Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


Supporting Information

# N-heterocyclic carbene catalysed oxidative esterification of aliphatic aldehydes

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## Experimental section

**General:** All reactions involving air or moisture sensitive reagents or intermediates were carried out in dried glassware under an argon atmosphere. THF was distilled from potassium under argon. Diethyl ether was distilled from sodium or potassium under argon. All other solvents and reagents were purified according to standard procedures or were used directly from *Sigma Aldrich, Acros Organics, ABCR, Alfa Aesar* or *Fluka* as received. NMR spectroscopy: *Bruker DPX 300* (at 300 K). Chemical shifts, δ (in ppm), are reported relative to TMS ($\delta(^{1}H)$ 0.0 ppm, $\delta(^{13}C)$ 0.0 ppm) which was used as the inner reference. Otherwise the solvents residual proton resonance and carbon resonance ($CDCl_3$, $\delta(^{1}H)$ 7.26 ppm, $\delta(^{13}C)$ 77.1 ppm; were used for calibration). TLC: *Merck* silica gel 60 F 254 plates; detection with UV light or by dipping into a solution of $KMnO_4$ (1.5 g in 400 mL $H_2O$, 5 g $NaHCO_3$) or a solution of $Ce(SO_4)_2$ x $H_2O$ (10 g), phosphormolybdic acid hydrate (25 g), and conc. $H_2SO_4$ (60 mL) in $H_2O$ (940 mL), followed by heating. Flash column chromatography (FC): *Merck* or *Fluka* silica gel 60 (40-63 μm) at approximately 0.4 bar. Infrared spectra were recorded on a *Varian Associates* FT-IR 3100 Excalibur and *Shimadzu* FTIR 8400S and reported as wavenumber ($cm^{-1}$). Mass spectra were recorded on a *Finnigan MAT 4200S,* a *Bruker Daltonics MicroTof,* a *Waters Micromass Quatro LCZ* (ESI), a *Finnigan MAT 95* (EI),a *Thermo Finnigan LTQ FT* (ESI) mass spectrometer; and peaks are given in *m/z* (% of basis peak).

All the aldehydes and alcohols used are either commercially available or synthesized by using the synthetic procedures mentioned in literature.[1,2]

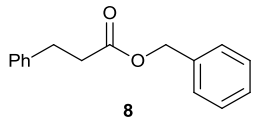
**General procedure A for the oxidative esterification:**

In a heatgun dried Schlenk tube, 1,3-dimethyl triazolium iodide (**4**) (7.5 mol%) and rubidium carbonate (2.0 equiv) were added to dry THF (0.1 M). The mixture was stirred at room temperature for 5 min prior to the addition of 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (**7**) (1.2 equiv) and the alcohol (1.0 or 1.5 equiv). Stirring was continued for another five min. Then the aldehyde (1.0 or 1.5 equiv) was added and the reaction mixture was allowed to stir at 60 $^{o}$C for 24-72 h. After consumption of the limiting reagent the reaction mixture was cooled to room temperature, the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography.

**General procedure B for the oxidative esterification**

In a heatgun dried Schlenk tube 1,3-dimethyl triazolium iodide (**4**) (7.5 mol%) and rubidium carbonate (2.0 equiv) were added to dry THF (0.1 M). The mixture was stirred at room temperature for 5 min prior to the addition of 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (**7**) (1.0 equiv) and the alcohol (1mL/mmol). Stirring was continued for another five min. Then the aldehyde (1.0 equiv) was added and the reaction mixture was allowed to stir at 60 $^{o}$C for 6-24 h. After consumption of the aldehyde the reaction mixture was cooled to room temperature, the solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography.

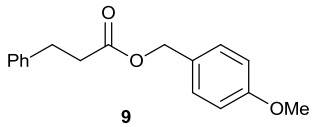
**Benzyl 3-phenylpropanoate (8):**



**8**

**8** was prepared according to GP-A with 3-phenylpropionaldehyde (27 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), benzyl alcohol (32 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **8** was obtained (39 mg, 81%). FTIR (neat): $\tilde{\nu}$ = 3030, 1732, 1496, 1454, 1148, 907, 730, 695 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) δ = 7.49 – 7.00 (m, 10H), 5.08 (s, 2H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.66 (t, *J* = 7.8 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ = 172.8, 140.5, 136.1, 128.7, 128.6, 128.4, 128.3, 126.4, 66.4, 36.0, 31.1. HRMS (ESI) Exact mass calculated for $C_{16}H_{16}O_2Na$ ($[M+Na]^+$): 263.1043. Found 263.10399.

**4-Methoxybenzyl 3-phenylpropanoate (9):**

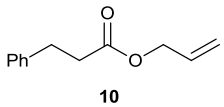


**9**

**9** was prepared according to GP-A with 3-phenylpropionaldehyde (27 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester 9 was obtained (48 mg, 88%). FTIR (neat): $\tilde{\nu}$ = 2956, 2837, 1730, 1613, 1514, 1454, 1245, 1148, 1032, 822 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) δ = 7.44 – 7.03 (m, 7H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.97 (s, 2H), 3.73 (s, 3H), 2.88 (t, *J* = 7.8 Hz, 2H), 2.58 (t, *J* = 7.8 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ = 172.9,

159.7, 140.6, 130.2, 128.6, 128.4, 128.2, 126.3, 114.1, 66.2, 55.4, 36.1, 31.1. HRMS (ESI) Exact mass calculated for $C_{17}H_{18}O_3Na$ ($[M+Na]^+$): 293.1148. Found 293.1156.

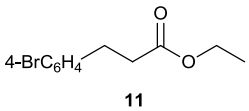
**Allyl 3-phenylpropanoate (10):**



**10**

**10** was prepared according to GP-B with 3-phenylpropionaldehyde (27 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), allyl alcohol (0.2 mL) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (82 mg, 0.20 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **10** was obtained (30 mg, 80%). FTIR (neat): $\tilde{\nu}$ = 2934, 1733, 1497, 1454, 1266, 1149, 987, 735, 698 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.46 – 6.88 (m, 5H), 5.89 (ddt, *J* = 16.4, 10.9, 5.7 Hz, 1H), 5.45 – 4.99 (m, 2H), 4.58 (d, *J* = 5.8, 2H), 2.97 (t, *J* = 7.8 Hz, 2H), 2.66 (t, 8.2 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 172.6, 140.6, 132.3, 128.6, 128.4, 126.9, 118.3, 65.2, 36.0, 31.1. HRMS (ESI) Exact mass calculated for $C_{12}H_{15}O_2$ ($[M+H]^+$): 191.1067, Found 191.1070; $C_{12}H_{14}O_2Na$ ($[M+Na]^+$): 213.0886, Found 213.0892.

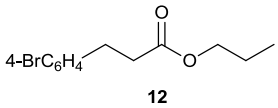
**Ethyl 3-(4-bromophenyl)propanoate (11):**



**11**

**11** was prepared according to GP-B with 3-(4-bromophenyl)propanal (43 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), ethyl alcohol (0.2 mL) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (82 mg, 0.20 mmol) in THF (2.0 mL) at 60 ˚C for 6 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **11** was obtained (36 mg, 70%). FTIR (neat): $\tilde{\nu}$ = 2981, 1731, 1489, 1178, 1156, 1072, 1011, 812 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.40 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 172.5, 139.5, 131.5, 130.1, 120.0, 60.5, 35.6, 30.3, 14.2. HRMS (ESI) Exact mass calculated for $C_{11}H_{14}BrO_2$ ($[M+H]^+$): 257.0172, Found 257.0172.

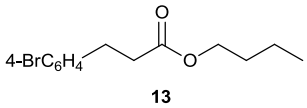
**Propyl 3-(4-bromophenyl)propanoate(12):**



**12**

**12** was prepared according to GP-B with 3-(4-bromophenyl)propanal (43 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), *n*-propyl alcohol (0.2 mL) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (82 mg, 0.20 mmol) in THF (2.0 mL) at 60 ˚C for 6 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **12** was obtained (40 mg, 74%). FTIR (neat): $\tilde{\nu}$ = 2969, 1728, 1489, 1012, 905, 727, 649 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.39 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 4.02 (t, *J* = 6.7 Hz, 2H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 8.2 Hz, 2H), 1.65–1.58 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 172.7, 139.7, 131.6, 130.2, 120.2, 66.3, 35.7, 30.5, 22.1, 10.4. HRMS (ESI) Exact mass calculated for C12H15BrNaO2+ ($[M+Na]^+$): 293.0148, Found 293.0143.

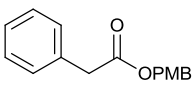
**Butyl 3-(4-bromophenyl)propanoate (13):**



**13**

**13** was prepared according to GP-B with 3-(4-bromophenyl)propanal (43 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), ethyl alcohol (0.2 mL) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (82 mg, 0.20 mmol) in THF (2.0 mL) at 60 ˚C for 6 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **13** was obtained (41 mg, 72%). FTIR (neat): $\tilde{\nu}$ = 2961, 1728, 1489, 1179, 1073, 1012, 905, 727 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.39 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 4.06 (t, *J* = 6.6 Hz, 2H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 1.63 – 1.52 (m, 2H), 1.39 – 1.26 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 172.7, 139.7, 131.6, 130.2, 120.2, 64.5, 35.8, 30.8, 30.5, 19.2, 13.8. HRMS (ESI) Exact mass calculated for $C_{13}H_{18}BrO_2$ ($[M+H]^+$): 285.0485, Found 285.0484; $C_{13}H_{17}BrNaO_2$ ($[M+Na]^+$): 307.0304, Found 307.0300.

**4-Methoxybenzyl 2-phenylacetate (14):**

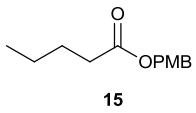


**14**

**14** was prepared according to GP-A with 2-phenylacetaldehyde (24 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After

$SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **14** was obtained (21 mg, 41%). FTIR (neat): $\tilde{\nu}$ = 2956, 2837, 1731, 1613, 1514, 1454, 1244, 1142, 1031, 972, 819, 696 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.51 – 7.09 (m, 7H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.03 (s, 2H), 3.76 (s, 3H), 3.60 (s, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 171.6, 159.8, 134.1, 130.1, 129.4, 128.7, 128.2, 127.2, 114.1, 66.6, 55.4, 41.5. HRMS (ESI) Exact mass calculated for $C_{16}H_{16}O_3Na$ ($[M+Na]^+$): 279.0992. Found 279.0999.

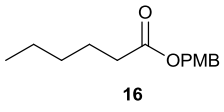
**4-Methoxybenzyl pentanoate (15):**



15

**15** was prepared according to GP-A with pentanal (17 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 36 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 50:1) ester **15** was obtained (32 mg, 72%). FTIR (neat): $\tilde{\nu}$ = 2958, 2874, 1731, 1613, 1515, 1465, 1303, 1245, 1162, 1034, 821 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.33 (t, *J* = 7.5 Hz, 2H), 1.86 – 1.51 (m, 2H), 1.48 – 1.23 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 173.8, 159.7, 130.1, 128.5, 114.1, 66.0, 55.4, 34.2, 27.2, 22.4, 13.8. HRMS (ESI) Exact mass calculated for $C_{13}H_{18}O_3Na$ ($[M+Na]^+$): 245.1148. Found 245.1146.

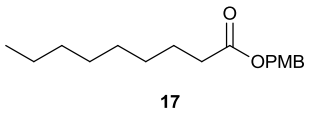
**4-Methoxybenzyl hexanoate (16):**



16

**16** was prepared according to GP-A with hexanal (20 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 36 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 25:1) ester **16** was obtained (35 mg, 75%). FTIR (neat): $\tilde{\nu}$ = 2956, 2932, 2861, 1732, 1613, 1515, 1303, 1245, 1161, 1111, 1034, 821 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.32 (t, *J* = 7.5 Hz, 2H), 1.82 – 1.47 (m, 2H), 1.39 – 1.21 (m, 4H), 0.88 (t, *J* = 6.7 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 173.9, 159.7, 130.1, 128.5, 114.1, 66.0, 55.4, 34.5, 31.4, 24.8, 22.4, 14.0. HRMS (ESI) Exact mass calculated for $C_{14}H_{20}O_3Na$ ($[M+Na]^+$): 259.1305. Found 259.1314.

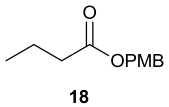
**4-Methoxybenzyl nonanoate (17):**



17

**17** was prepared according to GP-A with nonanal (29 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 72 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 50:1) ester **17** was obtained (38 mg, 67%). FTIR (neat): $\tilde{\nu}$ = 2954, 2925, 2855, 1733, 1613, 1515,1464, 1246, 1157, 1111, 1035, 821 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.32 (t, *J* = 7.5 Hz, 2H), 1.80 – 1.50 (m, 1H), 1.27 (m, 12H), 0.88 (t, *J* = 6.6 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 173.9, 159.7, 130.1, 128.5, 114.1, 66.0, 55.4, 34.5, 31.9, 29.34, 29.3, 29.2, 25.1, 22.8, 14.2. HRMS (ESI) Exact mass calculated for $C_{17}H_{26}O_3Na$ ($[M+Na]^+$): 301.1774. Found 301.1772.

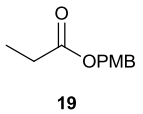
**4-Methoxybenzyl butyrate (18):**



18

**18** was prepared according to GP-A with butyraldehyde (22 mg, 0.30 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (28 mg, 0.20 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 30:1) ester **18** was obtained (41 mg, 99%). FTIR (neat): $\tilde{\nu}$ = 2964, 2937, 2877, 2838, 1731, 1613, 1515, 1463, 1303, 1245, 1166, 1034, 967, 820 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.31 (t, *J* = 7.4 Hz, 2H), 1.60-1.72 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 173.7, 159.7, 130.1, 128.5, 114.1, 66.0, 55.4, 36.4, 18.6, 13.8. HRMS (ESI) Exact mass calculated for $C_{12}H_{16}O_3Na$ ($[M+Na]^+$): 231.0992. Found 231.0993.

**4-Methoxybenzyl propionate (19):**

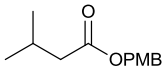


19

**19** was prepared according to GP-A with propionaldehyde (18 mg, 0.30 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (28 mg, 0.20 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 36 h. After $SiO_2$-

chromatography (pentane:$Et_2O$, 30:1) ester **19** was obtained (37 mg, 95%). FTIR (neat): $\tilde{\nu}$ = 2942, 2838, 1732, 1613, 1515, 1463, 1246, 1168, 1081, 1033, 757 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.30 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.35 (q, *J* = 7.6 Hz, 2H), 1.15 (t, *J* = 7.6 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 174.5, 159.8, 130.1, 128.4, 114.1, 66.1, 55.4, 27.8, 9.2. HRMS (ESI) Exact mass calculated for $C_{11}H_{14}O_3Na$ ($[M+Na]^+$): 217.0835. Found 217.0838.

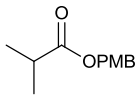
**4-Methoxybenzyl 3-methylbutanoate (20):**



**20**

**20** was prepared according to GP-A with 3-methylbutanal (26 mg, 0.30 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (28 mg, 0.20 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 40 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 50:1) ester **20** was obtained (33 mg, 74%). FTIR (neat): $\tilde{\nu}$ = 2959, 2872, 2838, 1731, 1613, 1515, 1465, 1293, 1245, 1164, 1113, 1034, 820 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.21 (d, *J* = 6.8 Hz, 2H), 2.18 – 2.03 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 173.1, 159.7, 130.1, 128.5, 114.1, 65.9, 55.4, 43.6, 25.9, 22.5. HRMS (ESI) Exact mass calculated for $C_{13}H_{18}O_3Na$ ($[M+Na]^+$): 245.1148. Found 245.1142.

