%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 6H), 3.37 (dd, *J* = 3.8 Hz, *J* = 1.9 Hz, 2H), 3.10 (s, 2H), 2.47 (q, *J* = 7.2 Hz, 2H), 2.02 (s, 3H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 172.0 (2C), 149.5, 132.0, 56.7, 53.1 (2C), 47.6, 41.6, 35.5, 16.3, 7.5; IR ν_{max} (film)/cm^{-1} 3473, 3280, 2849, 2367, 2343, 1995, 1739, 1684, 1657, 1623, 1436, 1376, 1267, 1201, 1169, 1075, 963, 893, 806; MS (CI) m/z (rel. intensity %) 255 ($M+H^+$, 32), 272 ($M+NH_4^+$, 100); HRMS (CI) calcd. $C_{13}H_{22}NO_5$ ($M+NH_4^+$) 272.1492, found 258.1496.

2.2.9. Compound **24**



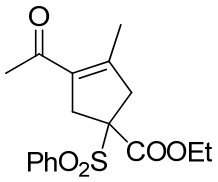
1,1-Dicarboxymethyl-4-methyl-3-(4-(thiophen-2-yl)butanoyl)-cyclopent-3-ene (**24**). The general procedure was followed, using dimethyl propargylmalonate (102 mg) and 6-(thiophen-2-yl)hex-1-en-3-one (72 μL) and stirring the mixture at RT for 72h; purification was accomplished by chromatography (Et_2O/toluene 1:50, R_f 0.49 in AcOEt/petroleum ether 1:2), affording the pure product as a colourless oil (105 mg, 75%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 5.0 Hz, 1H), 6.92 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.79 (d, *J* = 3.5 Hz, 1H), 3.75 (s, 6H), 3.30 (s, 2H), 3.15 (s, 2H), 2.87 (t, *J* = 7.0 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.06 (s, 3H), 1.98 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 198.3, 171.8, 149.8, 144.4, 131.9, 126.7, 124.3, 123.0, 56.5, 53.0, 47.5, 41.5, 41.0, 29.0, 25.2, 16.2; IR ν_{max} (film)/cm^{-1} 2953, 2851, 1996, 1737, 1682, 1656, 1622, 1555, 1435, 1371, 1265, 1200, 1168, 1073, 965, 849, 824; MS (CI) m/z (rel. intensity %) 373 ($M+Na^+$, 100); HRMS (CI) calcd. $C_{18}H_{22}NaO_5S$ ($M+Na^+$) 373.1080, found 373.1094.

2.2.10. Compound **25**



1,1-Dicarboxymethyl-4-methyl-3-(4-(3,4-dimethoxyphenyl)butanoyl)-cyclopent-3-ene (**25**). The general procedure was followed, using dimethyl propargylmalonate (105 mg) and 6-(3,4-dimethoxyphenyl)hex-1-en-3-one (97 mg) and stirring the mixture at RT for 72h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8,→1:2, R_f 0.31 in AcOEt/petroleum ether 1:2), affording the pure product as a colourless oil (135 mg, 79%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, *J* = 8.5 Hz, 1H), 6.71-6.70 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.74 (s, 3H), 3.29 (s, 2H), 3.15 (s, 2H), 2.58 (t, *J* = 7.5 Hz, 1H), 2.50 (t, *J* = 7.0 Hz, 1H), 2.05 (s, 3H), 1.94-1.88 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 198.7, 171.8, 149.6, 148.7, 141.0, 134.2, 132.0, 120.1, 111.5, 111.0, 56.5, 55.8, 55.6, 52.9, 47.5, 41.5, 41.3, 34.6, 25.0, 16.2; IR ν_{max} (film)/cm^{-1} 2952, 2837, 1995, 1737, 1681, 1654, 1621, 1516, 1436, 1370, 1261, 1200, 1157, 1072, 1029, 868, 809, 763; MS (CI) m/z (rel. intensity %) 405 ($M+H^+$, 100); HRMS (CI) calcd. $C_{22}H_{32}NO_7$ ($M+NH_4^+$) 422.2173, found 422.2163.

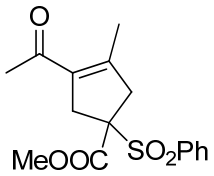
2.2.11. Compound **26**



3-Acetyl-1-carboxyethyl-4-methyl-1-(phenylsulphonyl)-cyclopent-3-ene (**26**). The general procedure was followed, using methyl vinyl ketone (35 μL) and ethyl 2-(phenylsulfonyl)pent-4-ynoate (156 mg) and stirring the mixture at RT for 72h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8, R_f 0.35 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish solid (94 mg, 71%): mp 71-72 ^{0}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.5 Hz, 2H), 7.70 (t, *J* = 7.5 Hz,

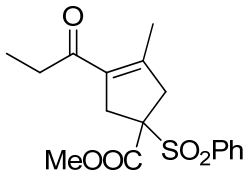
1H), 7.57 (dd, *J* = 7.5, 7.5 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 3.56 (d, *J* = 17.0 Hz, 1H), 3.49 (*J* = 19.0 Hz, 1H), 3.37 (d, *J* = 17.0 Hz, 1H), 3.33 (*J* = 19.0 Hz, 1H), 2.26 (s, 3H), 2.07 (s, 3H), 1.17 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 196.0, 167.8, 149.3, 136.1, 134.3, 132.5, 129.8 (2C), 128.9 (2C), 75.2, 62.9, 45.3, 39.8, 30.3, 16.3, 13.7; IR ν_{max} (KBr)/cm^{-1} 3069, 2988, 2915, 1378, 1909, 1737, 1690, 1625, 1584, 1471, 1450, 1430, 1358, 1306, 1279, 1241, 1222, 1209, 1144, 1085, 1066, 1028, 997, 962, 864, 763, 726, 691, 590, 580, 524; MS (CI) m/z (rel. intensity %) 354 ($M+NH_4^+$, 28); HRMS (CI) calcd. $C_{17}H_{24}NO_5S$ ($M+NH_4^+$) 354.1370, found 354.1362.

2.2.12. Compound **27**



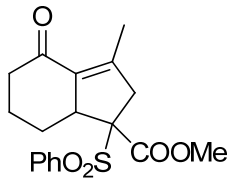
3-Acetyl-1-carboxymethyl-4-methyl-1-(phenylsulphonyl)-cyclopent-3-ene (**27**). The general procedure was followed, using methyl vinyl ketone (35 μL) and methyl 2-(phenylsulfonyl)pent-4-ynoate (159 mg) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8→1:2, R_f 0.20 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish oil (95 mg, 70%):^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 6.5 Hz, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.54 (dd, *J* = 7.5, 6.5 Hz, 2H), 3.65 (s, 3H), 3.53 (d, *J* = 17.0 Hz, 1H), 3.45 (d, *J* = 19.5 Hz, 1H), 3.35 (d, *J* = 17.0 Hz, 1H), 3.29 (d, *J* = 19.5 Hz, 1H), 2.21 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 195.9, 168.3, 149.2, 135.9, 134.4, 132.5, 129.7 (2C), 128.9 (2C), 75.2, 53.4, 45.3, 39.7, 30.2, 14.1; IR ν_{max} (film)/cm^{-1} 3066, 1001, 2954, 2924, 1995, 1737, 1685, 1655, 1623, 1583, 1447, 1434, 1365, 1310, 1258, 1213, 1163, 1083, 1023, 948, 844, 761, 723, 692; MS (CI) m/z (rel. intensity %) 323 ($M+H^+$, 3), 340 ($M+NH_4^+$, 100); HRMS (CI) calcd. $C_{16}H_{22}NO_5S$ ($M+NH_4^+$) 340.1213, found 340.1224.

2.2.13. Compound **28**



1-Carboxymethyl-4-methyl-1-(phenylsulphonyl)-3-propionyl-cyclopent-3-ene (**28**). The general procedure was followed, using ethyl vinyl ketone (40 μL) and methyl 2-(phenylsulfonyl)pent-4-ynoate (159 mg) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8→1:2, R_f 0.21 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish oil (93 mg, 66%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.56 (dd, *J* = 8.0, 7.5 Hz, 2H), 3.68 (s, 3H), 3.57 (d, *J* = 17.0 Hz, 1H), 3.44 (d, *J* = 19.5 Hz, 1H), 3.39 (d, *J* = 17.0 Hz, 1H), 3.27 (d, *J* = 19.5 Hz, 1H), 2.50 (q, *J* = 7.0 Hz, 2H), 2.05 (s, 3H), 1.05 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 198.8, 168.5, 148.7, 136.1, 134.4, 131.8, 129.8 (2C), 129.0 (2C), 75.5, 53.6, 45.2, 39.5, 35.5, 16.3, 7.4; IR ν_{max} (film)/cm^{-1} 3066, 2982, 2938, 2367, 1995, 1737, 1685, 1655, 1628, 1447, 1376, 1310, 1262, 1214, 1157, 1083, 951, 893, 761. 723, 691; MS (CI) m/z (rel. intensity %) 336 (M^+, 9); HRMS (CI) calcd. $C_{17}H_{24}NO_5S$ ($M+NH_4^+$) 354.1370, found 354.1364.

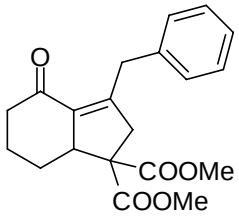
2.2.14. Compound **29**



5-Carboxymethyl-7-methyl-1-oxo-5-(phenylsulphonyl)-bicyclo[4.3.0]non-7-ene (**29**). The general procedure was followed, using methyl 2-(phenylsulfonyl)pent-4-ynoate (159 mg) and cyclohexenone (40 μL) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (Et_2O/petroleum ether 1:4→1:1, R_f 0.26 in AcOEt/petroleum ether 1:3), affording the pure product as a white solid (61 mg, 42%). Alternatively, the same procedure

was followed using NMP as solvent instead of MeOH, after purification affording the product with a 63% yield as a mixture of inseparable diasteromers (5:1 dr): mp 135-136 ^{0}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.5 Hz, 2H of major), 7.72 (d, *J* = 7.5 Hz, 2H of minor), 7.62 (t, *J* = 7.5 Hz, 1H of major and minor), 7.50 (t, *J* = 7.5 Hz, 2H of major and minor), 3.82-3.76 (m, 1H of major), 3.70 (s, 3H of minor), 3.62 (s, 3H of major and 1H of minor), 3.47 (d, *J* = 18.0 Hz, 1H of major), 3.06 (d, *J* = 18.0 Hz, 1H of major), 3.02 (d, *J* = 19.6 Hz, 1H of minor), 2.87 (d, *J* = 19.6 Hz, 1H of minor), 2.60-2.55 (m, 1H of minor), 2.46-2.23 (m, 1H of major and 3H of minor), 2.11-2.00 (m, 4H of major and 4H of minor), 1.93-1.86 (m, 1H of major), 1.83-1.77 (m, 1H of major), 1.69-1.57 (m, 1H of major and 1H of minor), 1.04 (qd, *J* = 12.7, 3.1 Hz, 1H of major); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0 (minor), 198.2 (major), 168.8 (minor), 167.2 (major), 150.0 (major), 147.2 (minor), 137.7 (major), 136.5 (minor), 134.4 (minor), 134.3 (major), 132.9 (minor), 130.6 (major), 130.2 (2C, major), 130.1 (2C, minor),128.8 (2C, major and minor), 80.2 (major), 79.0 (minor), 53.9 (minor), 53.4 (minor), 52.7 (major), 51.8 (major), 45.2 (minor), 44.0 (major), 40.8 (minor), 40.2 (major), 28.3 (major), 26.8 (minor), 24.1 (minor), 23.1 (major), 15.8 (major), 15.8 (minor); IR ν_{max} (KBr)/cm^{-1} 3068, 2962, 2877, 1734, 1682, 1618, 1448, 1440, 1415, 1322, 1299, 1241, 1208, 1189, 1143, 1082, 954, 922, 890, 836, 811, 756, 735, 714, 689, 594, 548, 512; MS (CI) m/z (rel. intensity %) 349 ($M+H^+$, 8), 366 ($M+NH_4^+$, 41); HRMS (CI) calcd. $C_{18}H_{24}NO_5S$ ($M+NH_4^+$) 366.1370, found 366.1366.

2.2.15. Compound **31**



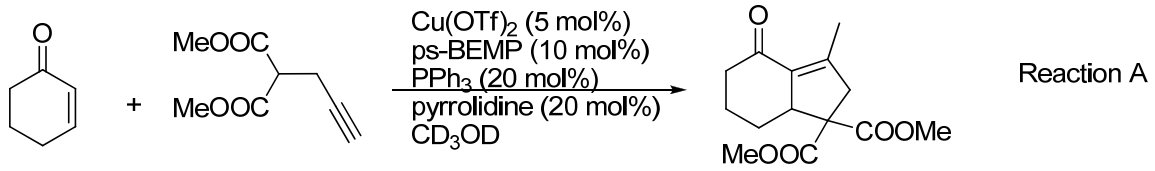
5,5-Dicarboxymethyl-7-benzyl-1-oxo-bicyclo[4.3.0]non-7-ene (**31**). The general procedure was followed, using cyclohexenone (40 μL) and dimethyl 2-(3-phenylprop-2-ynyl)malonate **30** (150 mg) and stirring the mixture at reflux for 16h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:20, R_f 0.30 in AcOEt/petroleum ether 1:4),

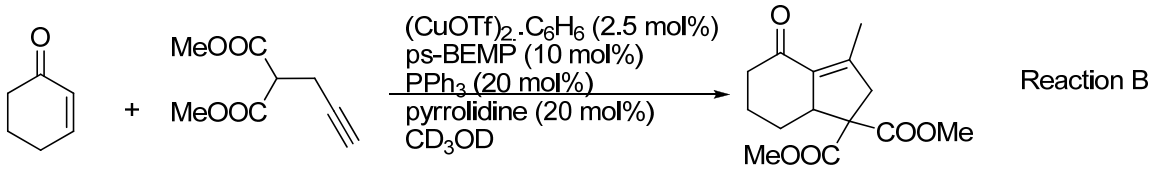
affording the pure product as a colorless oil (94 mg, 69%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.18 (m, 5H), 4.08 (d, *J* = 14.0 Hz, 1H), 3.76 (d, *J* = 14.0 Hz, 1H), 3.73-3.71 (m, 1H), 3.69 (s, 3H), 3.68 (s, 3H), 3.02 (d, *J* = 18.5, 1H), 2.63 (d, *J* = 18.5 Hz, 1H), 2.52 (ddd, *J* = 17.5, 2.0, 2.0 Hz, 1H), 2.25 (ddd, *J* = 19.5, 13.0, 6.0 Hz, 1H), 2.16-2.13 (m, 1H), 2.08-2.04 (m, 1H),1.84-1.75 (m, 1H), 1.25-1.20 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 198.9, 171.5, 170.6, 150.9, 138.1, 132.3, 129.0 (2C), 128.4 (2C), 126.3, 62.0, 52.7, 52.2, 52.0, 43.5, 40.9, 35.6, 27.5, 23.4; IR ν_{max} (film)/cm^{-1} 3027, 2952, 2867, 2360, 1735, 1681, 1623, 1494, 1435, 1326, 1269, 1221, 1198, 1172, 1090, 1034, 960, 934, 844, 803; MS (APCI) m/z (rel. intensity %) 343 ($M+H^+$, 100), 360 ($M+NH_4^+$, 11); HRMS (CI) calcd. $C_{20}H_{22}NO_5$ ($M+H^+$) 343.1545, found 343.1549.

