Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Ag_2O-catalysed nucleophilic isocyanation: selective formation of less-stable benzylic isonitriles

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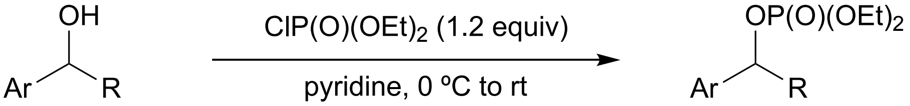
1. General Information

^{1}H NMR spectra were measured on a JEOL JNM-ECX400P (400 MHz) spectrometer and JNM-ECS400 (400 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane or the residual solvent as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = double-doublet, td = triple-doublet, q = quartet, m = multiplet, br = broad, and app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a JEOL JNM-ECX400P (100 MHz) spectrometer and a JNM-ECS400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm, from the residual solvent as an internal standard. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 and FT/IR-4600. Gel permeation chromatography (GPC) was performed using an LC-918 recycling preparative HPLC equipped with JAIGEL-1H and -2H columns in series (Japan Analytical Industry Co., Ltd.). The products were purified by flash column chromatography on silica gel 60N (Kanto Chemical Co. Inc.). All manipulations for isocyanation of benzylic phosphates were performed under an argon atmosphere using the standard Schlenk technique, unless otherwise noted. Trimethylsilyl cyanide (TMSCN) was purchased from Kanto Chemical Co. Inc., and was used after distillation. Dehydrated 1,4-dioxane was purchased from Kanto Chemical Co. Inc., and was used as received. Silver(I) oxide (Ag_2O) was purchased from Sigma-Aldrich Co. LLC., and was used as received.

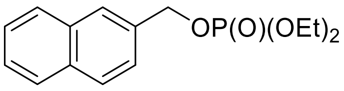
2. Preparation of Benzylic Phosphates

General Procedure

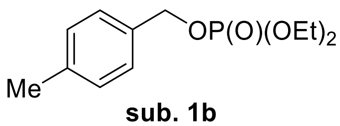


A dry round-bottomed flask was charged with benzylic alcohol (1.0 equiv) and pyridine to prepare 2M solution. The mixture was cooled to 0 ºC and diethyl chlorophosphate (1.2 equiv) was added dropwise. The reaction mixture was allowed to warm up to room temperature and stirred until the reaction was judged complete by TLC analysis. The reaction was quenched by the addition of 1 M H_2SO_4 aq. The layers were separated and the aqueous layer was extracted with AcOEt. The combined organic layers were washed with 1M H_2SO_4 aq., then brine, and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the collected filtrate was concentrated in vacuo. The crude residue was purified by silica-gel column chromatography. The isolated benzylic phosphates were repurified by distillation or gel permission chromatography.

The NMR data of **sub. 1a**,[1] **sub. 1b**,[1] **sub. 1c**,[2] **sub. 1d**,[1] **sub. 1e**,[1] **sub. 1f**,[1] **sub. 1g**,[3] **sub. 1h**,[1] **sub. 1i**,[4] **sub. 1j**,[3] **2a**,[1] **2b**,[5] **2c**,[5] **2d**,[6] and **2h**[7] were in accordance with those in the literature.



sub. 1a



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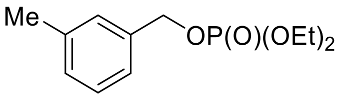

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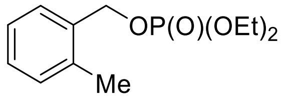

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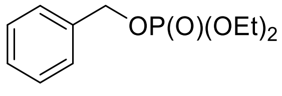
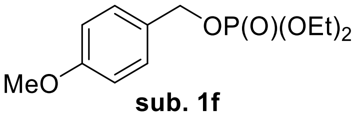


sub. 1e



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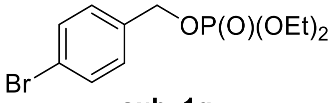
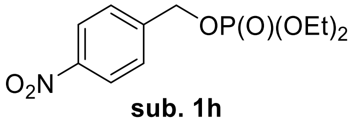
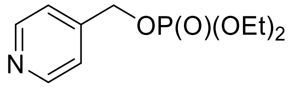


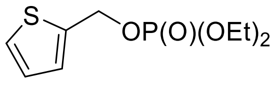
sub. 1g



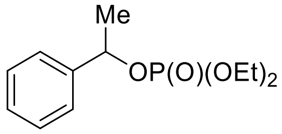
sub. 1h



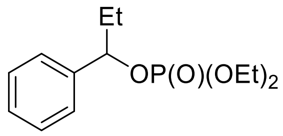
sub. 1i



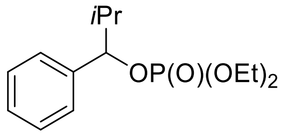
sub. 1j



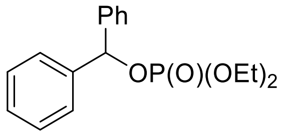
2a



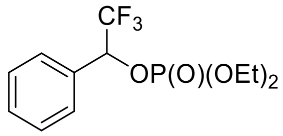
2b



2c

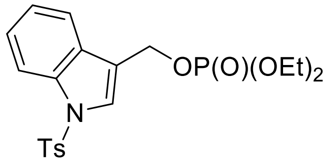


2d



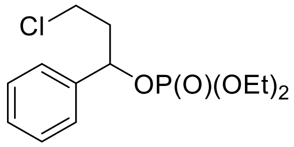
2h

3-(*N*-Tosyl)indolylmethyl diethyl phosphate (sub. 1j): colorless oil, 10% yield.



^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.4 Hz, 1H, Ar), 7.79 (d, *J* = 8.4 Hz, 2H, Ar), 7.65 (d, *J* = 6.4 Hz, 2H, Ar), 7.35 (app. t, *J* = 8.0 Hz, 1H, Ar), 7.28 (d, *J* = 8.0 Hz, 1H, Ar), 7.24 (d, *J* = 8.0 Hz, 2H, Ar), 5.20 (d, *J* = 8.0 Hz, 2H, ArCH_2), 4.08–3.99 (m, 4H, C$H_2$$CH_3$), 2.35 (s, 3H, ArC$H_3$), 1.24 (dt, *J* = 0.8 Hz, 7.0 Hz, 6H, CH_2CH_3) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ 145.1, 135.12, 135.08, 129.9, 129.2, 126.9, 125.5, 125.1, 123.5, 119.8, 117.7 (d, *J* = 7.6 Hz), 113.6, 63.9 (d, *J* = 6.7 Hz), 60.9 (d, *J* = 4.8 Hz), 21.6, 16.0 (d, *J* = 6.7 Hz) ppm.
^{31}P-NMR (162 MHz, $CDCl_3$): δ –0.21 ppm.
IR (neat): 2979, 1447, 1173, 1007, 969, 597, 535 cm^{-1}.
HRMS (ESI): calcd. for $C_{20}H_{24}O_6NNaPS$: 460.0954, [M+Na]$^+$ found: 460.0951.

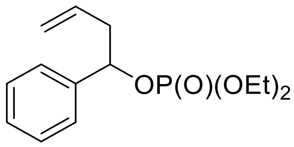
3-Chloro-1-phenylpropyl diethyl phosphate (2e): colorless oil, 25% yield.



^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.39–7.31 (m, 5H, Ar), 5.47 (dt, *J* = 5.6, 8.0 Hz, 1H, ArC*H*), 4.10–4.01

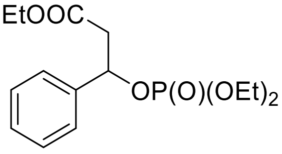
(m, 1H, C*H*$_2$CH$_3$), 3.96–3.87 (m, 3H, C*H*$_2$CH$_3$) 3.71–3.64 (m, 1H, C*H*HCl), 3.48 (dt, *J* = 11.2, 6.4 Hz, 1H, CH*H*Cl), 2.51–2.42 (m, 1H, ArCHC*H*H), 2.21–2.16 (m, 1H, ArCHCH*H*), 1.23–1.17 (m, 6H, (OCH$_2$C*H*$_3$)$_2$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 139.4 (d, *J* = 1.9 Hz), 128.6 (two peaks overlapped), 126.3, 77.4 (app d, *J* = 8.6 Hz) 63.69 (d, *J* = 4.7 Hz), 63.67 (d, *J* = 5.7 Hz), 40.7 (d, *J* = 7.7 Hz), 40.5, 15.9 (d, *J* = 7.7 Hz), 15.9 (d, *J* = 6.7 Hz) ppm.
^{31}P-NMR (162 MHz, CDCl$_3$): δ –1.22 ppm.
IR (neat): 2981, 1258, 1023, 975, 756, 699, 540 cm^{-1}.
HRMS (ESI): calcd. for $C_{13}H_{20}O_4ClNaP$: 329.0680, [M+Na]$^+$ found: 329.0677.

1-Phenylbut-3-en-1-yl diethyl phosphate (2f): colorless oil, 63% yield.



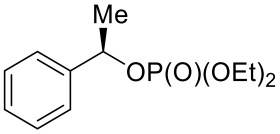
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.36–7.28 (m, 5H, Ar), 5.77–5.66 (m, 1H, C*H*=CH$_2$), 5.35–5.29 (m, 1H, ArC*H*), 5.12–5.05 (m, 2H, CH=C*H*$_2$), 4.13–3.92 (m, 2H, C*H*$_2$CH$_3$), 3.90–3.81 (m, 2H, C*H*$_2$CH$_3$), 2.78–2.71 (m, 1H, CHC*H*HCH=CH$_2$), 2.64–2.57 (m, 1H, CHCH*H*CH=CH$_2$), 1.25 (app t, *J* = 7.0 Hz, 3H, CH$_2$C*H*$_3$), 1.13 (app t, *J* = 7.0 Hz, 3H, CH$_2$C*H*$_3$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 139.9 (d, *J* = 2.9 Hz), 132.9, 128.3, 128.2, 126.5, 118.3, 79.6 (d, *J* = 6.7 Hz), 63.5 (d, *J* = 5.8 Hz), 63.5 (d, *J* = 5.7 Hz), 42.3 (d, *J* = 6.7 Hz), 16.0 (d, *J* = 7.7 Hz), 15.8 (d, *J* = 7.6 Hz) ppm.
^{31}P-NMR (162 MHz, CDCl$_3$): δ –1.19 ppm.
IR (neat): 2981, 1260, 1026, 973, 698, 538, 517 cm^{-1}.
HRMS (ESI): calcd. for $C_{14}H_{21}O_4NaP$: 307.1070, [M+Na]$^+$ found: 307.1069.

Ethyl 3-(diethylphosphoryl)oxy-3-phenylpropanoate (2g): colorless oil, 52% yield.

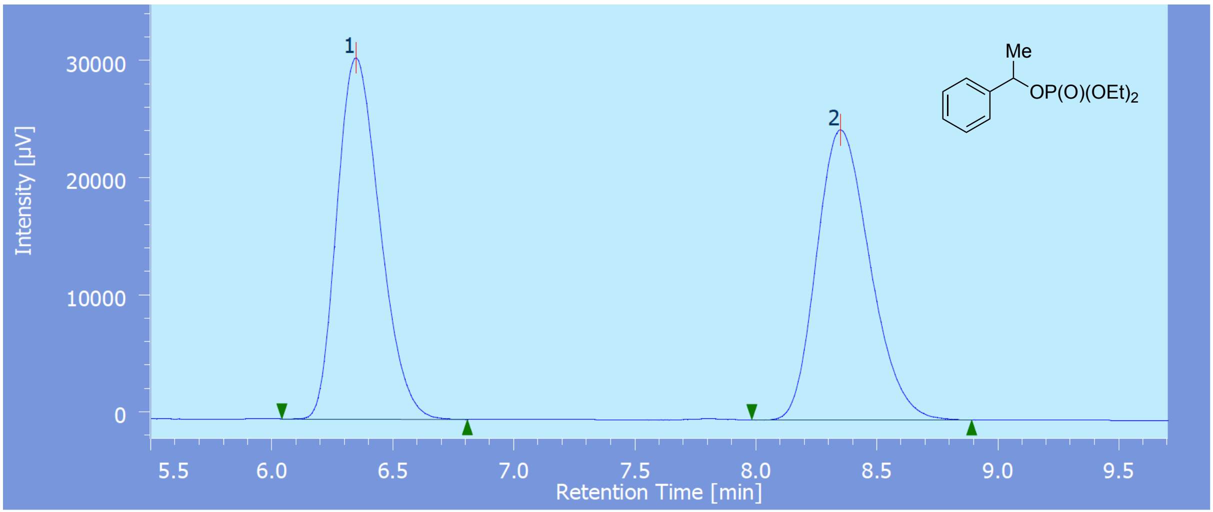


^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.43–7.32 (m, 5H, Ar), 5.76–5.70 (m, 1H, ArCH), 4.15–4.08 (m, 2H, C(O)OC*H*$_2$CH$_3$), 4.07–4.00 (m, 1H, P(O)(OC*H*$_2$CH$_3$)$_2$), 3.96–3.80 (m, 3H, P(O)(OC*H*$_2$CH$_3$)$_2$), 3.07 (ddd, *J* = 15.4, 10.0, 2.8 Hz,1H, ArCHC*H*H), 2.82–2.75 (m, 1H, ArCHCH*H*), 1.24–1.20 (m, 6H, P(O)(OCH$_2$C*H*$_3$)$_2$), 1.17–1.12 (m, 3H, C(O)OCH$_2$C*H*$_3$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 169.4, 139.1 (d, *J* = 2.0 Hz), 128.7, 128.5, 126.6, 76.5 (d, *J* = 4.8 Hz), 63.62 (d, *J* = 4.8 Hz), 63.58 (d, *J* = 4.8 Hz), 60.8, 43.1 (d, *J* = 7.6 Hz), 15.9 (d, *J* = 6.7 Hz), 15.8 (d, *J* = 6.7 Hz), 14.0 ppm.
^{31}P-NMR (162 MHz, CDCl$_3$): δ –1.60 ppm.
IR (neat): 2981, 1734, 1266, 1165, 1021, 970, 699, 514 cm^{-1}.
HRMS (ESI): calcd. for $C_{15}H_{23}O_6NaP$: 353.1125, [M+Na]$^+$ found: 353.1123.

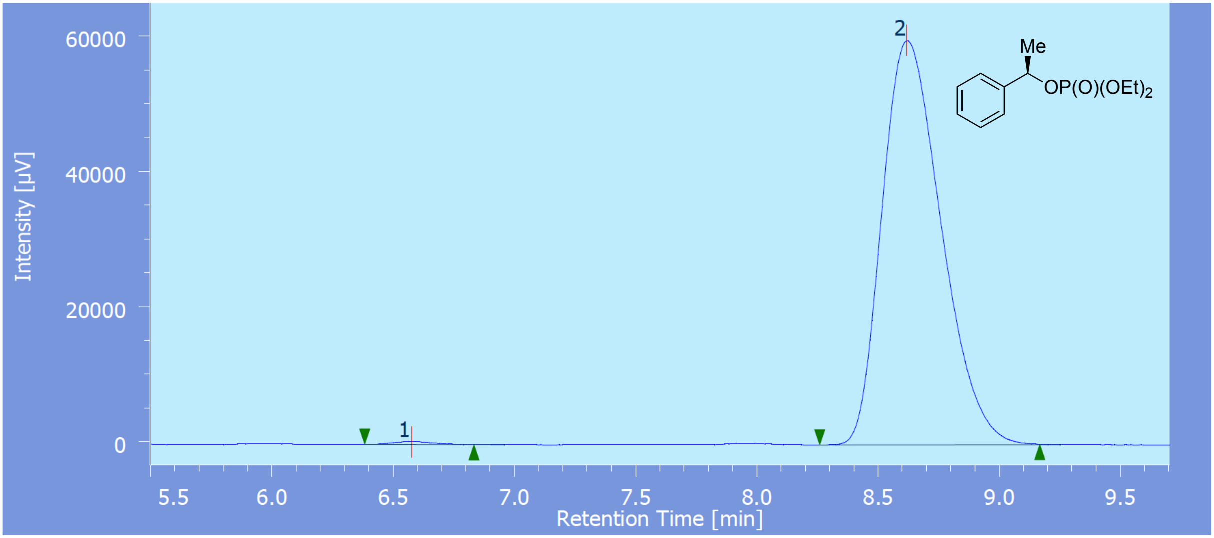
(*R*)-1-phenylethyl diethyl phosphate ((*R*)-2a)[8]: colorless oil, 64% yield, 99% *ee*.



^{1}H NMR data was in accordance with the racemic phosphate **2a**.
HPLC analysis: column, Chiralcel OJ-H, hexane/*i*PrOH = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time; t_R = 8.6 min (major), t_R = 6.6 min (minor)



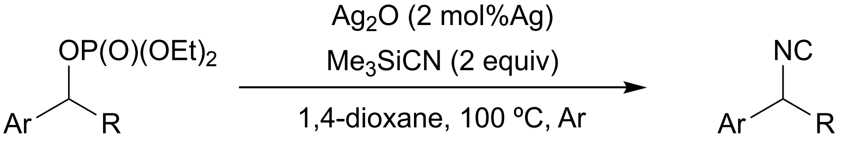
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	6.350	380008	30822	50.030	55.477	N/A	5973	5.455	1.232	
2	Unknown	1	8.350	379549	24736	49.970	44.523	N/A	6748	N/A	1.218	



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	6.575	5090	429	0.499	0.713	N/A	6757	5.302	1.231	
2	Unknown	1	8.617	1014573	59782	99.501	99.287	N/A	5806	N/A	1.328	

3. Ag_2O-Catalyzed Isocyanation of Benzylic Phosphates

General Procedure

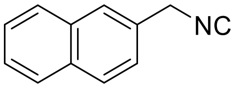


Caution: Trimethylsilyl cyanide (TMSCN) must be used in a well-ventilated hood due to its high toxicity. Most synthesized isonitriles have a distressing smell.

Ag-catalyzed benzylic isocyanation of naphthylmethyl diethylphosphate (**sub. 1a**) is described as a typical procedure.

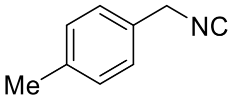
To a suspension of Ag_2O (1.2 mg, 0.010 mmol) in 1,4-dioxane (1.5 mL) was added naphthylmethyl diethylphosphate (**sub. 1a**, 149 mg, 0.50 mmol). The resulting mixture was stirred for 5 min at 100 ºC, followed by the addition of TMSCN (99 mg, 1.0 mmol). The reaction mixture was then continuously stirred at 100 ºC until completion of the reaction. Saturated $NaHCO_3$ aq. was added to quench the reaction, and the aqueous layer was extracted by AcOEt (10 mL × 3). The collected organic layer was washed with brine and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the resulting mixture was concentrated in vacuo. The yield of the product was calculated from ^{1}H NMR spectra of the crude **1a** with pyrazine as an internal standard (93% yield). The crude product was purified by silica-gel column chromatography (AcOEt/hexane = 1/60) to afford pure **1a** as a white solid (71 mg, 84% yield).

2-(Isocyanomethyl)naphthalene (**1a**)[9]**:** white solid, 84% yield (isolated yield).



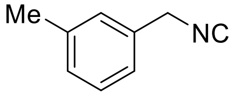
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.88–7.82 (m, 4H, Ar), 7.55–7.49 (m, 2H, Ar), 7.40 (dd, J = 8.0, 1.6 Hz, 1H, Ar), 4.80 (s, 2H, $ArCH_2$) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ 157.8 (t, J = 4.8 Hz), 133.1, 133.0, 129.6, 128.9, 127.9, 127.7, 126.7, 126.6, 125.6, 124.0, 45.7 (t, J = 7.6 Hz) ppm.
IR (neat): 3056, 2152, 1509, 1331, 938, 863, 824, 756, 474 cm^{-1}.

1-(Isocyanomethyl)-4-methylbenzene (1b)[10]**:** yellow oil, 77% yield (isolated yield).



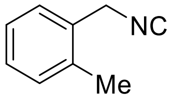
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.26–7.19 (m, 4H, Ar), 4.60 (s, 2H, $ArCH_2$), 2.37 (s, 3H, Me) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ 157.1 (t, J = 5.3 Hz), 138.1, 129.5, 129.3, 126.5, 45.2 (t, J = 7.2 Hz), 21.0 ppm.
IR (neat): 2920, 2858, 2147, 1516, 1439, 796, 731 cm^{-1}.

1-(Isocyanomethyl)-4-methylbenzene (1c): yellow oil, 74% yield (isolated yield).



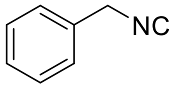
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.31–7.26 (m, 1H, Ar), 7.17–7.13 (m, 3H, Ar), 4.61 (s, 2H, ArCH$_2$), 2.38 (s, 3H, Me) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.4 (t, J = 5.5 Hz), 138.8, 132.2, 129.1, 128.8, 127.2, 123.6, 45.4 (t, J = 7.2 Hz), 21.3 ppm.
IR (neat): 2923, 2851, 2151, 1486, 1069, 1010, 793 cm^{-1}.
HRMS (EI): m/z calcd. for C_9H_9N: 131.0735 [M]$^+$; found: 131.0738.

1-(Isocyanomethyl)-2-methylbenzene (1d): yellow oil, 64% yield (isolated yield)



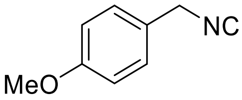
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.40–7.38 (m, 1H, Ar), 7.31–7.20 (m, 3H, Ar), 4.59 (s, 2H, ArCH$_2$), 2.34 (s, 3H, Me) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.5 (t, J = 5.0 Hz), 135.4, 130.5, 130.4, 128.6, 127.4, 126.5, 44.0 (t, J = 7.2 Hz), 18.7 ppm.
IR (neat): 2923, 2147, 1463, 1034, 918, 739, 612 cm^{-1}.
HRMS (EI): calcd. for C_9H_9N: 131.0735 [M]$^+$; found: 131.0736.

Isocyanomethylbenzene (1e)[11]: yellow oil, 64% yield (isolated yield).



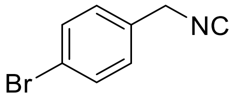
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.43–7.34 (m, 5H, Ar), 4.64 (s, 2H, ArCH$_2$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.5 (t, J = 5.3 Hz), 132.3, 128.9, 128.4, 126.5, 45.5 (t, J = 7.4 Hz) ppm.
IR (neat): 3033, 2925, 2149, 1454, 903, 731, 692, 601 cm^{-1}.

1-(Isocyanomethyl)-4-methoxybenzene (1f): yellow oil, 89% yield (isolated yield).



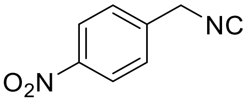
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.27 (app d, J = 8.4 Hz, 2H, Ar), 6.92 (app d, J = 8.8 Hz, 2H, Ar), 4.57 (s, 2H, ArCH$_2$), 3.82 (s, 3H, OMe) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 159.6, 156.9 (t, J = 4.8 Hz), 128.1, 124.5, 114.3, 55.3, 45.0 (t, J = 6.7 Hz) ppm.
IR (neat): 2360, 2936, 2838, 2146, 1613, 1512, 1246, 1177, 1031, 811, 572 cm^{-1}.
HRMS (EI): calcd. For C_9H_9NO: 147.0684 [M]$^+$; found: 147.0685.

1-(Isocyanomethyl)-4-bromobenzene (1g)[12]**:** yellow oil, 84% yield (isolated yield).