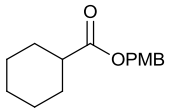
**4-Methoxybenzyl isobutyrate (21):**



**21**

**21** was prepared according to GP-A with isobutyraldehyde (22 mg, 0.30 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (28 mg, 0.20 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 30:1) ester **21** was obtained (39 mg, 94%). FTIR (neat): $\tilde{\nu}$ = 2937, 2838, 1729, 1614, 1515, 1467, 1246, 1148, 1034, 823 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.29 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.05 (s, 2H), 3.81 (s, 3H), 2.57 (hept, *J* = 7.0 Hz, 1H), 1.17 (d, *J* = 7.0 Hz, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 177.2, 159.7, 130.0, 128.6, 114.1, 66.0, 55.4, 34.2, 19.1. HRMS (ESI) Exact mass calculated for $C_{12}H_{16}O_3Na$ ($[M+Na]^+$): 231.0992. Found 231.0987.

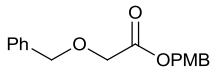
**4-Methoxybenzyl cyclohexanecarboxylate (22):**



**22**

**22** was prepared according to GP-A with cyclohexanecarbaldehyde (34 mg, 0.30 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (28 mg, 0.20 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 48 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 30:1) ester **22** was obtained (34 mg, 67%). FTIR (neat): $\tilde{\nu}$ = 2932, 2855, 1727, 1613, 1514, 1451, 1303, 1244, 1161, 1130, 1033, 963, 820 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.30 (d, *J* = 9.4 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 5.06 (s, 2H), 3.83 (s, 3H), 2.34 (tt, *J* = 11.3, 3.6 Hz, 1H), 1.95-1.09 (m, 2H), 1.78-1.74 (m, 2H), 1.52 – 1.39 (m, 2H), 1.21-1.36 (m, 4H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 176.1, 159.7, 129.9, 128.7, 114.1, 65.9, 55.4, 43.4, 29.2, 25.9, 25.6. HRMS (ESI) Exact mass calculated for $C_{15}H_{20}O_3Na$ ($[M+Na]^+$): 271.1305. Found 271.1300.

**4-Methoxybenzyl 2-(benzyloxy)acetate (23):**



**23**

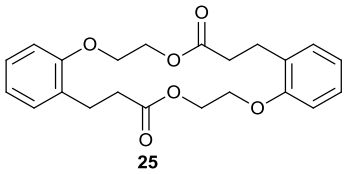
**23** was prepared according to GP-A with 2-(benzyloxy)acetaldehyde (30 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 36 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 30:1) ester **23** was obtained (40 mg, 70%). FTIR (neat): $\tilde{\nu}$ = 2936, 2838, 1749, 1613, 1515, 1454, 1246, 1173, 1112, 1029, 820,737, 697 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ = 7.39 – 7.23 (m, 8H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.15 (s, 2H), 4.63 (s, 2H), 4.12 (s, 2H), 3.81 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ = 170.4, 159.9, 137.2, 130.4, 128.6, 128.2, 128.1, 127.7, 114.1, 73.5, 67.4, 66.5, 55.4. HRMS (ESI) Exact mass calculated for $C_{17}H_{18}O_4Na$ ($[M+Na]^+$): 309.1097. Found 309.1094.

**Procedure for macrolactonization**

In a heatgun dried Schlenk tube 1,3-dimethyl triazolium iodide (**4**) (10 mol%) and rubidium carbonate (2.0 equiv) were added to dry THF (0.1 M). The mixture was stirred at room temperature for 5 min prior to the addition of 3,3′,5,5′-tetra-*tert*-butyldiphenoquinone (**7**) (1 equiv). Stirring was continued for another five min. Then the 3-(2-(2-

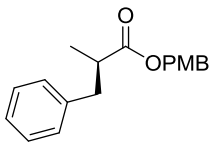
hydroxyethoxy)phenyl)propanal (**24**)[1] (1.0 equiv) was added and the reaction mixture was allowed to stir at 60 $^{o}$C for 2 h. The reaction mixture was cooled to room temperature, the solvent was evaporated under reduced pressure and the crude product was purified by silica gel flash column chromatography (pentane:ethylacetare, 5:1).

**6,7,10,11,17,18,21,22-Octahydrodibenzo[e,n][1,4,10,13]tetraoxacyclooctadecine-9,20-dione (25)**


**25**

FTIR (neat): $\tilde{\nu}$ = 2929, 1734, 1495, 1453, 1247, 1179, 1116, 1072, 928, 753 cm$^{-1}$. $^{1}$H NMR (300 MHz, $CDCl_3$) δ = 7.24 – 7.17 (m, 2H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 4.54 – 4.36 (m, 2H), 4.25 – 4.09 (m, 2H), 3.07 – 2.88 (m, 2H), 2.84 – 2.58 (m, 2H).$^{13}$C NMR (75 MHz, $CDCl_3$) δ = 173.7, 156.7, 130.6, 129.1, 127.9, 121.1, 110.9, 65.6, 62.8, 33.4, 27.2. HRMS (ESI) Exact mass calculated for $C_{22}H_{24}NaO_6$ ([M+Na]$^{+}$): 407.1465. Found 407.1455.

**Synthesis of 4-methoxybenzyl (R)-2-methyl-3-phenylpropanoate (27)**



**27**

**27** was prepared according to GP-A with (R)-2-methyl-3-phenylpropanal (26)[2] (30 mg, 0.20 mmol), 1,3-dimethyl triazolium iodide (3.4 mg, 15 μmol), rubidium carbonate (93 mg, 0.40 mmol), 4-methoxybenzyl alcohol (42 mg, 0.30 mmol) and 3,3',5,5'-tetra-*tert*-butyldiphenoquinone (98 mg, 0.24 mmol) in THF (2.0 mL) at 60 ˚C for 24 h. After $SiO_2$-chromatography (pentane:$Et_2O$, 20:1) ester **27** was obtained (40 mg, 71%). FTIR (neat): $\tilde{\nu}$ = 3029, 2937, 1728, 1613, 1515, 1454, 1382, 1265, 1247, 1161, 1112, 1033 cm$^{-1}$. $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.24-7.17 (m, 7H), 6.86-6.83 (m, 2H), 4.99 (s, 2H), 3.79 (s, 3H), 3.01 (dd, *J* = 12.9, 6.7 Hz, 1H), 2.81-2.63 (m, 2H), 1.14 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) δ 176.0, 159.7, 139.4, 130.0, 129.1, 128.5, 128.3, 126.4, 114.0, 66.1, 55.4, 41.6, 39.9, 16.9. HRMS (ESI) Exact mass calculated for $C_{18}H_{20}NaO_3$ ([M+Na]+): 307.1310. Found 307.1305.

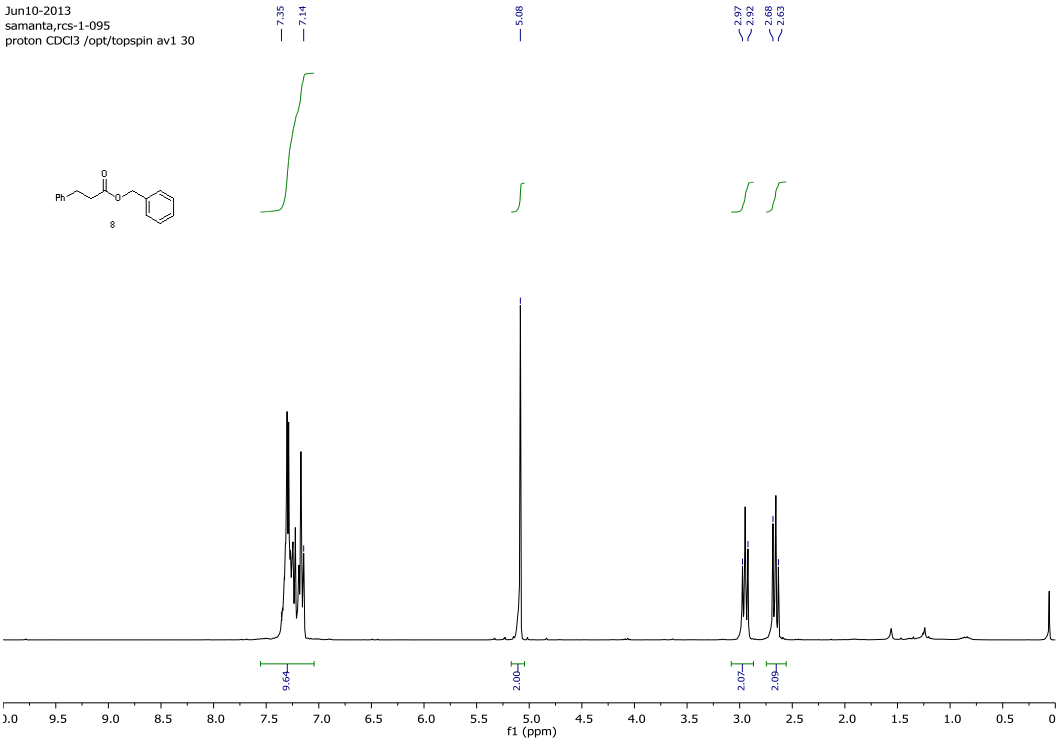
Enantiomeric excess was determined by using Chiralcel OJ-RH column with MeCN:$H_2O$ = 45:55 at 230 nm wavelength at 10 °C temperature.

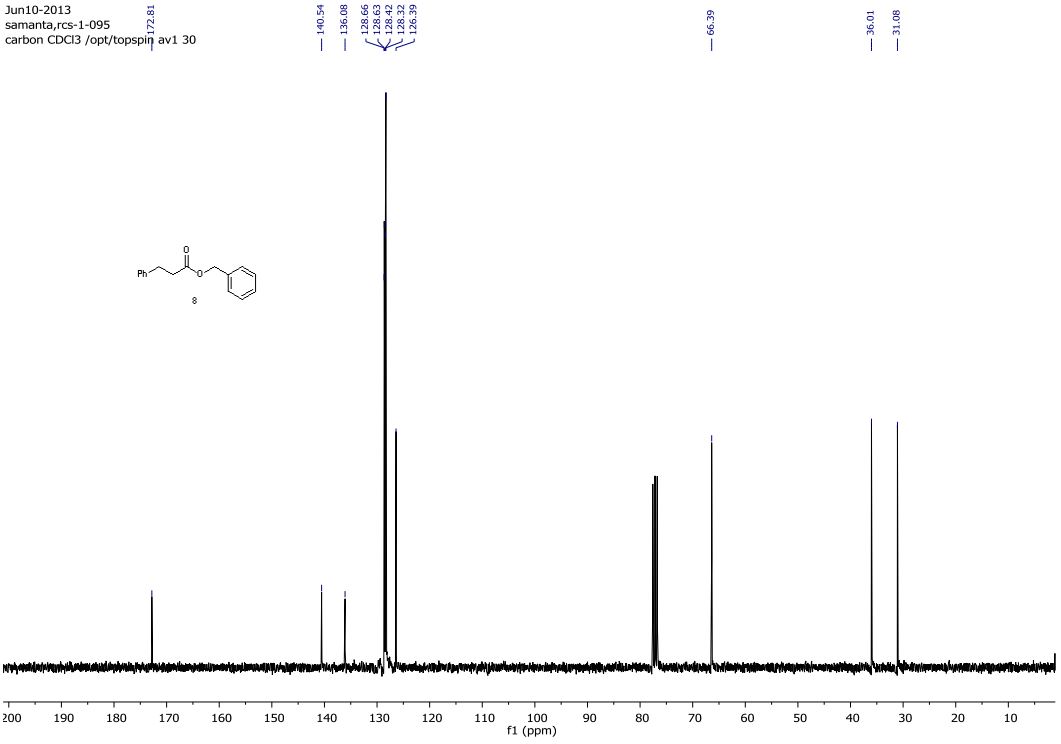
## References

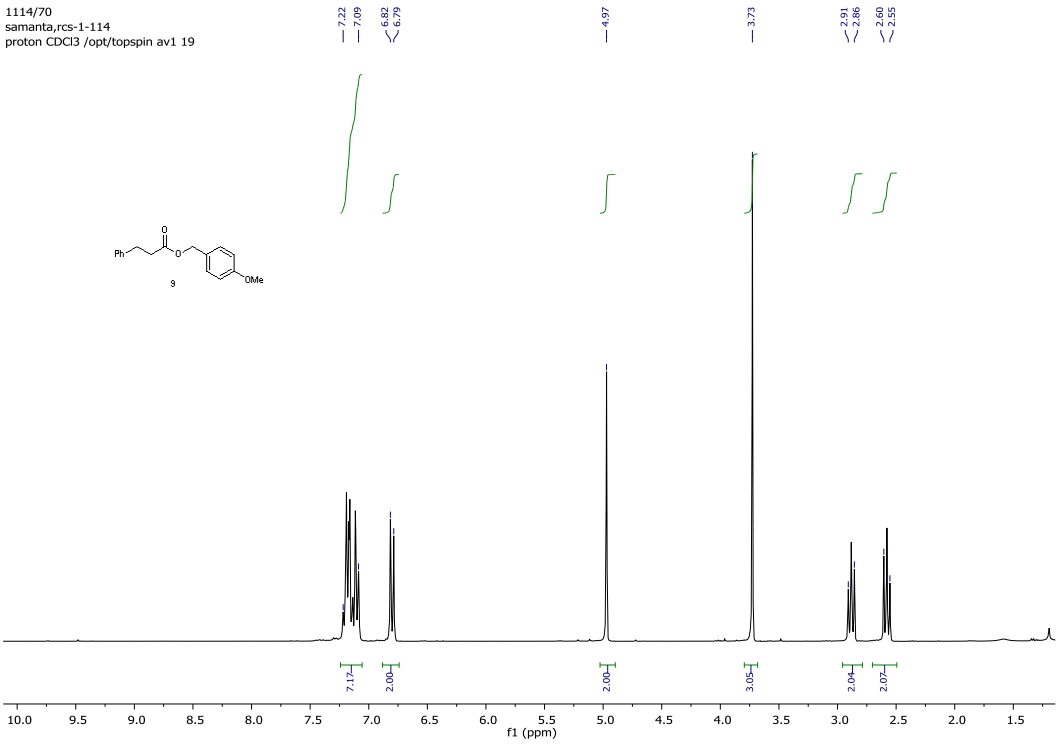

**1)** (*a*) J. Liu, S. He, T. Jian, P. H. Dobbelaar, I. K. Sebhat, L. S. Lin, A. Goodman, C. Guo, P. R. Guzzo, M. Hadden, A. J. Henderson, K. Pattamana, M. Ruenz, B. J. Sargent, B. Swenson, L. Yet, C. Tamvakopoulos, Q. Peng, J. Pan, Y. Kan, O. Palyha, T. M. Kelly, X.-M. Guan, A. D. Howard, D. J. Marsh, J. M. Metzger, M. L. Reitman, M. J. Wyvratt, and R. P. Nargund, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 2074; (*b*) D. B. Huple and R.-S. Liu, *Chem. Commun.*, 2012, **48**, 10975; (*c*) E. Elhalem, B. N. Bailey, R. Docampo, I. Ujvary, S. H. Szajnman, and J. B. Rodriguez, *J. Med. Chem.*, 2002, **45**, 3984.

