Supplementary Material (ESI) for Chemical Communications

Supporting information for

Anticancer Pt Complexes as non-Innocent Compounds for Catalysis in Aqueous Media**

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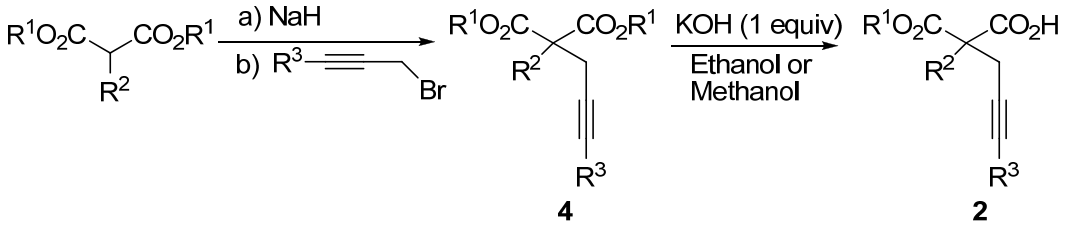
Contents

General Methods. NMR spectra were acquired on a Bruker 300 spectrometer, running at 300 and 75 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). ^{13}C NMR spectra were acquired on a broad band decoupled mode. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ dip. Purification of reaction products was carried out by flash chromatography (FC) using silica 60 A C_C 35-75 μm (SDS VOTRE PARTENAIRE CHIMIE).

Materials. The following compounds were synthesized according to literature procedures: (a) *trans* Pt(II) complexes[1] **1a**, **1k**, **1l**, **1m** and **1n;** (b) *cis* Pt(II)[2] complexes **1b**, **1c** and **1d;** (c) *cis* Pt(II)[3] complex with asymmetric amines **1j;** (d) *trans* Pt(IV)[4] complexes **1e**, **1f**, **1g** and **1h.**

Commercially available starting materials and solvents were used without further purification. The synthesis of alkyne-acids derivatives were also carried out following methods described in the literature (see Scheme SI-1).[5] The synthesis of the starting alkynyl malonates derivatives (**4d-e** and **4g-j**) were described before in the literature.[5]

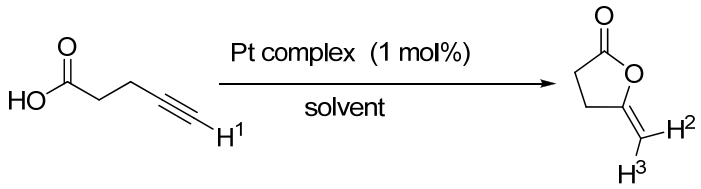


Scheme SI-1

Blood samples were obtained from patients that agreed to have their blood used for scientific purposes through signed consent. Blood was drawn from an arm vein into Vacutainer tubes containing EDTA (final concentration, 1.5 mg/ml). Samples were centrifuged immediately (15 min, 3.000 rpm, 4C). Plasma was collected by aspiration, and samples were immediately immersed in crushed ice. Plasma samples (1.5 ml aliquots) were frozen.

[1] González-Vadillo, A. M.; Álvarez-Valdés, A.; Moneo, V.; Blanco, F.; Díaz, R. G.; Carnero, A.; Navarro-Ranninger, C. *J. Inor. Biochem.* **2007**, *101*, 551.
[2] Cini, R., Donati, A., Giannettoni R. *Inorganica Chimica Acta* **2001**, *315* 73.
[3] Pantoja, E., Álvarez-Valdés, A., Pérez J. M., Navarro-Ranninger C., Reedijk J. *Inorganica Chimica Acta* **2002**, *339*, 525.
[4] Pérez, J. M.; Kelland, L. R.; Montero, E. I.; Boxall, F. E.; Fuertes, M. A.; Alonso, C.; Navarro-Ranninger, C. *Molecular Pharmacology* **2003**, *63*, 933.
[5] Genin E., Toullec P. Y., Marie P., Antoniotti S., Brancour C., Genêt J-P., Michelet V. *Arkivoc* **2007**, *(v)*, 67.

Kinetic studies. After addition of alkyne acid to a solution of the corresponding catalyst **1**, an aliquot of the reaction medium was taken periodically, and checked by ^{1}H NMR. Sampling intervals were 1, 3, 5, 10 and 19 hours. The conversion percentage was calculated by measuring the olefinic proton (H^2 and H^3) versus acetylenic proton (H^1) (Scheme SI-2).

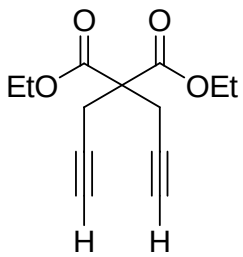


2a **3a**

Scheme SI-2

Experimental Procedures and Characterizations.

General Procedure for alkylation reaction of malonates. Under an argon inert atmosphere, NaH (1.1 eq.) was added portion wise at 0 °C to a solution of the corresponding malonate (1 eq.) in anhydrous THF. The mixture was allowed to warm to room temperature and the corresponding propargyl bromide was added. After the completion of the reaction (which is followed by TLC), the reaction was quenched with water, extracted with Et_2O and the organic phase were dried with anhydrous $MgSO_4$ and organic solvent eliminated under reduced pressure.



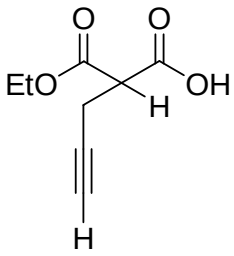
4f

Diethyl 2,2-di(prop-2-ynyl)malonate (4f).[6] The product was directly obtained following the standard procedure, starting from the commercial avariable diethyl propargylmalonate as yellow oil (70% yield) without further purification. The spectroscopical data is in accordance with the previously described compound.[6] ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.24 (q, *J* = 7.1 Hz, 4H), 2.99 (d, *J* = 2.52 Hz, 4H), 2.02 (s, 2H), 1.26 (t, *J* = 7.0 Hz, 6H).

General Procedure for the mono-hydrolysis of the substituted malonates. Under inert atmosphere (Ar) a solution of KOH (1.2 eq., M = 56) in anhydrous methanol or ethanol was added to a solution of substrate (1 eq). The mixture was stirred at room temperature for 18 hours. Then the reaction mixture was extracted with Et_2O and washed three times with aqueous saturated sodium bicarbonate. The aqueous

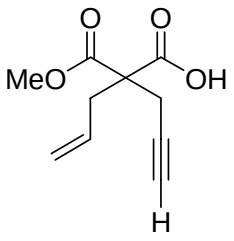
[6] Singh, Rajendra K. *Synthesis* **1985**, 54.

phase was acidified to pH=1 with concentrated HCl and then extracted with Et_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure, obtaining pure acid compounds.



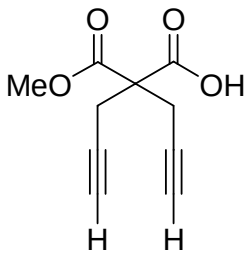
2d

2-(Methoxycarbonyl)pent-4-ynoic acid (2d).[7] The product was directly obtained following the standard procedure, starting from the commercial avariable dimethyl propargylmalonate and ethanol as solvent, as yellow oil (69% yield) without further purification). The spectroscopical data is in accordance with the previously described compound.[7] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.1-4.4 (bs, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.61 (t, *J* = 7.5 Hz, 1H), 2.81 (dt, *J* = 7.5 Hz, 2.5 Hz, 2H), 2.04 (t, *J* = 2.5 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H).



2e

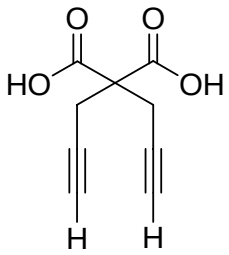
2-(Methoxycarbonyl)-2-(prop-2-ynyl)pent-4-enoic acid (2e). The product was directly obtained following the standard procedure using diethyl allylmalonate and propargyl bromide as colourless oil (77% yield) without further purification). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60-7.40 (bs, 1H), 5.65-5.51 (m, 1H), 5.17-5.06 (m, 2H), 3.70 (s, 3H), 2.73 (s, 4H), 2.00 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 170.1, 131.3, 120.2, 78.5, 71.8, 56.9, 53.0, 36.6, 22.7. MS (TOF ES^+): $[M+Na]^+$ calcd for $C_{10}H_{12}NaO_4$ 219.0627; found 219.0616.



2f

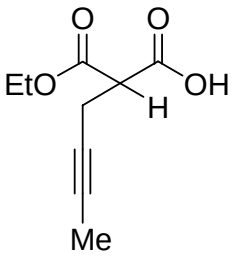
2-(Methoxycarbonyl)-2-(prop-2-ynyl)pent-4-ynoic acid (2f).[8] The product was directly obtained following the standard procedure and was described before,[8] starting from **4f** and 1.2 equivalents of KOH after 24 hours (69% yield) without further purification). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50-8.88 (bs, 1H), 3.82 (s, 3H), 3.00 (s, 4H), 2.06 (s, 2H).

[7] F. Neatu, Z. Li, R: Richards, P. Toullec, J.-P. Genet, K. Dumbuya, J. M. Gottfried, H.-P. Steinrueck, Hans, V. Parvulescu, V. Michelet, *Chem. Eur. J.* **2008** *14*, 9412.
[8] a) E. Genin, P. Y. Toullec, S. Antoniotti, C. Brancour, J.-P. Genet, V. Michelet *J. Am. Chem. Soc.* **2006**, 128, 3112; b) See also reference 5.



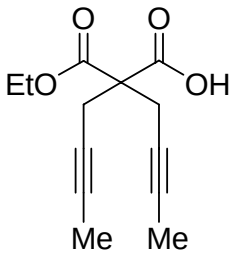
2g

2,2-Di(prop-2-ynyl)malonic acid (2g). [9] The product was directly obtained following the standard procedure and was described before,[9] starting from **4f** and 5 equivalents of KOH after 24 hours (51% yield) without further purification). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80-3.70 (bs, 2H), 3.02 (s, 4H), 2.10 (s, 2H).



2h

2-(Ethoxycarbonyl)hex-4-ynoic acid (2h). The product was directly obtained following the standard procedure as colourless oil (81% yield) without further purification). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.91-9.80 (bs, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.50 (t, *J* = 7.6 Hz, 1H), 2.68-2.66 (m, 2H), 1.68 (t, *J* = 2.3 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 168.2, 78.2, 74.3, 62.0, 51.4, 18.8, 14.0, 3.4. MS (TOF ES$^+$): $[M+Na]^+$ calcd for $C_9H_{12}NaO_4$ 207.0627; found 207.0616.

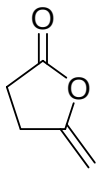


2i

2-(But-2-ynyl)-2-(ethoxycarbonyl)hex-4-ynoic acid (2i). The product was directly obtained following the standard procedure as white solid (70% yield) without further purification). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.44-9.23 (bs, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 2.84 (s, 4H), 1.68 (s, 6H), 1.21 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 169.2, 79.2, 72.9, 62.1, 57.1, 23.1, 13.9, 3.4. MS (TOF ES$^+$): $[M+Na]^+$ calcd for $C_{13}H_{16}O_4Na$ 259.0940; found 259.0937.

General Procedure for the alkyne-acid cyclization in aqueous media. In a ordinary vial the corresponding alkyne acid (0.2 mmol) was added to a stirred solution of catalyst **1** (1 mol%, 0.002 mmol) in 0.2 mL of water. After complete consumption of the alkyne acid (usually 6-10 hours, as monitored by ^{1}H NMR spectroscopy), the reaction mixture was extracted with 2x5 mL of CH_2Cl_2. The organic phase was dried with anhydrous Na_2SO_4 and finally the product was purified following the procedure indicated in each case.