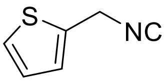
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.53 (d, *J* = 8.4 Hz, 2H, Ar), 7.22 (d, *J* = 8.8 Hz, 2H, Ar), 4.60 (s, 2H, ArCH$_2$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 158.2 (br), 132.0, 131.2, 128.2, 122.4, 44.9 (t, *J* = 7.3 Hz) ppm.
IR (neat): 2147, 1488, 1408, 1070, 1011, 794, 479 cm^{-1}.

1-(Isocyanomethyl)-4-nitrobenzene (1h)[13]**:** yellow solid, 32% yield (isolated yield).



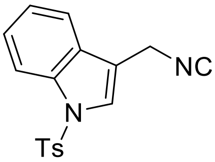
^{1}H-NMR (400 MHz, CDCl$_3$): δ 8.29 (d, *J* = 8.4 Hz, 2H, Ar), 7.57 (d, *J* = 8.8 Hz, 2H, Ar), 4.80 (s, 2H, ArCH$_2$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 159.6 (br), 147.9, 139.0, 127.3, 124.2, 44.9 (t, *J* = 7.7 Hz) ppm.
IR (neat): 3110, 2928, 2160, 1601, 1522, 1351, 1106, 737 cm^{-1}.

2-(Isocyanomethyl)thiophene (1j)[14]**:** yellow oil, 67% yield (isolated yield).



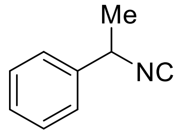
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.31 (d, *J* = 5.2 Hz, 1H, Ar), 7.07 (app d, *J* = 3.6 Hz, 1H, Ar), 6.99 (t, *J* = 4.4 Hz, 1H, Ar), 4.76 (s, 2H, ArCH$_2$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.6 (t, *J* = 4.7 Hz), 134.2, 127.0, 126.9, 126.3, 40.5 (t, *J* = 7.2 Hz) ppm.
IR (neat): 3107, 2145, 1437, 1219, 916, 852, 831, 701, 626 cm^{-1}.
HRMS (EI): calcd. For C_6H_5NS: 123.0143, [M]$^+$;found: 123.0142.

3-(Isocyanomethyl)-((4-methylphenyl)sulfonyl)indol (1k): white solid, 74% yield (isolated yield).



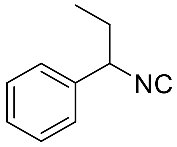
^{1}H-NMR (400 MHz, CDCl$_3$): δ 8.00 (d, *J* = 8.4 Hz, 1H, Ar), 7.78 (d, *J* = 8.4, 2H, Ar), 7.62 (s, 1H, Ar), 7.51 (d, *J* = 8.4 Hz, 1H, Ar), 7.38 (t, *J* = 8.4 Hz, 1H, Ar), 7.28 (t, *J* = 8.0 Hz, 1H, Ar), 7.23 (d, *J* = 8.4 Hz, 2H, Ar), 4.69 (s, 2H, ArCH$_2$), 2.33 (s, 3H, Me) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.7 (br), 145.3, 135.1, 134.7, 130.0, 128.0, 126.8, 125.4, 124.3, 123.6, 119.0, 114.2, 113.8, 37.4 (br), 21.5 ppm.
IR (KBr): 3126, 3055, 2163, 1597, 1363, 1175, 980, 570 cm^{-1}.
HRMS (EI): calcd. for $C_{17}H_{14}N_2O_2S$: 310.0776, [M]$^+$; found: 310.0761.

1-Isocyano-1-phenylethane (3a)[15]**:** colorless oil, 83% yield (isolated yield).



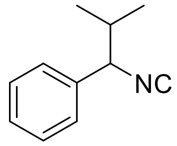
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.43–7.32 (m, 5H, Ar), 4.82 (qt, *J* = 7.2, 1.8 Hz, 1H, CH), 1.69 (dt, *J* = 7.2 Hz, 2.2 Hz, 3H, Me) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 156.1 (t, *J* = 4.8 Hz), 138.4, 128.8, 128.1, 125.2, 53.6 (t, *J* = 6.5 Hz), 25.0 ppm.
IR (neat): 2986, 2928, 2138, 1450, 1074, 756, 695, 610, 544 cm^{-1}.

1-Isocyano-1-phenyl-propane (3b): colorless oil, 73% yield (isolated yield).



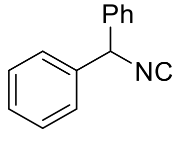
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.42–7.38 (m, 2H, Ar), 7.35–7.32 (m, 3H, Ar), 4.64 (app. t, *J* = 7.8 Hz, 1H, ArCH), 1.97–1.88 (m, 2H, C*H*$_2$CH$_3$), 1.05 (t, *J* = 7.4 Hz, CH2C*H*$_3$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 156.6 (t, *J* = 4.8 Hz), 137.2, 128.8, 128.2, 125.9, 60.2 (t, *J* = 6.7 Hz), 31.7, 10.1 ppm.
IR (neat): 2974, 2139, 1492, 1454, 891, 759, 743, 696, 533 cm^{-1}.
HRMS (EI): *m/z* calcd. for $C_{10}H_{11}N_1$: 145.0892 [M]$^+$; found: 145.0893.

1-Isocyano-1-phenyl-2-methyl-propane (3c): colorless oil, 89% yield (isolated yield).



^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.41–7.29 (m, 5H, Ar), 4.57–4.55 (m, 1H, ArC*H*), 2.14–2.04 (m, 1H, ArCHC*H*), 1.04 (d, *J* = 7.2 Hz, 3H, Me), 0.94 (d, *J* = 6.8 Hz, 3H, Me) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.0 (t, *J* = 5.0 Hz), 136.2, 128.6, 128.1, 126.4, 65.1 (t, *J* = 6.2 Hz), 35.0, 19.5, 16.8 ppm.
IR (neat): 2967, 2138, 1452, 735, 698 cm^{-1}
HRMS (EI): calcd. for $C_{11}H_{13}N$: 159.1048, [M]$^+$ found: 159.1049.

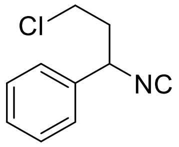
Benzhydrylisonitrile (3d): brown solid, 83% yield (isolated yield).



^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.39–7.30 (m, 10H, Ar), 5.90 (s, 1H, Ar$_2$CH) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 158.2 (br), 137.5, 128.9, 128.4, 126.5, 61.9 (t, *J* = 6.7 Hz) ppm.

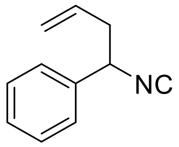
IR (neat): 3062, 3032, 2136, 1493, 1452, 961, 756, 735, 692, 647, 610, 532 cm^{-1}.
HRMS (EI): calcd. for $C_{14}H_{11}N_1$: 193.0892, $[M]^+$ found: 193.0892.

3-Chloro-1-isocyano-1-phenyl-propane (3e): colorless oil, 84% yield (isolated yield).



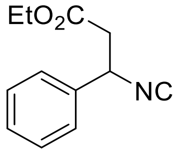
^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.44–7.34 (m, 5H, Ar), 4.99 (app. dd, *J* = 8.0, 6.4 Hz, 1H, ArC*H*), 3.79–3.72 (m, 1H, CH_2CH_2Cl), 3.60–3.55 (m, 1H, CH_2CH_2Cl), 2.42–2.33 (m, 1H, CH_2CH_2Cl), 2.27–2.17 (m, 1H, CH_2CH_2Cl) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 158.0 (t, *J* = 4.4 Hz), 136.1, 129.1, 128.7, 125.8, 55.7 (t, *J* = 6.4 Hz), 40.9, 40.5 ppm.
IR (neat): 3033, 2138, 1496, 1453, 1024, 960, 763, 696, 664, 532 cm^{-1}.
HRMS (EI): calcd. for $C_{10}H_{10}ClN$: 179.0502, $[M]^+$ found: 179.0504.

1-Isocyano-1-phenyl-3-butene (3f): colorless oil, 62% yield (isolated yield).



^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.41–7.38 (m, 2H, Ar), 7.35–7.32 (m, 3H, Ar), 5.82–5.72 (m, 1H, C*H*=CH$_2$), 5.20 (br s, 1H, CH=C*H*H), 5.17 (d, *J* = 6.0 Hz, 1H, CH=CH*H*), 4.73 (t, *J* = 6.8 Hz, 1H, ArC*H*), 2.61 (app t, *J* = 6.4 Hz, 2H, ArCH(NC)C*H*$_2$) ppm.
^{13}C-NMR (100 MHz, CDCl$_3$): δ 157.1 (app t, *J* = 4.4 Hz), 136.7, 131.8, 128.8, 128.3, 125.9, 119.6, 58.5 (t, *J* = 6.5 Hz), 42.7 ppm.
IR (neat): 3081, 2916, 2138, 1454, 994, 923, 753, 696, 610 cm^{-1}.
HRMS (ESI): calcd. for $C_{11}H_{11}NNa$: 180.0784, $[M+Na]^+$ found: 180.0789.

Ethyl 3-Isocyano-3-phenyl-propionate (3g): colorless oil, 59% yield (isolated yield).



^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.42–7.33 (m, 5H, Ar), 5.18 (dd, *J* = 8.8 Hz, 6.0 Hz, 1H, ArC*H*), 4.24–4.12 (m, 2H, $COOCH_2CH_3$), 2.99 (dd, *J* = 16.0, 8.8 Hz, 1H, ArCH(NC)CH*H*), 2.81 (br dd, *J* = 16.0 Hz, 5.6 Hz, 1H, ArCH(NC)C*H*H), 1.25 (t, *J* = 7.4 Hz, 3H, $COOCH_2CH_3$)
^{13}C-NMR (100 MHz, CDCl$_3$): δ 168.6, 158.0 (br), 135.9, 128.9, 128.7, 125.8, 61.2, 54.6 (t, *J* = 6.2 Hz), 43.3, 14.0 ppm.
IR (neat): 2986, 2139, 1731, 1370, 1161, 1004, 758, 697 cm^{-1}.
HRMS (EI): calcd. for $C_{12}H_{13}O_2NNa$: 226.0839, $[M+Na]^+$ found: 226.0842.

4. Determination of Catalytic Active Species

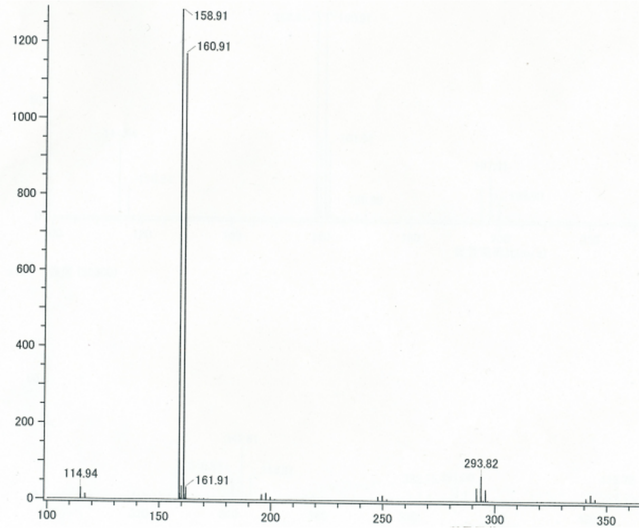
$$\mathrm{Ag_2O} \xrightarrow[\text{1,4-dioxane, 100 ºC, 18 h}]{\mathrm{Me_3SiCN}\text{ (100 equiv)}} \mathrm{AgCN}$$

A suspension of Ag_2O (11.3 mg, 0.049 mmol) in 1,4-dioxane (15 mL) was stirred at 100 ºC for 5 min, followed by the addition of TMSCN (992 mg, 10.0 mmol). The reaction mixture was then continuously stirred at 100 ºC for 18 h. The precipitate was collected by filtration, and was washed with 1,4-dioxane. AgCN (13.5 mg 0.10 mmol) was obtained as a white solid after drying in vacuo. The IR spectra were in accordance with those of the commercial AgCN.

IR (KBr): 2163 cm^{-1}.

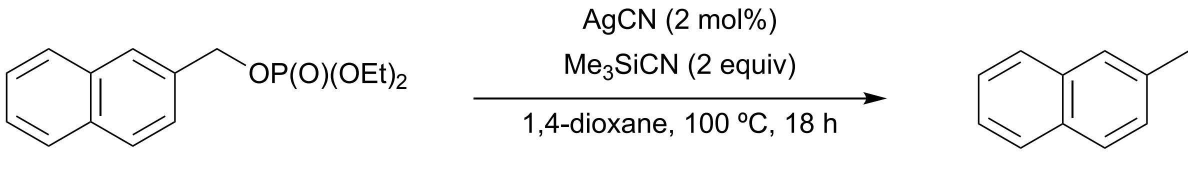
$$\mathrm{AgCN} \xrightarrow[\text{1,4-dioxane, 100 ºC, 30 min}]{\mathrm{Me_3SiCN}\text{ (100 equiv)}} \underset{\textit{in situ}}{\mathrm{(Me_3Si)[Ag(CN)_2]}}$$

A suspension of AgCN (11.3 mg, 0.049 mmol) in 1,4-dioxane (15 mL) was stirred at 100 ºC for 5 min, followed by the addition of TMSCN (992 mg, 10.0 mmol). The reaction mixture was then continuously stirred at 100 ºC for 30 min yielding a white powder. The signal assigned to $[Ag(CN)_2]^-$ was detected by ESI-MS (negative mode) measurement of the sample obtained from the supernatant of the resulting mixture.



HRMS (ESI⁻): calcd. for C_2AgN_2: 158.9112, $[M]^-$ found: 158.9111.

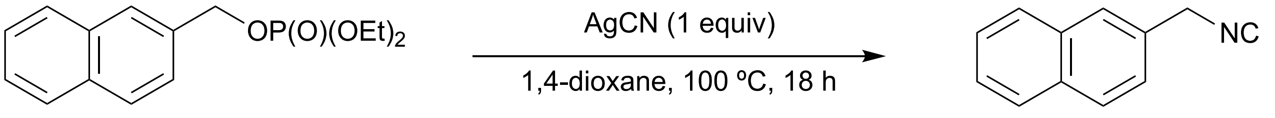
5. Reaction between Benzylic Phosphate and Several Cyanide Sources



sub. 1a

1a
89% yield

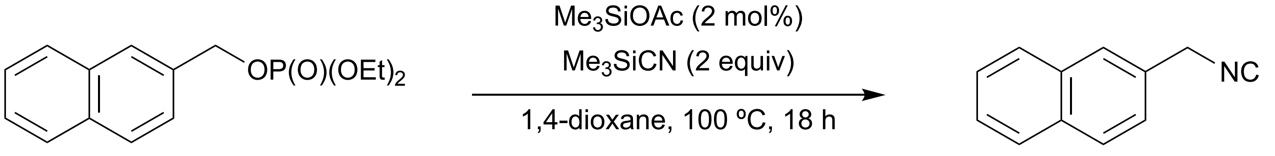
To a suspension of AgCN (1.3 mg, 0.010 mmol) in 1,4-dioxane (1.5 mL) was added naphthylmethyl diethylphosphate (**sub. 1a**, 149 mg, 0.50 mmol). The resulting mixture was stirred at 100 ºC for 5 min, followed by the addition of TMSCN (99 mg, 1.0 mmol). The reaction mixture was then continuously stirred at 100 °C until completion of the reaction. Saturated $NaHCO_3$ aq. was added to quench the reaction, and the aqueous layer was extracted by AcOEt (10 mL × 3). The collected organic layer was washed with brine and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the resulting mixture was concentrated in vacuo. The yield of the product was calculated from ^{1}H NMR spectra of the crude **1a** with pyrazine as an internal standard (89% yield).



sub. 1a

1a
0% yield

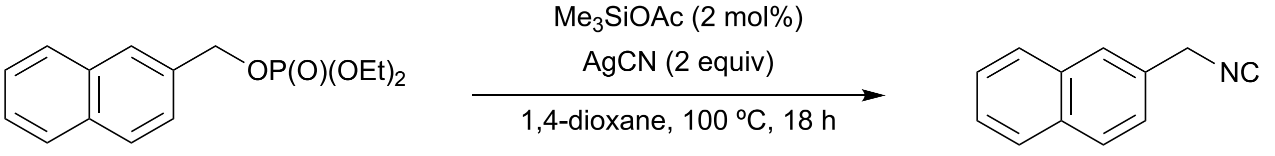
A suspension of AgCN (67 mg, 0.50 mmol) in 1,4-dioxane (1.5 mL) was stirred at 100 °C for 5 min, followed by the addition of naphthylmethyl diethylphosphate (**sub. 1a**, 149 mg, 0.51 mmol). The reaction mixture was then continuously stirred at 100 °C for 18 h. No consumption of the substrate was observed.



sub. 1a

1a
0% yield

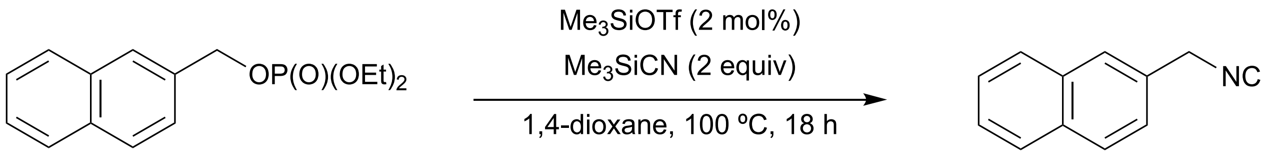
To a solution of TMSCN (99 mg, 9.99 mmol) in 1,4-dioxane (1.0 mL) was added naphthylmethyl diethylphosphate (**sub. 1a**, 149 mg, 0.51 mmol). The resulting mixture was stirred at 100 °C for 5 min, followed by the addition of the solution of TMSOAc in 1,4-dioxane (0.020 M, 0.50 mL, 0.010 mmol). The reaction mixture was then continuously stirred at 100 °C for 18 h. No consumption of the substrate was observed.



sub. 1a

1a
0% yield

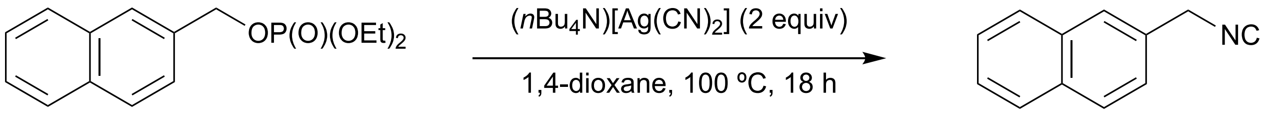
To a suspension of AgCN (136 mg, 1.02 mmol) in 1,4-dioxane (1.0 mL) was added naphthylmethyl diethylphosphate (**sub. 1a**, 149 mg, 0.51 mmol). The resulting mixture was stirred at 100 °C for 5 min, followed by the addition of the solution of TMSOAc in 1,4-dioxane (0.020 M, 0.50 mL, 0.010 mmol). The reaction mixture was then continuously stirred at 100 °C for 18 h. No consumption of the substrate was observed.



sub. 1a

1a
2% ^{1}H NMR yield

To a solution of TMSCN (99 mg, 0.99 mmol) in 1,4-dioxane (1.0 mL) was added naphthylmethyl diethylphosphate (**sub. 1a**, 149 mg, 0.51 mmol). The resulting mixture was stirred at 100 ºC for 5 min, followed by the addition of the solution of TMSOTf in 1,4-dioxane (0.020 M, 0.50 mL, 0.010 mmol). The reaction mixture was then continuously stirred at 100 ºC for 1 h. Saturated NaHCO$_3$ aq. was added to quench the reaction, and the aqueous layer was extracted by AcOEt (10 mL × 3). The collected organic layer was washed with brine and dried over Na$_2$SO$_4$. After Na$_2$SO$_4$ was filtered off, the resulting mixture was concentrated in vacuo. The yield of the product was calculated from ^{1}H NMR spectra of the crude **1a** with pyrazine as an internal standard (2% yield).



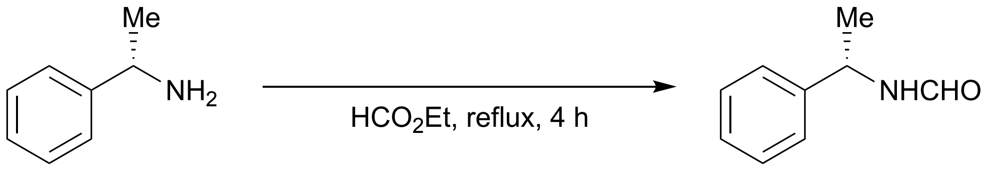
sub. 1a

1a
0% yield

(^{n}Bu$_4$N)[Ag(CN)$_2$] was prepared by the reported procedures.[16] A suspension of (^{n}Bu$_4$N)[Ag(CN)$_2$] (400 mg, 0.99 mmol) in 1,4-dioxane (1.5 mL) was heated to 100 ºC, followed by the addition of naphthylmethyl diethylphosphate (**sub. 1a**, 148 mg, 0.50 mmol). The reaction mixture was then continuously stirred at 100 ºC for 18 h. No consumption of the substrate was observed.