**2)** (a) J. Peed, I. P. Dominguez, I. R. Davies, M. Cheeseman, J. E. Taylor, G. Kociok-Köhn, S. D. Bull, *Org. Lett*., 2011, **13**, 3592. (b) R. H. Taaning, L. Thim, J. Karaffa, A. G. Campana, Anna-Mette Hansen, T. Skrydstrup, *Tetrahedron*, 2008, **64**, 11884. (c) S. D. Bull, S. G. Davies, R. L. Nicholson, H. J. Sanganee, A. D. Smith, *Org. Biomol. Chem*., 2003, **1**, 2886.

# $^{1}H$ and $^{13}C$ NMR spectra

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2.55
Ph
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OMe
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7.17
2.00
2.00
3.05
2.04
2.07
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
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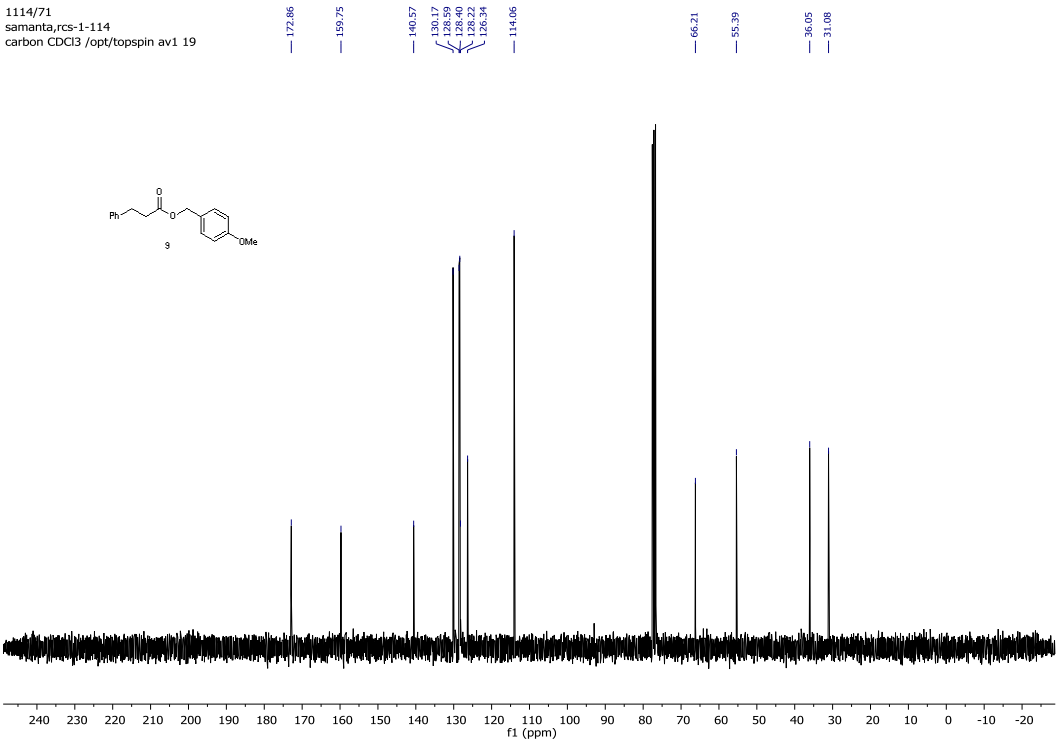
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OMe
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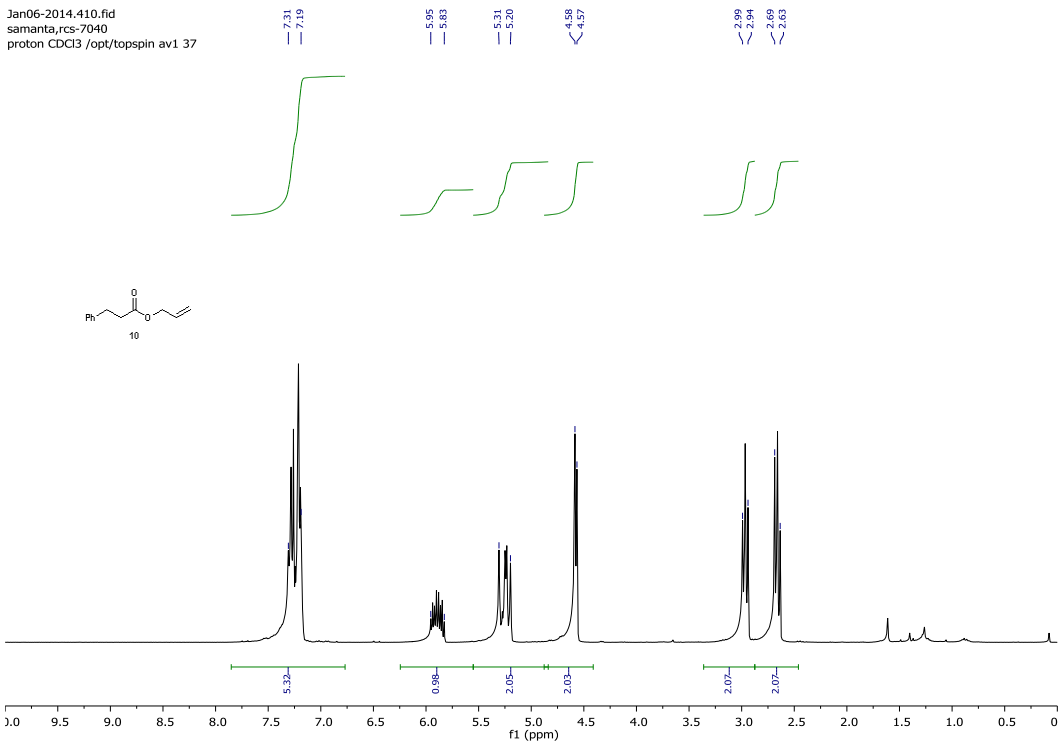
f1 (ppm)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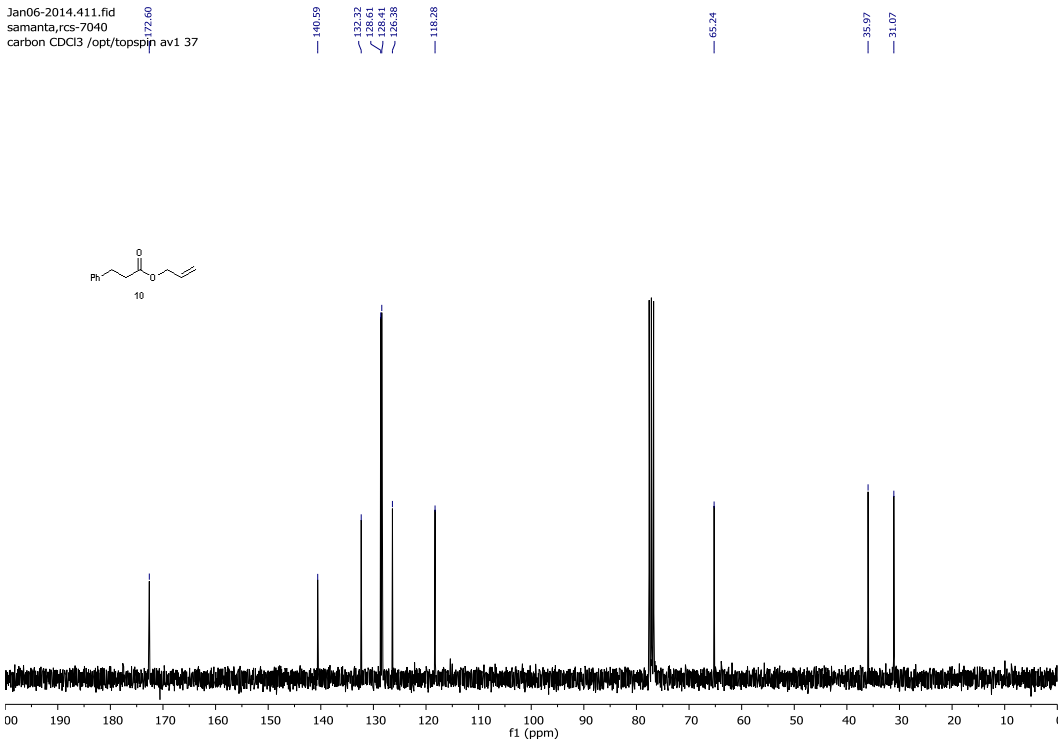