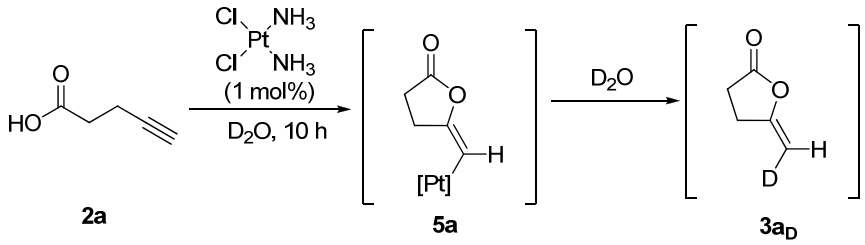
[9] Wakabayashi, T.; Ishi, Y.; Ishikawa, K.; Hida, M. *Angew. Chem. Int. Ed.* **1996**, *35*, 2123.



3a

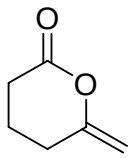
(*rac*)-Dihydro-5-methylenefuran-2(3H)-one (3a). [10] The product was directly obtained following the standard procedure using the catalyst indicated in Table 1 as yellow oil (70% yield) after FC (5:1 hexane:EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (d, *J* = 2.2 Hz, 1H), 4.26 (d, *J* = 2.2 Hz, 1H), 2.85-2.79 (m, 2H), 2.63-2.57 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 155.6, 88.4, 27.8, 24.9 MS (TOF ES$^+$): $[M]^+$ calcd for $C_5H_6O_2$ 98.0368; found 98.0373.

(*rac*)-Tetrahydro-5-(Deuteriummethylene)furan-2-one ($3a_D$).



2a **5a** **$3a_D$**

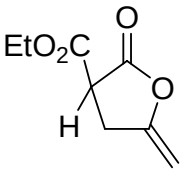
The product was directly obtained following the standard procedure using catalyst *cis*-platin (**1j**) D_2O as solvent (91% yield) without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (s, 1H), 2.85 (t, *J* = 8.4 Hz, 2H), 2.63 (t, *J* = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 155.8, 88.5, 88.2 (t, *J* = 24.7 Hz), 27.9, 25.0.



3b

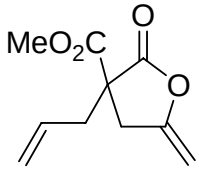
(*rac*)-6-Methylenetetrahydropyran-2-one (3b). The product was directly obtained following the standard procedure with catalyst **1b** as white solid (73% yield)[11] without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (s, 1H), 4.23 (s, 1H), 2.56 (t, *J* = 6.8 Hz, 2H), 2.42 (t, *J* = 6.4 Hz, 2H), 1.81 (qt, *J* = 6.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 155.3, 93.7, 30.3, 26.7, 18.5. MS (TOF ES$^+$): $[M]^+$ calcd for $C_6H_8O_2$ 112.0524; found 112.0521.

[10] Amos, R. A.; Katzenellenbogen, J. A. *J. Org. Chem.* **1978**, *43,* 560.
[11] Yield is based on recovered material.



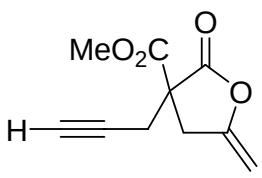
3d

(*rac*)-Ethyl tetrahydro-5-methylene-2-oxofuran-3-carboxylate (3d). The product was directly obtained following the standard procedure with catalyst **1c** as yellow oil (75% yield) without further purification). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.74 (dd, *J* = 4.6, 2.4 Hz, 1H), 4.34-4.32 (m, 1H) 4.19 (q, *J* = 7.0 Hz, 2H), 3.67 (dd, *J* = 10.3, 7.6 Hz, 1H), 3.21 (ddt, *J* = 16.6, 9.7, 2.2, 1H), 3.01 (ddt, *J* = 16.6, 10.4, 1.6 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 166.9, 153.2, 89.7, 62.5, 46.4, 29.4, 14.0. MS (TOF ES$^+$): $[M+Na]^+$ calcd for $C_8H_{10}NaO_4$ 193.0471; found 193.0461.



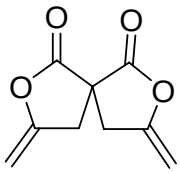
3e

(*rac*)-Methyl (3-allyl-5-methylene-2-oxotetrahydrofuran)-3-carboxylate (3e). The product was directly obtained following the standard procedure with catalyst **1c** as yellow oil (51% yield) without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70-5.56 (m, 1H), 5.14 (d, *J* = 11.7 Hz, 1H), 5.12 (d, *J* = 14.4 Hz, 1H), 4.72 (d, *J* = 2.2 Hz, 1H), 4.30 (d, *J* = 2.1 Hz, 1H), 3.72 (m, 3H), 3.22 (dt, *J* = 16.7, 1.7 Hz, 1H), 2.84 (dt, *J* = 16.7, 1.8 Hz, 1H), 2.75-2.67 (m, 1H), 2.60 (dd, *J* = 14.0, 7.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 169.3, 152.6, 131.0, 121.1, 89.6, 54.9, 53.4, 38.2, 34.4. MS (TOF ES$^+$): $[M]^+$ calcd for $C_{10}H_{12}O_4$ 196.0736; found 196.0739.



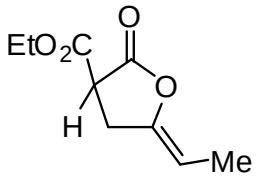
3f

(*rac*)-Methyl tetrahydro-5-methylene-2-oxo-3-(prop-2-ynyl)furan-3-carboxylate (3f). The product was directly obtained following the standard procedure with catalyst **1c** as yellow oil (73% yield) without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.81 (d, *J* = 2.0 Hz, 1H), 4.40 (d, *J* = 2.0 Hz, 1H), 3.77 (s, 3H), 3.30 (d, *J* = 16.7 Hz, 1H), 3.18 (d, *J* = 16.7 Hz, 1H), 2.87 (d, *J* = 2.5 Hz, 2H), 2.07 (t, *J* = 2.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 168.4, 152.4, 89.7, 72.3, 54.4, 53.6, 34.6, 23.7. MS (TOF ES$^+$): $[M+Na]^+$ calcd for $C_{10}H_{10}NaO_4$ 217.0471; found 217.0457.



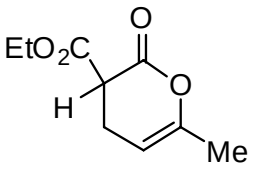
3g

Dihydro-5-methylenefuran-2(3H)-one-3-spiro-dihydro-5´-methylenefuran-2´(3H)-one (3g). The product was directly obtained following the standard procedure with catalyst **1c** as white solid (84% yield) without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.87 (d, *J* = 3.0 Hz, 1H), 4.44 (d, *J* = 3.0 Hz, 1H), 3.39 (d, *J* = 15.3 Hz, 1H), 2.88 (d, *J* = 15.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 151.3, 91.1, 51.9, 36.5. MS (TOF ES$^+$): $[M+Na]^+$ calcd for $C_9H_8NaO_4$ 203.0314; found 203.0304.



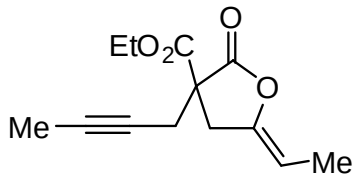
3h

(*rac*)-Ethyl 5-ethyliden-2-oxotetrahydrofuran-3-carboxylate (3h).[12] The product was directly obtained following the standard procedure with catalyst **1b** as inseparable mixture with compound **3h´** (70% combined yield) without further purification). Isomers were identified by comparison with the literature[12] and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (tq, *J* = 6.9, 1.5 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.68 (dd, *J* = 10.3, 7.9 Hz , 1H), 3.20 (ddt, *J* = 16.0, 7.8, 2.0 Hz, 1H), 3.00 (ddt, *J* = 16.0, 10.4, 1.5 Hz, 1H), 1.66 (dt, *J* = 6.9, 1.6 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 167.2, 145.9, 100.3, 62.4, 46.4, 29.3, 14.0, 10.4. MS (TOF ES^+): $[M]^+$ calcd for $C_9H_{12}O_4$ 184.0736; found 184.0745.



3h´

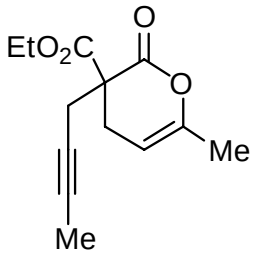
(*rac*)-Ethyl 6-methyl-2-oxo-3,4-dihydro-2H-pyran-3-carboxylate (3h´). The product was directly obtained following the standard procedure as inseparable mixture with compound **3h** (70% combined yield) without further purification.^{1}H NMR (300 MHz, $CDCl_3$) δ 5.00 (dt, *J* = 4.4, 0.7 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.52 (dd, *J* = 8.0, 7.0 Hz , 1H), 2.75-2.66 (m, 1H), 2.50-2.40 (m, 1H), 1.87 (d, *J* = 1.0 Hz, 3H), 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 165.3, 150.3, 98.6, 62.0, 45.6, 22.4, 18.4, 14.0. MS (TOF ES^+): $[M]^+$ calcd for $C_9H_{12}O_4$ 184.0736; found 184.0745.



3i

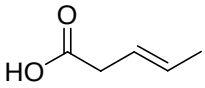
(*rac*)-Ethyl 3-(but-2-ynyl)-5-ehtylidene-2-oxotetrahydrofuran-3-carboxylate (3i).[11] The product was directly obtained with catalyst **1b** following the standard procedure as brown oil as inseparable mixture with compound **3i´**(59% combined yield) without further purification. Isomers were identified by comparison with the literature[11] and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.69 (tq, *J* = 6.9, 1.7 Hz, 1H), 4.22 (q, *J* = 7.0 Hz, 2H), 3.21 (dqt, *J* = 16.1, 1.6 Hz, 1H), 3.12 (dqt, *J* = 16.1, 2.0 Hz, 1H), 2.81 (qt, *J* = 2.4 Hz, 2H), 1.76 (t, *J* = 2.5 Hz, 3H), 1.70 (dt, *J* = 6.9, 1.8 Hz, 3H), 1.3 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 167.5, 144.6, 98.8, 78.6, 71.6, 61.5, 53.8, 33.8, 23.2, 12.9, 9.4, 2. MS (TOF ES^+): $[M+Na]^+$ calcd for $C_{13}H_{16}NaO_4$ 259.0940; found 259.0931.

[12] E. Genin, P. Y. Toullec, S. Antoniotti, C. Brancour, J.-P. Gent, V. Michelet *J. Am. Chem. Soc.* **2006**, 128, 3112;



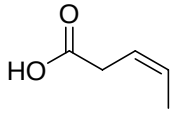
3i´

(*rac*)-Ethyl 3-(but-2-ynyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-3-carboxylate (3i´). The product was directly obtained following the standard procedure as brown oil as inseparable mixture with compound **3i** (59% combined yield) without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.02-5.00 (m, 1H), 4.23 (q, *J* = 7.0 Hz, 2H), 2.88 (q, *J* = 2.6 Hz, 2H), 2.76-2.69 (m, 2H), 1.87-1.86 (m, 3H), 1.74 (t, *J* = 2.5 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 165.5, 148.8, 98.2, 61.2, 77.9, 72.2, 51.2, 23.6, 21.8, 17.3, 12.9, 2.5. MS (TOF ES$^+$): $[M+Na]^+$ calcd for $C_{13}H_{16}NaO_4$ 259.0940; found 259.0931.



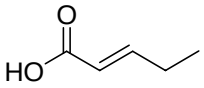
7b

(*E*)-Pent-3-enoic acid (7b).[13] The product was directly obtained with catalyst **1b** following the standard procedure as yellow oil as inseparable mixture with compound **7b'** and **7b''** (96% combined yield) without further purification. Isomers were identified by comparison with the literature[13] and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68-5.41 (m, 2H), 2.99 (d, *J* = 6.3 Hz, 2H), 1.64 (d, *J* = 5.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.9, 130.1, 122.0, 37.8, 17.9.



