Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

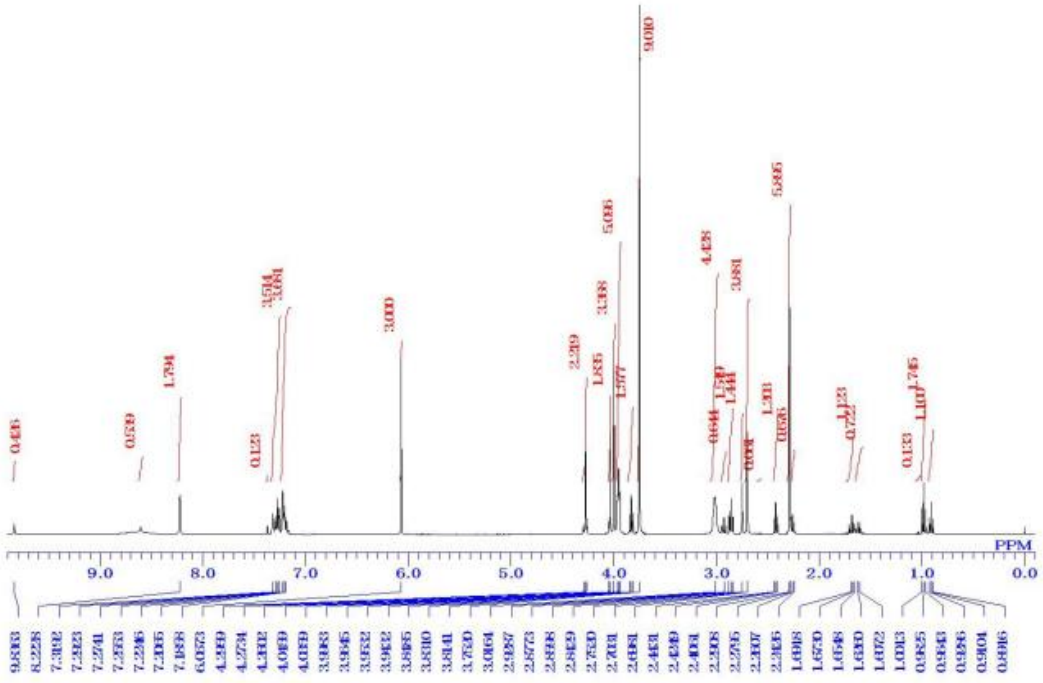
contents

1. General methods

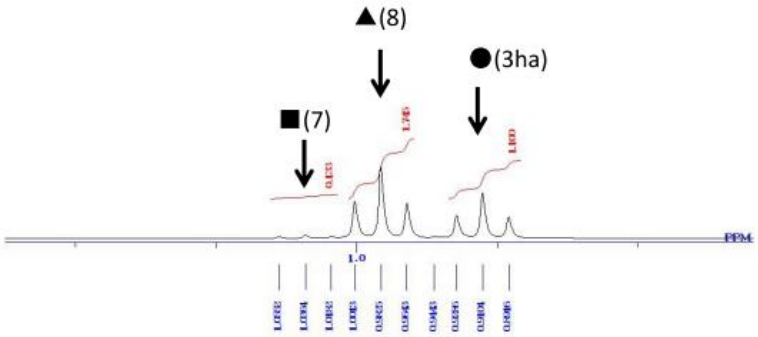
Nuclear magnetic resonance (^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz)) spectra were determined on a JEOL JNM-ECS400 spectrometer. Chemical shifts for ^{1}H NMR are reported as δ values relative to tetramethylsilane as the internal standard and coupling constants are in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. Chemical shifts for ^{13}C NMR were reported in ppm relative to the center line of a triplet at 77.16 ppm for deuteriochloroform. Mass spectra were measured on JMS-T100TD (DART). Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F_{254}. Preparative TLC separations were performed on Merck analytical plates (0.25 or 0.50 mm thick) precoated with silica gel 60 F_{254}. Flash chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 N (spherical, neutral, 40-100 mesh) unless otherwise noted. Amino acid derivatives, Cbz-phenylalanine **1f** and Boc-alanine **1g**, were purchased from Watanabe chemical industries, LTD and used without further purification. Other reagents were commercial grades and were used without any purification unless otherwise noted. All reactions sensitive to oxygen or moisture were conducted under a N_2 atmosphere.

2. NMR spectra for time-course study

FigureS1. NMR spectra for the reaction using DMT-3,5-LUT at 10 min after reaction initiation.
(a) overall picture



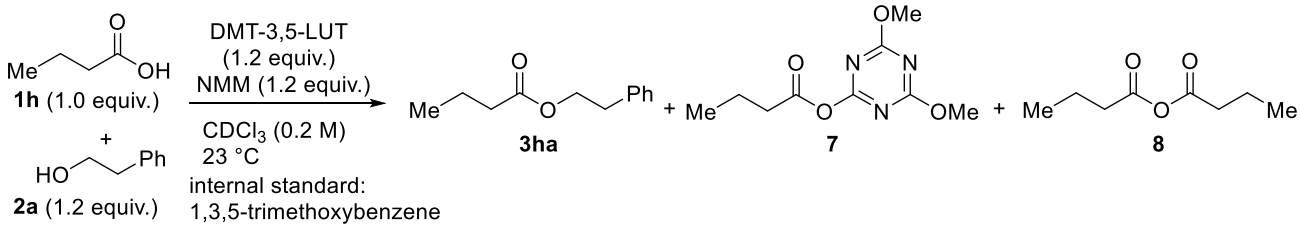
(b) Yields were determined based on these signals.

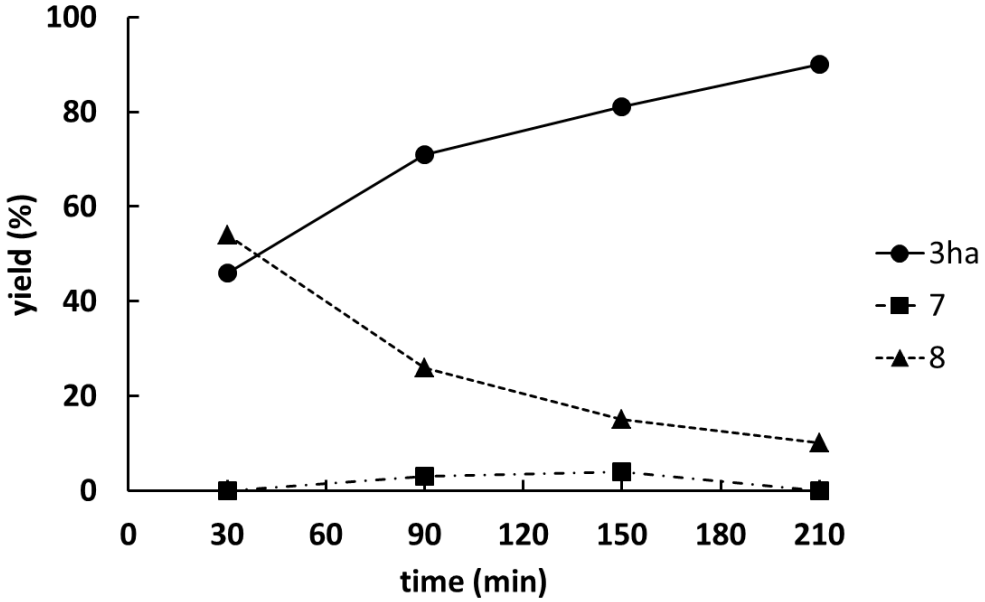


3. Reaction by dropwise addition

The reaction was conducted by dropwise addition of the solution of **1h** and NMM.

Figure S2

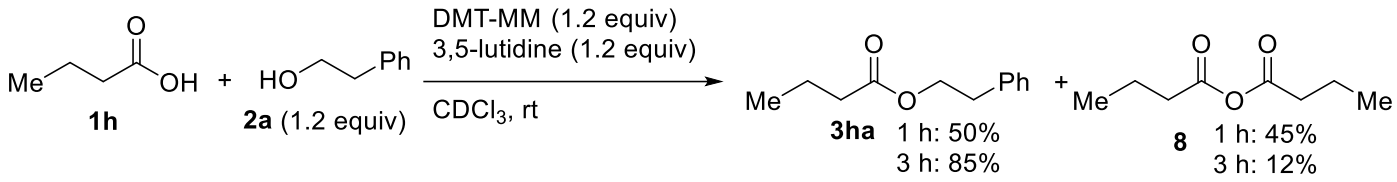




4. Esterification using DMT-MM and 3,5-lutidine

Esterification using a combination of DMT-MM and 3,5-lutidine for 1 h afforded products **3ha** and **8** in 50% and 45% yields, respectively (Scheme S2). After 3 hours, **3ha** increased to 85% and **8** decreased to 12%, respectively. These results are ascribed to the low solubility of DMT-MM in $CDCl_3$ and the low basicity of 3,5-lutidine, which is insufficient to generate carboxylate anions.

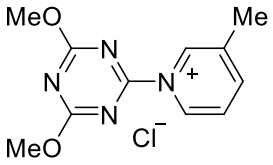
Scheme S1.



5. Experimental procedure and characterization data for products

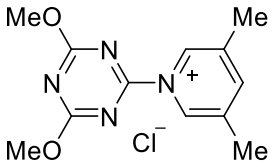
General procedure for the synthesis of the condensing reagents:
To a solution of CDMT (2.23 g, 12.7 mmol) in THF (25 mL) was added 3,5-lutidine (1.74 mL, 15.2 mmol) at room temperature. After stirring for 4 hours, a precipetate was filtered and washed with THF to give DMT-3,5-LUT (3.47 g, 97% yield) as a white solid.

1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-3-methylpyridin-1-ium chloride (DMT-3-PIC)



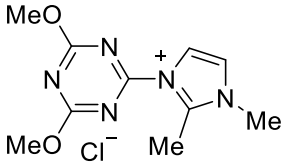
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.2 (d, J = 6.4 Hz, 1H), 10.1 (s, 1H), 9.01 (d, J = 8.2 Hz, 1H), 8.62 (dd, J = 6.4, 8.2 Hz, 1H), 4.30 (s, 6H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 164.6, 153.2, 140.2, 139.8, 138.6, 128.8, 57.4, 19.1; HRMS (ESI+) Calcd for $C_{11}H_{13}N_4O_2^+$ ([M]$^+$): 233.1039; found: 233.1046.

1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-3,5-dimethylpyridin-1-ium chloride (DMT-3,5-LUT)



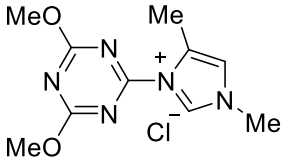
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 2H), 8.68 (s, 1H), 4.32 (s, 6H), 2.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 164.7, 153.6, 139.6, 137.8, 57.6, 19.1; HRMS (ESI+) Calcd for $C_{12}H_{15}N_4O_2^+$([M]$^+$): 247.1195; found: 247.1201.

3-(4,6-dimethoxy-1,3,5-triazin-2-yl)-1,5-dimethyl-1H-imidazol-3-ium chloride (DMT-1,2-M2Im)



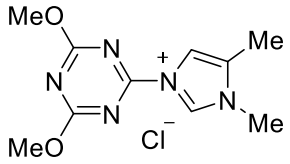
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, J = 2.3 Hz, 1H), 8.18 (d, J = 2.3 Hz, 1H), 4.31 (s, 3H), 4.16 (s, 6H), 3.33 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 163.2, 147.9, 124.8, 118.8, 56.7, 36.9, 15.0; HRMS (ESI+) Calcd for $C_{10}H_{14}N_5O_2^+$ ([M]$^+$): 236.1148; found: 236.1153.

3-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-1,4-dimethyl-1H-imidazol-3-ium chloride (DMT-1,4-M2Im)



^{1}H NMR (400 MHz, $CDCl_3$): δ 11.6 (s, 1H), 7.51 (s, 1H), 4.36 (s, 3H), 4.23 (s, 6H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 163.2, 140.1, 132.0, 122.8, 57.3, 37.5, 13.2; HRMS (ESI+) Calcd for $C_{10}H_{14}N_5O_2^+$ ([M]$^+$): 236.1148; found: 236.1142.

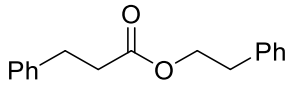
3-(4,6-dimethoxy-1,3,5-triazin-2-yl)-1,5-dimethyl-1*H*-imidazol-3-ium chloride (DMT-1,5-M2Im)



^{1}H NMR (400 MHz, $CDCl_3$): δ 11.94 (s, 1H), 7.87 (s, 1H), 4.28 (s, 3H), 4.24 (s, 6H) 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 161.5, 139.6, 133.0, 114.8, 57.4, 35.0, 9.6; HRMS (ESI+) Calcd for $C_{10}H_{14}N_5O_2^+$ ([M]$^+$): 236.1148; found: 236.1149.

