Conversion of Azides into Diazo Compounds in Water

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1. General Methods

Reagent chemicals were obtained from chemical sources and used without further purification. All glassware was flame-dried under vacuum, and reactions were performed under N_2(g) unless indicated otherwise. Dichloromethane, diethyl ether, tetrahydrofuran, and toluene were dried over a column of alumina. *N*,*N*-Dimethylformamide and triethylamine were dried over alumina and purified further by passage through an isocyanate scrubbing column. Chromatography was performed with columns of 40–63 Å silica gel, 230–400 mesh (Silicycle, Québec City, Canada). Thin-Layer chromatography (TLC) was performed on plates of EMD 250-μm silica 60-F_{254}. The phrase "concentrated under reduced pressure" refers to the removal of solvents and other volatile materials using a rotary evaporator at water aspirator pressure (<20 torr) while maintaining the water-bath temperature below 40 °C. Residual solvent was removed from samples at high vacuum (<0.1 torr). The term "high vacuum" refers to vacuum achieved by mechanical belt-drive oil pump. All NMR spectra were acquired at ambient temperature unless indicated otherwise with a Bruker DMX-400 Avance, Bruker Avance III 500i with a cryoprobe, or Bruker Avance III 500ii with a cryoprobe spectrometer at the National Magnetic Resonance Facility at

Madison (NMRFAM). ^{1}H NMR spectra were referenced to TMS or the residual protic solvent. ^{13}C NMR spectra were referenced to the residual solvent peak. ^{31}P NMR spectra were referenced to an external source of 85% w/v H_3PO_4(aq). Electrospray ionization (ESI) mass spectrometry was performed with a Micromass LCT at the Mass Spectrometry Facility in the Department of Chemistry at the University of Wisconsin–Madison.

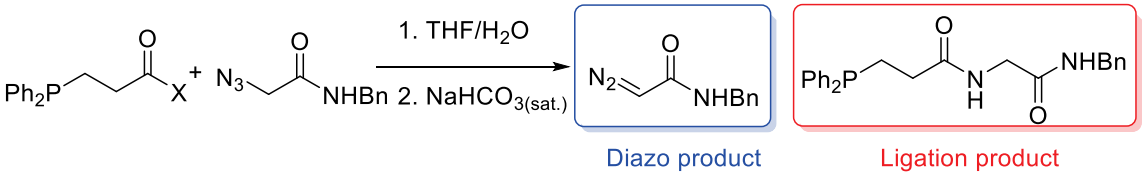
2. Experimental Procedures for Table 1

General procedure for the reaction of 2-azido-*N*-benzylacetamide with phosphines

2-Azido-*N*-benzylacetamide (10 mg, 0.526 mmol) was reacted with different phosphinopropanoates (1 equiv) in a solution containing 0.15 mL H_2O in 1 mL THF for 4 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and stirred for another 8 h. The resulting solution was extracted with CH_2Cl_2 (3 × 10 mL), and the organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The concentrated crude residue was assessed by ^{1}H NMR spectroscopy to determine the diazo:amide product ratio.

General procedure for assessing the water stability of different phosphines

A phosphine (15 mg) was dissolved in 1.0 mL of THF. The resulting solution was then diluted with 1.5 mL of 10 mM sodium phosphate buffer, pH 4.0, 7.0, 9.0, or 12.0. The resulting mixture was stirred for 16 h and then extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The concentrated crude residue was assessed by ^{1}H NMR spectroscopy to obtain the ratio of decomposition.



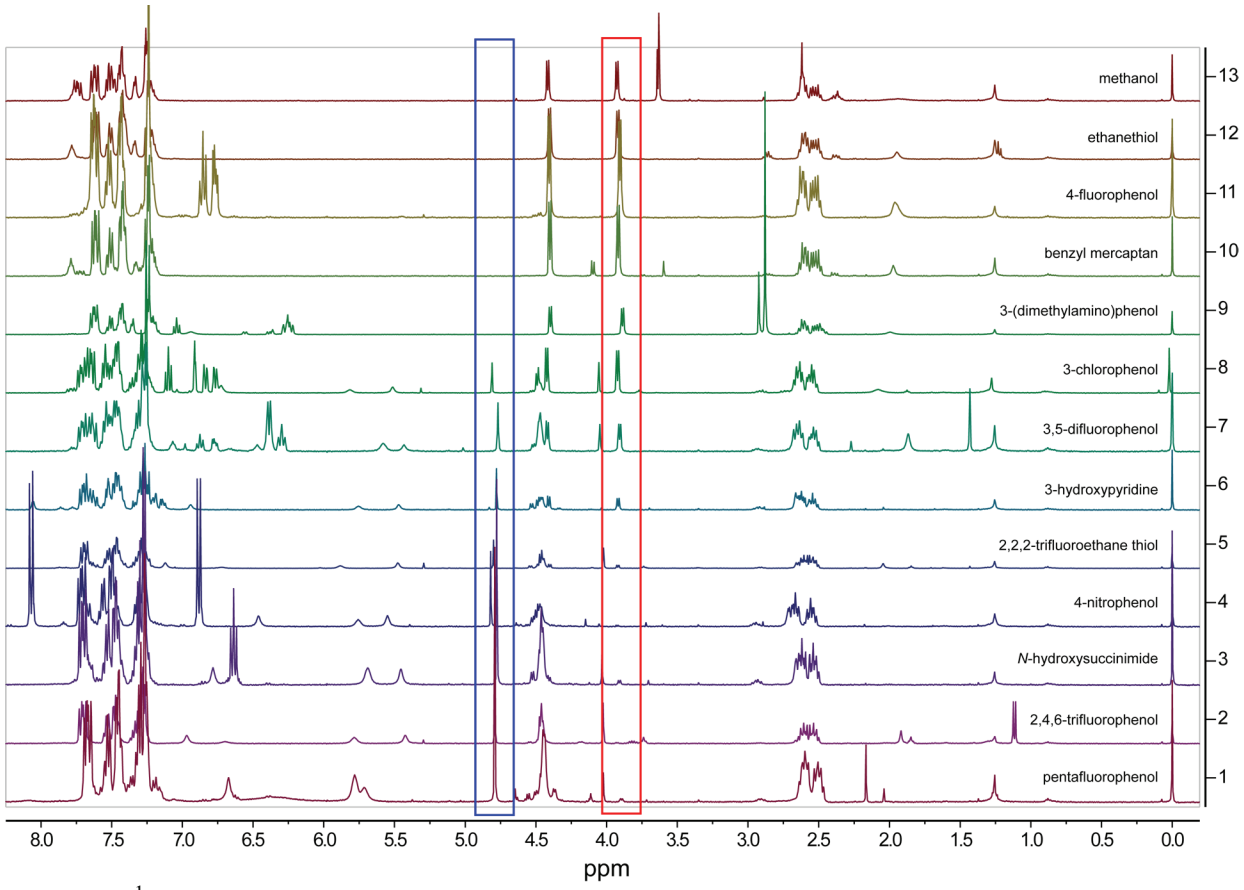


Figure S1. ^{1}H-NMR spectra of the products from the reaction of 2-azido-*N*-benzylacetamide with $Ph_2P(CH_2)_2C(O)X$, where XH is indicated explicitly. Diagnostic signals from the diazo product are circumscribed in blue, and diagnostic signals from the amide product are circumscribed in red.

Table S1. Product distribution based on pK_a of trapping agent

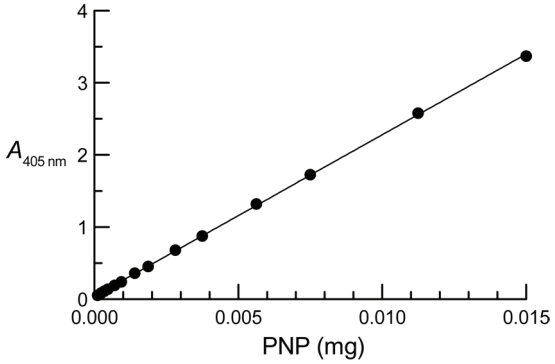
Conjugate acid of X	Integration of δ 4.8 (s, 1H)	Integration of δ 3.9 (d, 2H)	Ratio of Diazo:Amide[a]
methanol	0	1	0:100
ethanethiol	0	1	0:100
4-fluorophenol	0	1	0:100
benzyl mercaptan	0	1	0:100
3-(dimethylamino)phenol	0	1	0:100
3-chlorophenol	1	4.03	33:77
3,5-difluorophenol	1	1.20	63:27
3-hydroxypyridine	1	0.97	67:23
2,2,2-trifluoroethane thiol	1	0.40	83:17
4-nitrophenol	1	0.07	97:3
N-hydroxysuccinimide	1	0.05	98:2
2,4,6-trifluorophenol	1	0.07	97:3
pentafluorophenol	1	0.06	97:3

[a] Determined by ^{1}H-NMR spectroscopy, as shown in Figure S1.

3. Solubility Assay of Phosphinoester 1

A standard curve was developed by adding 200 μL of a 0.5 N NaOH solution to various amounts of *p*-nitrophenol and measuring the absorbance at 405 nm.[1]

Standard Curve

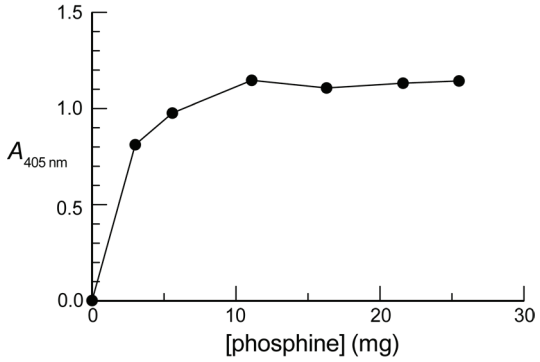


Sample	PNP (mg)	$A_{405\ nm}$	Sample	PNP (mg)	$A_{405\ nm}$
1	0.0150	3.38	11	0.00375	0.896
2	0.00750	1.71	12	0.00188	0.465
3	0.00375	0.863	13	0.000938	0.2495
4	0.00188	0.449	14	0.000469	0.138
5	0.000938	0.240	15	0.000234	0.0856
6	0.000469	0.139	16	0.0112	2.58
7	0.000234	0.0847	17	0.00562	1.32
8	0.000117	0.0566	18	0.00281	0.681
9	0.0150	3.37	19	0.00141	0.363
10	0.00750	1.74	20	0.000703	0.194

Phosphinoester **1** (11.1 mg, 0.0180 mmol) was placed in an Eppendorf tube. Deionized water (500 μL) was then added, and the mixture was stirred vigorously at room temperature for 1 h. After centrifugation, 100 μL of clear liquid was removed and treated with 100 μL of deionized water, and a background absorbance reading at 405 nm was recorded. Another 100 μL was then withdrawn and treated with 100 μL of 1 N NaOH(aq). The solution immediately turned yellow, and its absorbance at 405 nm was measured and found to be 1.208. This same process was then repeated with different amounts of phosphinoester **1**.

The PNP absorbance curve of phosphinoester **1** was found to be linear after 10 mg, indicative of a saturated solution. The average absorbance in this range was found to be 1.13. When this value is applied to the equation for the standard curve ($y = 224x + 0.0393$), it was determined that there was 0.00489 mg of PNP in the 200-μL solution. These data indicate that phosphinoester **1** has a solubility of 0.42 mg/mL in water.

Absorbance Curve



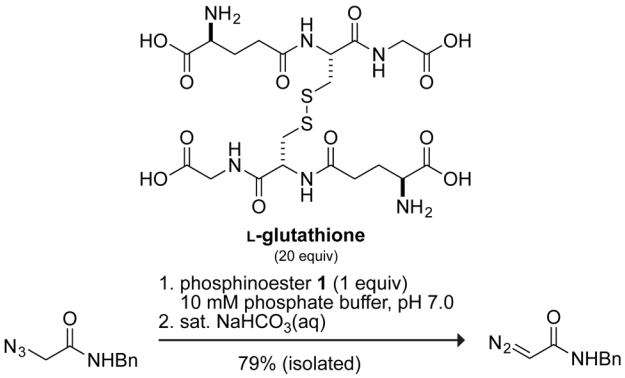
Phosphine (mg)	$A_{405\ nm}$ (before hydrolysis)	$A_{405\ nm}$ (after hydrolysis)	$A_{405\ nm}$ (background correction)
0	0.0305	0.0327	0.00220
3	0.0481	0.861	0.813
5.6	0.0517	1.03	0.978
11.1	0.0614	1.21	1.147
16.3	0.0667	1.17	1.11
21.6	0.0668	1.20	1.13
25.5	0.0738	1.22	1.14

4. Experimental Procedures for Table 2

Equimolar amounts of phosphinoester **1** (45.0 mg, 0.073 mmol) and 2-azido-*N*-benzylacetamide (13.9 mg, 0.073 mmol) were added to 1.2 mL of 10 mM sodium phosphate buffer, containing a co-solvent, and the resulting mixture was stirred for 24 h. The clear yellow solution was quenched with 5 mL of saturated aqueous $NaHCO_3$ for another 8 h and extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the corresponding diazo compound (11.7 mg, 0.067 mmol, 91% yield). This procedure was applied to different solvents (from pH 5.0 to 8.0, and co-solvent systems) for the generation of 2-diazo-*N*-benzylacetamide.

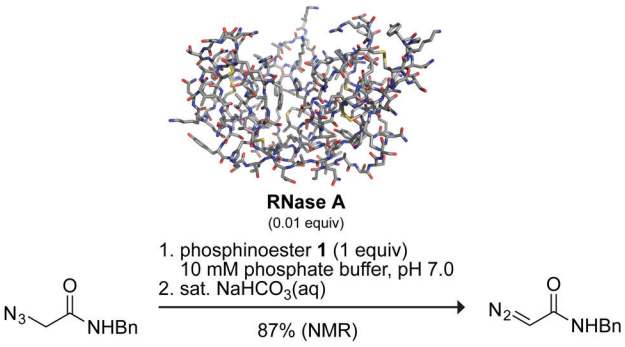
5. Biomolecular Compatibility

5.1 Reaction in the Presence of L-Glutathione



2-Azido-*N*-benzylacetamide (13.4 mg, 0.070 mmol) and phosphinoester **1** (44.3 mg, 0.072 mmol) were used in the general procedure for the synthesis of diazo compounds but in the presence of L-glutathione (881.6 mg, 1.438 mmol). The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to give *N*-benzyl-2-diazoacetamide (9.6 mg, 0.055 mmol, 79% yield) as a yellow solid.

5.2 Reaction in the Presence of Ribonuclease A



Ribonuclease A (26.0 mg, 1.9 μmol) from Sigma Chemical (St. Louis, MO) was dissolved in 1.9 mL of 10 mM sodium phosphate buffer, pH 7.0. To this 14 mg/mL solution of protein (which is near the solubility limit) was added a mixture of 2-azido-*N*-benzylacetamide (3.6 mg, 0.019 mmol) and phosphinoester **1** (11.7 mg, 0.019 mmol), and the resulting solution was stirred for 6 h before being quenched with saturated $NaHCO_3$(aq) for another 8 h. The resulting clear yellow solution was extracted with CH_2Cl_2 (3 × 15 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The yield of 2-azido-*N*-benzylacetamide (87%) was obtained by comparing the integration of the ^{1}H-NMR peaks at δ 5.16 (s, 1H) and δ 3.92 (s, 2H) in MeOH-d_4.

2-Azido-*N*-benzylacetamide: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.33–7.25 (m, 5H), 4.40 (s, 1H), 3.92 (s, 2H).

***N*-Benzyl-2-diazoacetamide: ^{1}H NMR (500 MHz, MeOH-d_4)** δ 7.33–7.23 (m, 5H), 5.16 (s, 1H), 4.40 (s, 1H).

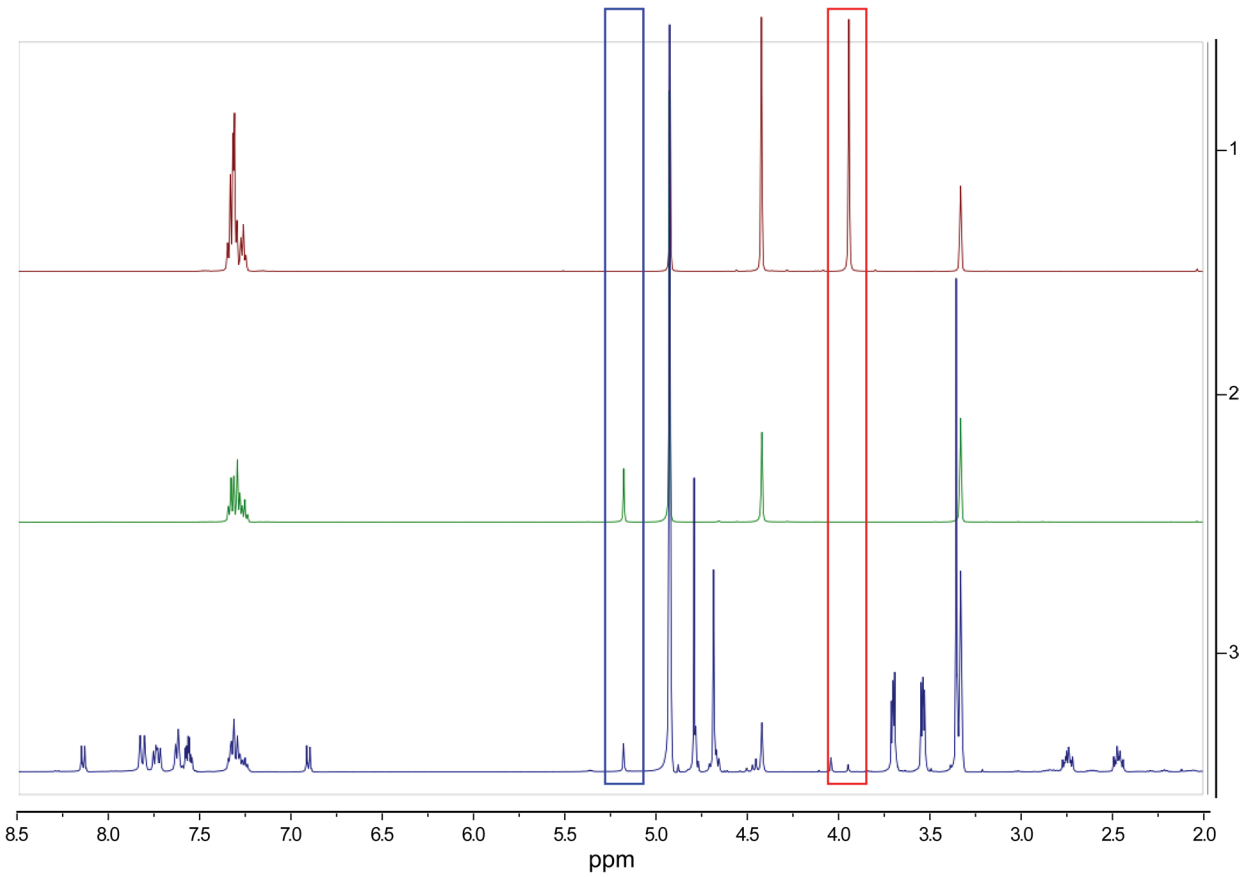


Figure S2. ^{1}H-NMR spectra of the products from the reaction of 2-azido-*N*-benzylacetamide with phosphinoester **1** in the presence of RNase A. Diagnostic signals from the diazo product are circumscribed in blue, and diagnostic signals from the azide starting material are circumscribed in red.