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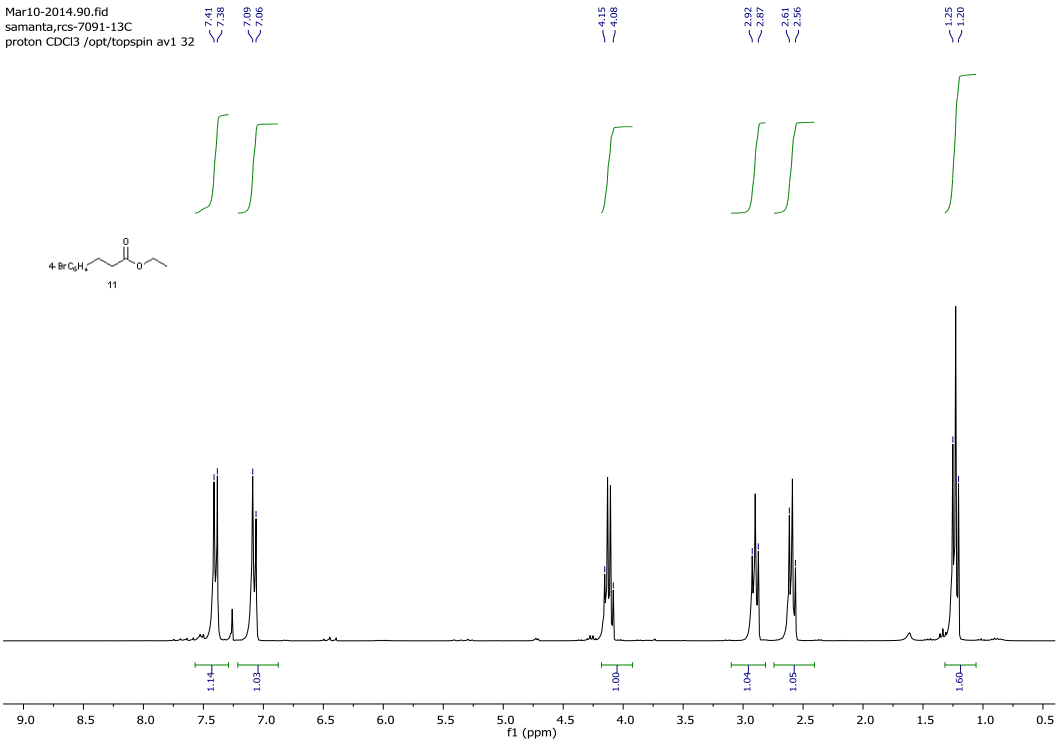
f1 (ppm)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1.14
1.03
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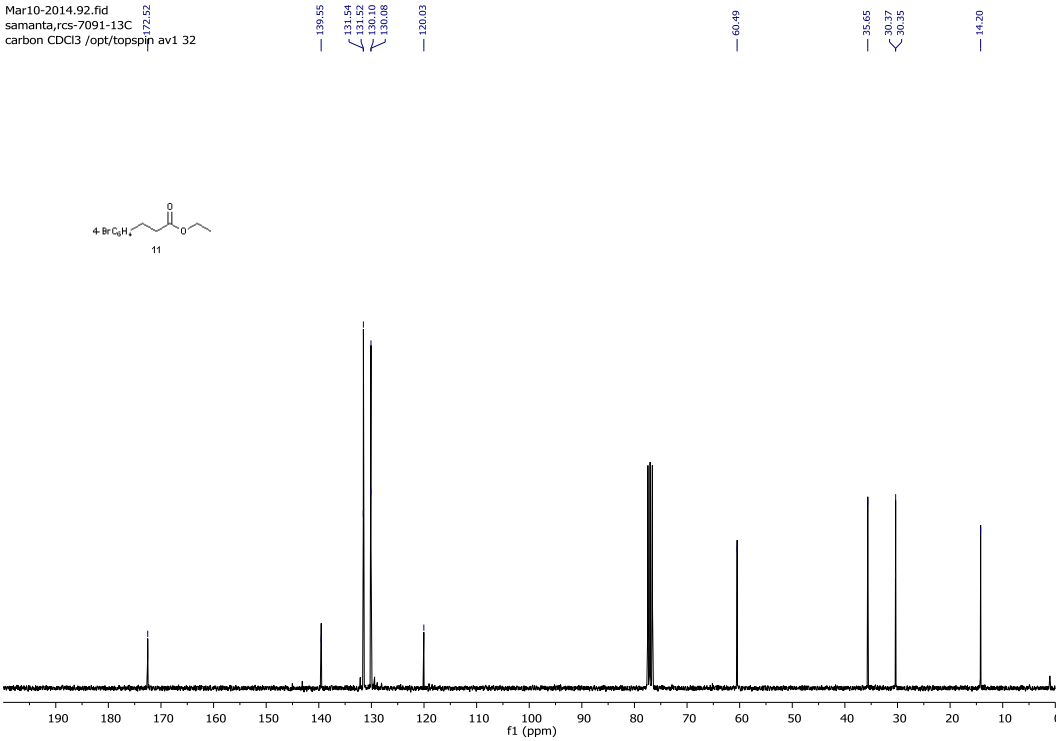
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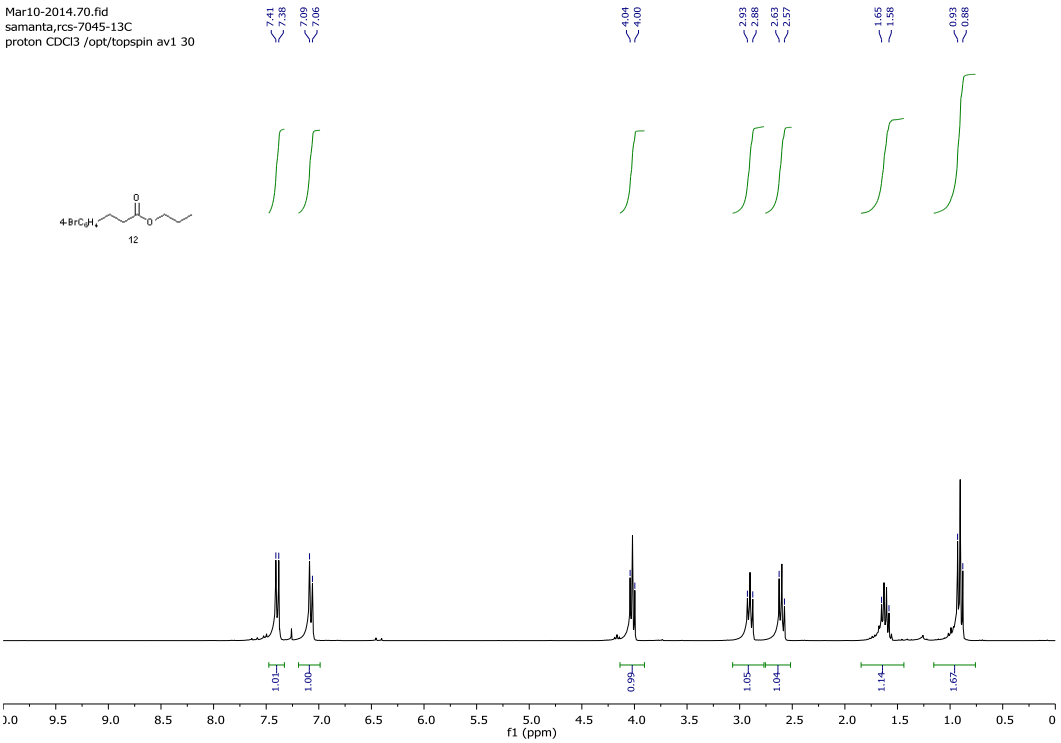
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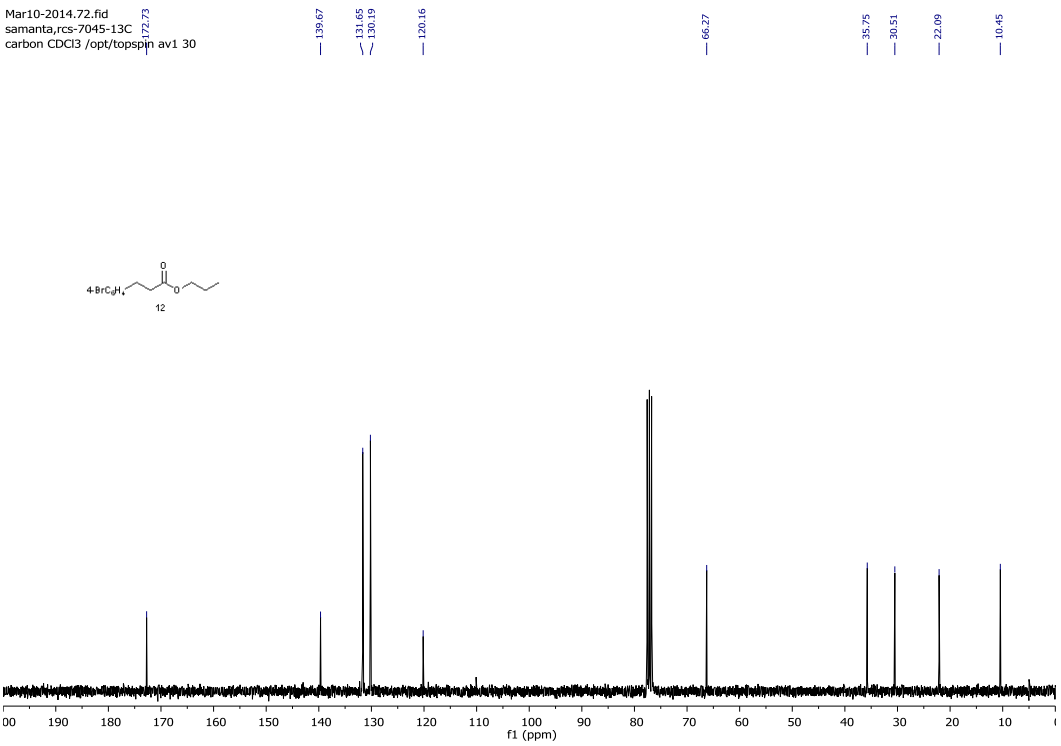
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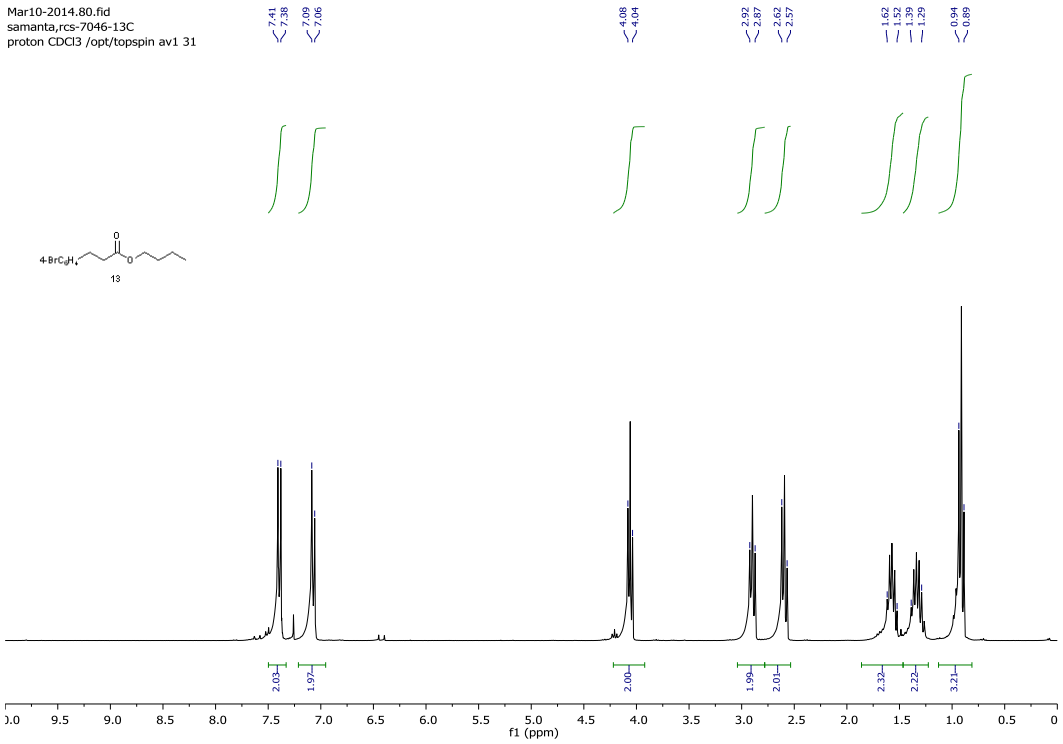
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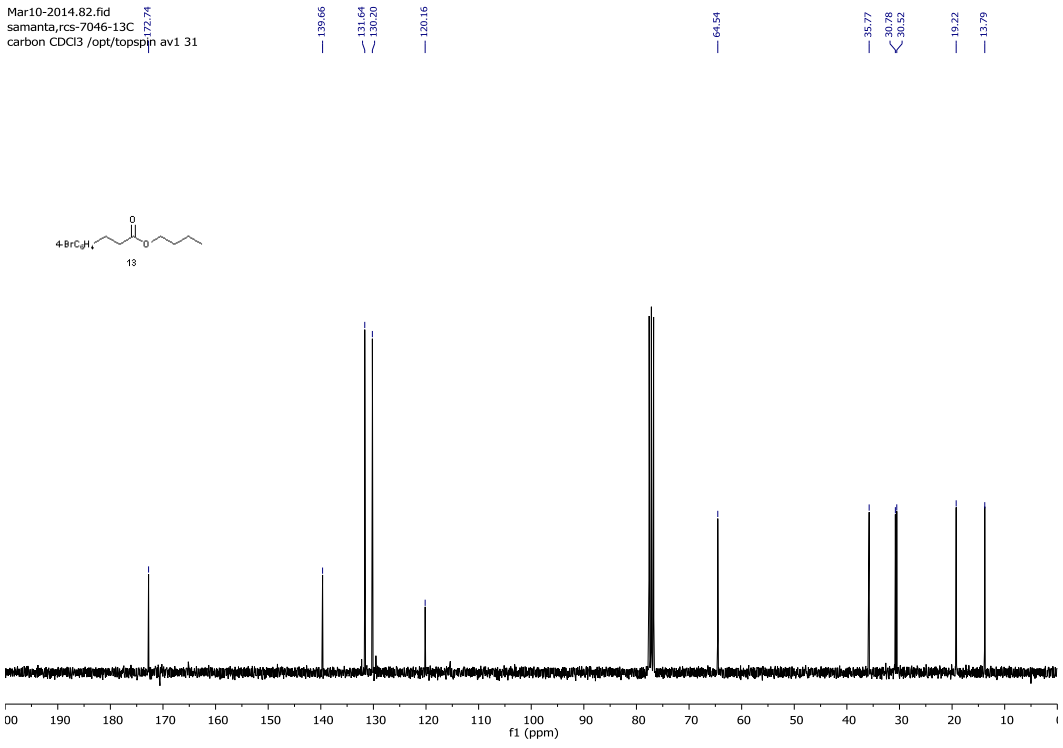
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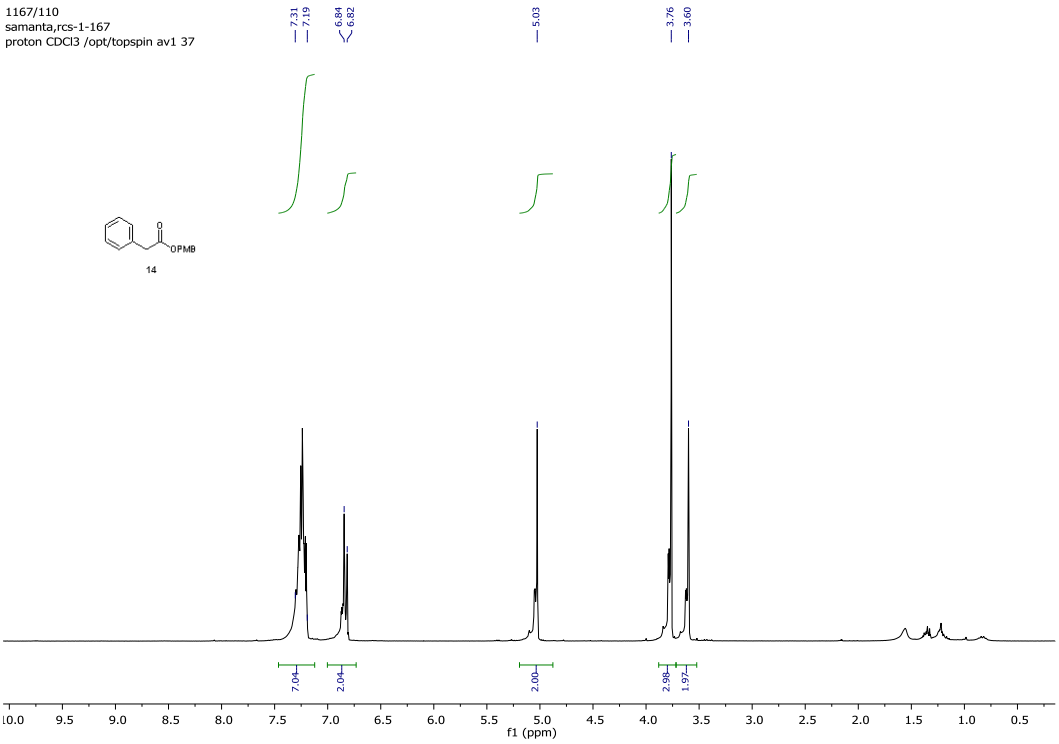
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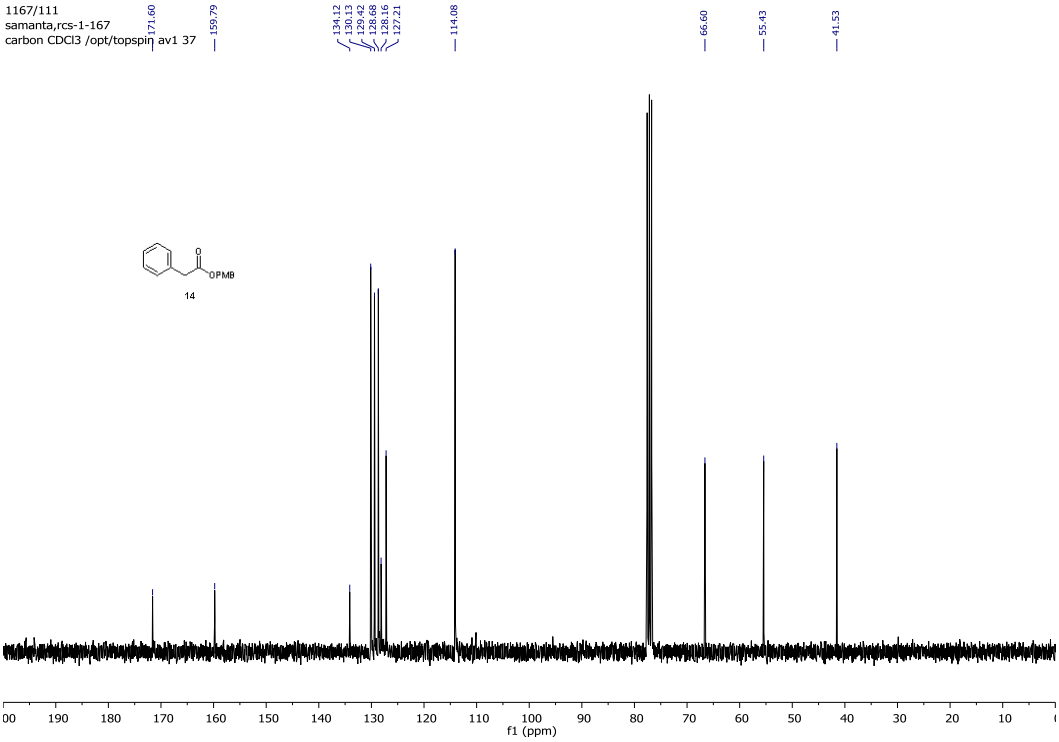
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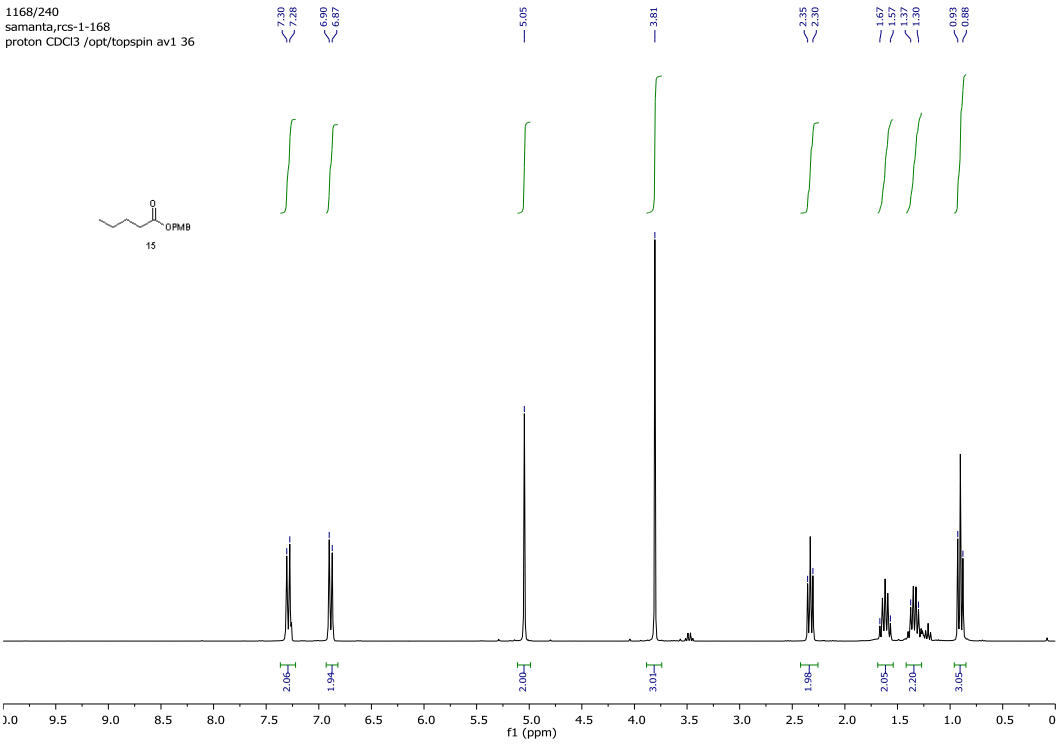
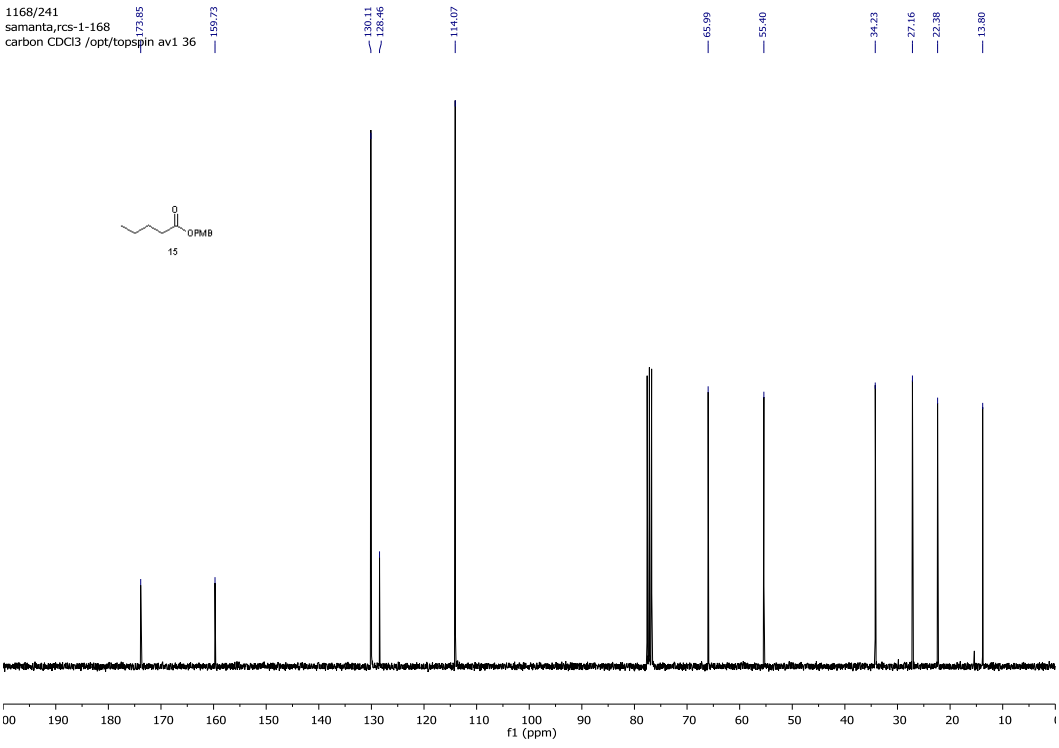
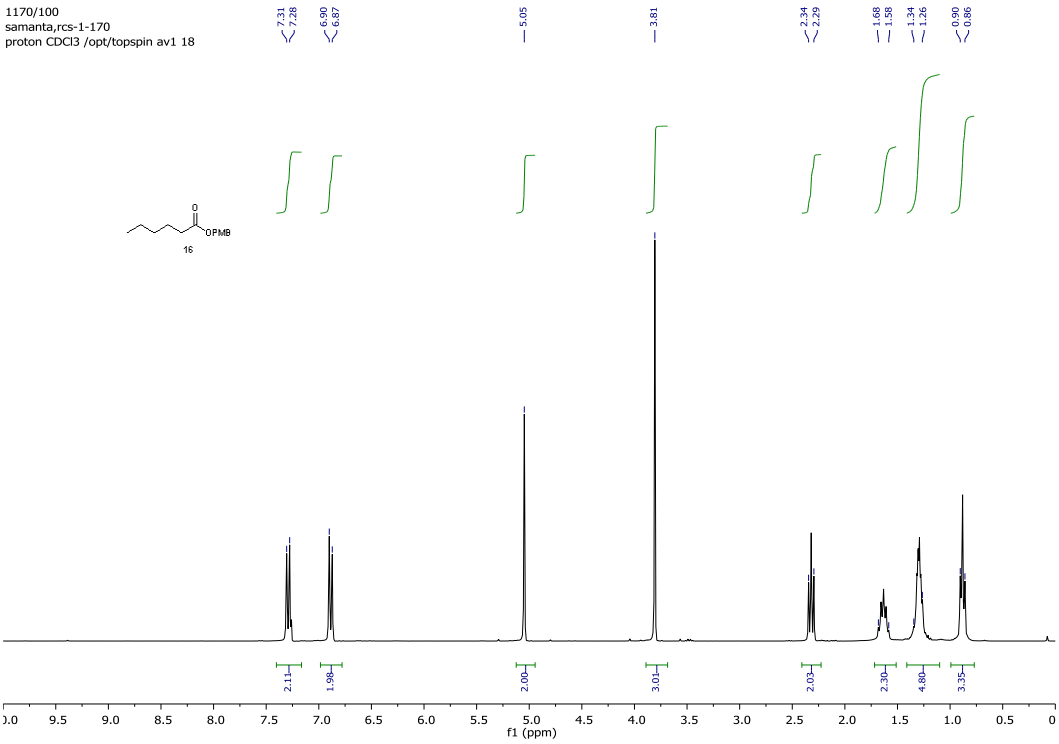
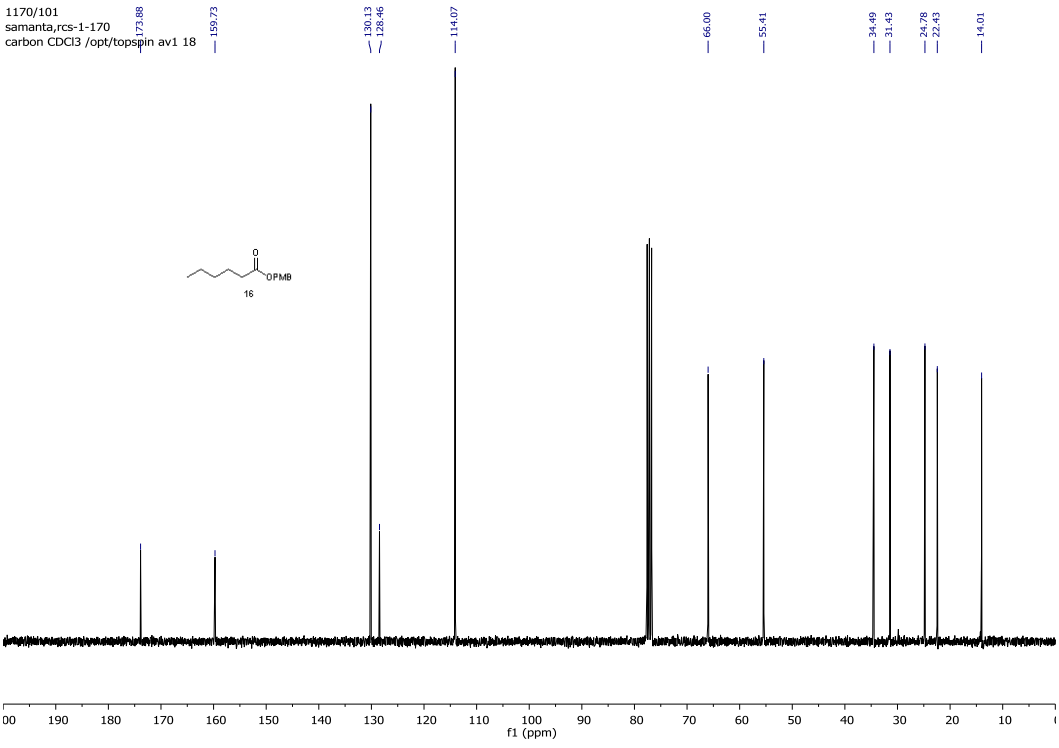
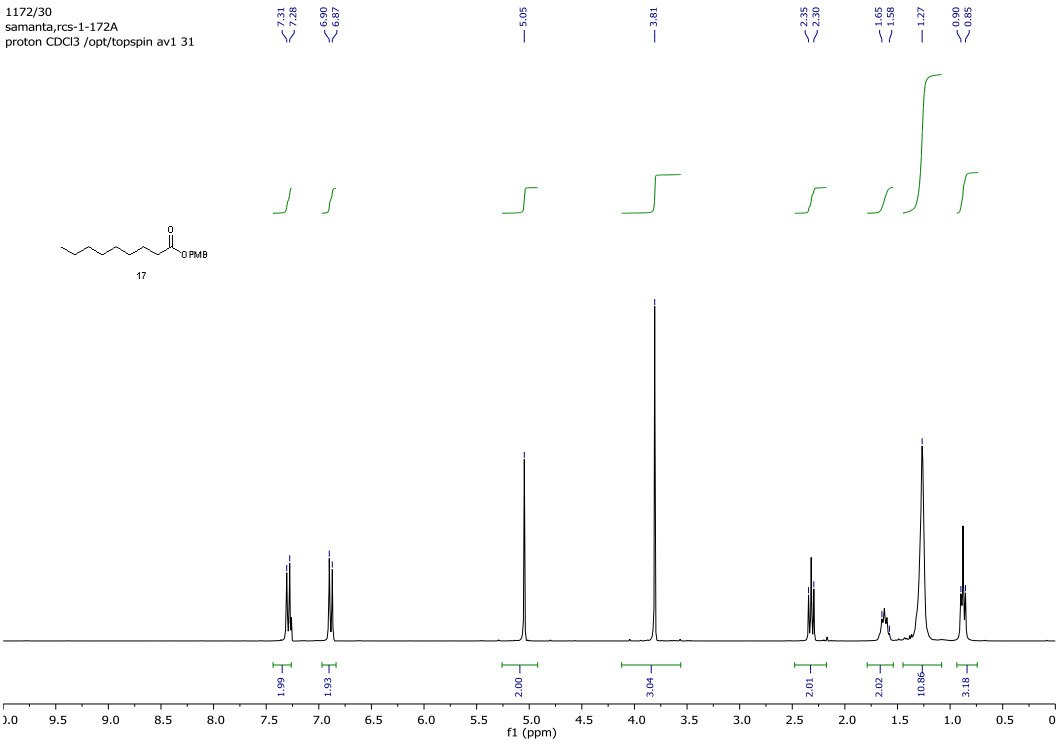
14
f1 (ppm)