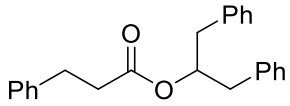
General procedure for esterification using DMT-3,5-LUT:
To a suspension of DMT-3,5-LUT (271 mg, 0.96 mmol) in CH_2Cl_2 (1 mL) was added a solution of 3-phenylpropionic acid **1a** (120 mg, 0.80 mmol), 1,3-diphenylpropan-2-ol **2b** (192 µL, 0.96 mmol), and *N*-methylmorpholine (106 µL, 0.96 mmol) in CH_2Cl_2 (1 mL) at room temperature. After stirring for 9 hours, the reaction mixuture was washed with 1 M HCl, sat. aq. $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/AcOEt 95:5) to afford **3ab** (254 mg, 92%) as a liquid.

Phenethyl 3-phenylpropanoate (3aa)[1)]



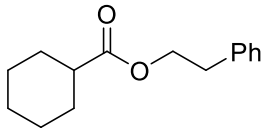
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.10 (m, 10H), 4.28 (t, J = 6.9 Hz, 2H), 2.95-2.87 (m, 4H), 2.61 (t, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 140.6, 137.9, 129.0, 128.6, 128.4, 126.7, 126.4, 65.1, 36.0, 35.2,31.0; HRMS (DART+) Calcd for $C_{17}H_{19}O_2$ ([M+H]$^+$): 255.1385; found: 255.1379.

1,3-Diphenylpropan-2-yl 3-phenylpropanoate (3ab)



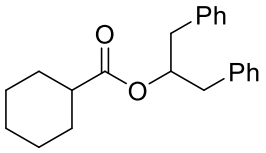
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.13 (m, 13H), 7.12-7.07 (m, 2H), 5.31 (quint, J = 6.4 Hz, 1H), 2.90-2.79 (m, 4H), 2.78 (t, J = 7.8 Hz, 2H), 2.49 (t, J = 7.8 Hz, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 140.7, 137.6, 129.6, 128.6, 128.5, 128.4, 126.7, 126.3, 75.4, 40.1, 36.1, 31.0; HRMS (DART+) Calcd for $C_{24}H_{24}O_2$ ([M+H]$^+$): 345.1855; found: 345.1844.

Phenethyl cyclohexanecarboxylate (3ba)[2)]



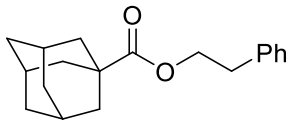
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.27 (m, 2H), 7.26-7.19 (m, 3H), 4.28 (t, J = 6.9 Hz, 2H), 2.93 (t, J = 6.9 Hz, 2H), 2.27 (tt, J = 12.0,4.0 Hz, 1H), 1.90-1.82 (m, 2H), 1.78-1.67 (m, 2H), 1.67-1.57 (m, 1H), 1.47-1.30 (m, 2H) 1.32-1.13 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.2, 138.2, 129.1, 128.6, 126.6, 64.7, 43.3, 35.3, 29.1, 25.9, 25.6; HRMS (DART+) Calcd for $C_{15}H_{21}O_2$ ([M+H]$^+$): 233.1542; found: 233.1538.

1,3-Diphenylpropan-2-yl cyclohexanecarboxylate (3bb)



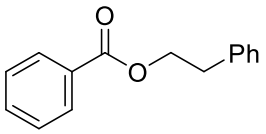
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.10 (m, 10H), 5.31 (quint, J = 6.4 Hz, 1H), 2.86 (d, J = 6.4 Hz, 4H), 2.20-2.10 (m, 1H), 1.75-1.54 (m, 5H), 1.35-1.09 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 137.7, 129.6, 128.4, 126.6, 74.7, 43.5, 40.2, 29.0, 25.9, 25.5; HRMS (DART+) Calcd for $C_{22}H_{26}O_2$ ([M+H]$^+$): 323.2011; found: 323.2017.

Phenethyl (3r,5r,7r)-adamantane-1-carboxylate (3ca)[3)]



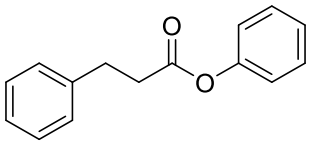
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.27 (m, 2H), 7.25-7.19 (m, 3H), 4.26 (t, J = 6.9 Hz, 2H), 2.93 (t, J = 6.9, 2H), 2.05-1.60 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8, 138.2, 129.1, 128.6, 126.6, 64.7, 40.8, 39.0, 36.7, 35.3, 28.1; LRMS (DART+) Calcd for $C_{19}H_{25}O_2$([M+H]$^+$): 285.1855; found: 285.1860.

Phenethyl benzoate (3da)[1)]



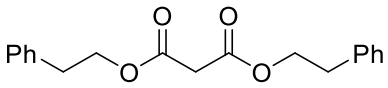
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05-7.95 (m, 2H), 7.59-7.51 (m, 1H), 7.47-7.40 (m, 2H), 7.37-7.20 (m, 5H), 4.54 (t, J = 6.9 Hz, 2H), 3.09 (t, J = 6.9, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 138.0, 133.0, 130.4, 129.7, 129.1, 128.6, 128.4, 126.7, 65.6, 35.3; HRMS (DART+) Calcd for $C_{15}H_{14}O_2$ ([M+H]$^+$): 227.1072; found:227.1065.

Phenyl 3-phenylpropanoate (3ad)[4)]



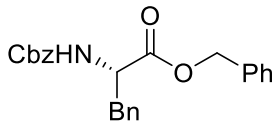
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.18 (m, 8H), 7.04-6.98 (m, 2H), 3.08 (t, J = 7.8 Hz, 2H), 2.89 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 150.8, 140.3, 129.5, 128.7, 128.6, 126.6, 126.0, 121.7, 36.1, 31.1; HRMS (DART+) Calcd for $C_{15}H_{15}O_2$ ([M+H]$^+$): 227.1072; found: 227.1078.

Diphenethyl malonate (3ea)[5)]



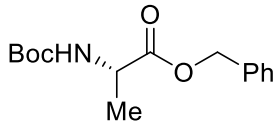
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.13 (m, 10H), 4.34 (t, J = 7.1 Hz, 4H), 3.35 (s, 2H), 2.93 (t, J = 7.1 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 137.5, 129.0, 128.7, 126.8, 66.1, 41.7, 35.0; HRMS (DART+) Calcd for $C_{19}H_{21}O_4$ ([M+H]$^+$): 313.1440; found: 313.1446.

Benzyl ((benzyloxy)carbonyl)-L-phenylalaninate (3fe)[6)]



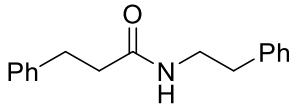
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.15 (m, 13H), 7.05-6.96 (m, 2H), 5.23 (d, J = 7.7 Hz, 1H), 5.16 (d, J = 11.9 Hz, 1H), 5.11 (d, J = 11.9 Hz, 1H), 5.15 (d, J = 12.8 Hz, 1H), 5.07 (d, J = 12.8 Hz, 1H), 4.71 (td, J = 5.96, 7.7 Hz, 1H), 3.15-3.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 155.7, 136.3, 135.6, 135.2, 129.5, 128.75, 128.71, 128.66, 128.3, 128.2, 127.2, 67.4, 67.1, 54.9, 38.3; HRMS (DART+) Calcd for $C_{24}H_{24}NO_4$ ([M+H]$^+$): 390.1705; found: 390.1702.

Benzyl (*tert*-butoxycarbonyl)-L-alaninate (3ge)[7)]



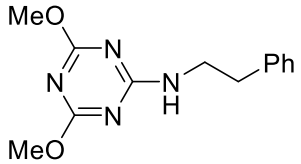
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.30 (m, 5H), 5.20 (d, J = 12.4 Hz, 2H), 5.14 (d, J = 12.4 Hz, 2H), 5.04 (brs, 1H), 4.37 (quint, J = 7.2 Hz, 1H), 1.44 (s, 9H), 1.39 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 155.2, 135.6, 128.7, 128.5, 128.3, 80.0, 67.1, 49.4, 28.4, 18.8; HRMS (DART+) Calcd for $C_{15}H_{22}NO_4$ ([M+H]$^+$): 280.1549; found: 280.1545.

***N*-phenethyl-3-phenylpropanamide (5)[8)]**



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.15 (m, 8H), 7.10-6.98 (m, 2H), 5.31 (br s, 1H), 3.48 (td, J = 7.0, 6.1 Hz, 2H), 2.94 (t, J = 7.8 Hz, 2H), 2.74 (t, J = 7.0 Hz, 2H), 2.42 (t, J = 7.8 Hz, 2H).

4,6-dimethoxy-*N*-phenethyl-1,3,5-triazin-2-amine (6)[8)]



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.15 (m, 5H), 5.34 (br s, 1H), 3.98 (s, 3H), 3.91 (s, 3H), 3.72 (td, J = 7.0, 6.2 Hz, 2H), 2.90 (t, J = 7.0 Hz, 2H).

6. References

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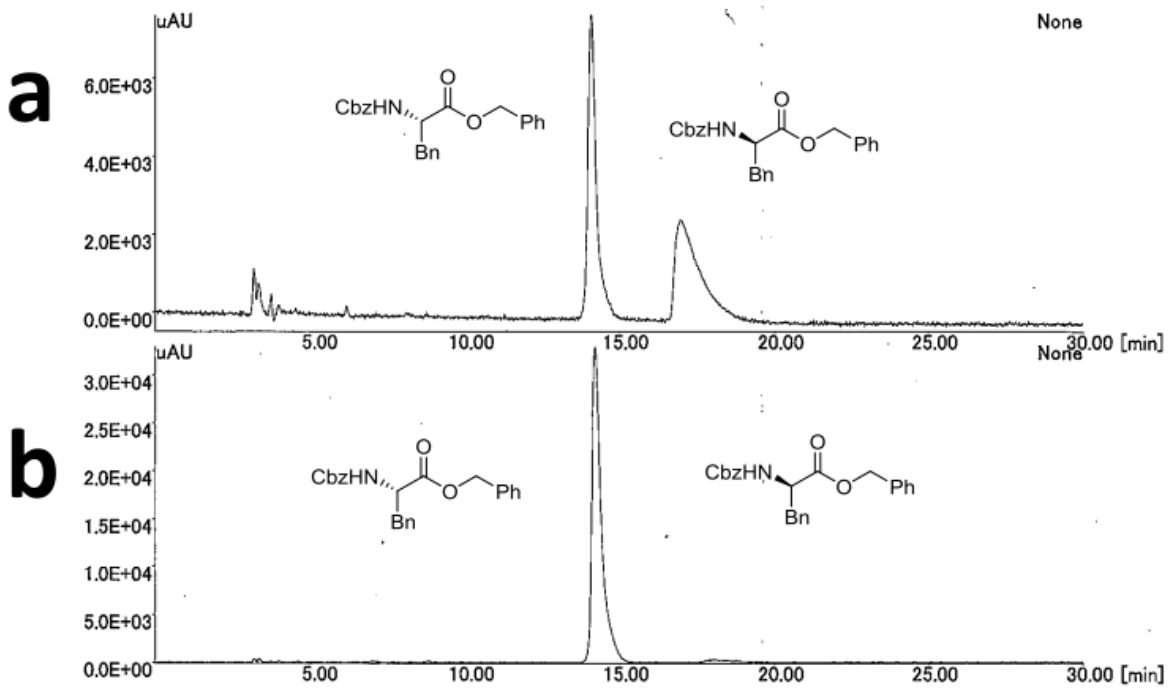
7. HPLC analyses

Benzyl ((benzyloxy)carbonyl)-L-phenylalaninate (3fe)