Mass Spectrometry and Ribonucleolytic Activity Assay

To determine whether the deimidogenation reaction mixture affected RNase A, the molecular mass and catalytic activity of the enzyme were assessed before and after the reaction. A control reaction mixture was prepared with RNase A under identical conditions but without reactants. Samples were collected at three time points: (1) prior to the reaction, (2) after 6 h of reaction but before quenching with saturated $NaHCO_3$(aq), and (3) after 8 h of quenching with saturated $NaHCO_3$(aq). Dilutions (50 μM) were desalted using C18 tips from Thermo Scientific (Rockford, IL) and analyzed by MALDI–TOF mass spectrometry. Enzymatic activity was assayed by monitoring the cleavage of a fluorogenic substrate, 6-FAM–dArUdGdA–6-TAMRA.[2] Fluoresence at 515 nm after excitation at 492 nm was monitored with a M1000 microplate reader from Tecan (Mannedorf, Germany). Assays were performed in duplicate in oligo(vinylsulfonic acid)-free 0.10 M MES buffer, pH 6.0, containing NaCl (0.10 M). The increase in fluorescence was converted into activity with the equation:

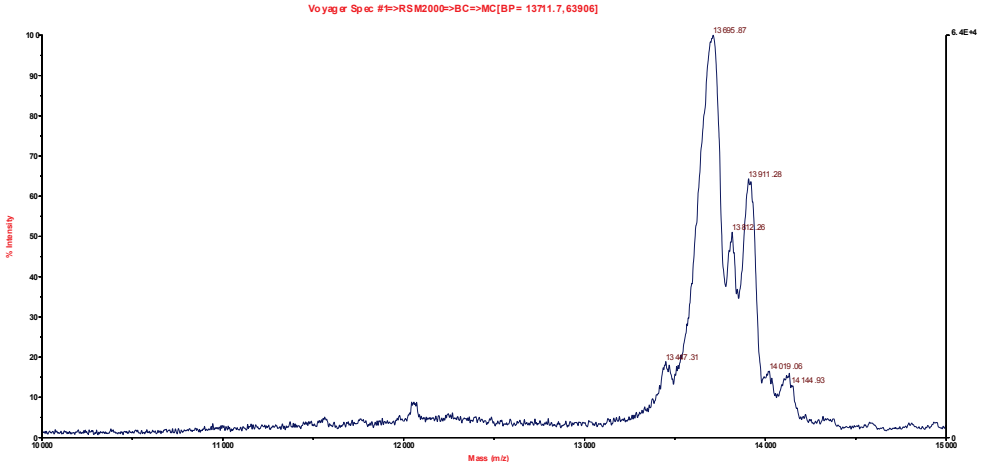
$$k_{cat}/K_M = \frac{\Delta I/\Delta t}{(I_{max} - I_0)[\text{RNase A}]}$$

Where $\Delta I/\Delta t$ is the initial reaction velocity, I_{max} is the maximum fluorescence detectable after all substrate is cleaved with additional RNase A, and I_0 is the background fluorescence in the initial assay mixture.

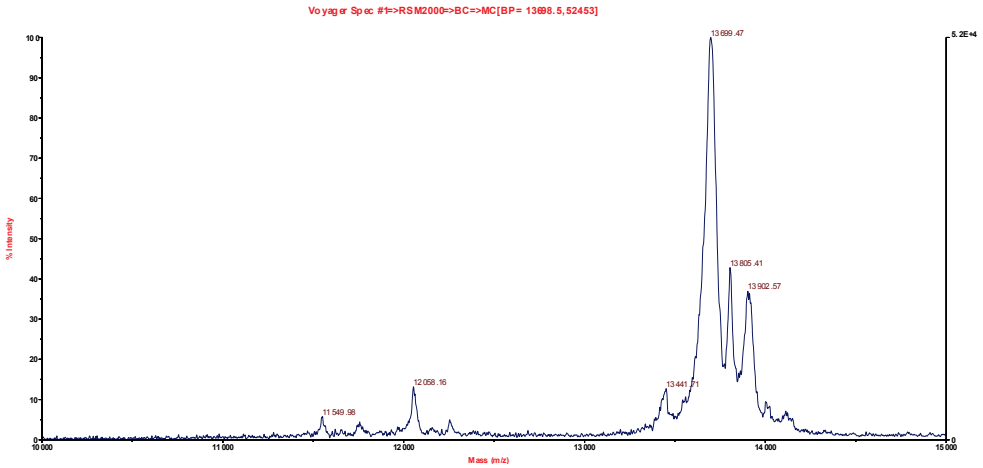
Table S2. Molecular Mass and Catalytic Activity of RNase A Exposed to a Deimidogenation Reaction Mixture

Sample	Condition	*m/z*	(k_{cat}/K_M ± SE) (10^6 $M^{-1}s^{-1}$)
C1	No Reactants	13,696	4.2 ± 2.2
C2	No Reactants + 6 h	13,699	4.1 ± 1.9
C3	No Reactants + 6 h + sat. $NaHCO_3$(aq) + 8 h	13,707	5.1 ± 3.6
E1	+ Reactants	13,695	5.8 ± 2.7
E2	+ Reactants + 6 h	13,699	7.0 ± 4.7
E3	+ Reactants + 6 h + sat. $NaHCO_3$(aq) + 8 h	13,702	6.7 ± 2.4

C1



C2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13902.57
12058.16
13441.71
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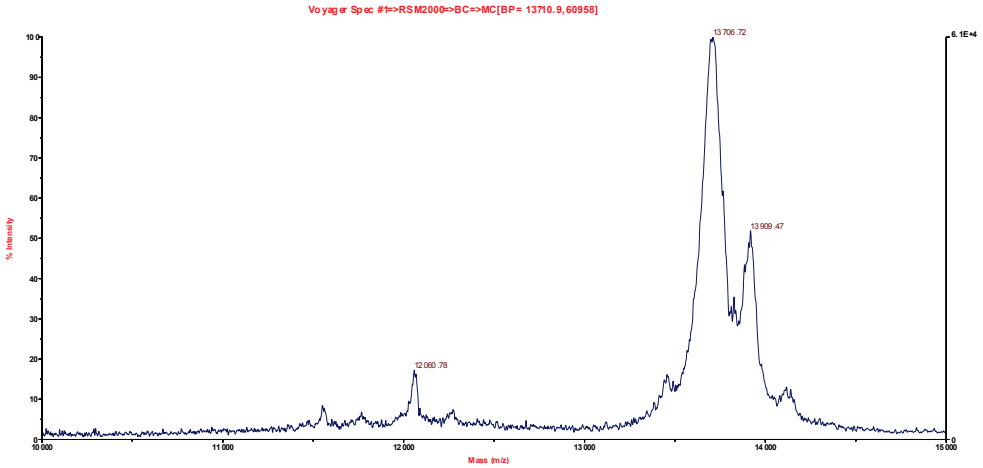
% Intensity
Mass (m/z)

C3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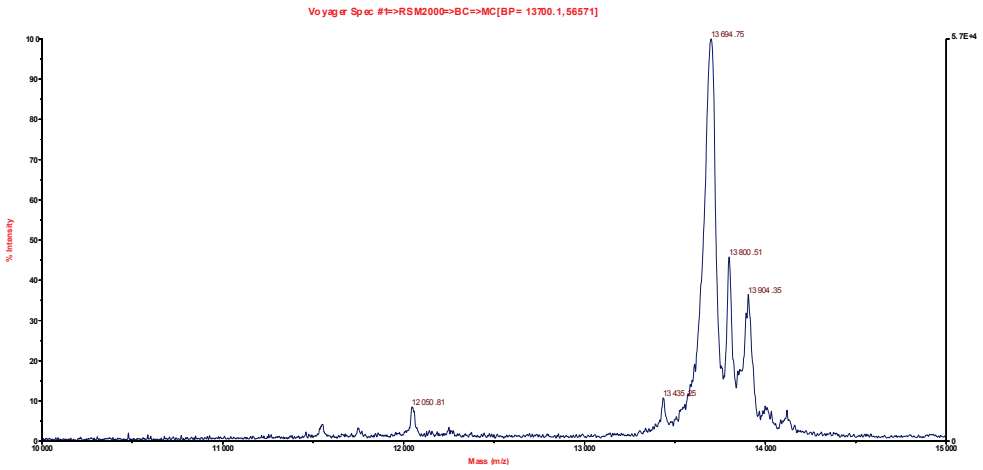
12060.78
% Intensity
Mass (m/z)

E1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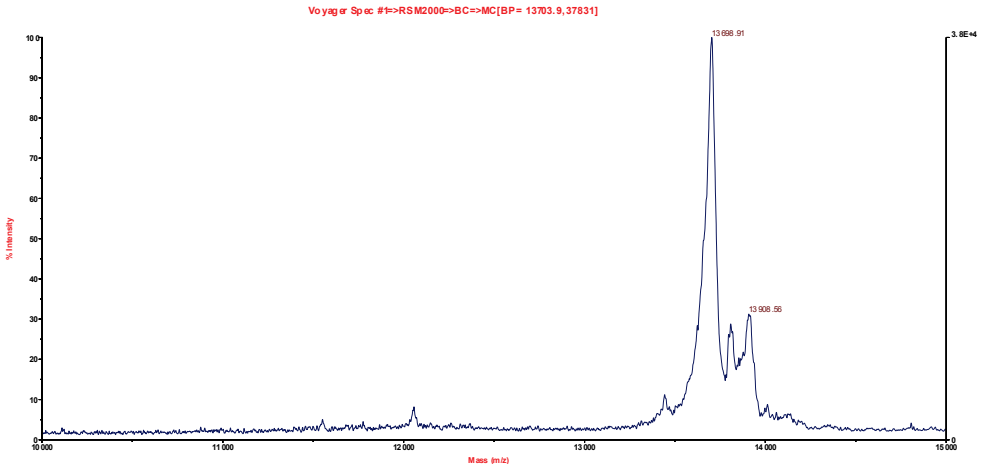
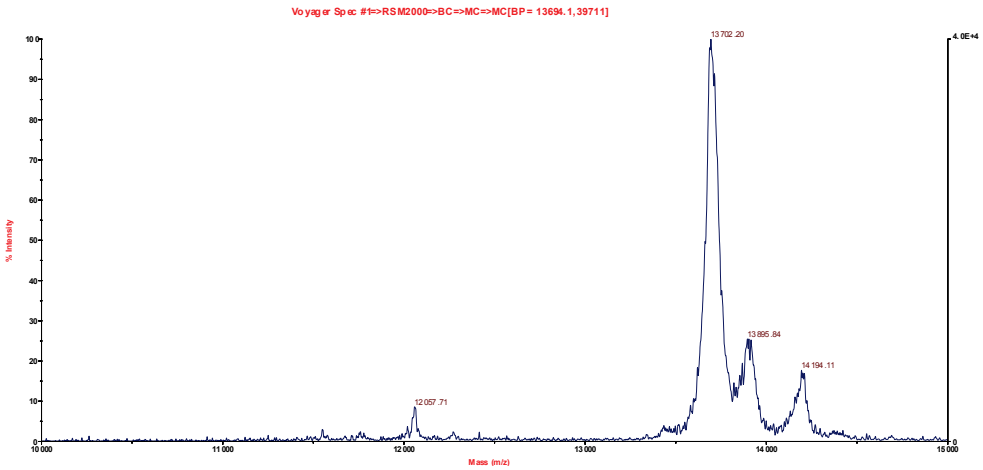
12050.81
13435.45
% Intensity
Mass (m/z)

E2

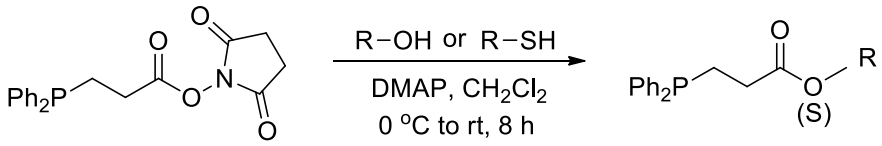


E3



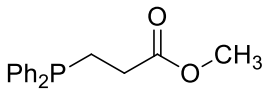
6. Compound Synthesis and Characterization

General Procedure for the Synthesis of 3-(Diphenylphosphino)propanoate Esters



N-Succinimidyl 3-(diphenylphosphino)propanoate (1.0 equiv) and alcohol/thiol (1.5 or 2.0 equiv) were dissolved in anhydrous CH_2Cl_2 at 0 °C under N_2(g). To this solution was added 4-(dimethylamino)pyridine (DMAP) (1.0 equiv). The resulting solution was allowed to warm to room temperature and stirred for 8 h. The mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel.

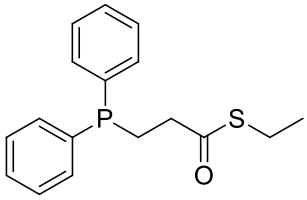
Methyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.153 g, 0.431 mmol), methanol (26 μL, 0.647 mmol), and DMAP (0.053 g, 0.435 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenylphosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a clear liquid (0.093 g, 0.343 mmol, 80% yield).

Methyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.32 (m, 10H), 3.64 (s, 3H), 2.44–2.32 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 173.6, 173.5, 137.7, 137.6, 132.8, 132.6, 128.8, 128.5, 128.5, 51.7, 30.6, 30.4, 23.0, 22.9; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.6; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{16}H_{17}O_2P+H)^+$ 273.1039, measured 273.1034.

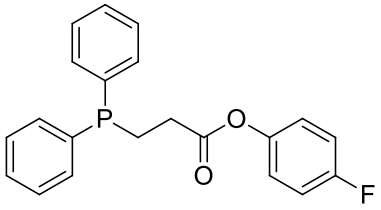
Ethyl 3-(diphenylphosphino)propanethioate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.150 g, 0.422 mmol), ethanethiol (46 μL, 0.633 mmol), and DMAP (0.052 g, 0.426 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenylphosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a white solid (0.084 g, 0.279 mmol, 66% yield).

Ethyl 3-(diphenylphosphino)propanethioate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.40 (m, 4H), 7.36–7.33 (m, 6H), 2.87 (q, J = 7.4 Hz, 2H), 2.64–2.57 (m, 2H), 2.40–2.36 (m, 2H), 1.23 (t, J = 7.5 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 199.0, 137.6, 137.5, 132.8, 132.6, 128.8, 128.6, 128.5, 40.3, 40.1, 23.5, 23.4, 14.7; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.7; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{17}H_{19}OPS+H)^+$ 303.0968, measured 303.0961.

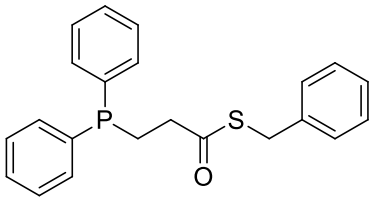
4-Fluorophenyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.158 g, 0.445 mmol), 4-fluorophenol (0.076 g, 0.678 mmol), and DMAP (0.055 g, 0.450 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenyl-phosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a white solid (0.132 g, 0.375 mmol, 84% yield).

4-Fluorophenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.43 (m, 4H), 7.40–7.35 (m, 6H), 7.06–6.99 (m, 4H), 2.67–2.61 (m, 2H), 2.48–2.44 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P and ^{19}F-coupled; ^{1}H-decoupled, observed signals)** δ 177.7, 171.6, 161.4, 158.9, 146.4, 137.5, 132.8, 132.8, 132.6, 128.9, 128.6, 128.6, 122.9, 122.8, 116.1, 115.9, 30.9, 30.7, 23.0, 22.9; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.7; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{21}H_{18}FO_2P+H)^+$ 353.1102, measured 353.1102.

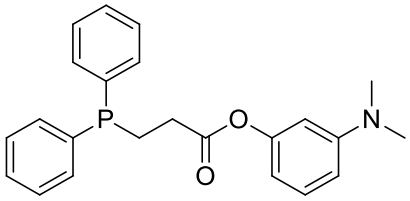
***S*-Benzyl 3-(diphenylphosphino)propanethioate**



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.150 g, 0.422 mmol), 4-fluoro-phenol (74 μL, 0.633 mmol), and DMAP (0.052 g, 0.426 mmol) in anhydrous CH_2Cl_2 (5.0 mL) were used in the general procedure for the synthesis of 3-(diphenyl-phosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a white solid (0.132 g, 0.364 mmol, 86% yield).

***S*-Benzyl 3-(diphenylphosphino)propanethioate: ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43–7.23 (m, 15H), 4.11 (s, 2H), 2.66–2.60 (m, 2H), 2.41–2.37 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 198.1, 198.0, 137.5, 137.4, 132.7, 132.5, 128.8, 128.8, 128.8, 128..6, 128.5, 127.2 40.0, 39.8, 33.3, 23.4, 23.3; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.7; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{22}H_{21}OPS+H)^+$ 365.1124, measured 365.1119.

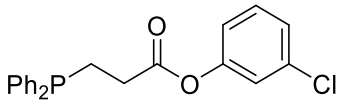
3-(Dimethylamino)phenyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.150 g, 0.422 mmol), 3-dimethyl-aminophenol (0.137 g, 0.844 mmol), and DMAP (0.053 g, 0.434 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenyl-phosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 10% v/v EtOAc in hexanes, to give the ester as a yellow liquid (0.137 g, 0.363 mmol, 86% yield).

3-(Dimethylamino)phenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.44 (m, 4H), 7.36–7.35 (m, 6H), 7.19 (dd, J = 10.4, 10.4 Hz, 1H), 6.56 (dd, J = 10.4, 3.0 Hz, 1H), 6.41–6.38 (m, 1H), 6.36 (dd, J = 3.0, 3.0 Hz, 1H), 2.93 (s, 6H), 2.66–2.60 (m, 2H), 2.49-2.45 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 171.8, 171.6, 151.7, 151.5, 137.6, 137.5, 132.8, 132.6, 129.5, 128.8, 128.5, 128.5, 109.8, 109.0, 105.3, 104.9, 40.3, 31.0, 30.8, 23.0, 22.8; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.5; **HRMS** (ESI^+) m/z calculated for $(C_{23}H_{24}NO_2P+H)^+$ 378.1618, measured 378.1621.

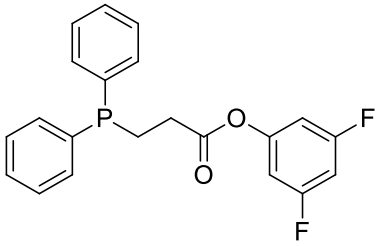
3-Chlorophenyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.254 g, 0.715 mmol), 4-fluoro-phenol (90 μL, 0.858 mmol), and triethylamine (0.12 mL, 0.858 mmol) in anhydrous CH_2Cl_2 (5.0 mL) were used in the general procedure for the synthesis of 3-(diphenyl-phosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 5% v/v EtOAc in hexanes, to give the ester as a white solid (0.213 g, 0.578 mmol, 81% yield).