7b'

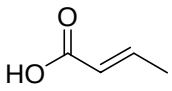
(*Z*)-Pent-3-enoic acid (7b').[14] The product was directly obtained with catalyst **1b** following the standard procedure as yellow oil as inseparable mixture with compound **7b** and **7b''**(96% combined yield) without further purification. Isomers were identified by comparison with the literature[14] and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68-5.41 (m, 2H), 3.08 (d, *J* = 6.9 Hz, 2H), 1.58 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 128.1, 121.0, 32.4, 12.9.



7b''

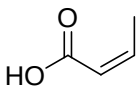
(*E*)-Pent-2-enoic acid (7b'').[15] The product was directly obtained with catalyst **1b** following the standard procedure as yellow oil as inseparable mixture with compound **7b** and **7b'** (96% combined yield) without further purification. Isomers were identified by comparison with the literature[15] and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 (dt, *J* = 15.6, 6.4 Hz, 1H), 5.75 (d, *J* = 15.6 Hz, 1H), 2.19 (qt, *J* = 6.8 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 153.8, 119.7, 25.4, 11.9.

[13] S˘mejkal T., Bernhard B. *Angew. Chem. Int. Ed* **2007**, *47* (2), 311-315.
[14] Ortiz, A.; Quesada, A.; Sanchez, A. *Journal of Chemical Ecology*, **2004**, 30 (5), 991-1000.
[15] MacPeek, D. L. *Journal of the American Chemical Society* **1959**, *81*, 680-683.



7a

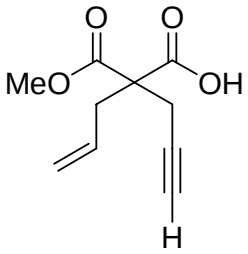
(*E*)-Buten-2-enoic acid (7a).[16] The product was directly obtained with catalyst **1b** following the standard procedure as brown oil as inseparable mixture with compound **7a'** (37% yield) without further purification. Isomers were identified by comparison with the literature[16] and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (dq, *J* = 15.5, 6.9 Hz, 1H), 5.92-5.75 (m, 1H), 1.84 (dd, *J* = 6.9, 1.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 147.6, 122.1, 18.1.



7a'

(*Z*)-Buten-2-enoic acid (7a').[16] The product was directly obtained with catalyst **1b** following the standard procedure as brown oil as inseparable mixture with compound **7a** (37% yield) without further purification. Isomers were identified by comparison with the literature and also by 2D-NMR experiments. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92-5.75 (m, 1H), 5.13 (d, *J* = 12.1 Hz, 1H), 3.06 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 129.7, 119.0, 18.1.

[16] Jasicka-Misiak I., Wieczorek, P. P., Kafarski P. *Phytochemistry*, **2005**, *66*, 1485–1491.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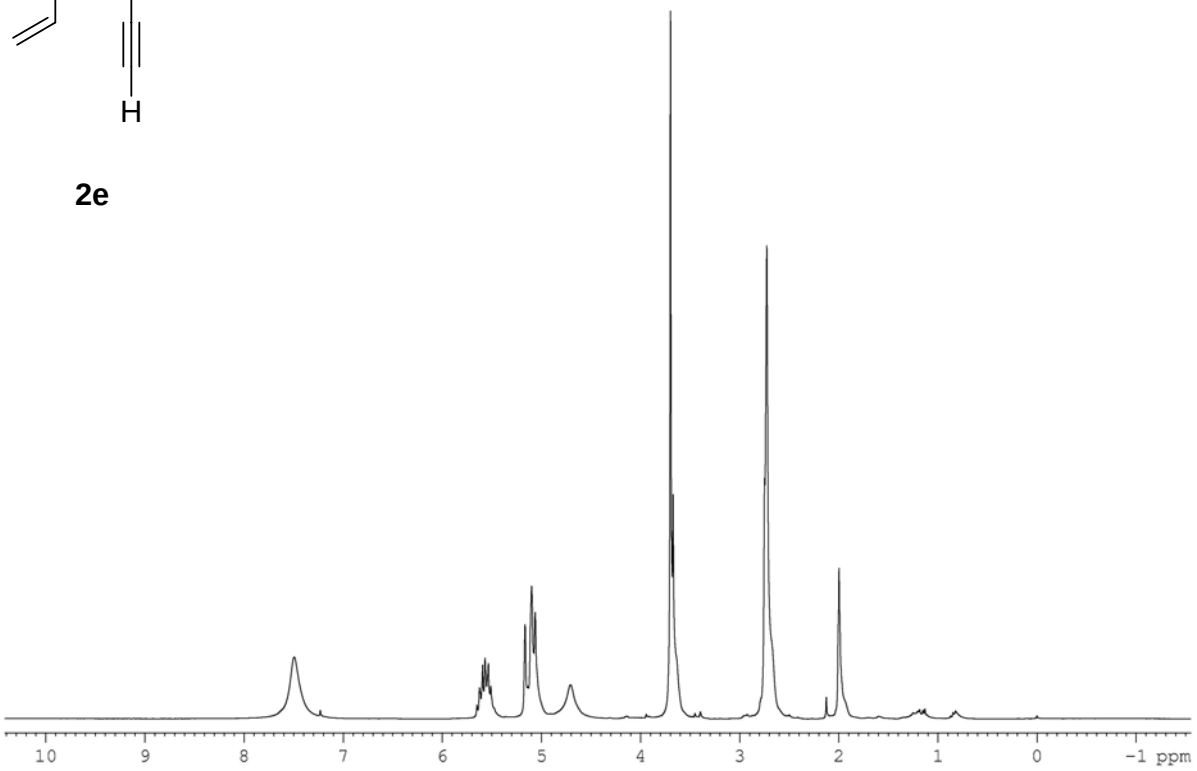
OH
H

2e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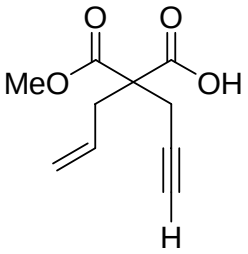
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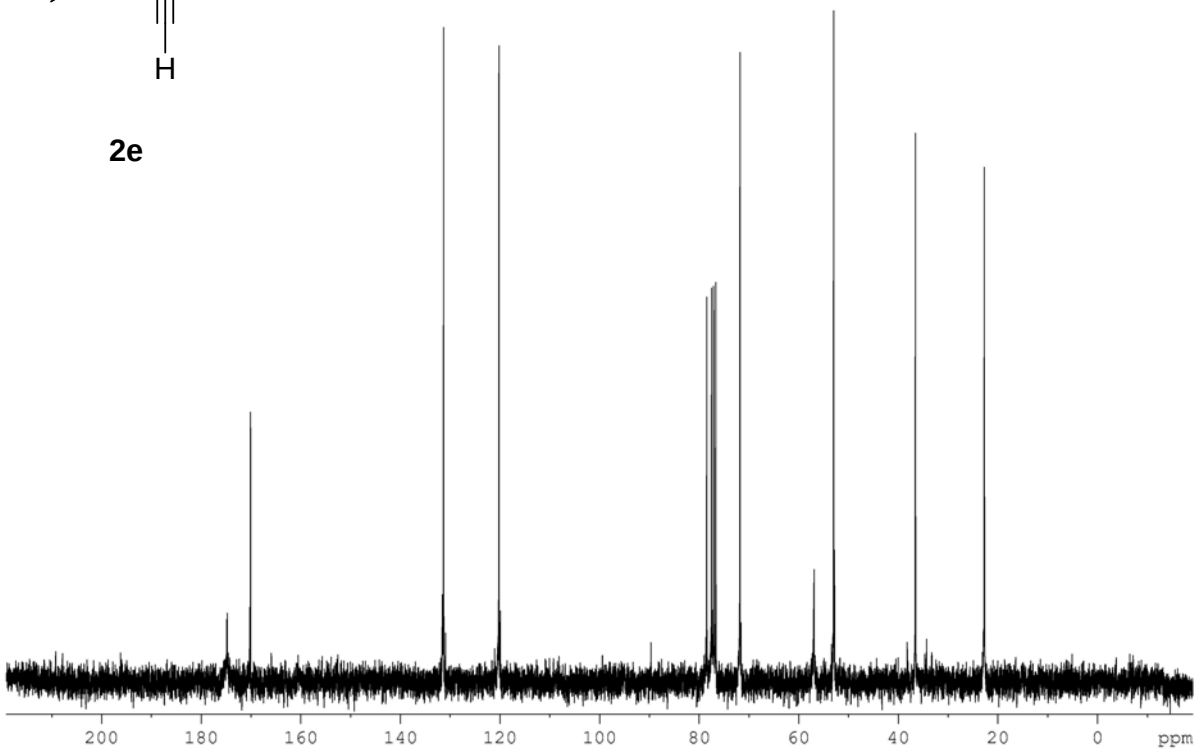
2e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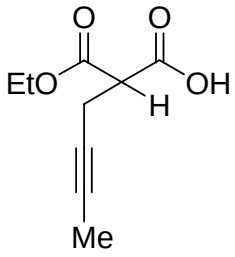
ppm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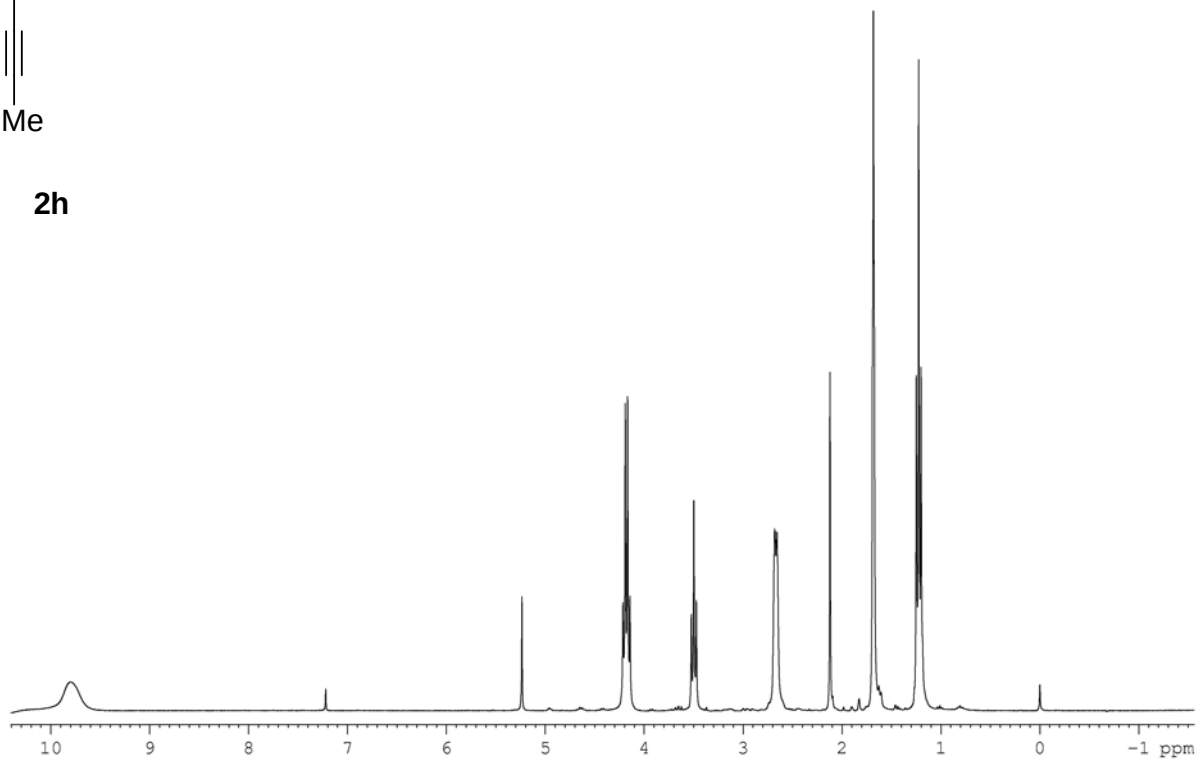
H
Me