Conditions

Chiralpak IB-3 4.6×25 cm

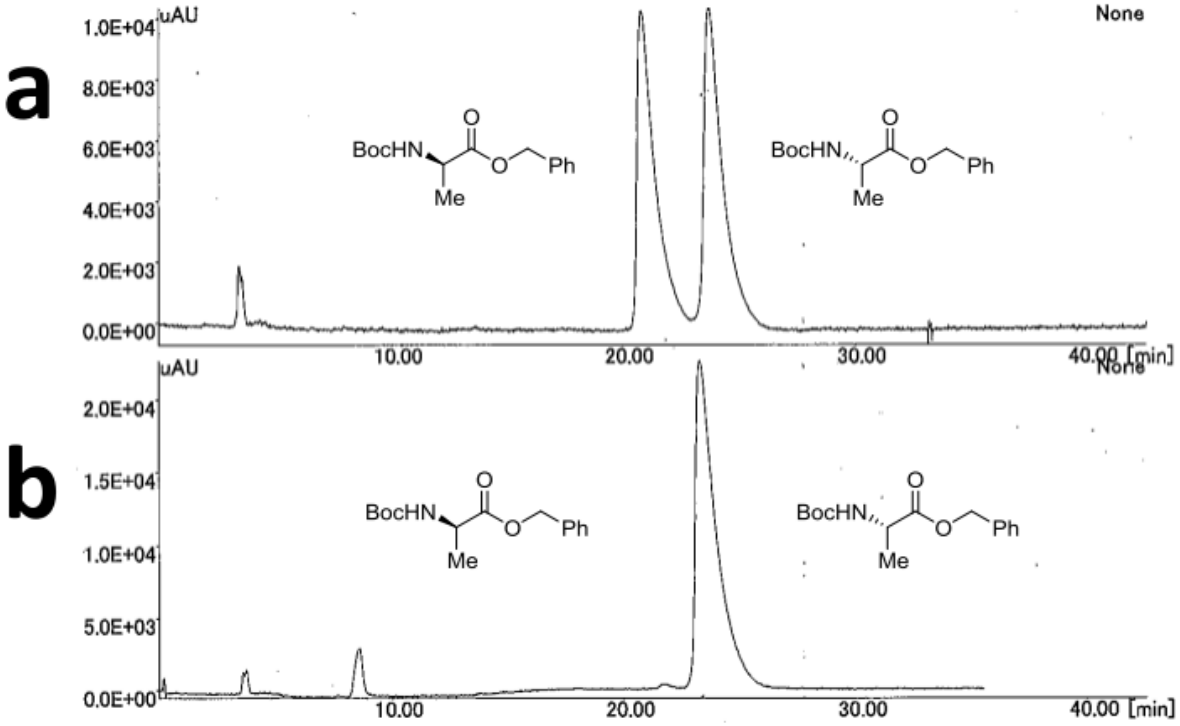
Flow: 1.0 mL/min (hexane/2-propanol = 95:5)

Detection at 254 nm

panel a: 1. Benzyl ((benzyloxy)carbonyl)-L-phenylalaninate, 14.1 min, 50%
2. Benzyl ((benzyloxy)carbonyl)-D-phenylalaninate, 17.0 min, 50%

panel b: 1. Benzyl ((benzyloxy)carbonyl)-L-phenylalaninate, 14.2 min, 98%
2. Benzyl ((benzyloxy)carbonyl)-D-phenylalaninate, 18.1 min, 2%

Benzyl (*tert*-butoxycarbonyl)-L-alaninate (3ge)



Conditions
Chiralpak IB-3 4.6×25 cm

Flow: 0.5 mL/min (hexane/2-propanol = 99.5:0.5)

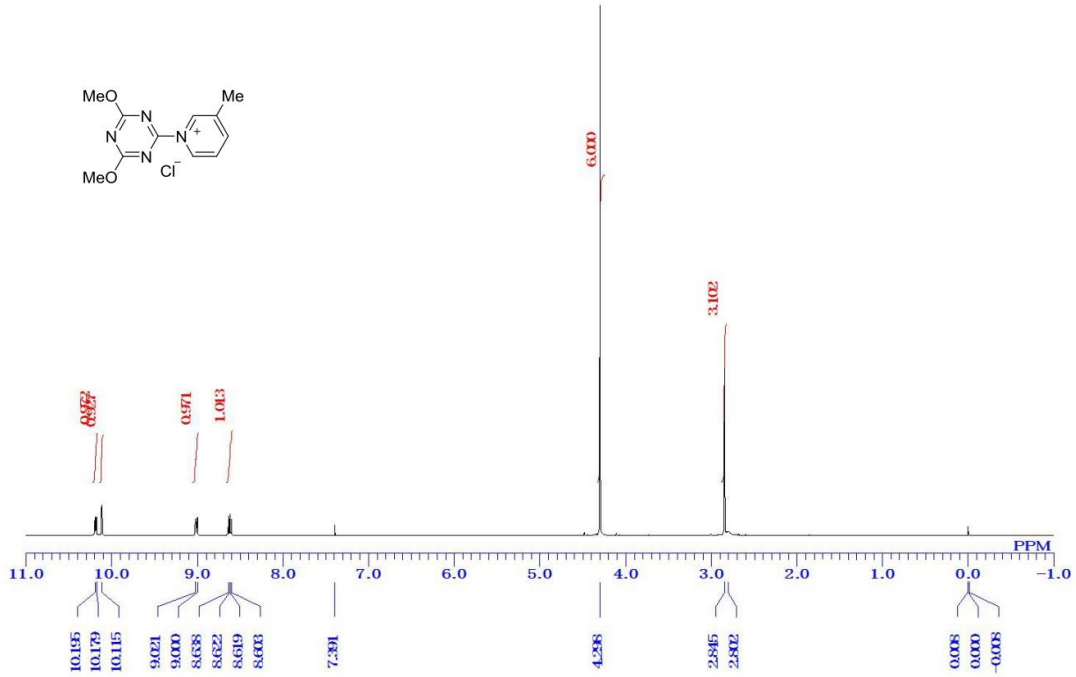
Detection at 208 nm

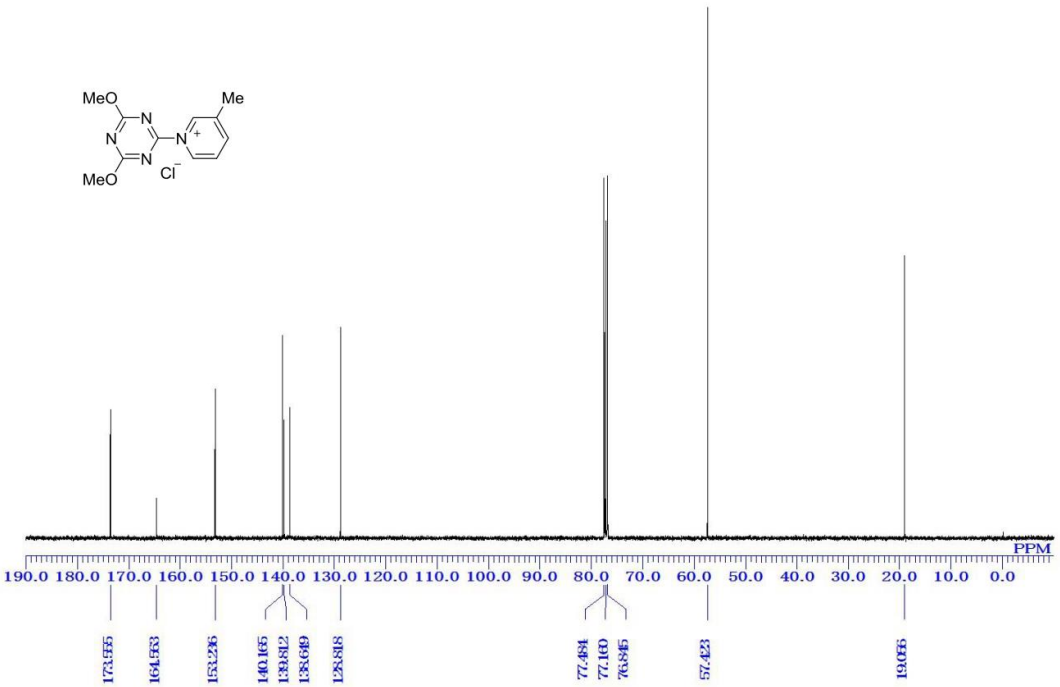
panel a: 1. Benzyl (*tert*-butoxycarbonyl)-D-alaninate, 20.8 min, 50%
2. Benzyl (*tert*-butoxycarbonyl)-L-alaninate, 23.7 min, 50%

panel b: 1. Benzyl (*tert*-butoxycarbonyl)-D-alaninate, 21.7 min, 1%
2. Benzyl (*tert*-butoxycarbonyl)-L-alaninate, 23.3 min, 99%

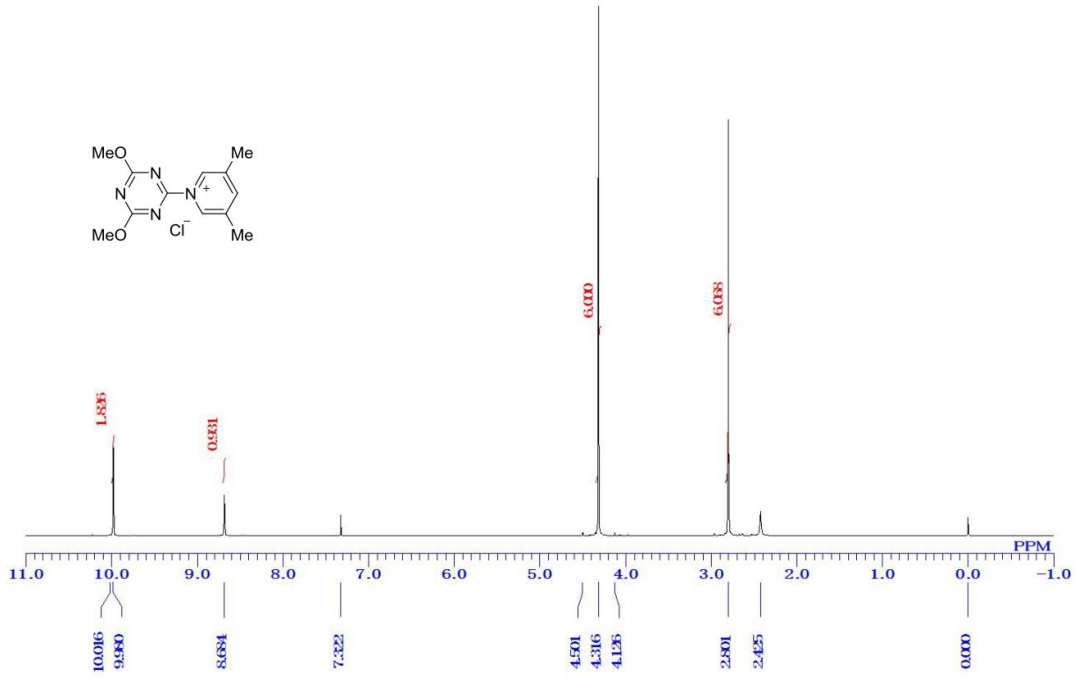
8. ^{1}H and ^{13}C NMR spectra

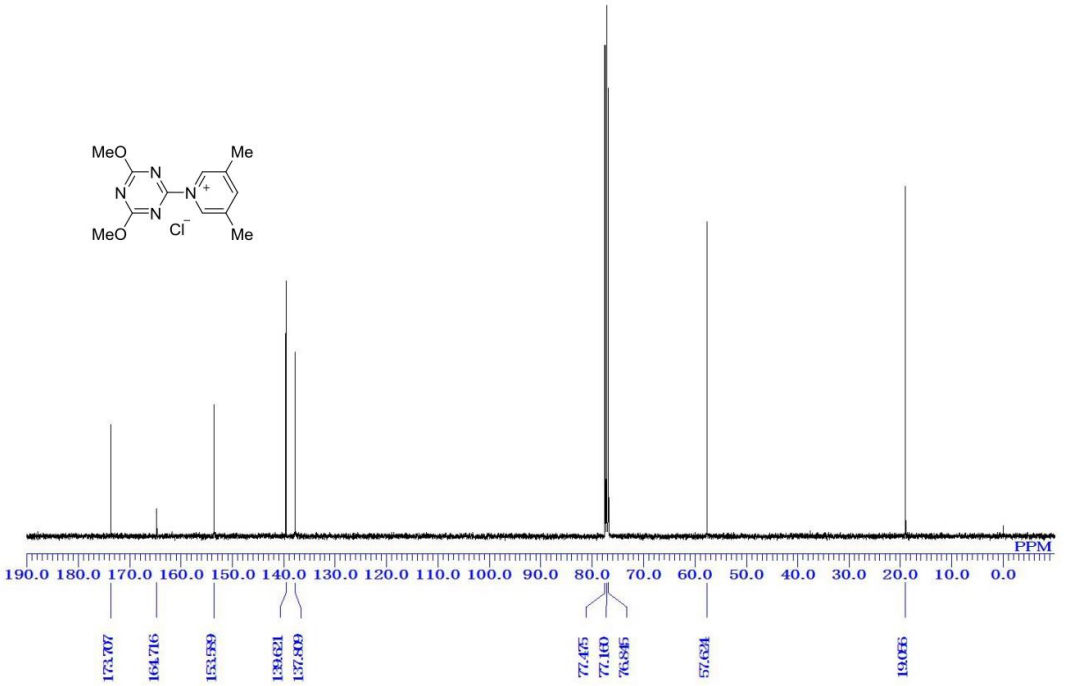
1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-3-methylpyridin-1-ium chloride (DMT-3-PIC)