6. Synthesis of the Optically Active Secondary Benzylic Isonitrile

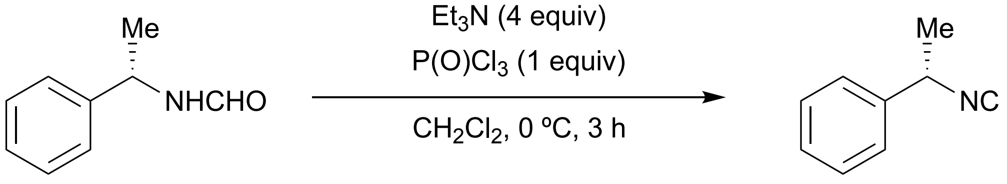
Synthesis of (*S*)-*N*-Formyl-1-phenylethylamine



86% yield

A dry round-bottomed flask was charged with (*S*)-1-phenylethylamine (606 mg, 5.00 mmol) and ethyl formate (16 mL). The mixture was stirred under reflux conditions for 4 h. The reaction mixture was evaporated in vacuo. The obtained (*S*)-*N*-formyl-1-phenylethylamine was purified by silica-gel column chromatography (AcOEt/hexane = 1/4, 644 mg, 86% yield). ^{1}H NMR data were in accordance with those in the literature.[17]

Synthesis of (*S*)-1-Isocyano-1-phenylethane ((*S*)-3a)

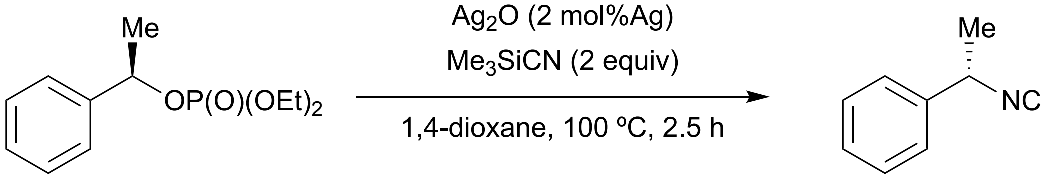


(*S*)-**3a**
37% yield
99% *ee*

A dry round-bottomed flask was charged with (*S*)-*N*-formyl-1-phenylethylamine (644 mg, 4.32 mmol) and CH_2Cl_2 (10 mL). Et_3N (1740 mg, 17.2 mmol, 4 equiv) was then added to the solution. After the mixture was cooled to 0 ºC, $P(O)Cl_3$ (251 mg, 1.64 mmol, 1 equiv) was added dropwise, and the mixture was stirred for 3 h. The reaction mixture was poured into saturated $NaHCO_3$ aq. cooled to 0 ºC. Then, the mixture was warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine, and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the collected filtrate was concentrated in vacuo. The obtained (*S*)-1-isocyano-1-phenyl-ethane ((*S*)-**3**) was purified by silica-gel column chromatography (Et_2O/hexane = 1/20, 208 mg, 37% yield, 99% *ee*, yellow oil). ^1H and ^{13}C NMR data were in accordance with those in the literature.[18]

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.43–7.32 (m, 5H, Ar), 4.82 (qt, *J* = 7.2 Hz, 1.8 Hz 1H, CH), 1.69 (dt, *J* = 7.2 Hz, 2.2 Hz, 3H, Me) ppm.
^{13}C-NMR (100 MHz, $CDCl_3$): δ 156.1 (t, *J* = 4.8 Hz), 138.4, 128.8, 128.1, 125.2, 53.6 (t, *J* = 6.2 Hz), 25.0 ppm.
IR (neat): 2986, 2928, 2138, 1450, 1074, 756, 695, 610, 544 cm^{-1}.
HPLC analysis: column, Chiralcel OB-H, hexane/*i*PrOH = 95/5, flow rate = 1.0 mL/min, λ = 254 nm, retention time; t_R = 5.9 min (major), t_R = 6.6 min (minor)

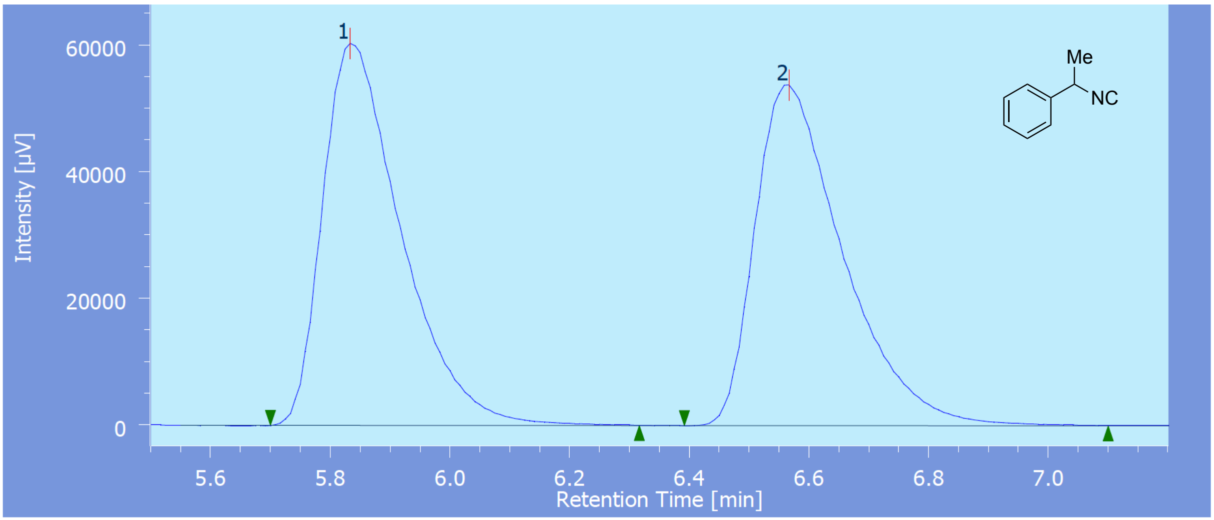
7. Catalytic Isocyanation of Optically Active Secondary Benzylic Phosphate



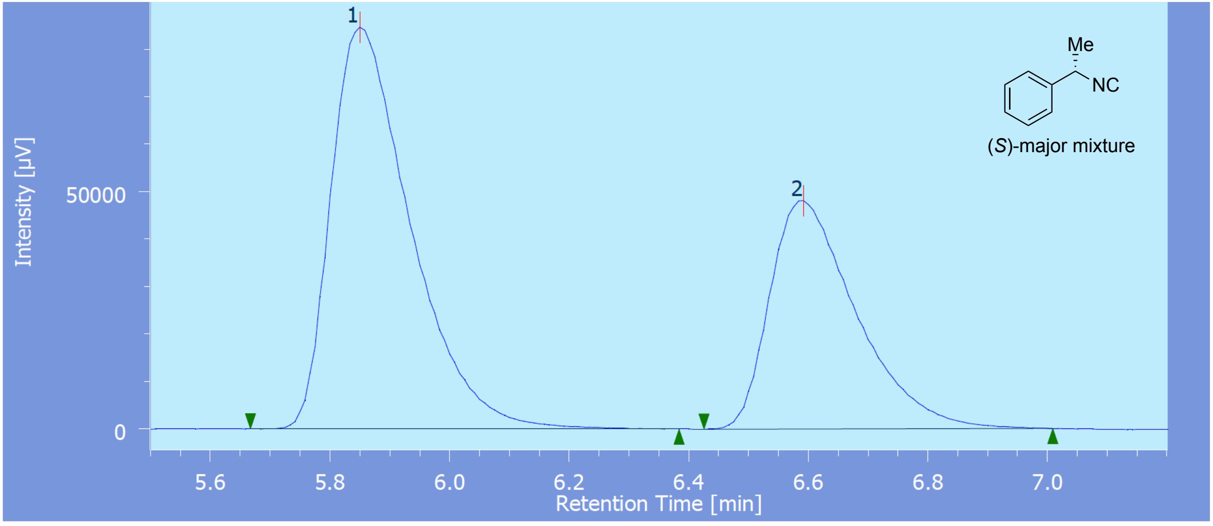
(*R*)-**2a**
99% *ee*

(*S*)-**3a**
83% yield
24% *ee*

To a suspension of Ag_2O (1.2 mg, 0.010 mmol) in 1,4-dioxane (1.5 mL) was added (*R*)-1-phenylethyl diethyl phosphate (**(*R*)-2a**, 129 mg, 0.50 mmol). The resulting mixture was stirred at 100 ºC for 5 min, followed by the addition of TMSCN (99 mg, 0.99 mmol). The reaction mixture was then continuously stirred at 100 ºC for 2.5 h. Saturated $NaHCO_3$ aq. was added to quench the reaction, and the aqueous layer was extracted by AcOEt (10 mL × 3). The collected organic layer was washed with brine and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the resulting mixture was concentrated in vacuo. The yield of the product was calculated from ^1H NMR spectra of the crude **3a** with pyrazine as an internal standard (87% yield). The crude product was purified by silica-gel column chromatography (Et_2O/hexane = 1/40) to afford pure **3a** as a yellow oil (54 mg, 83% yield). The value of *ee* was measured by HPLC analysis using Chiralcel OB-H, showing 24% *ee*.

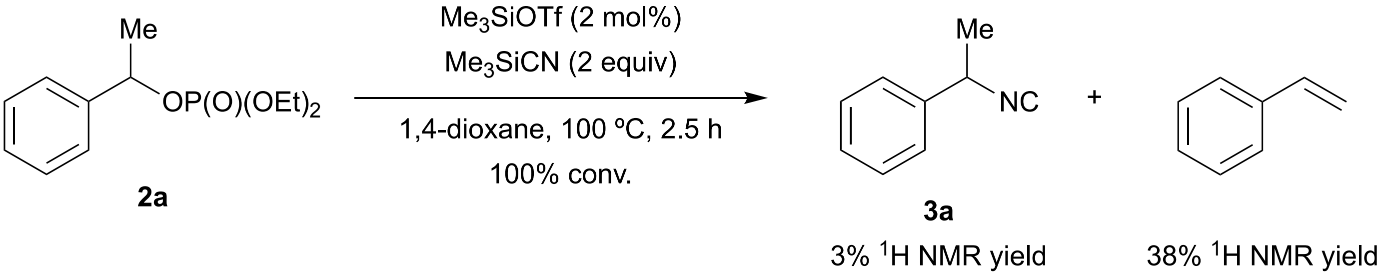


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	5.833	551088	60278	50.015	52.864	N/A	10024	2.980	1.654	
2	Unknown	1	6.567	550762	53746	49.985	47.136	N/A	10176	N/A	1.604	

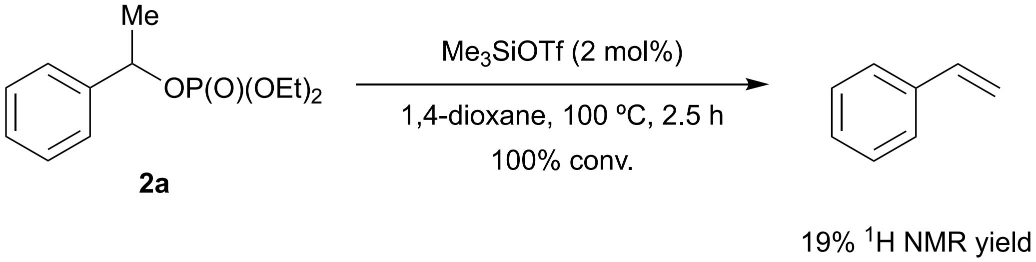


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	5.850	785145	84633	61.878	63.753	N/A	9716	3.004	1.630	
2	Unknown	1	6.592	483721	48118	38.122	36.247	N/A	10467	N/A	1.559	

8. Activation of Secondary Benzylic Phosphate by Me_3SiOTf



To a solution of TMSCN (99 mg, 0.99 mmol) in 1,4-dioxane (1.0 mL) was added 1-phenylethyl diethyl phosphate (**2a**, 129 mg, 0.50 mmol). The resulting mixture was stirred at 100 ºC for 5 min, followed by the addition of the solution of TMSOTf in 1,4-dioxane (0.020 M, 0.50 mL, 0.010 mmol). The reaction mixture was then continuously stirred at 100 ºC for 2.5 h. Saturated $NaHCO_3$ aq. was added to quench the reaction, and the aqueous layer was extracted by AcOEt (10 mL × 3). The collected organic layer was washed with brine and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the resulting mixture was concentrated in vacuo. The yield of the product was calculated from ^{1}H NMR spectra of the crude mixture with pyrazine as an internal standard (**3a:** 3% yield; styrene: 38% yield).



A solution of 1-phenylethyl diethyl phosphate (**2a**, 129 mg, 0.50 mmol) in 1,4-dioxane (1.0 mL) was stirred at 100 ºC for 5 min, followed by the addition of the solution of TMSOTf in 1,4-dioxane (0.020 M, 0.50 mL, 0.010 mmol). The reaction mixture was then continuously stirred at 100 ºC for 2.5 h. Saturated $NaHCO_3$ aq. was added to quench the reaction, and the aqueous layer was extracted by AcOEt (10 mL × 3). The collected organic layer was washed with brine and dried over Na_2SO_4. After Na_2SO_4 was filtered off, the resulting mixture was concentrated in vacuo. The yield of styrene was calculated from ^{1}H NMR spectra of the crude mixture with pyrazine as an internal standard (19% yield).

9. Reference

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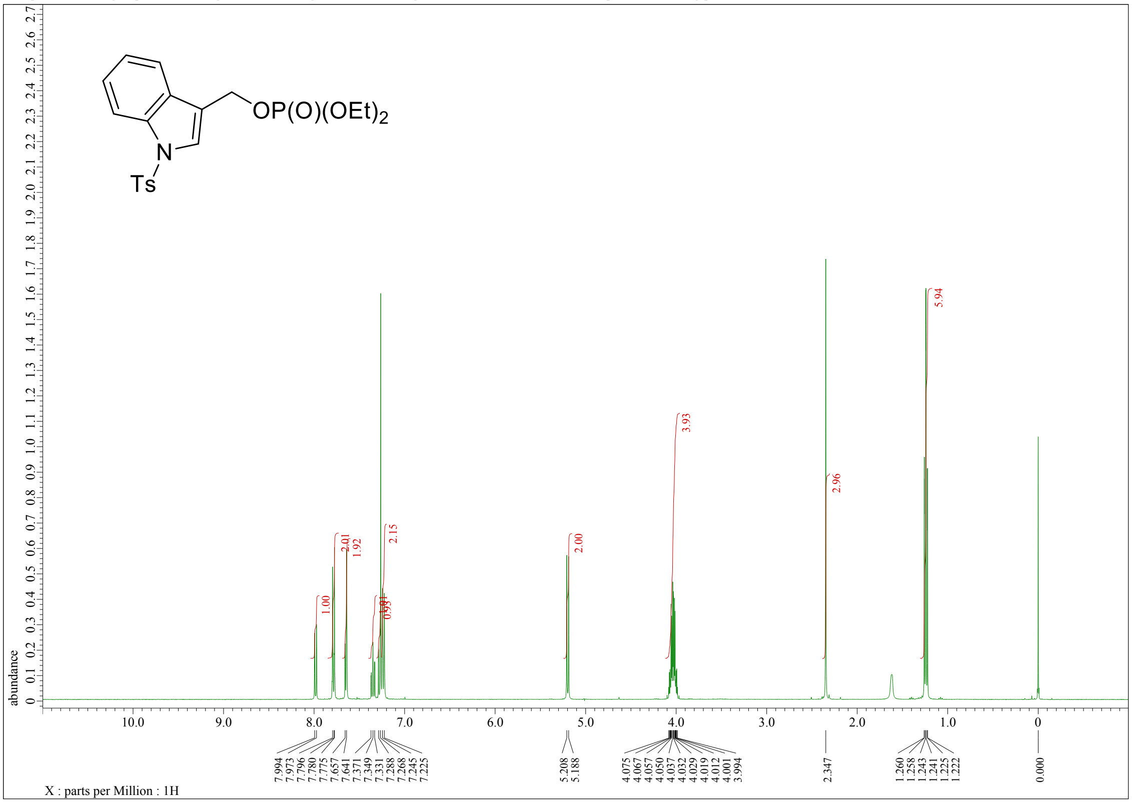
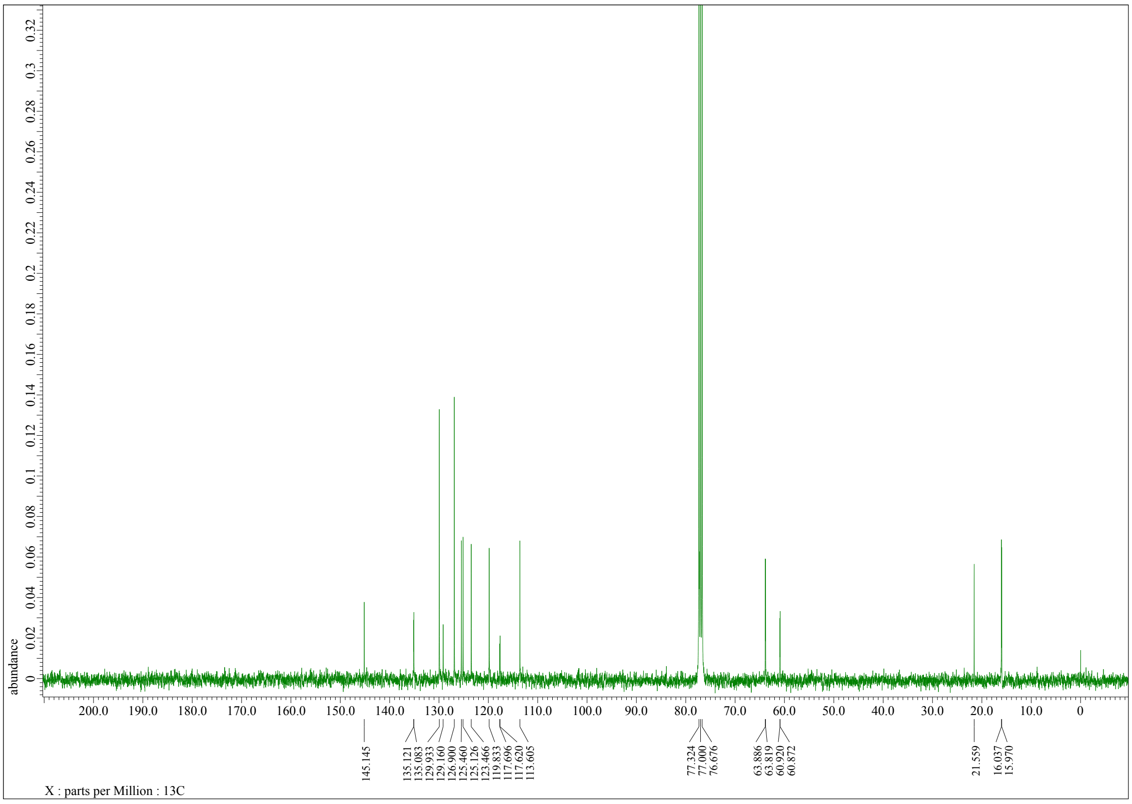
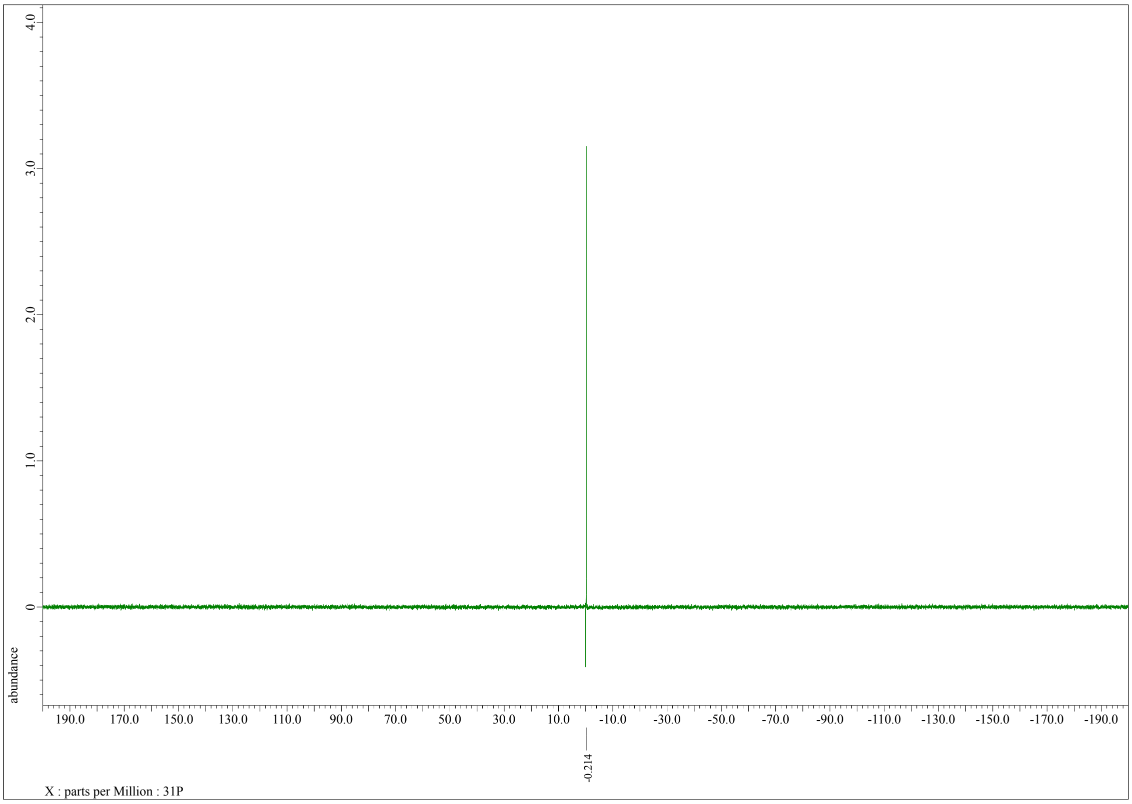
10. ^{1}H, ^{13}C, and ^{31}P NMR Spectra

3-(*N*-tosyl)indolylmethyl diethyl phosphate (sub. 1j)



