

Supporting information

Cyanide Ion Promoted Addition of Acylphosphonates to Ethyl Cyanofornate: Synthesis of Tertiary Carbinols via Tandem Carbon-Carbon Bond Formations

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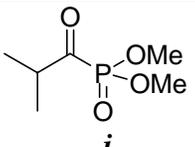
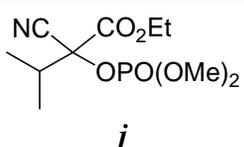
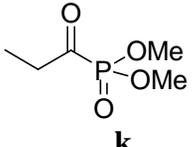
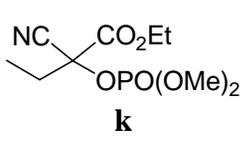
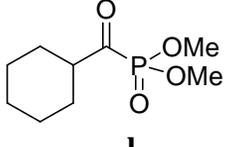
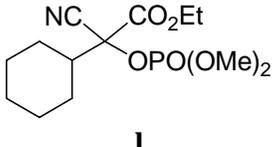
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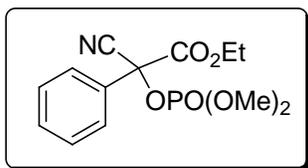
General Information. THF was freshly distilled from sodium-benzophenone. Purification of products was carried out by automatic flash column chromatography. Analytical thin layer chromatography was performed on aluminium sheets precoted with silica gel 60F254. Visualization was accomplished with UV light and anisaldehyde or 2,4-dinitrophenylhydrazine followed by heating. ¹H-NMR spectra are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Acylphosphonates were prepared according to well established procedures and purified by vacuum distillation.¹ All acylphosphonates were stored in flasks under nitrogen and they were stable at least for months. KCN was dried under vacuum at 100 °C. 18-crown-6 was recrystallized from acetonitrile and dried under vacuum at ambient temperature.

General Procedure: An oven dried Schlenk flask with a magnetic stir bar was charged with 0.5 mmol of acylphosphonate. Subsequently, 1 mL dry THF, 0.6 mmol ethyl cyanoformate, 0.025 mmol 18-crown-6, and a tip of spatula KCN was added under argon. The reaction was monitored by TLC (completed within 15-20 min.). After the completion of the reaction, the reaction was extracted with ether and brine three times. The organic phases were combined and concentrated under reduced vacuum. If needed, the crude product was purified with automatic flash column chromatography ether-petroleum ether as eluent.

Table 2. Addition of acylphosphonates to ethyl cyanofomate

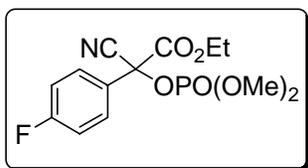
Entry	Acylphosphonate 1	Product 5	Yield (%)
1	 a	 a	91
2	 b	 b	86
3	 c	 c	88
4	 d	 d	95
5	 e	 e	90
6	 f	 f	90
7	 g	 g	90
8	 h	 h	90
9	 i	 i	87

10	 <p style="text-align: center;">j</p>	 <p style="text-align: center;">j</p>	75
11	 <p style="text-align: center;">k</p>	 <p style="text-align: center;">k</p>	74
12	 <p style="text-align: center;">l</p>	 <p style="text-align: center;">l</p>	90



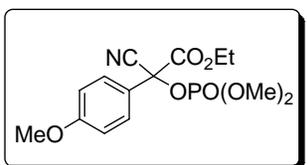
(Ethoxycarbonyl)(cyano)(phenyl)methyl dimethyl

phosphate (5a): Yield 142 mg (91%) yellow liq.; IR (neat) : ν = 2963, 1769, 1255, 1042 cm^{-1} .; ^1H NMR (CDCl_3) δ 1.21 (3H, t, $J=7.3$ Hz), 3.79 (3H, d, $J=11.5$ Hz), 3.88 (3H, d, $J=11.5$ Hz), 4.20-4.30 (2H, m), 7.37-7.41 (3H, m), 7.62-7.64 (2H, m); ^{13}C NMR (CDCl_3) δ 12.6, 54.0 (d, $J=5.5$ Hz), 54.3 (d, $J=5.5$ Hz), 63.3, 76.7 (d, $J=6.3$ Hz), 115.3, 124.6, 128.0, 129.6, 131.6 (d, $J=9.6$ Hz), 163.3 (d, $J=2.3$ Hz); ^{31}P NMR (CDCl_3) δ -1.64 ppm . Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{NO}_6\text{P}$: C, 49.85; H, 5.15; N, 4.47. Found: C, 49.66; H, 5.35; N, 4.78.



(Ethoxycarbonyl)(cyano)(4-fluorophenyl)methyl dimethyl

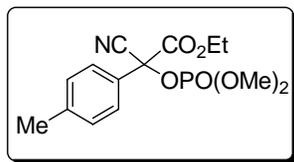
phosphate (5b): Yield 142 mg (86%) yellow liq.; IR (neat) : ν = 2964, 1769, 1252, 1040 cm^{-1} .; ^1H NMR (CDCl_3) δ 1.22 (3H, t, $J=6.3$ Hz), 3.79 (3H, d, $J=11.7$ Hz), 3.88 (3H, d, $J=11.7$ Hz), 4.20-4.31 (2H, m), 7.05-7.11 (2H, m), 7.60-7.65 (2H, m); ^{13}C NMR (CDCl_3) δ 13.6, 55.0 (d, $J=6.0$ Hz), 55.3 (d, $J=6.0$ Hz), 64.4, 76.1 (d, $J=6.1$ Hz), 115.2, 116.2 (d, $J=22.4$ Hz), 127.9 (d, $J=8.8$ Hz), 128.6 (d, $J=67$ Hz), 163.4 (d, $J=150.6$ Hz), 165.1; ^{31}P NMR (CDCl_3) δ -1.64 ppm . Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{FNO}_6\text{P}$ (331.23): C, 47.14; H, 4.56; N, 4.23. Found: C, 47.37; H, 4.77; N, 4.59.



(Ethoxycarbonyl)(cyano)(4-methoxyphenyl)methyl

dimethyl phosphate (5c): Yield 151 mg (88%) yellow liq.; IR (neat) : ν = 2962, 1761, 1511, 1257, 1046 cm^{-1} .; ^1H NMR (CDCl_3) δ 1.21 (3H, t, $J=6.7$ Hz), 3.76 (3H, s), 3.77 (3H, d, $J=11.5$ Hz), 3.86 (3H, d, $J=11.5$ Hz), 4.19-4.30 (2H, m), 6.88 (2H, d, $J=8.5$ Hz), 7.54 (2H, d, $J=9.1$ Hz); ^{13}C NMR (CDCl_3) δ 12.7, 53.9 (d, $J=6.6$ Hz), 54.2 (d, $J=6.6$ Hz), 54.4, 63.2, 75.5 (d, $J=6.7$ Hz), 113.4, 114.4,

123.4 (d, $J=9.4$ Hz), 126.3, 160.3, 163.4; ^{31}P NMR (CDCl_3) δ -2.29 ppm. Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_7\text{P}$ (343.27): C, 48.98; H, 5.29; N, 4.08. Found: C, 48.71; H, 5.55; N, 3.87.



(Ethoxycarbonyl)(cyano)(4-methylphenyl)methyl dimethyl

phosphate (5d): Yield 155 mg (95%) yellow liq.; IR (neat) : ν

= 2962, 1766, 1451, 1282, 1037 cm^{-1} ; ^1H NMR (CDCl_3 , 400

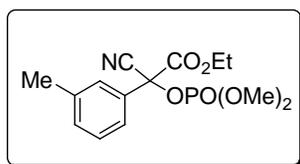
MHz) δ : 1.23 (3H, t, $J=7.0$ Hz), 2.32 (3H, s), 3.77 (3H, d, $J=11.7$ Hz), 3.87 (3H, d, $J=11.6$

Hz), 4.16-4.35 (2H, m), 7.17 (2H, d, $J=8.1$ Hz), 7.49 (2H, d, $J=8.2$ Hz); ^{13}C NMR (CDCl_3) δ :

13.7, 21.2, 54.8 (d, $J=6$ Hz), 55.1 (d, $J=6$ Hz), 64.0, 76.5 (d, $J=6.7$ Hz), 115.3, 125.7, 129.7,

137.2, 140.7, 164.3; ^{31}P NMR (CDCl_3) δ : -1.90 ppm. Anal. Calcd for

$\text{C}_{14}\text{H}_{18}\text{NO}_6\text{P}$ (327.27): C, 51.38; H, 5.54; N, 4.28. Found: C, 51.67; H, 5.74; N, 4.08.



(Ethoxycarbonyl)(cyano)(3-methylphenyl)methyl dimethyl

phosphate (5e): Yield 147 mg (90%) yellow liq.; IR (neat) : ν

= 3435, 1764, 1257, 1048 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.21 (3H, t,

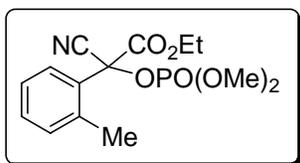
$J=7.1$ Hz), 2.32 (3H, s), 3.78 (3H, d, $J=11.6$ Hz), 3.87 (3H, d, $J=11.6$ Hz), 4.17-4.33 (2H,

m), 7.18-7.20 (1H, m), 7.24-7.29 (1H, m), 7.40-7.41 (2H, m); ^{13}C NMR (CDCl_3) δ 13.6, 21.4,

54.9 (d, $J=6.0$ Hz), 55.3 (d, $J=6.0$ Hz), 64.2, 76.7, 115.5, 122.7, 126.1, 128.9, 131.3, 132.6

(d, $J=9.2$ Hz), 139.1, 164.3; ^{31}P NMR (CDCl_3) δ -2.20 ppm. Anal. Calcd for

$\text{C}_{14}\text{H}_{18}\text{NO}_6\text{P}$ (327.27): C, 51.38; H, 5.54; N, 4.28. Found: C, 51.67; H, 5.74; N, 4.11.



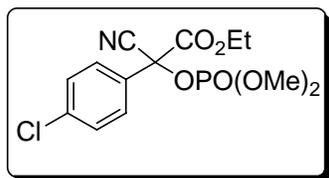
(Ethoxycarbonyl)(cyano)(2-methylphenyl)methyl dimethyl

phosphate (5f): Yield 147 mg (90%) yellow liq.; IR (neat) : ν

= 2962, 1767, 1283, 1034 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.26 (3H, t,

$J=7.6$ Hz), 2.46 (3H, s), 3.74 (3H, d, $J=11.0$ Hz), 3.82 (3H, d, $J=11.0$ Hz), 4.27-4.39 (2H,

m), 7.15-7.24 (2H, m), 7.26-7.31 (1H, m), 7.52 (1H, d, $J=8.5$ Hz); ^{13}C NMR (CDCl_3) δ 13.7, 20.1, 54.9 (d, $J=5.3$ Hz), 55.1 (d, $J=6.1$ Hz), 64.3, 77.2 (d, $J=6.9$ Hz), 115.0, 126.4, 127.5, 130.5, 130.6, 132.8, 137.1, 164.0; ^{31}P NMR (CDCl_3) δ -2.60 ppm. Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_6\text{P}$ (327.27): Found: C, 51.12; H, 5.34; N, 3.98.

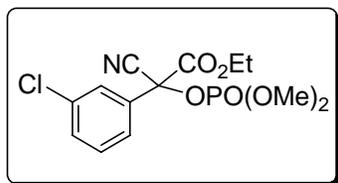


(Ethoxycarbonyl)(cyano)(4-chlorophenyl)methyl

dimethyl phosphate (5g): Yield 156 mg (90%) yellow liq.;

IR (neat) : $\nu = 2960, 1761, 1279, 1037 \text{ cm}^{-1}$.; ^1H NMR

(CDCl_3) δ 1.23 (3H, t, $J=7.3$ Hz), 3.83 (3H, d, $J=11.9$ Hz), 3.88 (3H, d, $J=11.7$ Hz), 4.24-4.34 (2H, m), 7.37 (2H, d, $J=8.6$ Hz), 7.57 (2H, d, $J=8.6$ Hz); ^{13}C NMR (CDCl_3) δ 13.6, 55.0 (d, $J=5.9$ Hz), 55.3 (d, $J=6.0$ Hz), 64.5, 76.1 (d, $J=6.2$ Hz), 115.0, 127.1, 129.3, 131.2 (d, $J=9.4$ Hz), 136.9, 163.9; ^{31}P NMR (CDCl_3) δ -2.10 ppm. Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{ClNO}_6\text{P}$ (347.69): C, 44.91; H, 4.35; N, 4.03. Found: C, 44.68; H, 4.23; N, 3.88.

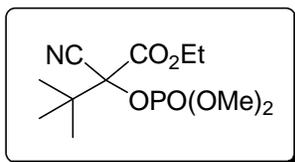


(Ethoxycarbonyl)(cyano)(3-chlorophenyl)methyl

dimethyl phosphate (5h): Yield 156 mg (90%) yellow liq.;

IR (neat) : $\nu = 2962, 1765, 1275, 1035 \text{ cm}^{-1}$.; ^1H NMR

(CDCl_3) δ 1.24 (3H, t, $J=7.1$ Hz), 3.81 (3H, d, $J=11.6$ Hz), 3.90 (3H, d, $J=11.6$ Hz), 4.23-4.35 (2H, m), 7.32-7.40 (2H, m), 7.52-7.54 (1H, m), 7.60-7.63 (1H, m); ^{13}C NMR (CDCl_3) δ 13.7, 55.1 (d, $J=6.0$ Hz), 55.4 (d, $J=6.1$ Hz), 64.6, 76.2, 115.0, 123.9, 125.9, 126.8, 130.3, 130.8, 134.6 (d, $J=9.3$ Hz), 135.2, 152.2, 163.9; ^{31}P NMR (CDCl_3) δ -2.10 ppm. Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{ClNO}_6\text{P}$ (347.69): C, 44.91; H, 4.35; N, 4.03. Found: C, 44.71; H, 4.41; N, 3.93.

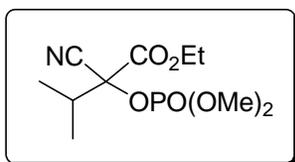


1-(Ethoxycarbonyl)-1-cyano-2,2-dimethylpropyl dimethyl

phosphate (5i): Yield 127 mg (87%) colorless liq.; IR (neat) : ν = 3435, 2962, 1756, 1259, 1045, 800 cm^{-1} .; ^1H NMR (CDCl_3)

δ 1.11 (9H, s), 1.31 (3H, t, $J=6.7$ Hz), 3.79 (3H, d, $J=8.4$ Hz), 3.82 (3H, d, $J=8.4$ Hz), 4.29-4.34 (2H, m); ^{13}C NMR (CDCl_3) δ 12.9, 23.8, 39.2 (d, $J=8$), 53.8 (d, $J=5.7$ Hz), 54.0 (d, $J=5.7$ Hz), 62.5, 81.3 (d, $J=8.3$ Hz), 114.3, 163.0; ^{31}P NMR (CDCl_3) δ -0.96 ppm. Anal.