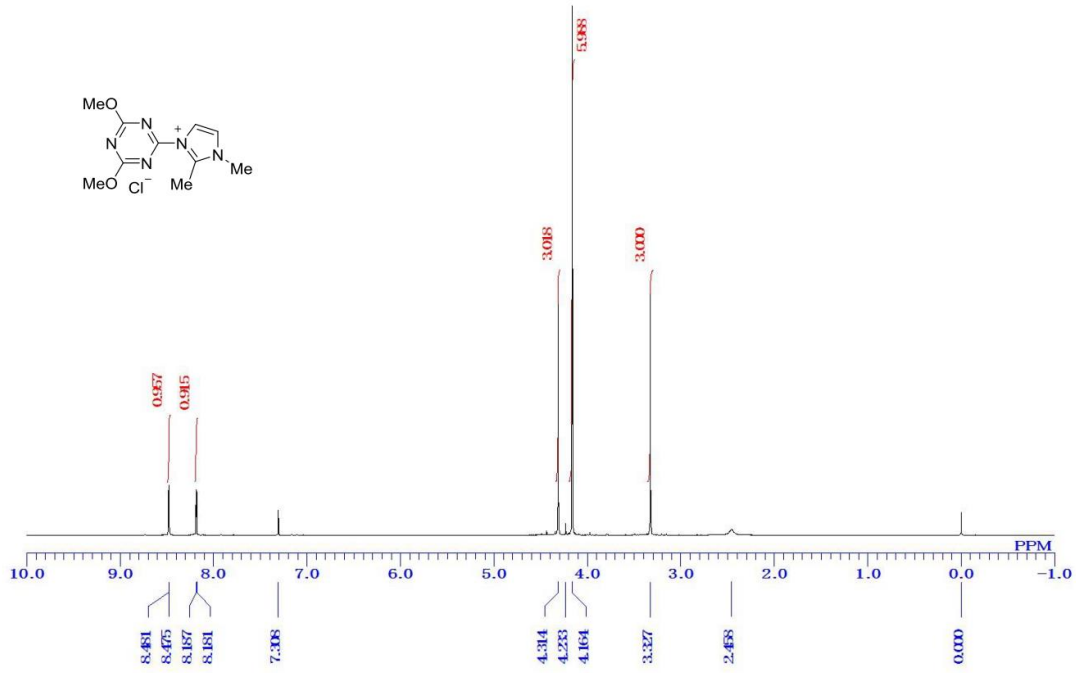


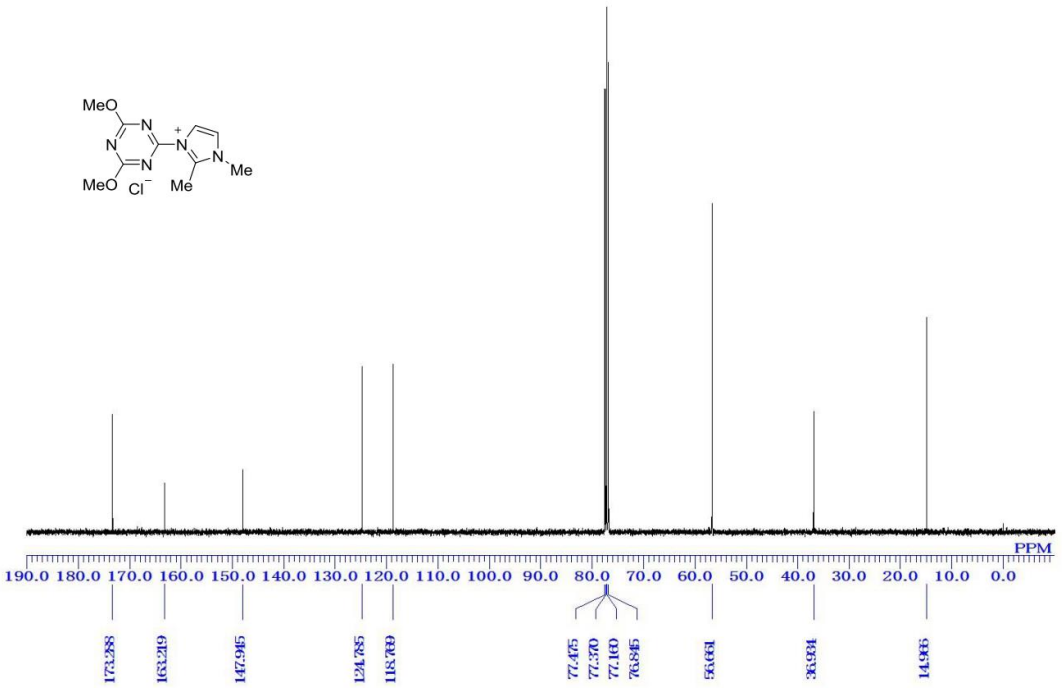
1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-3,5-dimethylpyridin-1-ium chloride (DMT-3,5-LUT)



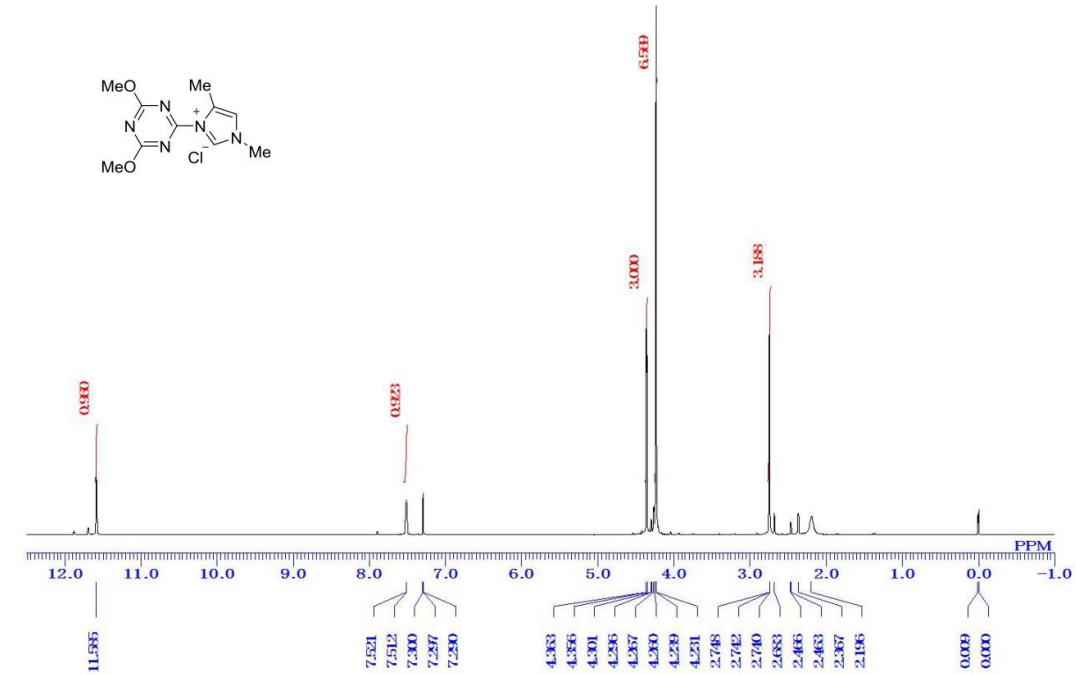


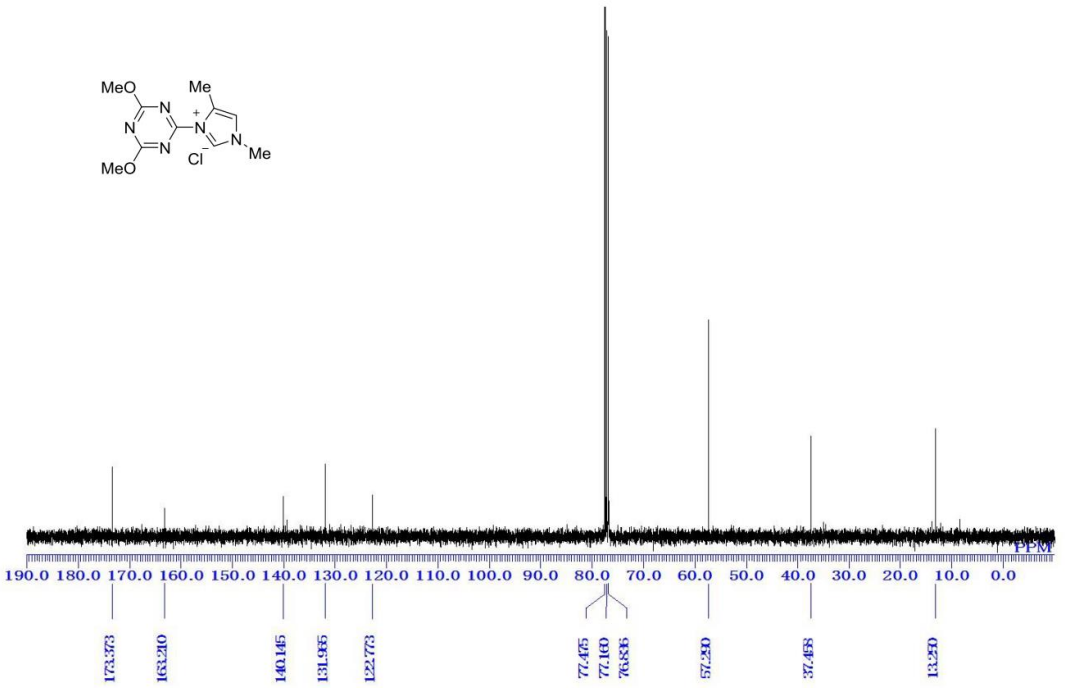
3-(4,6-dimethoxy-1,3,5-triazin-2-yl)-1,5-dimethyl-1H-imidazol-3-ium chloride (DMT-1,2-M2Im)



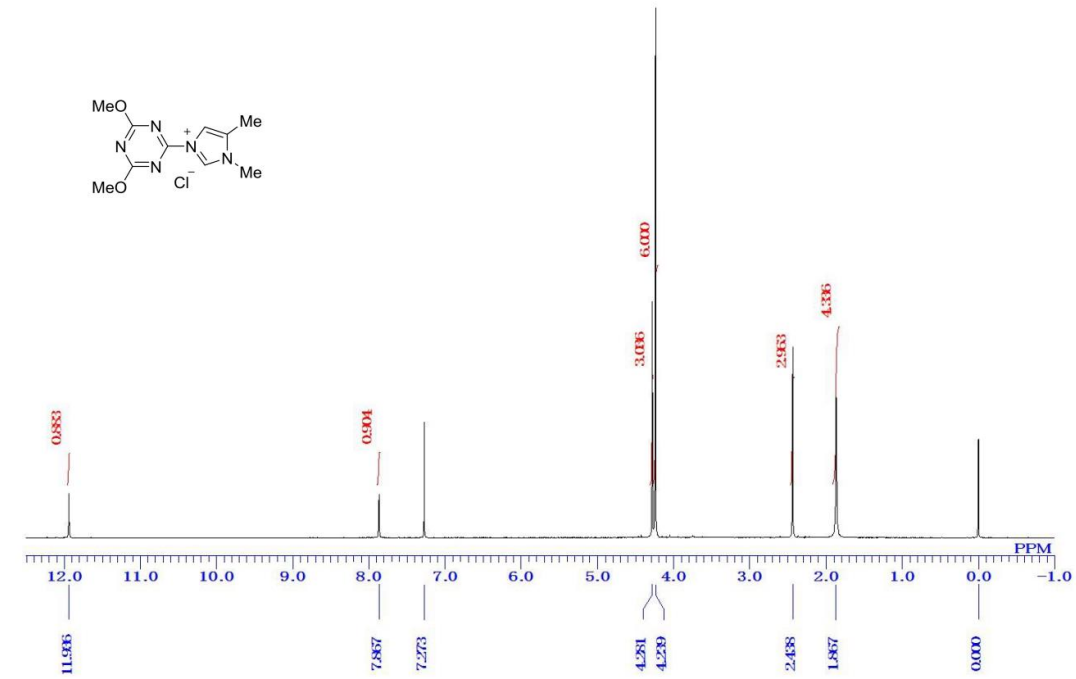


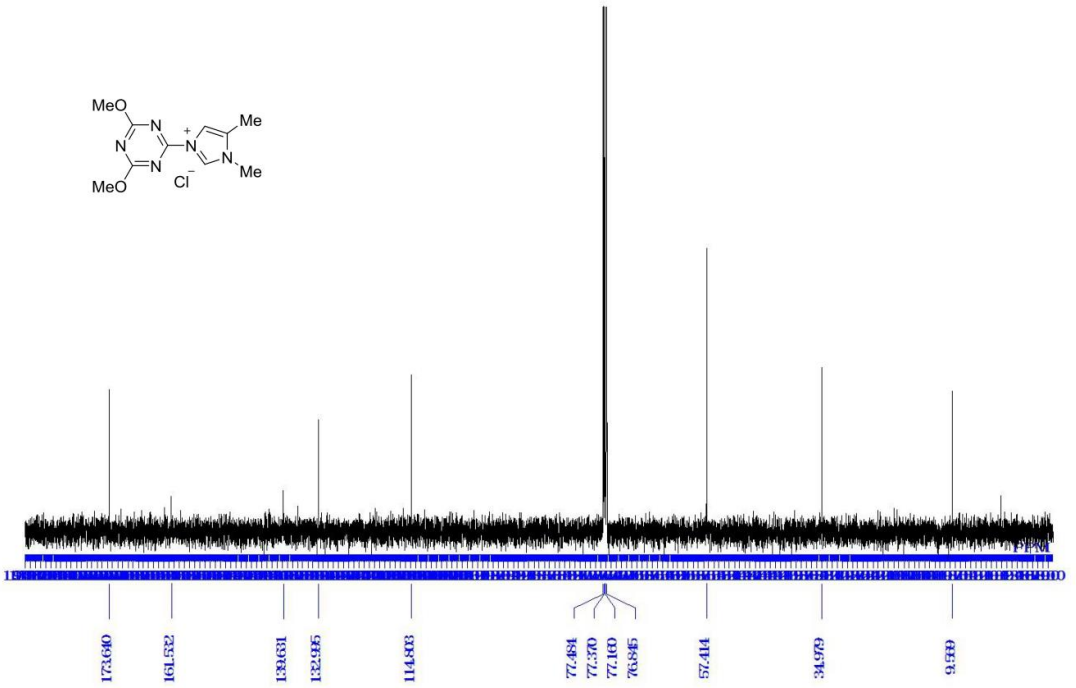
3-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-1,4-dimethyl-1H-imidazol-3-ium chloride (DMT-1,4-M2Im)