2h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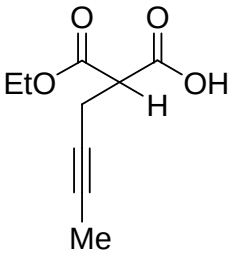
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OH
H
Me

2h

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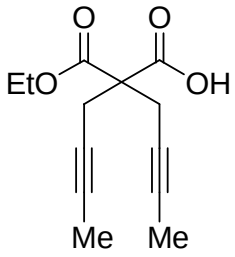
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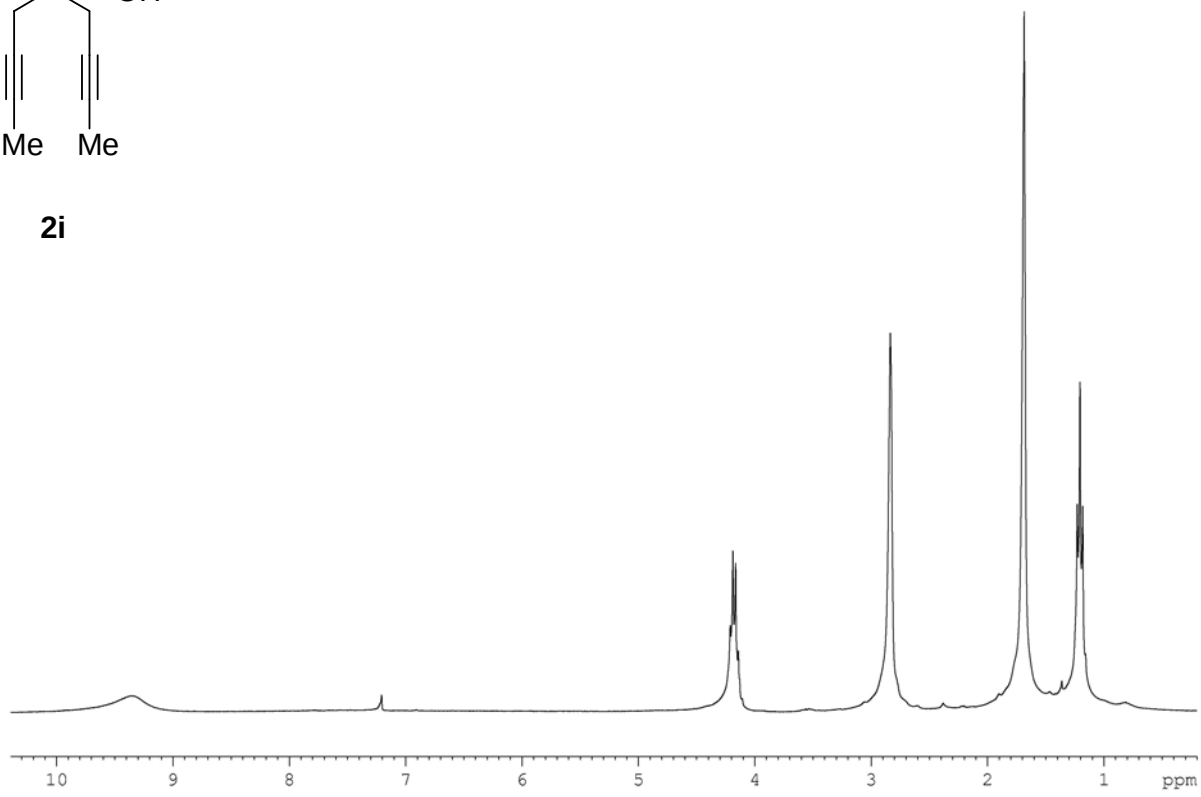
Me
Me

2i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3
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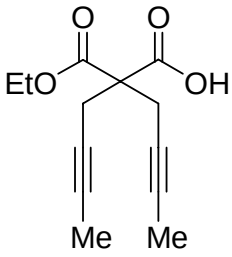
ppm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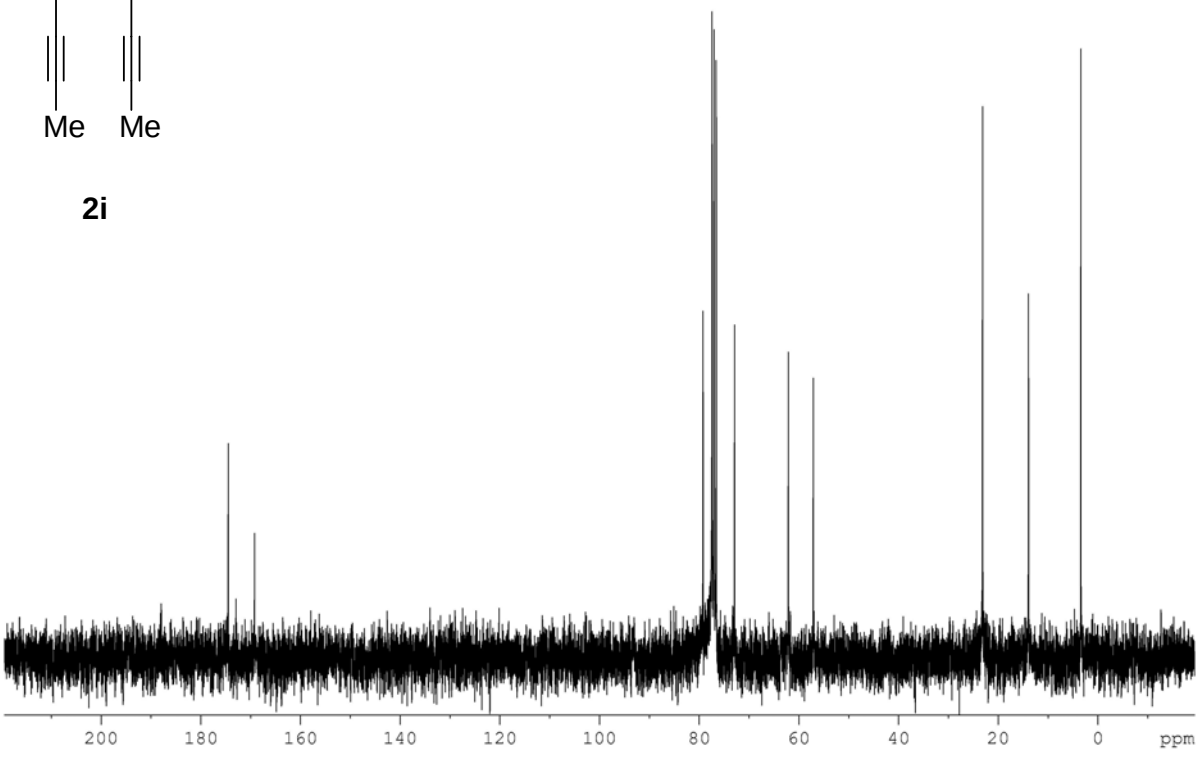
OH
Me
Me

2i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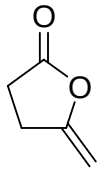

3a

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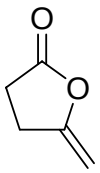

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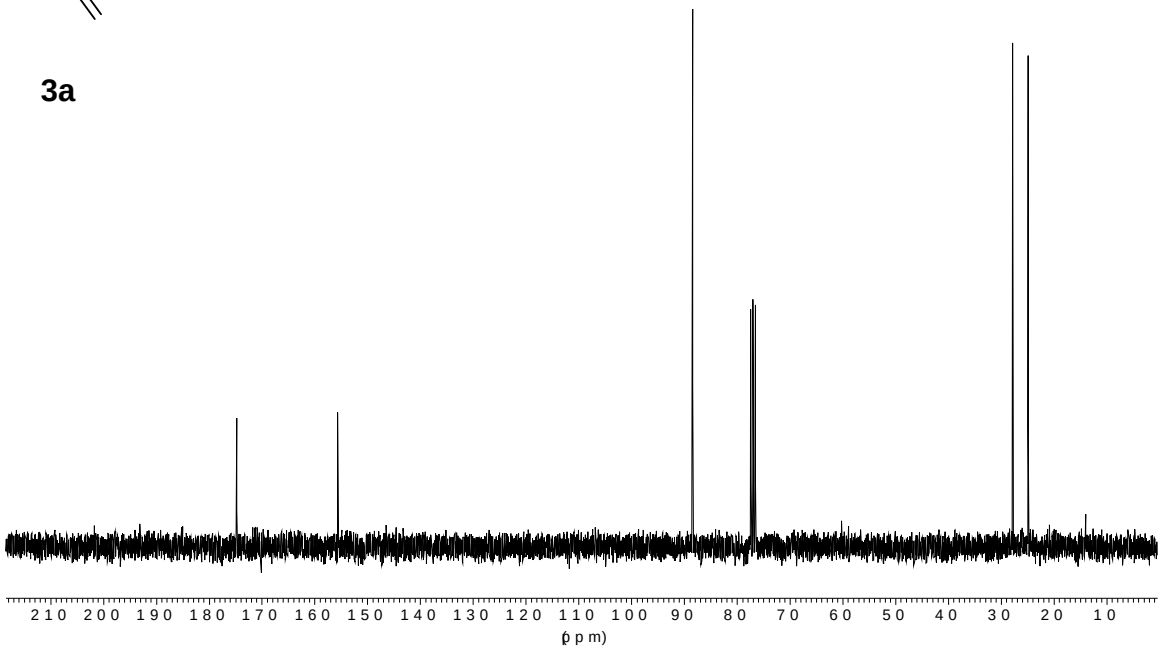
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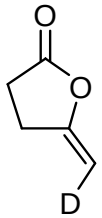
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D

3a$_D$

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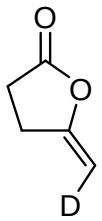
(ppm)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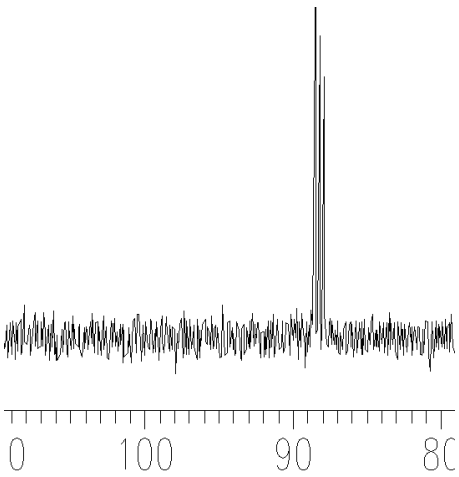
O
D