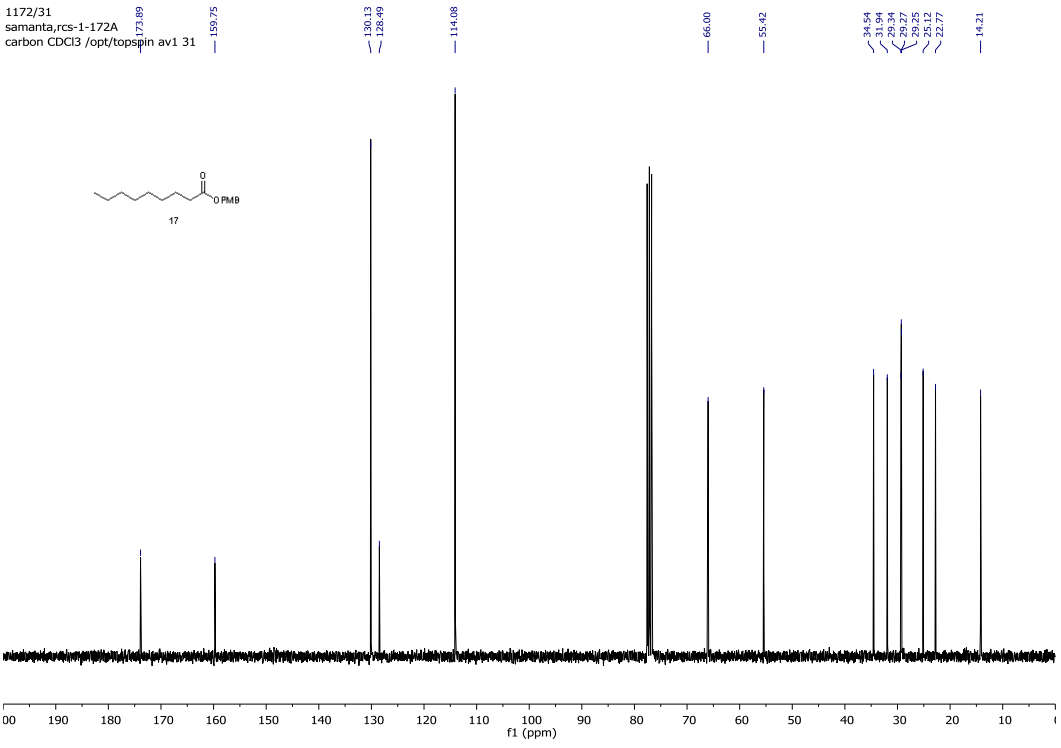

1168/240
samanta,rcs-1-168
proton CDCl3 /opt/topspin av1 36
7.30
7.28
6.90
6.87
5.05
3.81
2.35
2.30
1.67
1.57
1.37
1.30
0.93
0.88
OPMB
15
2.06
1.94
2.00
3.01
1.98
2.05
2.20
3.05
f1 (ppm)

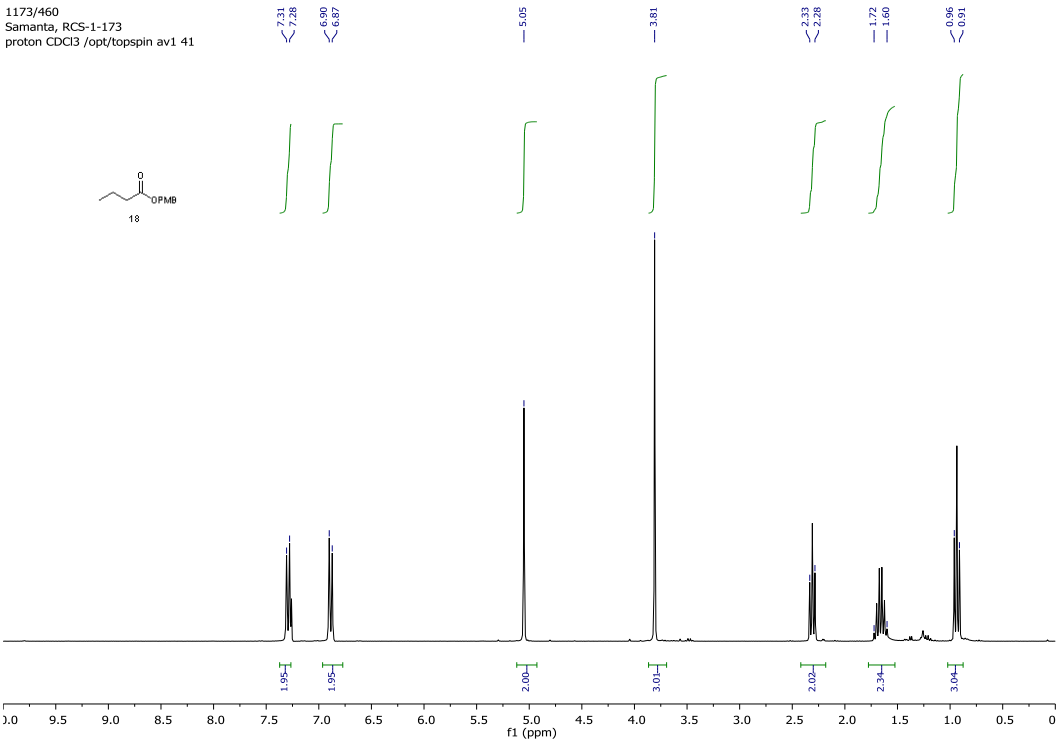

1168/241
samanta,rcs-1-168
carbon CDCl3 /opt/topspin av1 36
173.85
159.73
130.11
128.46
114.07
65.99
55.40
34.23
27.16
22.38
13.80
OPMB
15
f1 (ppm)