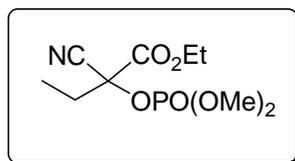
Calcd for $\text{C}_{11}\text{H}_{20}\text{NO}_6\text{P}$ (293.25): C, 45.05; H, 6.87; N, 4.78. Found: C, 44.85; H, 6.71; N, 4.52.



1-(Ethoxycarbonyl)-1-cyano-2-methylpropyl dimethyl

phosphate (5j): Yield 105 mg (75%) colorless liq.; IR (neat) : ν = 2955, 1752, 1451, 1030, 810 cm^{-1} .; ^1H NMR (CDCl_3 , 400

MHz) δ : 1.05 (d, $J=6.8$ Hz, 3H), 1.09 (3H, d, $J=6.7$ Hz), 1.33 (3H, t, $J=7.1$ Hz), 2.30 (1H, m), 3.78 (3H, s), 3.81 (3H, s), 4.31 (2H, dq, $J_1=1.8$ Hz, $J_2=7.1$ Hz) ^{13}C NMR (CDCl_3) δ : 13.9, 16.6, 16.7, 37.3 (d, $J=9$ Hz), 54.9 (d, $J=6$ Hz), 55.0 (d, $J=6$ Hz), 63.7, 80.1 (d, $J=8$ Hz), 114.6, 164.9; ^{31}P NMR (CDCl_3) δ : -1.44 ppm. Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{NO}_6\text{P}$ (279.23): C, 43.01; H, 6.50; N, 5.02. Found: C, 43.28; H, 6.330; N, 4.83.

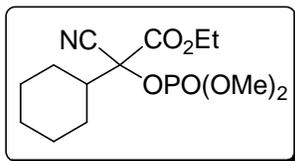


1-(ethoxycarbonyl)-1-cyanopropyl dimethyl phosphate

(5k): Yield 98 mg (74%) colorless liq.; IR (neat) : ν = 2968,

1756, 1028, 803 cm^{-1} .; ^1H NMR (CDCl_3 , 400 MHz) δ : 1.08 (3H, t, $J=7.4$ Hz), 1.31 (3H, t, $J=7.1$ Hz), 2.08-2.15 (2H, m) 3.78(3H, d, $J=4.3$ Hz) 3.81(3H, d, $J=4.3$ Hz), 4.28-4.33(2H, m); ^{13}C NMR (CDCl_3) δ : 7.0, 13.0, 31.6, 31.8, 54.4 (d, $J=6$ Hz), 54.7 (d, $J=6$ Hz), 62.9, 75.5 (d, $J=7.6$ Hz), 114.3, 164.0; ^{31}P NMR (CDCl_3) δ : -2.18 ppm.

Anal. Calcd for C₉H₁₆NO₆P(265.07): C, 40.76; H, 6.08; N, 5.28. Found: C, 40.58; H, 6.21; N, 4.97.



(Ethoxycarbonyl)(cyano)(cyclohexyl)methyl dimethyl

phosphate (5): Yield 144 mg (90%) colorless liq.; IR (neat) : ν

= 2962, 1759, 1450, 1261, 1026, 801 cm⁻¹.; ¹H NMR (CDCl₃)

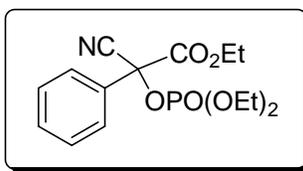
δ 1.06-1.33 (8H, m), 1.62-1.87 (5H, m), 1.96-2.02 (1H, m), 3.78 (3H, d, $J=5.4$ Hz), 3.81 (3H,

d, $J=5.4$ Hz), 4.27-4.34 (2H, m); ¹³C NMR (CDCl₃) δ 13.9, 25.4 (d, $J=9.3$ Hz), 26.7 (d,

$J=11.8$ Hz), 30.3, 46.0 (d, $J=8.2$ Hz), 54.8 (d, $J=5.4$ Hz), 55.0 (d, $J=5.9$ Hz), 63.6, 79.6, (d,

$J=8$ Hz), 114.8, 164.8; ³¹P NMR (CDCl₃) δ -1.64 ppm. Anal. Calcd for

C₁₃H₂₂NO₆P(312.12): C, 48.90; H, 6.94; N, 4.39. Found: C, 48.78; H, 6.73; N, 4.18.



(Ethoxycarbonyl)(cyano)(phenyl)methyl diethyl phosphate

(7): Yield 153 mg (90%) yellow liq.; IR (neat) : ν = 2985, 1767,

1259, 1024 cm⁻¹.; ¹H NMR (CDCl₃, 400 MHz) δ : 1.21 (3H, t,

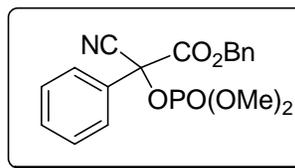
$J=7.2$ Hz), 1.28 (3H, t, $J=7.0$ Hz), 1.34 (3H, t, $J=7.2$ Hz), 4.10-4.30 (6H,m), 7.34-7.41(3H, m

), 7.60-7.65 (2H,m); ¹³C NMR (CDCl₃) δ : 12.7, 14.9 (d, $J=7.3$ Hz), 15.0 (d, $J=7.5$ Hz), 63.1,

63.8 (d, $J=6.1$ Hz), 64.1 (d, $J=6.0$ Hz), 75.6, 114.3, 124.6, 128.0, 129.5, 131.9 (d, $J=9.4$ Hz),

163.4; ³¹P NMR (CDCl₃) δ : -4.60 ppm. Anal. Calcd for C₁₅H₂₀NO₆P(341.10): C, 52.79; H,

5.91; N, 4.10. Found: C, 52.56; H, 5.721; N, 3.87.



((benzyloxy)carbonyl)(cyano)(phenyl)methyl dimethyl

phosphate (9): Yield 165 mg (88%) yellow liq.; IR (neat) : ν =

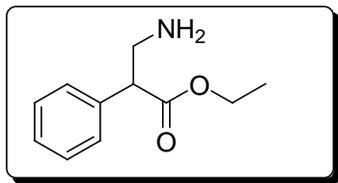
2961, 1770, 1453, 1282, 1041 cm⁻¹.; ¹H NMR (CDCl₃, 400

MHz) δ : 3.76 (3H, d, $J=11.6$ Hz), 3.80 (3H, d, $J=11.6$ Hz), 5.18 (1H, d, $J=12.2$ Hz), 5.22

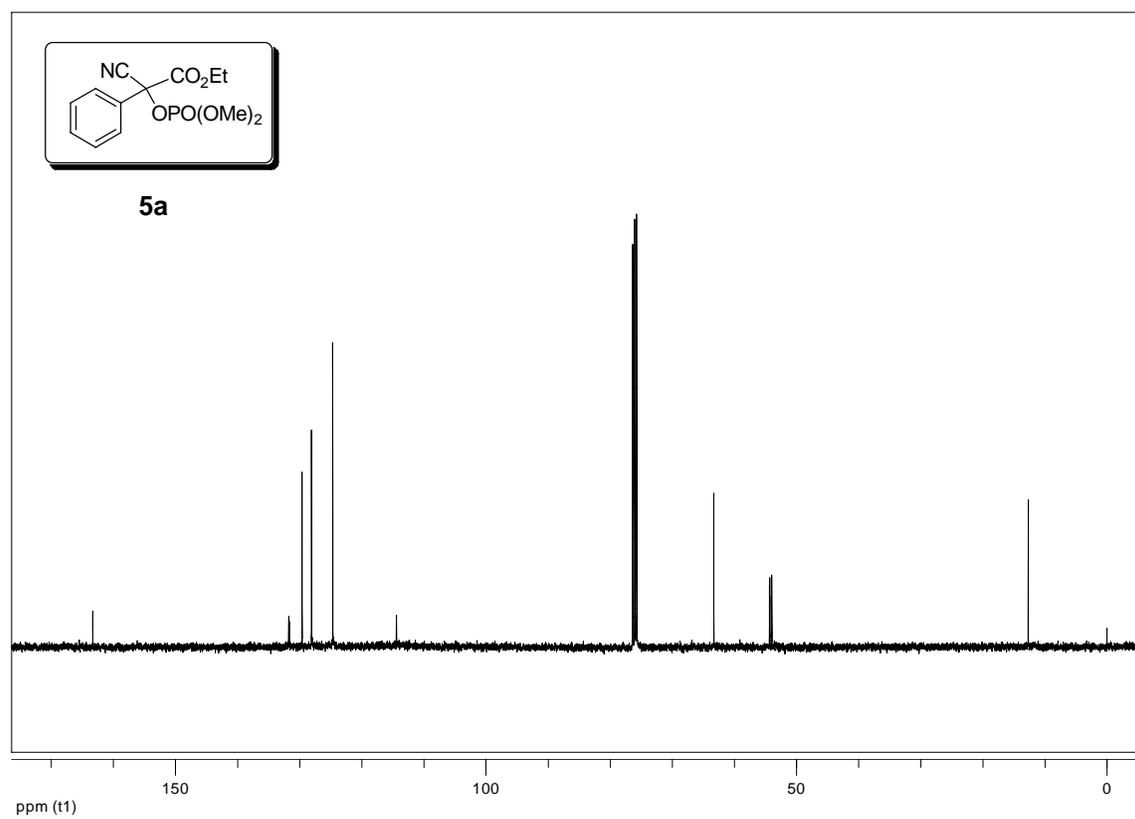
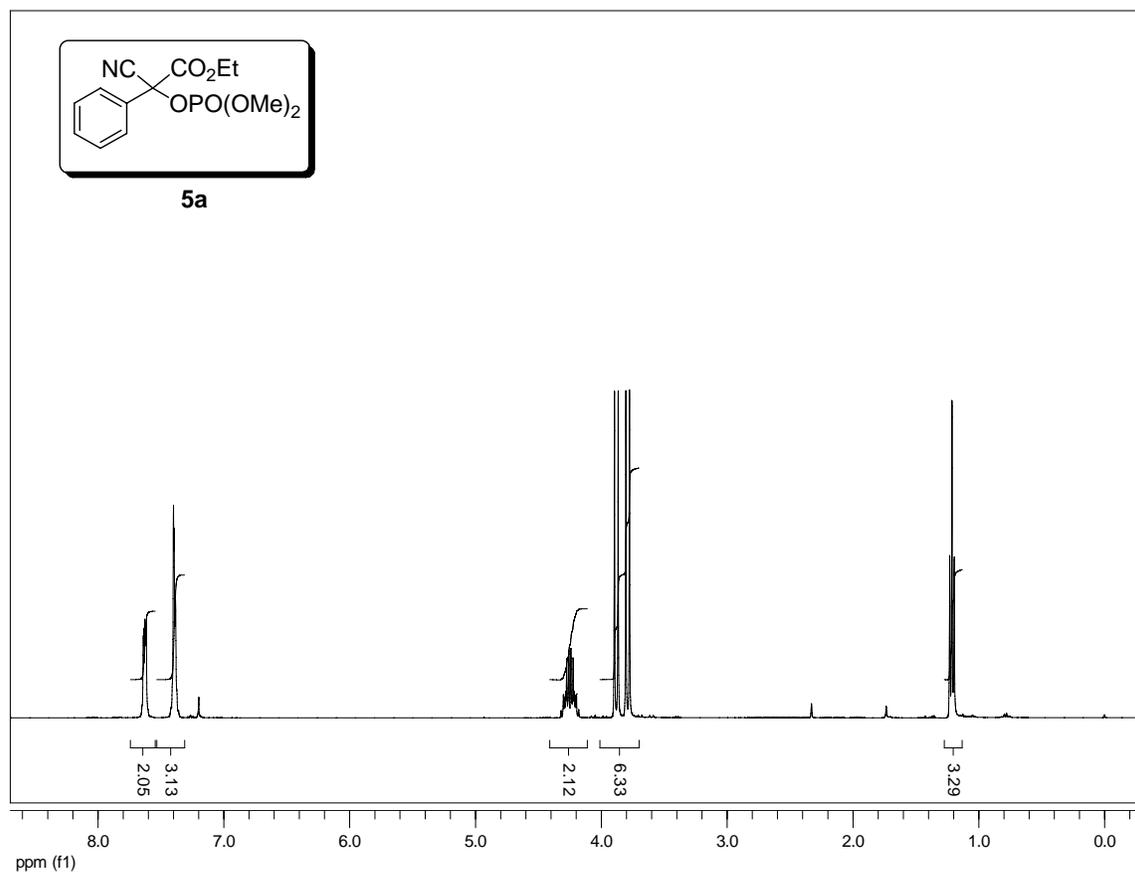
(1H, d, $J=12.2$ Hz), 7.12-7.19 (2H, m), 7.20-7.25 (3H, m), 7.30-7.40 (3H, m), 7.55-7.60(