3a$_D$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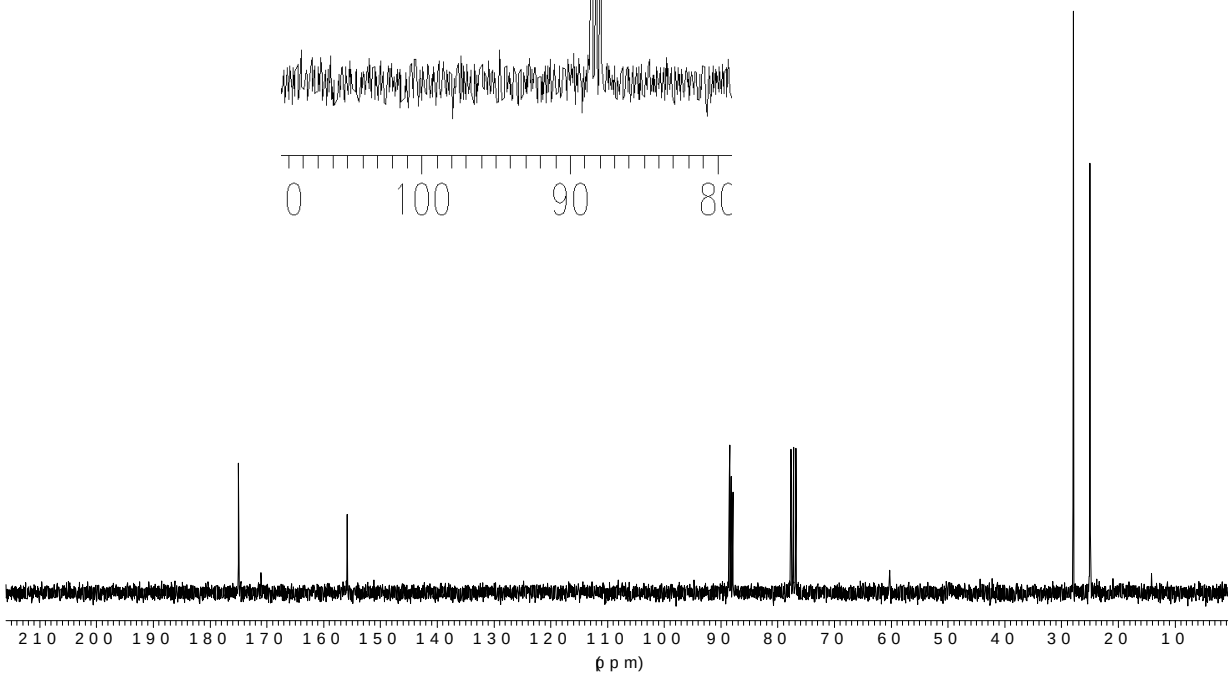
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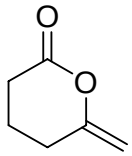

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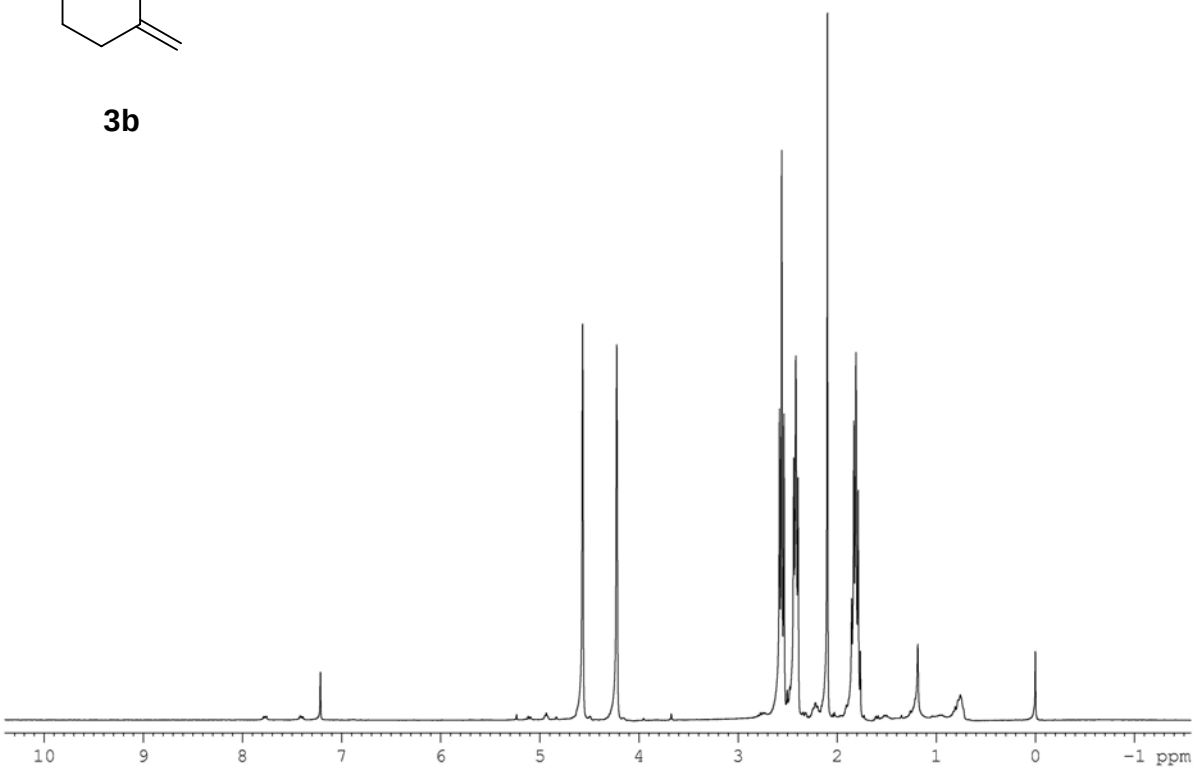
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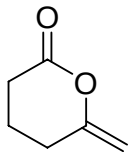

3b

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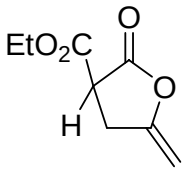
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H

3d

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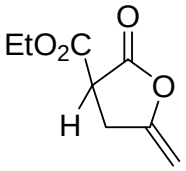
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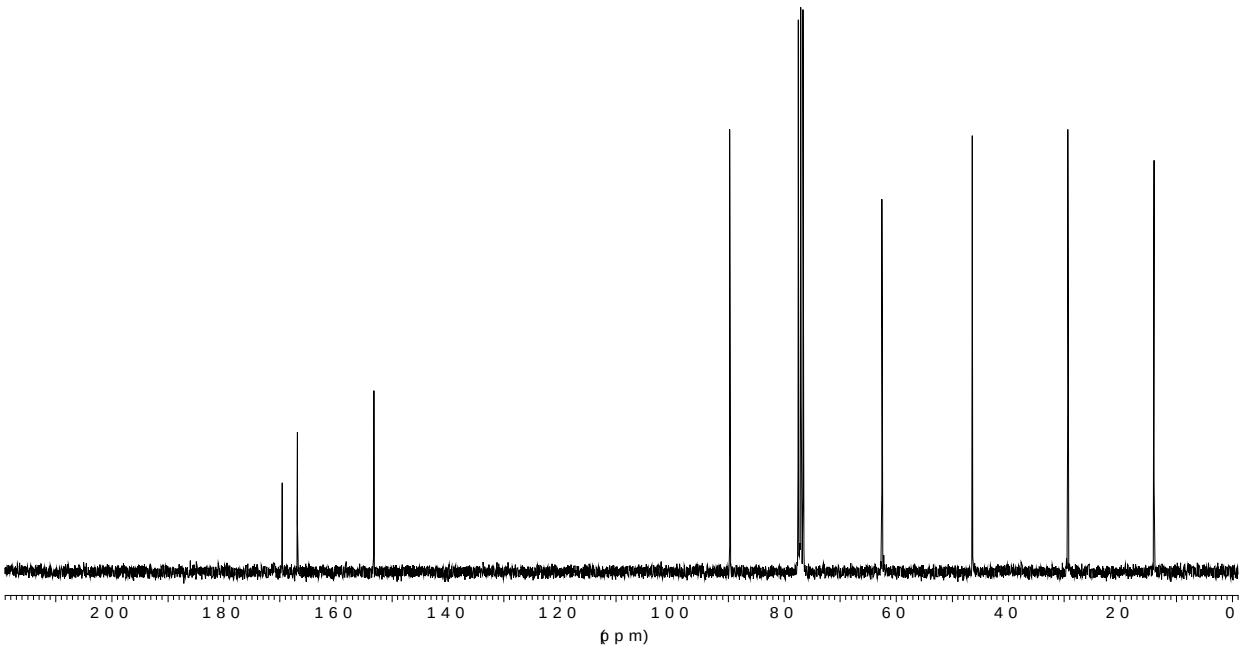
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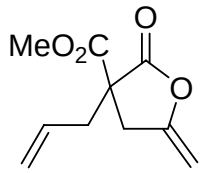
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3e

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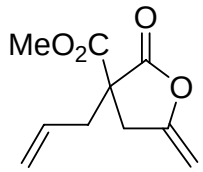
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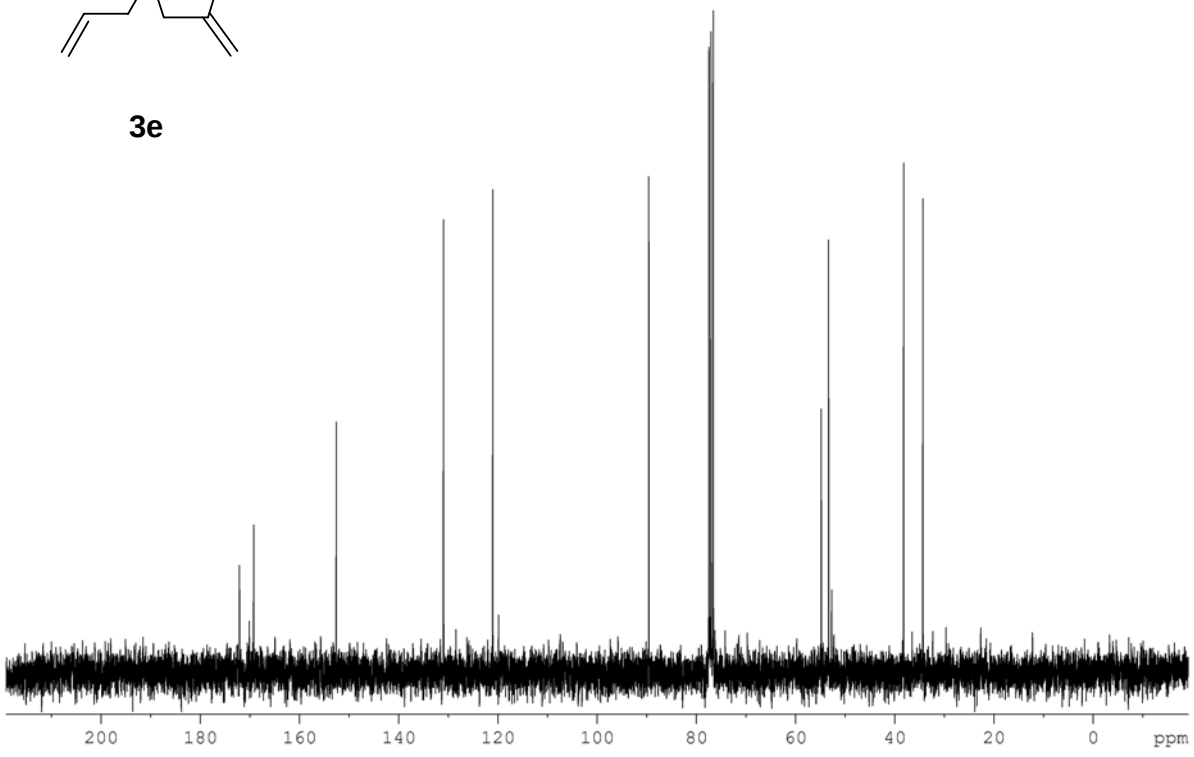
3e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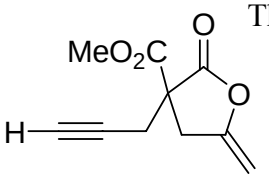
MeO2C
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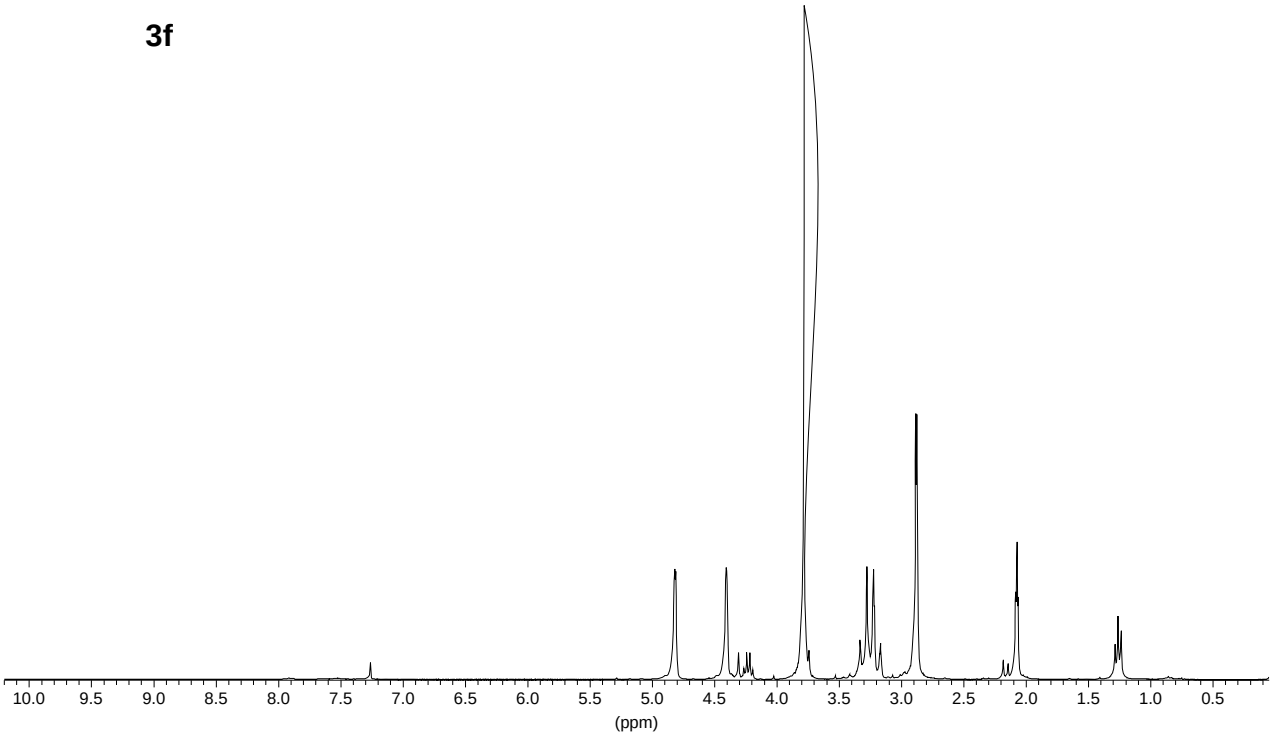
O
H