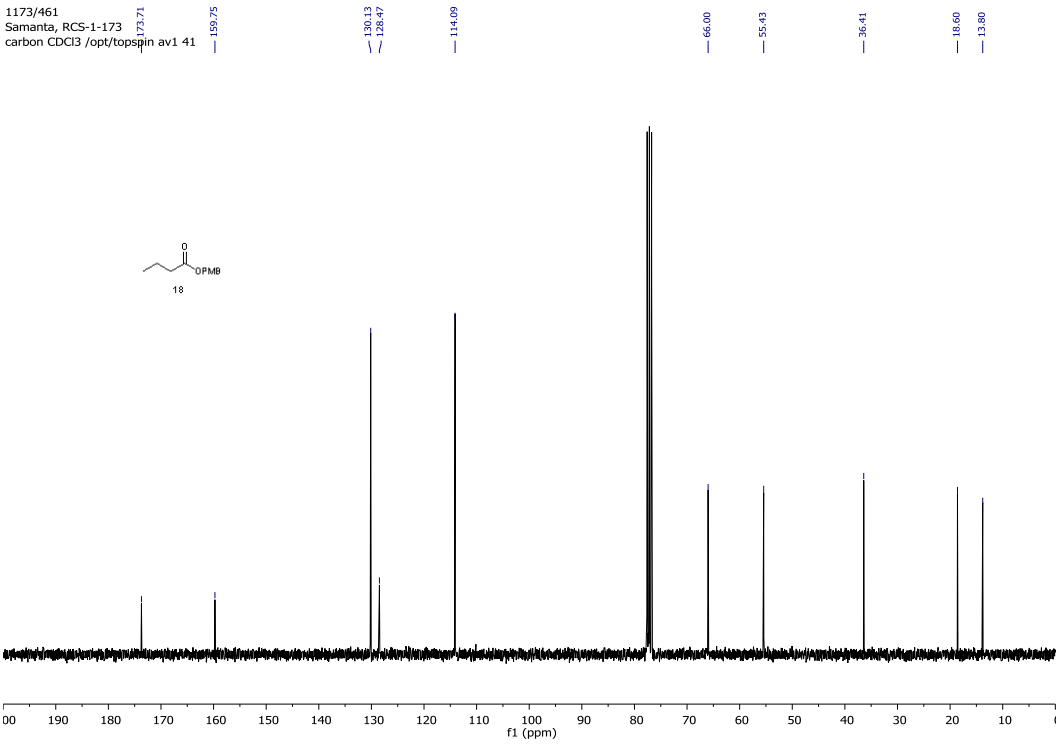

1170/100
samanta,rcs-1-170
proton CDCl3 /opt/topspin av1 18
7.31
7.28
6.90
6.87
5.05
3.81
2.34
2.29
1.68
1.58
1.34
1.26
0.90
0.86
OPMB
16
2.11
1.98
2.00
3.01
2.03
2.30
4.80
3.35
f1 (ppm)

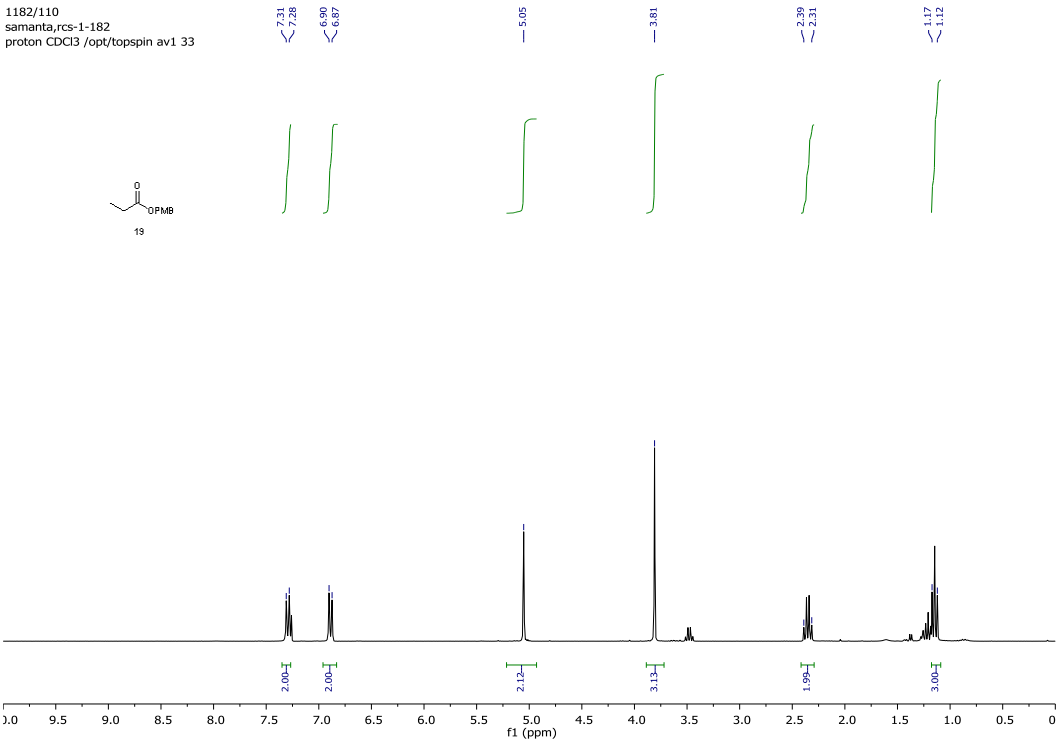

1170/101
samanta,rcs-1-170
carbon CDCl3 /opt/topspin av1 18
173.88
159.73
130.13
128.46
114.07
66.00
55.41
34.49
31.43
24.78
22.43
14.01
OPMB
16
f1 (ppm)

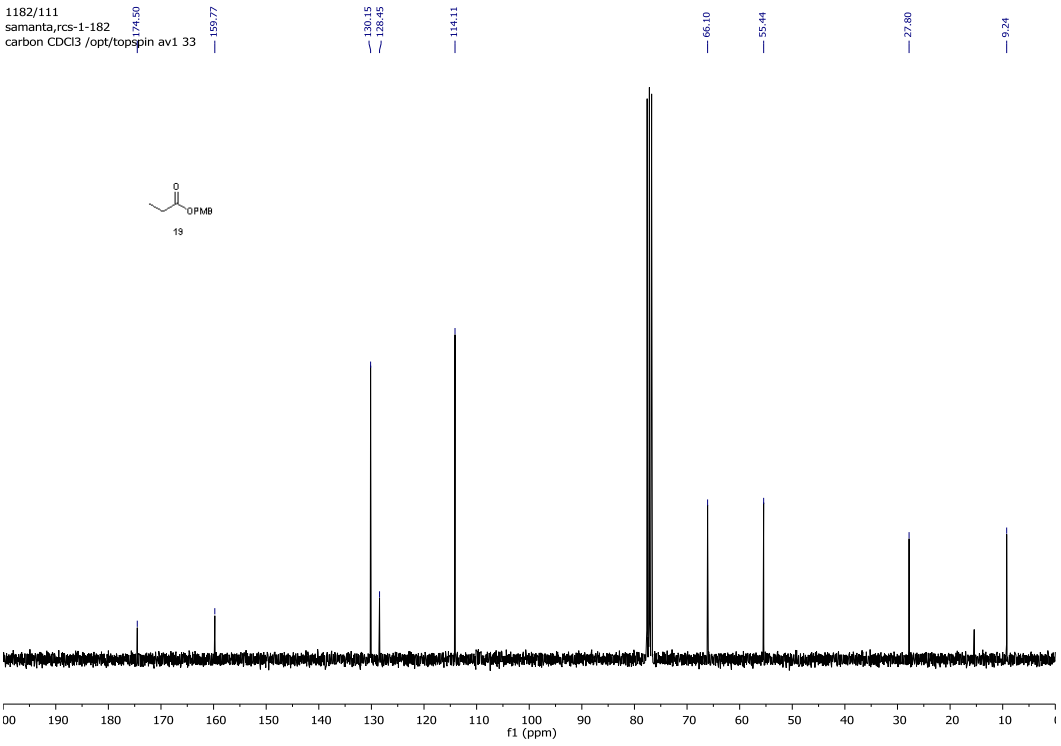

1172/30
samanta,rcs-1-172A
proton CDCl3 /opt/topspin av1 31
7.31
7.28
6.90
6.87
5.05
3.81
2.35
2.30
1.65
1.58
1.27
0.90
0.85
O
O PMB
17
1.99
1.93
2.00
3.04
2.01
2.02
10.86
3.18
f1 (ppm)

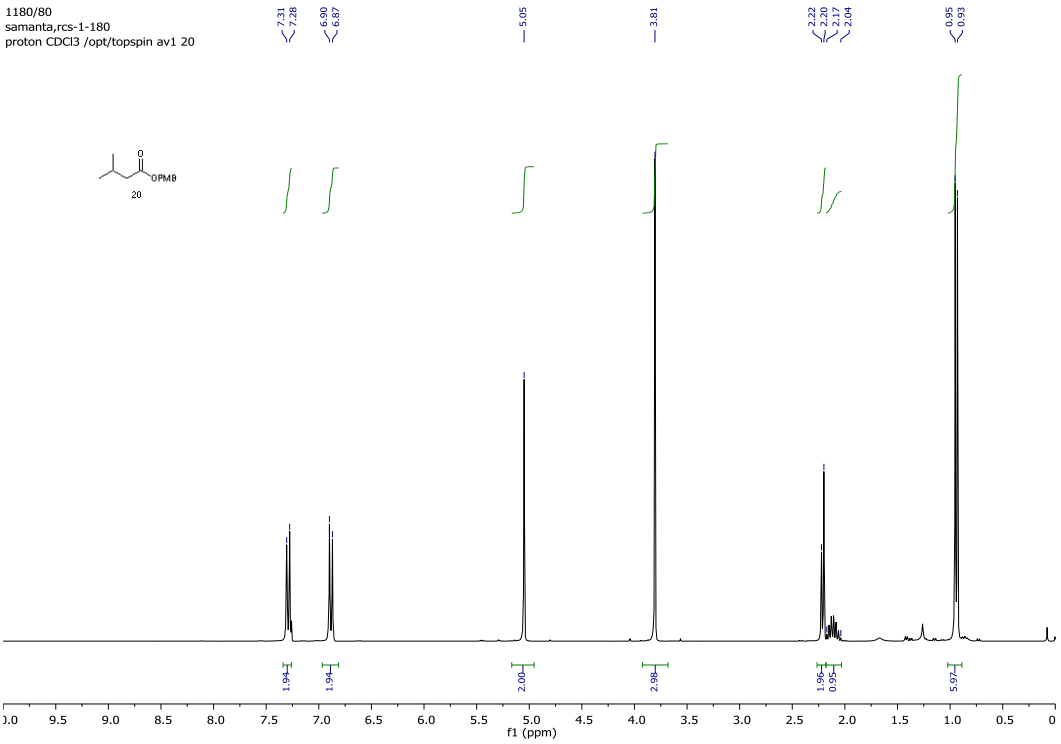

1172/31
samanta,rcs-1-172A
carbon CDCl3 /opt/topspin av1 31
173.89
159.75
130.13
128.49
114.08
66.00
55.42
34.54
31.94
29.34
29.27
29.25
25.12
22.77
14.21
O
O PMB
17
f1 (ppm)

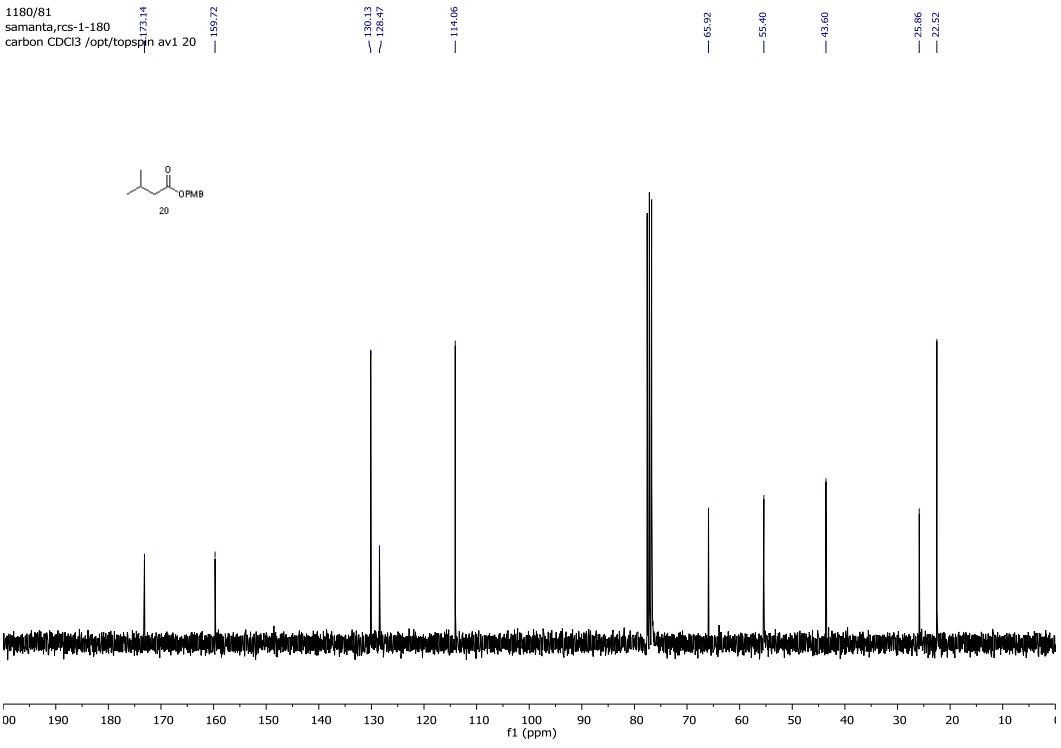

1173/460
Samanta, RCS-1-173
proton CDCl3 /opt/topspin av1 41
7.31
7.28
6.90
6.87
5.05
3.81
2.33
2.28
1.72
1.60
0.96
0.91
OPMB
18
1.95
1.95
2.00
3.01
2.02
2.34
3.04
f1 (ppm)