3. Mechanism study

3.1. Identification of Cu-PPh_3 complex

Two reactions were performed in the NMR tube:





Reaction A, the general procedure was followed, using dimethyl propargylmalonate (51 mg) and cyclohexenone (20 μL) in 0.7 ml of methanol-d_4; ^{31}P NMR was taken when the reaction finished: ^{31}P NMR (162 MHz, CD_3OD) δ 32.2 (s, $P(O)Ph_3$), -1.7 (br s, complex of Cu-PPh_3).

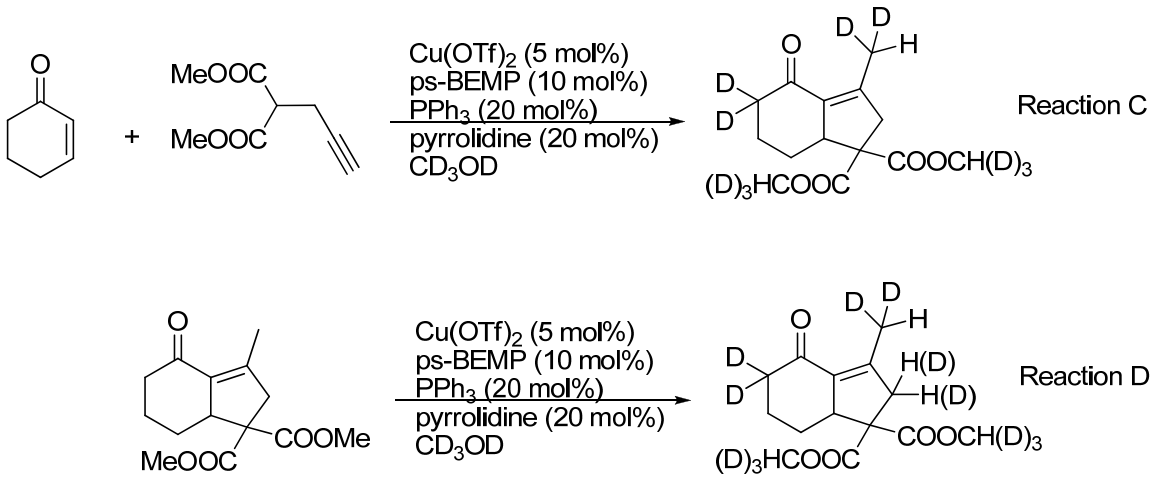
Reaction B, the general procedure was followed, using dimethyl propargylmalonate (51 mg) and cyclohexenone (20 μL) in 0.7 ml of methanol-d_4, $(CuOTf)_2.C_6H_6$ (3 mg) was used

instead of $Cu(OTf)_2$; ^{31}P NMR was taken when the reaction finished: ^{31}P NMR (162 MHz, CD_3OD) δ 32.2 (s, $P(O)Ph_3$), -1.1 (br s, complex of Cu-PPh_3).

^{31}P NMR of a 1:1 mixture of reaction A and reaction B showed the same catalyst complex in the two reactions: ^{31}P NMR (162 MHz, CD_3OD) δ 32.2 (s, $P(O)Ph_3$), -1.2 (br s, complex of Cu-PPh_3).

3.2. Reactions in CD_3OD

Two reactions were performed in the NMR tube:



Reaction C, the general procedure was followed, using dimethyl propargylmalonate (51 mg) and cyclohexenone (20 μL) in 0.7 ml of methanol-d_4. The reaction was followed by ^1H NMR. Cyclohexenone was consumed after 3.5h. Solvent was removed. The obtained crude was immediately purified by chromatography (Et_2O/petroleum ether 1:4 to 1:2, R_f 0.29 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (46 mg, 87%).

Reaction D, the general procedure was followed, compound **16** (53 mg) was added in 0.7 ml of methanol-d_4 instead of dimethyl propargylmalonate and cyclohexenone. Reaction was put on and worked up at the same as reaction C. The obtained crude was immediately purified by chromatography (Et_2O/petroleum ether 1:4 to 1:2, R_f 0.29 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (50 mg, 94%).

4. References

[S1] Brillon, D.; Deslongchamps, P. *Can. J. Chem*. **1987**, *65*, 43.

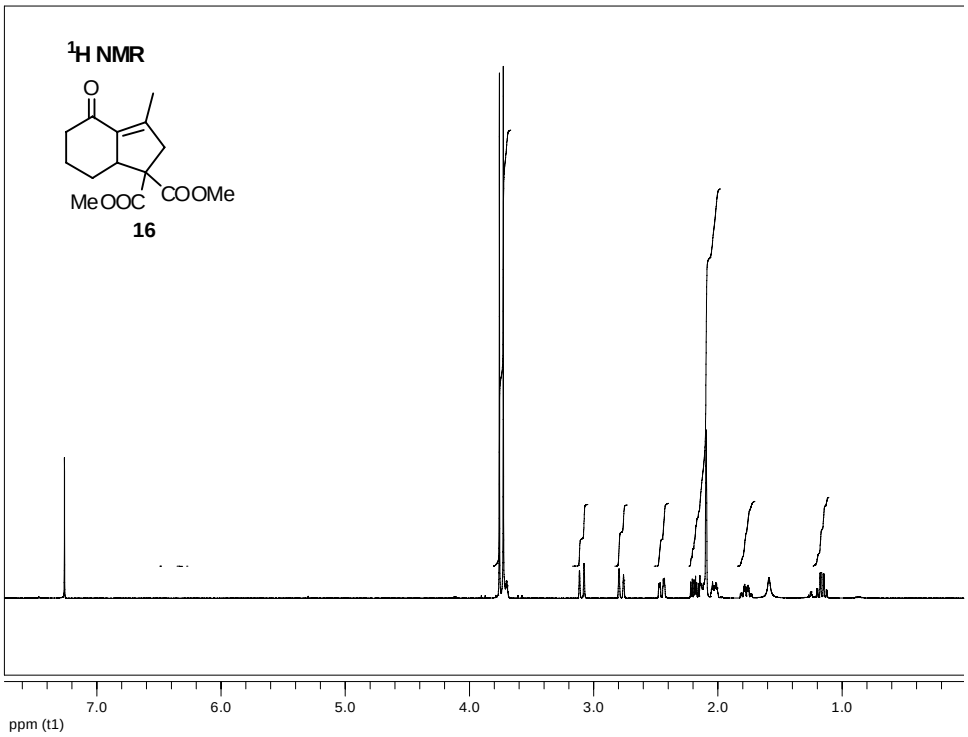
[S2] Schiller, R. ; Pour, M. ; Fáková, H. ; Kuneš, J . ; Císařová, I. *J. Org. Chem.* **2004**, *69*, 6761.

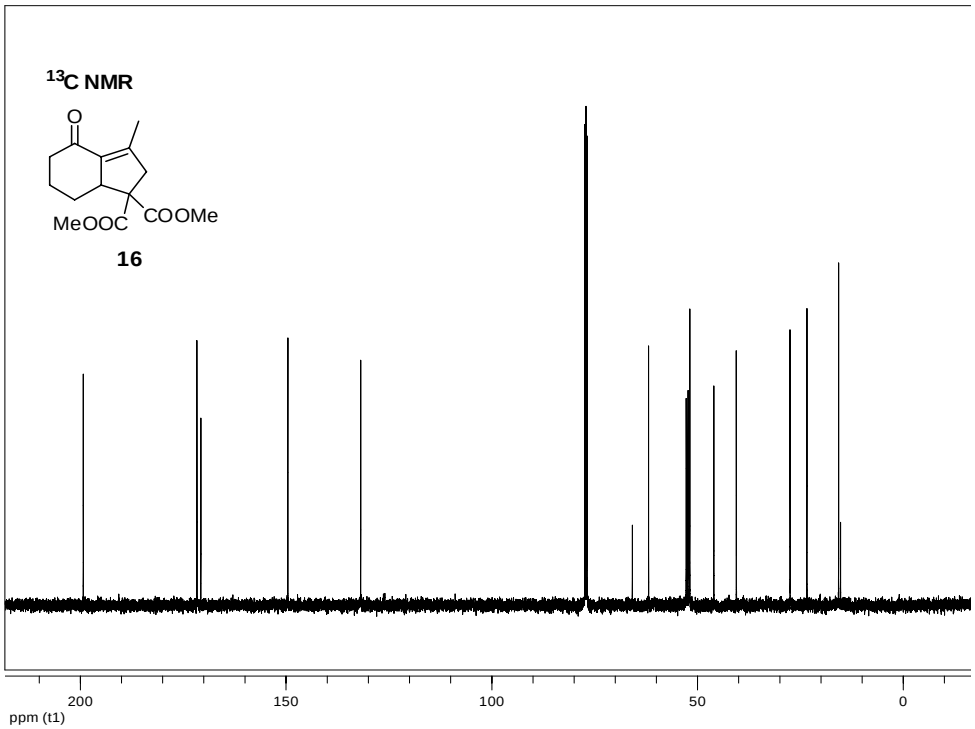
[S3] Chong, B. D.; Ji, Y. I.; Oh, S. S.; Yang, J. D.; Baik, W.; Koo, S. *J Org. Chem*. **1997**, *62*, 9323.

5. Spectra

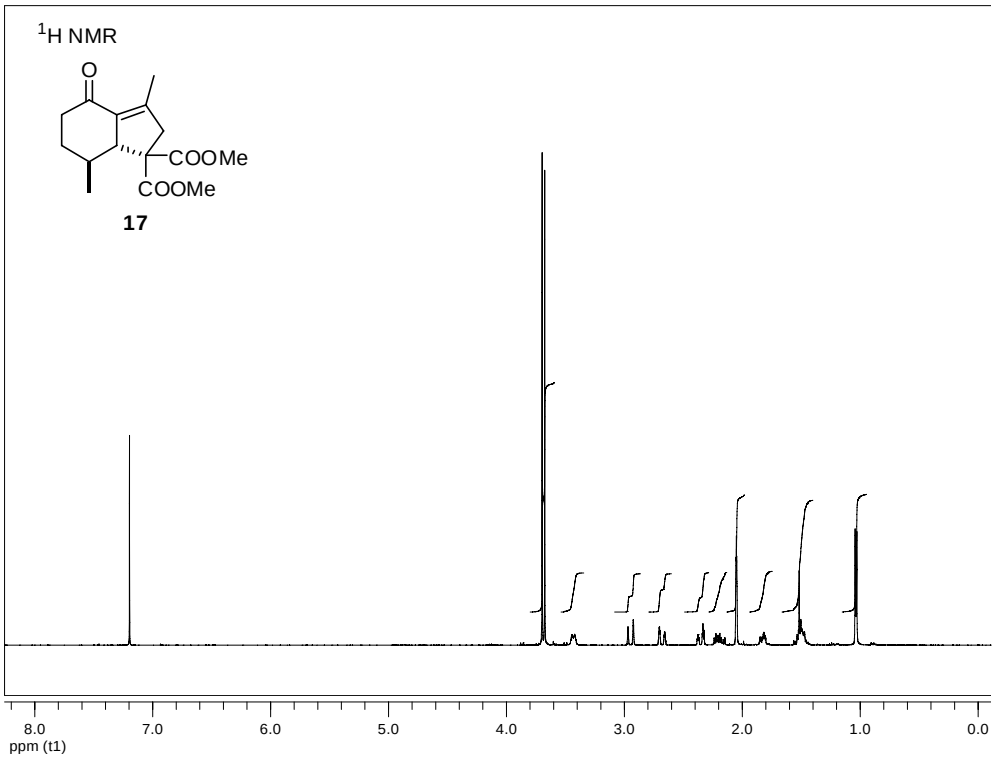
5.1. Spectra for reaction scope :