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150.0
130.0
110.0
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50.0
30.0
10.0
-10.0
-30.0
-50.0
-70.0
-90.0
-110.0
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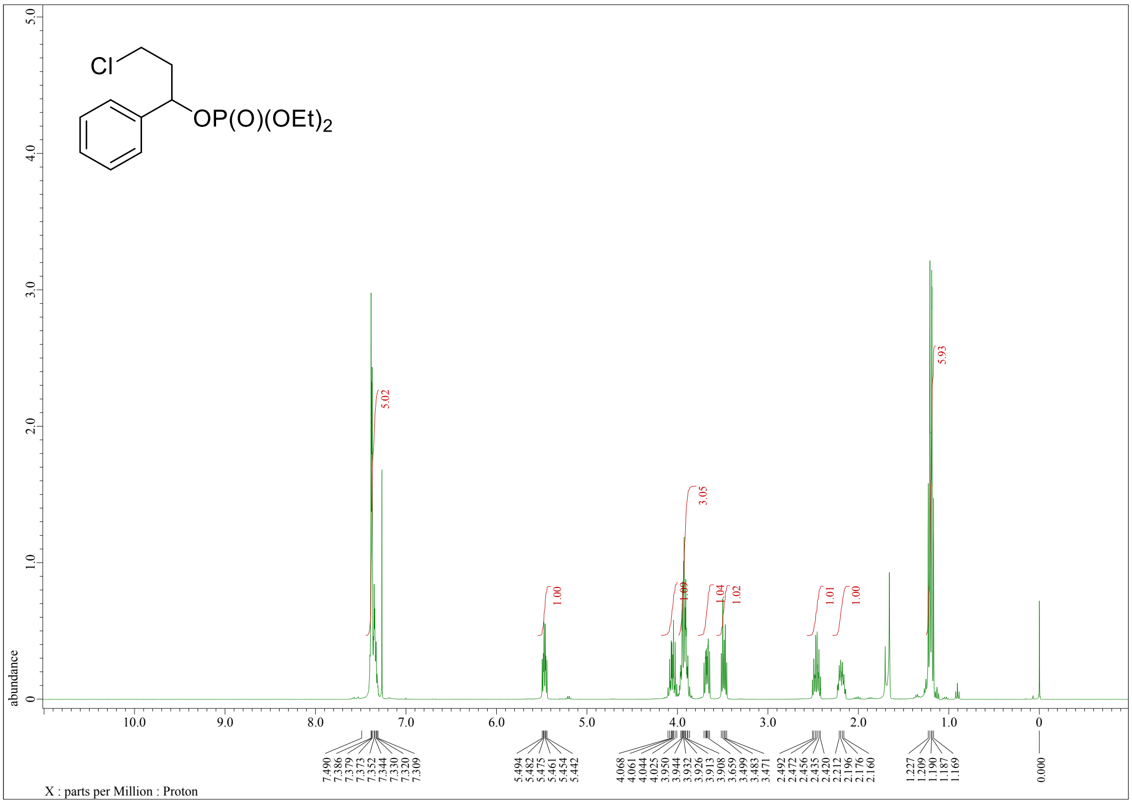
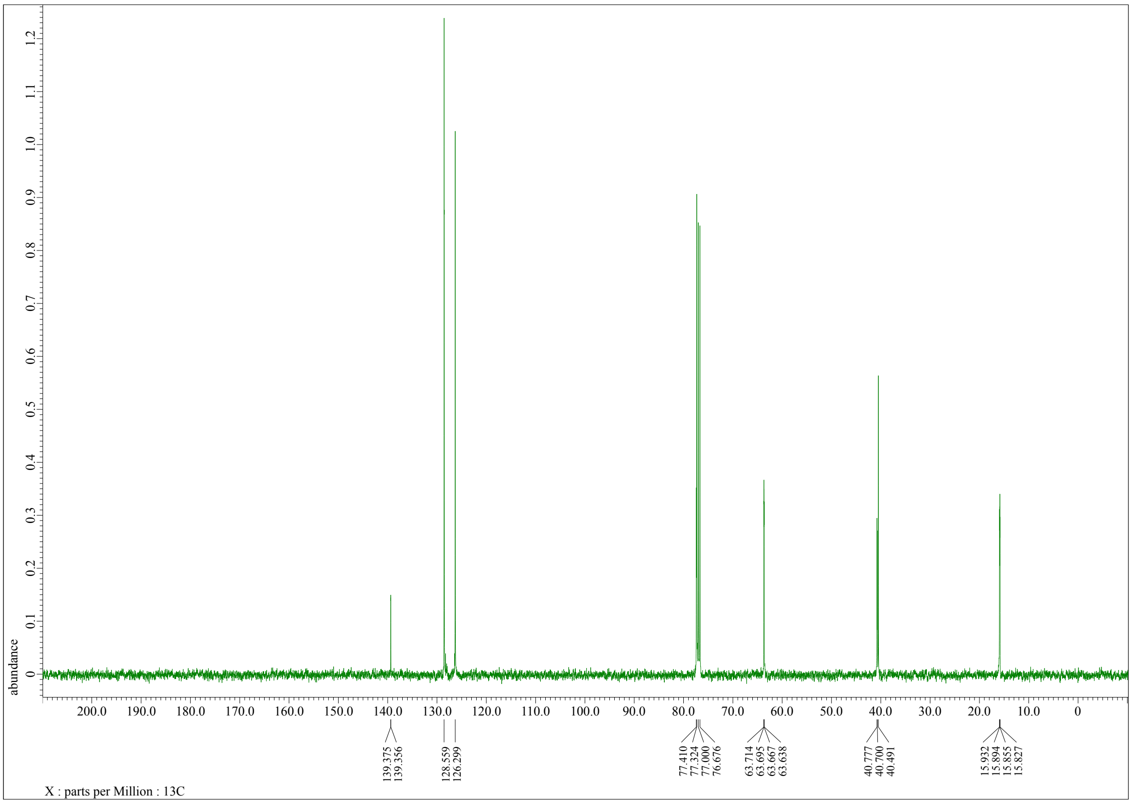
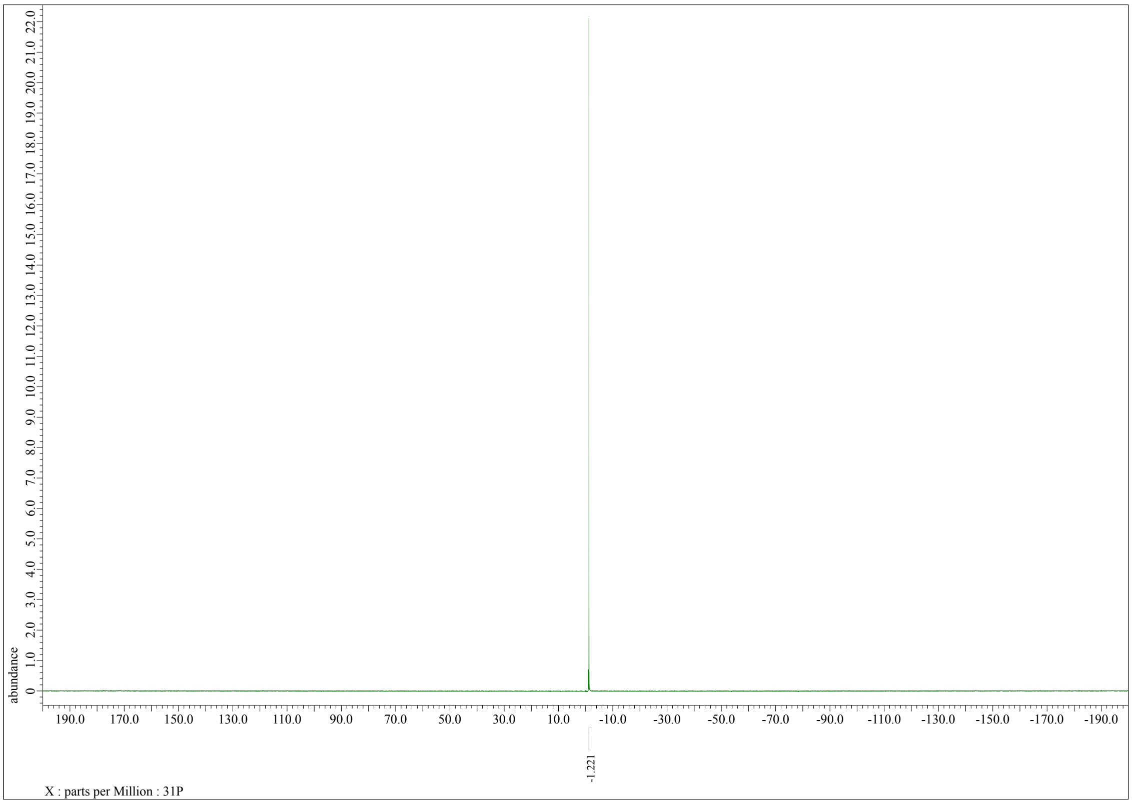
X : parts per Million : 31P

(3-Chloro-1-phenyl)propyl diethyl phosphate (2e)



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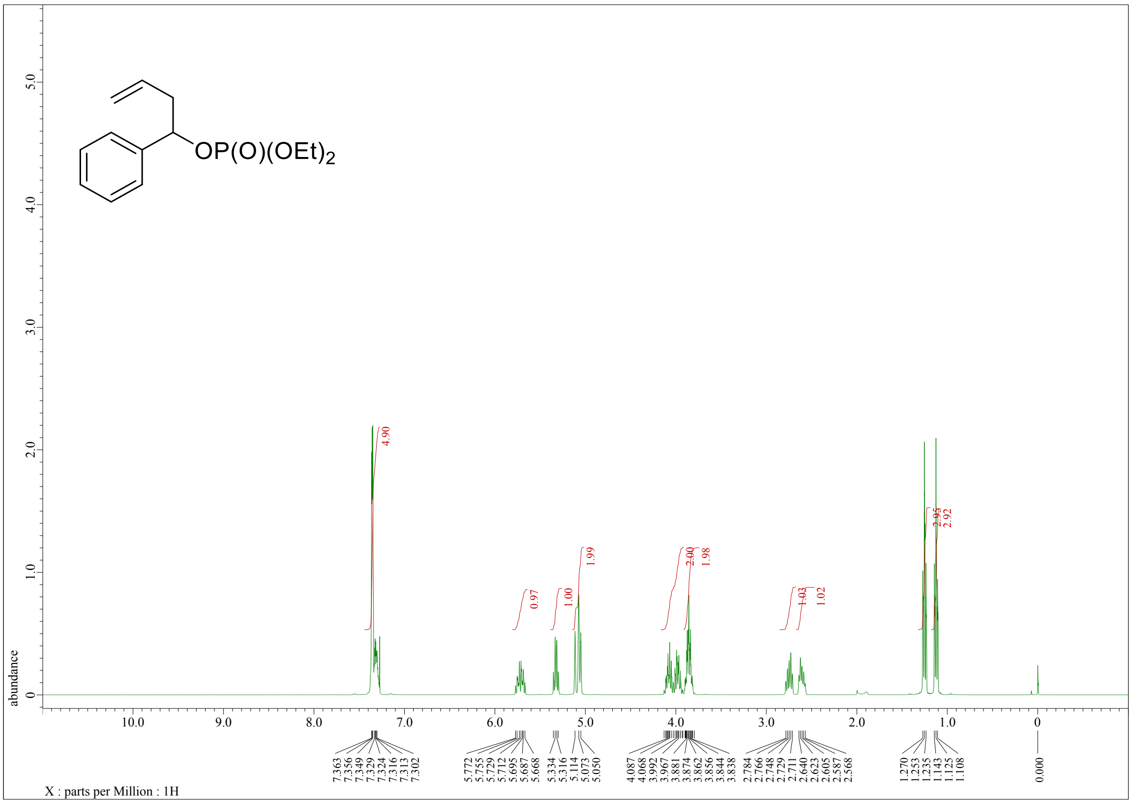
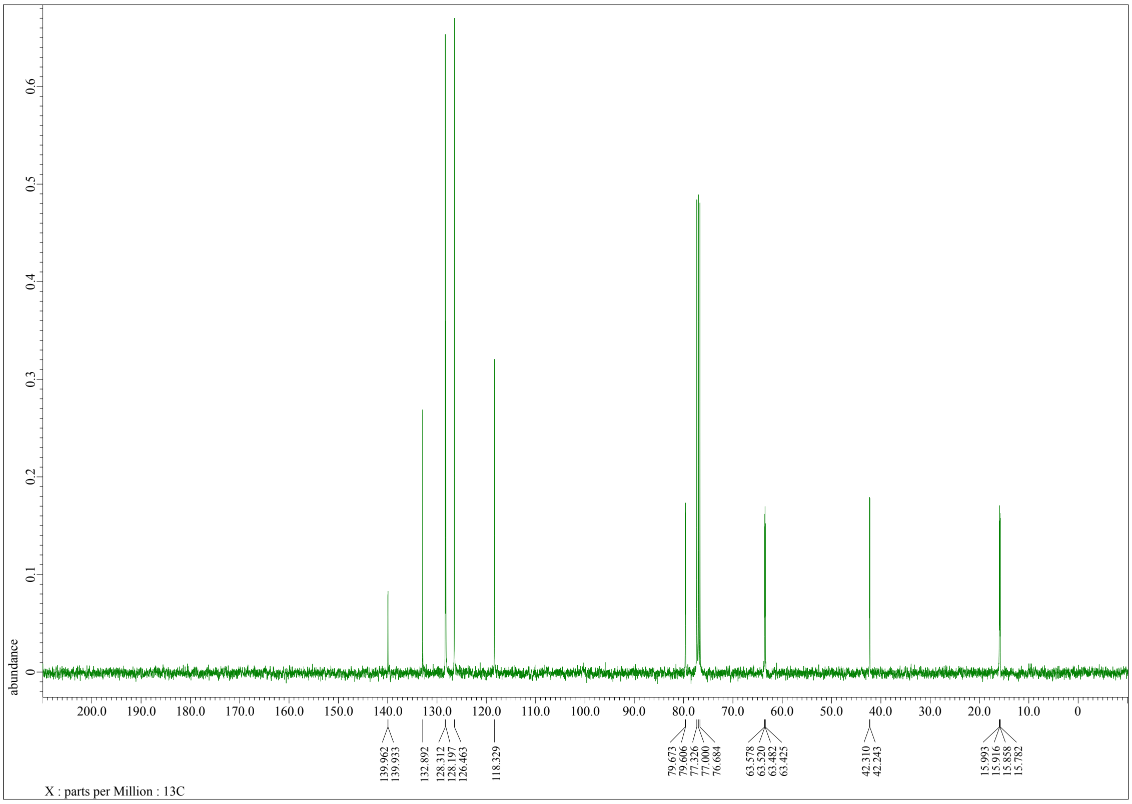
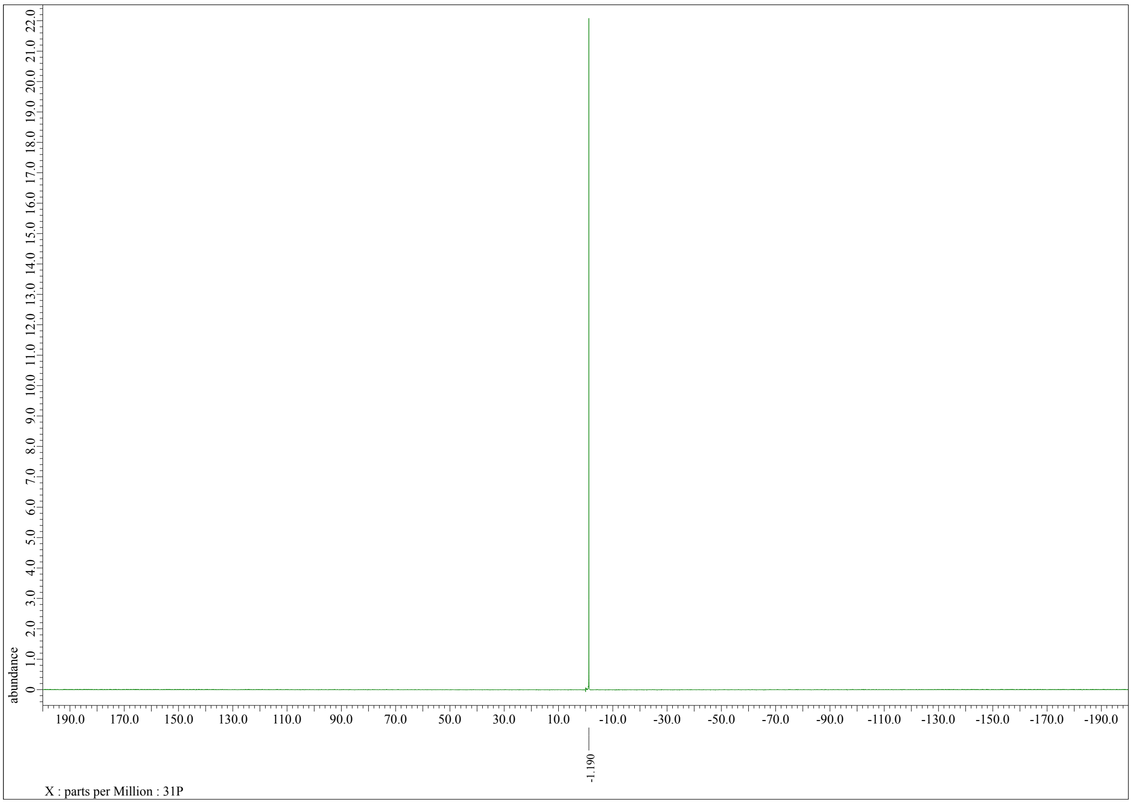
X : parts per Million : 31P

1-Phenyl-3-butenyl diethyl phosphate (2f)



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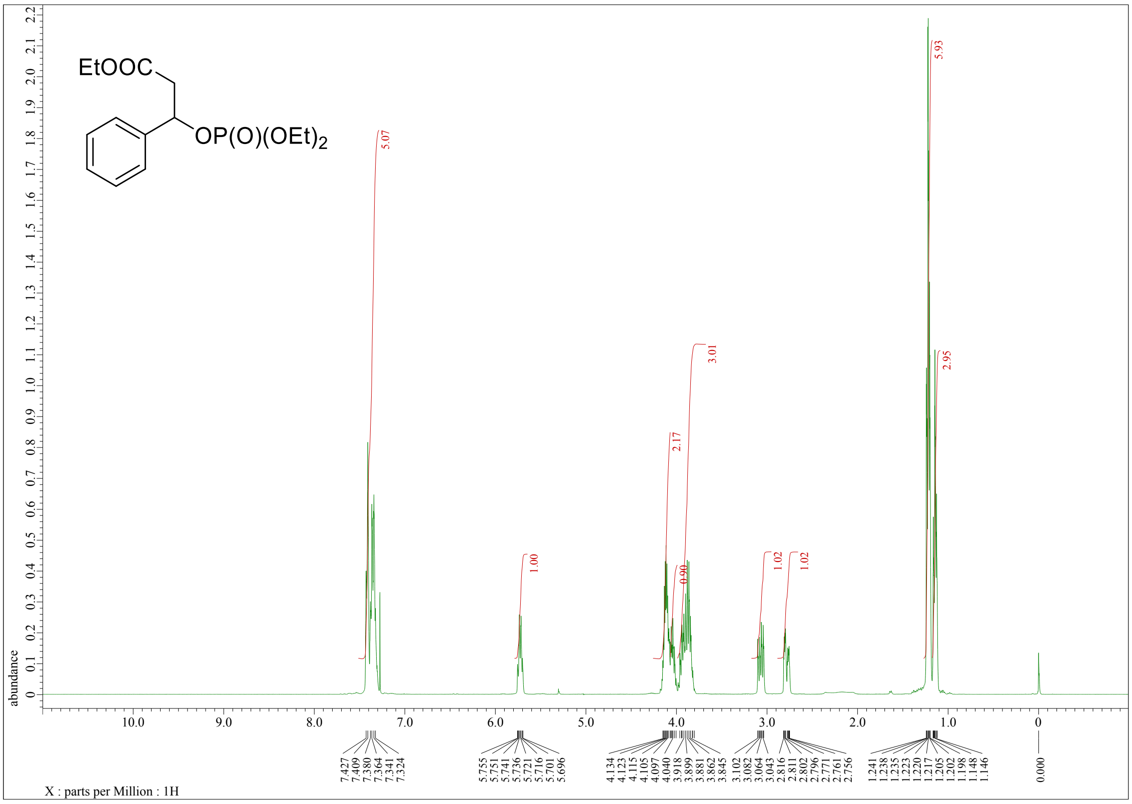
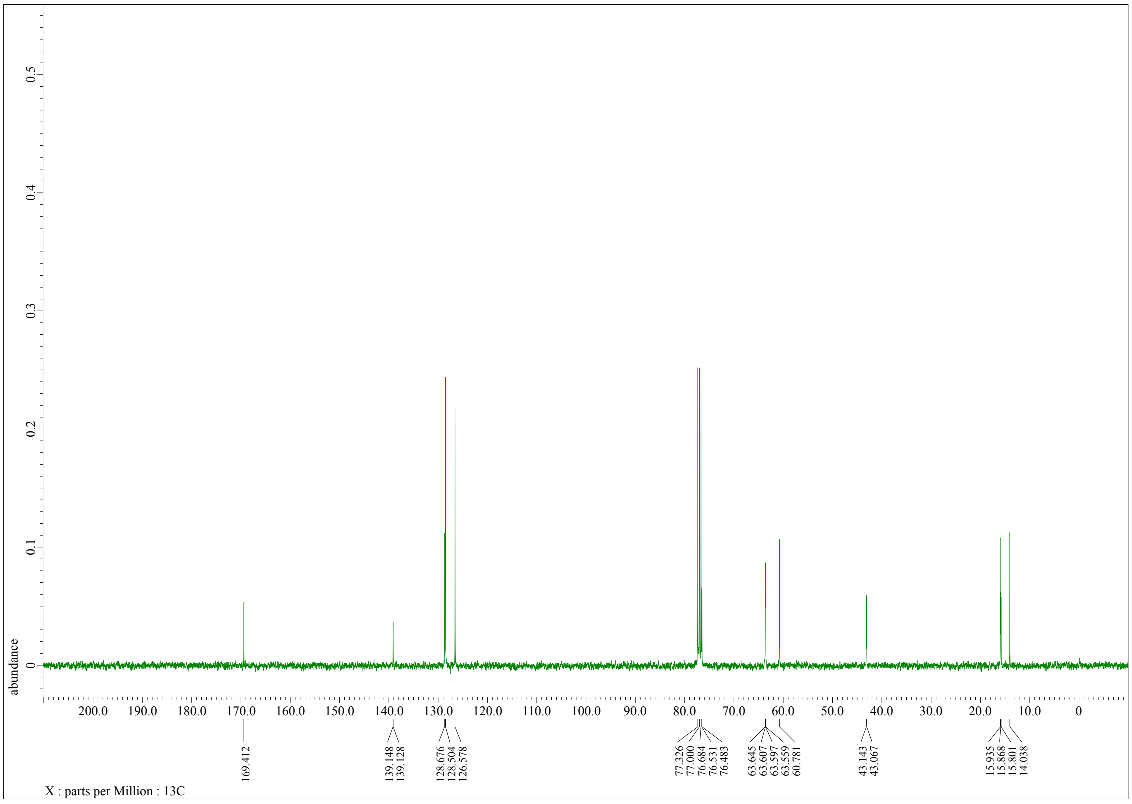
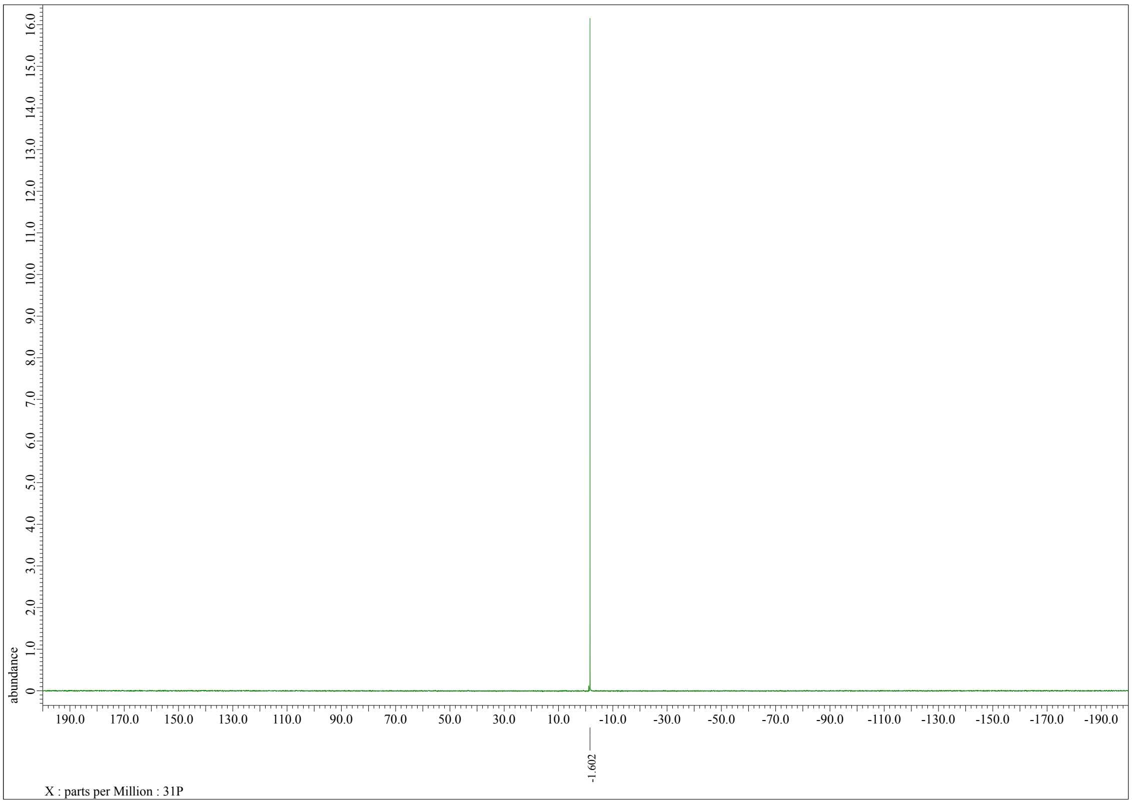
X : parts per Million : 31P

(1-Phenyl-2-carboethoxy)ethyl diethyl phosphate (2g)