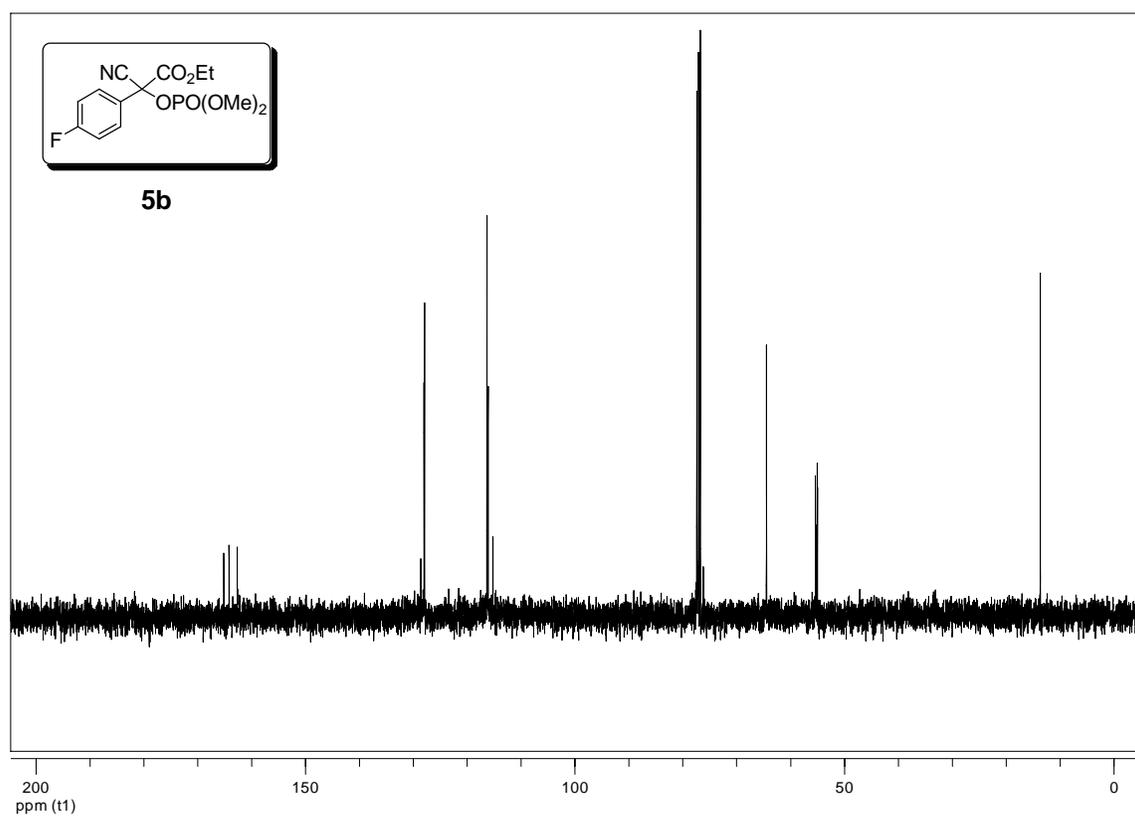
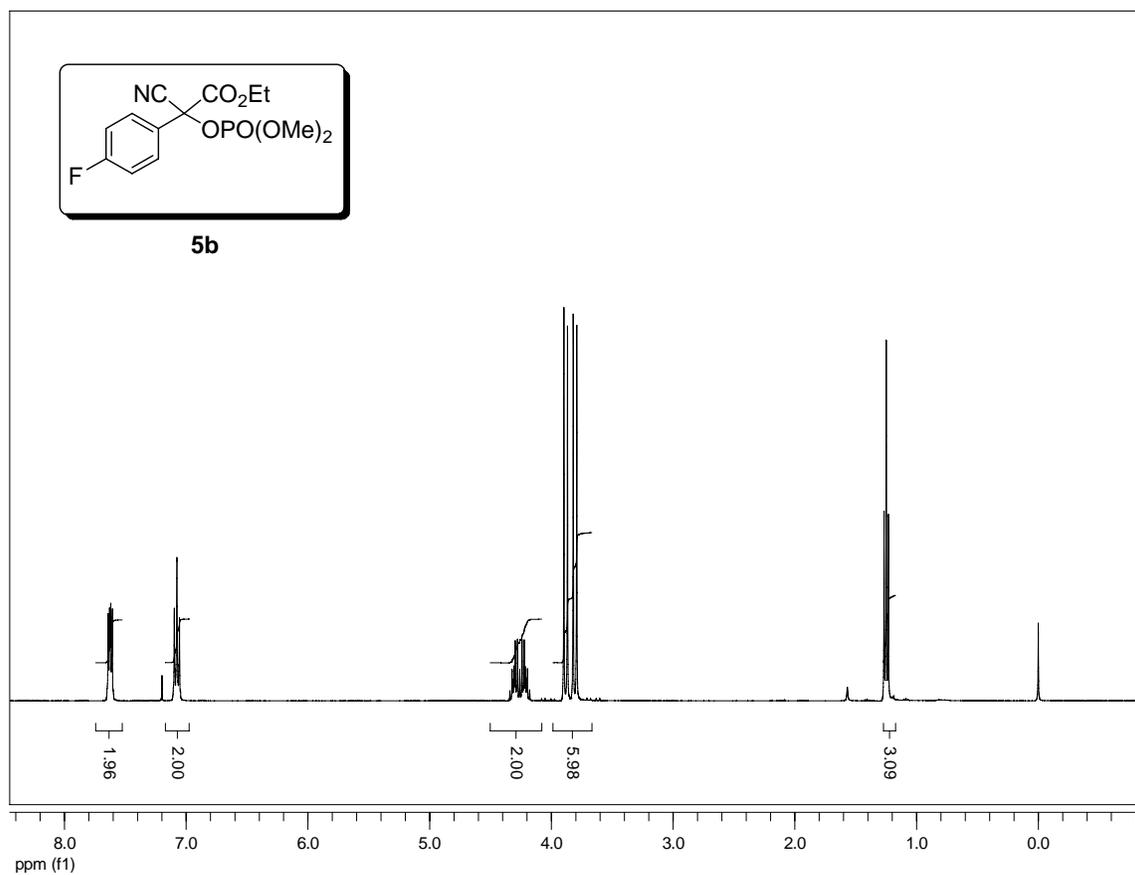
2H,m), ¹³C NMR (CDCl₃) δ : 55.0(d, $J=6.0$ Hz), 55.3(d, $J=5.9$ Hz), 69.5, 115.2, 125.7,

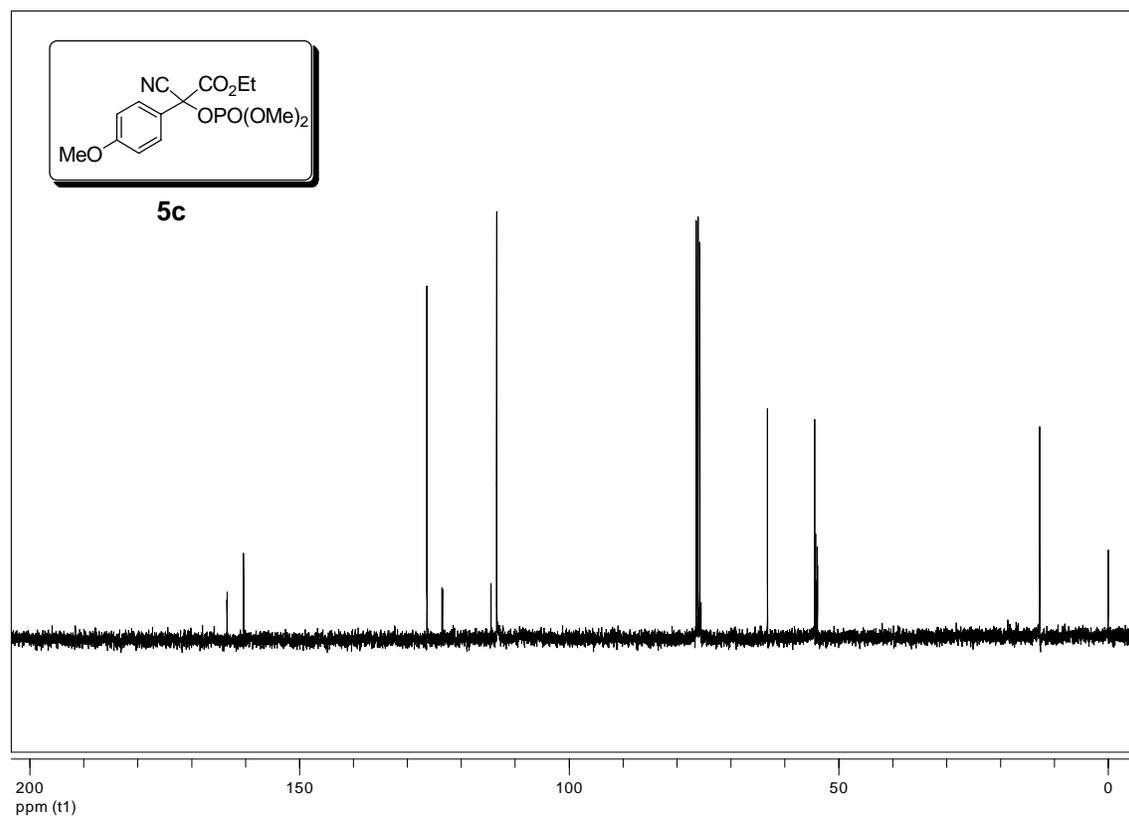
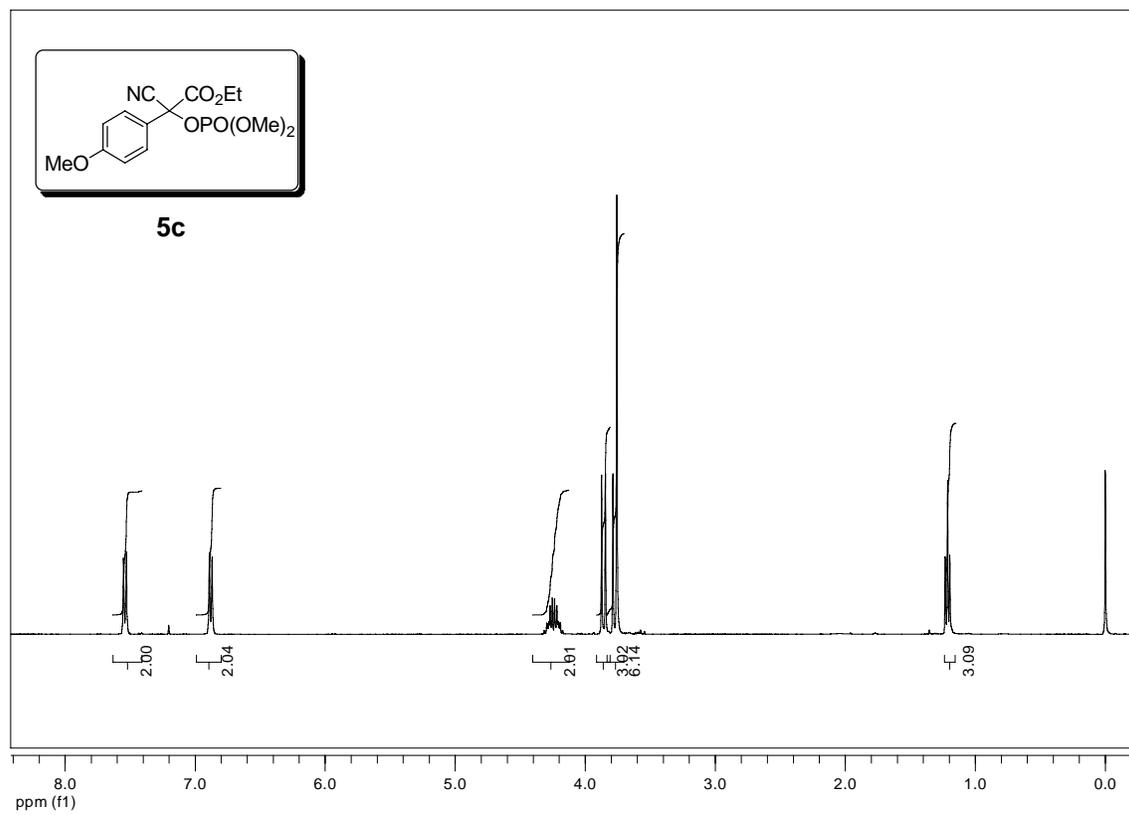
128.1, 128.6, 128.7, 129.1, 130.6, 132.4, 132.5, 133.9, 164.1; ^{31}P NMR (CDCl_3) δ : -2.20 ppm. Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{NO}_6\text{P}$ (375.31): C, 57.60; H, 4.83; N, 3.73. Found: C, 57.38; H, 4.61; N, 3.48.