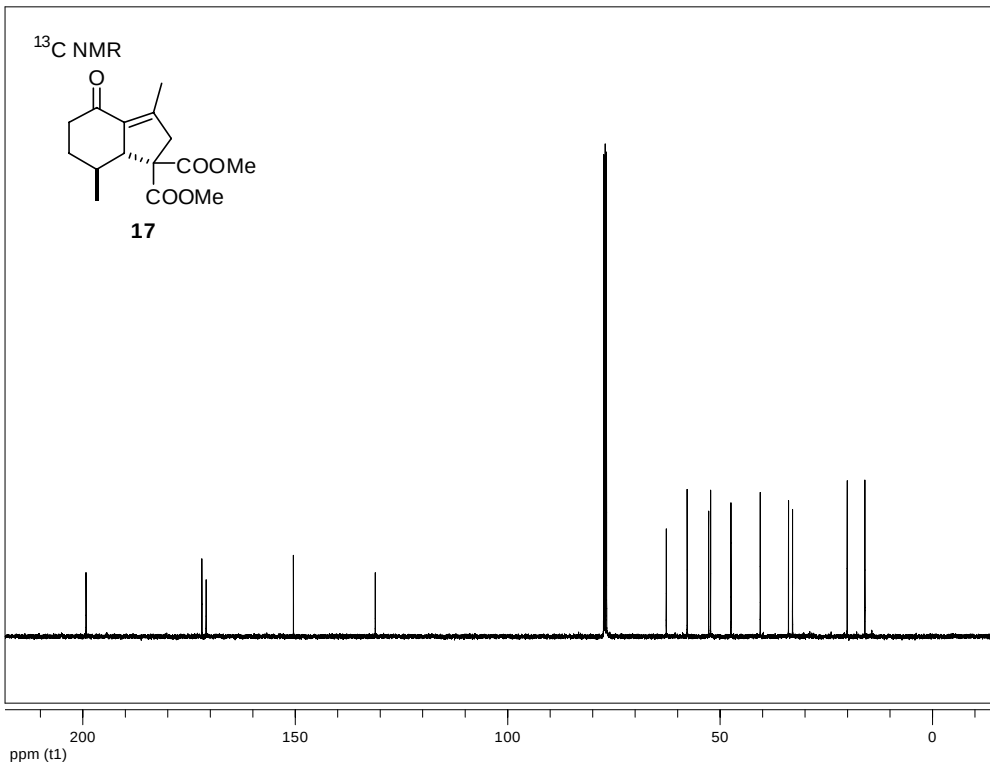
5.1.1. Compound **16**



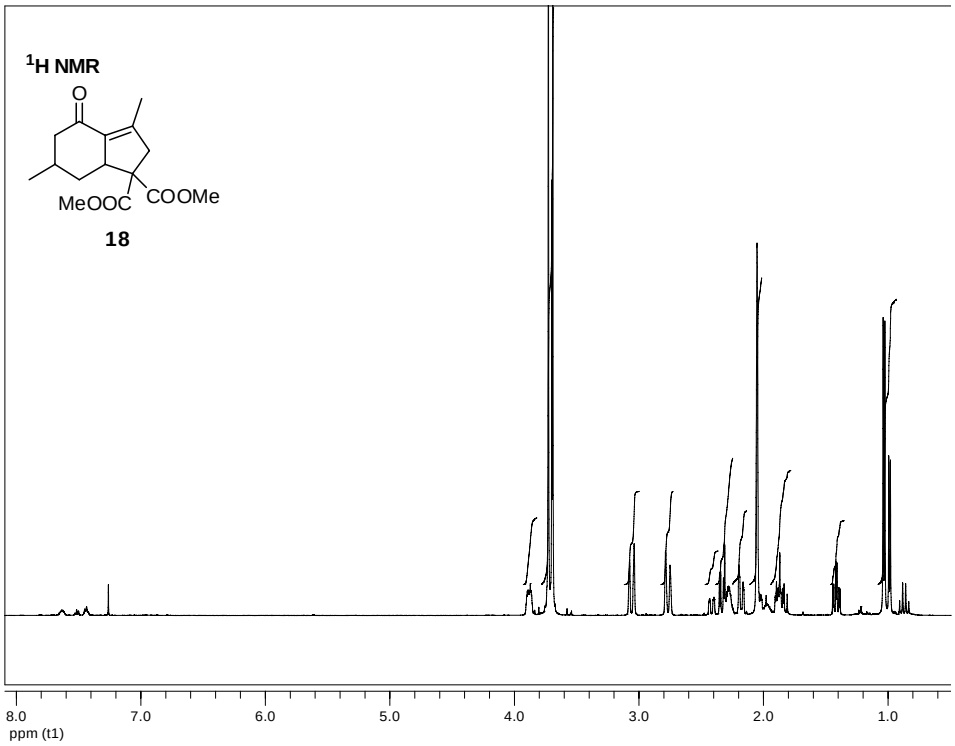


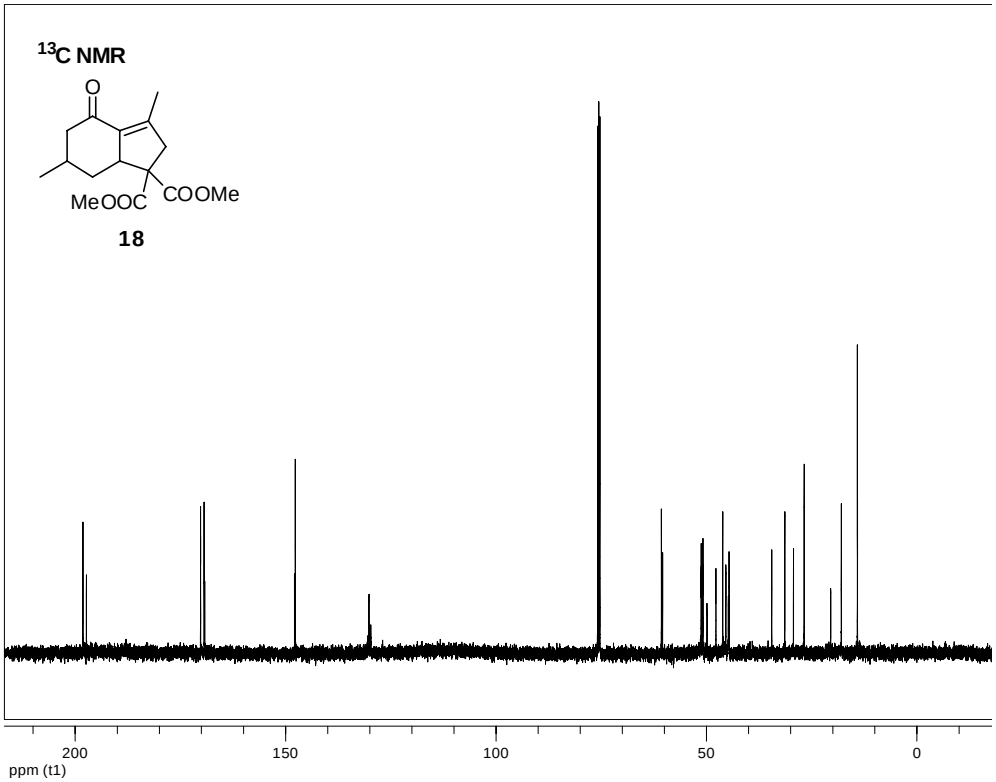
5.1.2. Compound **17**



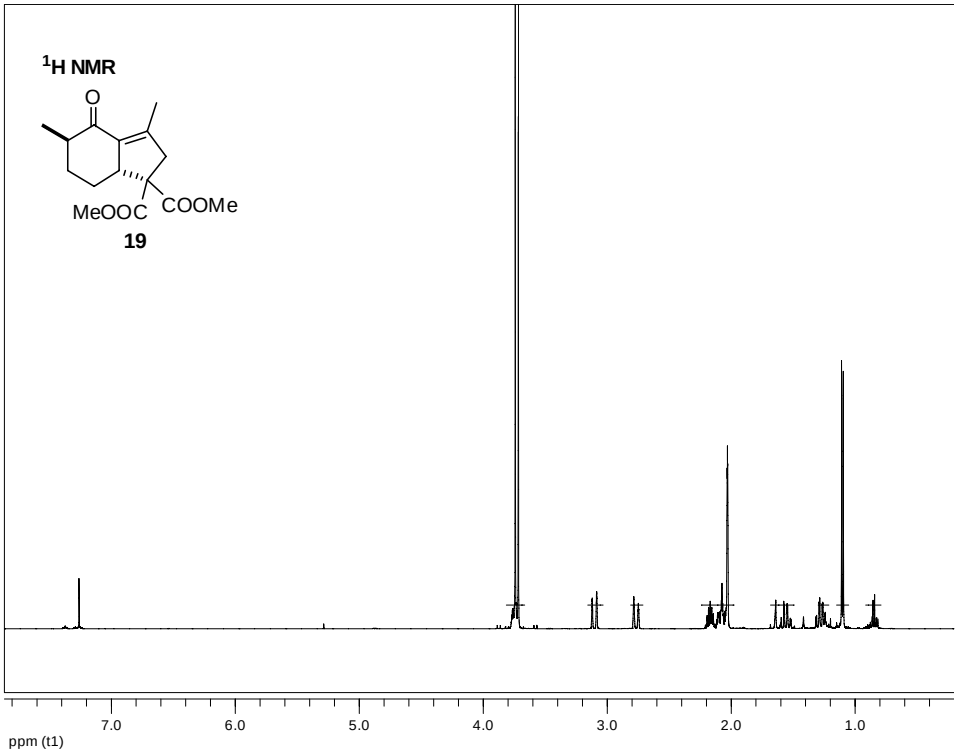


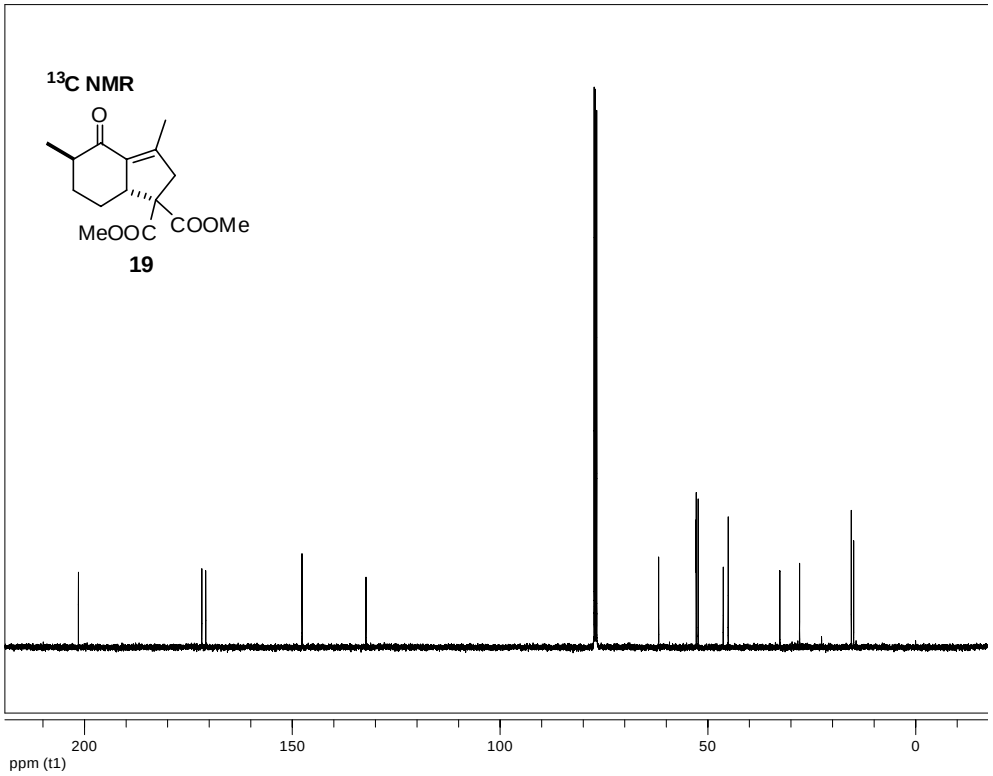
5.1.3. Compound **18**



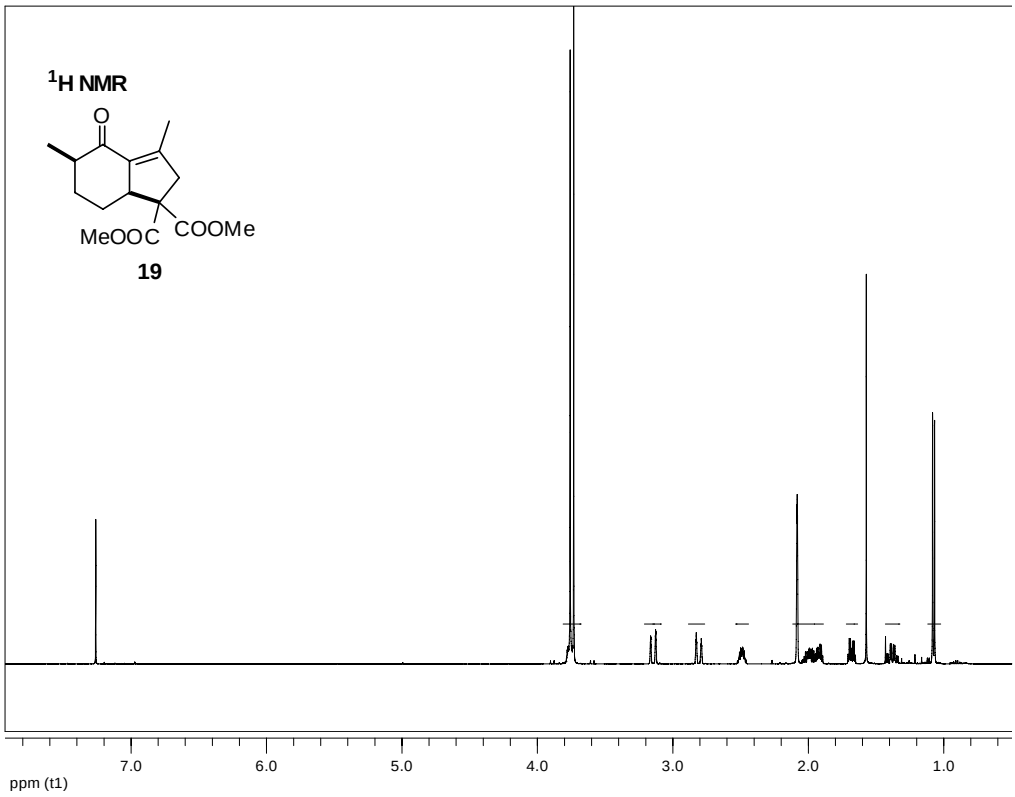


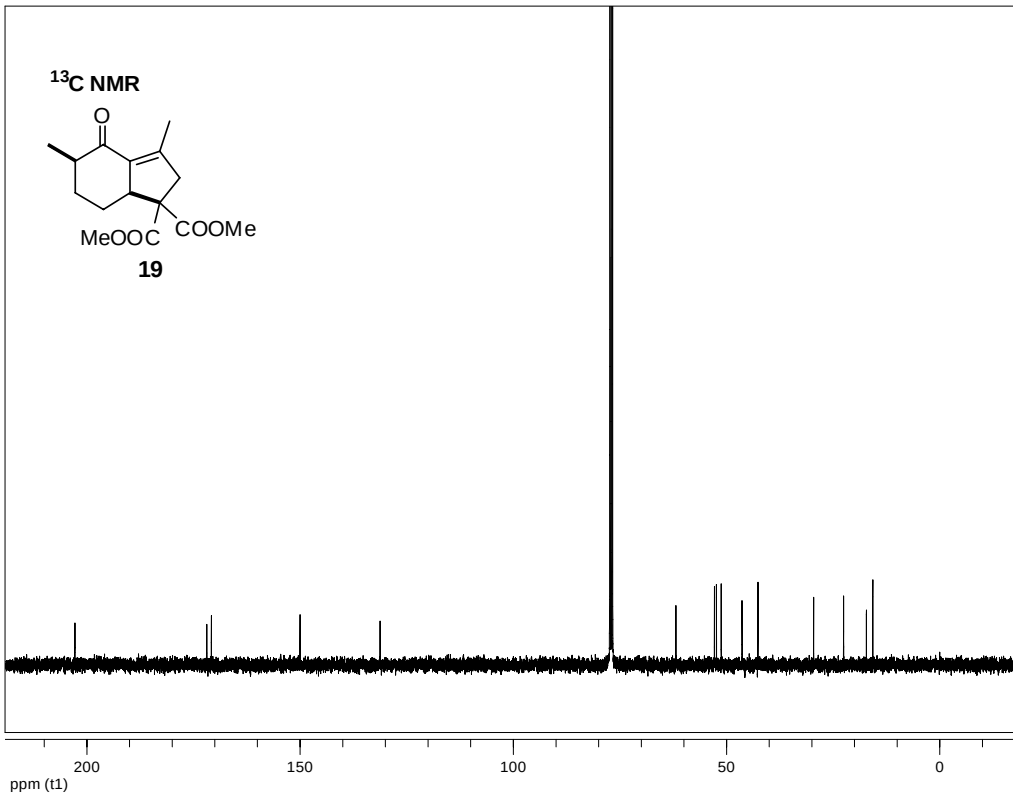
5.1.4. Compound **19** (major isomer)