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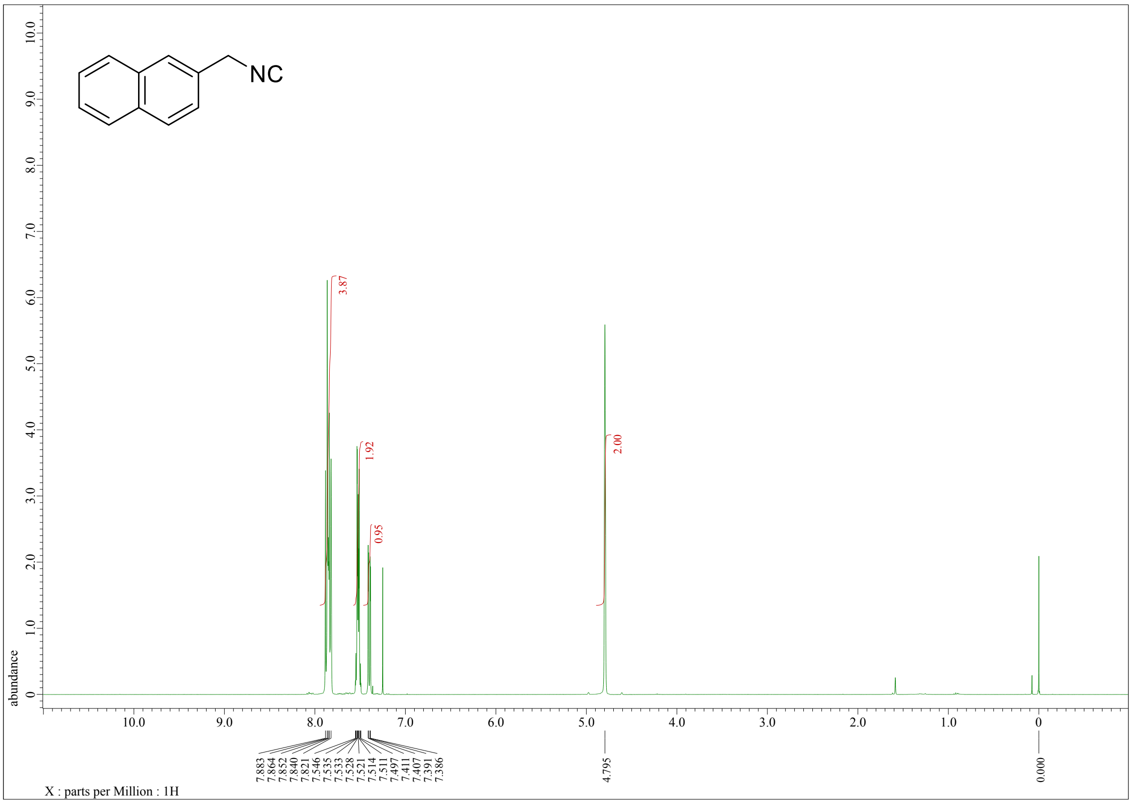
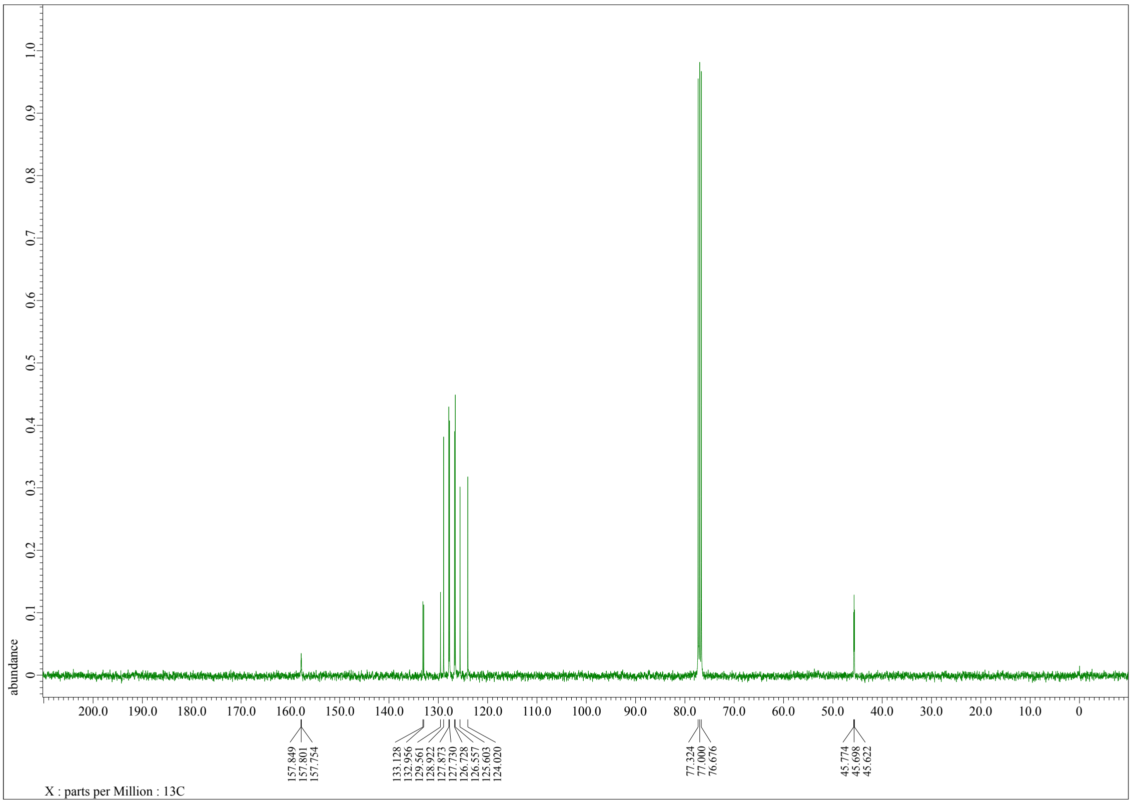
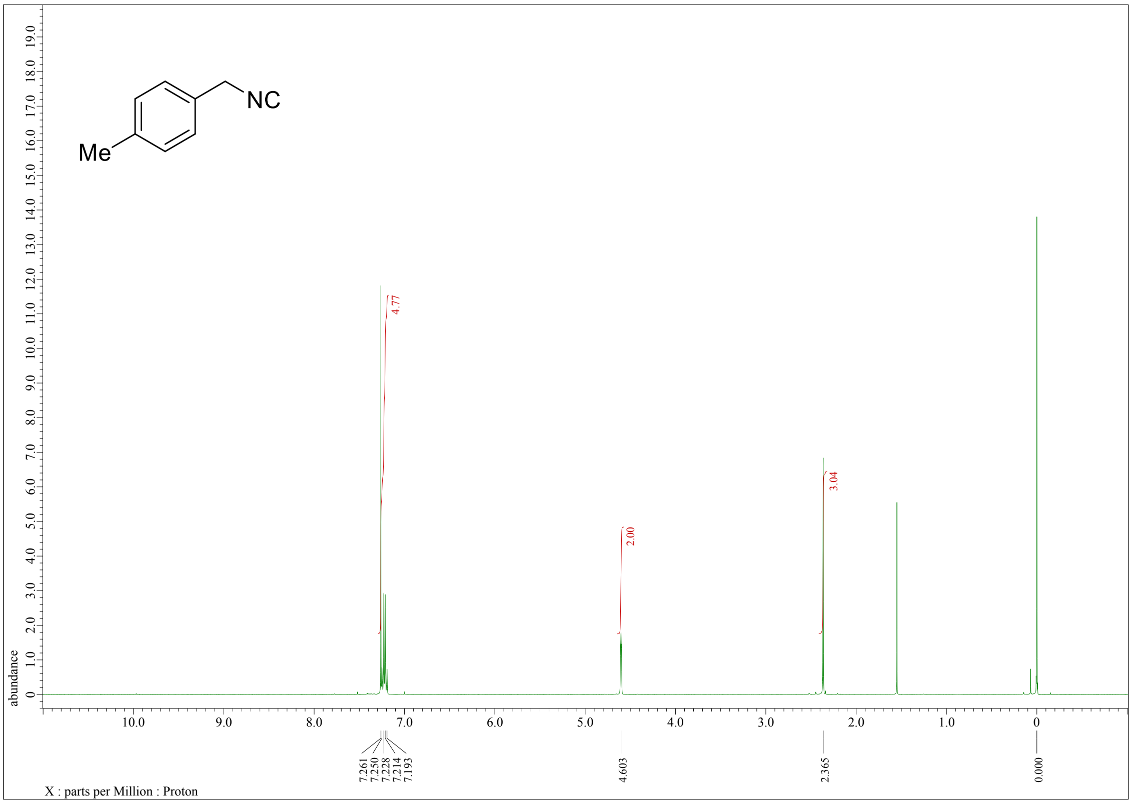
X : parts per Million : 31P

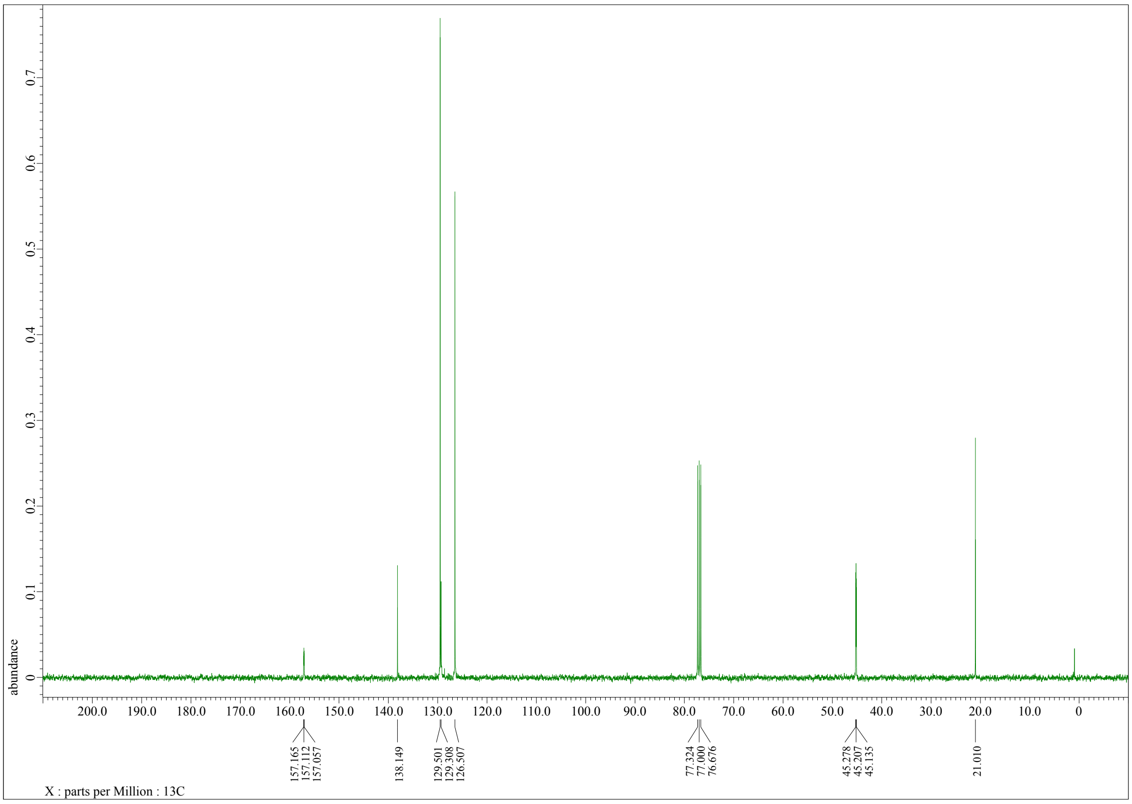
2-(Isocyanomethyl) naphthalene (1a)



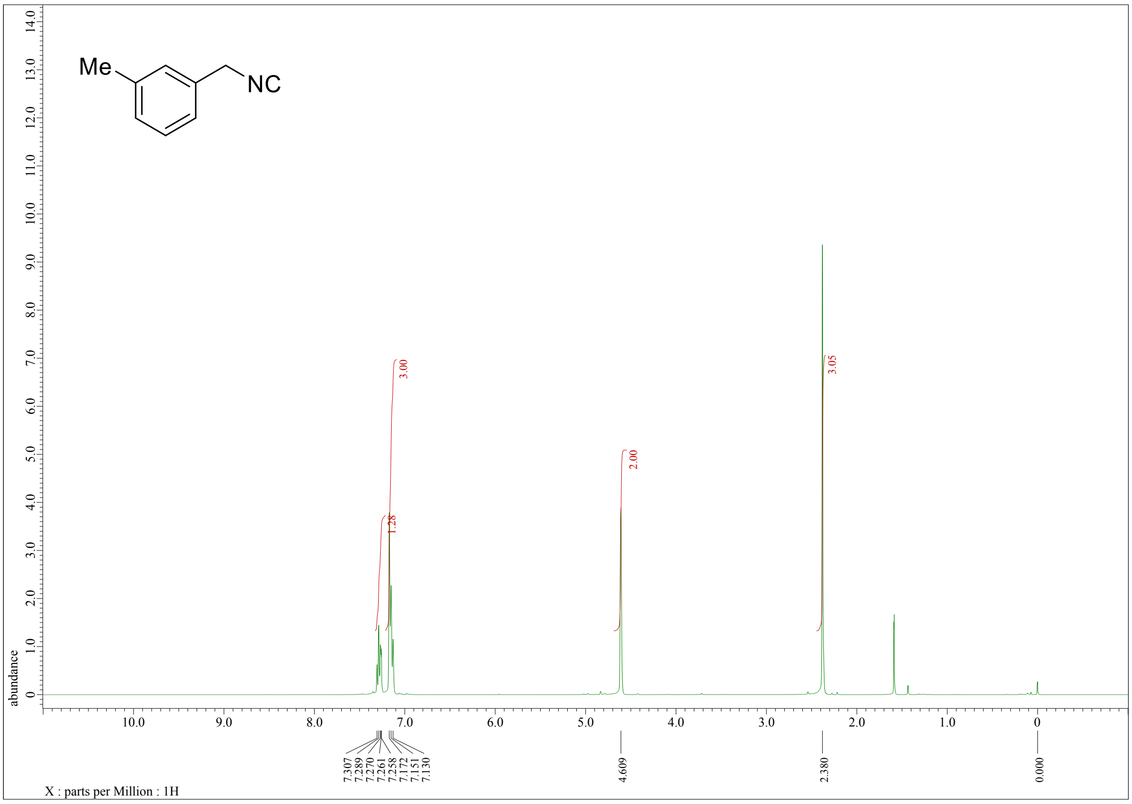


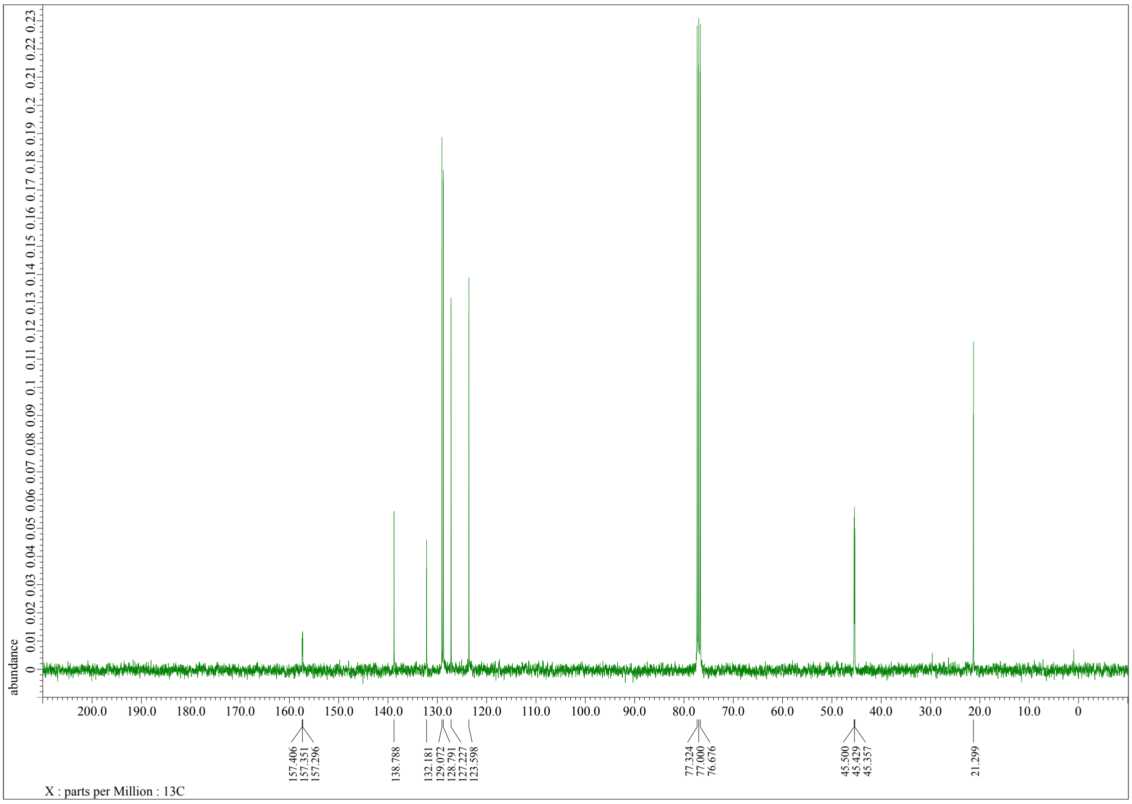
1-(Isocyanomethyl)-4-methylbenzene (1b)



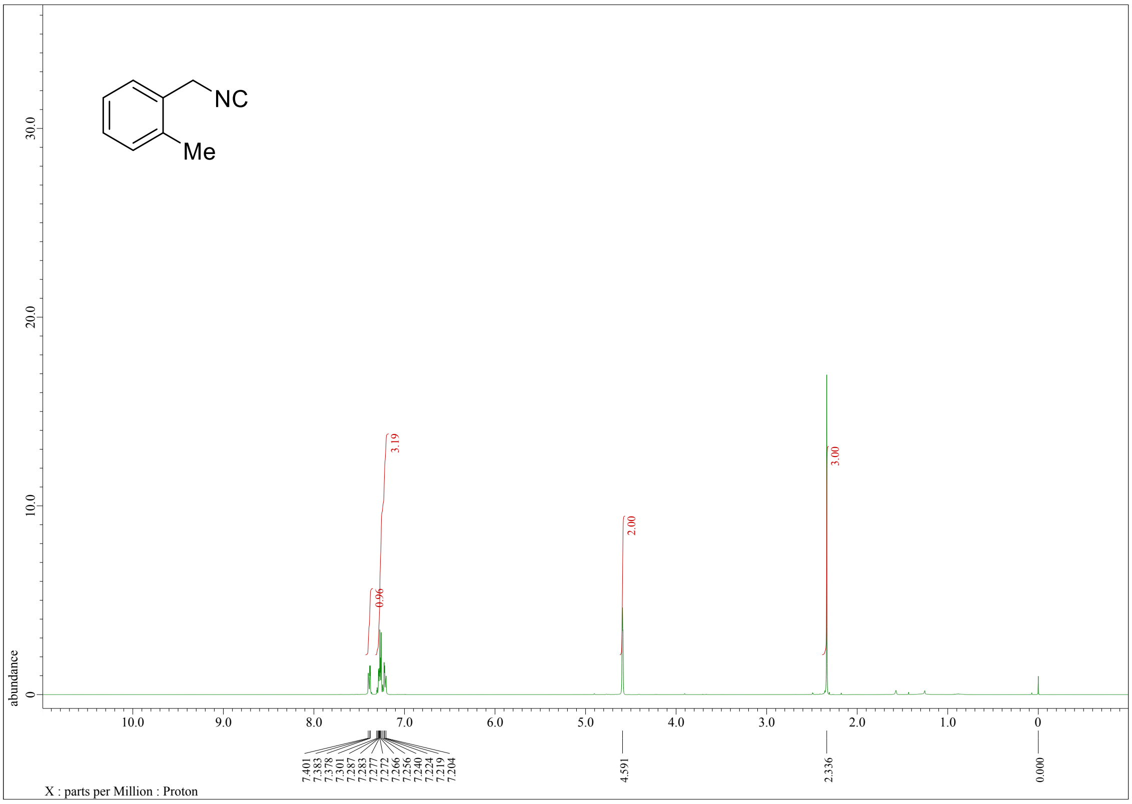


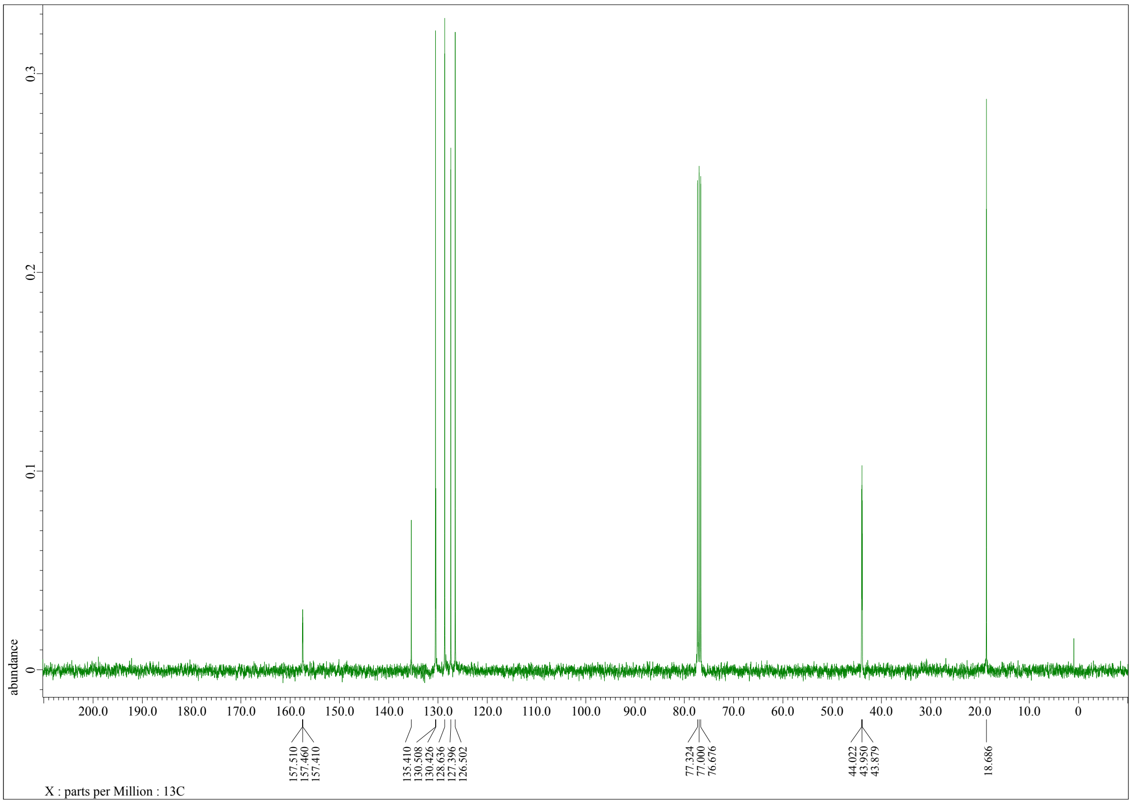
1-(Isocyanomethyl)-4-methylbenzene (1c)