3f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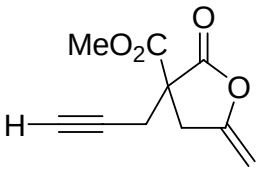
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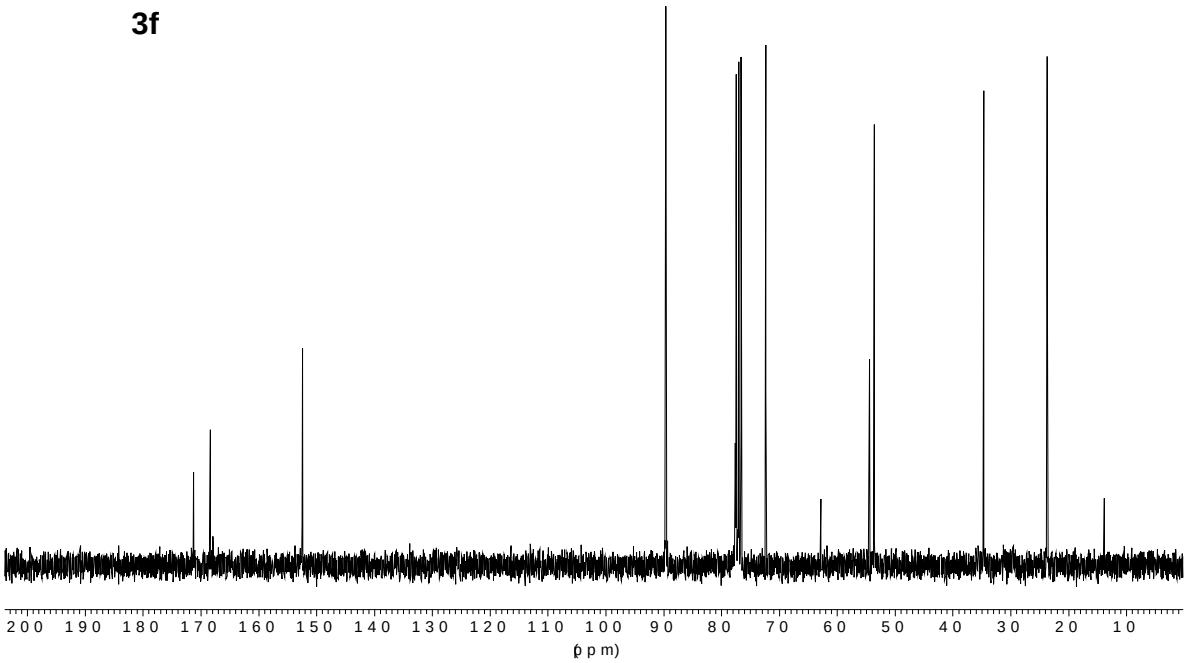
3f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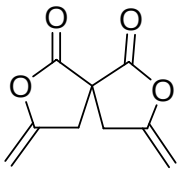
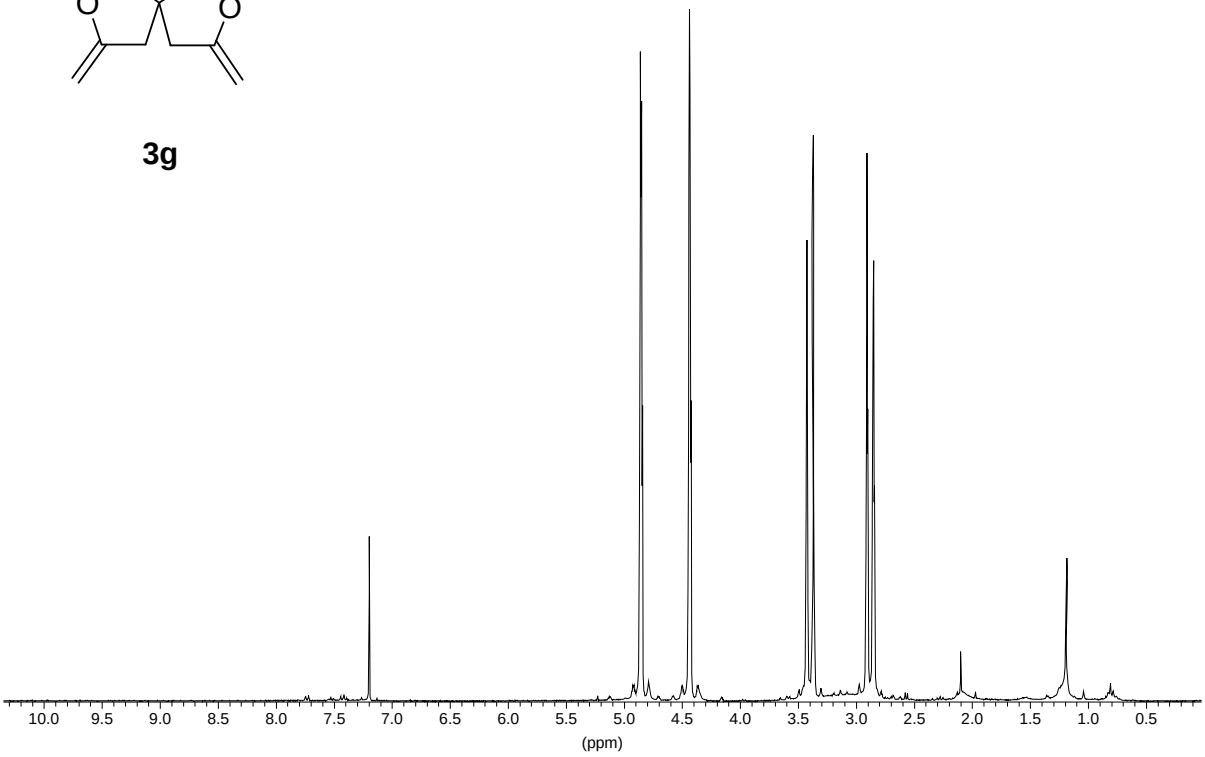
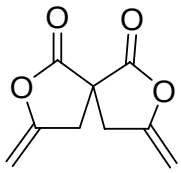
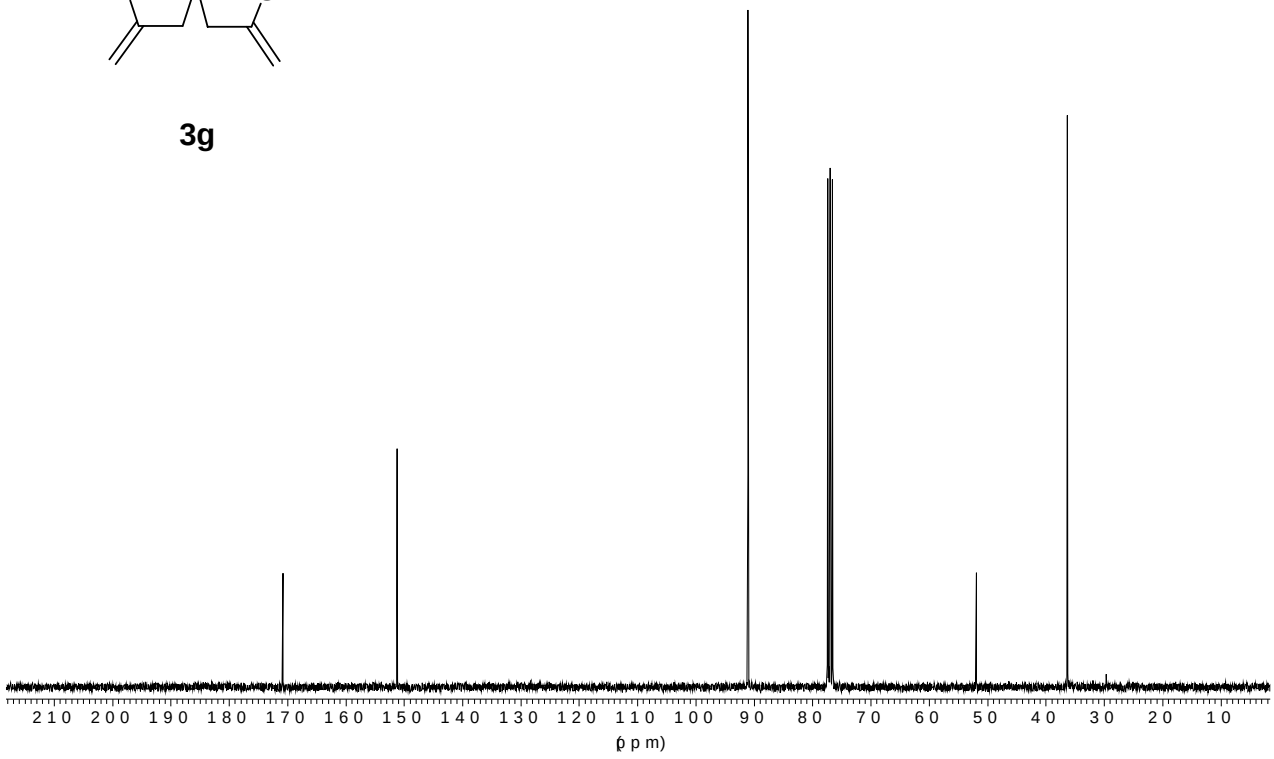