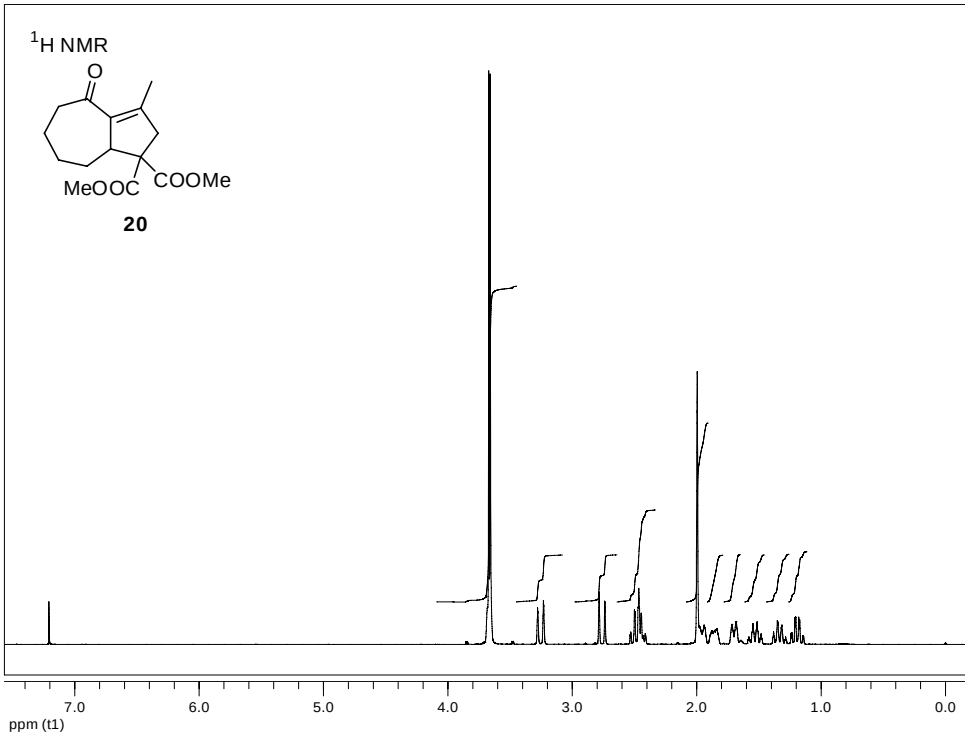


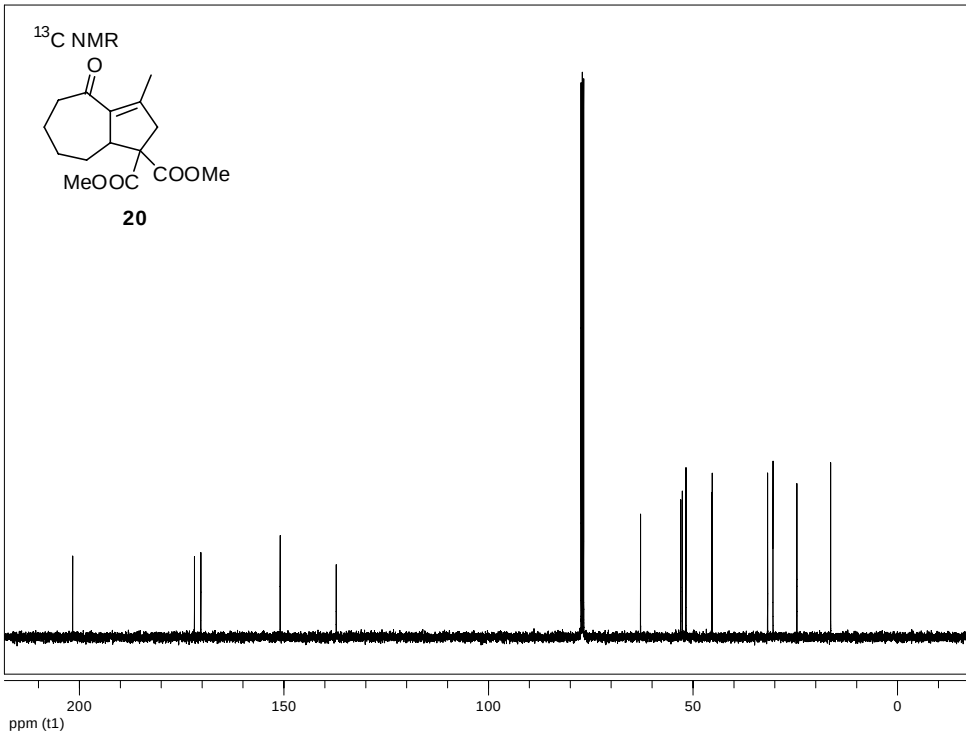
5.1.5. Compound **19** (minor isomer)