3-Chlorophenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.44 (m, 4H), 7.37–7.36 (m, 6H), 7.29 (dd, J = 10.2, 10.2 Hz, 1H), 7.22–7.19 (m, 1H), 7.08 (dd, J = 2.6, 2.6 Hz, 1H), 6.98–6.95 (m, 1H), 2.68–2.62 (m, 2H), 2.48–2.44 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 171.3, 171.2, 151.1, 137.5, 137.4, 134.6, 132.8, 132.6, 130.1, 129.0, 128.7, 128.6, 126.1, 122.2, 119.9, 31.0, 30.8, 23.0, 22.8; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.8; **HRMS** (ESI^+) m/z calculated for $(C_{21}H_{18}ClO_2P+H)^+$ 369.0806, measured 369.0818.

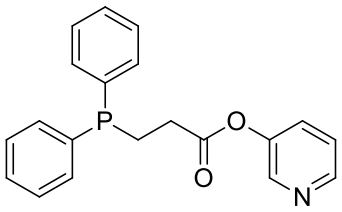
3,5-Difluorophenyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.148 g, 0.417 mmol), 3,5-difluoro-phenol (0.112 g, 0.861 mmol), and DMAP (0.054 g, 0.442 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenyl-phosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a white solid (0.029 g, 0.079 mmol, 19% yield).

3,5-Difluorophenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.43 (m, 4H), 7.40–7.34 (m, 6H), 6.71–6.63 (m, 3H), 2.68–2.61 (m, 2H), 2.47-2.43 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P and ^{19}F-coupled; ^{1}H-decoupled, observed signals)** δ 170.9, 170.7, 164.2, 164.0, 161.7, 161.6, 152.0, 151.8, 151.7, 137.4, 137.3, 132.8, 132.6, 129.0, 128.7, 128.6, 106.9, 106.8, 106.7, 106.6, 101.9, 101.6, 101.3, 30.9, 30.7, 22.9, 22.7; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.8; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{21}H_{17}F_2O_2P+H)^+$ 371.1007, measured 371.0996.

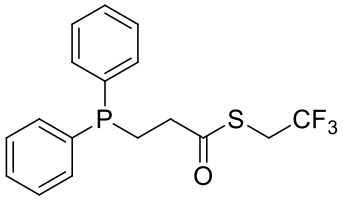
3-Pyridyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.150 g, 0.422 mmol), 3-hydroxy-pyridinium (0.060 g, 0.633 mmol), and DMAP (0.051 g, 0.417 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenylphosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 30% v/v EtOAc in hexanes, to give the ester as a white solid (0.070 g, 0.209 mmol, 49% yield).

3,5-Difluorophenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dd, J = 4.8, 1.4 Hz, 1H), 8.39 (d, J = 2.7 Hz, 1H), 7.48–7.30 (m, 12H), 2.69 (m, 2H), 2.47 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 171.3, 171.1, 147.3, 146.9, 143.3, 137.4, 137.3, 132.8, 132.6, 129.1, 129.0, 128.7, 128.6, 123.8, 30.9, 30.7, 23.0, 22.8; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.8; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{20}H_{18}NO_2P+H)^+$ 336.1148, measured 336.1155.

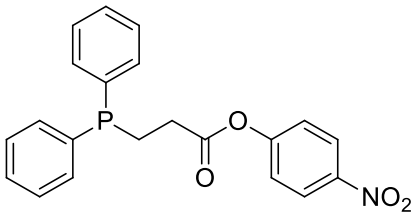
***S*-2,2,2-Trifluoroethyl 3-(diphenylphosphino)propanethioate**



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.313 g, 0.881 mmol), 2,2,2-trifluoroethane thiol (0.11 mL, 1.321 mmol), and DMAP (0.108 g, 0.884 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenylphosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a white solid (0.186 g, 0.524 mmol, 59% yield).

***S*-2,2,2-Trifluoroethyl 3-(diphenylphosphino) propanethioate: ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47–7.28 (m, 10H), 3.57 (q, J = 9.8 Hz, 2H), 2.75–2.62 (m, 2H), 2.45–2.34 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P and ^{19}F-coupled; ^{1}H-decoupled, observed signals)** δ 194.9, 194.8, 137.2, 137.1, 132.7, 132.6, 129.0, 128.7, 128.6, 126.0, 123.2, 120.5, 40.1, 39.9, 31.1, 30.8, 30.4, 30.1, 23.3, 23.1; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.8; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{17}H_{16}F_3OPS+H)^+$ 357.0685, measured 357.0684.

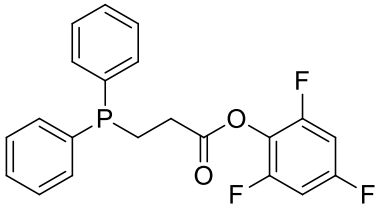
4-Nitrophenyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.300 g, 0.844 mmol), 4-nitrophenol (0.178 g, 1.280 mmol), and DMAP (0.102 g, 0.835 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenylphosphino) propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 10% v/v EtOAc in hexanes, to give the ester as a yellow solid (0.175 g, 0.460 mmol, 55% yield).

4-Nitrophenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.8 Hz, 2H), 7.48–7.44 (m, 4H), 7.38–7.36 (m, 6H), 7.25 (d, J = 8.8 Hz, 2H), 2.73–2.67 (m, 2H), 2.49-2.45 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 170.8, 170.6, 155.3, 145.3, 137.3, 137.2, 132.8, 132.6, 129.0, 128.7, 128.6, 125.2, 122.4, 31.1, 30.9, 22.9, 22.8; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.9; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{21}H_{18}NO_4P+H)^+$ 380.1047, measured 380.1046.

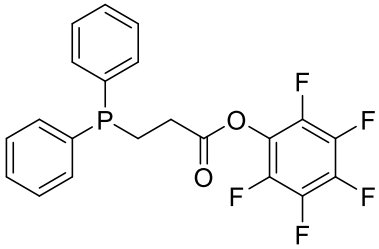
2,4,6-Trifluorophenyl 3-(diphenylphosphino)propanoate



N-Succinimidyl 3-(diphenylphosphino)propanoate (0.154 g, 0.433 mmol), 2,4,6-trifluorophenol (0.095 g, 1.975 mmol), and DMAP (0.055 g, 0.450 mmol) in anhydrous CH_2Cl_2 (4.0 mL) were used in the general procedure for the synthesis of 3-(diphenylphosphino)propanoate esters. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give the ester as a white solid (0.104 g, 0.269 mmol, 62% yield).

2,4,6-Trifluorophenyl 3-(diphenylphosphino)propanoate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.44 (m, 4H), 7.38–7.36 (m, 6H), 6.75 (t, J = 8.0 Hz, 2H), 2.73–2.67(m, 2H), 2.49–2.45 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P and ^{19}F-coupled; ^{1}H-decoupled, observed signals)** δ 169.9, 169.7, 160.8, 160.6, 160.5, 158.3, 158.2, 158.0, 156.5, 156.4, 156.4, 156.3, 154.0, 153.9, 153.9, 153.8, 137.4, 132.8, 132.6, 129.0, 128.7, 128.6, 124.0, 123.9, 101.1, 100.8, 100.6, 30.1, 29.9, 22.9, 22.8; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.6; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{21}H_{16}F_3O_2P+H)^+$ 389.0913, measured 389.0902.

Pentafluorophenyl 3-(diphenylphosphino)propanoate



A solution of 3-(dipheylphosphino)propanic acid (0.073 g, 0.281 mmol) in CH_2Cl_2 (2.0 mL) was cooled to 0 °C followed by the addition of pentafluorophenol (0.106 g, 0.576 mmol) and EDC hydrochloride (0.066 g, 0.337 mmol). The mixture was warmed gradually to room temperature and stirred overnight. The reaction mixture was quenched with water (5.0 mL) and extracted with CH_2Cl_2 (2 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 3% v/v EtOAc in hexanes, to give pentafluorophenyl 3-(diphenylphosphino)propanoate as a white solid (0.104 g, 0.246 mmol, 88% yield).

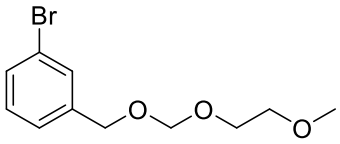
Pentafluorophenyl 3-(diphenylphosphino)propanoate : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.36 (m, 10H), 2.77–2.71 (m, 2H), 2.49–2.45 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P and ^{19}F-coupled; ^{1}H-decoupled, observed signals)** δ 169.2, 169.1, 142.4, 142.3, 140.7, 139.8, 139.7, 139.1, 137.2, 137.0, 132.8, 132.6, 129.1, 128.7, 128.7, 125.0, 30.1, 29.9, 22.9, 22.7; **^{31}P NMR**

(162 MHZ, $CDCl_3$) δ –16.8; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{21}H_{14}F_5O_2P+H)^+$ 425.0725, measured 425.0746.

6.1 Phosphinoester 1

The first functional groups tested to afford water solubility to the phosphine were $–CH_2N(Me)_2$ or $–O-(CH_2CH_2O)_2-CH_3$. With the tertiary amine, we observed decomposition of the 4-nitrophenol ester during column chromatography with $MeOH/CH_2Cl_2$ (1:1) as an elution solvent. With the ethylene glycol, we could not generate the requisite Grignard reagent. Accordingly, we tested $–CH_2OCH_2OCH_2CH_2OCH_3$ (methoxyethoxymethyl; MEM).

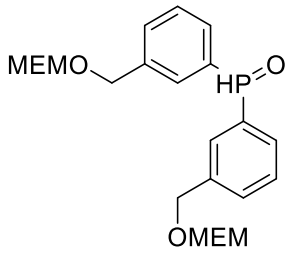
1-Bromo-3-[(2-methoxyethoxy)methoxymethyl]benzene



A solution of 3-bromobenzyl alcohol (10.012 g, 53.532 mmol) in THF (50 mL) was added slowly into a suspension of NaH (60%, 2.620 g, 53.467 mmol) in THF (50.0 mL) under N_2(g). The mixture was stirred for 1 h. Then, a solution methoxyethoxymethyl chloride (12.2 mL, of 106.935 mmol) in THF (30 mL) was added. The reaction mixture was stirred for another 8 h, and then quenched with water (20 mL). After condensation under reduced pressure, the residue was re-dissolved and extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes, to give 1-bromo-3-[(2-methoxyethoxy)methoxy]methyl]-benzene as a colorless liquid (11.920 g, 43.309 mmol, 81% yield).

1-Bromo-3-[(2-methoxyethoxy)methoxymethyl]benzene: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 7.2 Hz, 1H),), 7.21 (m, 1H) 7.7 Hz, 1H), 4.80 (s, 2H), 4.59 (s, 2H), 3.75 -3.73 (m, 2H), 3.58–3.56 (m, 2H), 3.39 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 140.2, 130.7, 130.7, 129.9, 126.2, 122.5, 94.9, 71.7, 68.4, 67.0, 59.0; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{11}H_{15}BrO_3+Na)^+$ 297.0097, measured 297.0089.

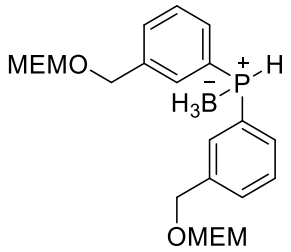
Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine oxide



Grinded Mg(s) (1.077 g, 44.875 mmol) was weighed in a two-neck round-bottom flask equipped with a condenser. The apparatus was flame-dried under vacuum and purged with N_2(g). A suspension of the Mg(s) in THF (15 mL) was activated by adding a few drops of 1,2-dibromoethane and heating to reflux. A solution of 1-bromo-3-[(2-methoxyethoxy)methoxymethyl]benzene (13.045 g, 47.436 mmol) in THF (50 mL) was added dropwise and with stirring to the refluxing solution, which turned dark yellow-green in color after 2 h. The reaction mixture was cooled to 0 °C, and diethyl phosphite (1.649 g, 11.946 mmol) in THF (10 mL) was added. The resulting solution was warmed gradually to room temperature and stirred for another 10 h. The reaction mixture was quenched with a saturated aqueous solution of ammonium chloride and acidified to pH 2 with 2 N HCl(aq). After condensation under reduced pressure, the residue was dissolved and extracted with CH_2Cl_2 (3 × 150 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 5% v/v MeOH in CH_2Cl_2 to give bis{3-[(2-methoxyethoxy)-methoxymethyl]phenyl}phosphine oxide as a colorless liquid (4.988 g, 11.389 mmol, 95% yield).

Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine oxide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, $J_{P\text{-}H}$= 481.6 Hz, 1H), 7.74 (d, J = 14.4 Hz, 2 H), 7.63–7.56 (m, 4H), 7.51–7.46 (m, 2H), 4.81 (s, 4H), 4.66 (s, 4H), 3.74–3.72 (m, 4H), 3.57–3.55 (m, 4H), 3. 39 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 139.0, 138.9, 131.9, 131.7, 130.8, 129.7, 129.6, 129.5, 128.9, 128.8, 94.9, 71.5, 68.5, 66.9, 58.9; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ 20.38; **HRMS** (ESI$^+$) *m*/*z* calculated for $(C_{22}H_{31}O_7P+H)^+$ 439.1881, measured 439.1891.

Borane bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine complex

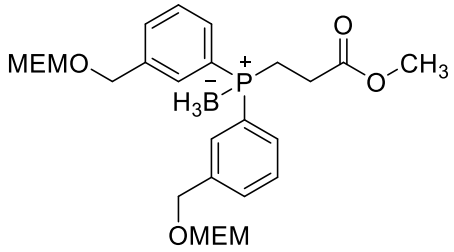


Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine oxide (2.041 g, 4.660 mmol) was dissolved in THF (40 mL) at 0 °C under N_2(g) and followed by adding borane-dimethyl sulfide (2.65 mL, 27.954 mmol). The reaction mixture was allowed to warm gradually to room

temperature and stirred for another 2 h before moving into ice bath and quenching with anhydrous MeOH (3.4 mL, 83.862 mmol) under N_2(g) (CAUTION: violent reaction). After 30 min, another portion of anhydrous MeOH (3.4 mL, 83.862 mmol) was adding for the completion of quenching the excess borane-dimethyl sulfide. The reaction mixture was concentrated under reduced pressure, re-dissolved with MeOH (30 mL), concentrated under reduced pressure again, washed with H_2O (20 mL), and extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes to give the borane bis{3-[(2-methoxyethoxy)methoxymethyl]-phenyl}phosphine complex as a colorless liquid (1.991 g, 4.567 mmol, 98% yield).

Borane bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine complex: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 11.6 Hz, 2 H), 7.60–7.54 (m, 2H), 7.52–7.49 (m, 2H), 7.46–7.41 (m, 2H), 6.31 (dq, J = 380.0, 7.0 Hz, 1H), 4.81 (s, 4H), 4.64 (s, 4H), 3.74–3.72 (m, 4H), 3.57-3.54 (m, 4H), 3.39 (s, 6H), 1.45–0.45 (br, 3H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 139.2, 139.1, 132.1, 132.0, 131.9, 131.8, 130.9, 129.1, 129.0, 126.5, 126.0, 95.0, 95.0, 71.6, 68.6, 66.97, 58.9; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ 0.92; **HRMS** (ESI$^-$) m/z calculated for $(C_{22}H_{34}BO_6P\text{-}H)^-$ 434.2149, measured 434.2167.

Borane methyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphino-propanoate complex

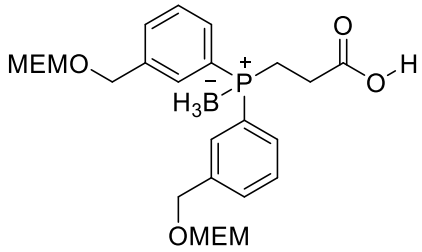


Borane bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine complex (1.024 g, 2.347 mmol) in MeOH (5 mL) was added slowly into the suspension of sodium methoxide (160 mg, 2.347 mmol) in anhydrous MeOH (10 mL) at 0 °C. After reacting at room temperature for 30 min, methyl acrylate (0.63 mL, 7.042 mmol) was dropwise adding into the reaction and kept reacting for ovrnight before quenching with water (5 mL). The reaction mixture was acidified to neutral by 2 N HCl(aq) and extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 70% v/v EtOAc in hexanes, to give borane methyl 3-bis{3-[(2-methoxyethoxy)-methoxymethyl]phenyl}phosphino-propanoate complex as a colorless liquid (871 mg, 1.669 mmol, 71% yield).

Borane methyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopro-panoate complex: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.66 (m, 2 H), 7.61–7.56 (m, 2H), 7.51–7.50 (m, 2H), 7.46–7.42 (m, 2H), 4.81 (s, 4H), 4.64 (s, 4H), 3.74–3.72 (m, 4H), 3.64 (s. 3H), 3.57–3.55 (m, 4H), 3.39 (s, 6H), 2.60–2.49 (m, 4H), 1.40–0.36 (br, 3H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 172.6, 172.4, 139.0, 139.0, 138.9, 131.2, 131.1,

131.0, 130.7, 129.0, 128.9, 128.80, 128.3, 94.9, 71.6, 68.6, 66.9, 58.9, 51.9, 27.6, 20.9, 20.5; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ 15.35; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{26}H_{40}BO_8P+NH_4)^+$539.2929, measured 539.2936.

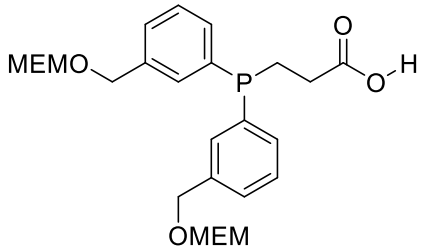
Borane 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid complex



Borane methyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoate complex (1.582 g, 3.222 mmol) was dissolved in MeOH (5 mL), and hydrolyzed by the addition of 7 N KOH(aq) (1.5 mL, 10.500 mmol) at room temperature. The reaction mixture was stirred for 30 min and then acidified to pH 2.0 with 2 N HCl. The reaction mixture was then concentrated under reduced pressure, and the residue was extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, washed with saturated aqueous NaCl, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 5% v/v MeOH in CH_2Cl_2, to give borane methyl 3-bis{3-[(2-methoxyethoxy)methoxy-methyl]phenyl}phosphinopropanoic acid complex as a white solid (1.604 mg, 3.158 mmol, 98% yield).

Borane 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid complex: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.66 (m, 2 H), 7.61–7.55 (m, 2H), 7.51–7.49 (m, 2H), 7.46–7.41 (m, 2H), 4.80 (s, 4H), 4.63 (s, 4H), 3.74–3.72 (m, 4H), 3.57–3.55 (m, 4H), 3.39 (s, 6H), 2.59–2.53 (m, 4H), 1.40–0.36 (br, 3H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 176.3, 176.1, 138.9, 138.8, 131.2, 131.1, 131.0, 130.7, 128.9, 128.8, 128.7, 128.1, 94.8, 71.5, 68.6, 66.8, 58.7, 27.5, 20.6, 20.2; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ 15.51; **HRMS** (ESI^-) *m*/*z* calculated for $(C_{25}H_{38}BO_8P\text{-}H)^-$ 506.2350, measured 506.2351.