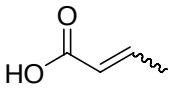
3g


10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

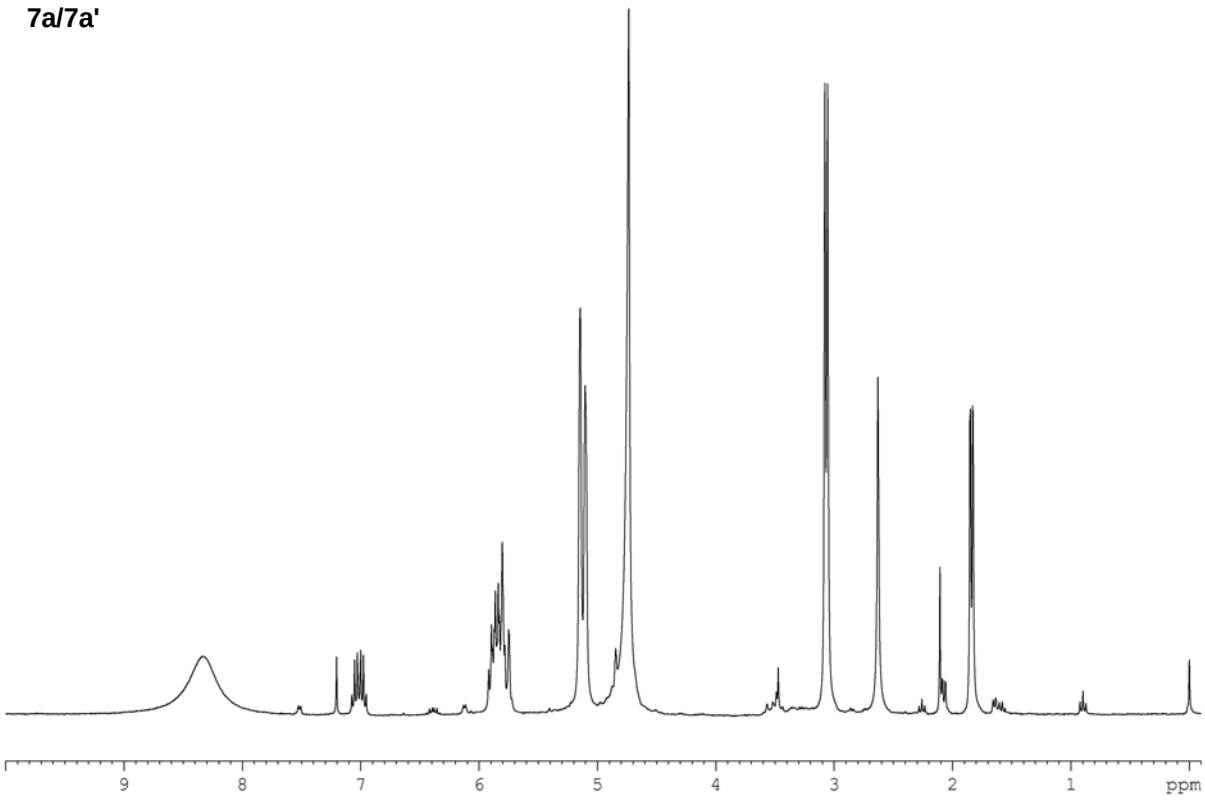


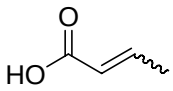
3g


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

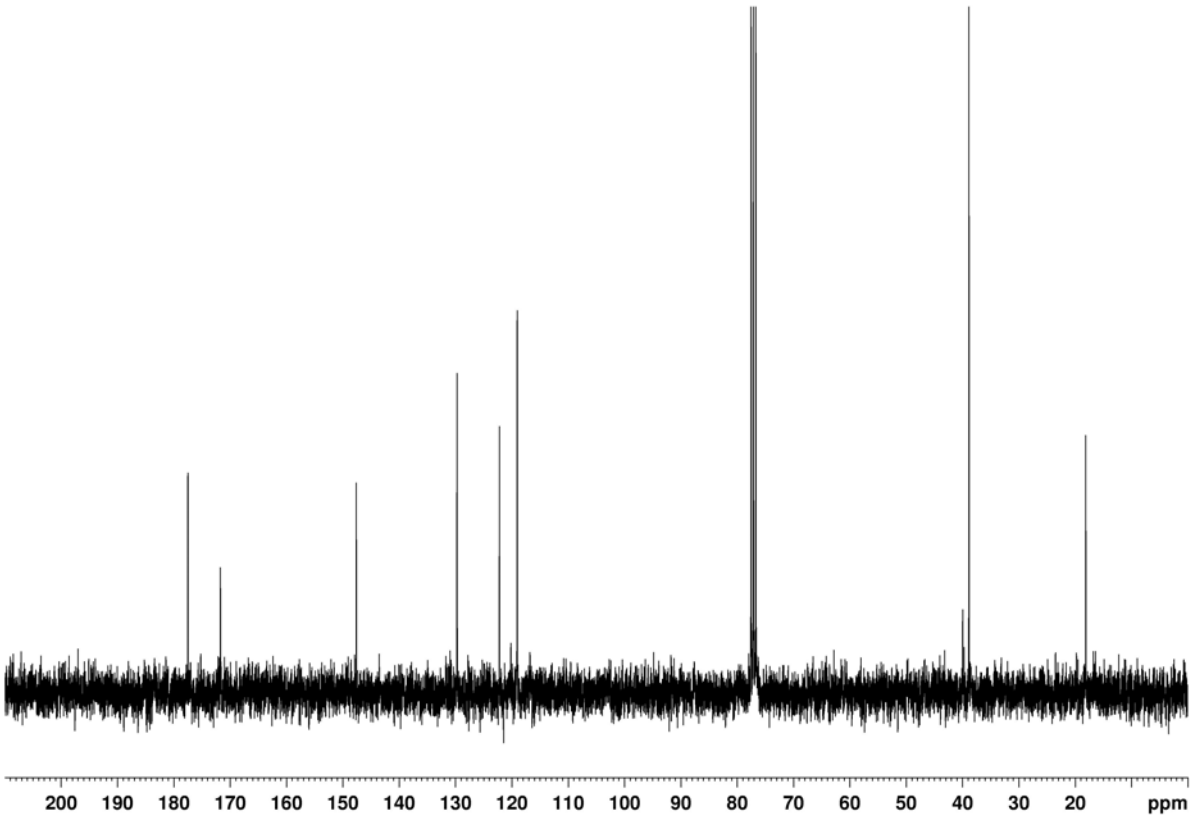


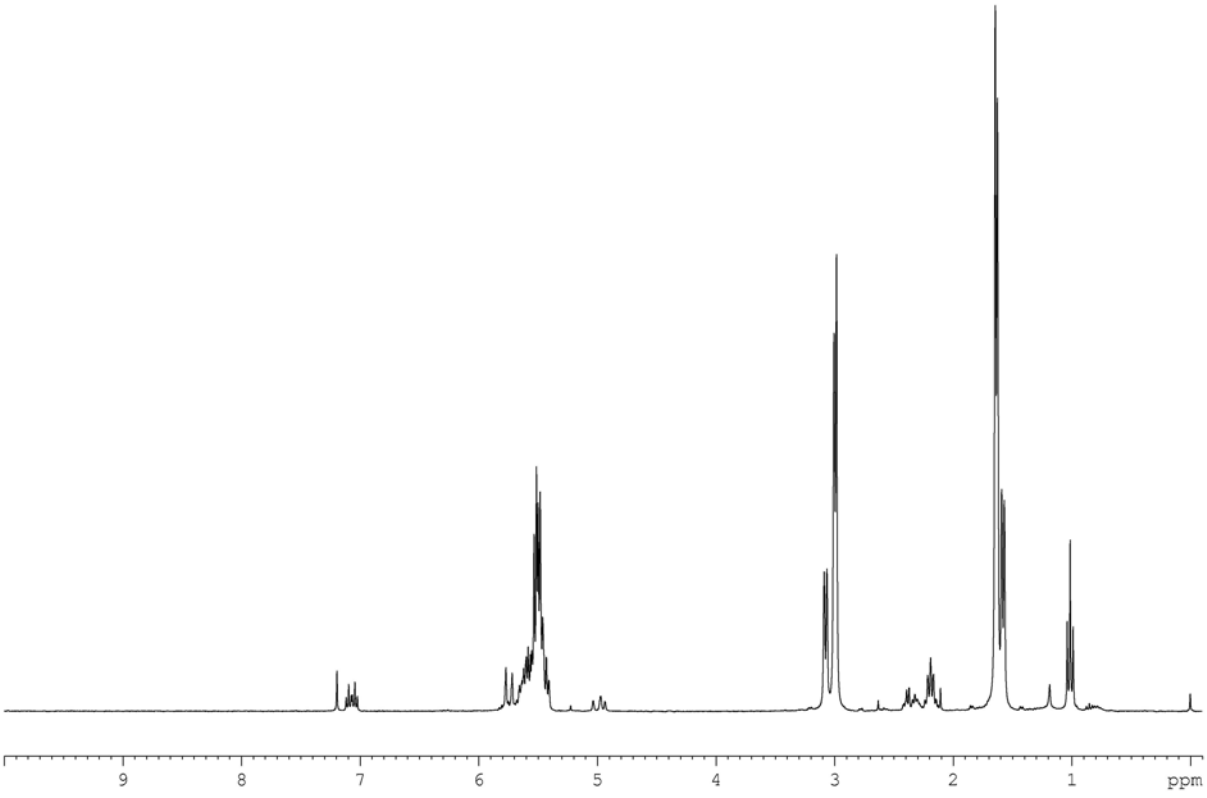
7a/7a'