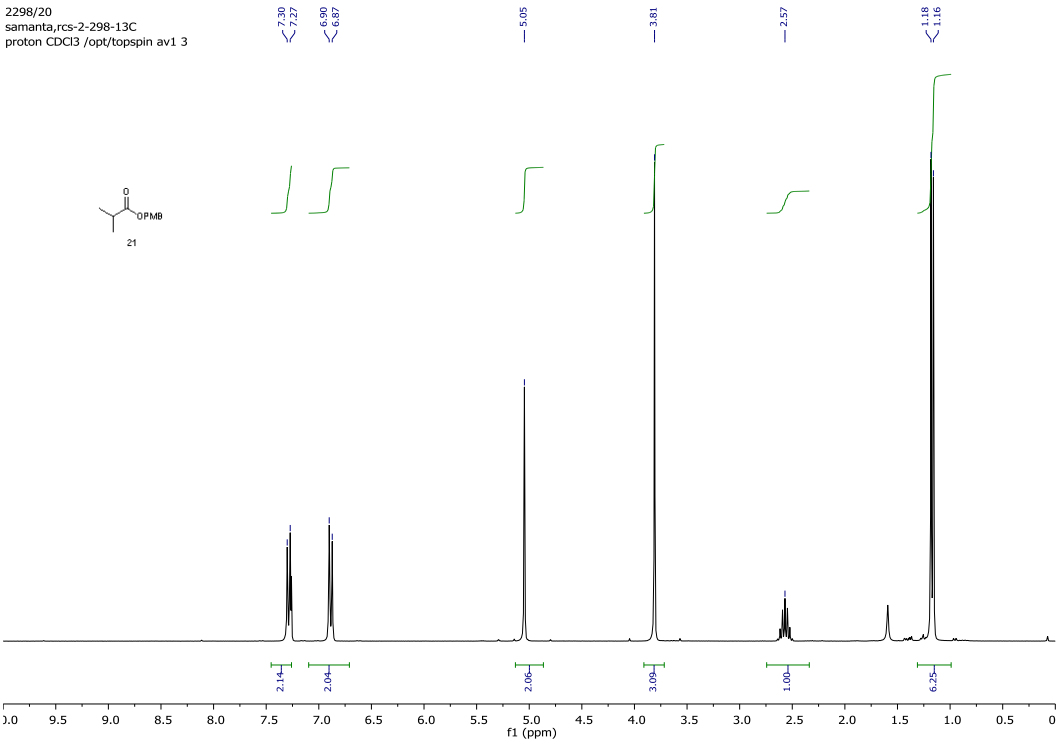

1173/461
Samanta, RCS-1-173
carbon CDCl3 /opt/topspin av1 41
173.71
159.75
130.13
128.47
114.09
66.00
55.43
36.41
18.60
13.80
OPMB
18
f1 (ppm)

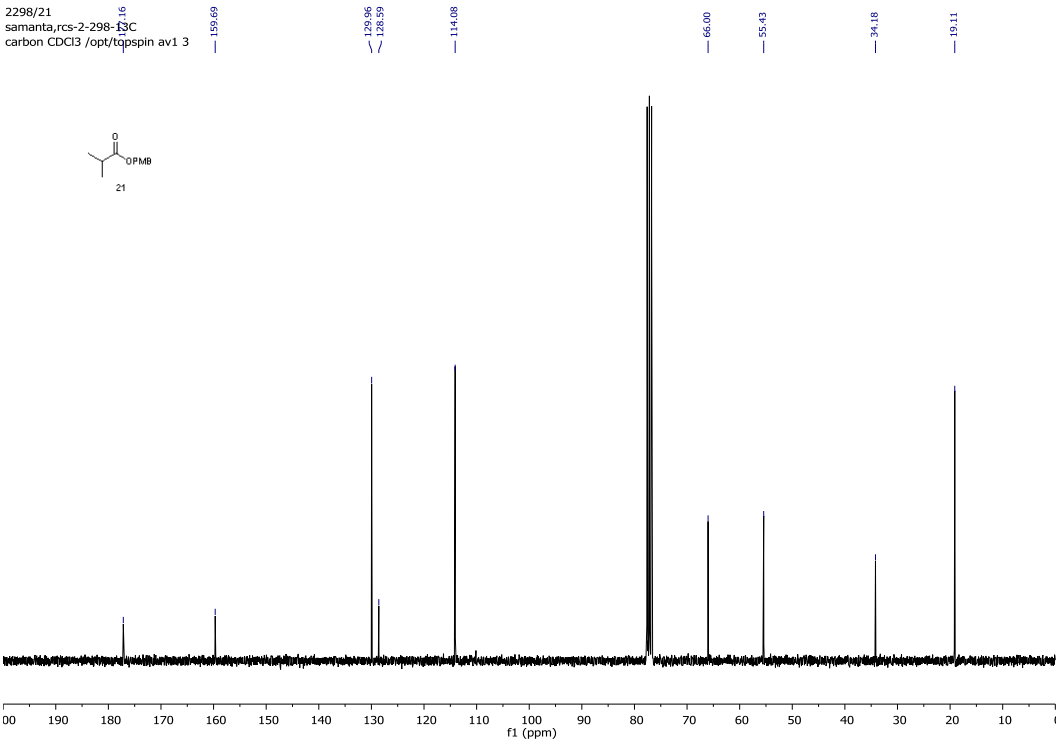

1182/110
samanta,rcs-1-182
proton CDCl3 /opt/topspin av1 33
7.31
7.28
6.90
6.87
5.05
3.81
2.39
2.31
1.17
1.12
OPMB
19
2.00
2.00
2.12
3.13
1.99
3.00
f1 (ppm)

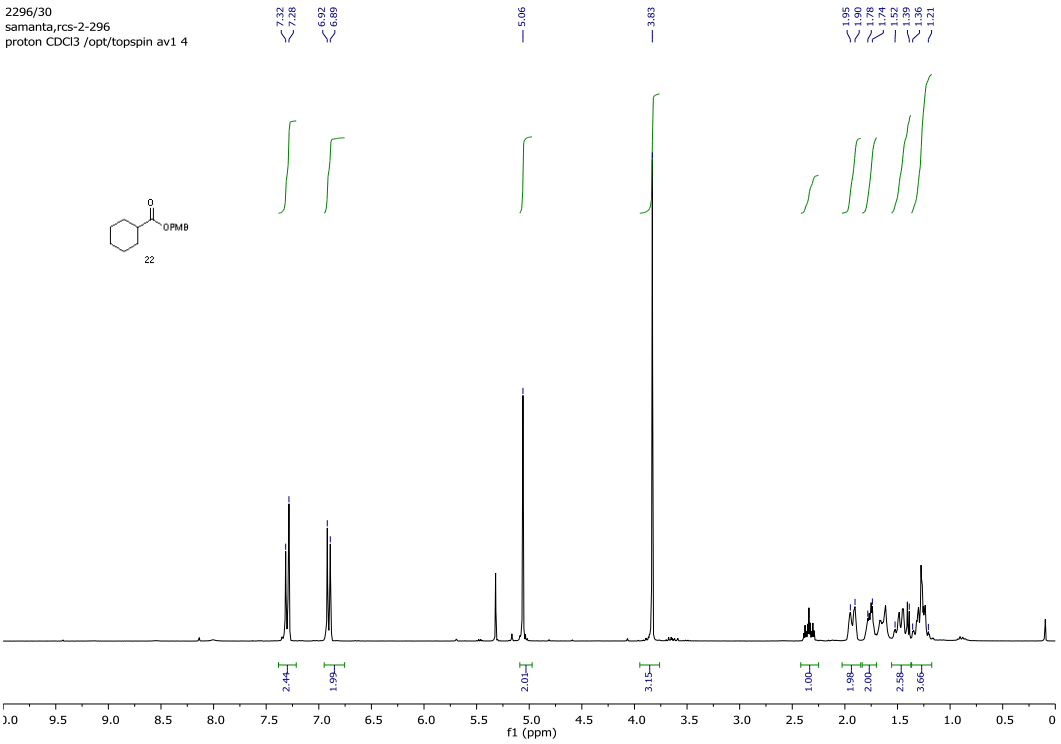

1182/111
samanta,rcs-1-182
carbon CDCl3 /opt/topspin av1 33
174.50
159.77
130.15
128.45
114.11
66.10
55.44
27.80
9.24
OPMB
19
f1 (ppm)

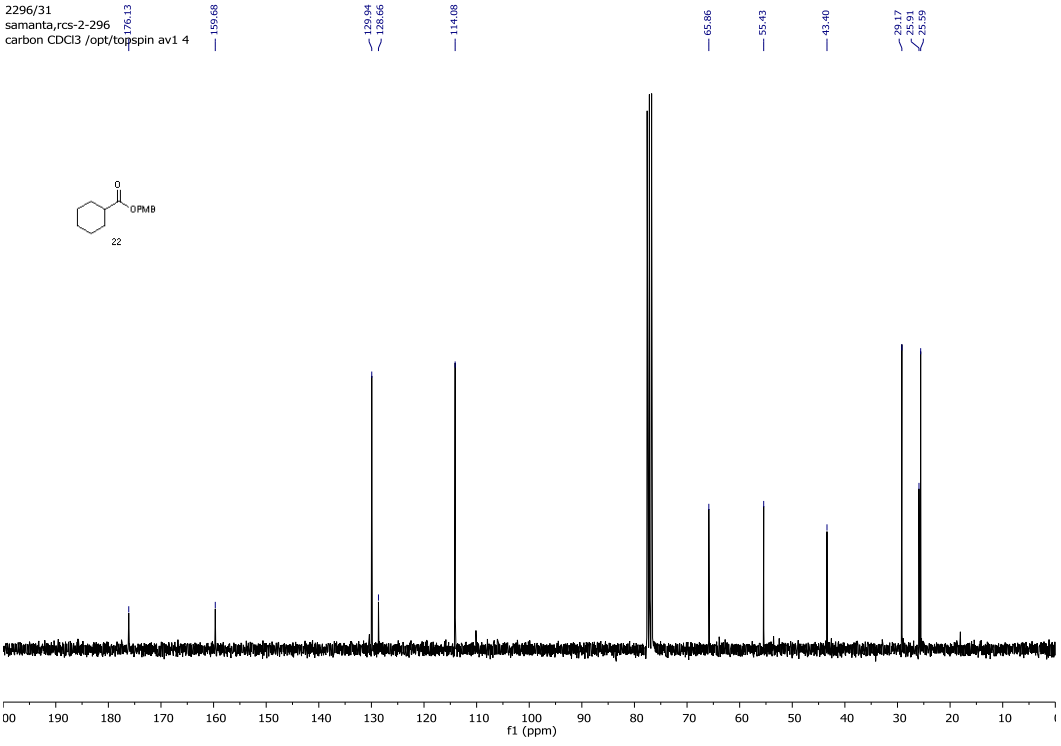

1180/80
samanta,rcs-1-180
proton CDCl3 /opt/topspin av1 20
7.31
7.28
6.90
6.87
5.05
3.81
2.22
2.20
2.17
2.04
0.95
0.93
OPMB
20
1.94
1.94
2.00
2.98
1.96
0.95
5.97
f1 (ppm)

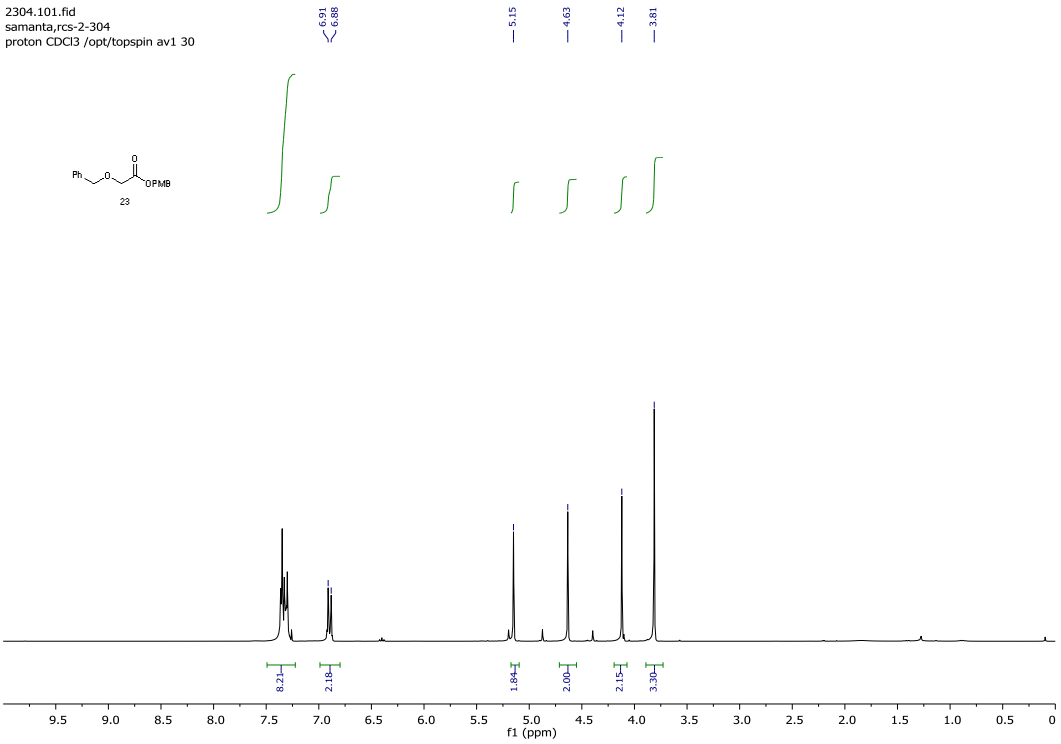

1180/81
samanta,rcs-1-180
carbon CDCl3 /opt/topspin av1 20
173.14
159.72
130.13
128.47
114.06
65.92
55.40
43.60
25.86
22.52
OPMB
20
f1 (ppm)

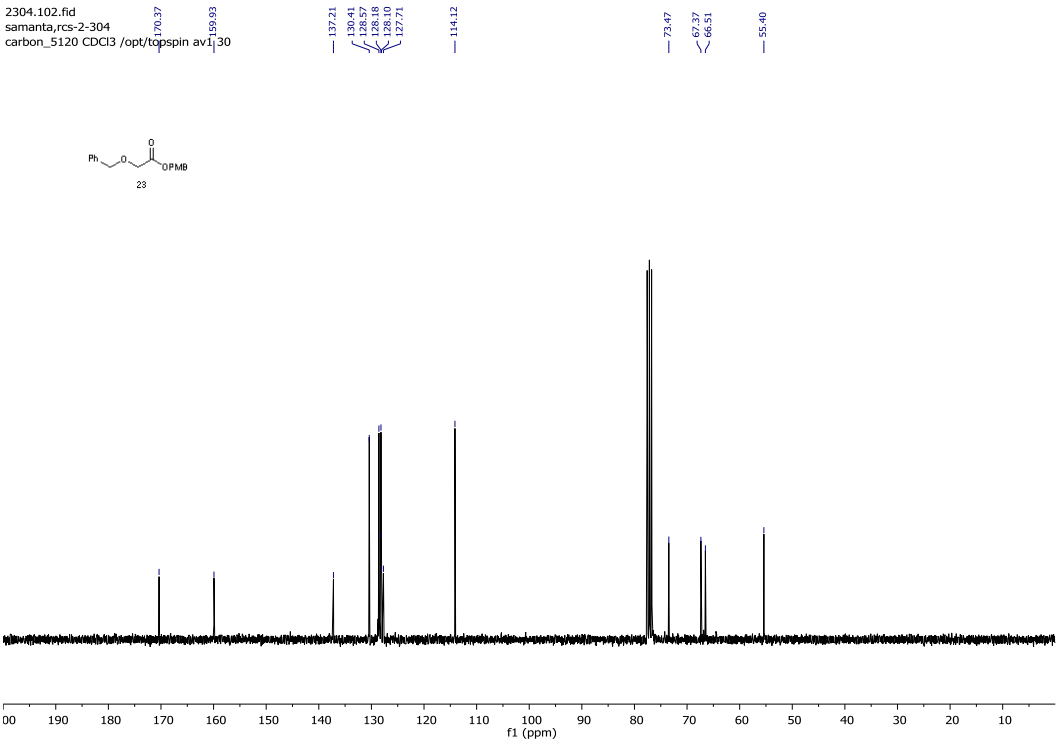

2298/20
samanta,rcs-2-298-13C
proton CDCl3 /opt/topspin av1 3
7.30
7.27
6.90
6.87
5.05
3.81
2.57
1.18
1.16
OPMB
21
2.14
2.04
2.06
3.09
1.00
6.25
f1 (ppm)