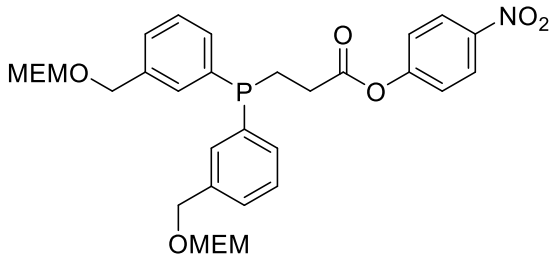
3-Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid



Borane 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid complex (871 mg, 1.715 mmol) was dissolved in the mixture of degas anhydrous MeOH (40 mL) and toluene (40 mL) under N_2(g), and heated to 60 °C for 4 h. The reaction mixture was concentrated under reduced pressure. The colorless liquid was found to be pure by ^{1}H-NMR analysis and used without further purification (820 mg, 1.660 mmol, 97% yield).

3-Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 6.4 Hz, 2H), 7.33–7.32 (m, 6H), 4.79 (s, 4H), 4.59 (s, 4H), 3.73–3.71 (m, 4H), 3.57–3.55 (m, 4H), 3.40 (s, 6H), 2.44–2.41 (m, 2H), 2.37–2.34 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 176.8, 176.7, 138.2, 138.1, 137.7, 137.6, 132.3, 132.2, 132.1, 131.9, 128.7, 128.7, 128.5, 94.9, 71.8, 69.2, 66.9, 59.1, 30.3, 30.1, 22.6, 22.5; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.40; **HRMS** (ESI$^+$) *m/z* calculated for $(C_{25}H_{35}O_8P+Na)^+$ 517.1962, measured 517.1988.

4-Nitrophenyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanate

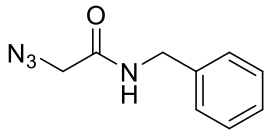


3-Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid (192 mg, 0.389 mmol) and 4-nitrophenol (60 mg, 0.428 mmol) were dissolved in CH_2Cl_2 (4 mL) under N_2(g) at 0 °C. After pouring *N*-(3-Dimethylaminopropyl)-*N′*-ethylcarbodiimide hydrochloride (84 mg, 0.428 mmol), the reaction mixture was removed to room temperature and stirred overnight. Then, the reaction mixture was quenched with water (5 mL) and extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes to give 4-nitrophenyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanate as a yellow liquid (172 mg, 0.280 mmol, 72% yield).

4-Nitrophenyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.35–7.32 (m, 6H), 7.25 (d, J = 8.4 Hz, 2H), 4.80 (s, 4H), 4.61 (s, 4H), 3.74–3.72 (m, 4H), 3.57–3.55 (m, 4H), 3.39 (s, 6H), 2.72–2.65 (m, 2H), 2.49–2.45 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$, ^{31}P-coupled; ^{1}H-decoupled, observed signals)** δ 170.6, 170.5, 155.2, 145.2, 138.3, 138.2, 137.4, 137.3, 132.2, 132.0, 131.9, 131.7, 128.7, 128.6, 128.5, 125.1, 122.3, 94.8, 94.8, 71.6, 69.0, 66.9, 58.9, 30.9, 30.7, 22.7, 22.6; **^{31}P NMR (162 MHZ, $CDCl_3$)** δ –16.68; **HRMS** (ESI$^+$) *m/z* calculated for $(C_{31}H_{38}NO_{10}P+H)^+$ 616.2307, measured 616.2313.

6.2 Azides

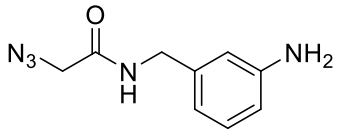
2-Azido-*N*-benzylacetamide



Benzylamine (0.56 mL, 5.162 mmol) was added into the solution of succinimidyl 2-azidoacetate[3] (1.012 g, 5.111 mmol) in CH_2Cl_2 (10 mL) at 0 °C under N_2(g) and stirred at room temperature for overnight. The reaction mixture was quenched with water (2 mL) and extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in Hexanes to give 2-azido-*N*-benzylacetamide (748 mg, 3.933 mmol, 77% yield) as a white solid.

2-Azido-*N*-benzylacetamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.28 (m, 5H), 4.48 (d, J = 5.8 Hz, 2H), 4.05 (s, 2H).

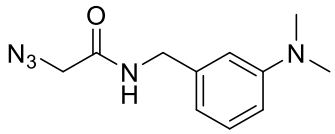
2-Azido-*N*-(3-aminobenzyl)acetamide



3-Aminomethylaniline (88 mg, 0.721 mmol), succinimidyl 2-azidoacetate (143 mg, 0.722 mmol), and DIEA (0.13 mL, 0.722 mmol) in anhydrous CH_2Cl_2 (5 mL) were used in the procedure for the synthesis of 2-azido-*N*-benzylacetamide. The residue was purified by column chromatography on silica gel, eluting with 70% v/v EtOAc in hexanes, to give the 2-azido-*N*-(3-aminobenzyl)acetamide as a white solid (129 mg, 0.629 mmol, 87% yield).

2-Azido-*N*-(3-aminobenzyl)acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (ddd, J = 7.7, 7.7, 0.9 Hz, 1H), 6.68–6.61 (m, 3H), 6.55 (br, 1H), 4.38 (d, J = 5.8 Hz, 2H), 4.05 (s, 2H), 3.71 (br, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 166.4, 146.8, 138.6, 129.7, 117.8, 114.4, 114.3, 52.6, 43.4; **HRMS** (ESI^+) m/z calculated for $(C_9H_{11}N_5O+H)^+$ 206.1037, measured 206.1044.

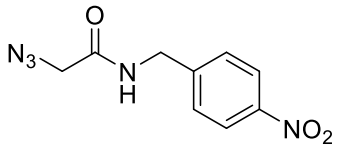
2-Azido-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide



N-[3-(Aminomethyl)phenyl]-*N*,*N*-dimethylamine (252 mg, 1.664 mmol), succinimidyl 2-azidoacetate (331 mg, 1.673 mmol), and DIEA (0.23 mL, 1.664 mmol) in anhydrous CH_2Cl_2 (5 mL) were used in the procedure for the synthesis of 2-azido-*N*-benzylacetamide. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes, to give the 2-azido-*N*-[3-(*N*,*N*-dimethylamino)-benzyl]acetamide as a yellow solid (351 mg, 1.504 mmol, 90% yield).

2-Azido-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (dd, J = 8.2, 8.2 Hz, 1H), 6.69–6.67 (m, 1H), 6.65–6.63 (m, 2H), 6.54 (br, 1H), 4.43 (d, J = 5.7 Hz, 2H), 4.04 (s, 2H), 2.96 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 166.3, 150.9, 138.1, 129.6, 115.9, 111.9, 111.9, 52.7, 44.1, 40.5; **HRMS** (ESI^+) *m/z* calculated for $(C_{11}H_{15}N_5O+H)^+$ 234.1350, measured 234.1349.

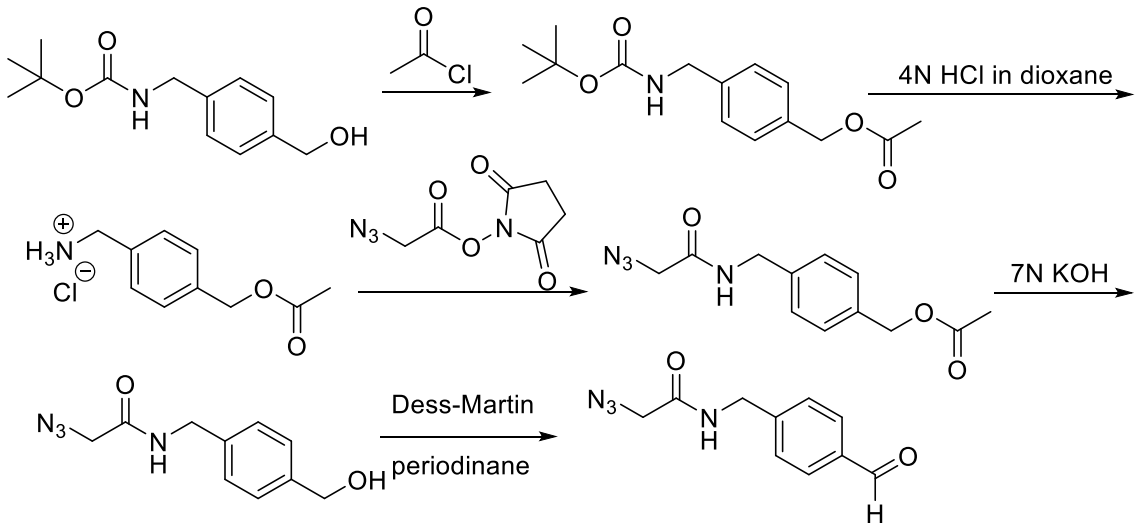
2-Azido-*N*-(4-nitrobenzyl)acetamide



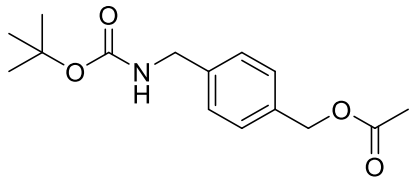
4-Nitrobenzylamine hydrochloride (259 mg, 1.325 mmol), succinimidyl 2-azidoacetate (282.5 mg, 1.427 mmol), and DIEA (0.46 mL, 2.651 mmol) in anhydrous CH_2Cl_2 (10 mL) were used in the procedure for the synthesis of 2-azido-*N*-benzylacetamide. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes, to give the 2-azido-*N*-(4-nitrobenzyl)acetamide as a yellow solid (363 mg, 1.544 mmol, 80% yield).

2-Azido-*N*-(4-nitrobenzyl)acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 8.7, 2H), 7.46 (d, J = 8.7 Hz, 2H), 6.81 (br, 1H), 4.59 (d, J = 6.3 Hz, 2H), 4.11 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 166.8, 147.4, 144.9, 128.3, 124.0, 52.6, 42.6; **HRMS** (EI^+) *m/z* calculated for $C_9H_9N_5O_3^+$ 205.0700, measured 235.0698.

Synthetic scheme for 2-azido-*N*-[4-(hydroxymethyl)benzyl]acetamide and 2-azido-*N*-(4-formylbenyl)acetamide



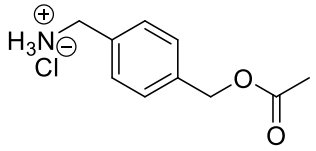
4-(*tert*-Butoxycarbonylaminomethyl)benzyl acetate



The synthesis of starting material 4-(*tert*-Butoxycarbonylaminoaminomethyl)benzyl alcohol was followed by the reference procedure,[4] and the ^{1}H-NMR spectrum was the same as report. The synthesized alcohol (980 mg, 4.130 mmol) was dissolved in CH_2Cl_2 (10 mL) with pyridine (0.33 mL, 4.130 mmol) and followed by adding acetic anhydride (1.95 g, 20.650 mmol) at room temperature. The reaction mwas stirred for 30 min, quenched with H_2O (8 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 20% v/v EtOAc in hexanes to give 4-(*tert*-butoxycarbonylaminomethyl)benzyl acetate (447 mg, 1.600 mmol, 39% yield) as a white solid.

4-(*tert*-Butoxycarbonylaminomethyl)benzyl acetate: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.34, 7.25 (ABq, J_{AB} = 7.9 Hz,4H), 7.13 (br, 1H), 5.08 (s, 2H), 4.22 (s, 2H), 2.06 (s, 3H), 1.45 (s, 9H); **^{13}C NMR (125 MHz, MeOH-d_4)** δ 172.7, 158.7, 141.2, 136.5, 129.6, 128.4, 80.4, 67.2, 44.9, 28.9, 21.0.

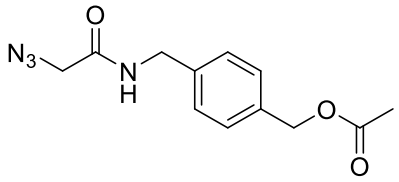
4-(Aminomethyl)benzyl acetate hydrochloride



4 N HCl in dioxane (4 mL, 16 mmol) was added to 4-(*tert*-butoxy-carbonylaminomethyl)benzyl acetate (447 mg, 1.598 mmol), and the resulting solution was stirred for 1 h at room temperature. The reaction mixture was concentrated under reduced pressure, and the crude product was dissolved in MeOH. Precipitation with diethyl ether gave 4-(aminomethyl)-benzyl acetate hydrochloride (301 mg, 1.396 mmol, 87% yield) as a white solid.

4-(Aminomethyl)benzyl acetate hydrochloride: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (br, 3H), 7.50 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 5.20 (s, 2H), 4.47 (s, 2H), 4.01 (s, 2H); **^{13}C NMR (125 MHz, DMSO-d_6)** δ 170.3, 136.6, 133.8, 129.0, 128.2, 65.0, 41.9, 20.7.

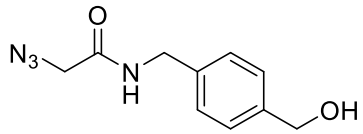
2-Azido-*N*-[4-(acetyloxymethyl)benzyl]acetamide



A suspension of 4-(aminomethyl)benzyl acetate hydrochloride (300 mg, 1.391 mmol) in CH_2Cl_2 (2 mL) was treated with DIEA (0.48 mL, 2.782 mmol), succinimidyl 2-azidoacetate (275 mg, 1.391 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for overnight before quenching with H_2O (3 mL). The solution was extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes, to give 2-azido-*N*-[4-(acetyloxymethyl)benzyl]acetamide as a white solid (244 mg, 0.930 mmol, 67% yield).

2-Azido-*N*-[4-(acetyloxymethyl)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35, 7.29 (ABq, J_{AB} = 8.1 Hz, 4H), 6.64 (br, 1H), 5.09 (s, 2H), 4.48 (d, J = 5.9 Hz, 2H), 4.05 (s, 2H), 2.10 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 170.8, 166.4, 137.5, 135.5, 128.7, 128.1, 65.9, 52.7, 43.1, 21.0; **HRMS** (ESI$^+$) m/z calculated for $(C_{12}H_{14}N_4O_3+NH_4)^+$ 280.1405, measured 280.1400.

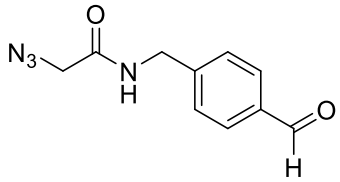
2-Azido-*N*-[4-(hydroxymethyl)benzyl]acetamide



2-Azido-*N*-[4-(acetyloxymethyl)benzyl]acetamide (206 mg, 0.785 mmol) was dissolved in MeOH (2 mL), and the resulting solution was added to 7 N KOH(aq) (0.12 mL, 0840 mmol) at room temperature, and the resulting solution was stirred for 1 h. The reaction mixture was acidified to pH 2 with 4 N HCl(aq) and then extracted with EtOAc (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 5% v/v MeOH in CH_2Cl_2 to give 2-azido-*N*-[4-(hydroxymethyl)benzyl]acetamide (166 mg, 0.754 mmol, 96% yield) as a white solid.

2-Azido-*N*-[4-(hydroxymethyl)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36, 7.29 (ABq, J_{AB} = 8.1 Hz, 4H), 6.61 (br, 1H), 4.70 (d, J = 5.9 Hz, 2H), 4.47 (d, J = 5.9 Hz, 2H), 4.05 (s, 2H), 1.75 (t, J = 5.9 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 166.4, 140.5, 136.8, 128.1, 127.4, 64.9, 52.7, 43.2; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{10}H_{12}N_4O_2+Na)^+$ 243.0853, measured 243.0865.

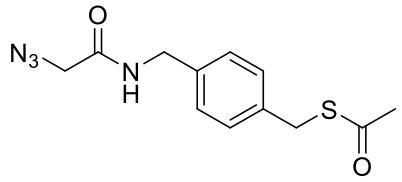
2-Azido-*N*-(4-formylbenyl)acetamide



2-Azido-*N*-[4-(hydroxymethyl)benzyl]acetamide (72 mg, 0.327 mmol) was dissolved in CH_2Cl_2 (5 mL), and to this solution was added Dess–Martin periodinane (138 mg, 0.327 mmol) and $NaHCO_3$(s) (137 mg). The resulting solution was stirred for 4 h. The reaction mixture was quenched with H_2O (2 mL) and extracted with EtOAc (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to give 2-azido-*N*-(4-formylbenzyl)acetamide (60 mg, 0.275 mmol, 84% yield) as a white solid.

2-Azido-*N*-(4-formylbenzyl)acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (s), 7.88 (d, J = 8.1 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 6.75 (br, 1H), 4.57 (d, J = 6.2 Hz, 2H), 4.11 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 191.7, 166.6, 144.3, 135.8, 130.2, 128.2, 52.7, 43.1; **HRMS** (EI^+) *m*/*z* calculated for $(C_{10}H_{10}N_4O_2\text{-}N_2)^+$ 190.0737, measured 190.0730.

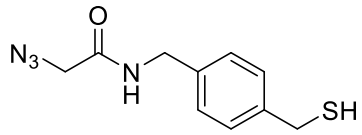
2-Azido-*N*-[4-(acetylmercaptomethyl)benzyl]acetamide



S-4-(Aminomethyl)benzyl ethanethiolate hydrochloride salt[5] (150 mg, 0.764 mmol), succinimidyl 2-azidoacetate (150 mg, 0.757 mmol), and triethylamine (0.21 mL, 1.528 mmol) in anhydrous CH_2Cl_2 (5 mL) were used in the procedure for the synthesis of 2-azido-*N*-[4-(acetyloxymethyl)benzyl]acetamide. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes, to give 2-azido-*N*-[4-(acetylmercaptomethyl)benzyl]acetamide as a white solid (178 mg, 0.640 mmol, 85% yield).

2-Azido-*N*-[4-(acetylmercaptomethyl)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28, 7.22 (ABq, J_{AB} = 8.1 Hz, 4H), 6.58 (br, 1H), 4.44 (d, J = 5.9 Hz, 2H), 4.10 (s, 2H), 4.05 (s, 2H), 2.35 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 195.1, 166.3, 137.4, 136.4, 129.3, 128.2, 52.7, 43.1, 33.0, 30.3; **HRMS** (ESI^+) *m/z* calculated for $(C_{12}H_{14}N_4O_2S+NH_4)^+$ 296.1176, measured 296.1170.