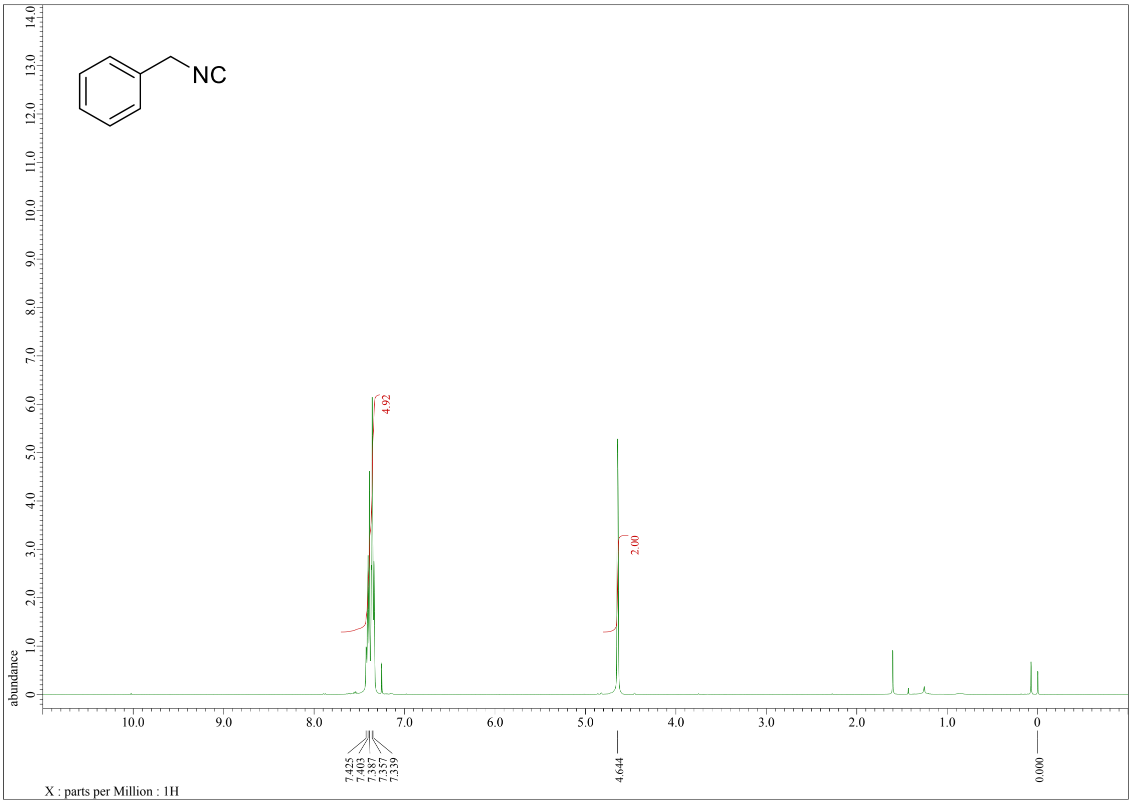


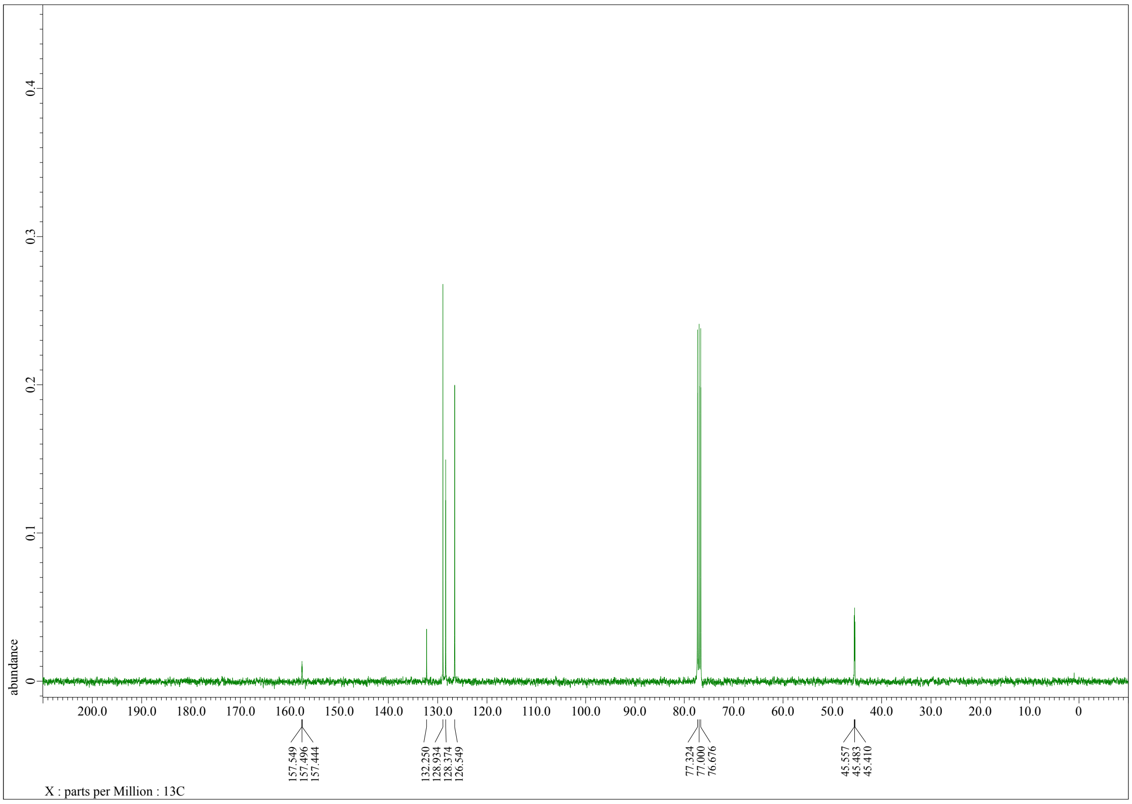
1-(Isocyanomethyl)-2-methylbenzene (1d)



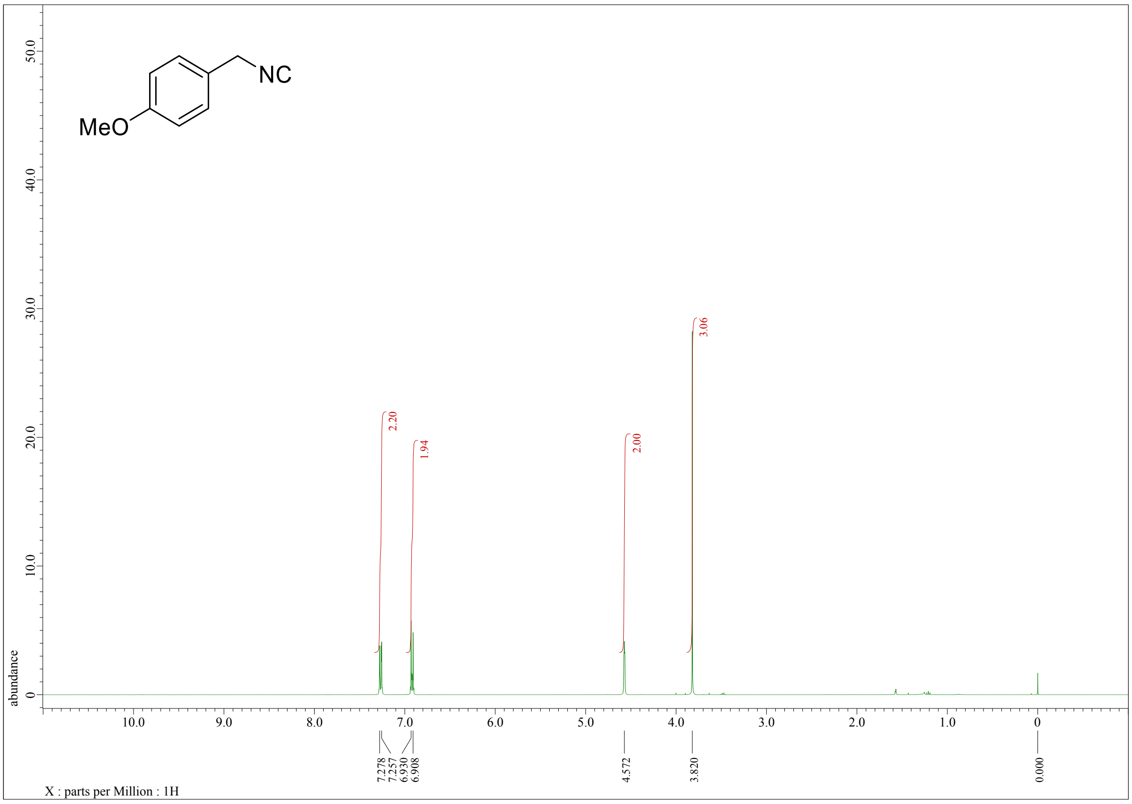


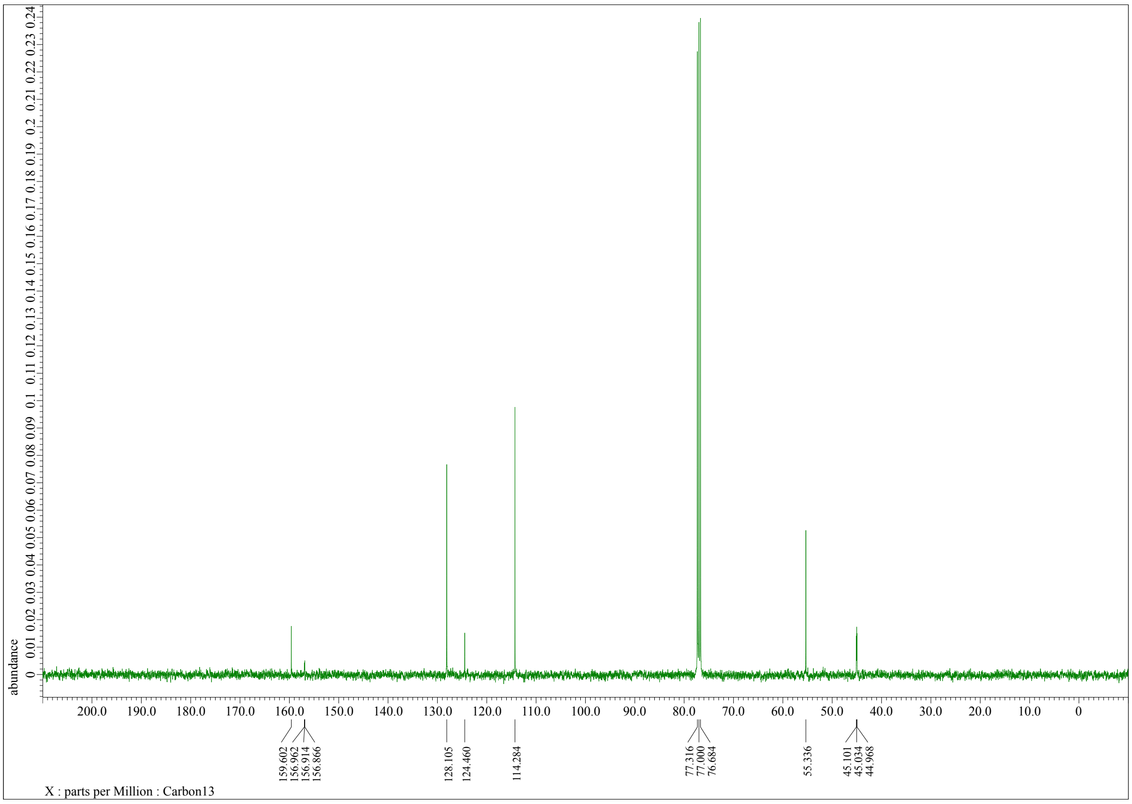
Isocyanomethylbenzene (1e)



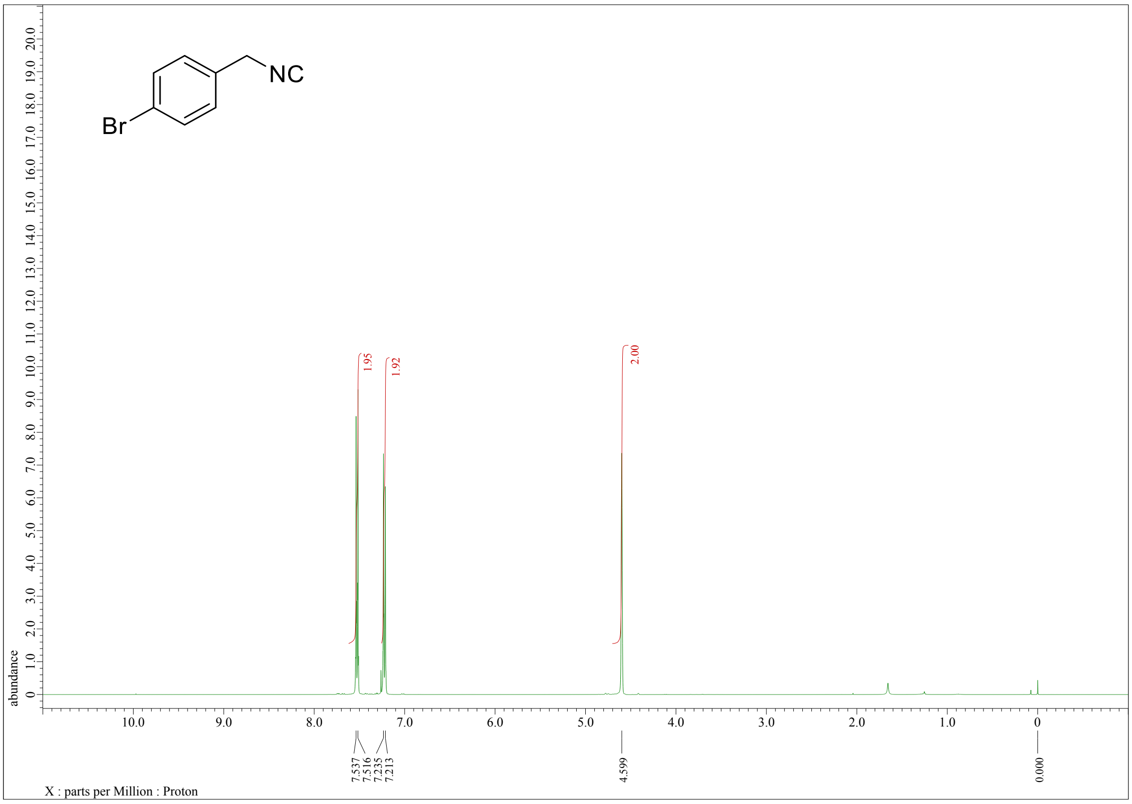


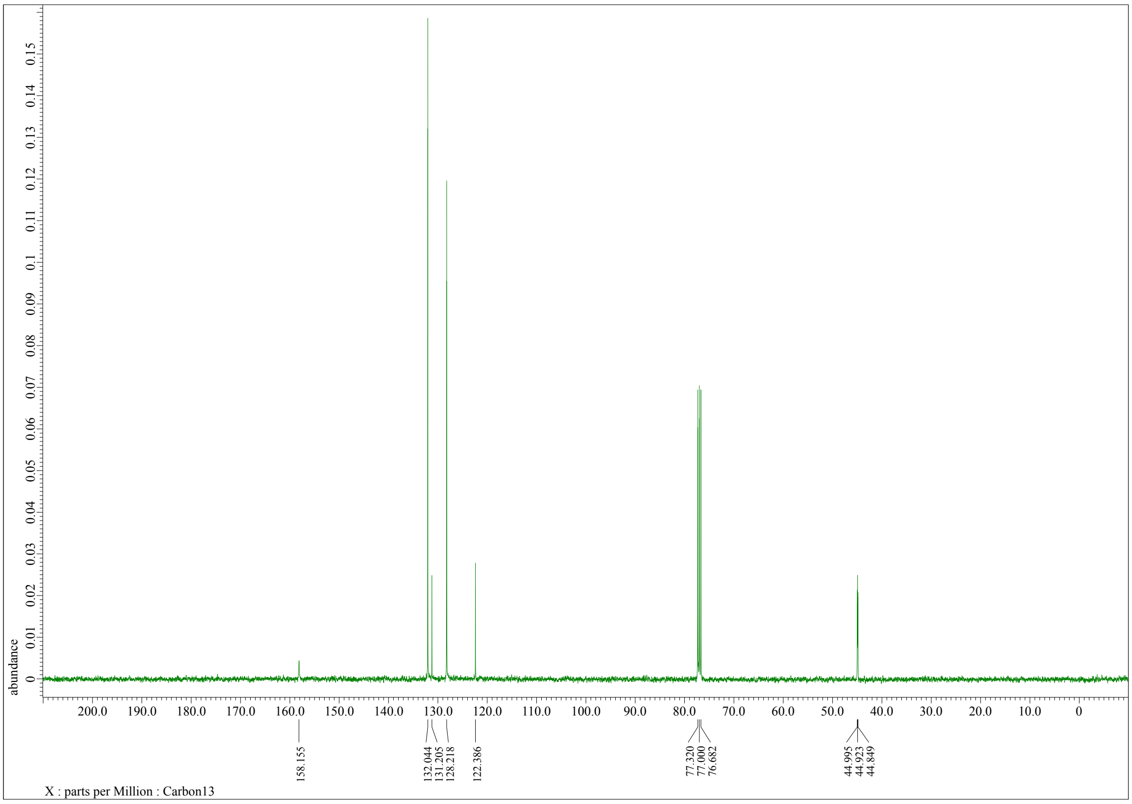
1-(Isocyanomethyl)-4-methoxybenzene (1f)



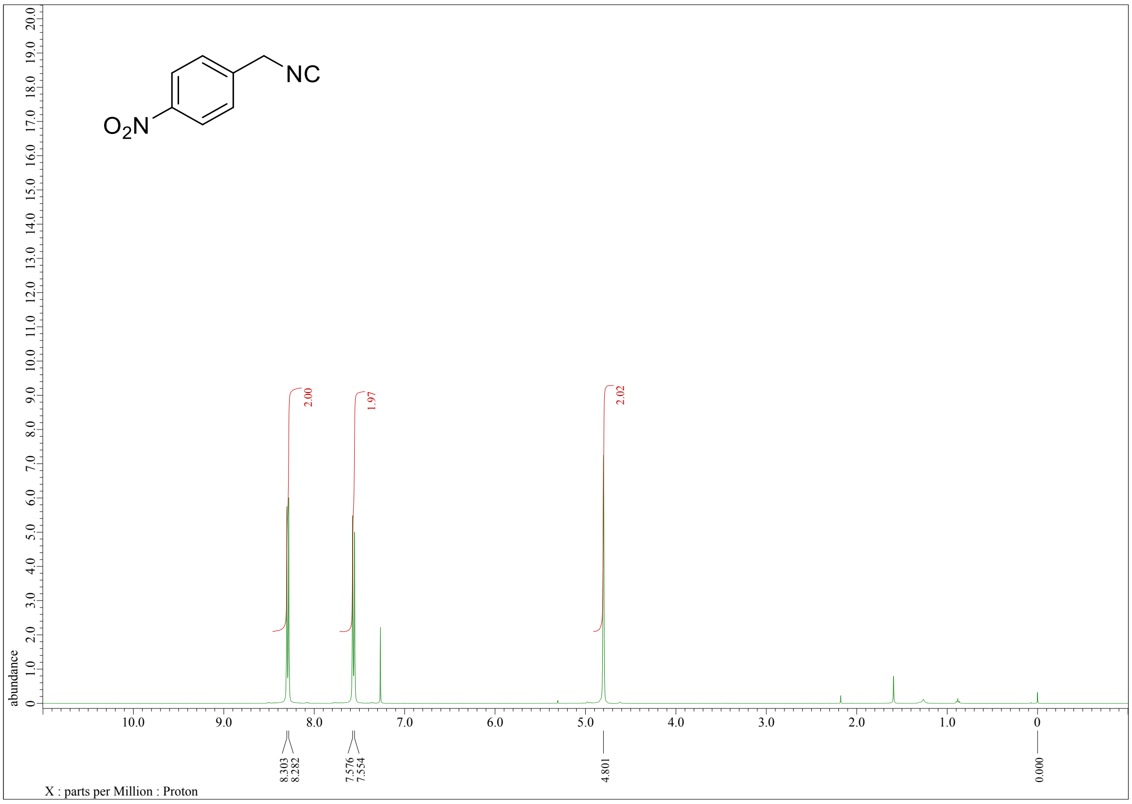


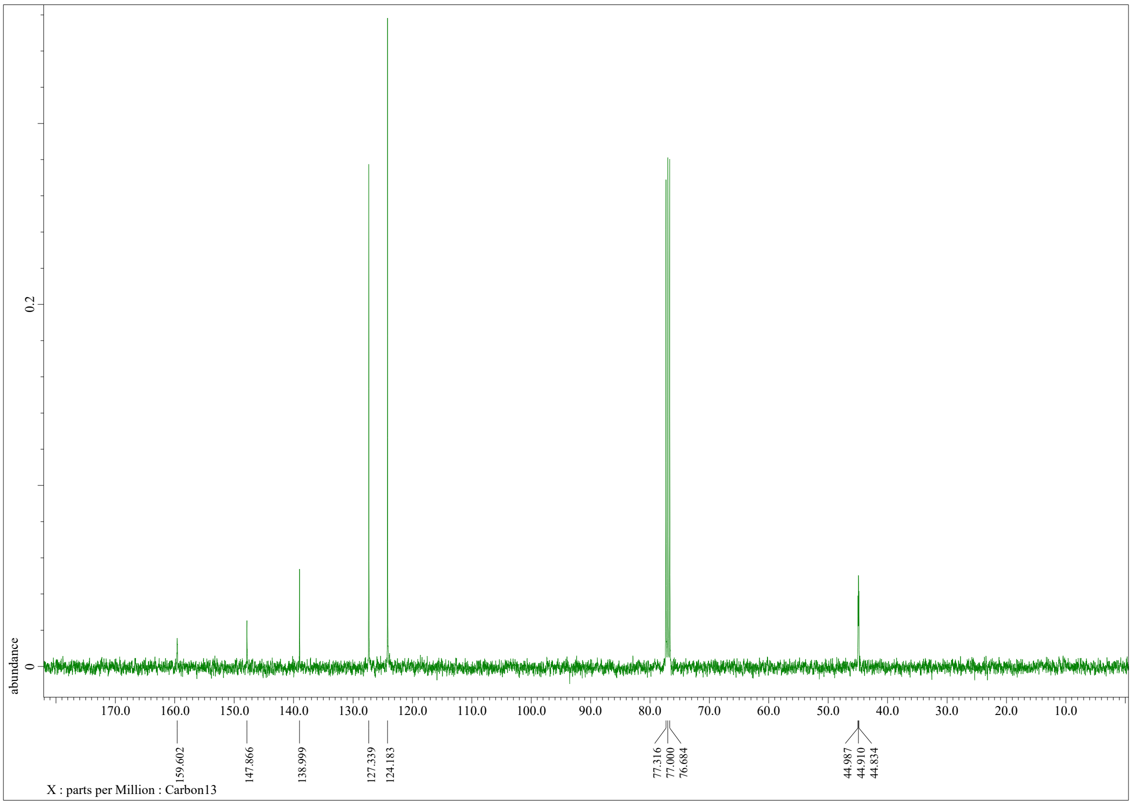
1-(Isocyanomethyl)-4-bromobenzene (1g)