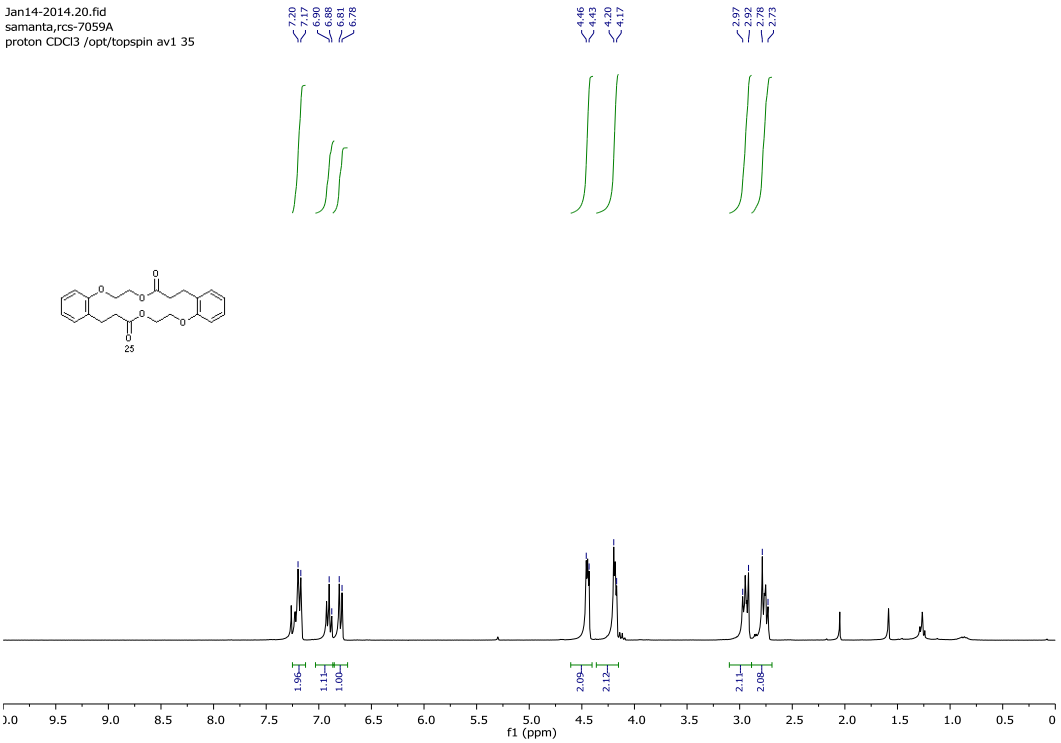

2298/21
samanta,rcs-2-298-13C
carbon CDCl3 /opt/topspin av1 3
159.69
129.96
128.59
114.08
66.00
55.43
34.18
19.11
OPMB
21
f1 (ppm)

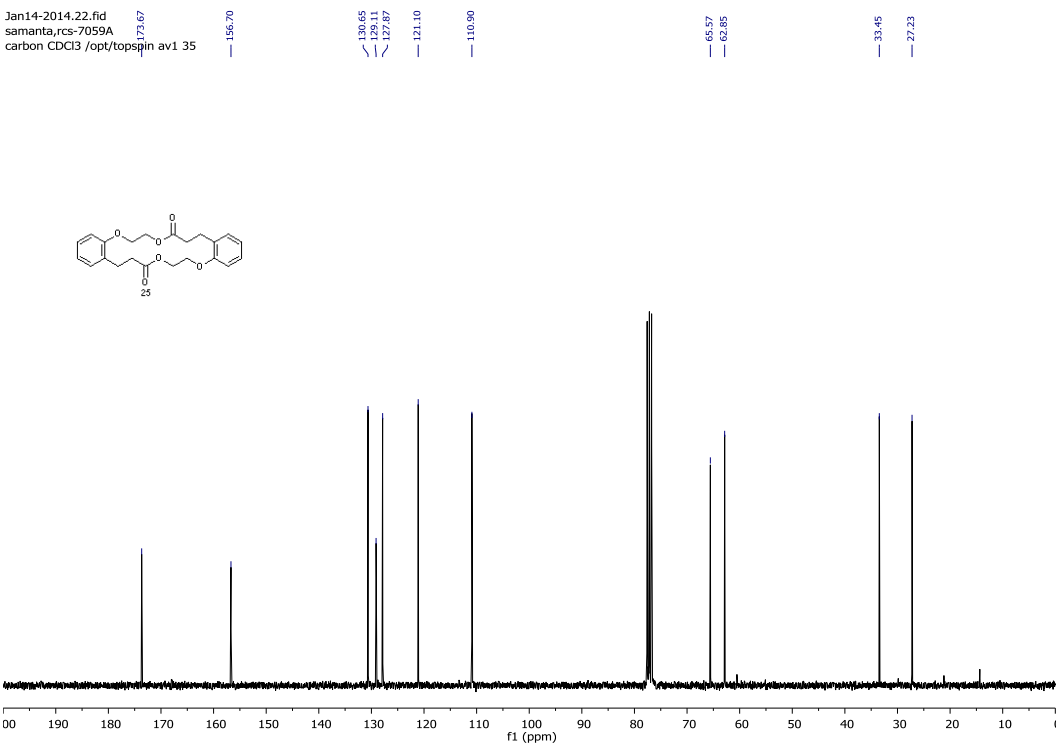

2296/30
samanta,rcs-2-296
proton CDCl3 /opt/topspin av1 4
7.32
7.28
6.92
6.89
5.06
3.83
1.95
1.90
1.78
1.74
1.52
1.39
1.36
1.21
OPMB
22
2.44
1.99
2.01
3.15
1.00
1.98
2.00
2.59
3.66
f1 (ppm)


2296/31
samanta,rcs-2-296
carbon CDCl3 /opt/topspin av1 4
176.13
159.68
129.94
128.66
114.08
65.86
55.43
43.40
29.17
25.91
25.59
OPMB
22
f1 (ppm)

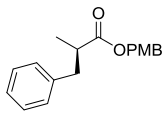

2304.101.fid
samanta,rcs-2-304
proton CDCl3 /opt/topspin av1 30
6.91
6.88
5.15
4.63
4.12
3.81
Ph
O
OPMB
23
8.21
2.18
1.84
2.00
2.15
3.30
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)


2304.102.fid
samanta,rcs-2-304
carbon_5120 CDCl3 /opt/topspin av1 30
170.37
159.93
137.21
130.41
128.57
128.18
128.10
127.71
114.12
73.47
67.37
66.51
55.40
Ph
O
OPMB
23
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

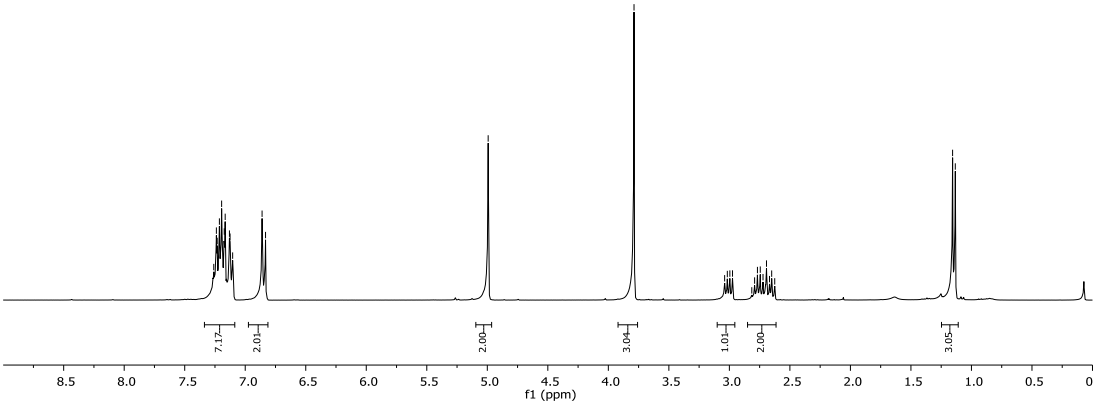

Jan14-2014.20.fid
samanta,rcs-7059A
proton CDCl3 /opt/topspin av1 35
7.20
7.17
6.90
6.88
6.81
6.78
4.46
4.43
4.20
4.17
2.97
2.93
2.78
2.73
25
1.96
1.11
1.00
2.09
2.12
2.11
2.08
f1 (ppm)


Jan14-2014.22.fid
samanta,rcs-7059A
carbon CDCl3 /opt/topspin av1 35
173.67
156.70
130.65
129.11
127.87
121.10
110.90
65.57
62.85
33.45
27.23
25
f1 (ppm)

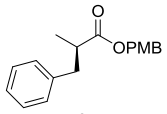

7.26 CDCl3
7.24
7.23
7.21
7.20
7.17
7.17
7.13
7.13
7.10
6.86
6.83
4.99
3.79
3.04
3.02
3.00
2.97
2.81
2.79
2.77
2.74
2.72
2.69
2.67
2.65
2.63
1.16
1.13


O
OPMB

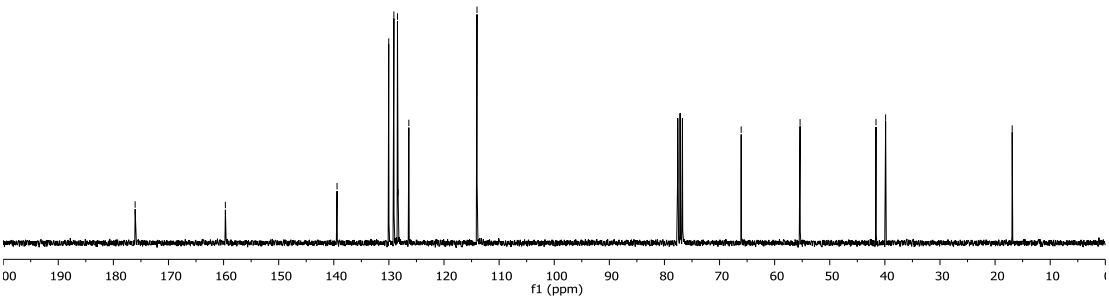
**27**


7.17
2.01
2.00
3.04
1.01
2.00
3.05
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
0
f1 (ppm)

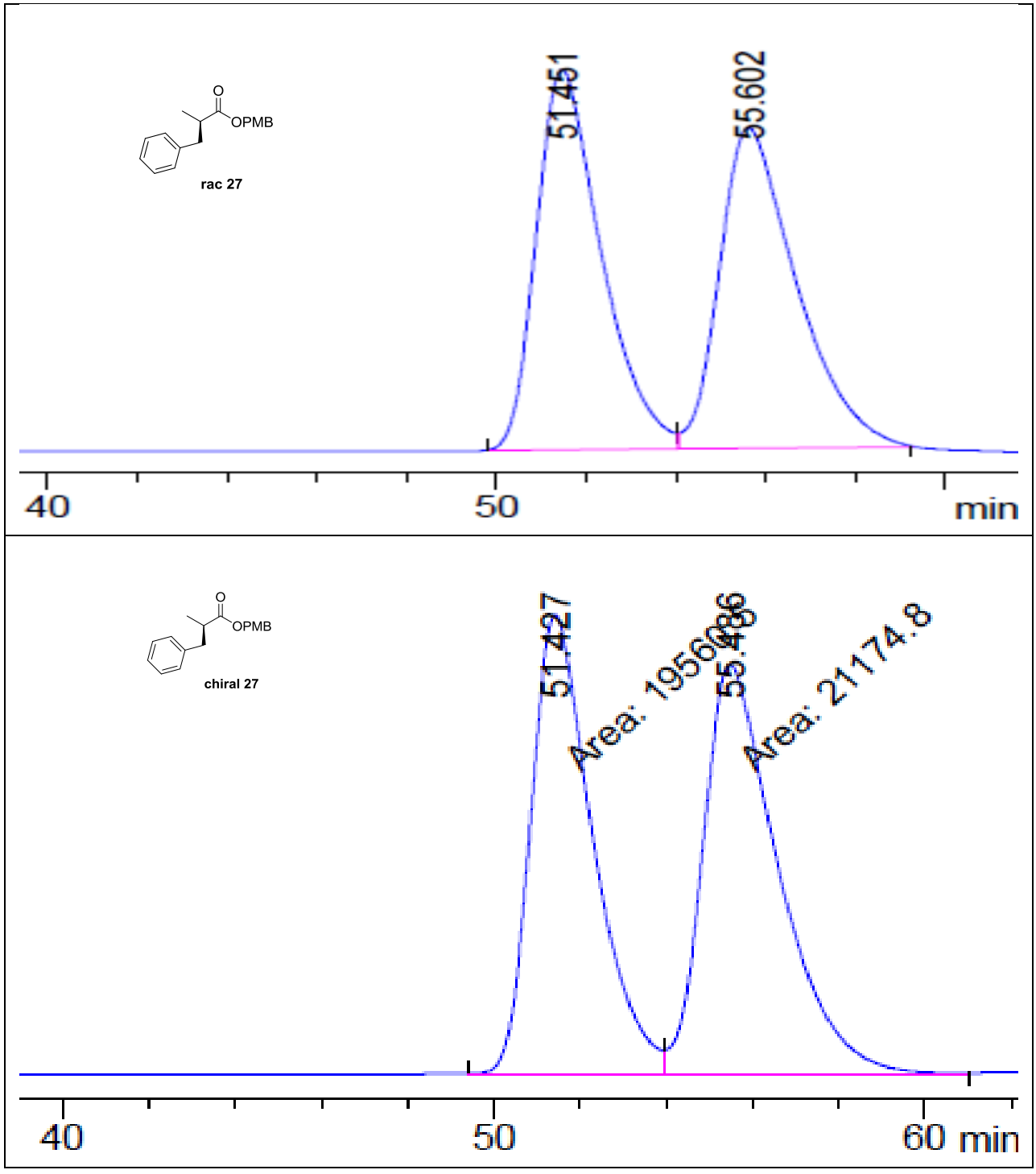

176.05
159.68
139.41
130.03
129.10
128.45
128.33
126.38
114.01
66.07
55.39
41.61
39.86
16.90


O
OPMB

**27**


00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

**HPLC:**


O
OPMB
rac 27
51.451
55.602
40
50
min
O
OPMB
chiral 27
51.427
Area: 19560
55.486
Area: 21174.8
40
50
60 min