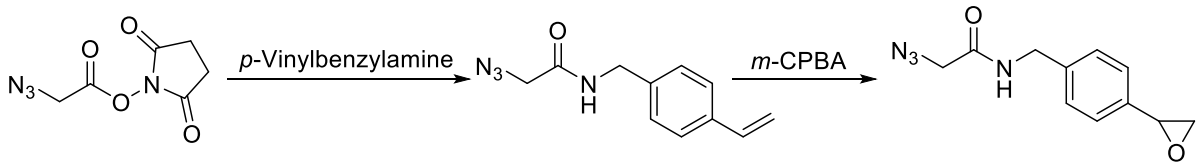
2-Azido-*N*-[4-(mercaptomethyl)benzyl]acetamide



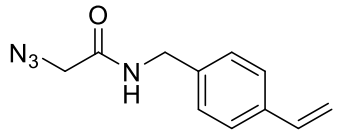
2-Azido-*N*-[4-(acetylmercaptomethyl)benzyl]acetamide (130 mg, 0.468 mmol) dissolved in MeOH (2 mL) was added to 7 N KOH(aq) (0.1 mL, 0.701 mmol) at room temperature and stirred for 1 h. The reaction mixture was acidified to pH 2 with 4 N HCl(aq) and extracted with EtOAc (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 3% v/v MeOH in CH_2Cl_2 to give 2-azido-*N*-[4-(mercaptomethyl)benzyl]acetamide (101 mg, 0.427 mmol, 91% yield) as a yellow solid.

2-Azido-*N*-[4-(mercaptomethyl)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31, 7.25 (ABq, J_{AB} = 7.8 Hz, 4H), 6.64 (br, 1H), 4.45 (d, J = 5.9 Hz, 2H), 4.01 (s, 2H), 3.74 (d, J = 7.6 Hz, 2H), 1.77 (t, J = 7.6 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 166.4, 140.8, 136.2, 128.5, 128.2, 52.6, 43.1, 28.6; **HRMS** (ESI^+) *m/z* calculated for $(C_{10}H_{12}N_4OS+NH_4)^+$ 254.1071, measured 254.1073.

Synthetic scheme for 2-azido-*N*-(4-vinylbenzyl)acetamide and 2-azido-*N*-(4-oxiranylbenzyl)acetamide



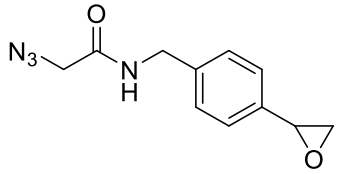
2-Azido-*N*-(4-vinylbenzyl)acetamide



p-Vinylbenzylamine (0.27 mL, 2.019 mmol) was added to a solution of succinimidyl 2-azidoacetate (400 mg, 2.019 mmol) in CH_2Cl_2 (2 mL) at 0 °C under N_2(g), and the resulting solution was stirred at room temperature for overnight. The reaction mixture was quenched with water (2 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 40% in EtOAc in hexanes to give 2-azido-*N*-(4-vinylbenzyl)acetamide (321 mg, 1.485 mmol, 74% yield) as a white solid.

2-Azido-*N*-(4-vinylbenzyl)acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.71 (dd, J = 17.5, 11.0 Hz, 1H), 6.60 (br, 1H), 5.75 (dd, J = 17.5, 0.9 Hz, 1H), 5.26 (dd, J = 11.0, 0.9 Hz, 1H), 4.46 (d, J = 5.5 Hz, 2H), 4.06 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 166.4, 137.2, 136.9, 136.2, 128.1, 126.6, 114.2, 52.7, 43.2; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{11}H_{12}N_4O+NH_4)^+$ 234.1350, measured 234.1345.

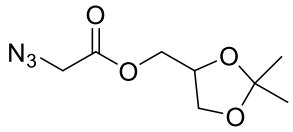
2-Azido-*N*-(4-oxiranylbenzyl)acetamide



2-Azido-*N*-(4-vinylbenzyl)acetamide (80 mg, 0.379 mmol) in CH_2Cl_2 (2 mL) was added to a solution of *m*-chloroperoxybenzoic acid (136 mg, 0.552 mmol) in CH_2Cl_2 (2 mL) at 0 °C under N_2(g), and the resulting solution was stirred at room temperature overnight. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to give 2-azido-*N*-(4-oxyranylbenzyl)acetamide (68 mg, 0.293 mmol, 77% yield) as a colorless solid.

2-Azido-*N*-(4-oxiranylbenzyl)acetamide: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.28,7.26 (ABq, J_{AB} = 8.3 Hz, 4H), 4.40 (s, 2H), 3.93 (s, 2H), 3.86 (dd, J = 4.1, 2.6 Hz, 1H), 3.11 (dd, J = 5.5, 4.1 Hz, 1H), 2.77 (dd, J = 5.5, 2.6 Hz, 1H); **^{13}C NMR (125 MHz, MeOH-d_4)** δ 170.3, 139.8, 138.5, 128.9, 127.0, 53.1, 53.1, 51.9, 43.9; **HRMS** (ESI^+) *m/z* calculated for $(C_{11}H_{12}N_4O_2+Na)^+$ 255.0853, measured 255.0844.

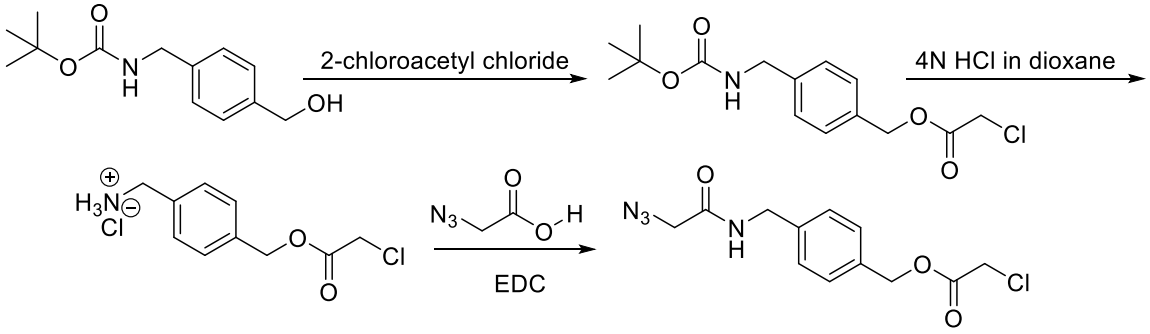
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-azidoacetate



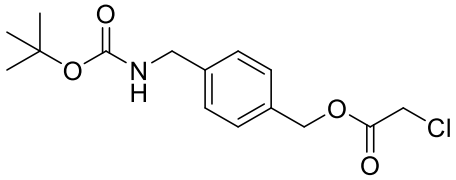
2,2-Dimethyl-1,3-dioxolane-4-methanol (260 mg, 1.967 mmol), succinimidyl 2-azidoacetate (300 mg, 1.515 mmol) in anhydrous CH_2Cl_2 (10 mL) were used in the procedure for the synthesis of 2-azido-*N*-benzylacetamide. The residue was purified by column chromatography on silica gel, eluting with 20% v/v EtOAc in hexanes, to give the (2,2-dimethyl-1,3-dioxolan-4-yl)methyl 2-azidoacetate as a white solid (267 mg, 1.242 mmol, 82% yield).

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-azidoacetate: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.38–4.34 (m, 1H), 4.32–4.28 (m, 1H), 4.23–4.19 (m, 1H), 4.11 (dd, J = 15.7, 8.6 Hz, 1H), 3.94 (s, 2H), 3.77 (dd, J = 8.6, 5.9 Hz, 1H), 1.44 (s, 3H), 1.37 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 168.2, 110.0, 73.2, 66.1, 65.9, 50.2, 26.6, 25.2; **HRMS** (EI^+) *m/z* calculated for $(C_8H_{13}N_3O_4-CH_3)^+$ 200.0666, measured 200.0659.

Synthetic scheme for 2-azido-*N*-{[4-(2-chloroacetyloxy)methyl]benzyl}acetamide



4-(*tert*-Butoxycarbonylaminomethyl)benzyl 2-chloroacetate

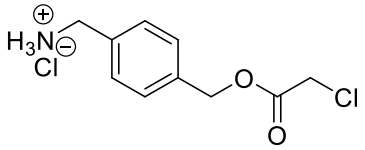


The synthesis of starting material 4-(*tert*-Butoxycarbonylaminoaminomethyl)benzyl alcohol was followed by the reference procedure[4], and the ^{1}H-NMR spectrum was the same as report. The

synthesized alcohol (1.079 g, 4.546 mmol) was dissolved in CH_2Cl_2 (10 mL) with pyridine (0.37 mL, 4.546 mmol) and followed by adding 2-chloroacetic anhydride (3.885 g, 22.73 mmol) at room temperature. The reaction mixture was stirred for 30 min, quenched with H_2O (8 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 20% v/v EtOAc in hexanes to give 4-(*tert*-butoxycarbonylaminomethyl)benzyl 2-chloroacetate (1.395 g, 4.190 mmol, 92% yield) as a white solid.

4-(*tert*-Butoxycarbonylaminomethyl)benzyl 2-chloroacetate: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.31, 7.28 (ABq, J_{AB} = 8.0 Hz,4H), 5.18 (s, 2H), 4.22 (s, 2H), 4.21 (s, 2H), 1.45 (s, 9H); **^{13}C NMR (125 MHz, MeOH-d_4)** δ 176.9, 165.4, 150.1, 143.4, 138.0, 136.7, 87.5, 76.5, 52.8, 50.8, 37.9; **HRMS** (ESI$^+$) *m*/*z* calculated for $(C_{15}H_{20}ClNO_4+Na)^+$ 336.0974, measured 336.0971.

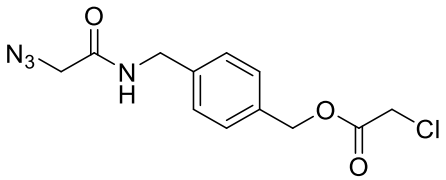
4-(Aminomethyl)benzyl 2-chloroacetate hydrochloride



4 N HCl in dioxane (0.89 mL, 3.540 mmol) was added in to the solution of 4-(*tert*-butoxycarbonylaminomethyl)benzyl 2-chloroacetate (550 mg, 1.753 mmol) in THF (2 mL) and stirred for 4 h at room temperature. The solvent was removed under reduced pressure, and the crude product was dissolved in MeOH. Precipitation with diethyl ether gave 4-(aminomethyl)-benzyl 2-chloroacetate hydrochloride (375 mg, 1.499 mmol, 86% yield) as a solid.

4-(Aminomethyl)benzyl 2-chloroacetate hydrochloride: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 (br, 3H), 7.50 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 5.20 (s, 2H), 4.47 (s, 2H), 4.01 (s, 2H); **^{13}C NMR (125 MHz, DMSO-d_6)** δ 167.3, 135.8, 134.1, 129.1, 128.3, 66.5, 41.9, 41.2; **HRMS** (ESI$^+$) *m*/*z* calculated for $(C_{10}H_{13}Cl_2NO_2\text{-}Cl)^+$ 214.0630, measured 214.0640.

2-Azido-*N*-{[4-(2-chloroacetyloxy)methyl]benzyl}acetamide

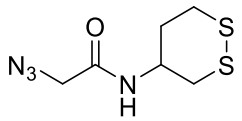


A suspension of 4-(aminomethyl)-benzyl 2-chloroacetate hydrochloride (100 mg, 0.400 mmol) in CH_2Cl_2 (2 mL) was treated with DIEA (0.14 mL, 0.800 mmol), 2-azidoacetic acid (56 mg, 0.554 mmol), and EDC (107 mg, 0.560 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight before quenching with H_2O (3 mL). The solution was extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, dried over

Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to give 2-azido *N*-[[4-[(2-chloroacetyloxy)methyl]phenyl]methyl]-acetamide (52 mg, 0.177 mmol, 44% yield based on hydrochloride salt) as a white solid.

2-Azido-*N*-{[4-(2-chloroacetyloxy)methyl]benzyl}acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34, 7.32 (ABq, J_{AB} = 8.2 Hz, 4H), 6.63 (br, 1H), 5.21 (s, 2H), 4.48 (d, J = 5.9 Hz, 2H), 4.10 (s, 2H), 4.06 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 167.1, 166.4, 138.0, 134.5, 129.0, 128.2, 67.5, 52.7, 43.1, 40.9; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{12}H_{13}ClN_4O_3+NH_4)^+$ 314.1015, measured 324.1001.

2-Azido-*N*-(3,4-dithianyl)acetamide



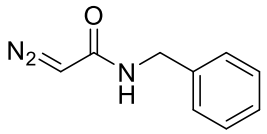
A suspension of 1,2-dithian-4-amine hydrochloride (50 mg, 0.292 mmol) in CH_2Cl_2 (2 mL) was treated with DIEA (87 μL, 0.585 mmol) and succinimidyl 2-azidoacetate (58 mg, 0.292 mmol) at 0 °C. The reaction mixture was removed to room temperature and stirred overnight before quenching with H_2O (3 mL). The solution was extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes to give 2-azido-*N*-(3,4-dithianyl)-acetamide (62 mg, 0.282 mmol, 97%) as a white solid.

2-Azido-*N*-(3,4-dithianyl)acetamide: ^{1}H NMR (500 MHz, DMSO-d_6 at 60 °C) δ 8.18 (d, J = 7.8, 1H), 3.93–3.87 (m, 1H), 3.82 (d, J = 1.8 Hz, 2H), 3.08–3.06 (m, 1H), 2.99–2.93 (m, 2H), 2.70 (dd, J = 13.2, 9.9 Hz, 1H), 2.13–2.07 (m, 1H), 1.78–1.70 (m, 1H); **^{13}C NMR (125 MHz, DMSO-d_6 at 60 °C, observed signals)** δ 166.0, 50.7, 46.7, 36.5, 33.0; **HRMS** (ESI^+) *m*/*z* calculated for $(C_6H_{10}N_4OS_2+NH_4)^+$ 236.0635, measured 236.0643.

6.3 Diazo Compounds/Experimental Procedures for Table 3

Equimolar amounts of phosphinoester **1** and an azide (~0.1 mmol, see below for details with a particular azide) were added to 1.0 mL of 10 mM sodium phosphate buffer, pH 7.0, and the resulting mixture was stirred for 6 h. The resulting clear yellow solution was quenched with 5 mL of saturated aqueous $NaHCO_3$ for another 8 h and extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, dried over Na_2SO_4(s), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the corresponding diazo compound.

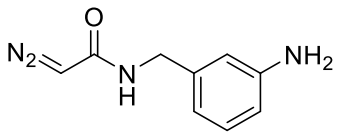
_N_-Benzyl-2-diazoacetamide



2-Azido-*N*-benzylacetamide (14 mg, 0.074 mmol) and phosphinoester **1** (45 mg, 0.074 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to give *N*-benzyl-2-diazoacetamide (11.7 mg, 0.068 mmol, 91%) as a yellow solid.

***N*-Benzyl-2-diazoacetamide: ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37–7.23 (m, 5H), 5.72 (br, 1H), 4.73 (s, 1H), 4.44 (d, J = 5.6 Hz, 2H).

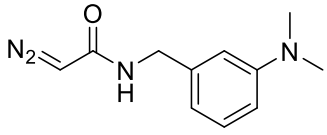
_N_-(3-Aminobenzyl)-2-diazoacetamide



2-Azido-*N*-(3-aminobenzyl)acetamide (13 mg, 0.063 mmol) and phosphinoester **1** (45 mg, 0.074 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 66% v/v EtOAc in hexanes to give *N*-(3-aminobenzyl)-2-diazoacetamide (11 mg, 0.058 mmol, 92%) as a yellow solid.

***N*-(3-Aminobenzyl)-2-diazoacetamide: ^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.11 (dd, J = 7.7, 7.7 Hz, 1H), 6.66–6.59 (m, 3H), 5.26 (br, 1H), 4.71 (s, 1H), 4.39 (s, 2H), 3.69 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 165.3, 146.8, 139.5, 129.7, 117.8, 114.3 (×2), 47.2, 44.0; **HRMS** (ESI^+) m/z calculated for $(C_9H_{10}N_4O+H)^+$ 191.0928, measured 191.0930.

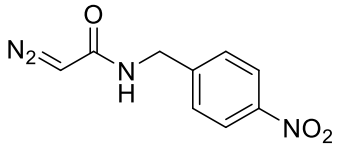
2-Diazo-_N_-[3-(_N_,_N_-dimethylamino)benzyl]acetamide



2-Azido-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide (21 mg, 0.091 mmol) and phosphinoester **1** (57 mg, 0.093 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes to give 2-diazo-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide (17 mg, 0.078 mmol, 86%) as a yellow solid.

2-Diazo-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (dd, J = 8.0, 8.0 Hz, 1H), 6.67–6.62 (m, 3H), 5.33 (br, 1H), 4.71 (s, 1H), 4.42 (s, 2H), 2.94 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 165.3, 151.0, 139.1, 129.5,111.9 (x 2), 47.0, 44.8, 40.5; **HRMS** (ESI^+) m/z calculated for $(C_{11}H_{14}N_4O+H)^+$ 219.1241, measured 219.1232.

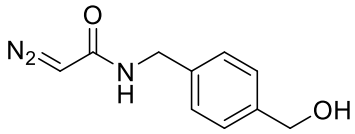
2-Diazo-*N*-(4-nitrobenzyl)acetamide



2-Azido-*N*-(4-nitrobenzyl)acetamide (18 mg, 0.077 mmol) and phosphinoester **1** (46 mg, 0.075 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 3% v/v MeOH in CH_2Cl_2 to give 2-diazo-*N*-(4-nitrobenzyl)acetamide (12 mg, 0.056 mmol, 72%) as a yellow solid.

2-Diazo-*N*-(4-nitrobenzyl)acetamide: ^{1}H NMR (500 MHz, MeOH-d_4) δ 8.21 (d, J = 8.7, 2H), 7.53 (d, J = 8.7 Hz, 2H), 5.22 (s, 1H), 4.52 (s, 2H); **^{13}C NMR (125 MHz, MeOH-d_4 at 45 °C)** δ 169.0, 148.8, 148.4, 129.4, 124.8, 47.9, 43.9; **HRMS** (ESI^+) m/z calculated for $(C_9H_8N_4O_3+H)^+$ 221.0670, measured 221.0674.

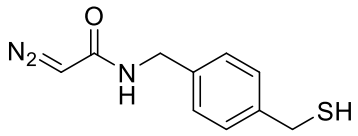
2-Diazo-*N*-[4-(hydroxymethyl)benzyl]acetamide



2-Azido-*N*-[4-(hydroxymethyl)benzyl]acetamide (23 mg, 0.105 mmol) and phosphinoester **1** (67 mg, 0.109 mmol) were used in the general procedure for the synthesis of diazo compounds, but before extracting with CH_2Cl_2, the aqueous solution was neutralized with saturated aqueous NH_4Cl. The residue was purified by column chromatography on silica gel, eluting with 3% v/v MeOH in CH_2Cl_2 to give 2-diazo-*N*-[4-(hydroxymethyl)-benzyl]acetamide (19 mg, 0.093 mmol, 88%) as a yellow solid.

2-Diazo-*N*-[4-(hydroxymethyl)benzyl]acetamide: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.30, 7.28 (ABq, J_{AB} = 7.9 Hz, 4H), 5.16 (s, 1H), 4.58 (s, 2H), 4.40 (s, 2H); **^{13}C NMR (125 MHz, MeOH-d_4)** δ 168.7, 141.9, 139.4, 128.7, 128.4, 65.1, 47.8, 44.3; **HRMS** (ESI^+) m/z calculated for $(C_{10}H_{11}N_3O_2+Na)^+$ 228.0744, measured 228.0744.