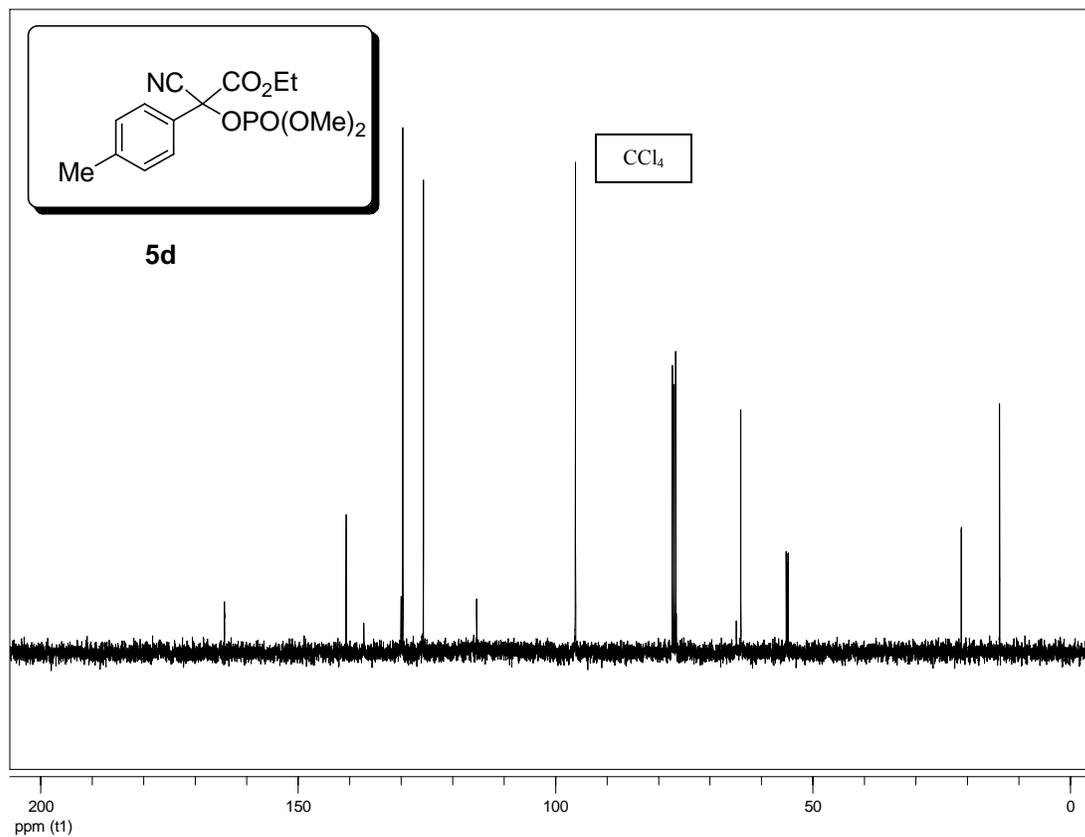
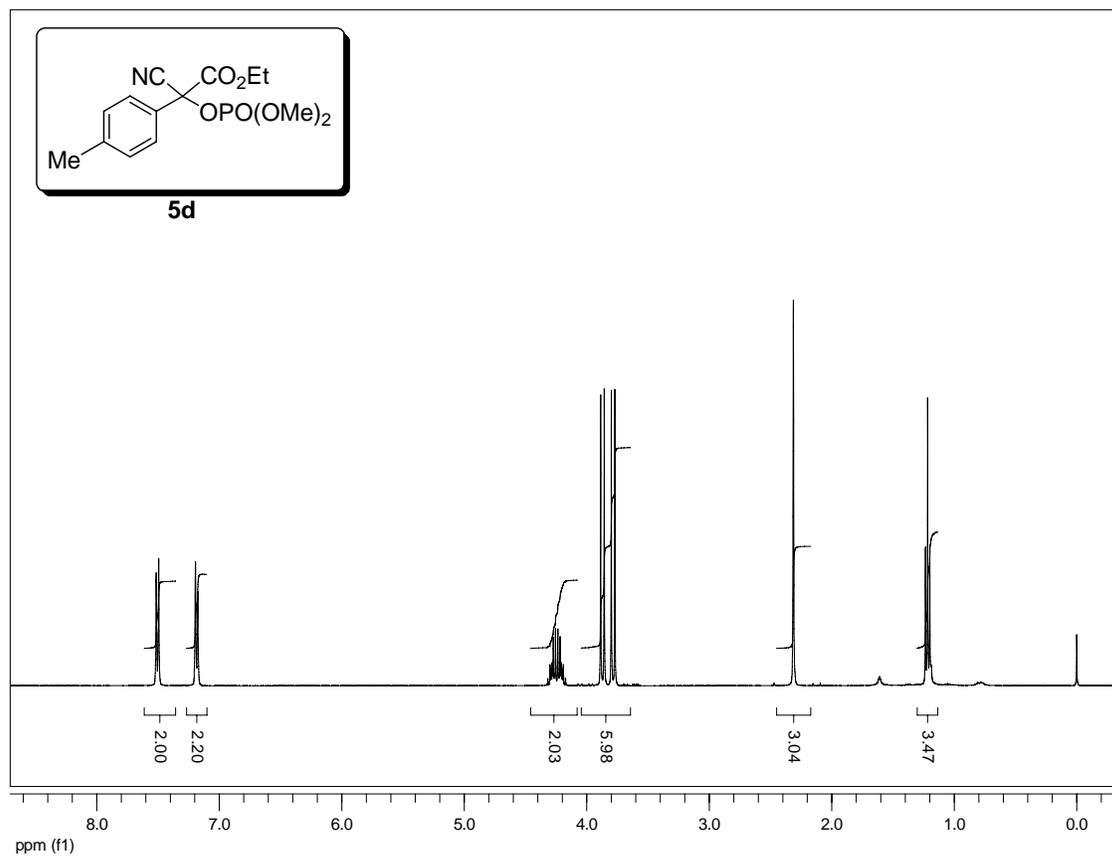


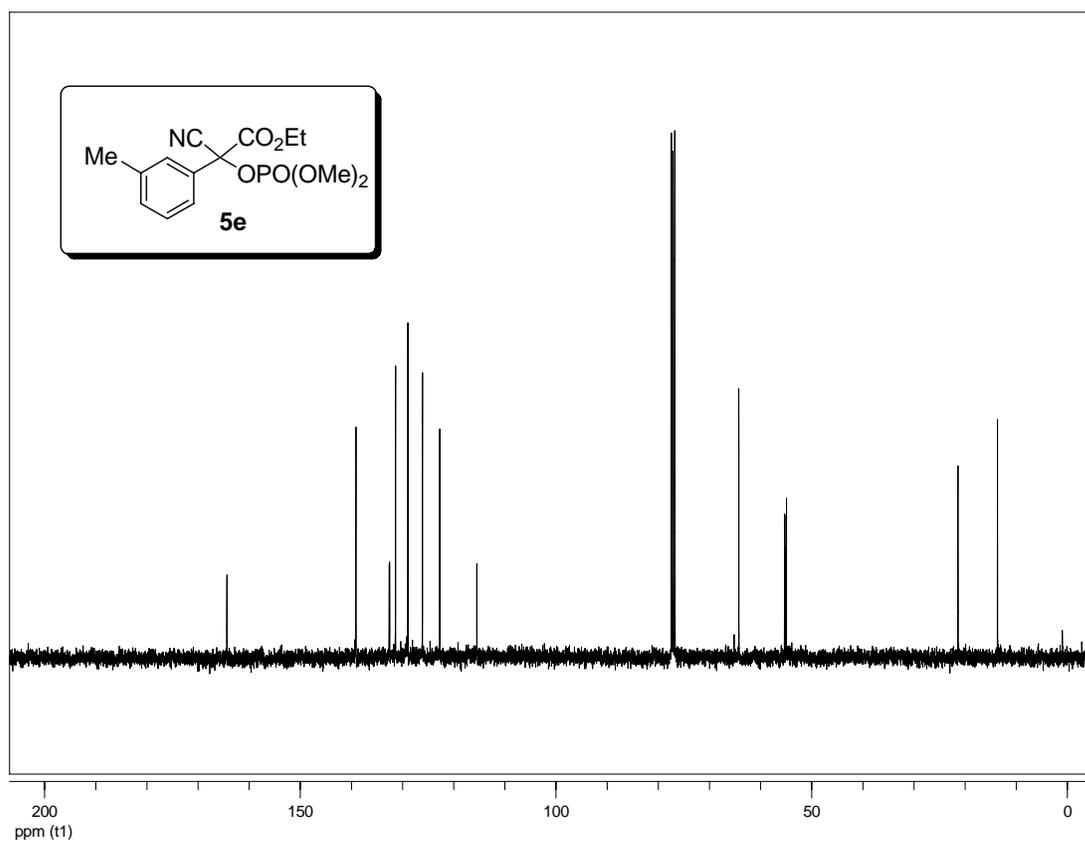
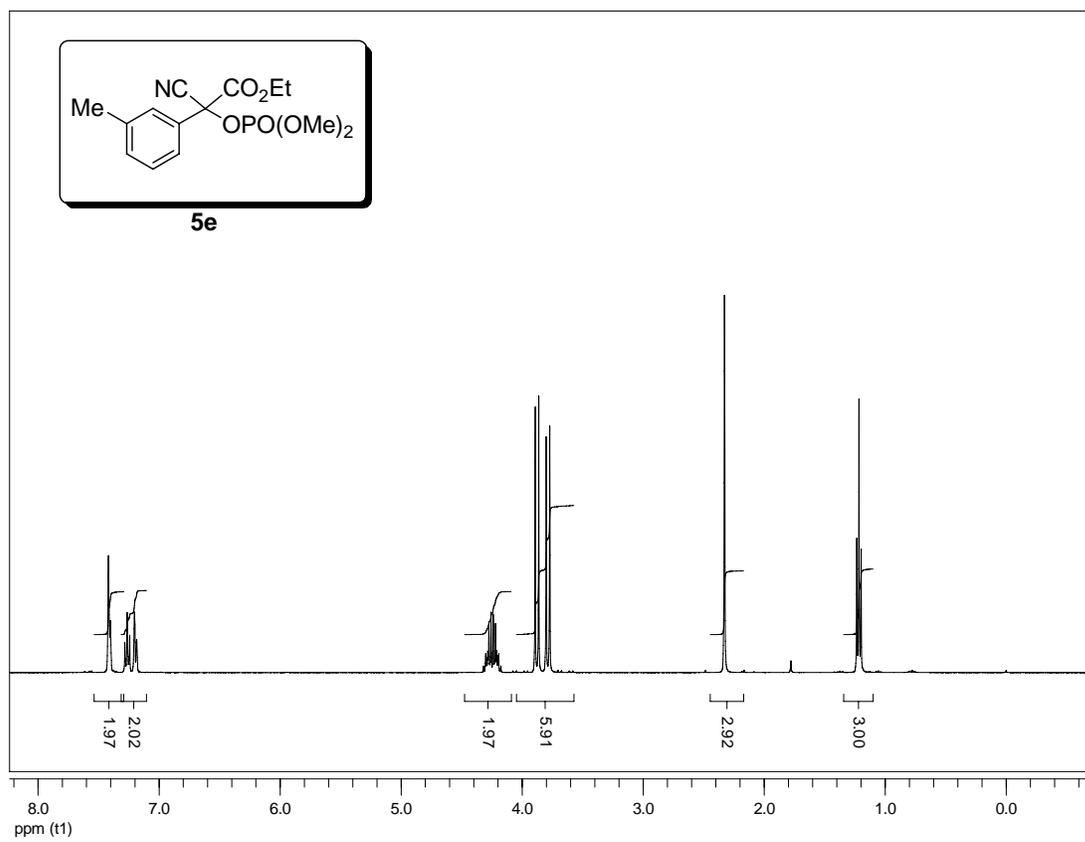
Ethyl 3-amino- 2-phenylpropanoate (11): A mixture of 1.5 g. (0.48 mmole) of **5a**, 150 ml. of absolute alcohol, 2.5 ml. of concd. hydrochloric acid, and 400 mg of 10% palladium on carbon catalyst was shaken in Paar hydrogenation apparatus at 60 p.s.i. initial pressure of hydrogen for 4h. The reaction mixture concentrated *in vacuo* and the residue was washed with ether and recrystallized twice in ethyl alcohol . Yield, 0.81 g. (74 %) of **12**. Mp: 163-166 °C (lit.² 164-165°C). This salt is dissolved in 8ml of water and neutralized with Na_2CO_3 solution. The precipitate is dissolved in ether and washed with water, dried over MgSO_4 . Evaporation of the solvent gave almost pure amine **11**. Yield, 0,65 g (96%) colorles solid (Mp: 76-78°C; Lit.² 78-79°C). ^1H NMR (CDCl_3) δ 1.02-1.19 (5H, m), 2.86-2.91 (1H, m), 3.14-3.20 (1H, m), 3.50-3.54 (1H, m), 3.95-4.08 (2H, m), 7.11-7.22 (5H, m); ^{13}C NMR (CDCl_3) 14.0, 45.5, 55.5, 60.6, 127.3, 128.0, 128.6, 137.2, 172.9 ppm.

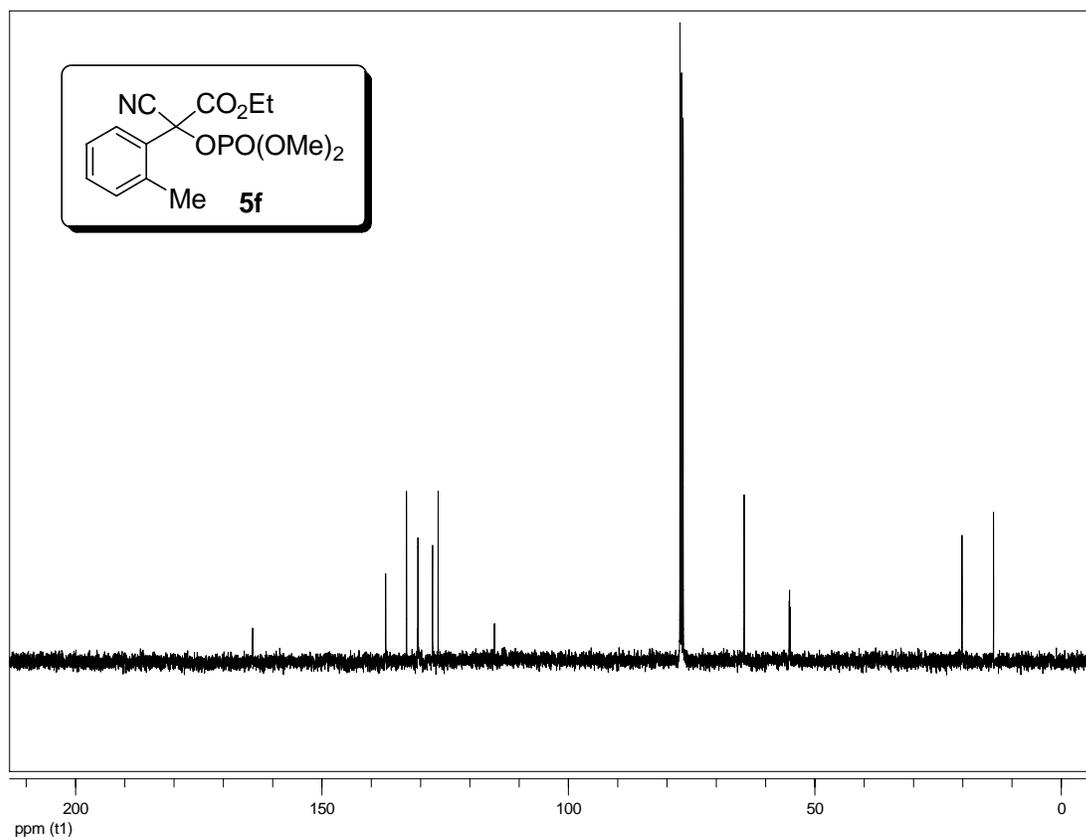
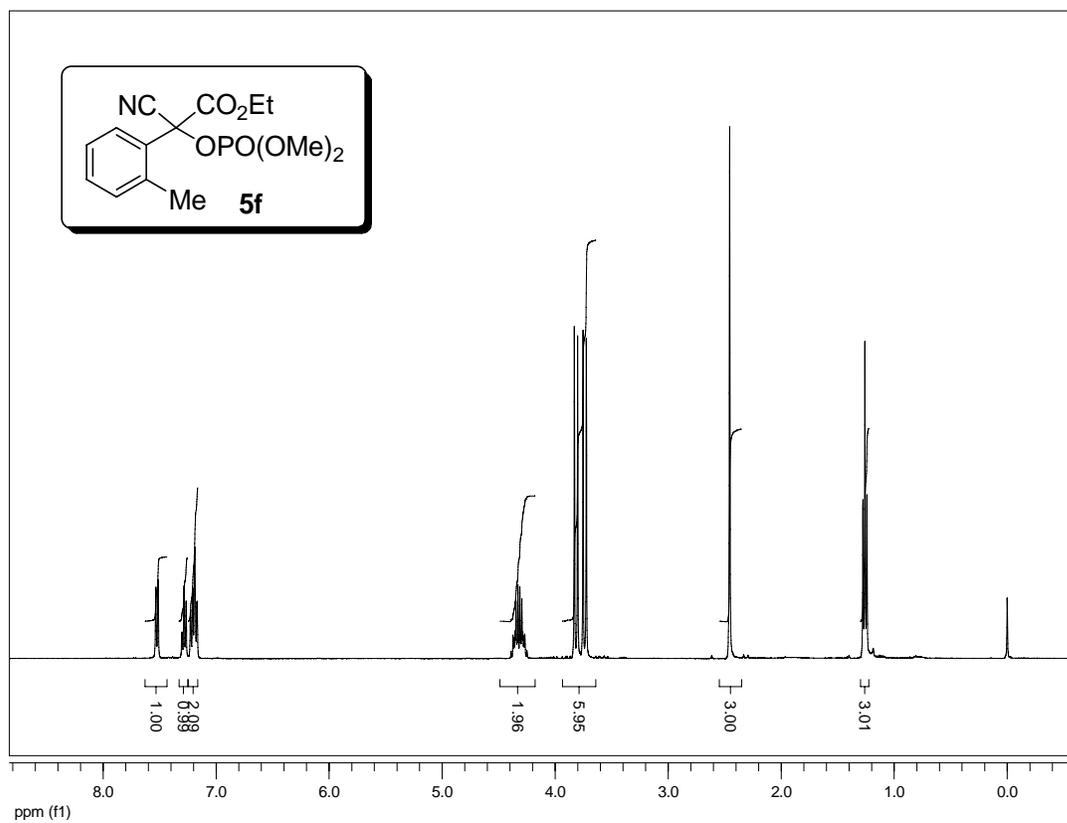