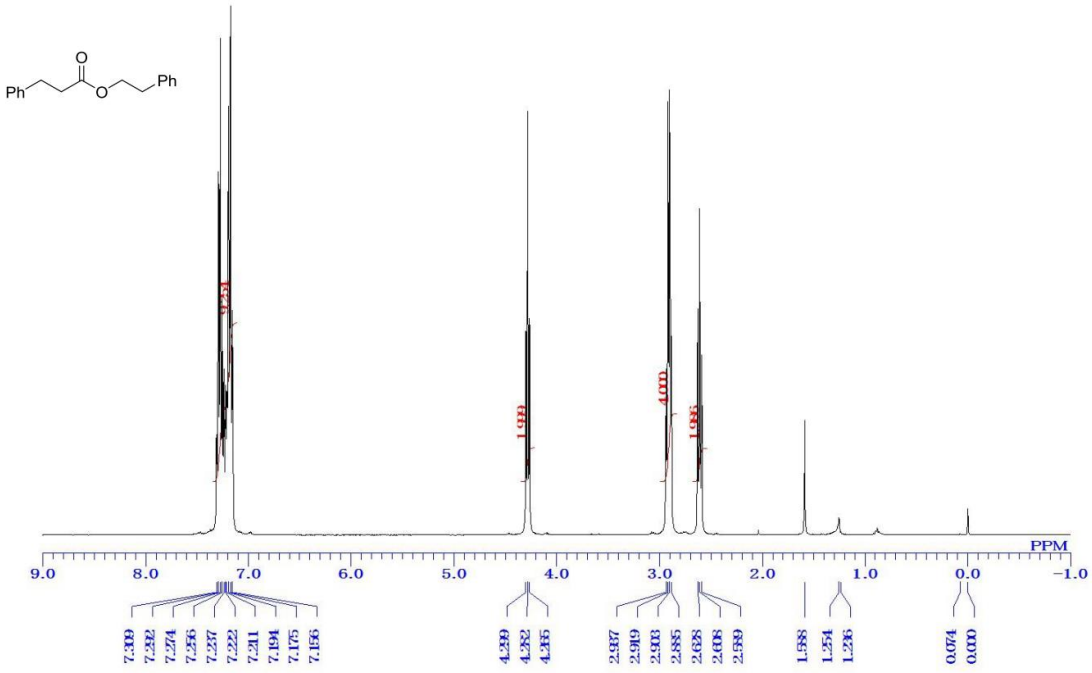


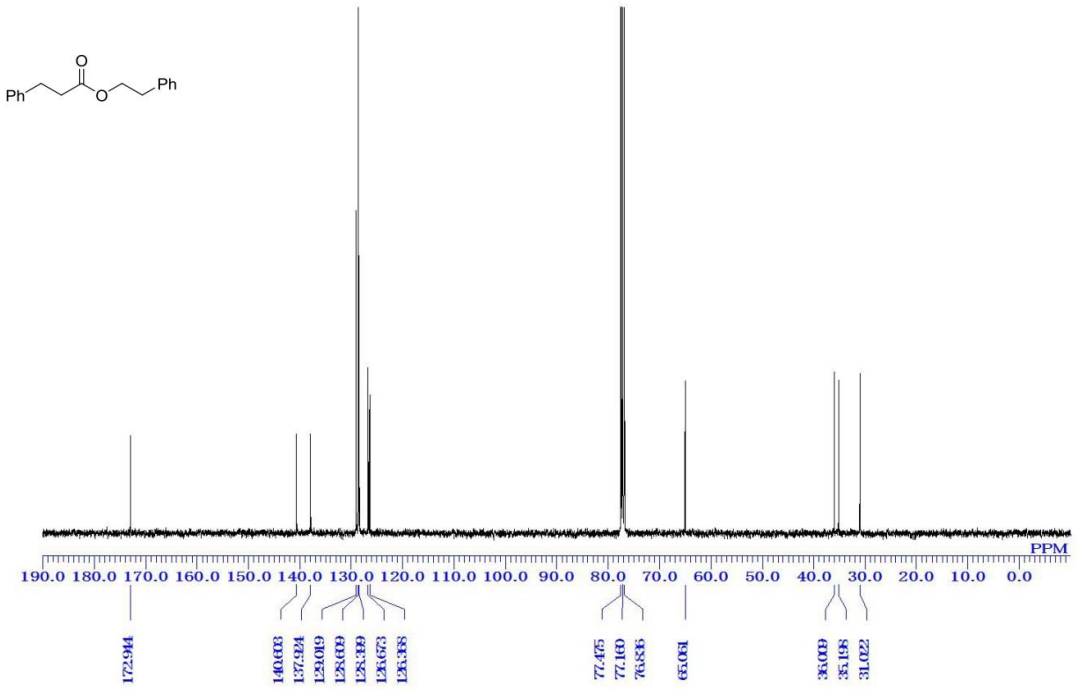
3-(4,6-dimethoxy-1,3,5-triazin-2-yl)-1,5-dimethyl-1*H*-imidazol-3-ium chloride (DMT-1,5-M2Im)



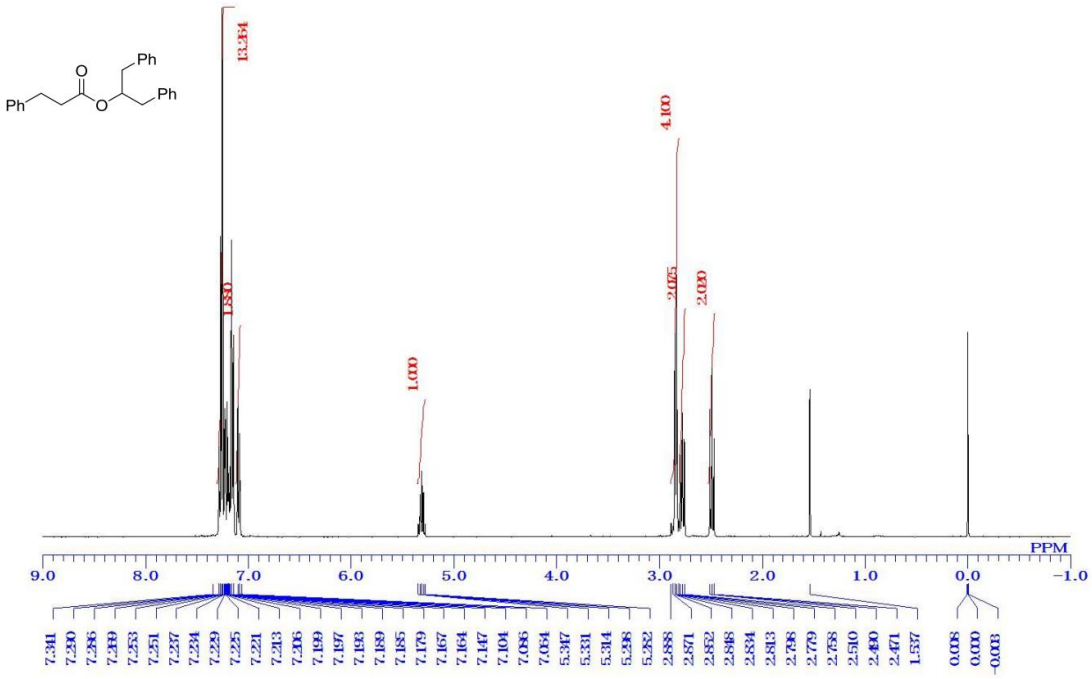


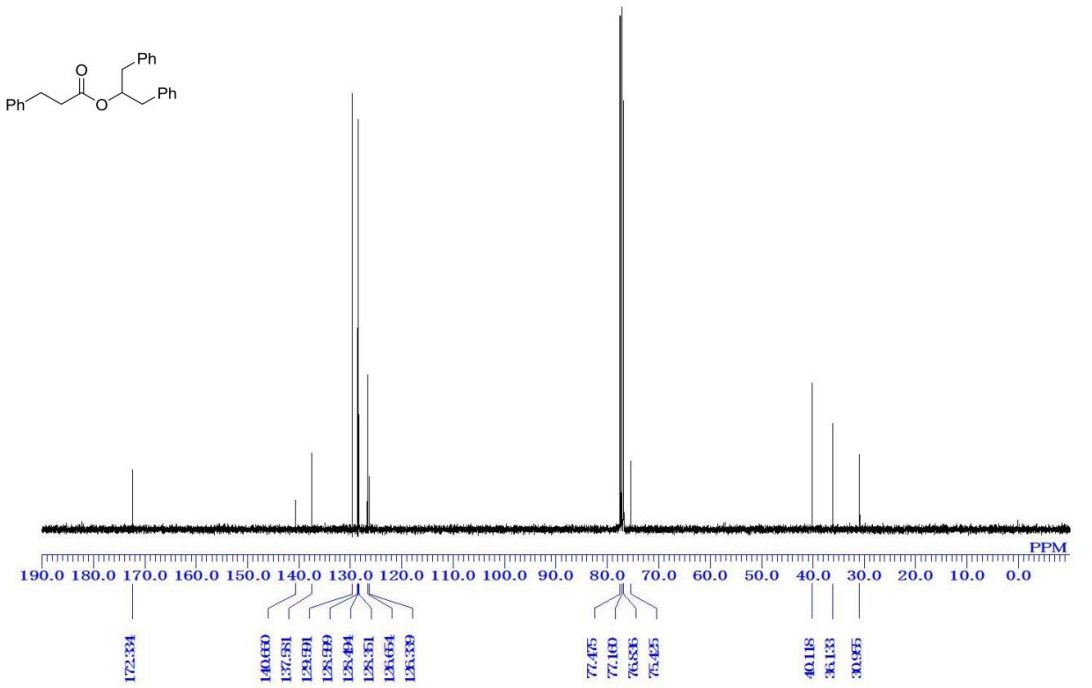
Phenethyl 3-phenylpropanoate (3aa)