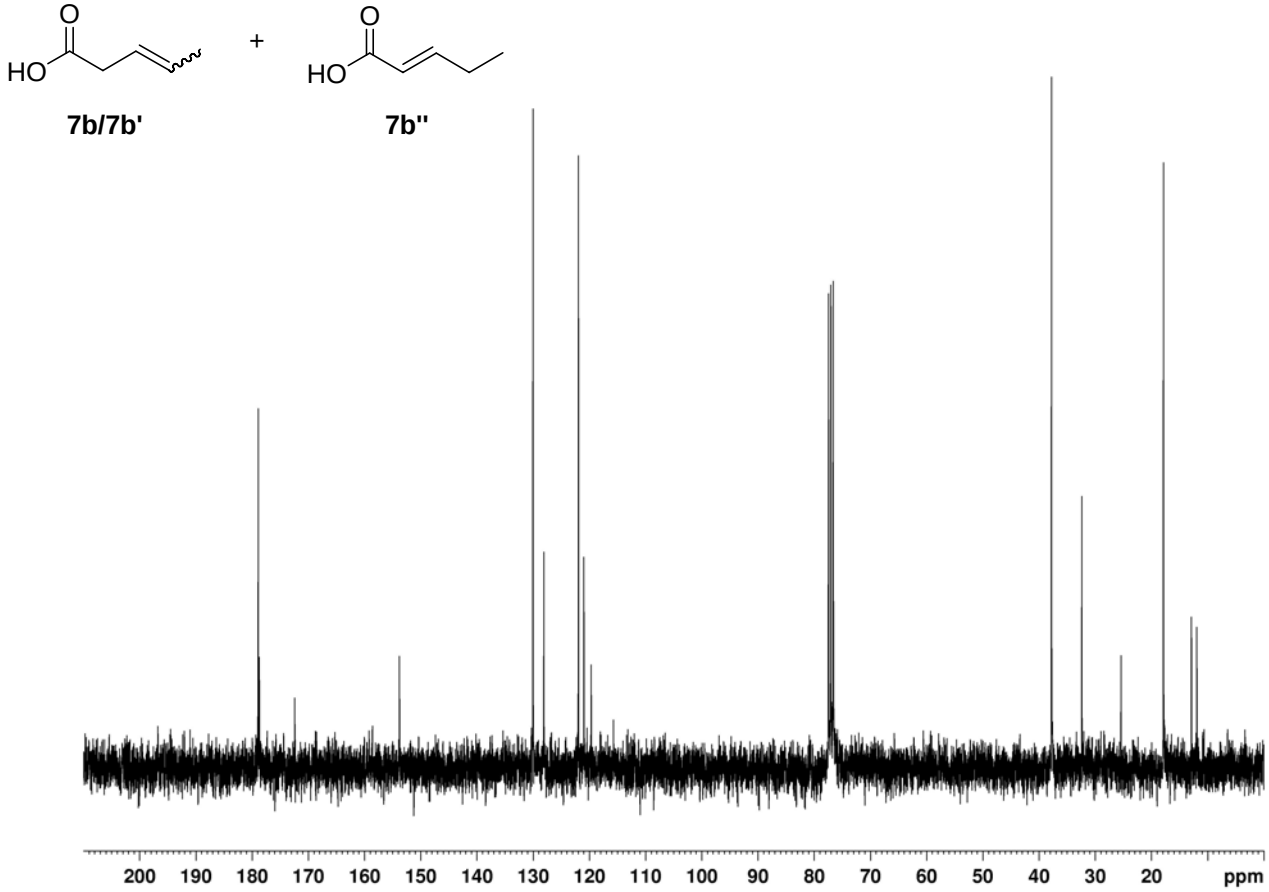


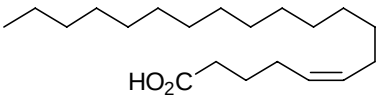
7a/7a'


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

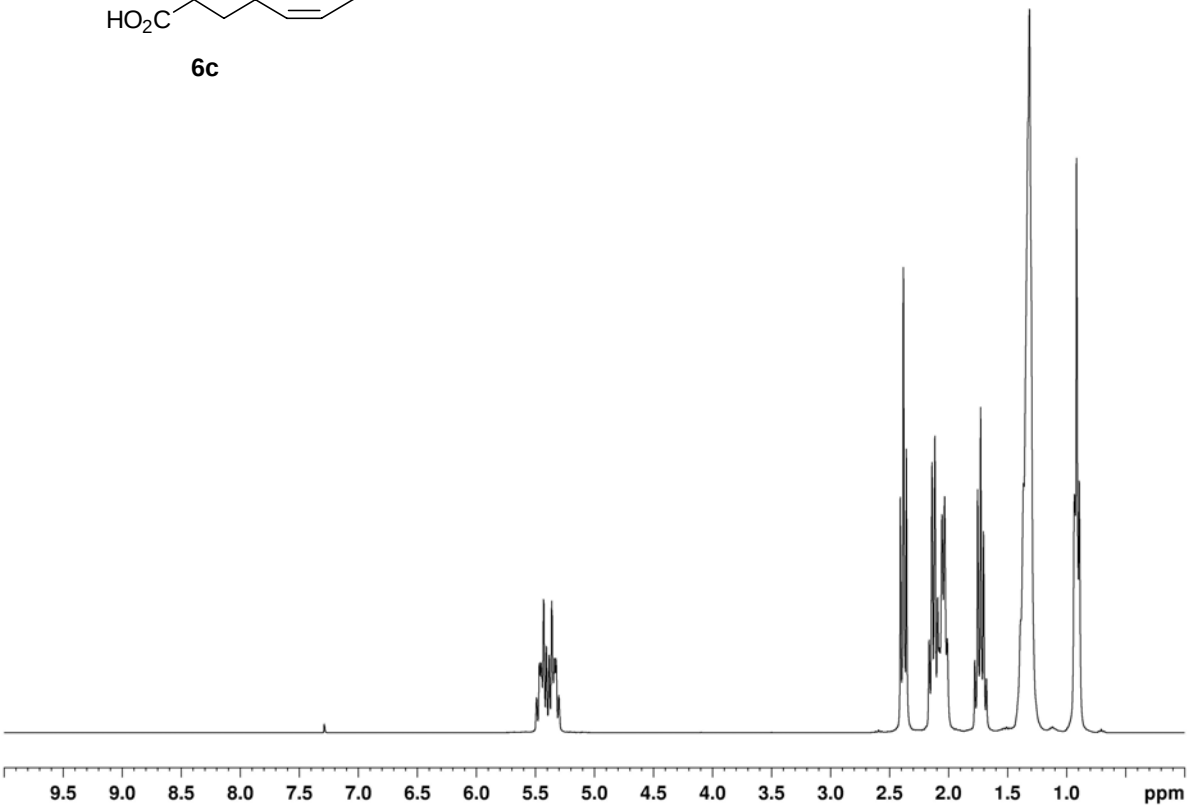


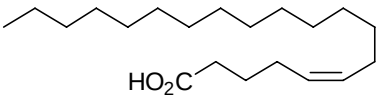
7b/7b' **7b''**


O
HO
+
O
HO
7b/7b'
7b''
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

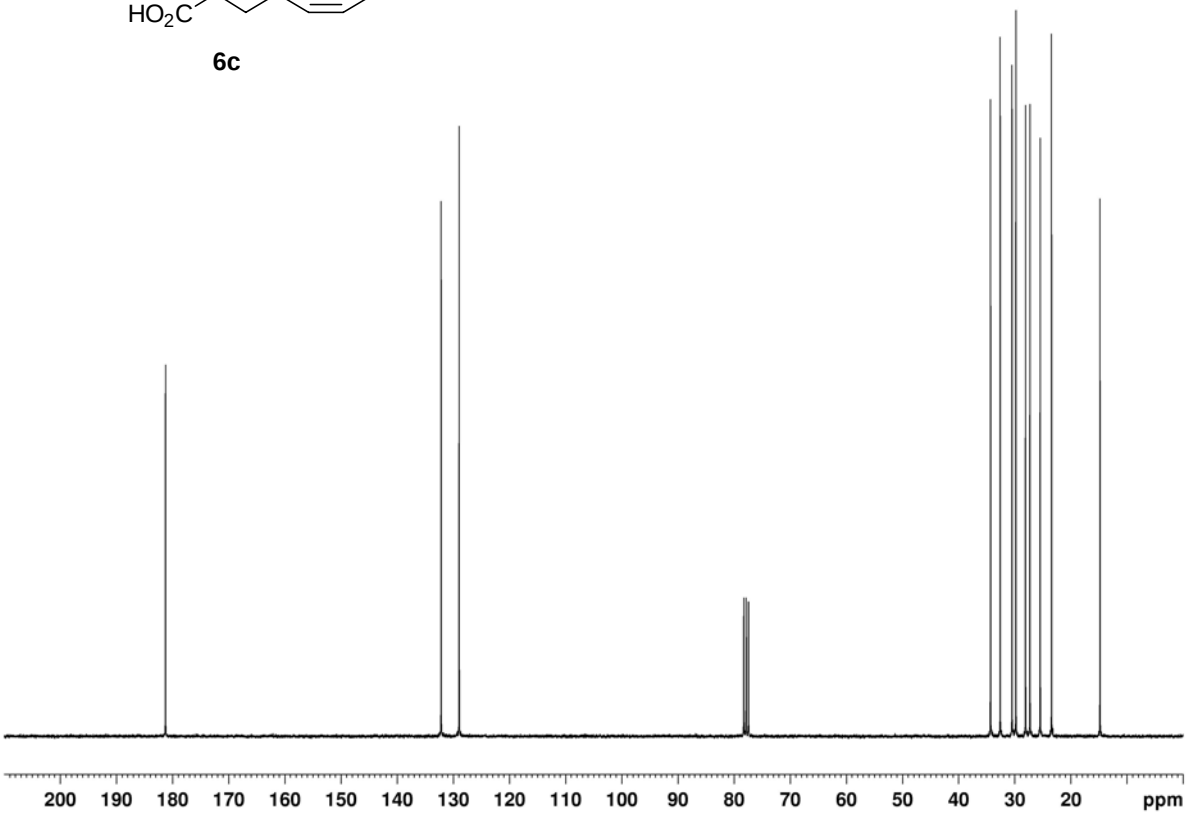

HO2C

6c

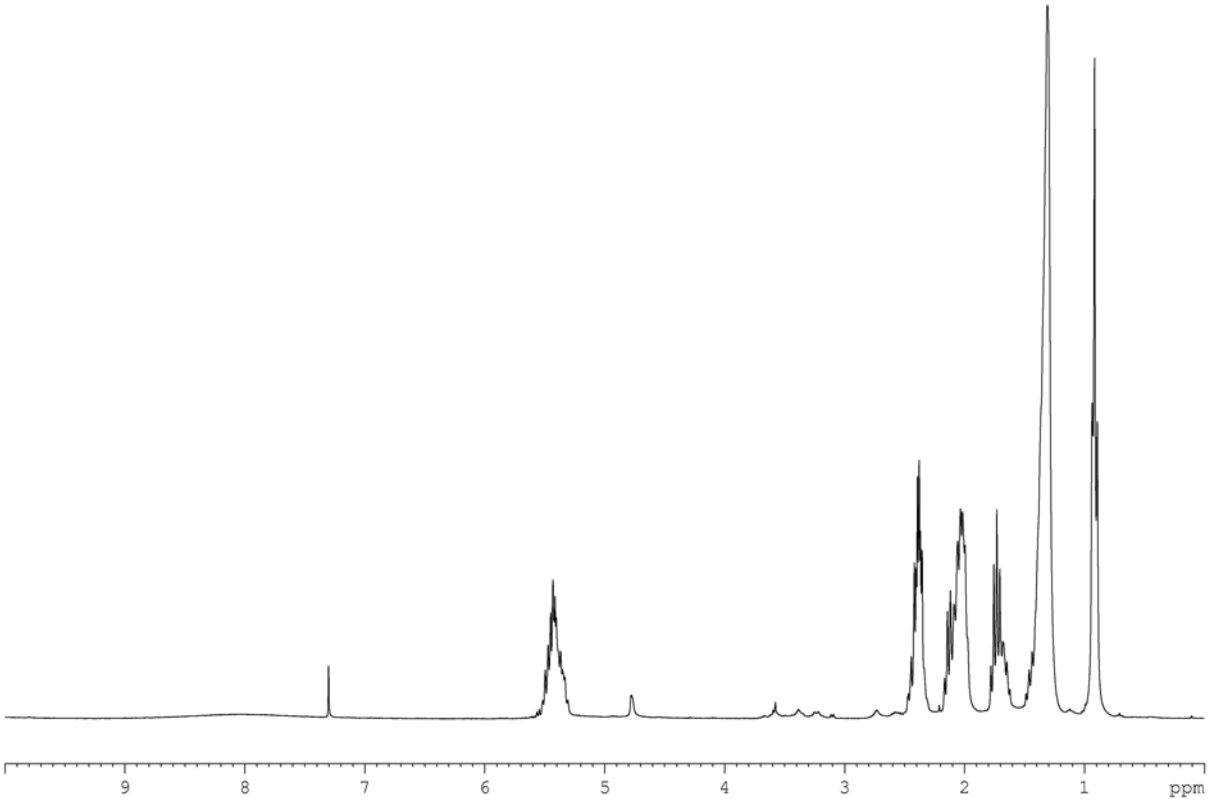

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm


HO2C

6c


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

mixture of different alkene-acids from reaction **6c** with catalyst **1b**



mixture of different alkene-acids from reaction **6c** with catalyst **1b**