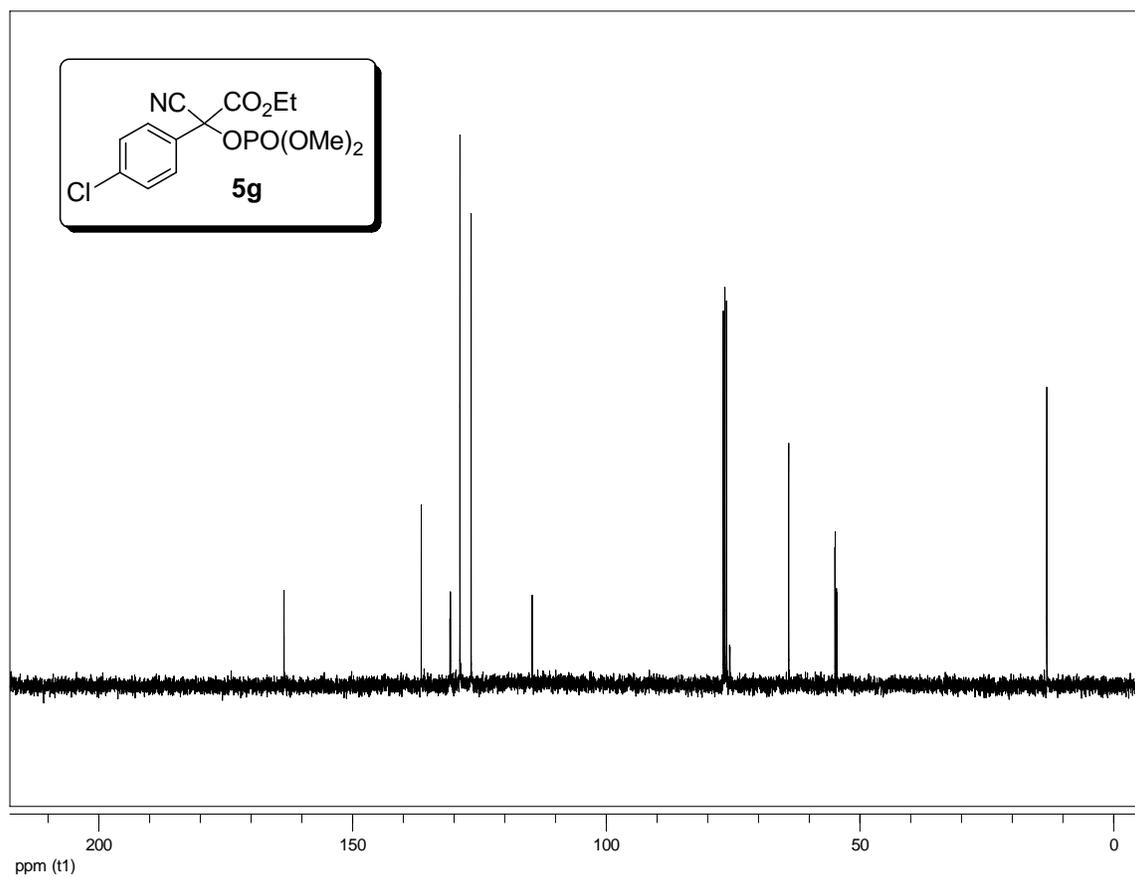
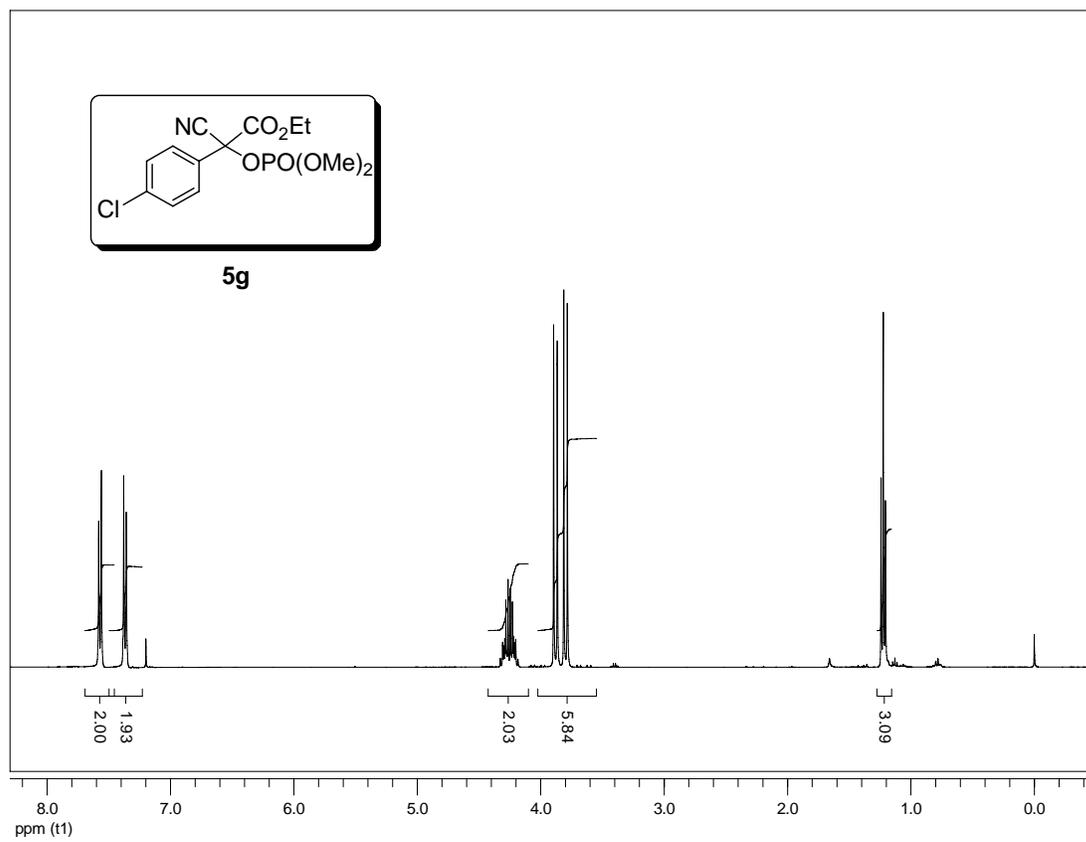


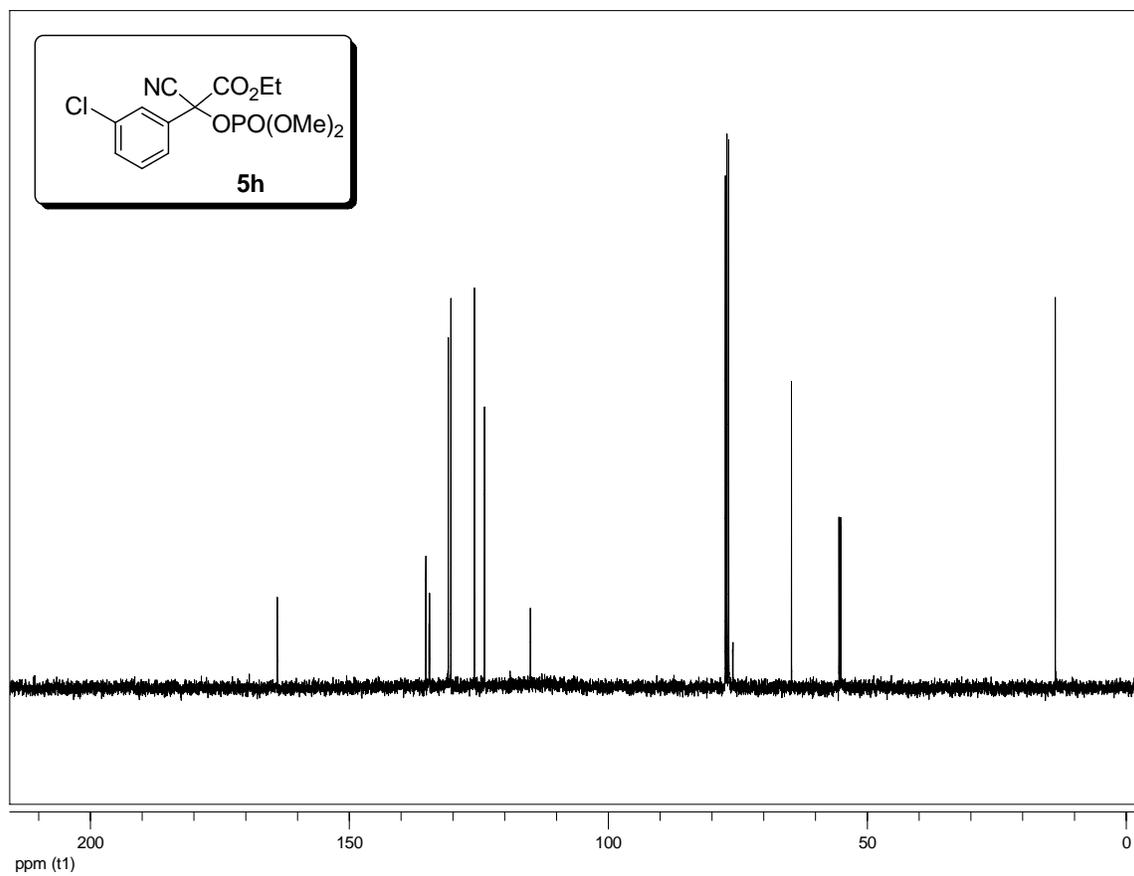
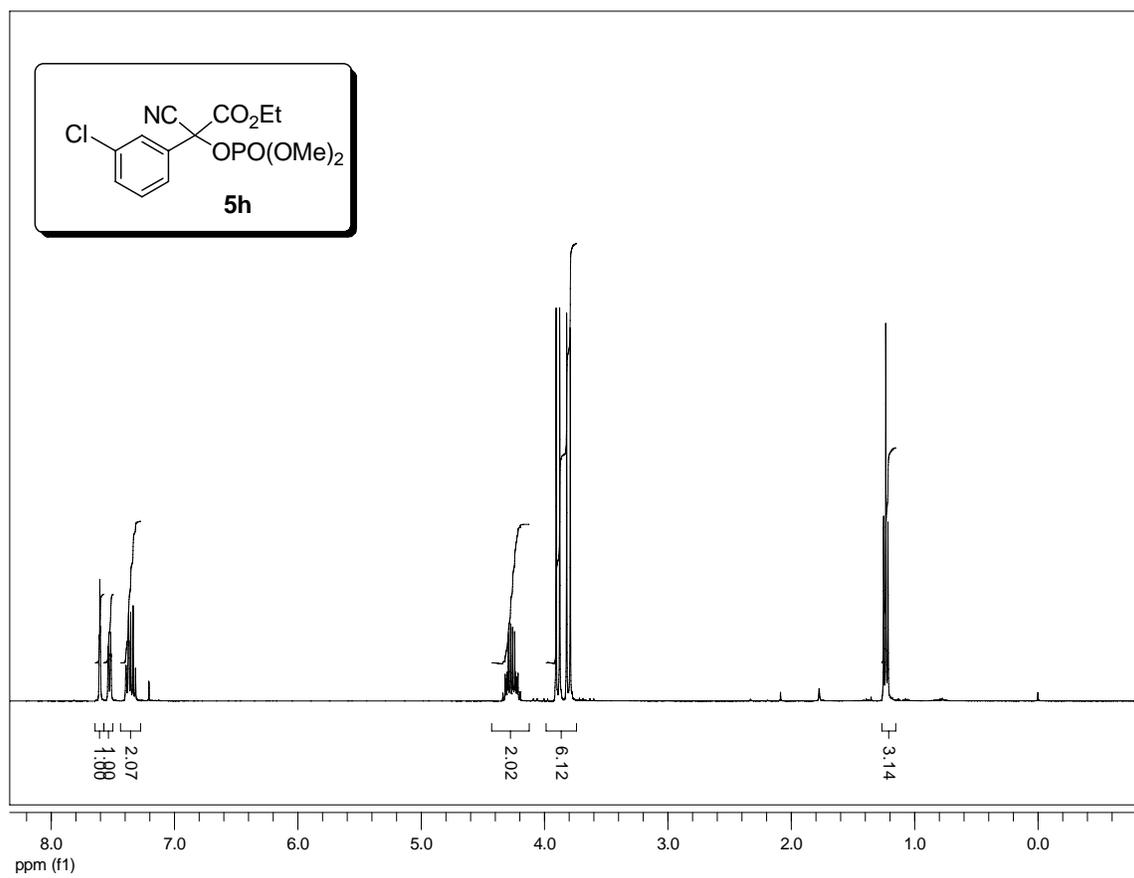