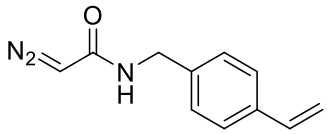
2-Diazo-*N*-[4-(mercaptomethyl)benzyl]acetamide



2-Azido-*N*-[4-(mercaptomethyl)benzyl]acetamide (15 mg, 0.062 mmol) and phosphinoester **1** (39 mg, 0.063 mmol) were used in the general procedure for the synthesis of diazo compounds. But before extracting with CH_2Cl_2, the aqueous solution was neutralized with $NH_4Cl_{(sat.)}$ solution. The residue was purified by column chromatography on silica gel, eluting with 3% v/v MeOH in CH_2Cl_2 to give 2-diazo-*N*-[4-(mercaptomethyl)-benzyl]acetamide (11 mg, 0.051 mmol, 82%) as a yellow solid.

2-Diazo-*N*-[4-(mercaptomethyl)benzyl]acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28, 7.26 (ABq, J_{AB} = 8.2 Hz, 4H), 5.28 (s, 1H), 4.72 (s, 1H), 4.46 (d, J = 5.7 Hz, 2H), 3.73 (d, J = 7.6 Hz, 2H), 1.75 (t, J = 7.6 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 165.3, 140.6, 137.1, 128.4, 128.2, 47.3, 43.7, 28.6; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{10}H_{11}N_3OS+H)^+$ 222.0696, measured 222.0690.

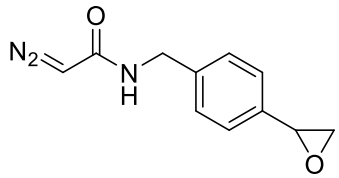
2-Diazo-*N*-(4-vinylbenzyl)acetamide



2-Azido-*N*-(4-vinylbenzyl)acetamide (14 mg, 0.065 mmol) and phosphinoester **1** (42 mg, 0.068 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to 2-diazo-N-(4-vinylbenzyl)acetamide (12 mg, 0.059 mmol, 90%) as a yellow solid.

2-Diazo-*N*-(4-vinylbenzyl)acetamide: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.39 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 6.71 (dd, J = 17.6, 10.9 Hz, 1H), 5.76 (dd, J = 17.6, 1.0 Hz, 1H), 5.20 (dd, J = 10.9, 1.0 Hz, 1H), 5.16 (s, 1H), 4.39 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 168.7, 140.0, 138.2, 137.9, 128.9, 127.5, 114.0, 47.8, 44.2; **HRMS** (ESI^+) *m*/*z* calculated for $(C_{11}H_{11}N_3O+H)^+$ 202.0975, measured 202.0984.

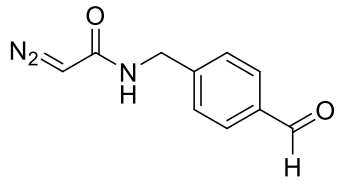
2-Diazo-*N*-(4-oxiranylbenzyl)acetamide



2-Azido-*N*-(4-oxiranylbenzyl)acetamide (18 mg, 0.078 mmol) and phosphinoester **1** (49 mg, 0.080 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to give 2-diazo-*N*-(4-oxiranylbenzyl)acetamide (14 mg, 0.064 mmol, 82%) as a yellow solid.

2-Diazo-*N*-(4-oxiranylbenzyl)acetamide: ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.27,7.25 (ABq, J_{AB} = 8.4 Hz, 4H), 5.16 (s, 1H), 4.40 (s, 2H), 3.85 (dd, J = 4.1, 2.6 Hz, 1H), 3.11 (dd, J = 5.5, 4.1 Hz, 1H), 2.78 (dd, J = 5.5, 2.6 Hz, 1H); **^{13}C NMR (125 MHz, MeOH-d_4)** δ 180.7, 140.5, 138.4, 128.8, 127.0, 53.1, 51.8, 47.8, 44.2; **HRMS** (ESI^+) m/z calculated for $(C_{11}H_{11}N_3O_2+NH_4)^+$ 235.1190, measured 235.1186.

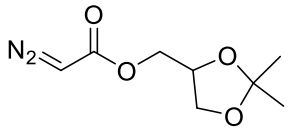
2-Diazo-*N*-(4-formylbenzyl)acetamide



2-Azido-*N*-(4-formylbenzyl)acetamide (22 mg, 0.101 mmol) and phosphinoester **1** (62 mg, 0.101 mmol) were used in the general procedure for the synthesis of **diazo compounds.** The residue was purified by column chromatography on silica gel, eluting with 40% v/v EtOAc in hexanes to 2-diazo-*N*-(4-formylbenzyl)acetamide (16 mg, 0.082 mmol, 81%) as a yellow solid.

2-Diazo-*N*-(4-formylbenzyl)acetamide: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s), 7.85 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 5.49 (br, 1H), 4.80 (s, 1H), 4.58 (d, J = 6.1 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 191.8, 156.8, 145.5, 135.6, 130.1, 128.0, 47.4, 43.5; **HRMS** (EI^+) m/z calculated for $(C_{10}H_9N_3O_2-H)^+$ 203.0690, measured 203.0698.

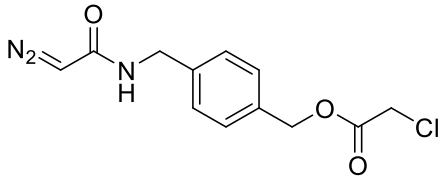
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-diazoacetate



(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-azidoacetate (26 mg, 0.121 mmol) and phosphinoester **1** (82 mg, 0.133 mmol) were used in the general procedure for the synthesis of diazo compounds**.** The residue was purified by column chromatography on silica gel, eluting with 25% v/v EtOAc in hexanes to give (2,2-dimethyl-1,3-dioxolan-4-yl)methyl 2-diazoacetate (17 mg, 0.086 mmol, 71%) as a yellow liquid. The starting material was recovered for (7 mg, 0.033 mmol, 27%)

(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-diazoacetate: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.36–4.31 (m, 1H), 4.27–4.21 (m, 1H), 4.20–4.16 (m, 1H), 4.09 (dd, J = 8.6, 6.6 Hz, 1H), 3.75 (dd, J = 8.6, 6.2 Hz, 1H), 1.44 (s, 3H), 1.37 (s, 3H); **^{13}C NMR (125 MHz, $CDCl_3$)** δ 168.2, 109.9, 73.6, 66.1, 64.9, 46.4, 26.6, 25.3; **HRMS** (EI^+) m/z calculated for $(C_8H_{12}N_2O_4+Na)^+$ 223.0690, measured 223.0699.

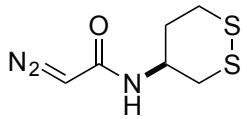
***N*-{[4-(2-Chloroacetyloxy)methyl]benzyl}-2-diazoacetamide**



2-Azido *N*-{[4-[(2-chloroacetyloxy)methyl]phenyl]methyl}acetamide (25 mg, 0.084 mmol) and phosphinoester **1** (54 mg, 0.089 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 50% v/v EtOAc in hexanes to *N*-{[4-(2-chloroacetyloxy)methyl]benzyl}-2-diazoacetamide (20 mg, 0.071 mmol, 84%) as a yellow solid.

***N*-{[4-(2-chloroacetyloxy)methyl]benzyl}-2-diazoacetamide: ^{1}H NMR (500 MHz, $CDCl_3$ at 65 °C)** δ 7.33, 7.29 (ABq, J_{AB} = 8.2 Hz, 4H), 5.22 (br, 1H), 5.19 (s, 2H), 4.68 (s, 1H), 4.47 (d, J = 5.9 Hz, 2H), 4.05 (s, 2H); **^{13}C NMR (125 MHz, $CDCl_3$ at 65 °C)** δ 167.0, 165.3, 139.0, 128.8, 128.0, 67.4, 46.9, 43.8, 40.7; **HRMS** (ESI^+) m/z calculated for $(C_{12}H_{12}ClN_3O_3+H)^+$ 282.0640, measured 282.0634.

2-Diazo-*N*-(3,4-dithianyl)acetamide



2-Azido-*N*-(3,4-dithianyl)acetamide (20 mg, 0.092 mmol) and phosphinoester **1** (60 mg, 0.098 mmol) were used in the general procedure for the synthesis of diazo compounds. The residue was purified by column chromatography on silica gel, eluting with 50% v/v in EtOAc in hexanes to 2-diazo-*N*-(3,4-dithianyl)acetamide (13 mg, 0.064 mmol, 70%) as a yellow solid.

2-Diazo-*N*-(3,4-dithianyl)acetamide: ^{1}H NMR (500 MHz, DMSO-d_6 at 65 °C, observed signals) δ 7.69 (br 0.67 H), 5.26 (s, 0.49H), 3.92–3.87 (m, 1H), 3.103.06 (m, 1H), 2.99–2.91 (m, 2H), 2.67–2.62 (m, 1H), 2.13–2.08 (m, 1H), 1.72–1.65 (m, 1H); **^{13}C NMR (125 MHz, DMSO-d_6 at 65 °C)** δ 163.8, 46.7, 45.8, 37.1, 33.3, 32.9; **HRMS** (ESI^+) *m*/*z* calculated for $(C_6H_9N_3OS_2+H)^+$ 204.0260, measured 204.0253.

7. References

(1) (a) Scott, R.; Vinogradov, S. *J. Phys. Chem.* **1969**, *73*, 1890-1897. (b) Pshezhetskii, V. S.; Murtazaeva, G. A.; Kabanov, V. A. *Eur. Polym. J.* **1974**, *10*, 571-580. (c) Ando, R. A.; Borin, A. C.; Santos, P. S. *J. Phys. Chem. A* **2007**, *111*, 7194-7199.

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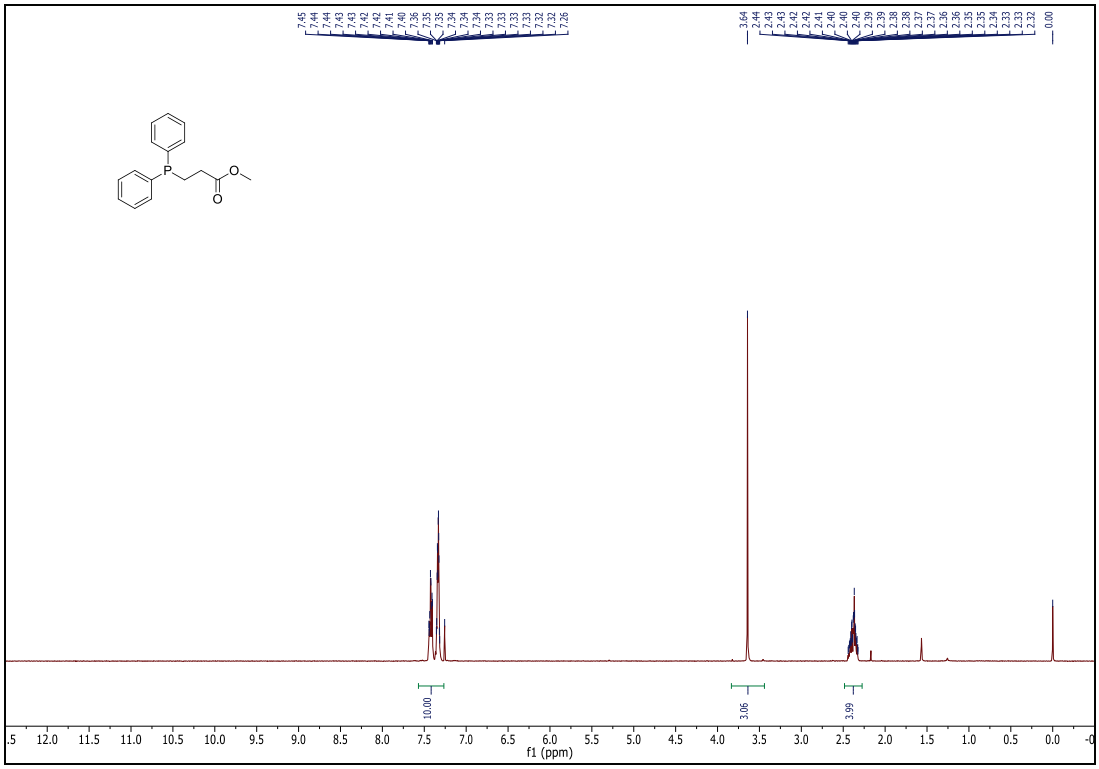
(3) Loka, R. S.; Sadek, C. M.; Romaniuk, N. A.; Cairo, C. W. *Bioconjugate Chem.* **2010**, *21*, 1842-1849.

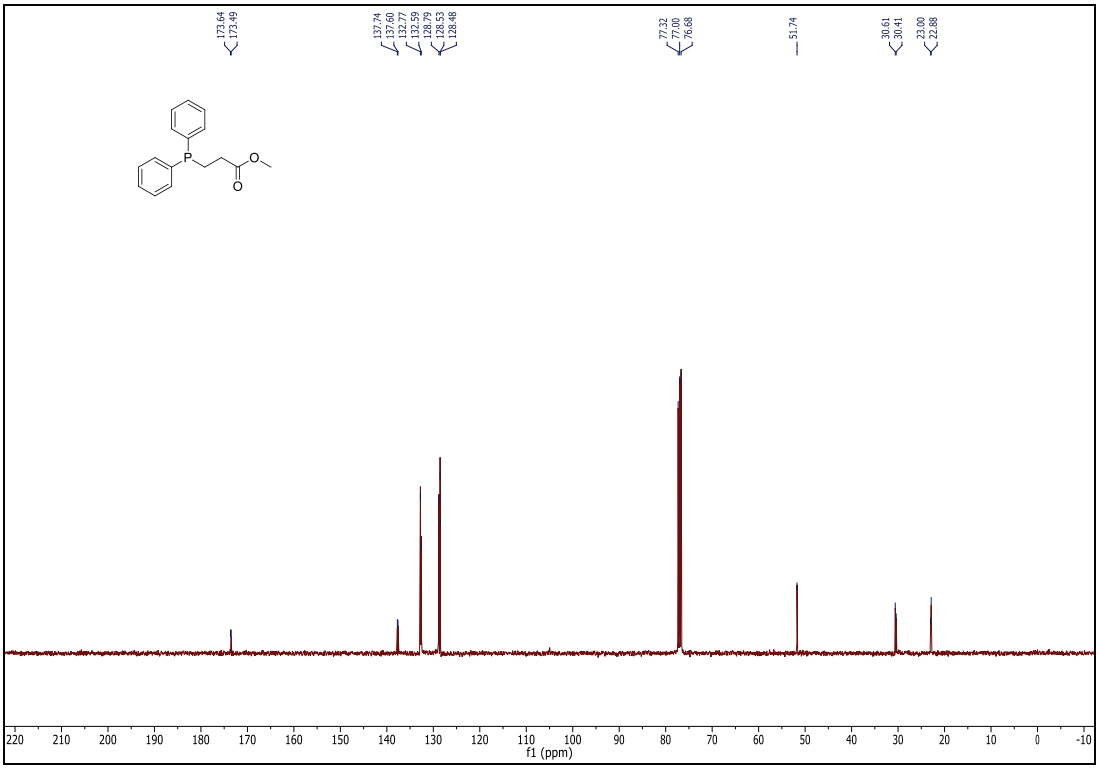
(4) (a) Zistler, A.; Koch, S.; Dieter Schluter, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, *0*, 501-508. (b) Yang, X.; Dai, C.; Dayan Calderon Molina, A.; Wang, B. *Chem. Commun.* **2010**, *46*, 1073-1075.

(5) Bernardes, G. J. L.; Casi, G.; Trüssel, S.; Hartmann, I.; Schwager, K.; Scheuermann, J.; Neri, D. *Angew. Chem. Int. Ed.* **2012**, *51*, 941-944.