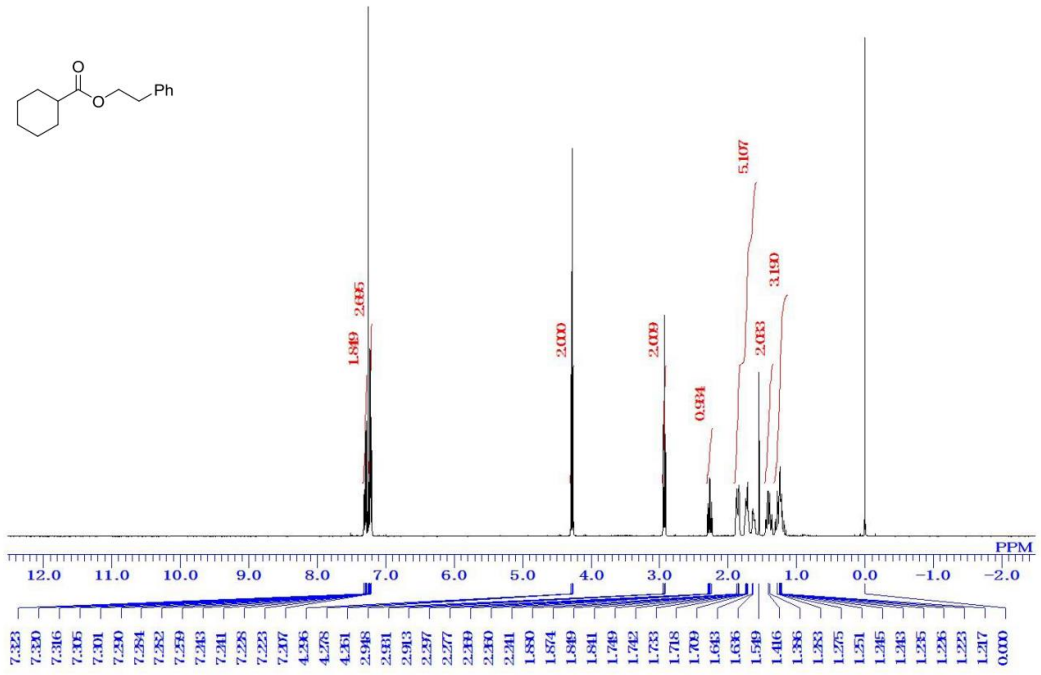


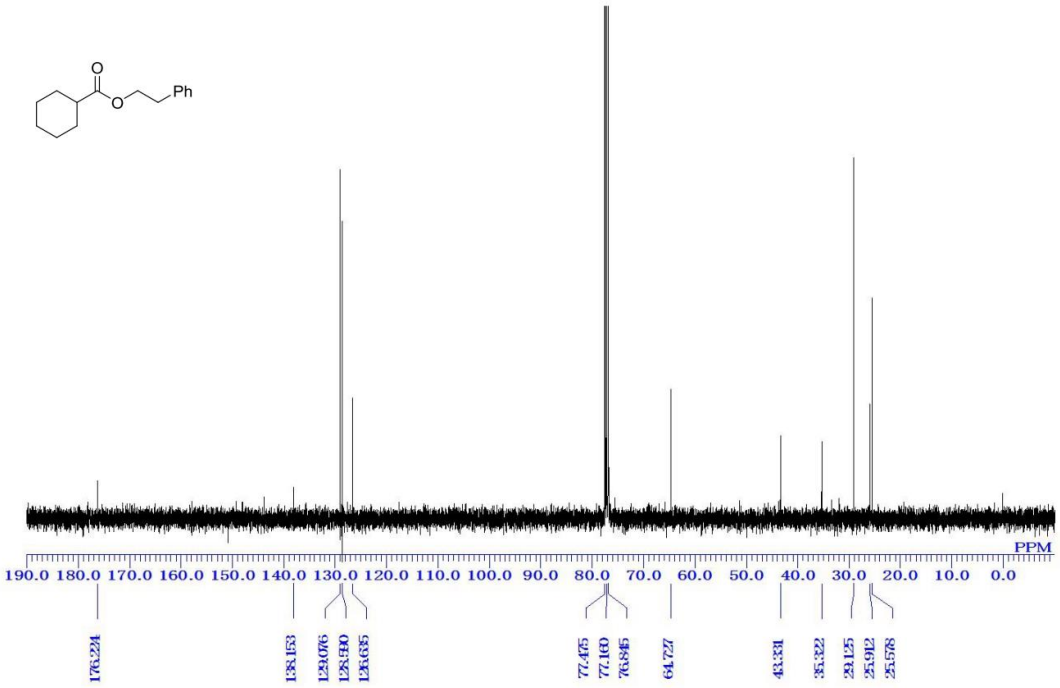
1,3-Diphenylpropan-2-yl 3-phenylpropanoate (3ab)



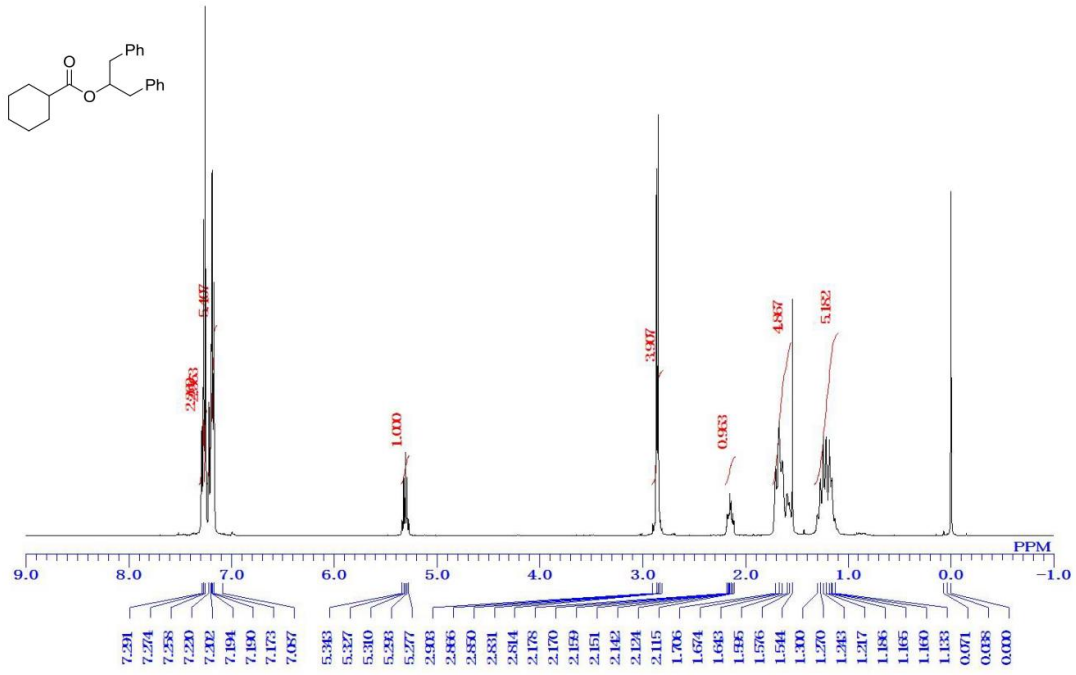


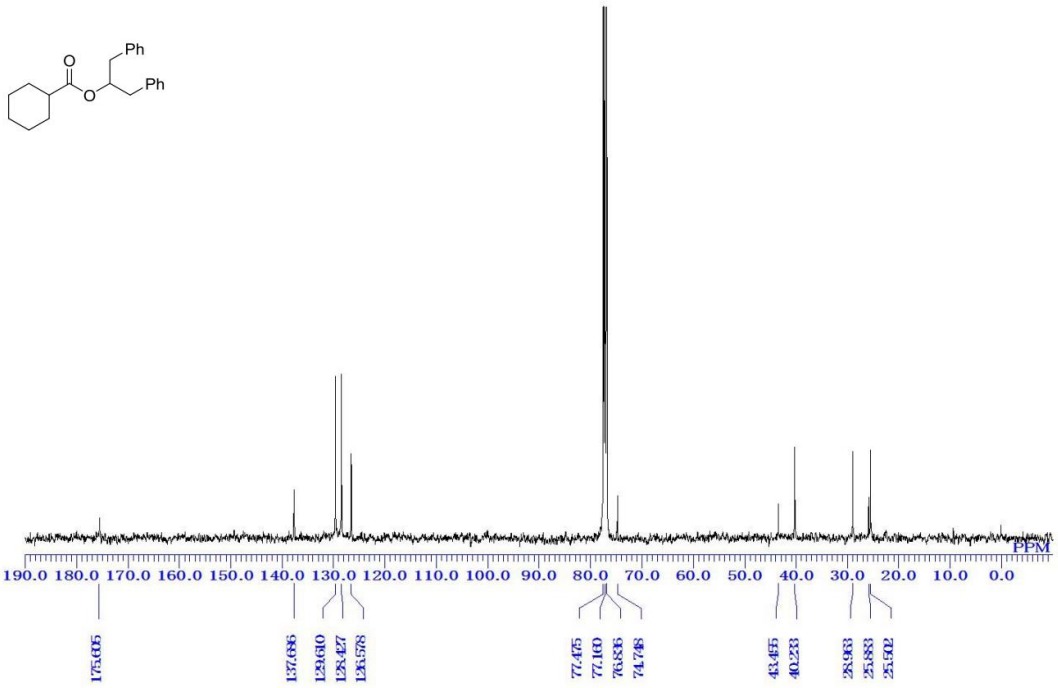
Phenethyl cyclohexanecarboxylate (3ba)



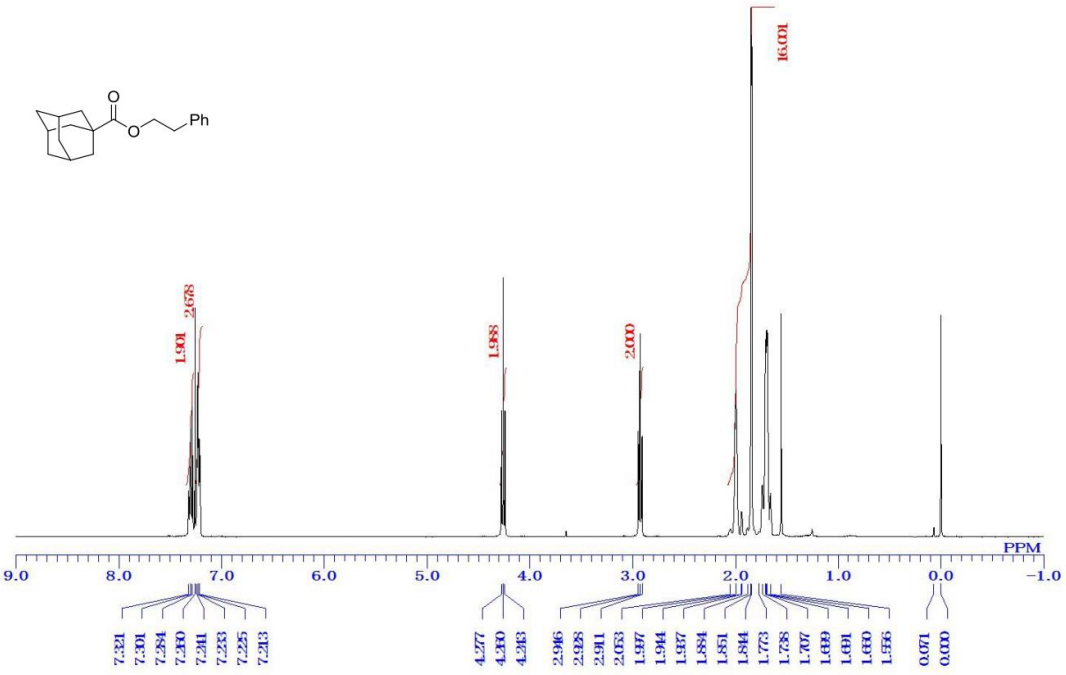


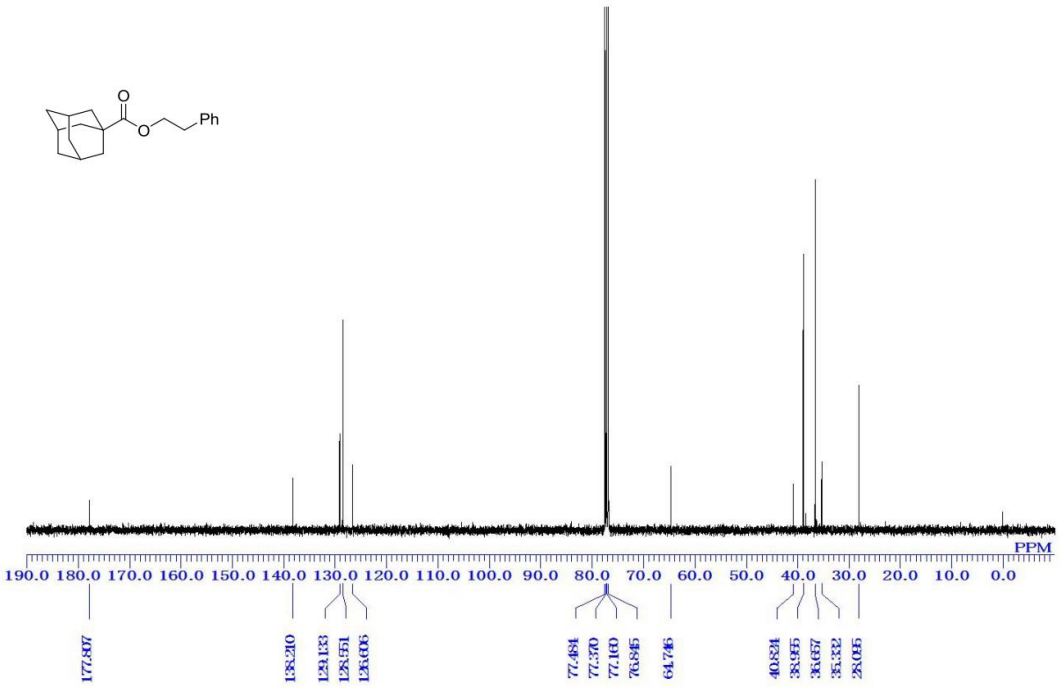
1,3-Diphenylpropan-2-yl cyclohexanecarboxylate (3bb)