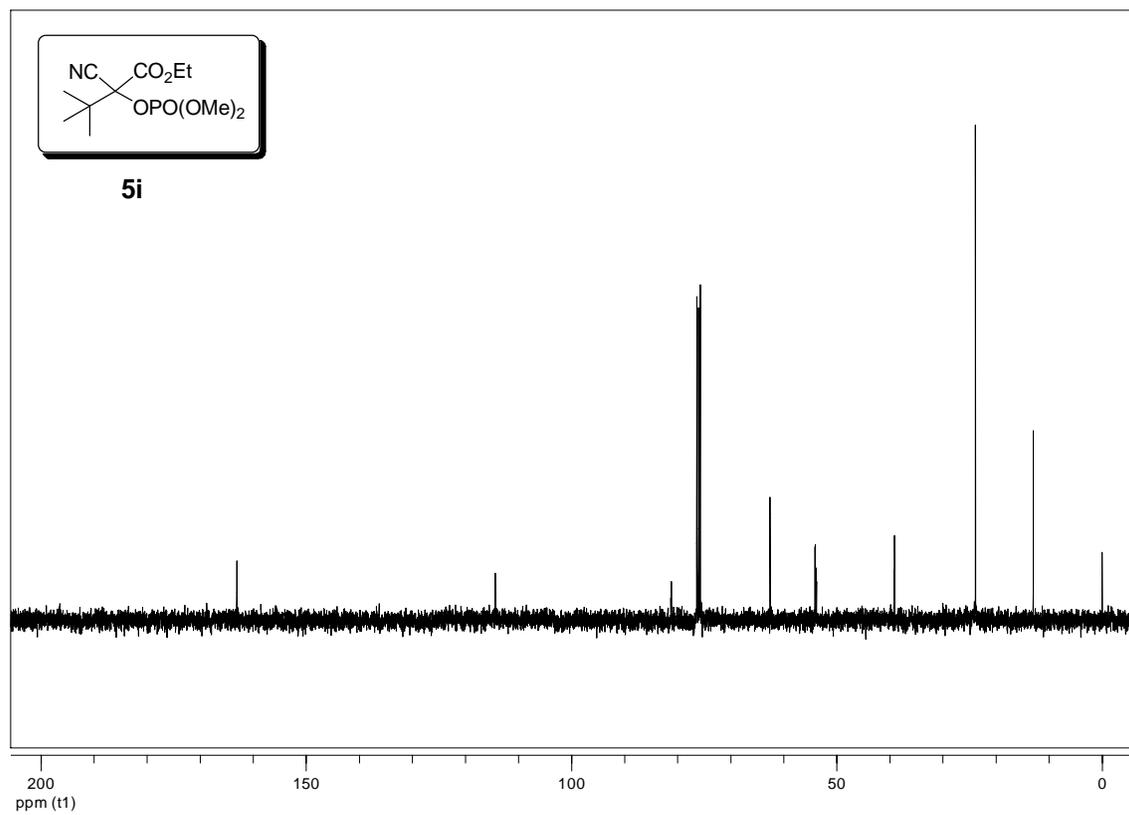
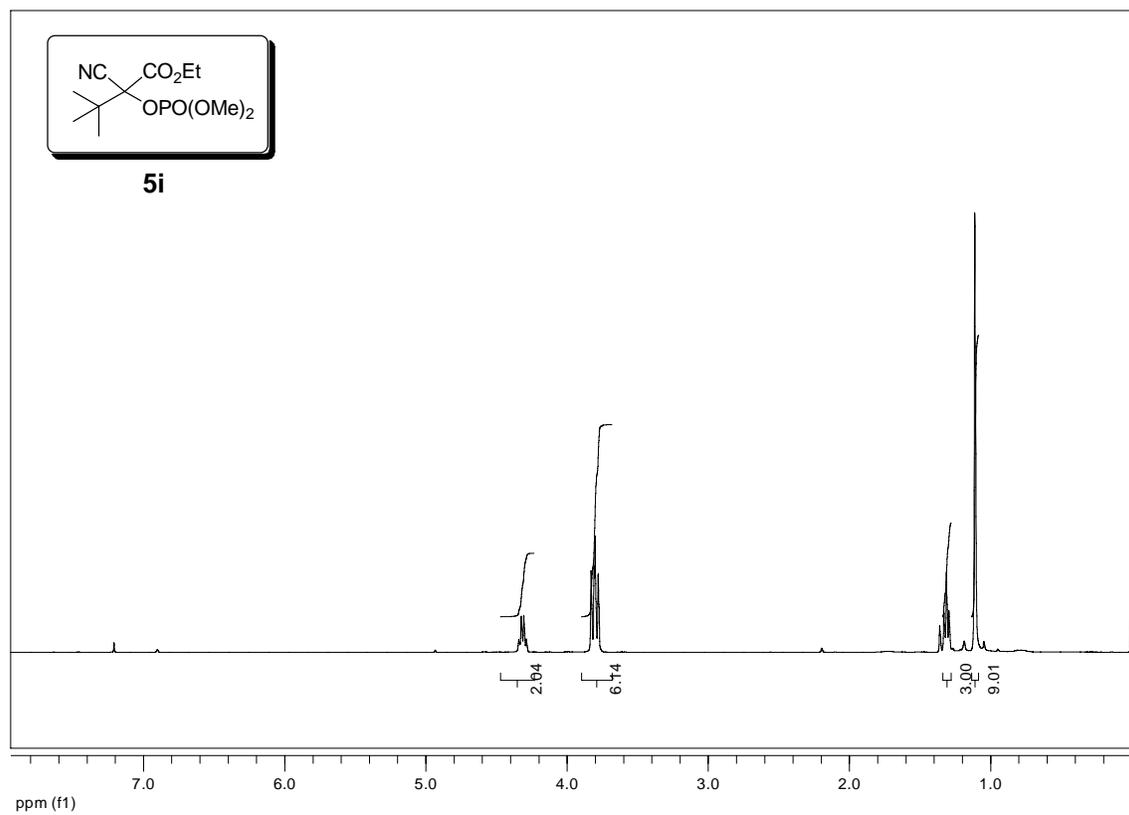


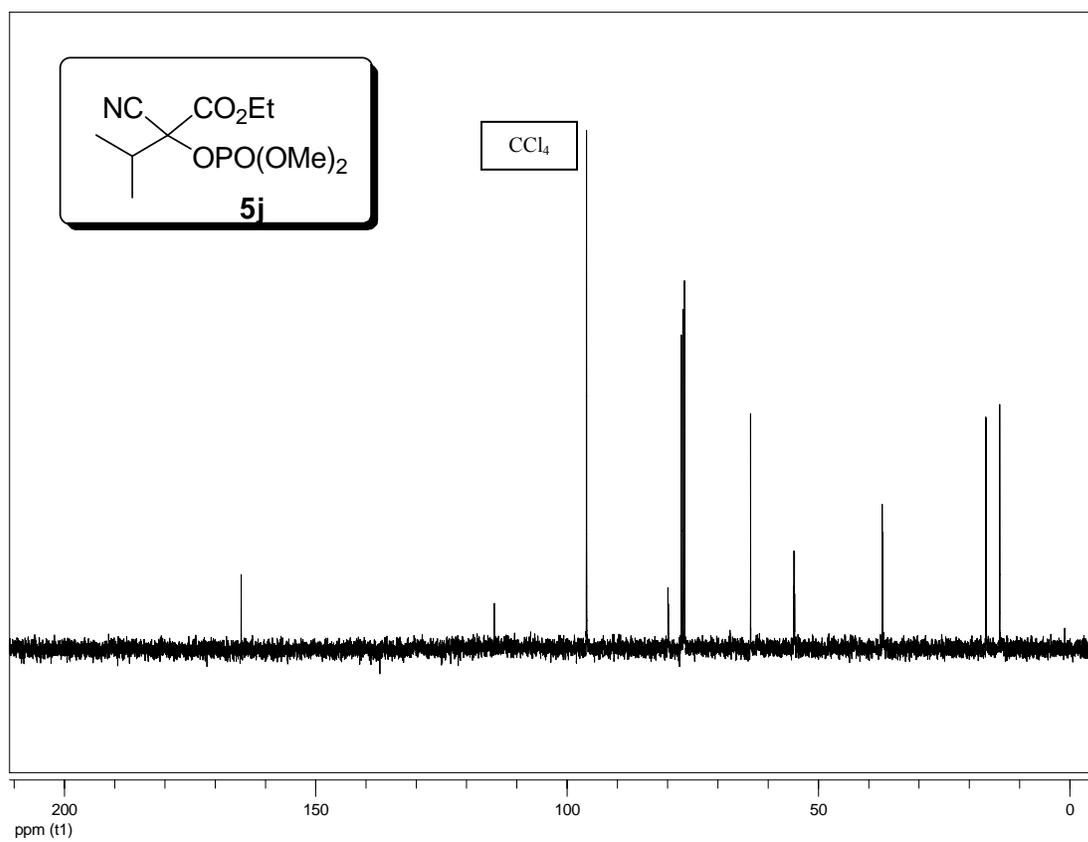
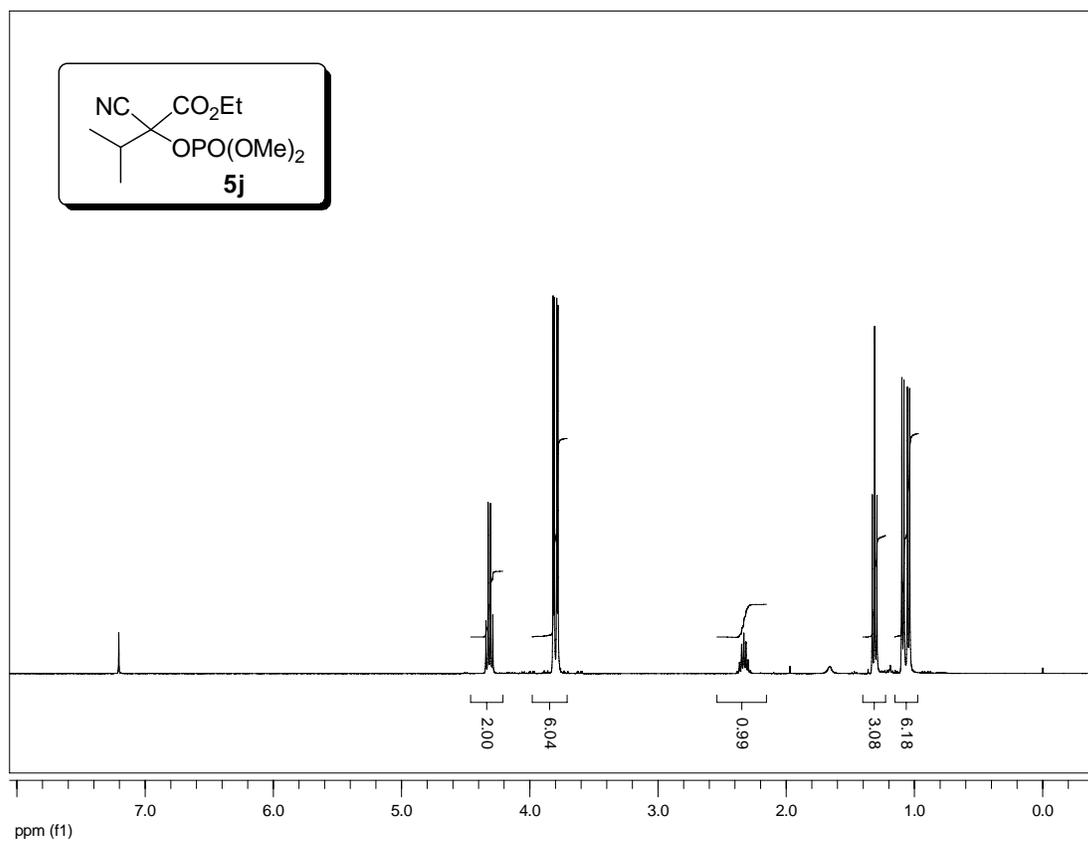