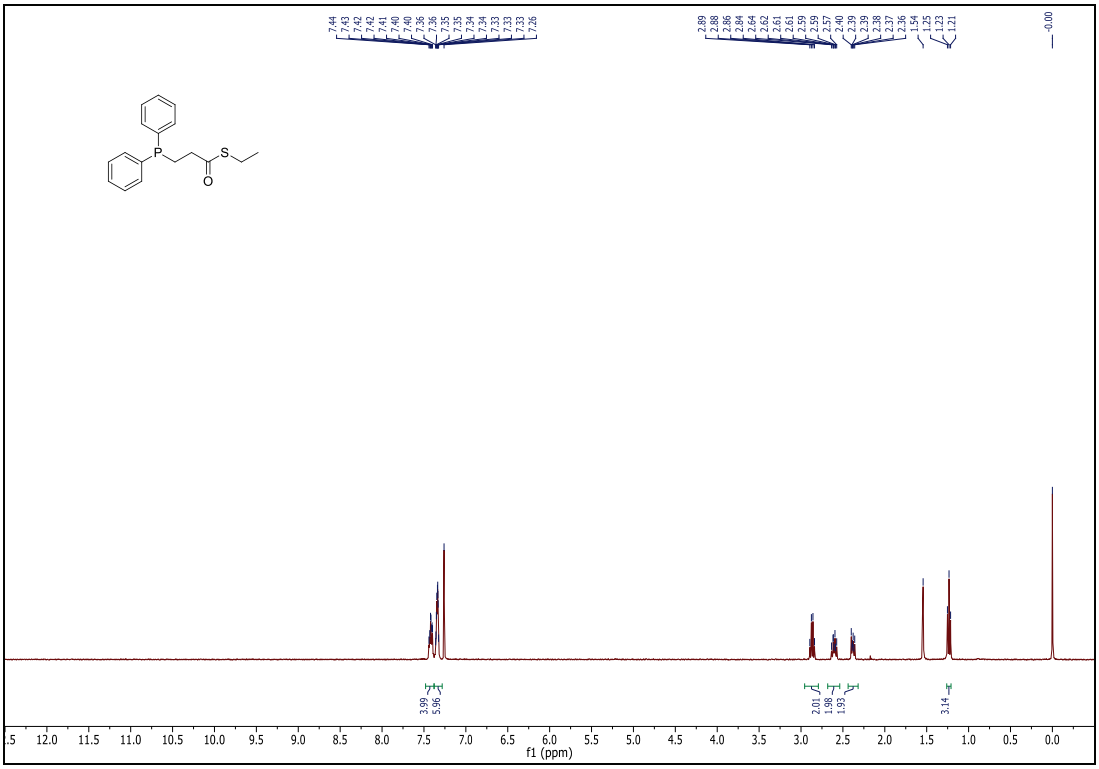
8. NMR Spectra

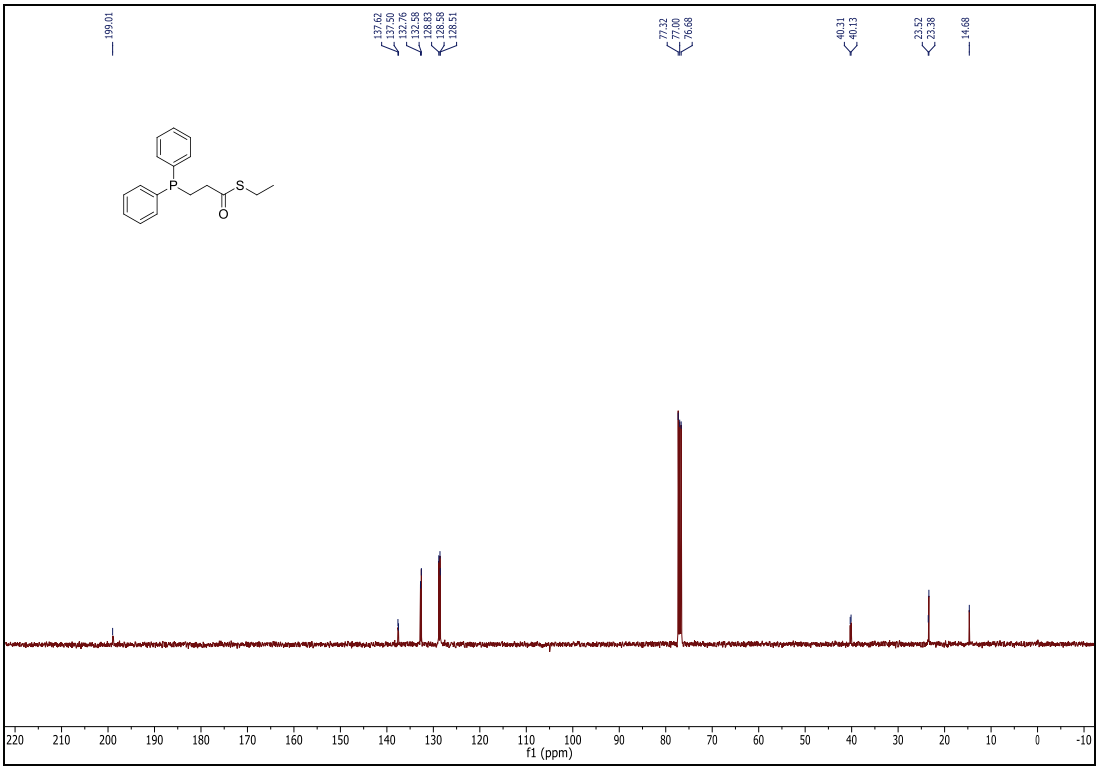
Methyl 3-(diphenylphosphino)propanoate



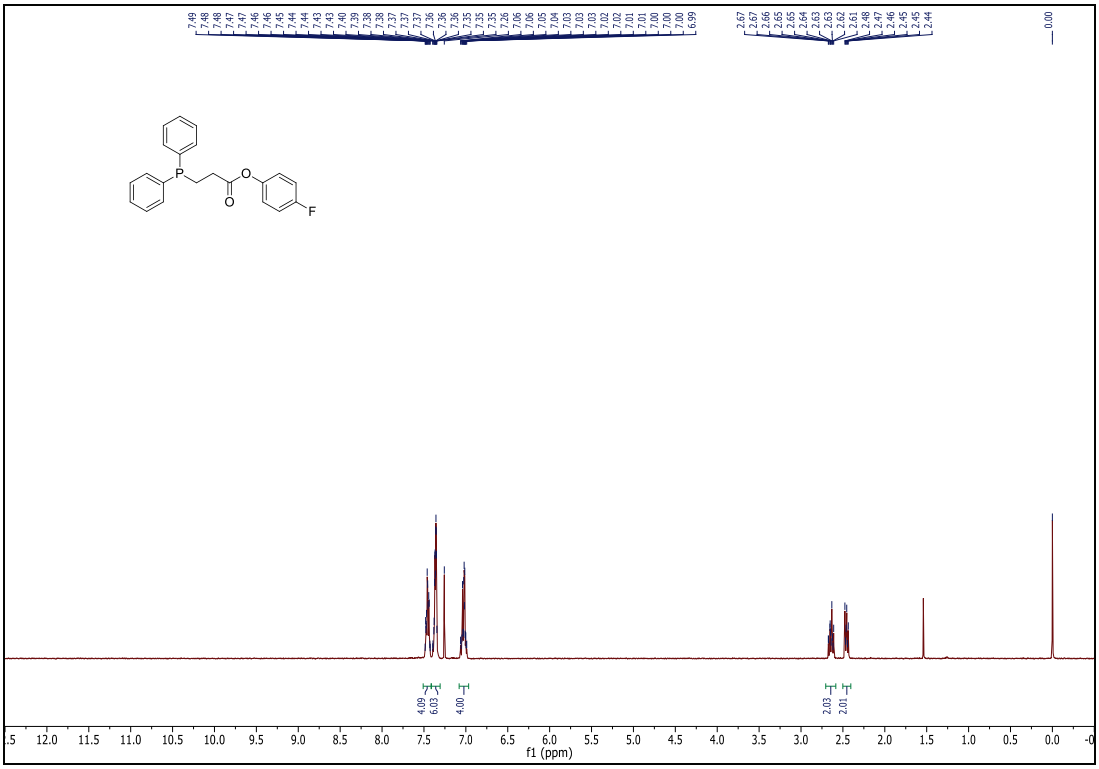


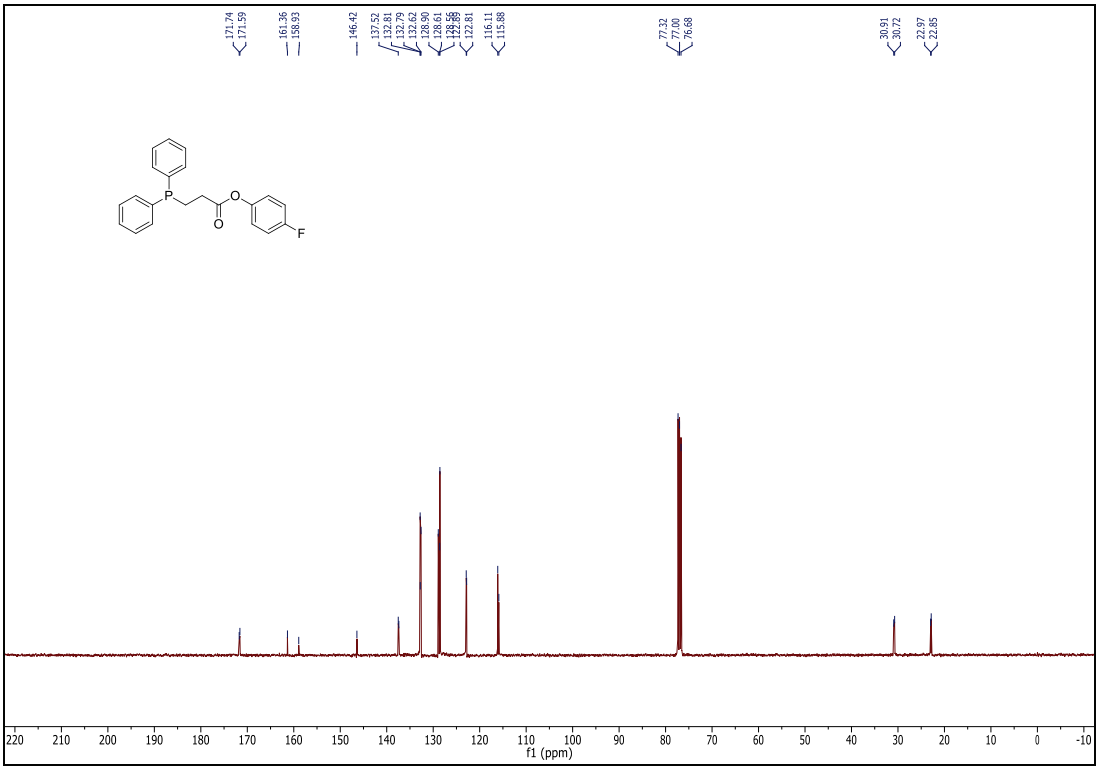
Ethyl 3-(diphenylphosphino)propanethioate



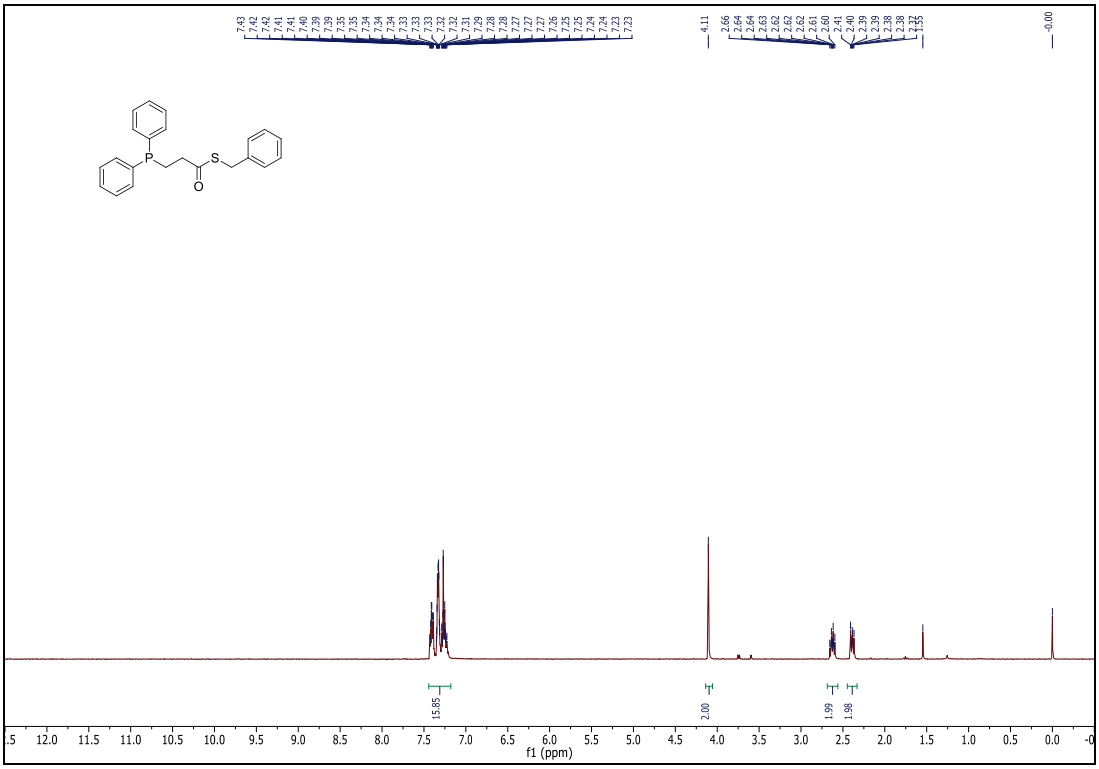


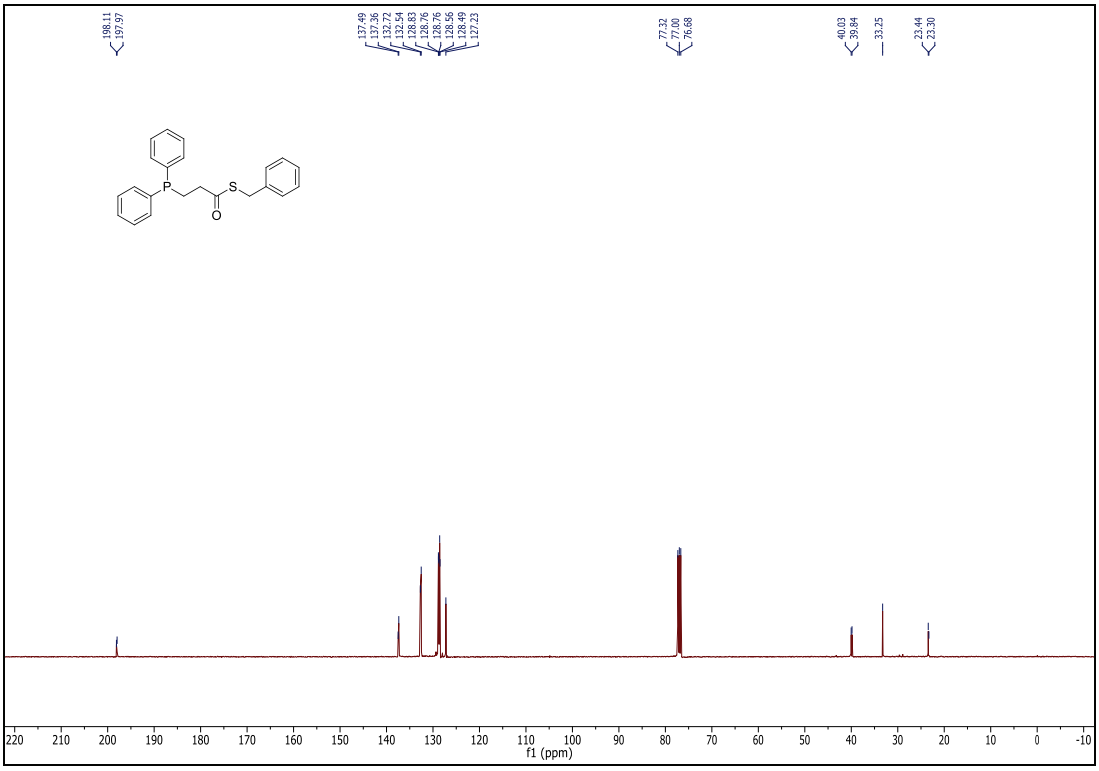
4-Fluorophenyl 3-(diphenylphosphino)propanoate



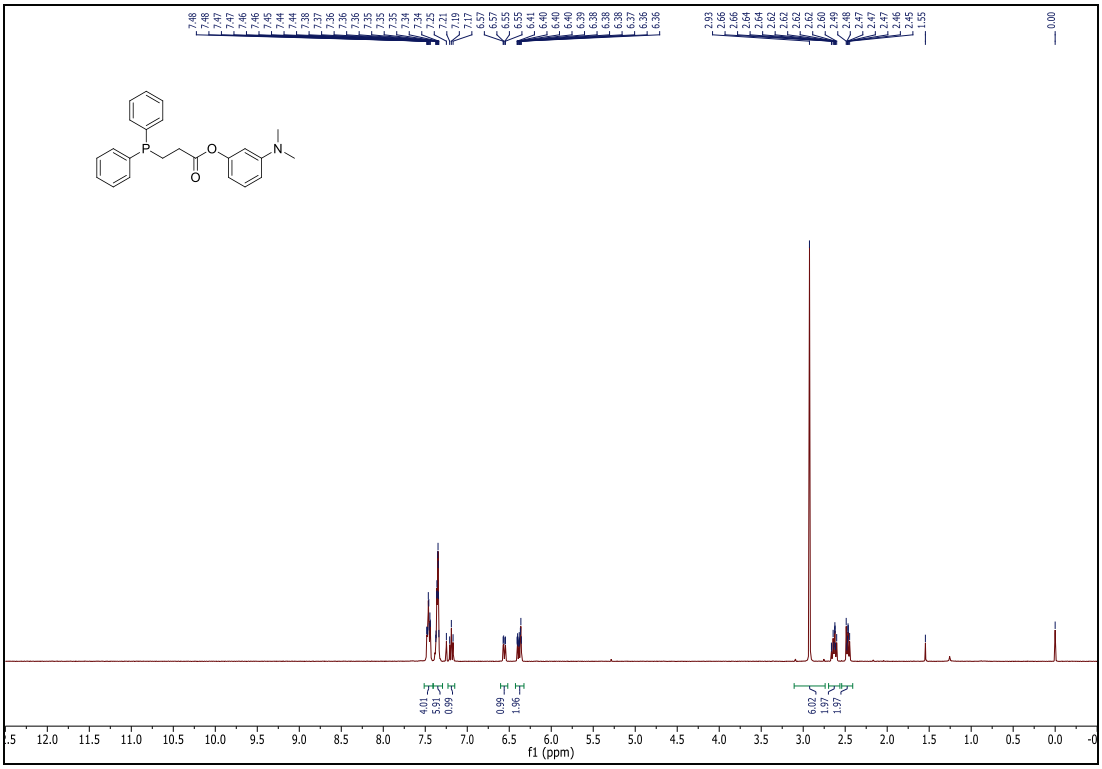


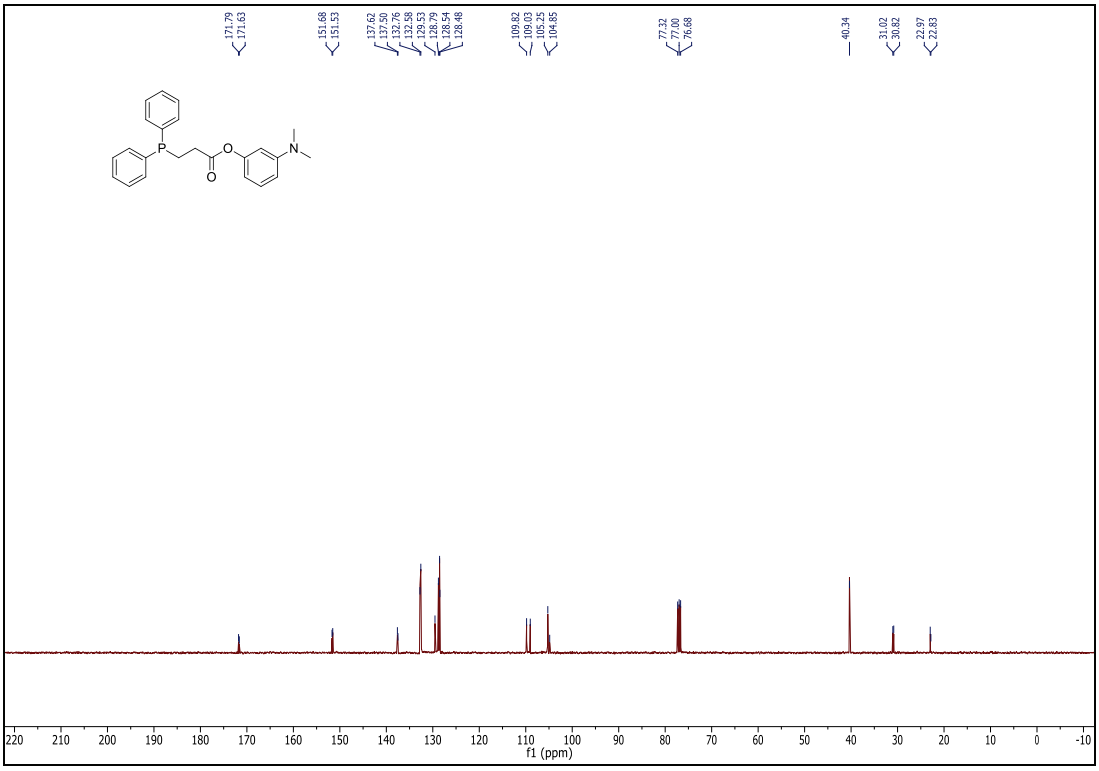
S-Benzyl 3-(diphenylphosphino)propanethioate