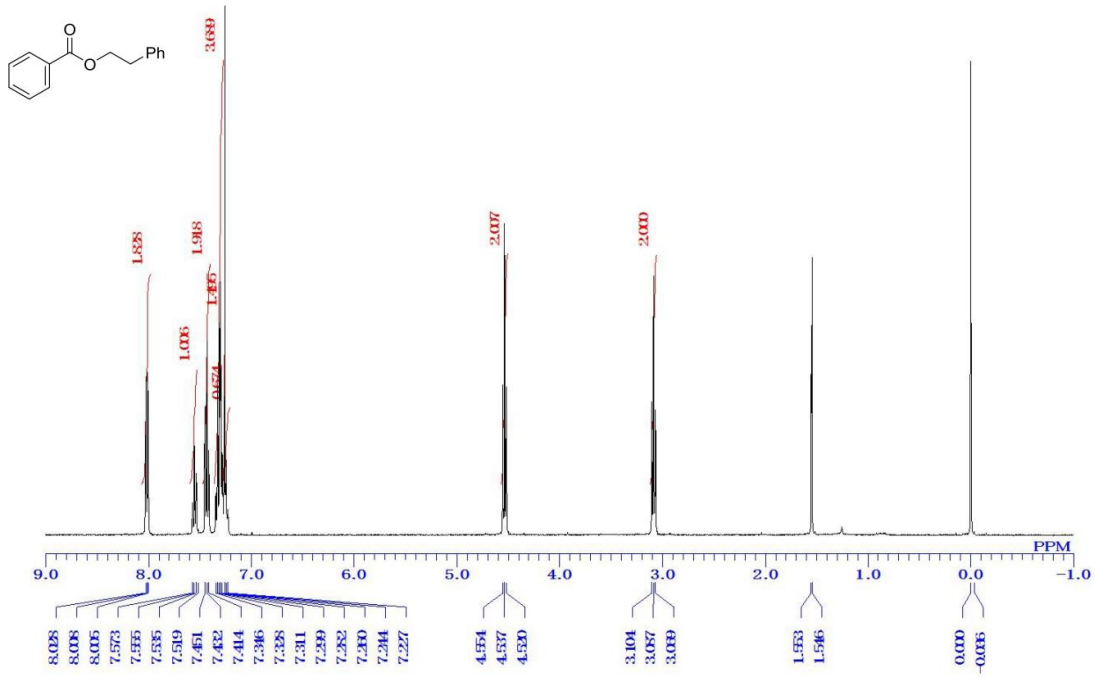


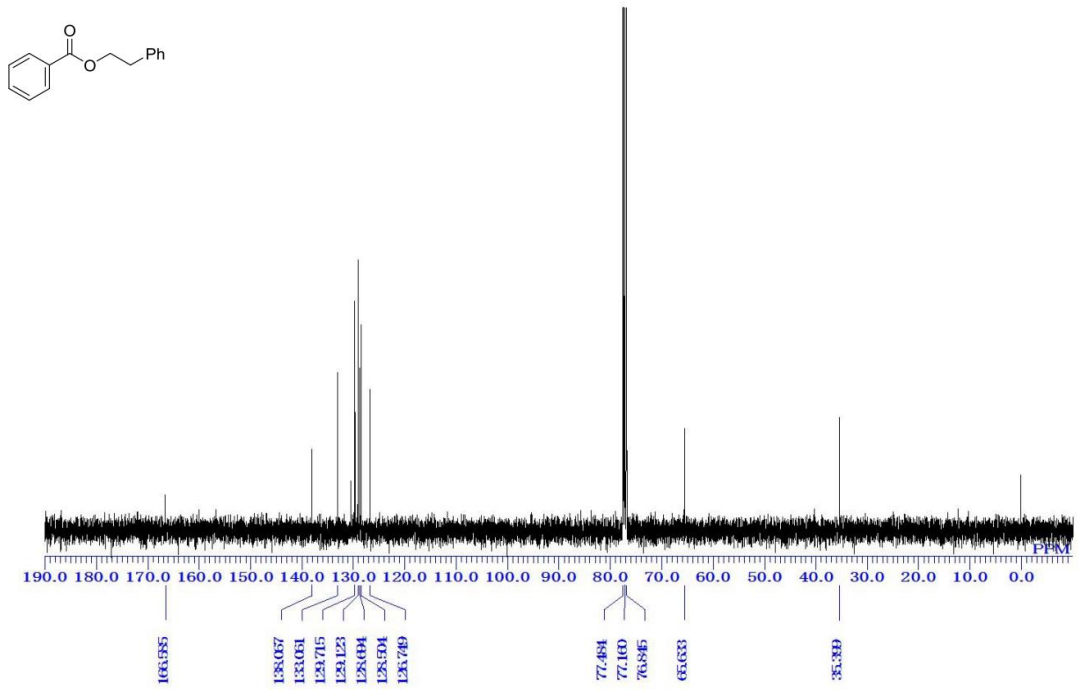
Phenethyl (3r,5r,7r)-adamantane-1-carboxylate (3ca)[3]



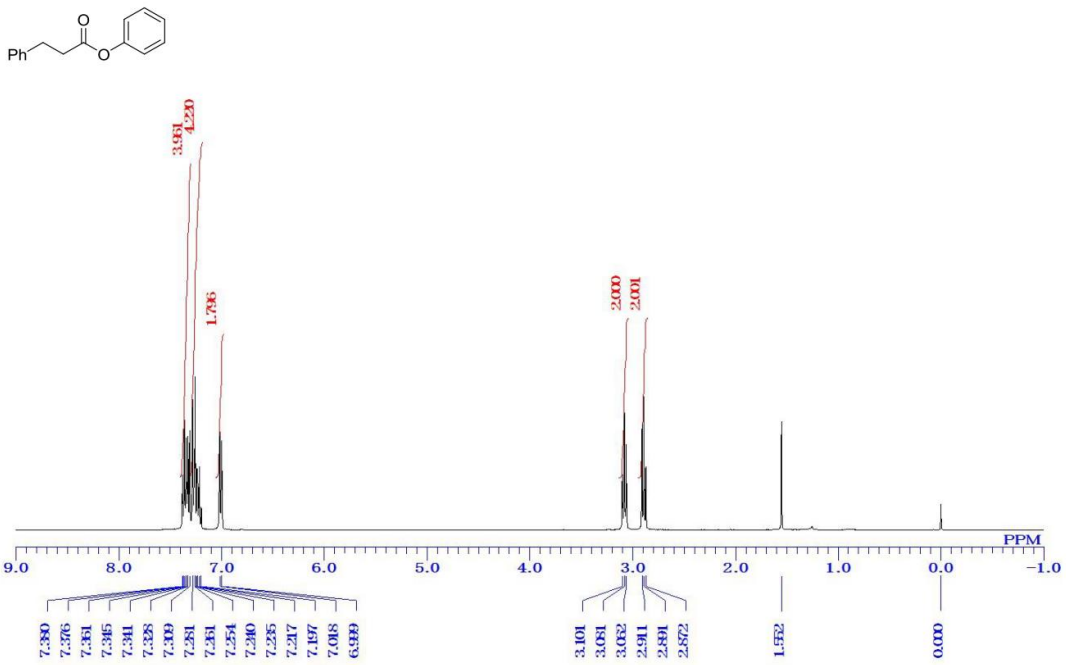


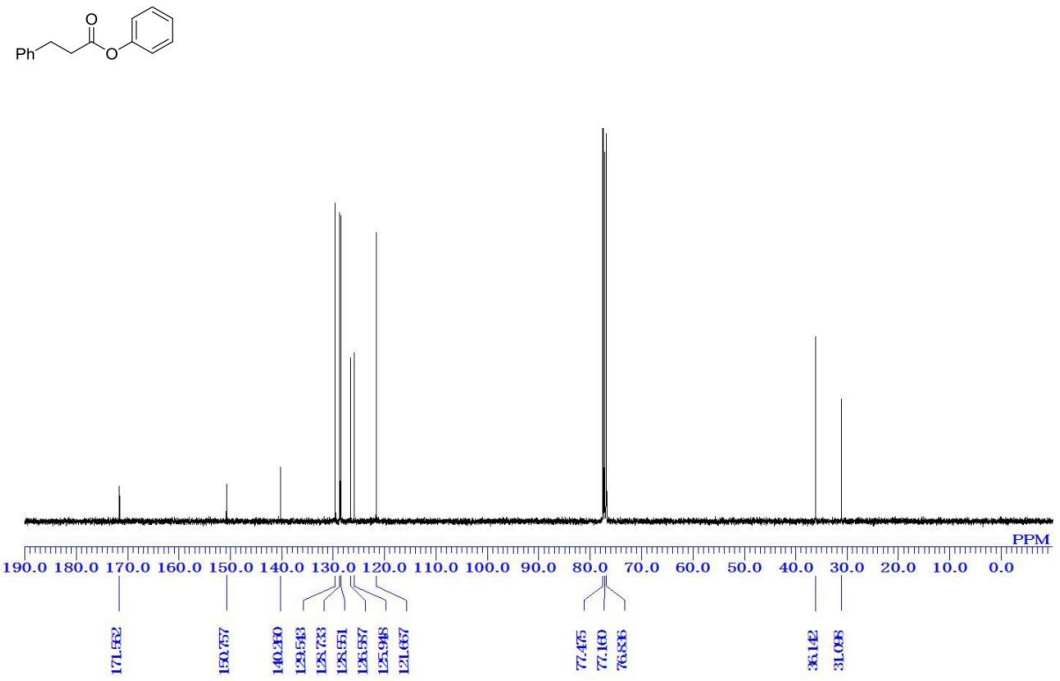
Phenethyl benzoate (3da)



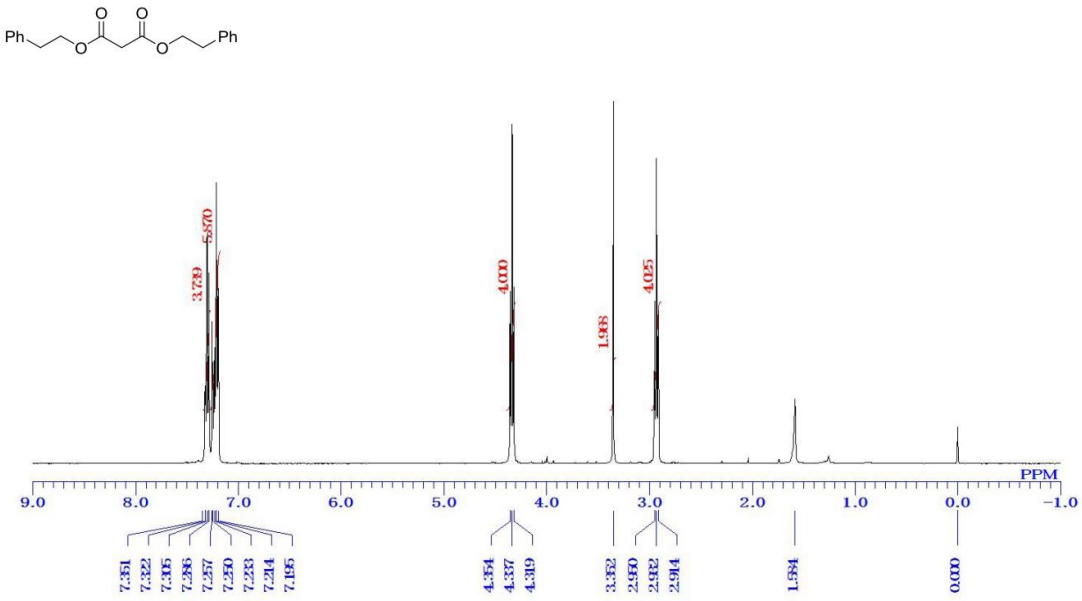


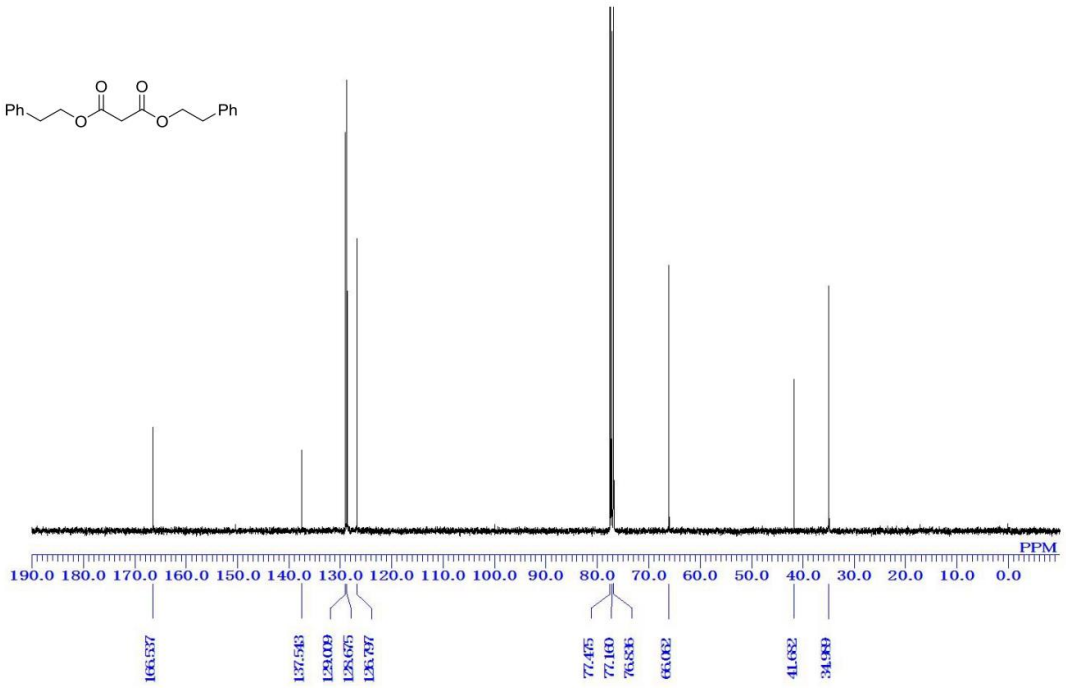
Phenyl 3-phenylpropanoate (3ad)[4]