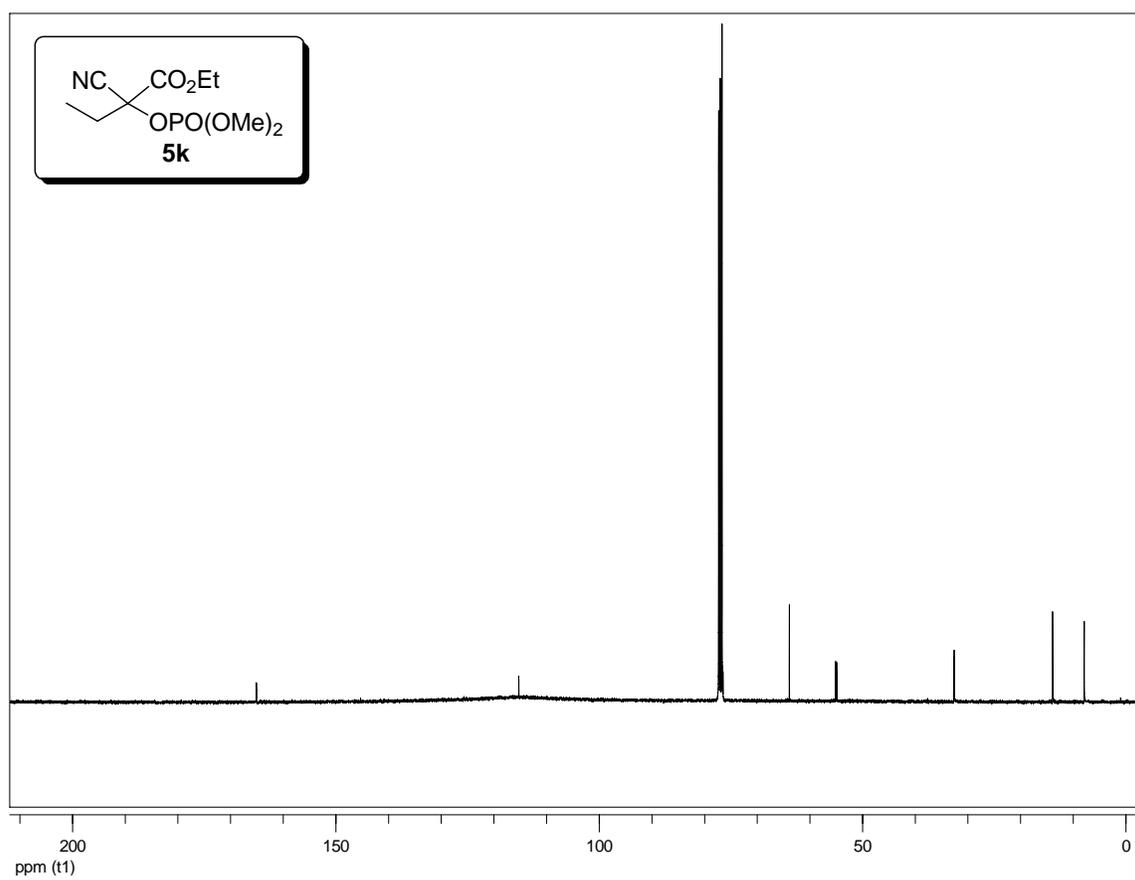
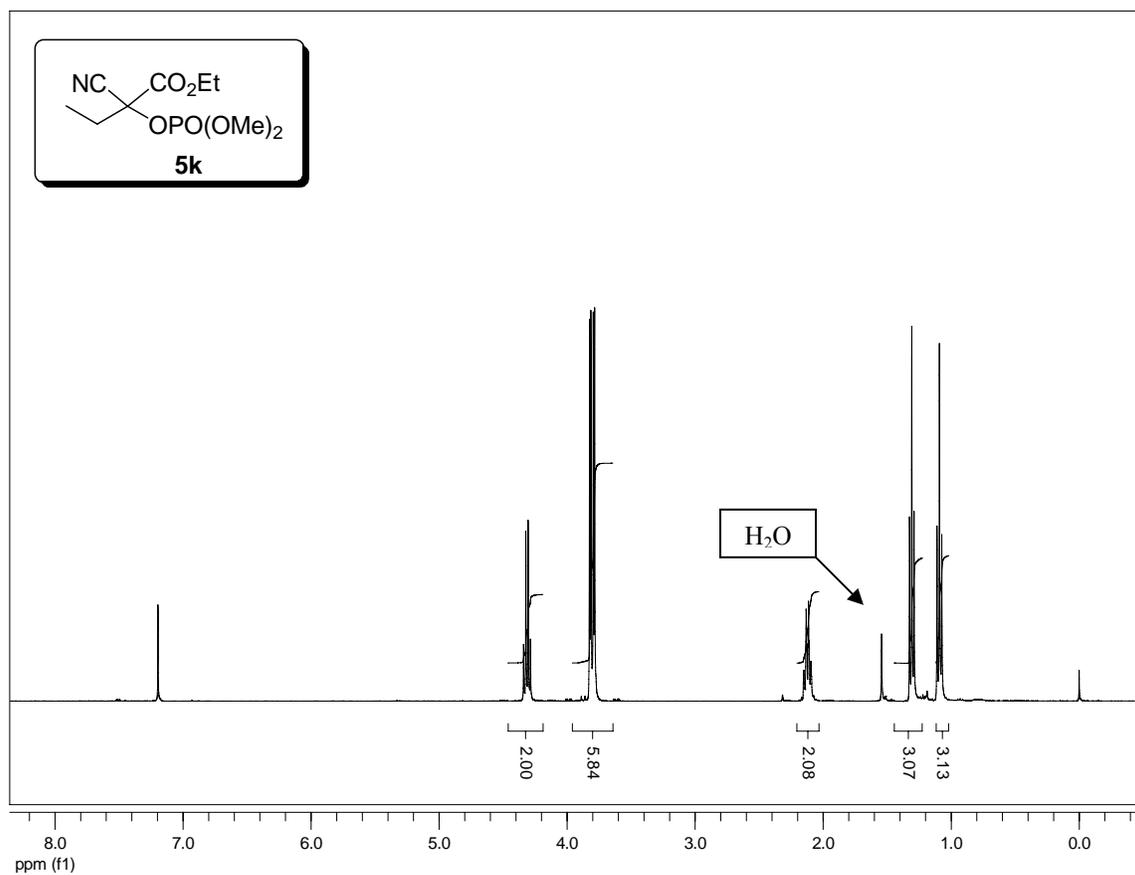


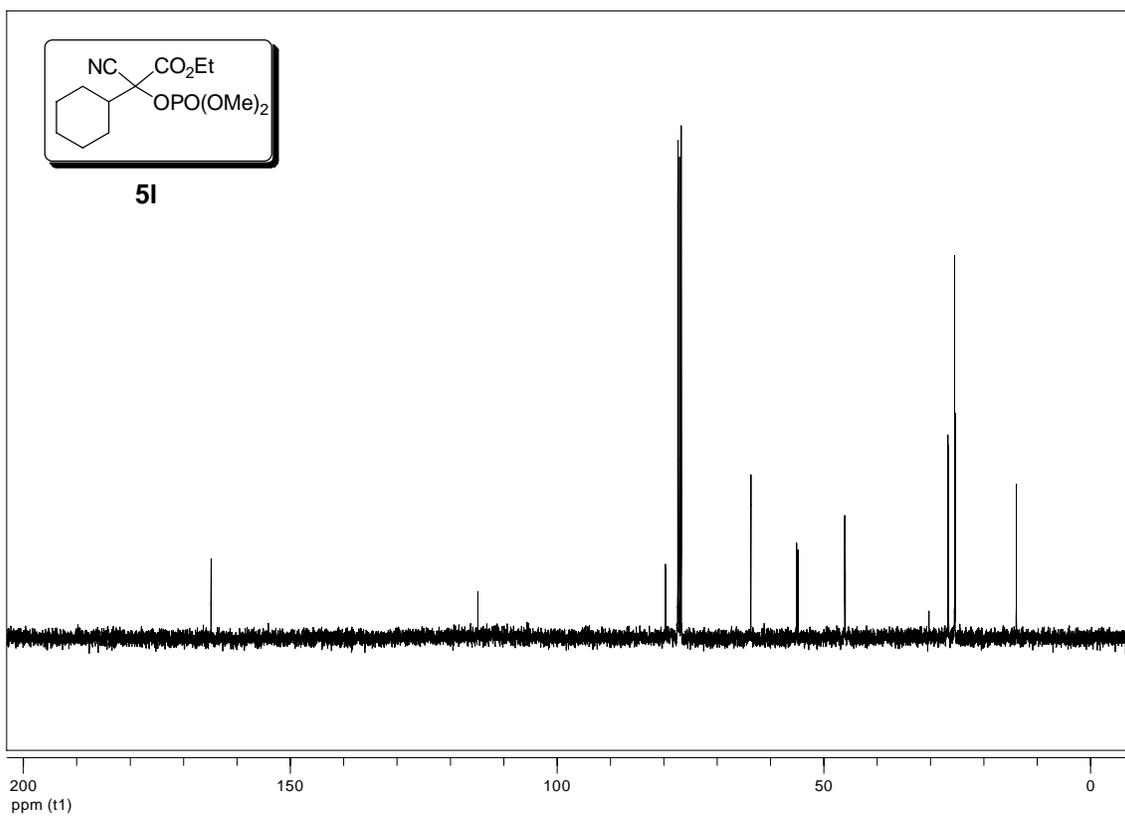
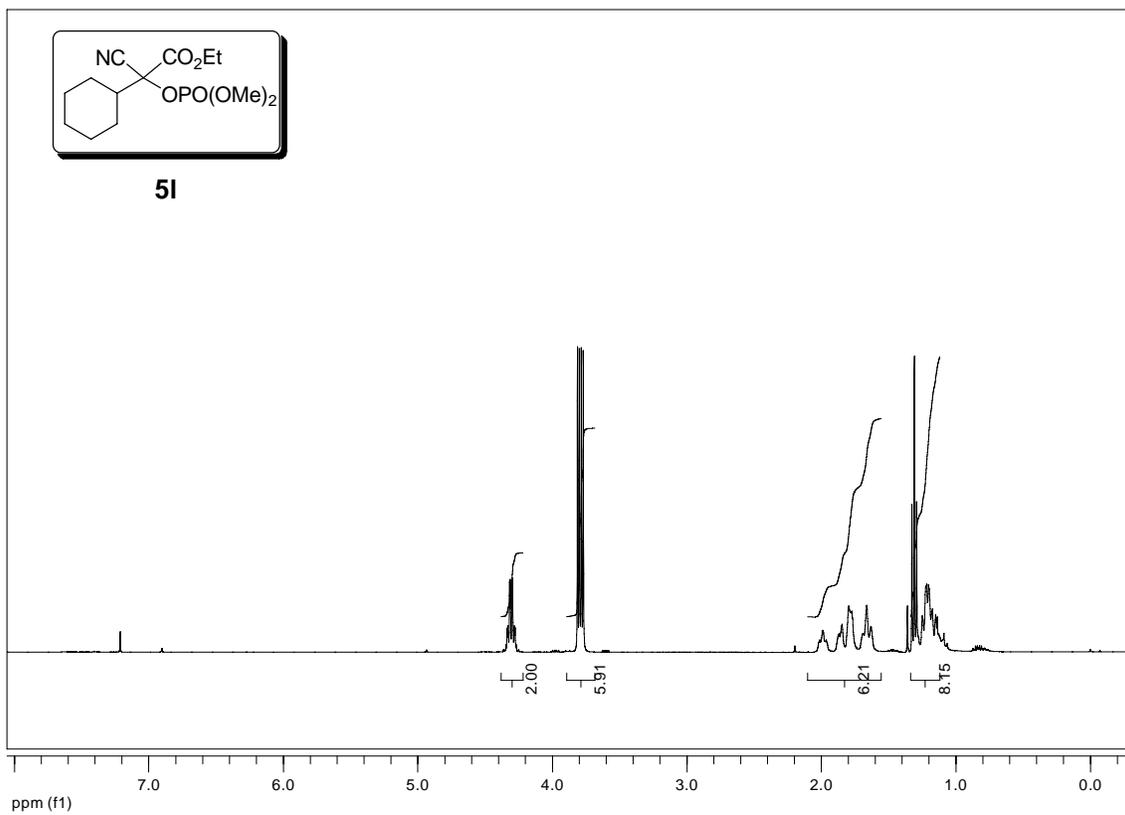


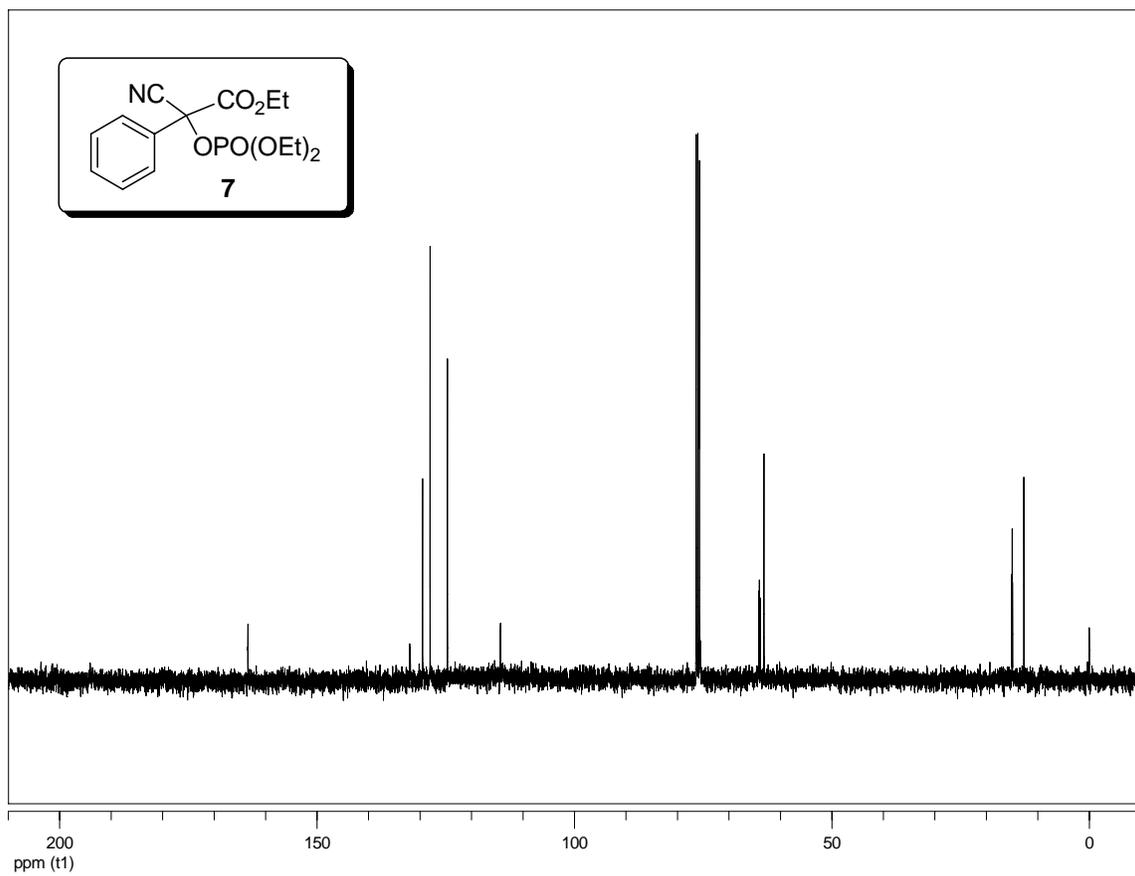
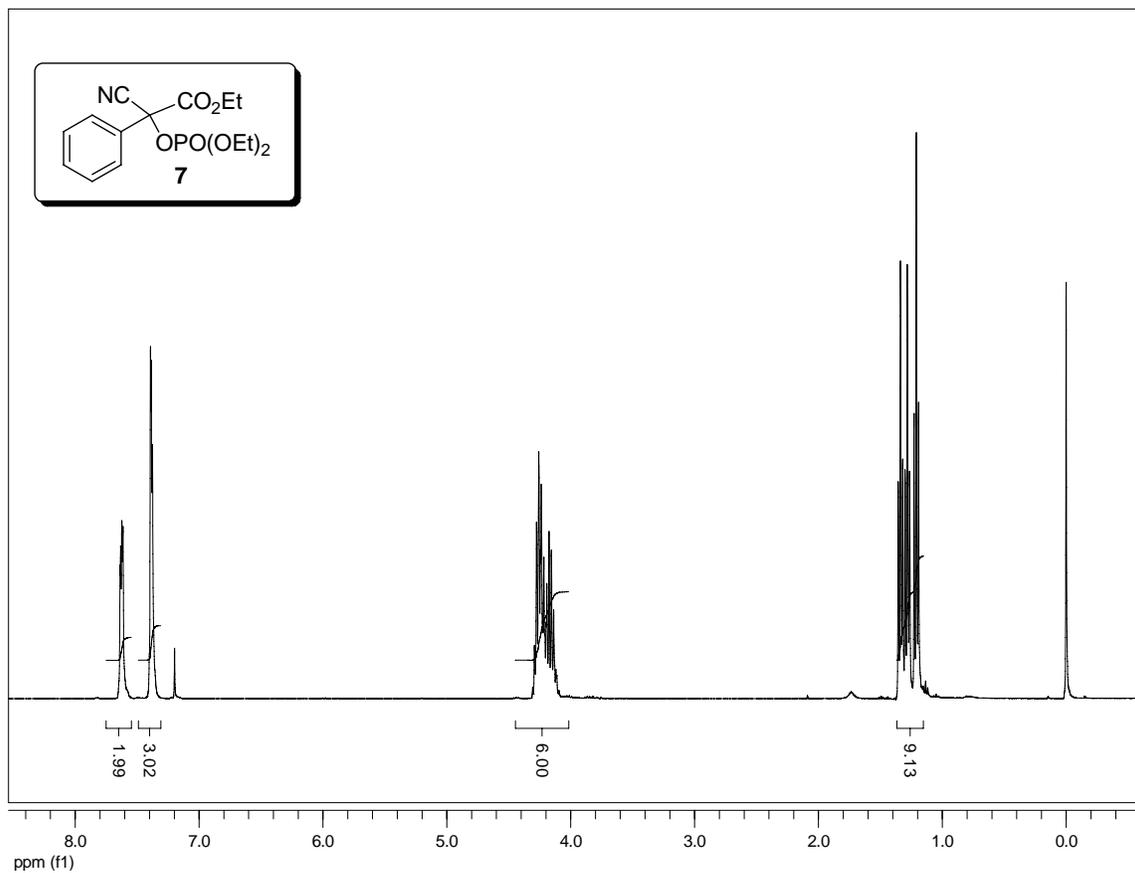