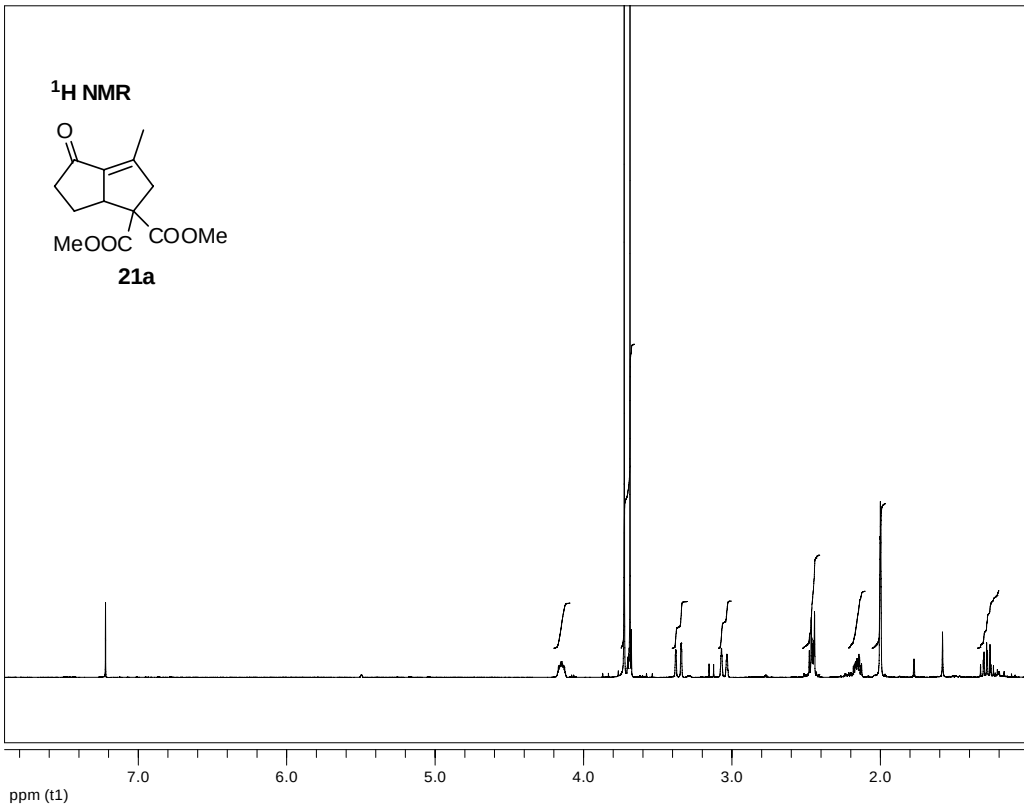


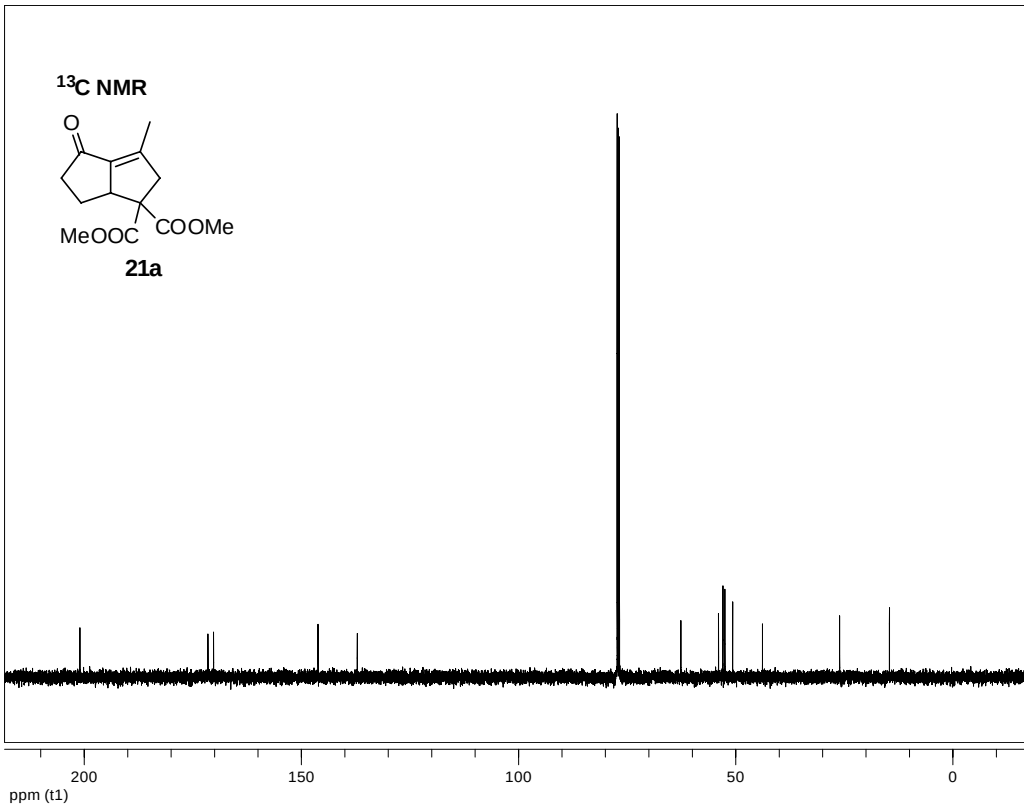
5.1.6. Compound **20**



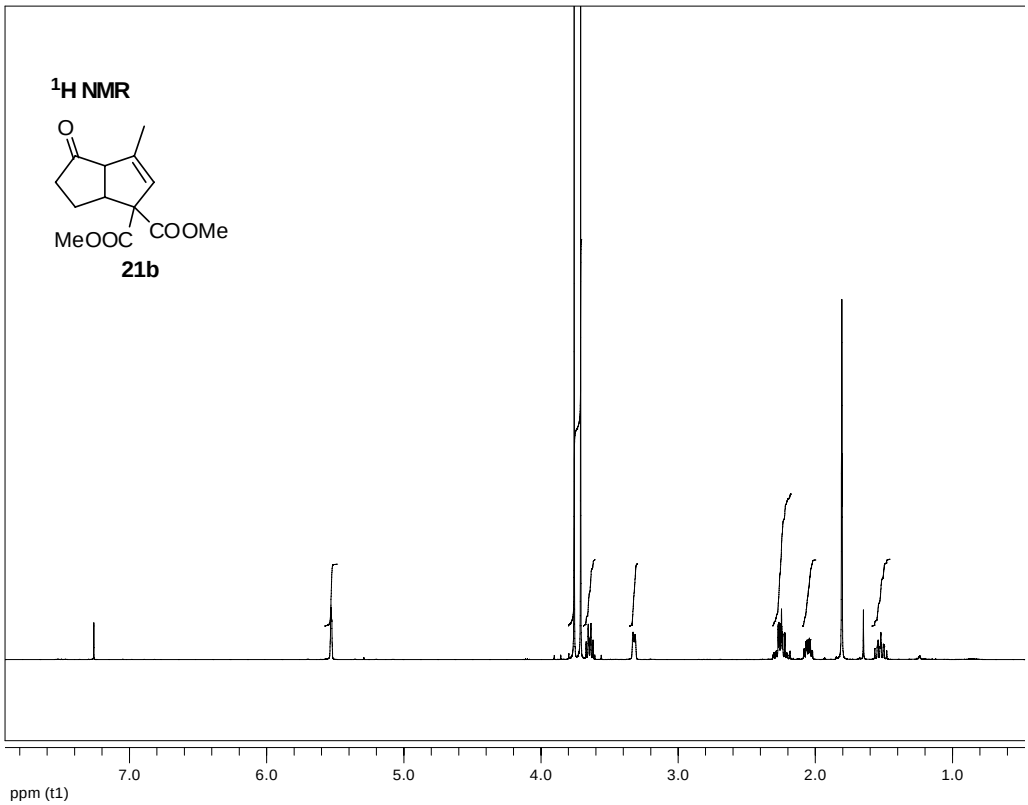


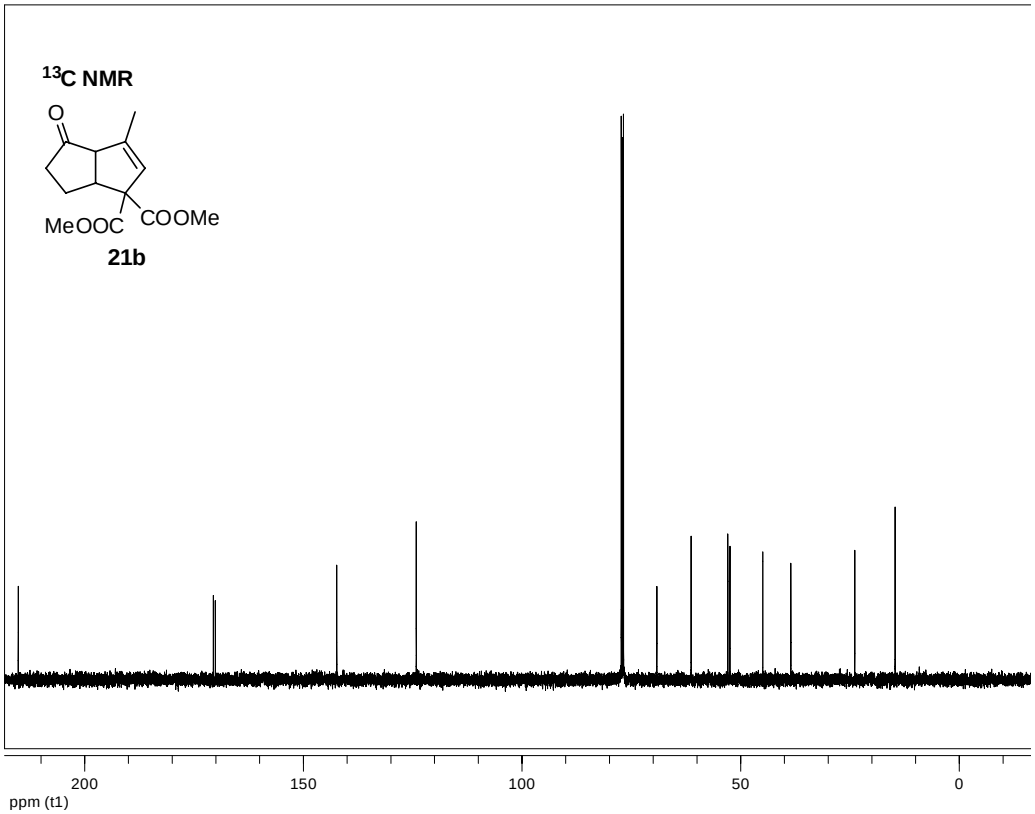
5.1.7. Compound **21a**



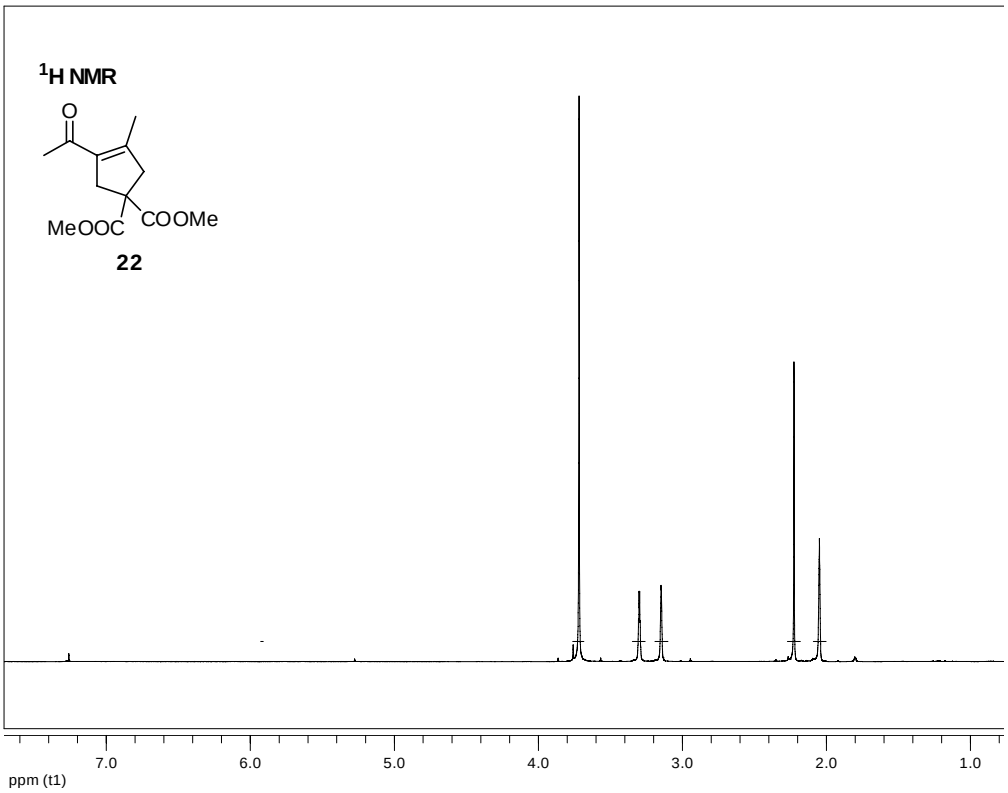


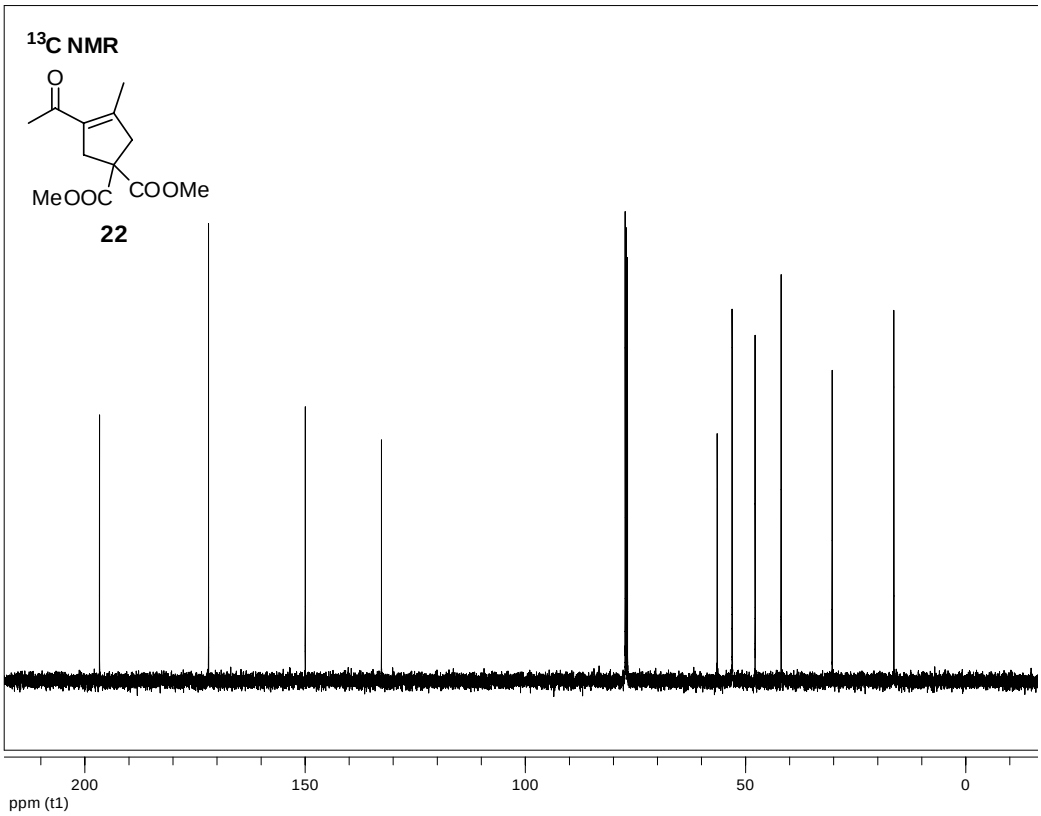
5.1.8. Compound **21b**



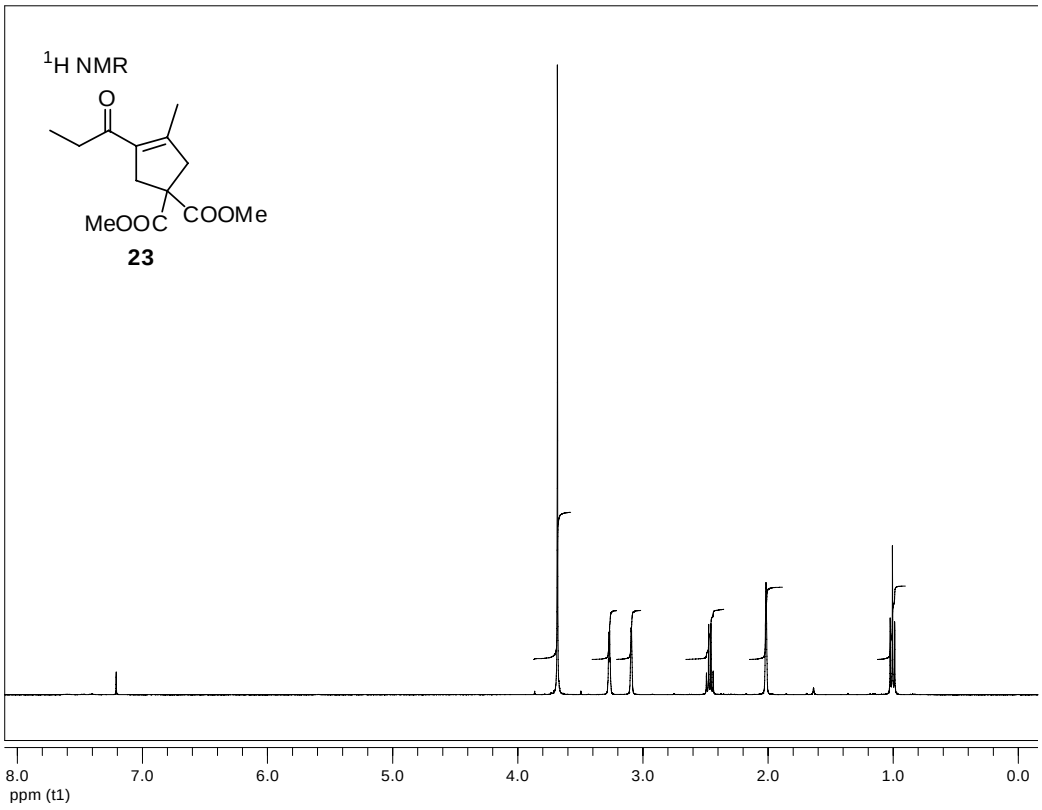