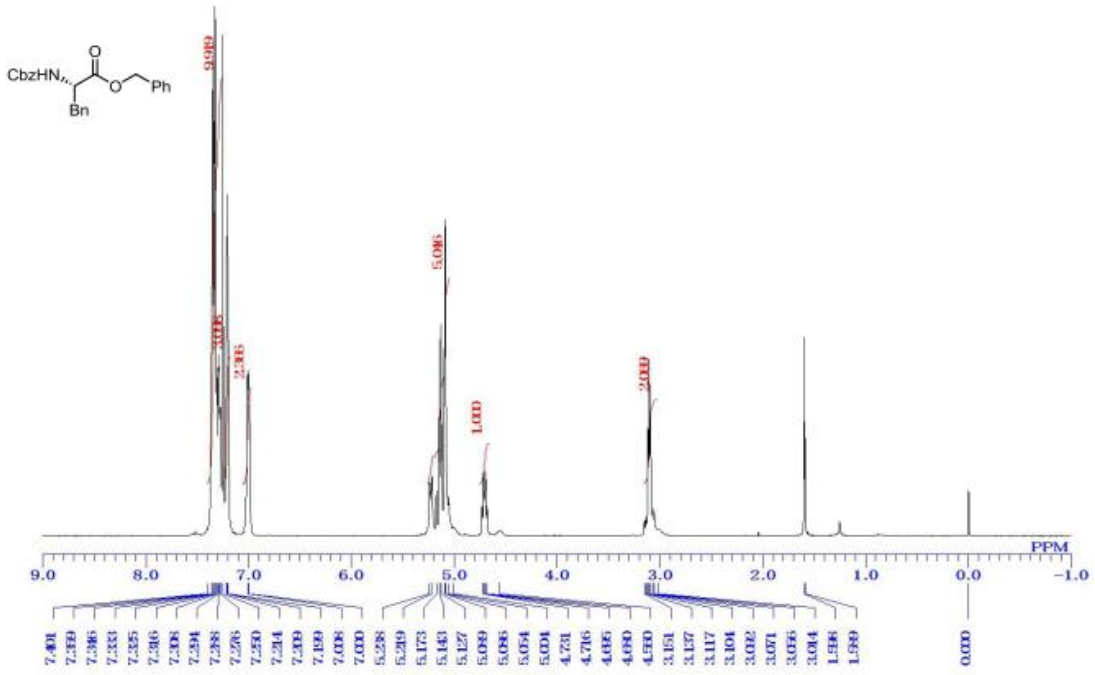


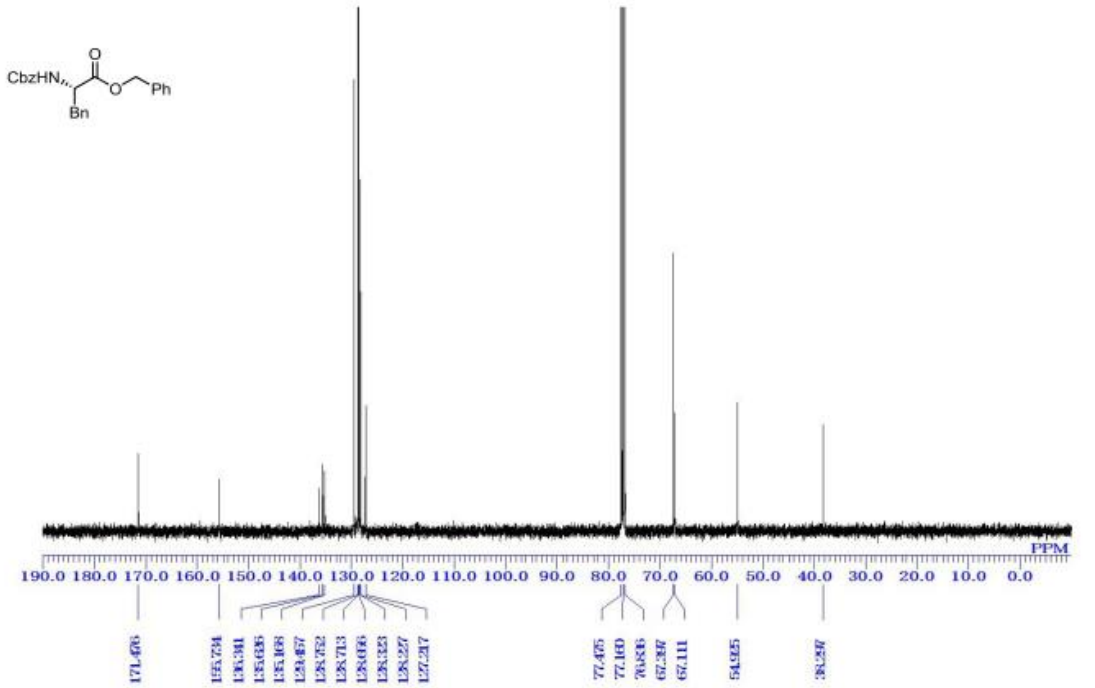
Diphenethyl malonate (3ea)



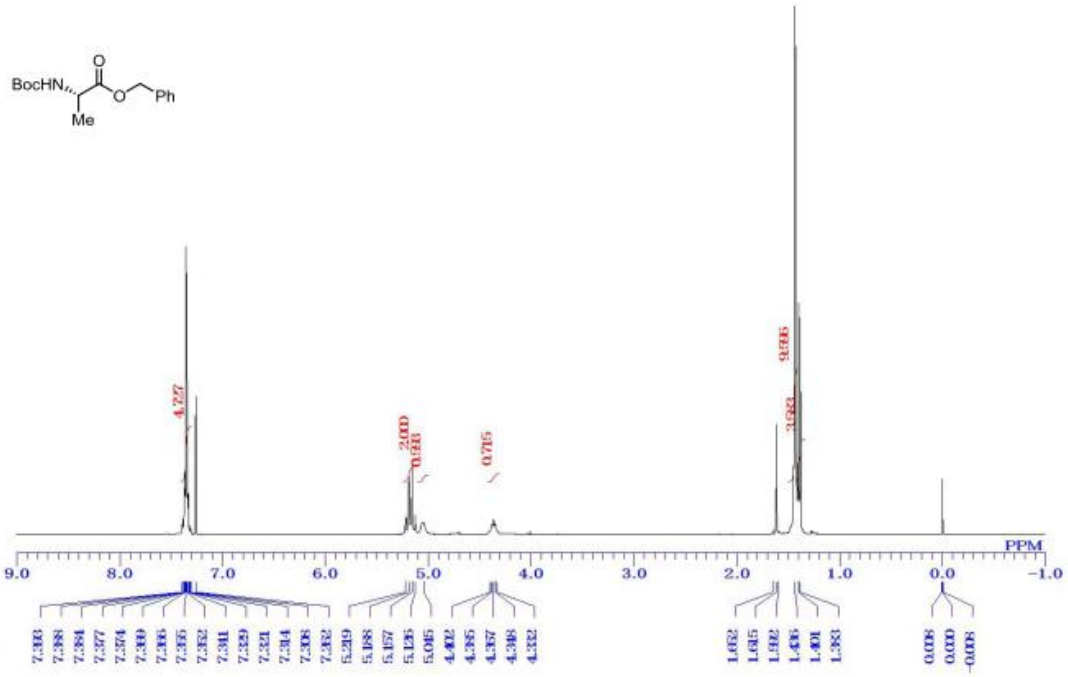


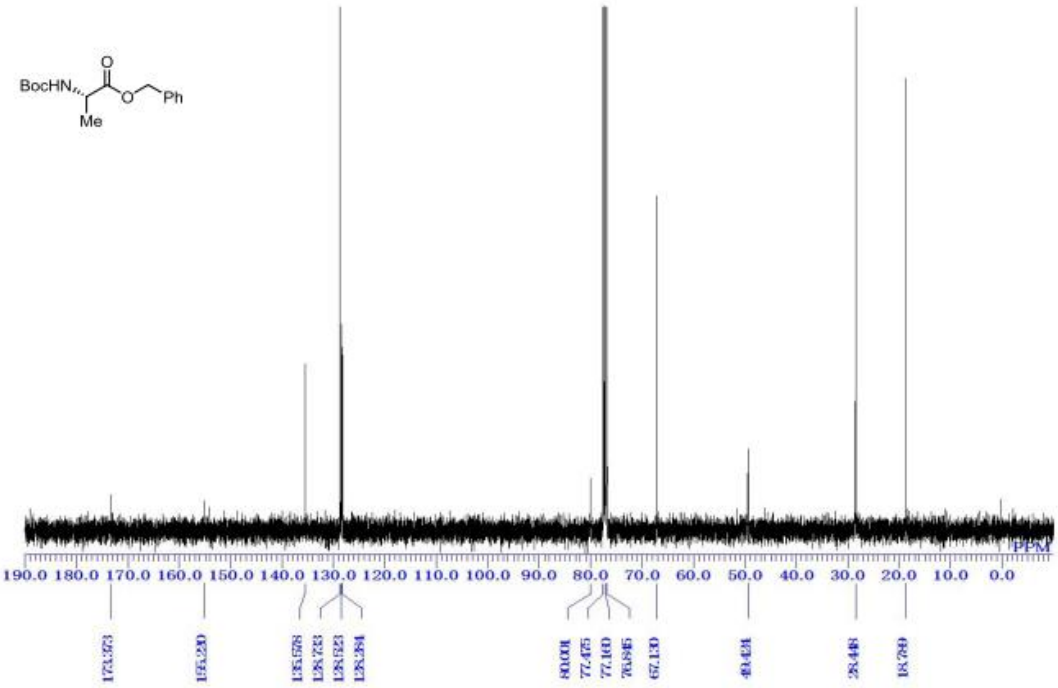
Benzyl ((benzyloxy)carbonyl)-L-phenylalaninate (3fe)



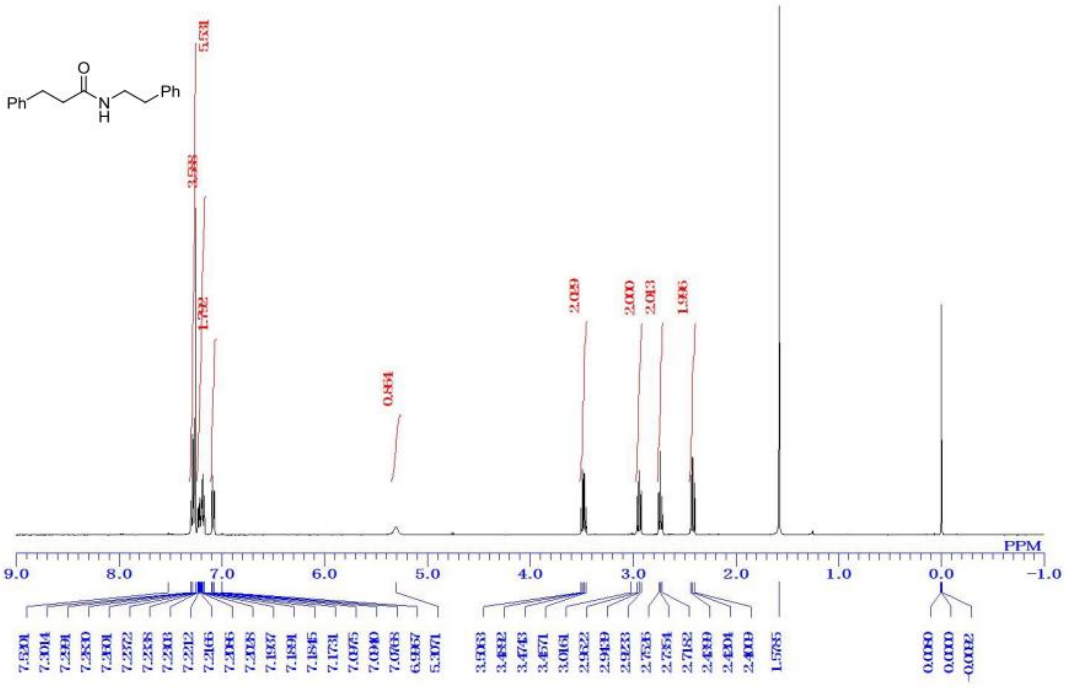


Benzyl (*tert*-butoxycarbonyl)-L-alaninate (3ge)





_N_-phenethyl-3-phenylpropanamide (5)



4,6-dimethoxy-_N_-phenethyl-1,3,5-triazin-2-amine (6)