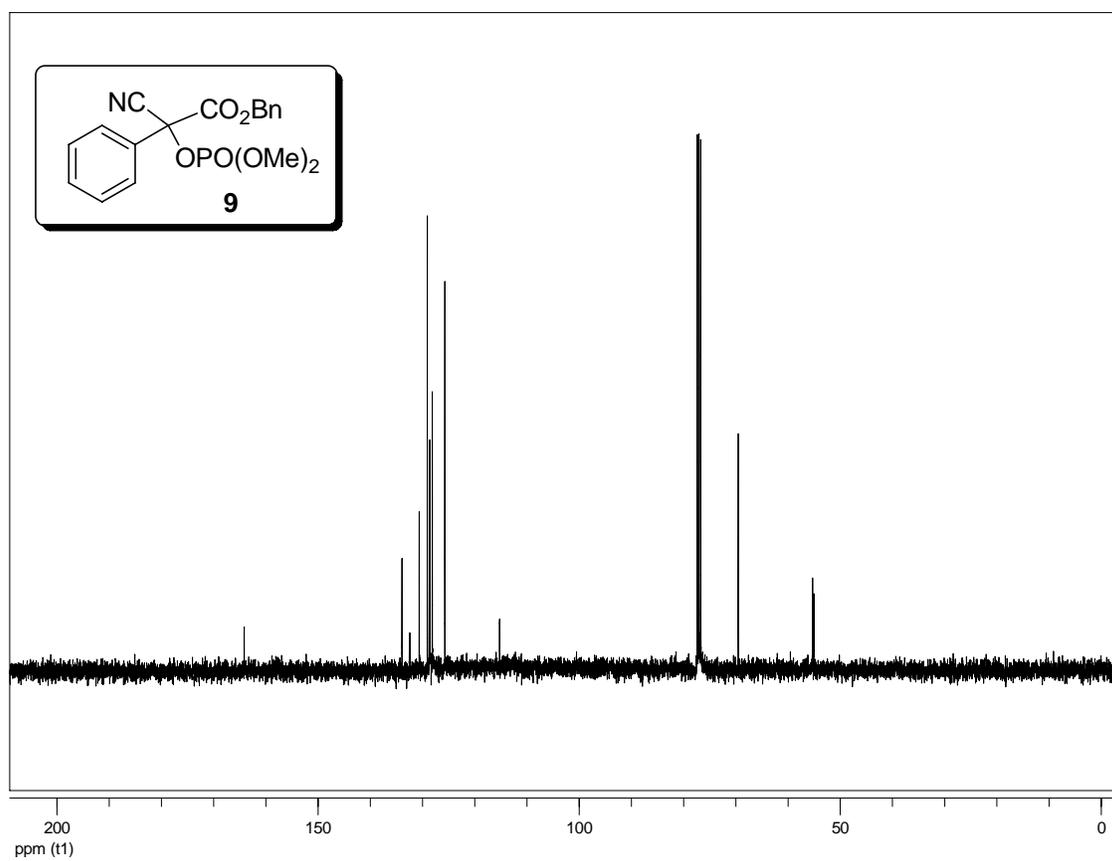
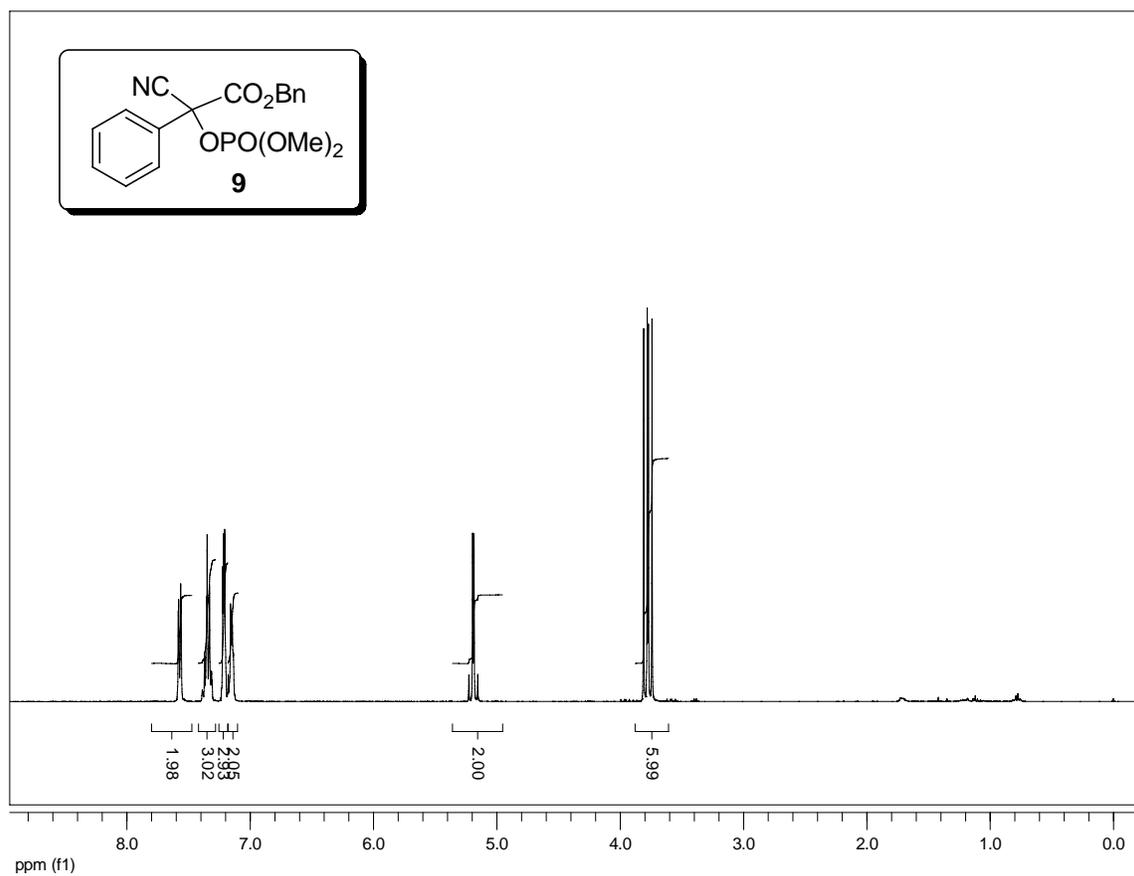


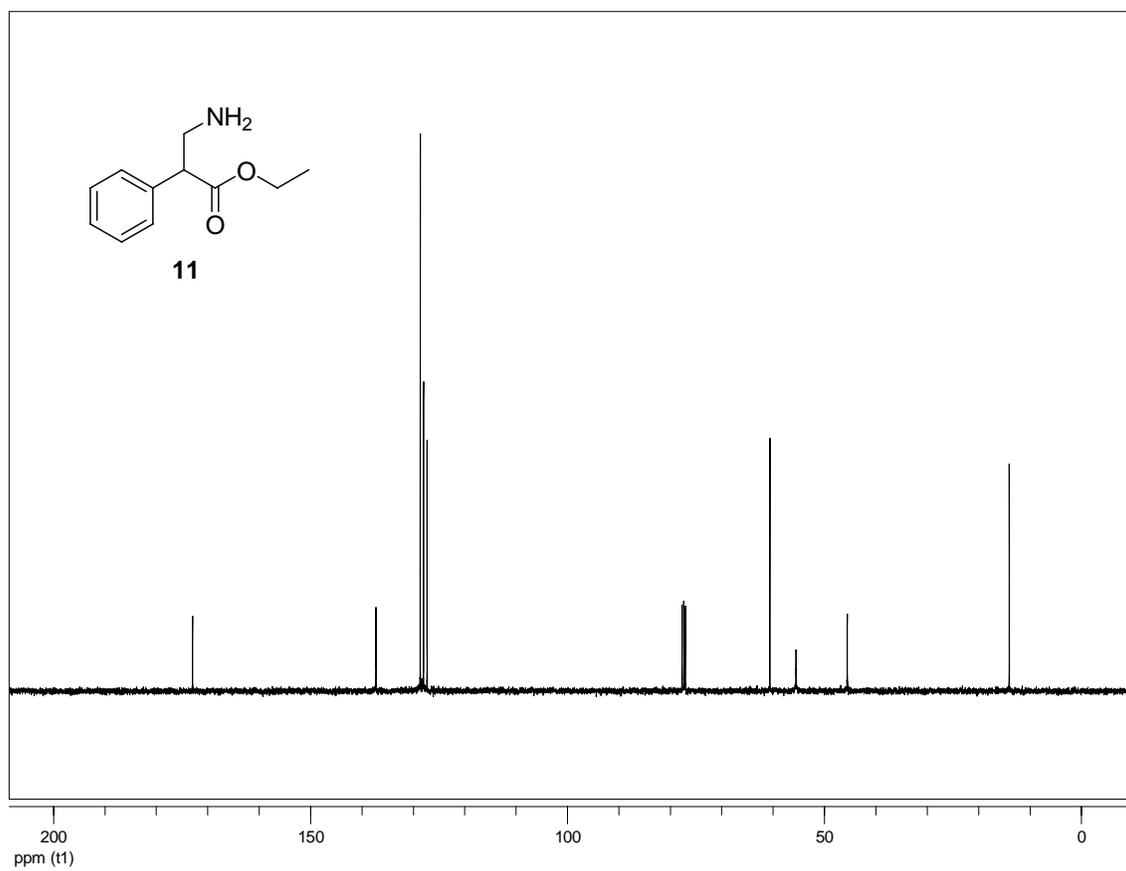
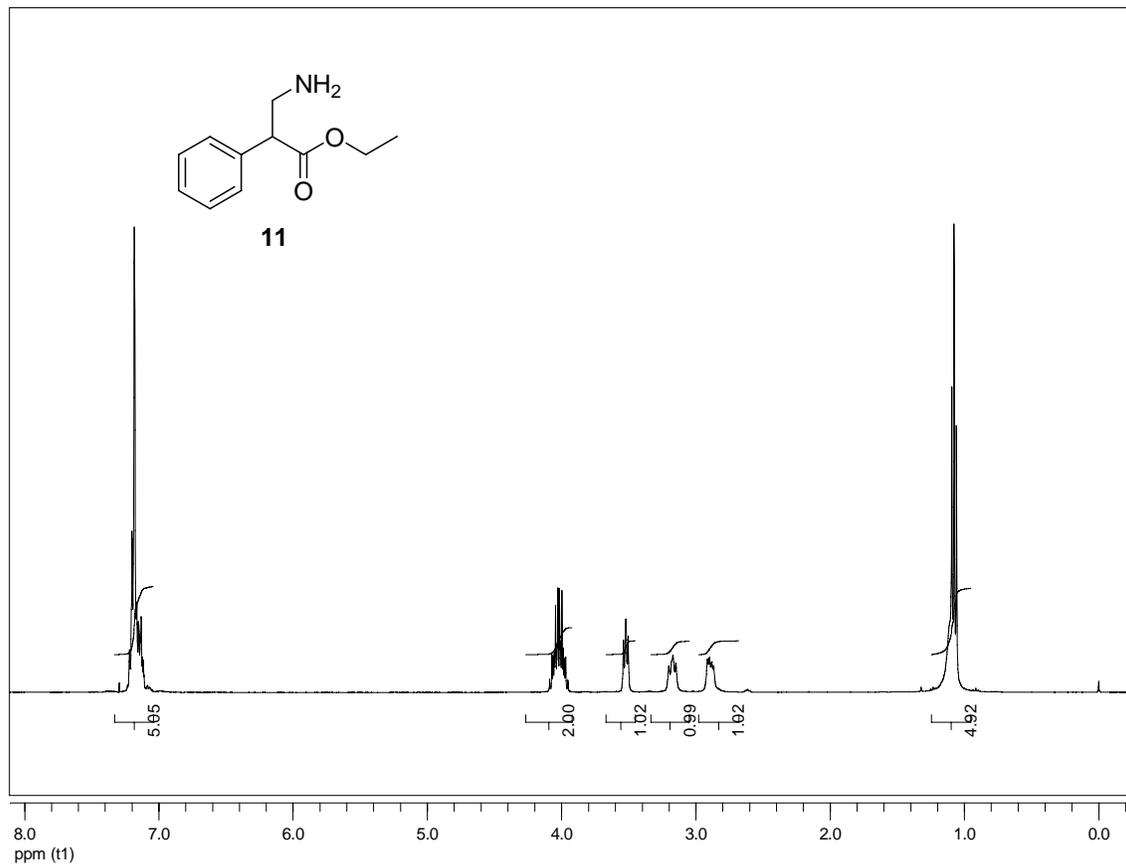












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(b) Berlin, K. D.; Taylor, H. A. *J. Am. Chem. Soc.* **1964**, *86*, 3862-3866. (c) Kim, S.; Cho, C. H.; Lim, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9574.
2. (a) Testa, E.; Fontanella, L.; Bovara, M. *Liebigs Ann. Chem.* **1964**, *671*, 97. (b) *Testa, E.; Fontanella, L.; Cristiani, G. F.; Mariani, L. Liebigs Ann. Chem.* **1961**, *639*, 166.