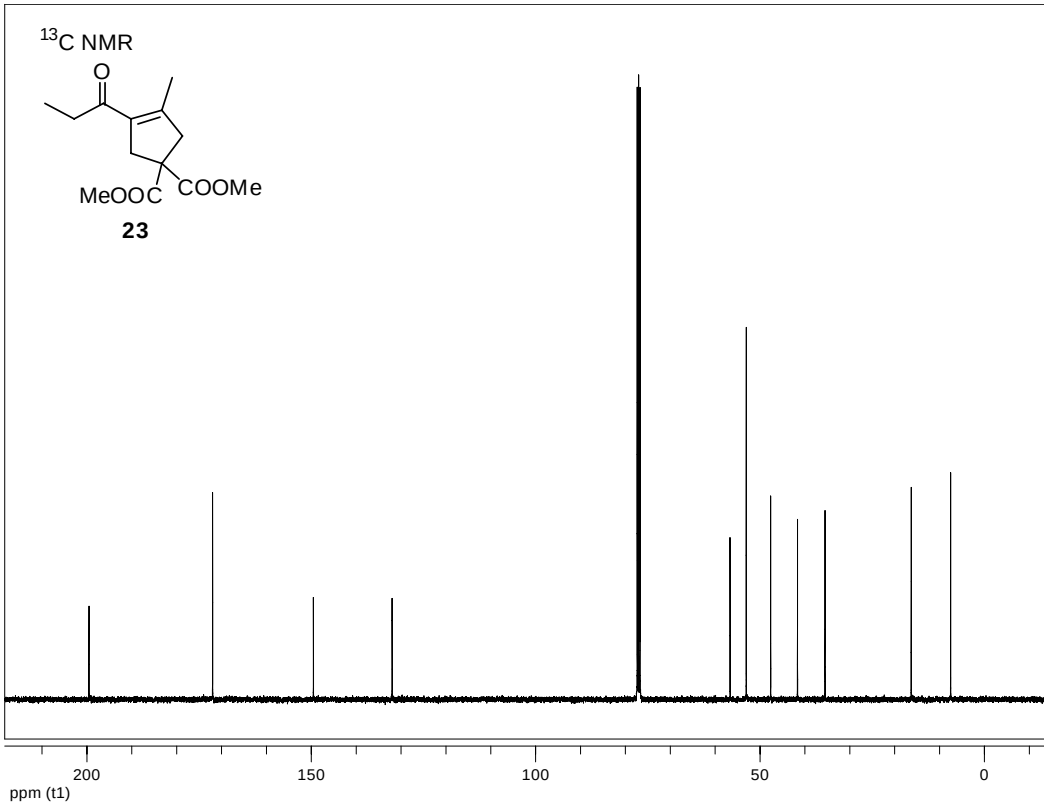
5.1.9. Compound **22**



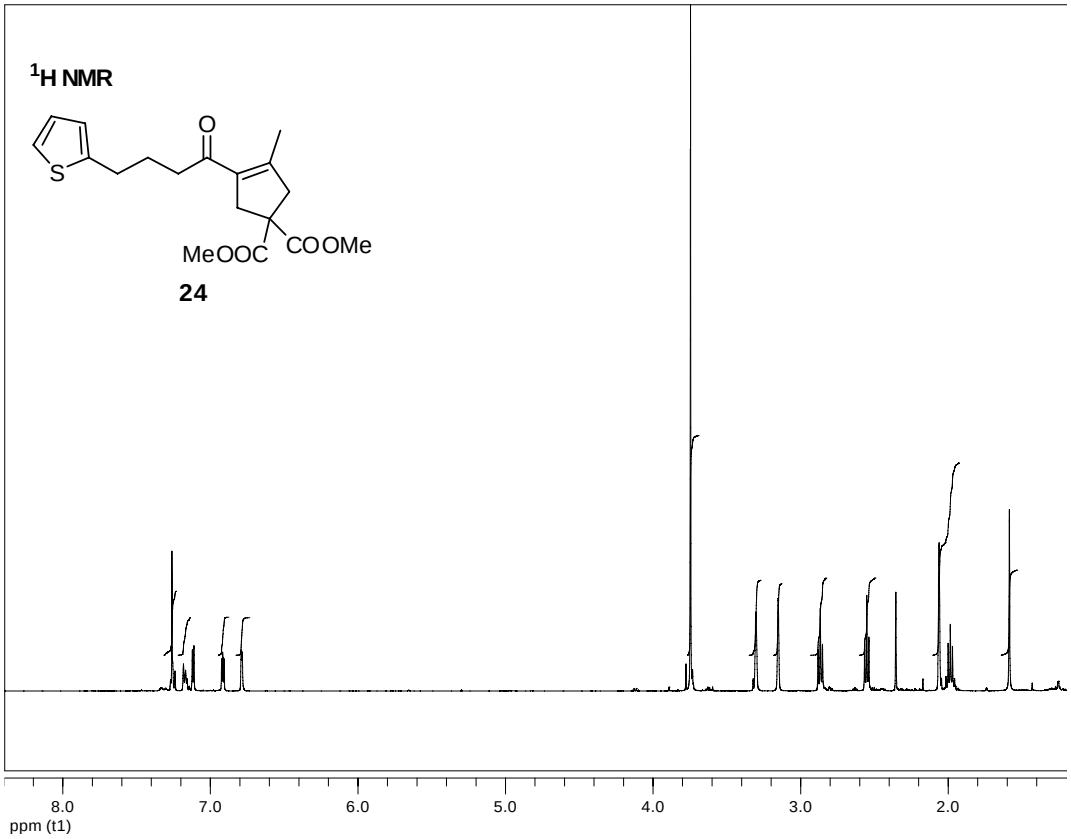


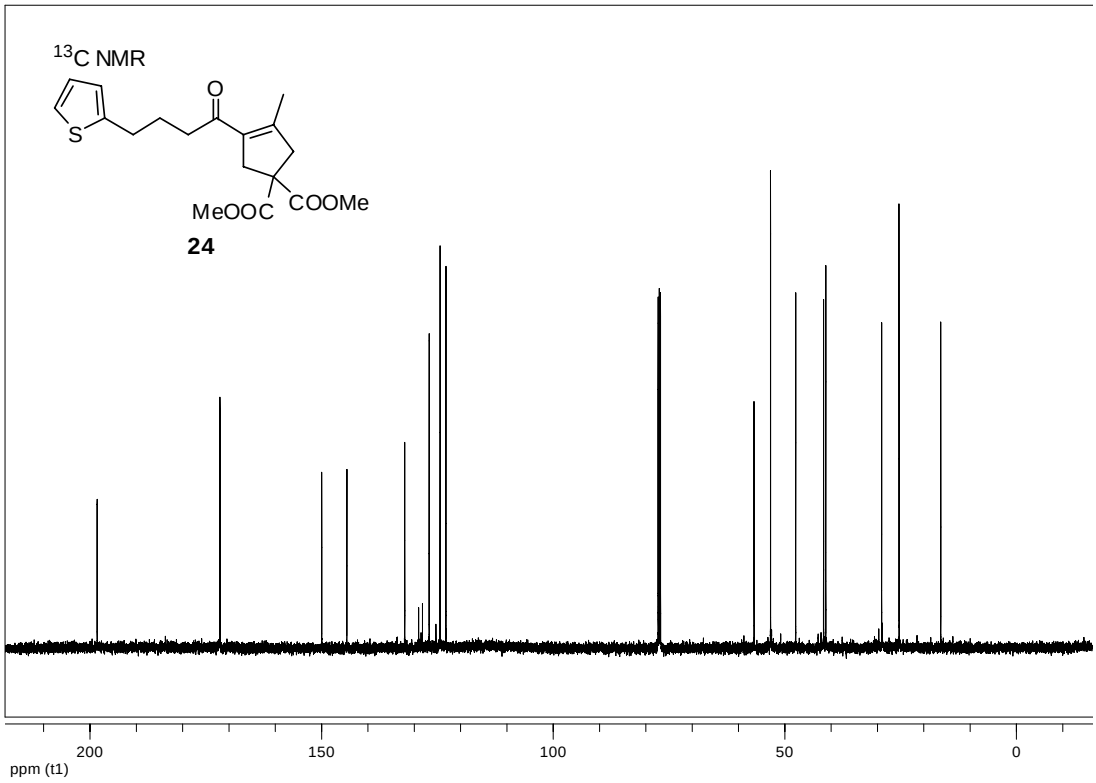
5.1.10. Compound **23**



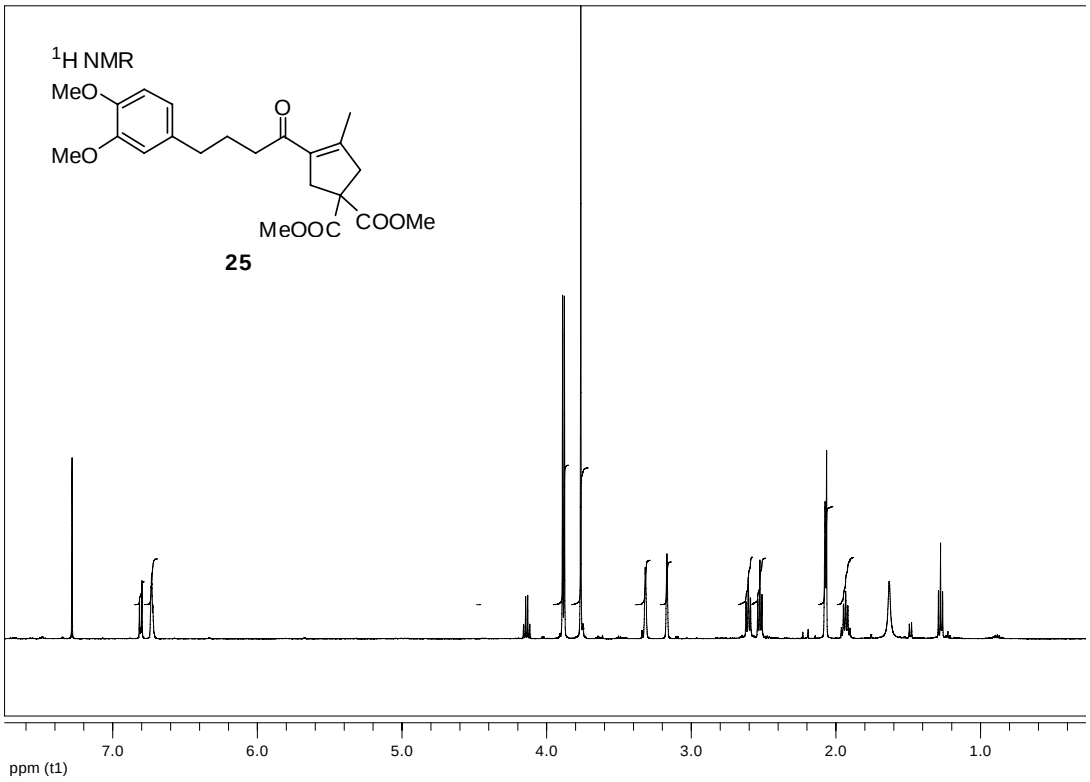


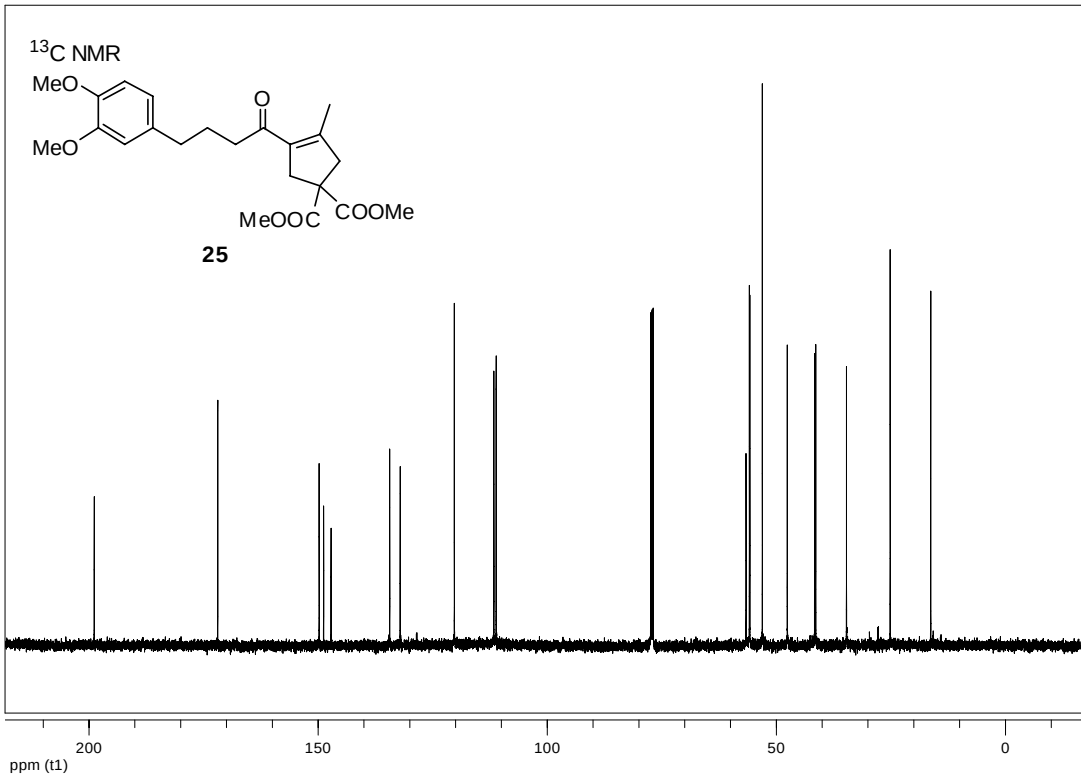
5.1.11. Compound **24**



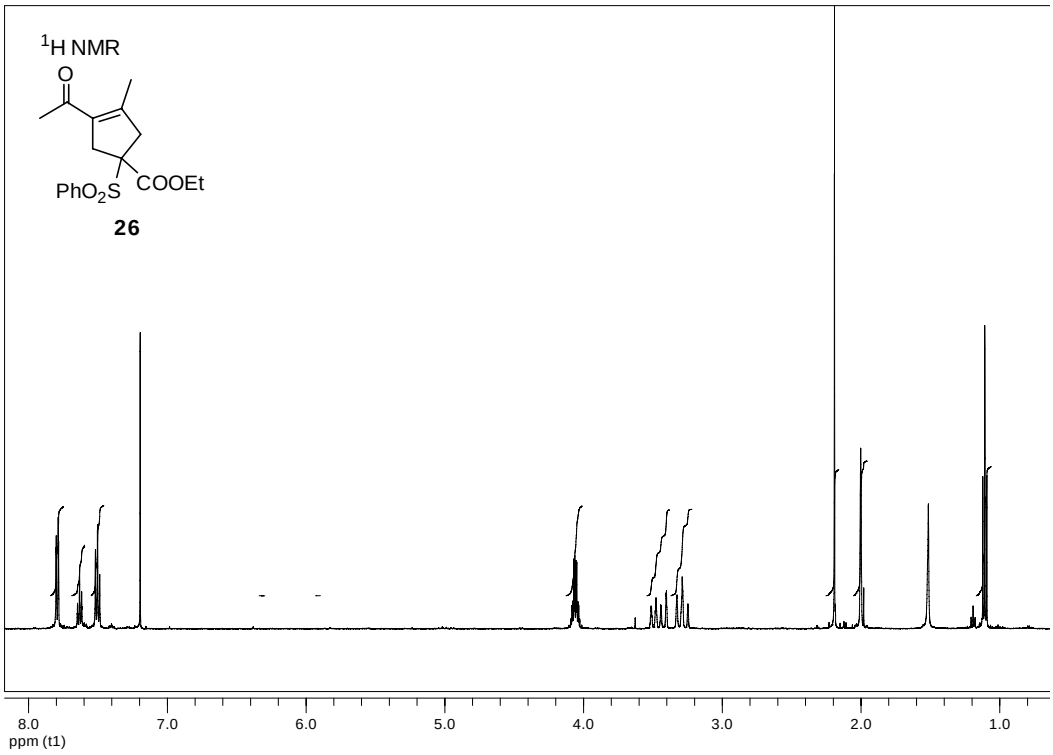


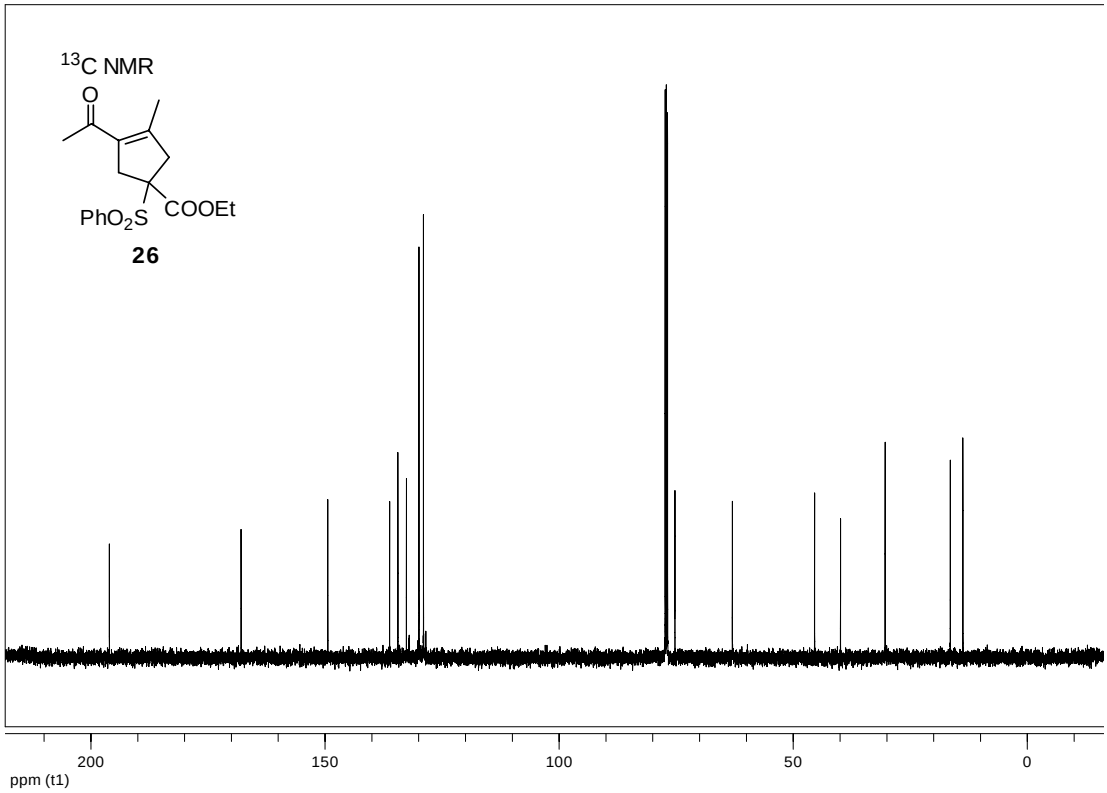