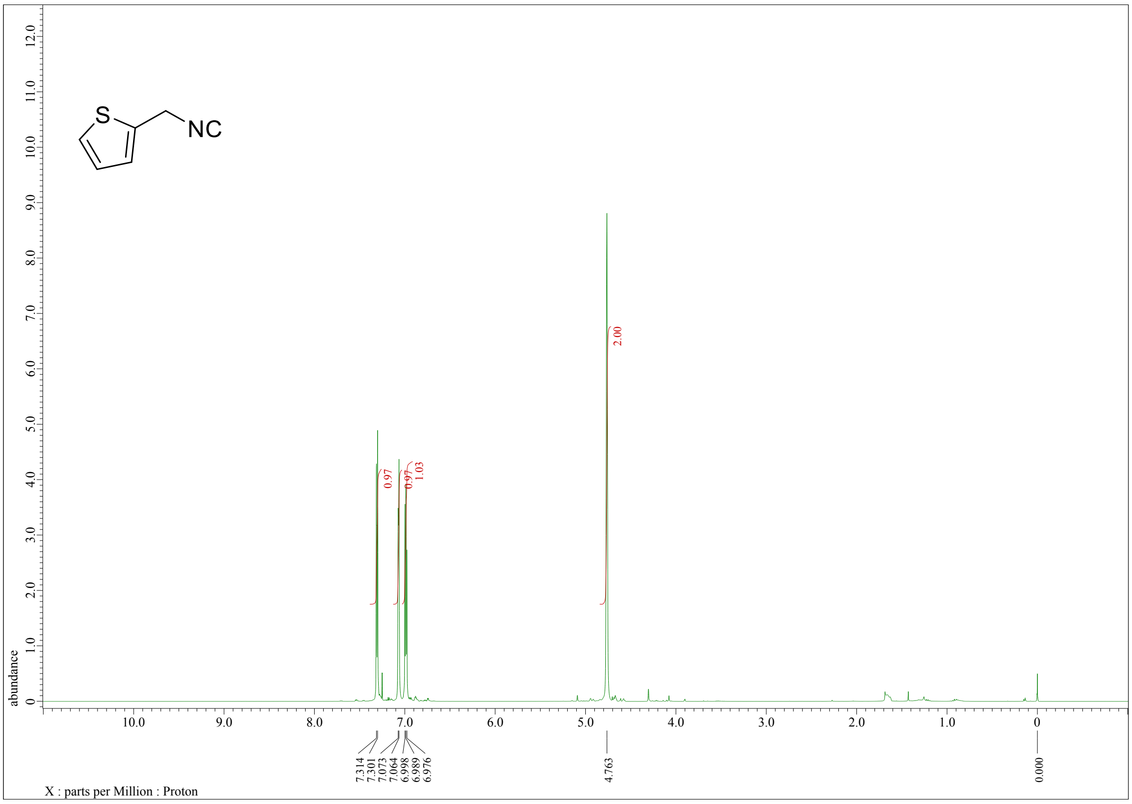


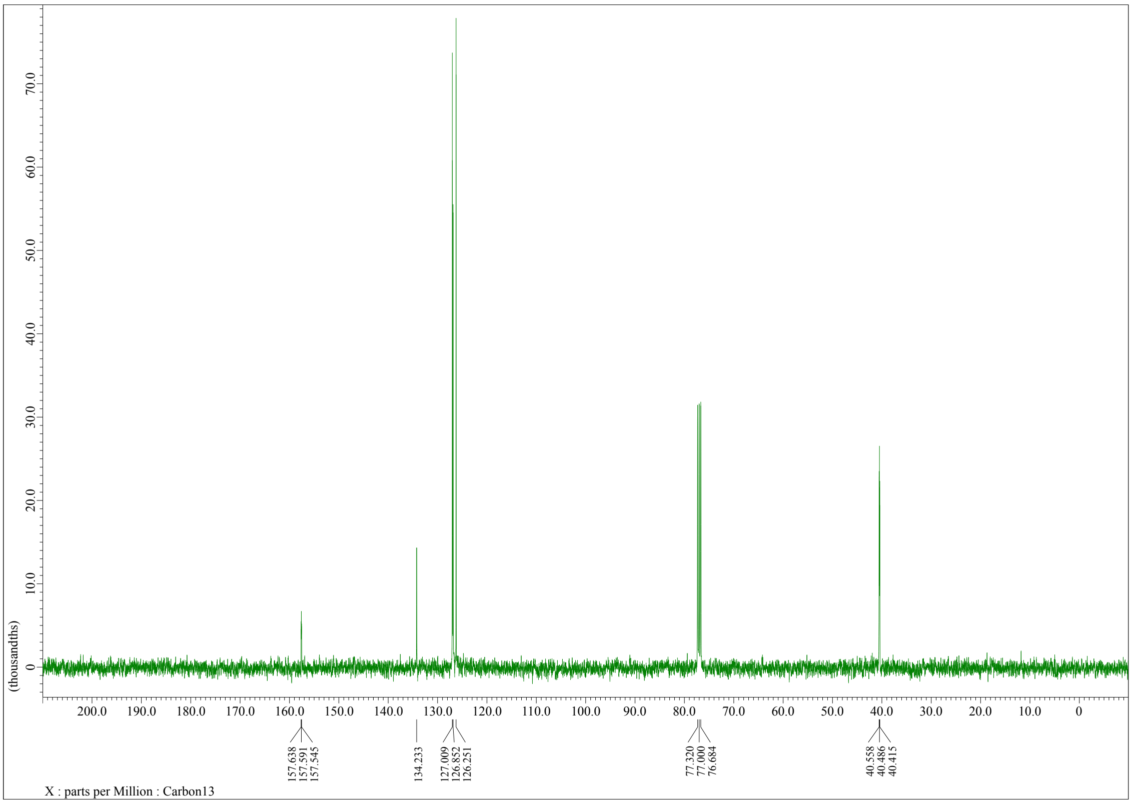
1-(Isocyanomethyl)-4-nitrobenzene (1h)



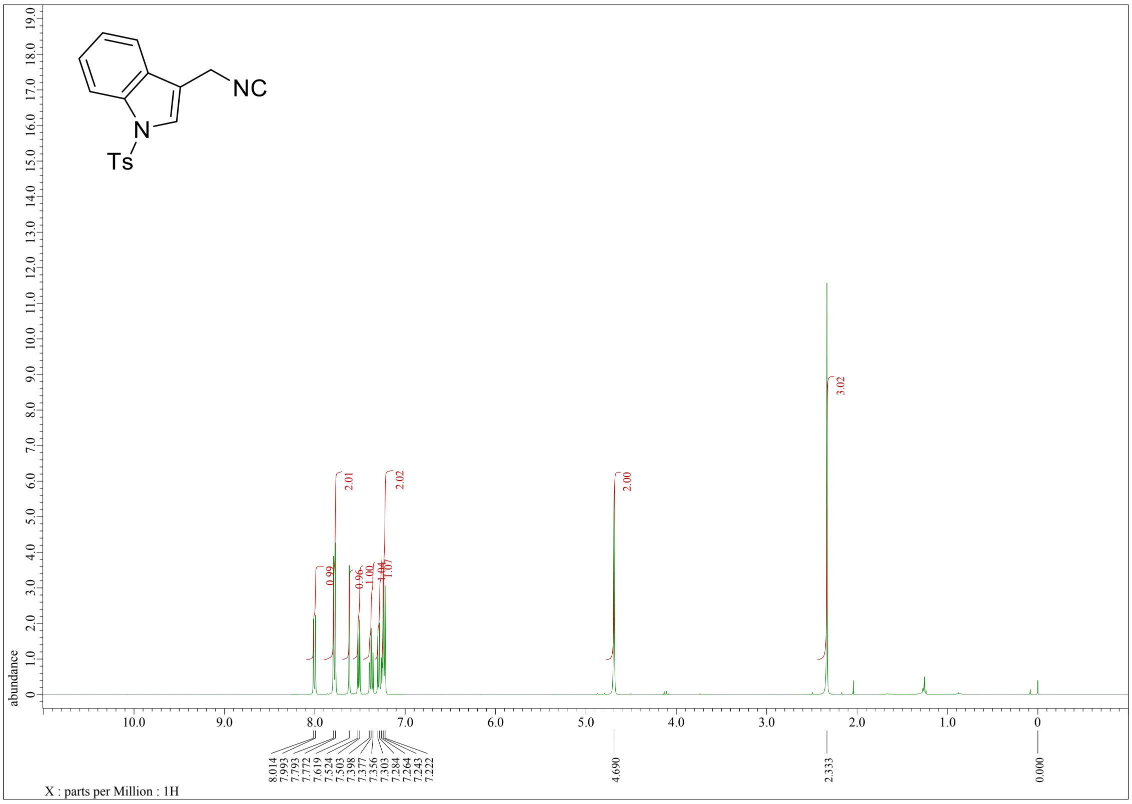


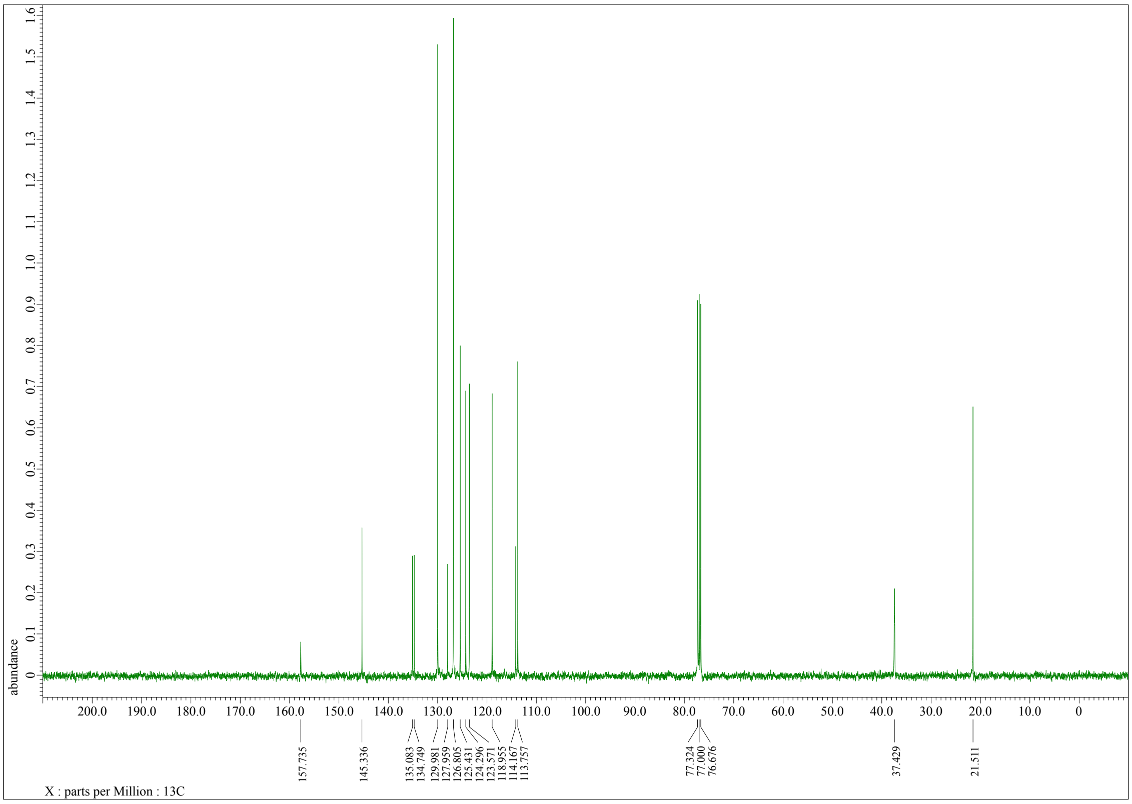
2-(Isocyanomethyl)thiophene (1j)



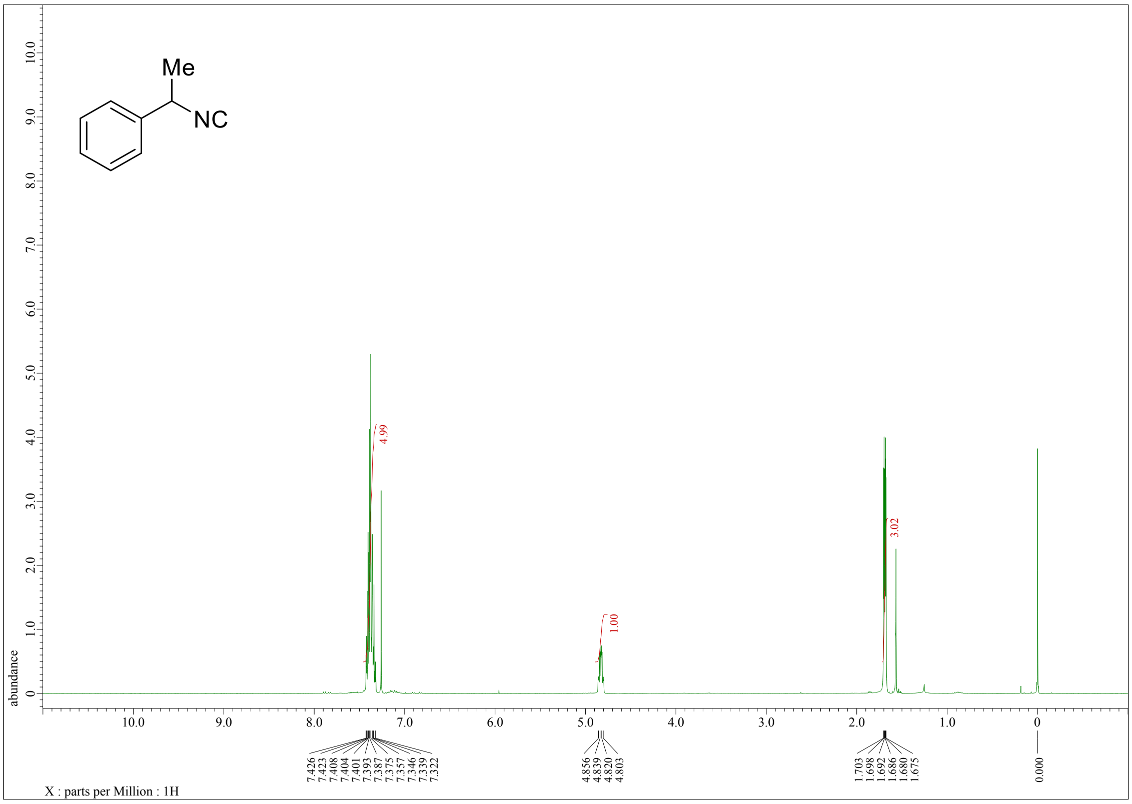


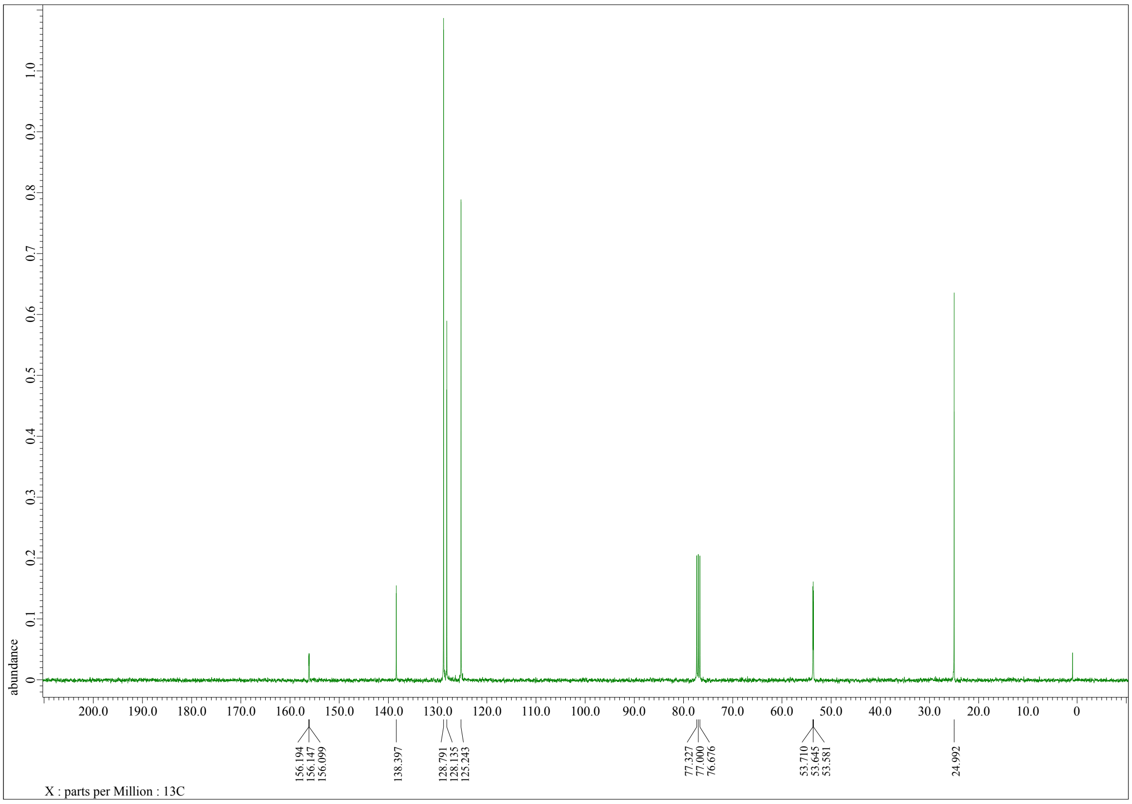
3-(Isocyanomethyl)-[(4-methylphenyl)sulfonyl]indol (1k)



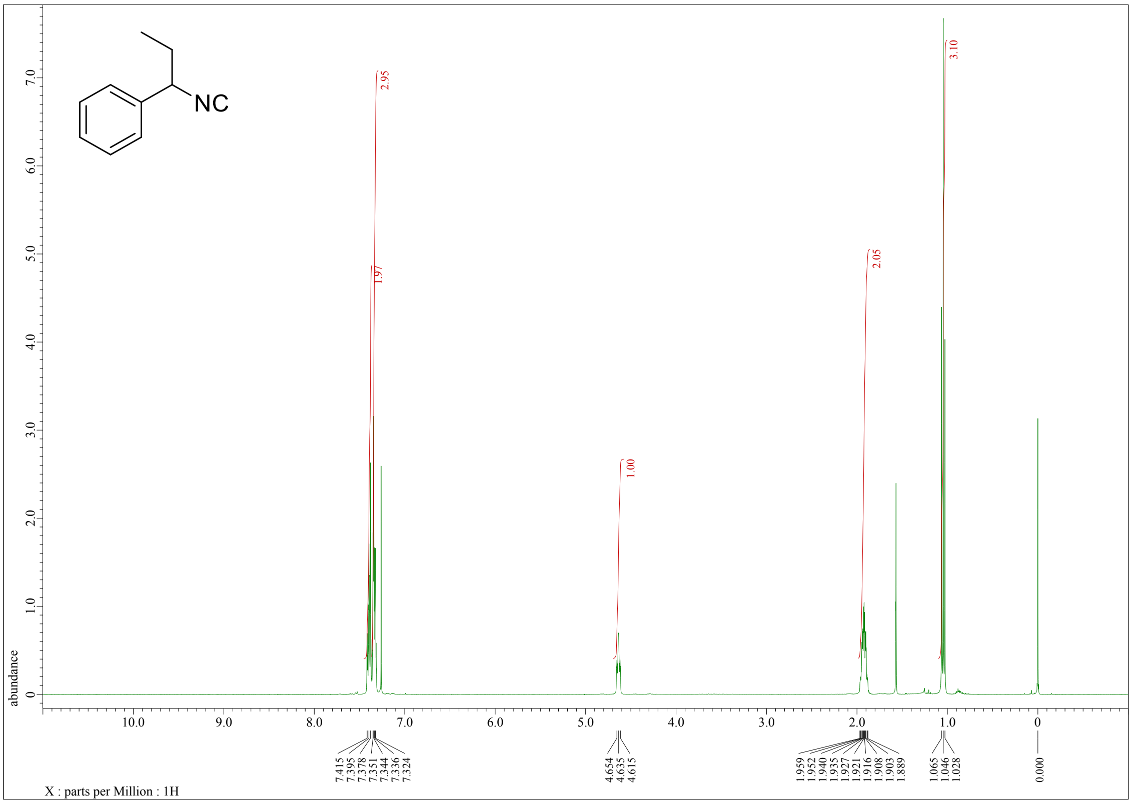


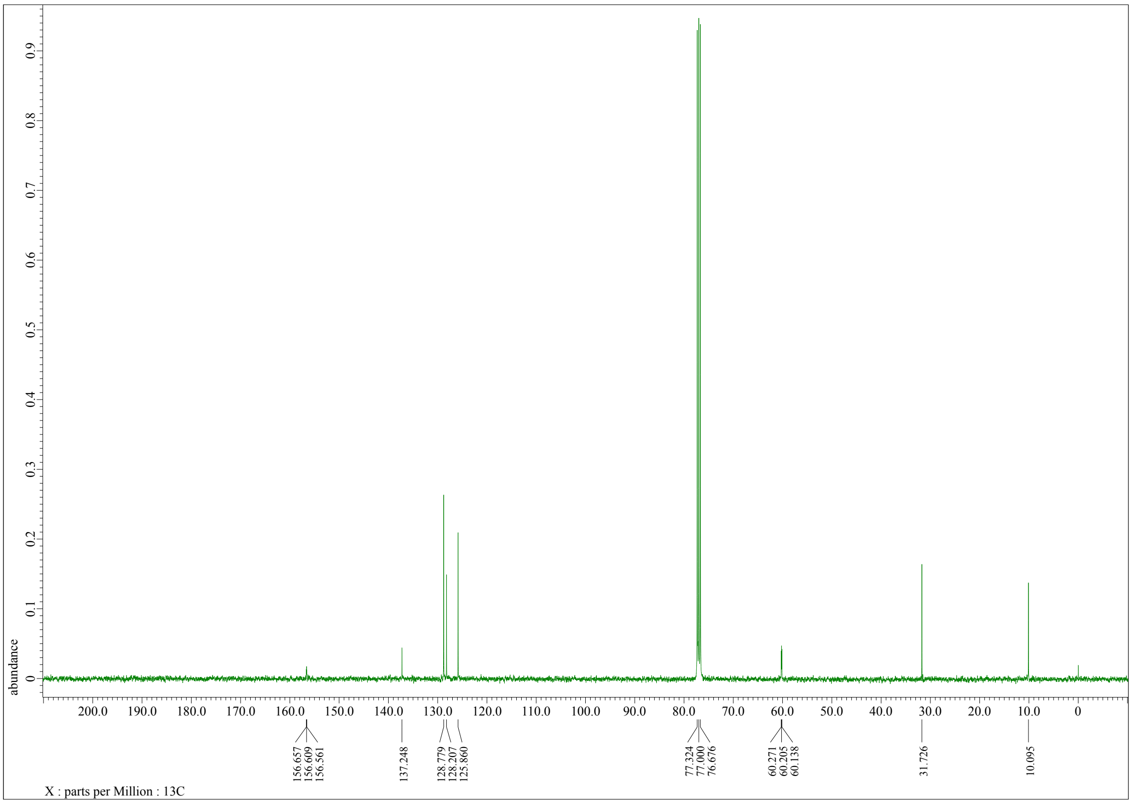
1-Isocyano-1-phenyl-ethane (3a)



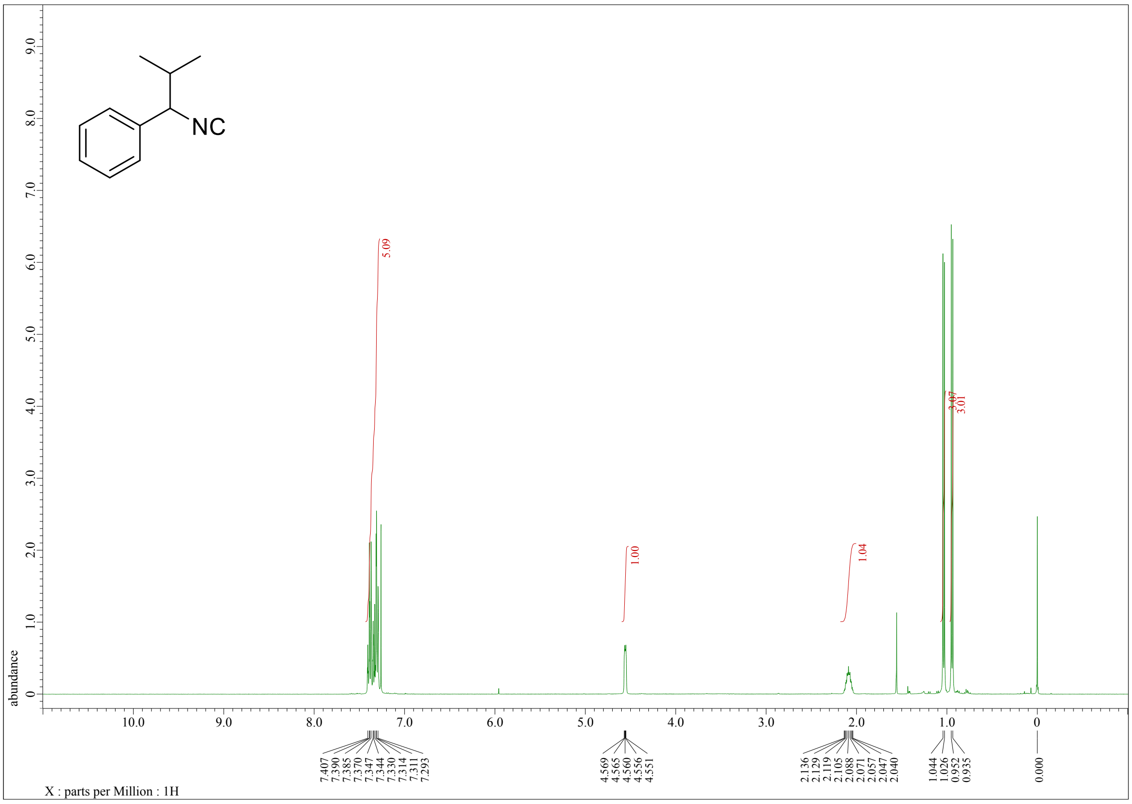


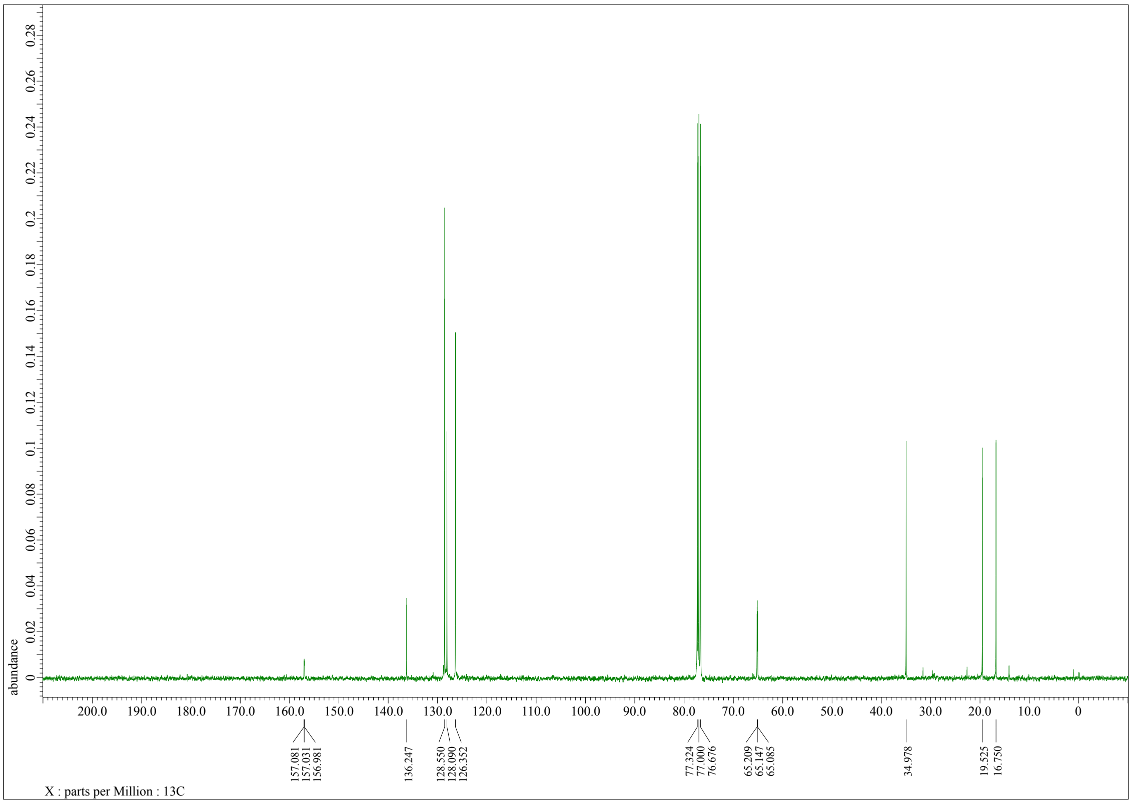
1-Isocyano-1-phenyl-propane (3b)



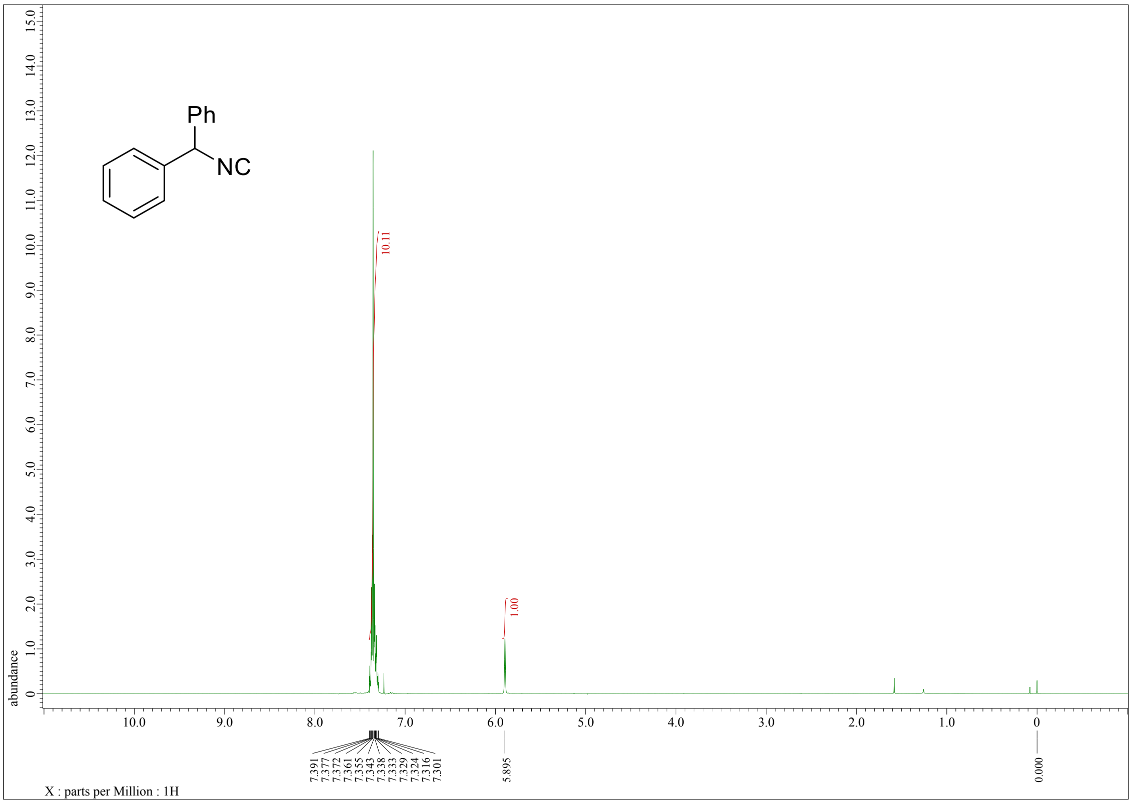


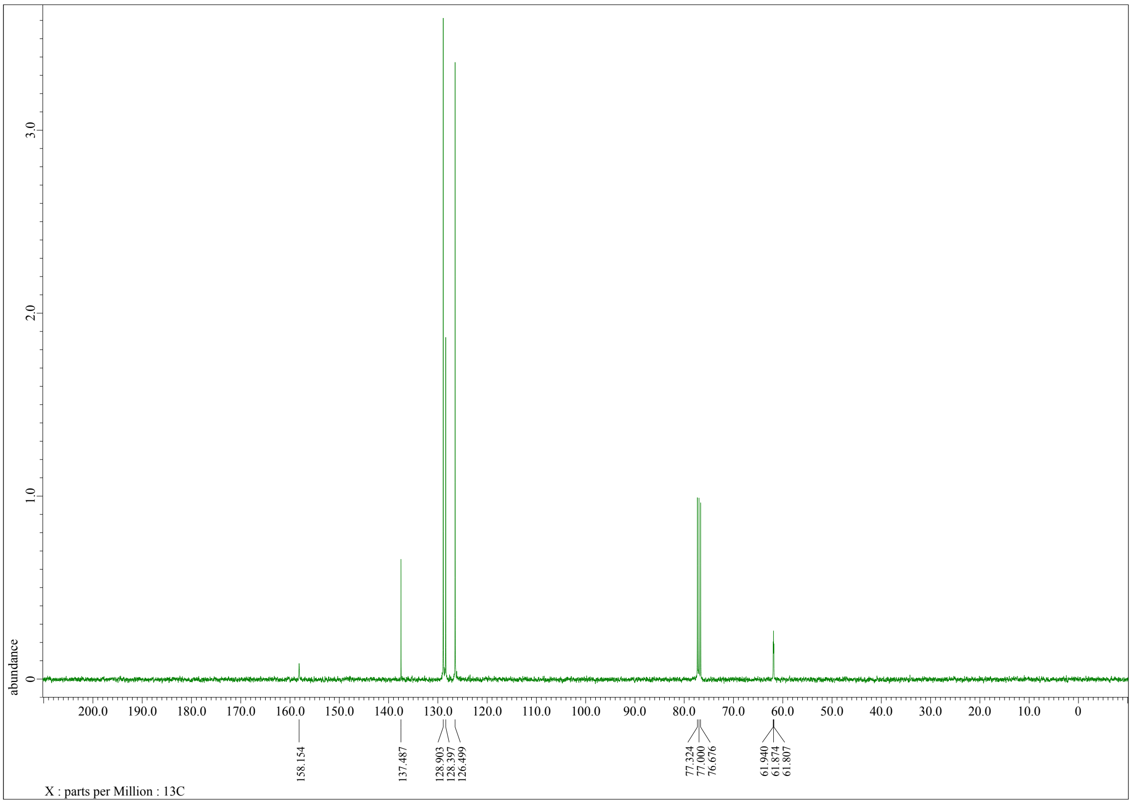
1-Isocyano-1-phenyl-2-methyl-propane (3c)



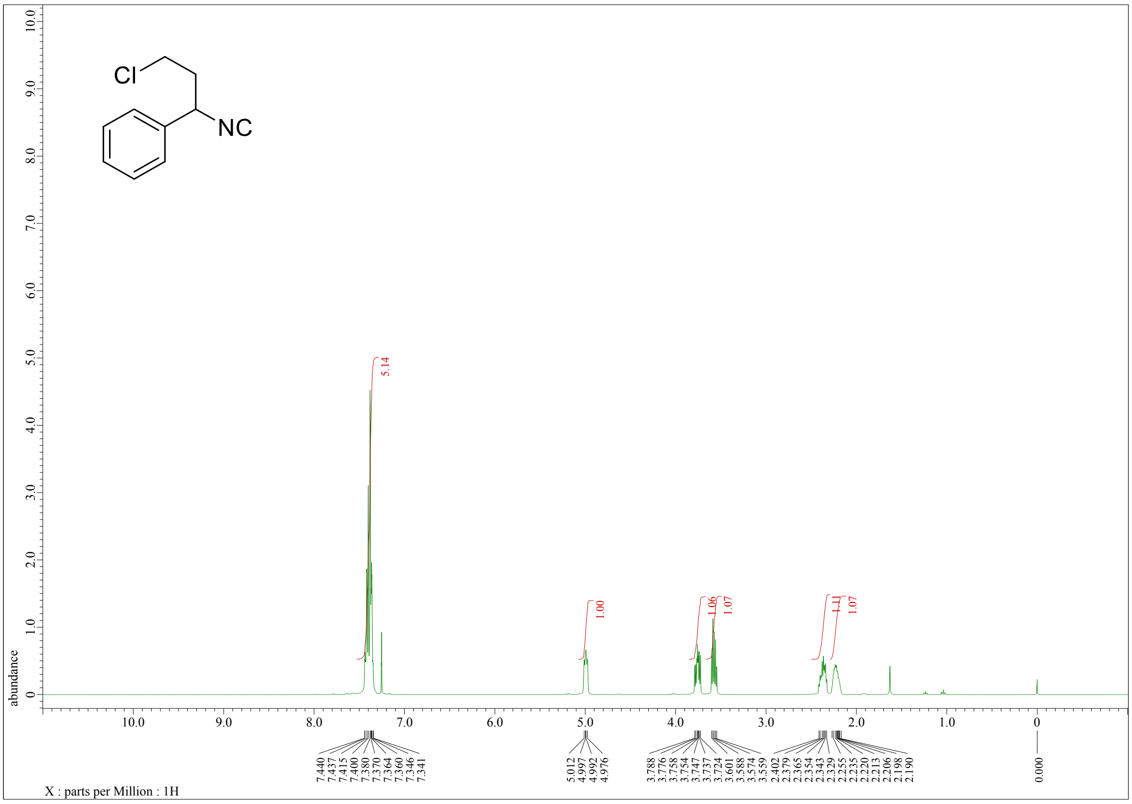


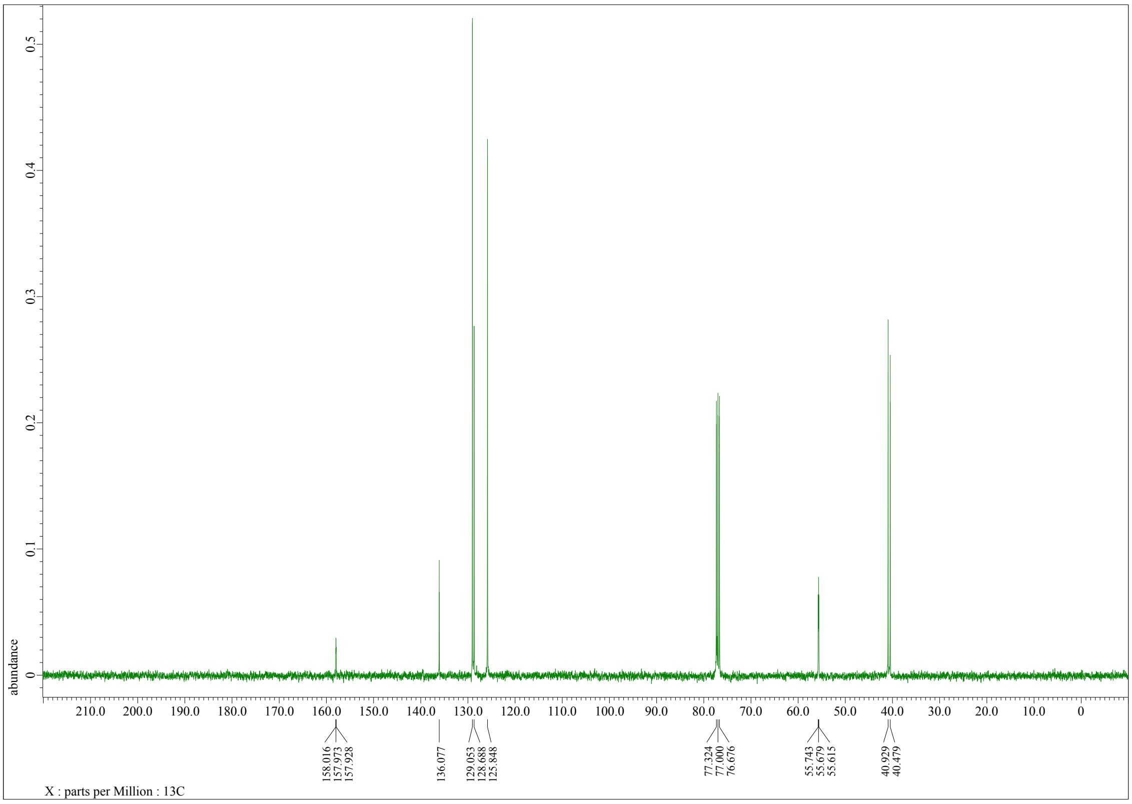
Benzhydrylisonitrile (3d)



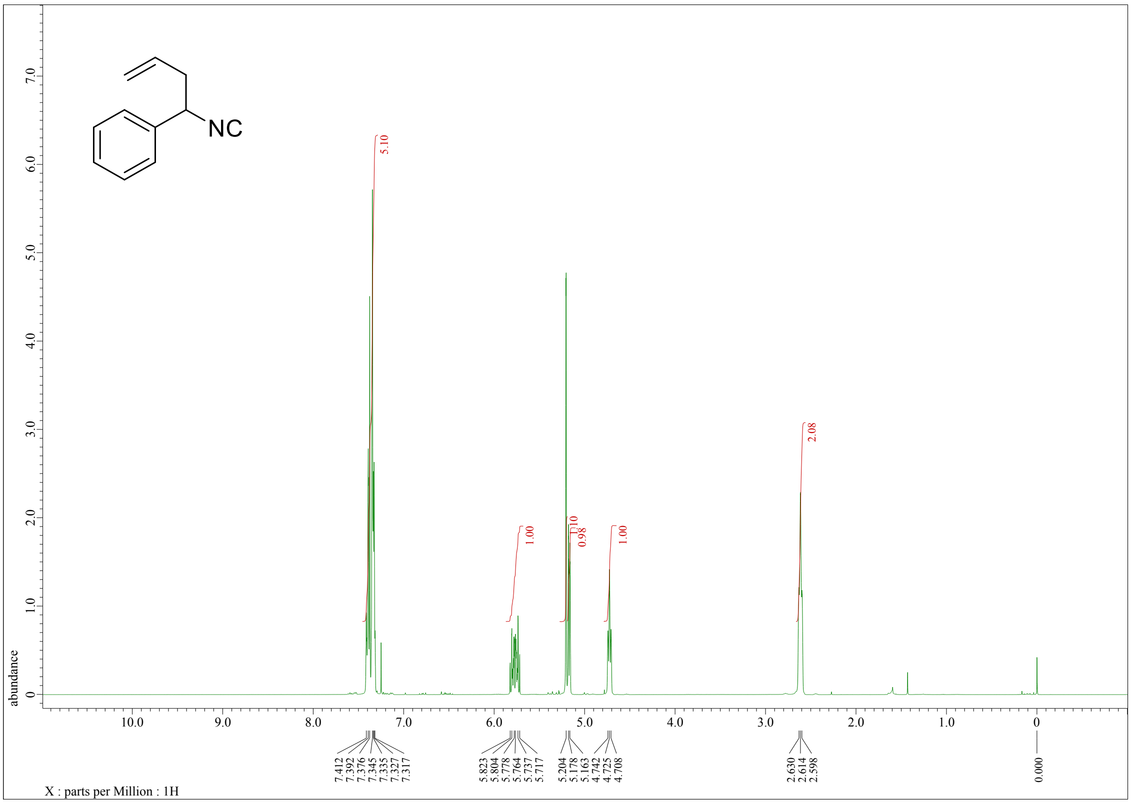


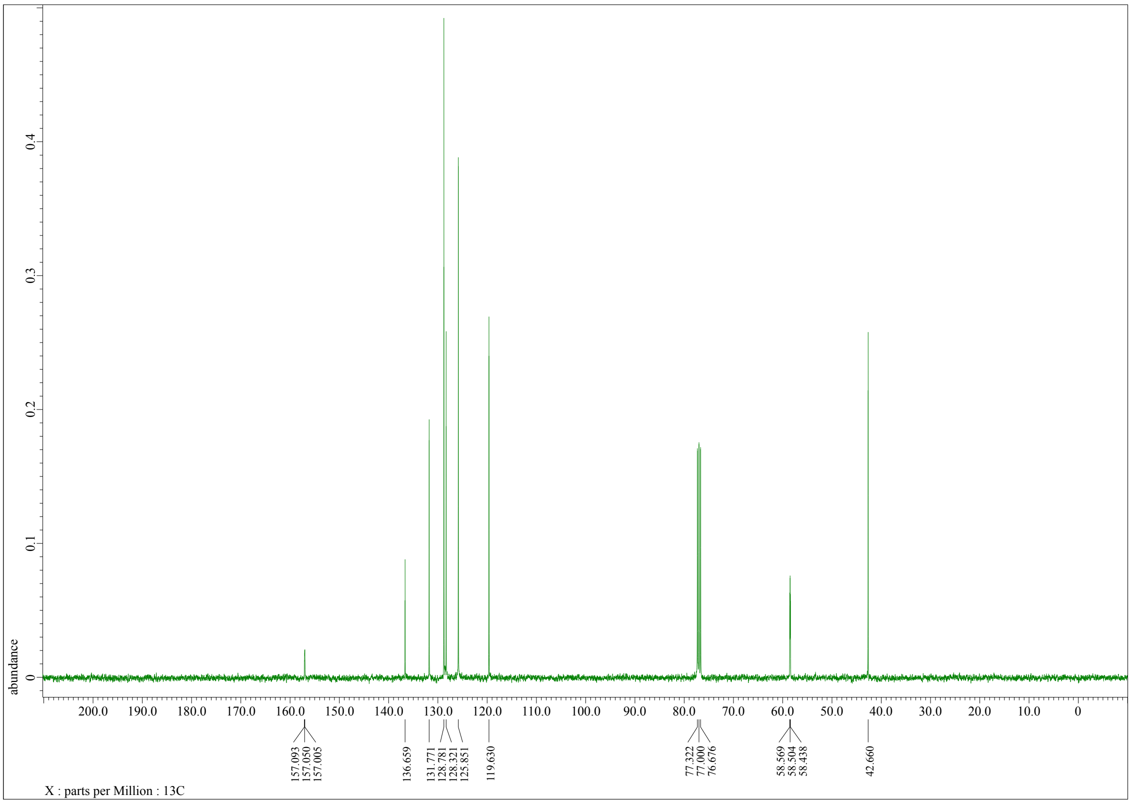
3-Chloro-1-isocyano-1-phenyl-propane (3e)





1-Isocyano-1-phenyl-3-butene (3f)





Methyl 3-Isocyano-3-phenyl-propionate (3g)