5.1.12. Compound **25**



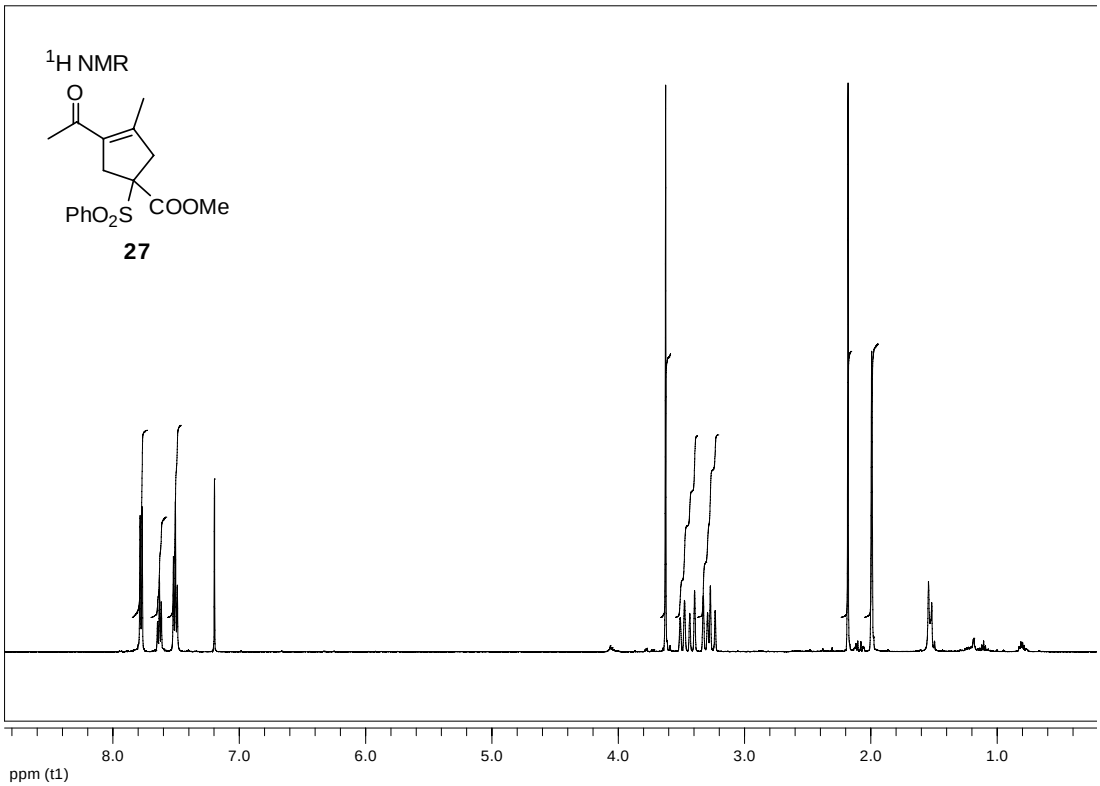


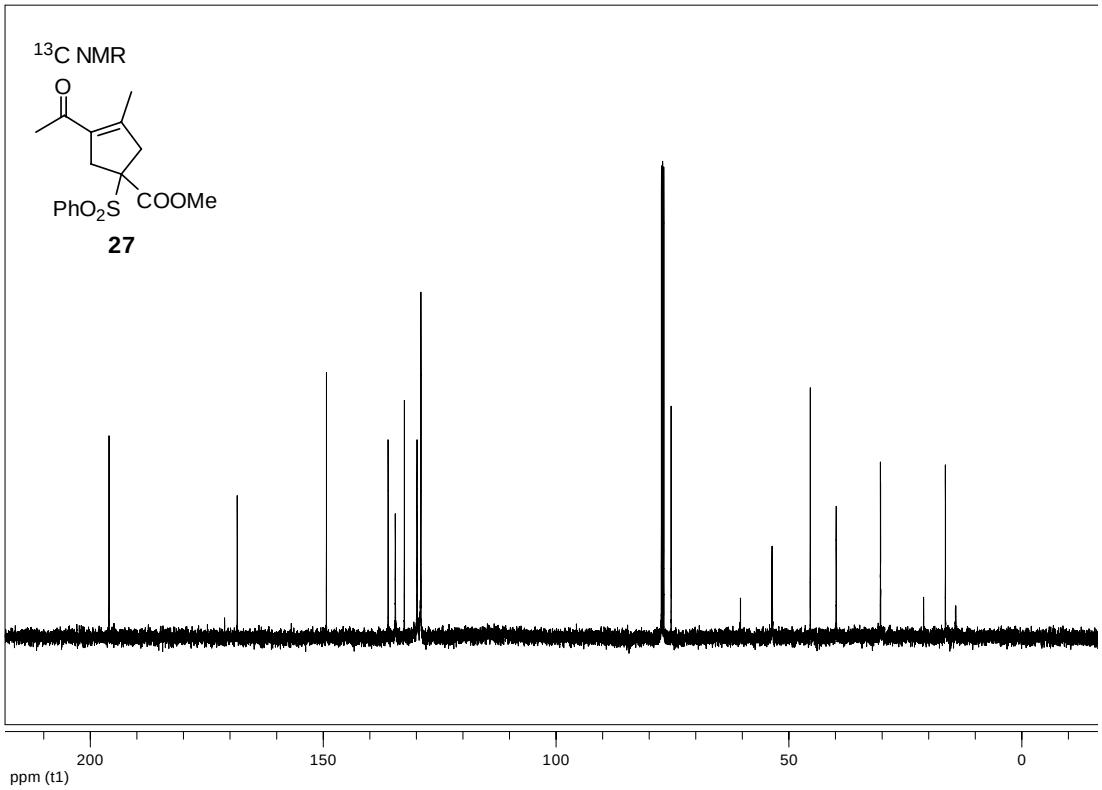
5.1.13. Compound **26**



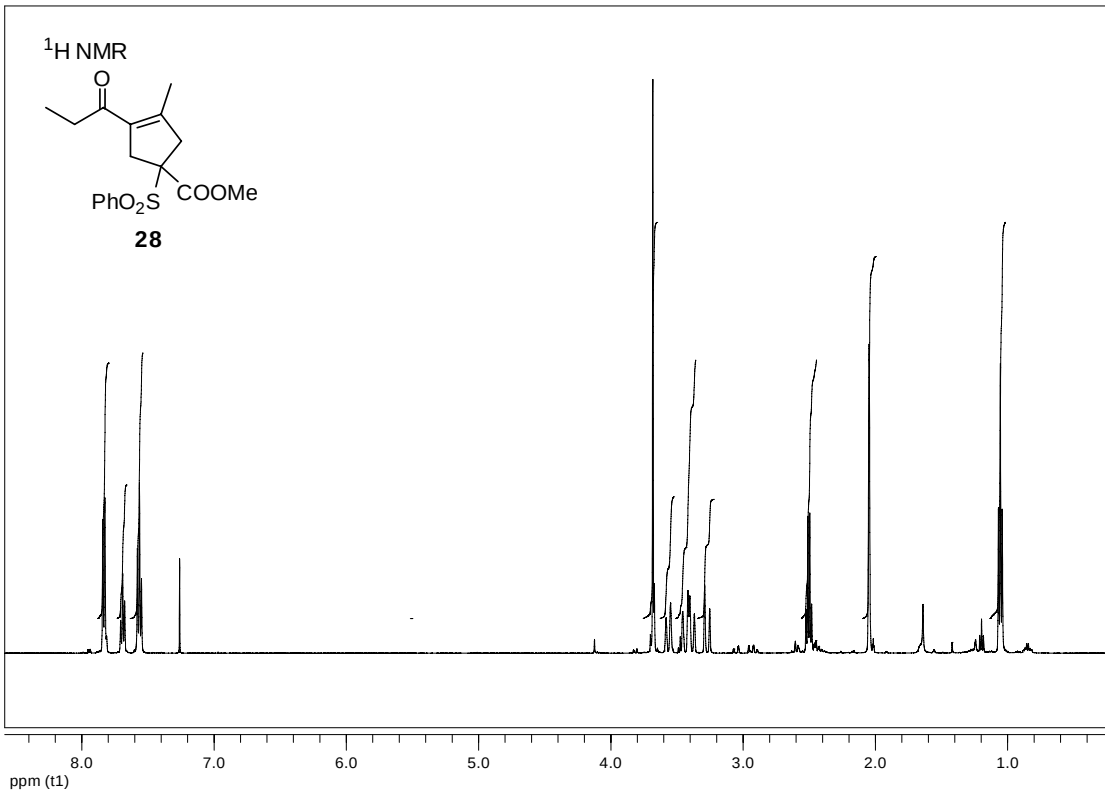


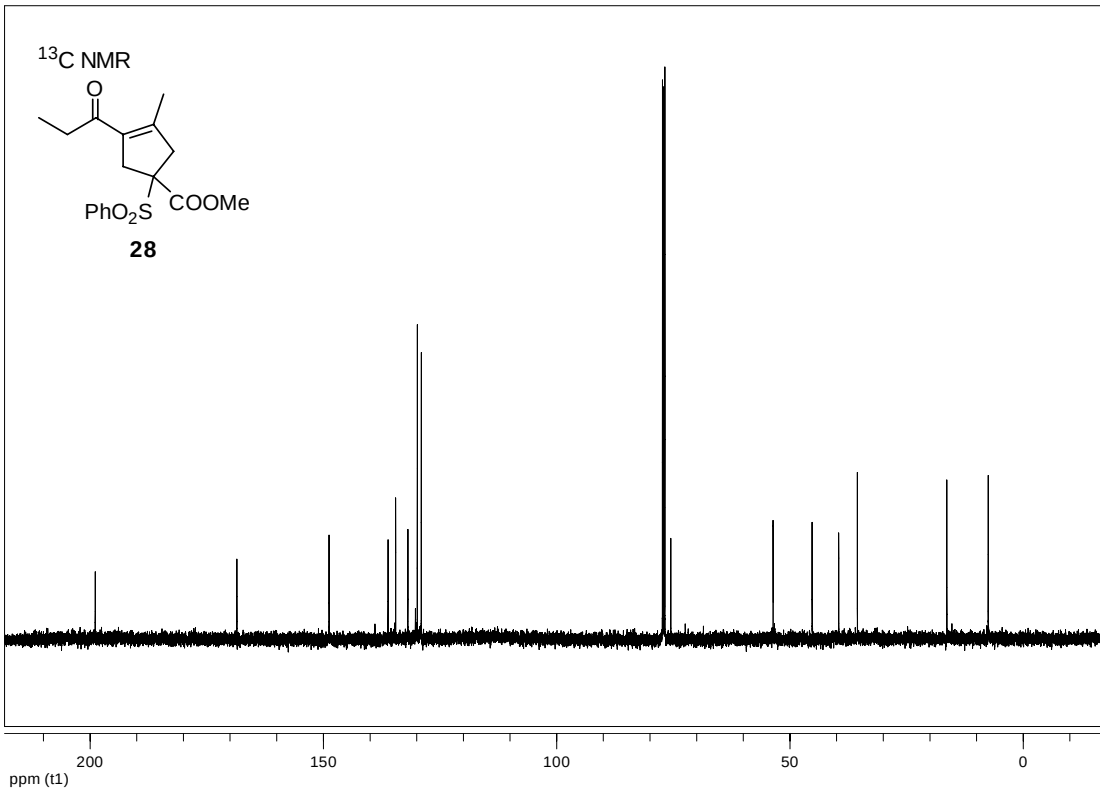
5.1.14. Compound **27**



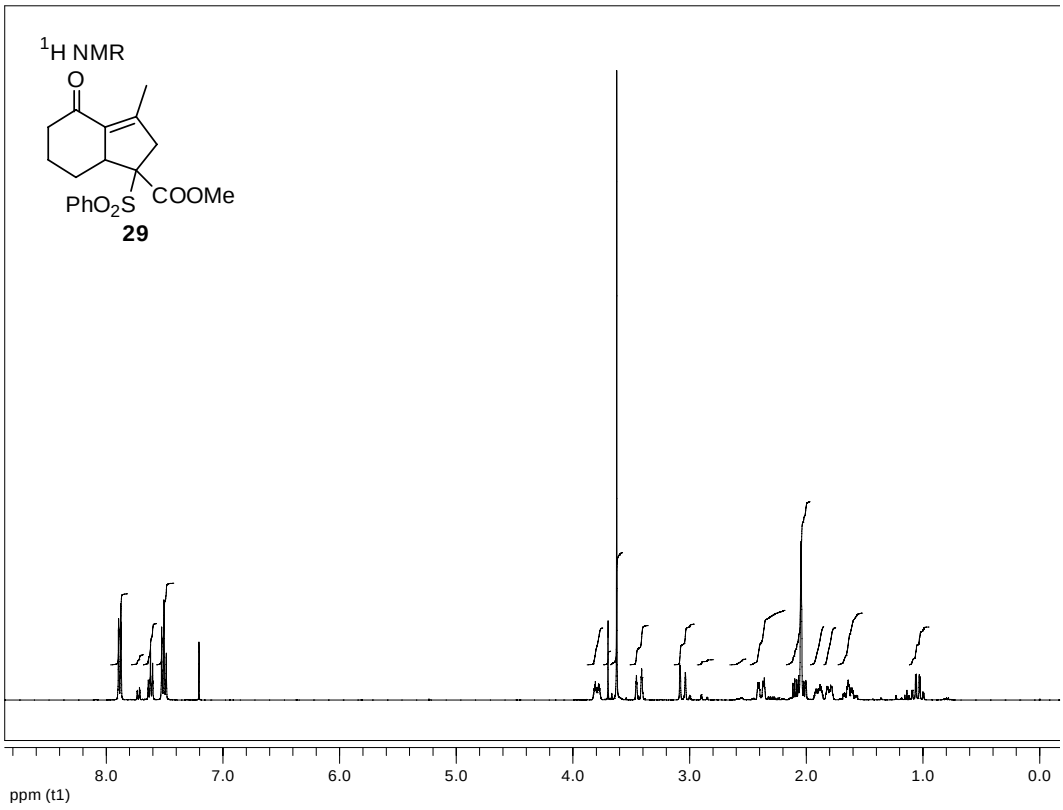


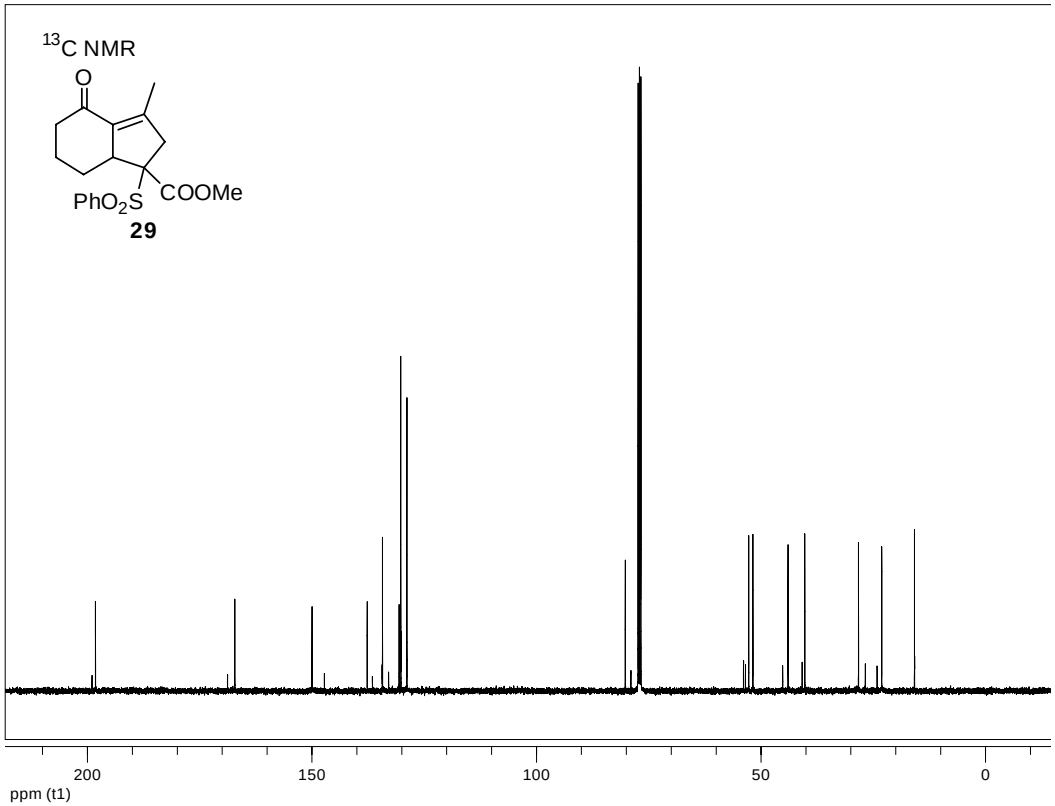
5.1.15. Compound **28**



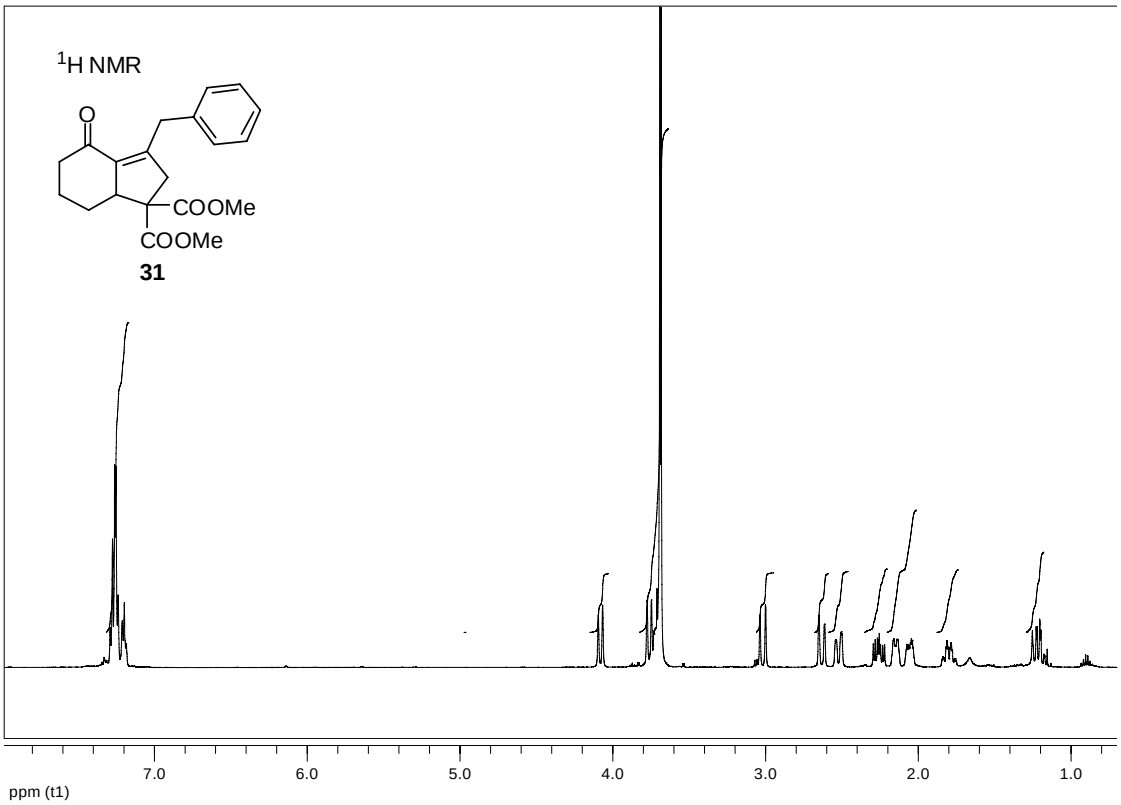


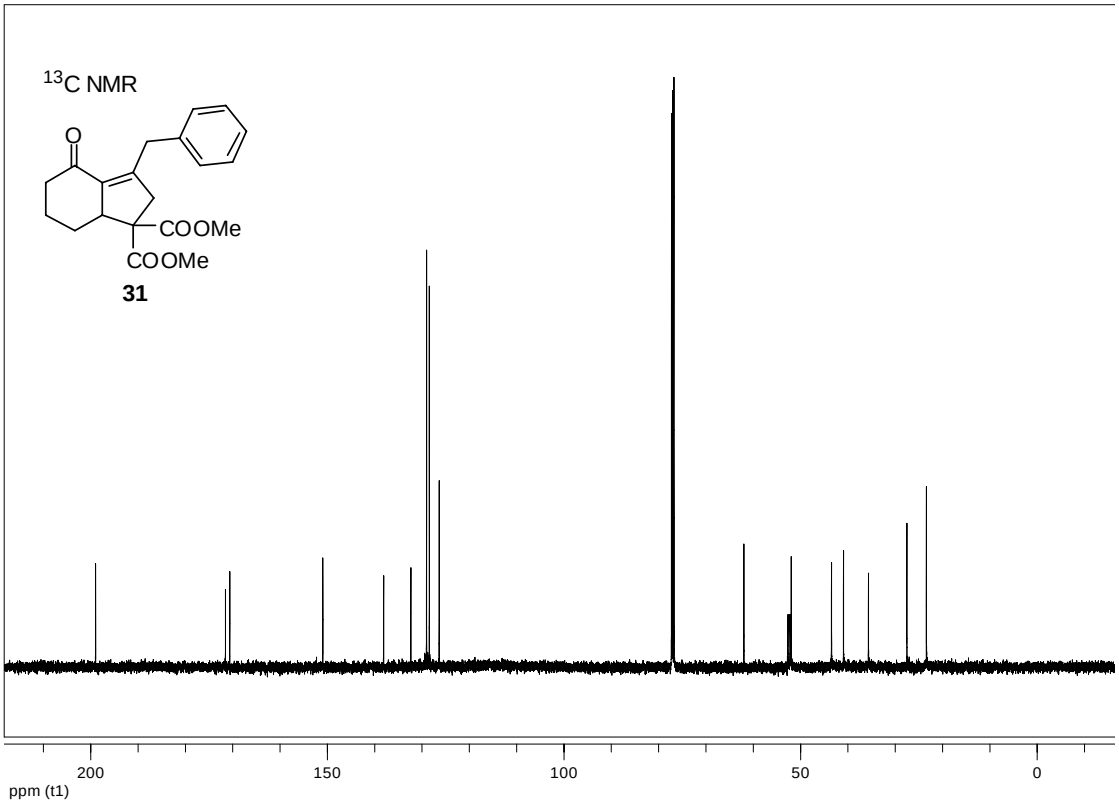
5.1.16. Compound **29**





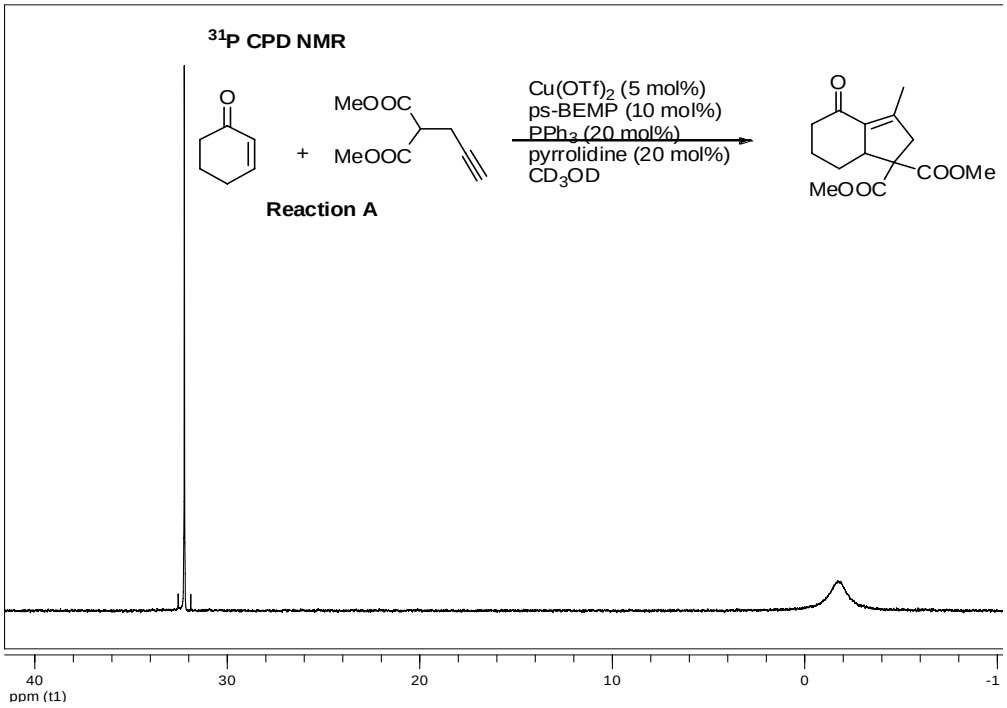
5.1.17. Compound **31**



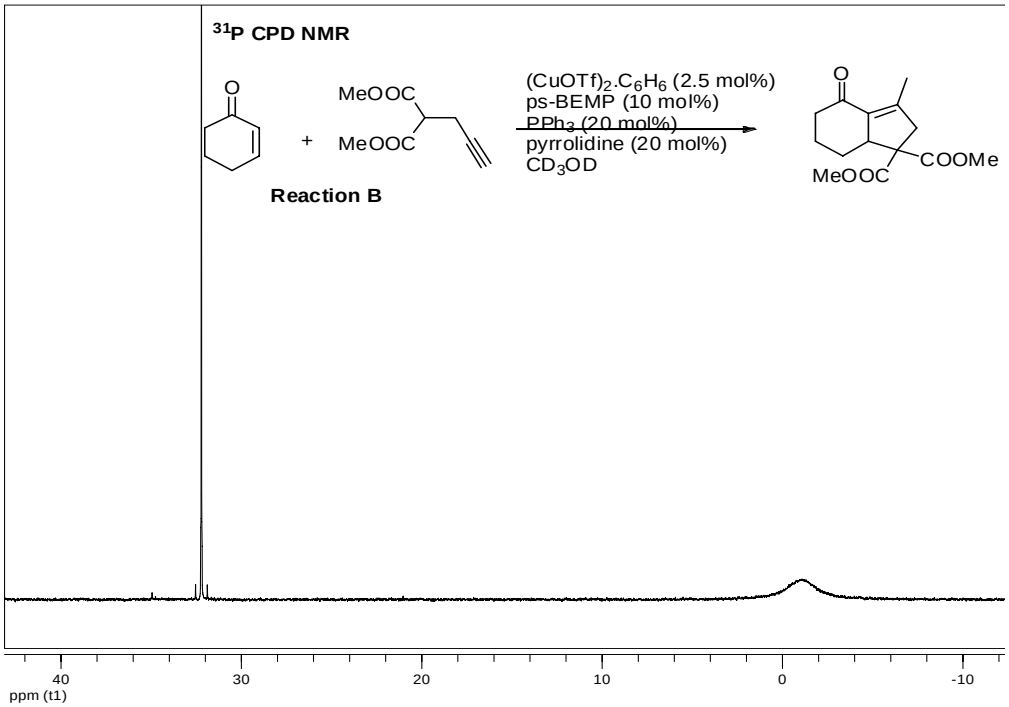


5.2. Mechanism study

5.2.1. ^{31}P NMR of reaction A



5.2.2. ^{31}P NMR of reaction B



5.2.3. ^{31}P NMR of a mixture of reaction A and reaction B