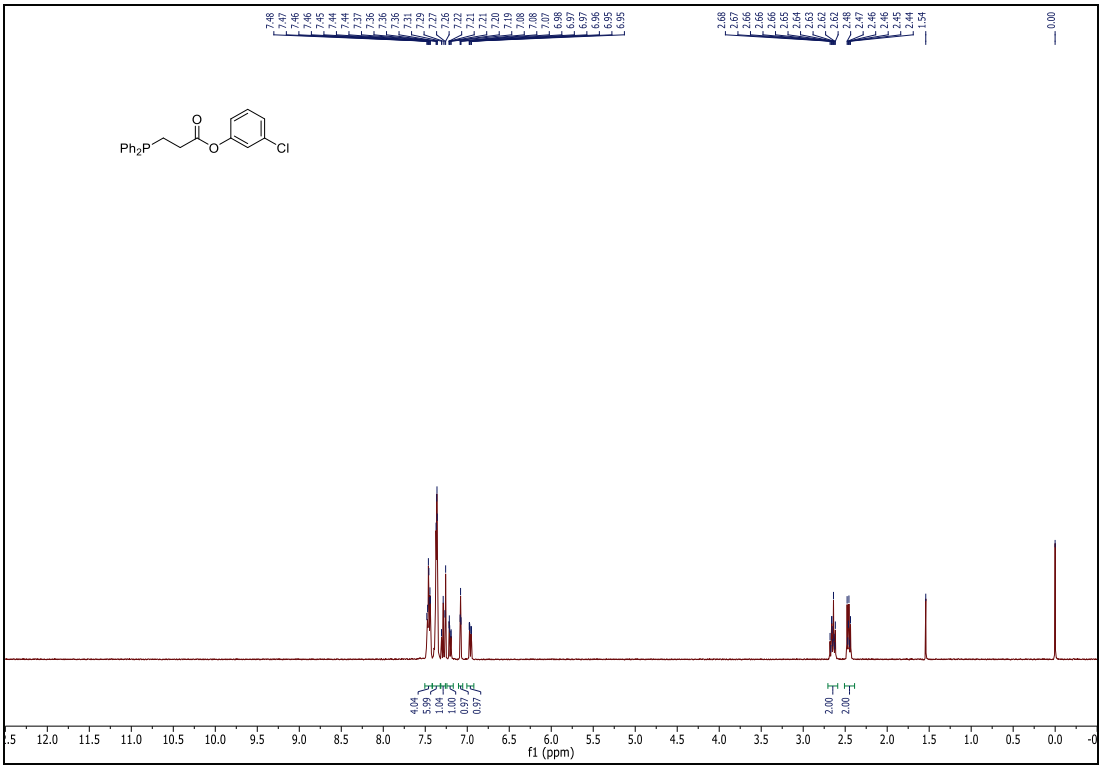


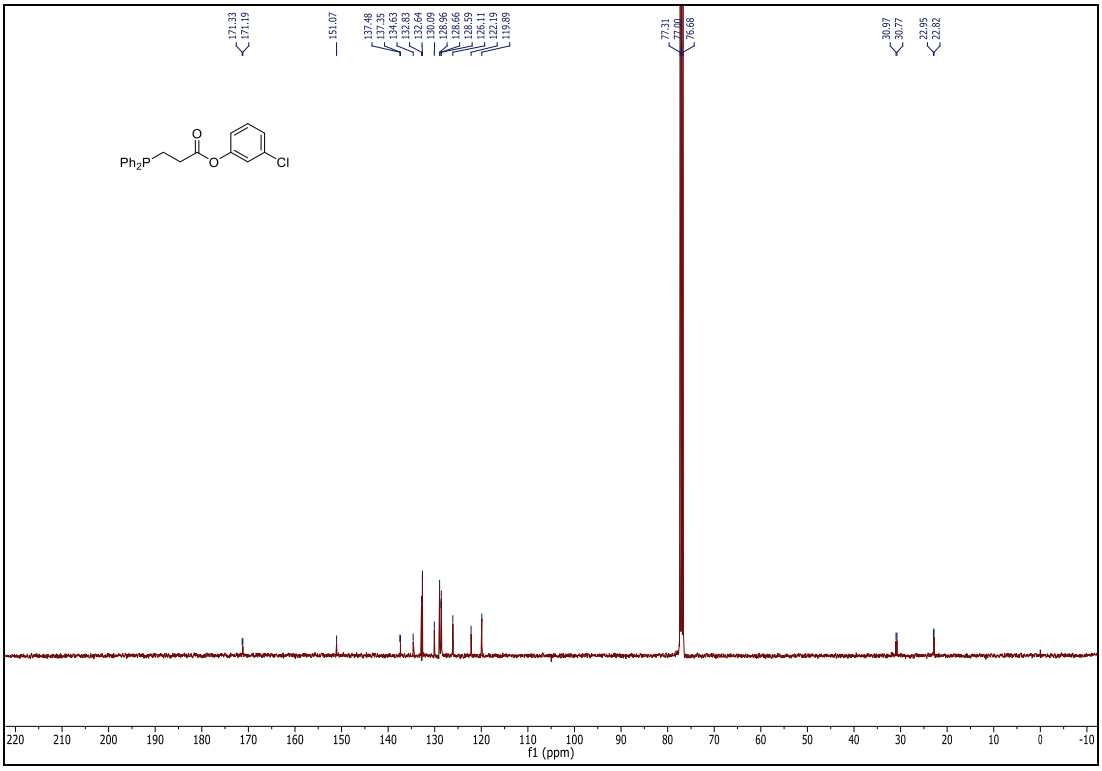
3-(Dimethylamino)phenyl 3-(diphenylphosphino)propanoate



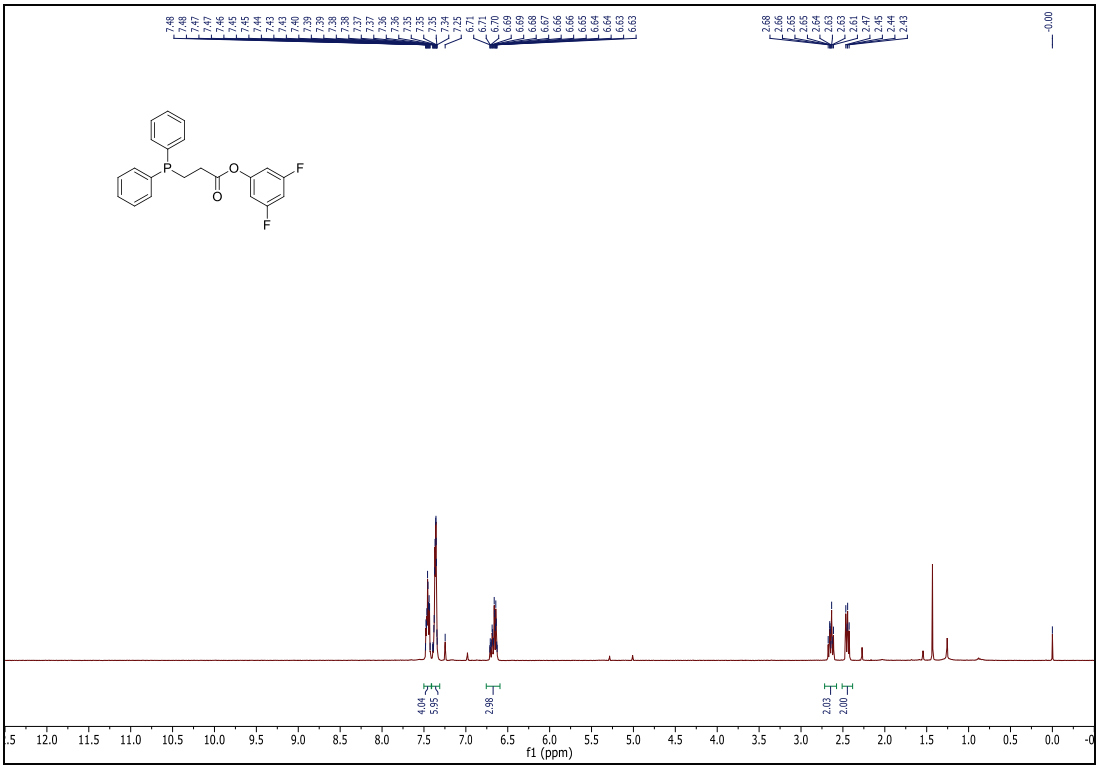


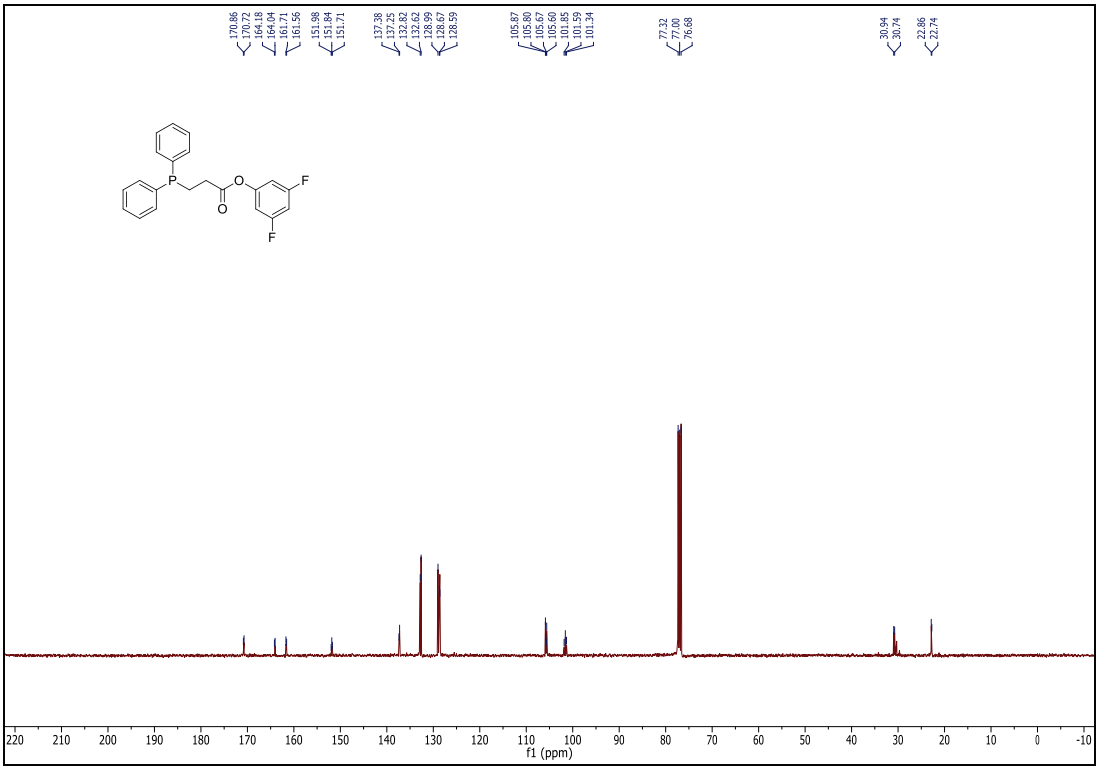
3-Chlorophenyl 3-(diphenylphosphino)propanoate



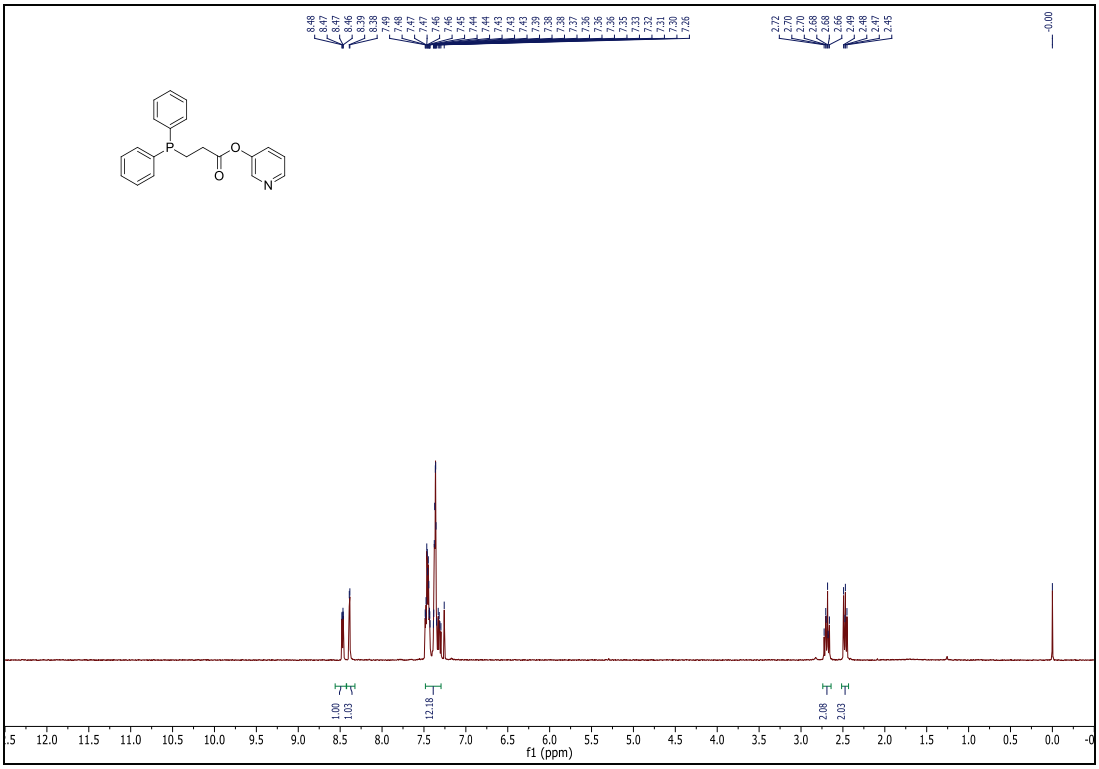


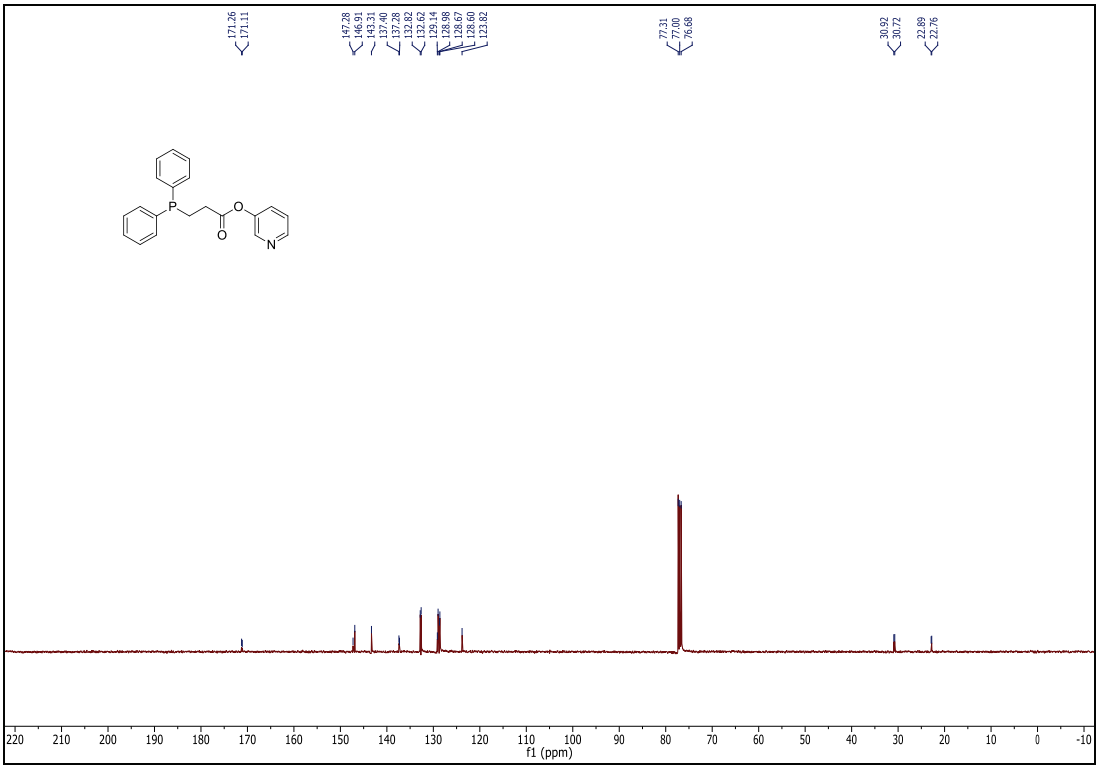
3,5-Difluorophenyl 3-(diphenylphosphino)propanoate



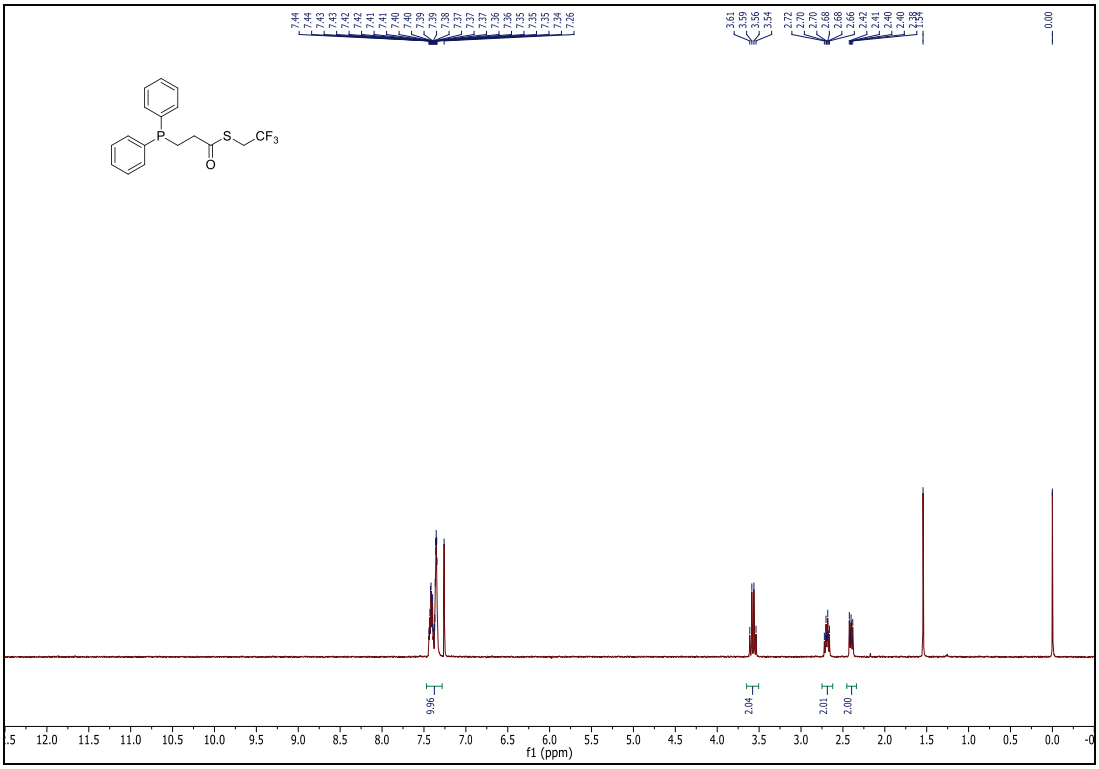


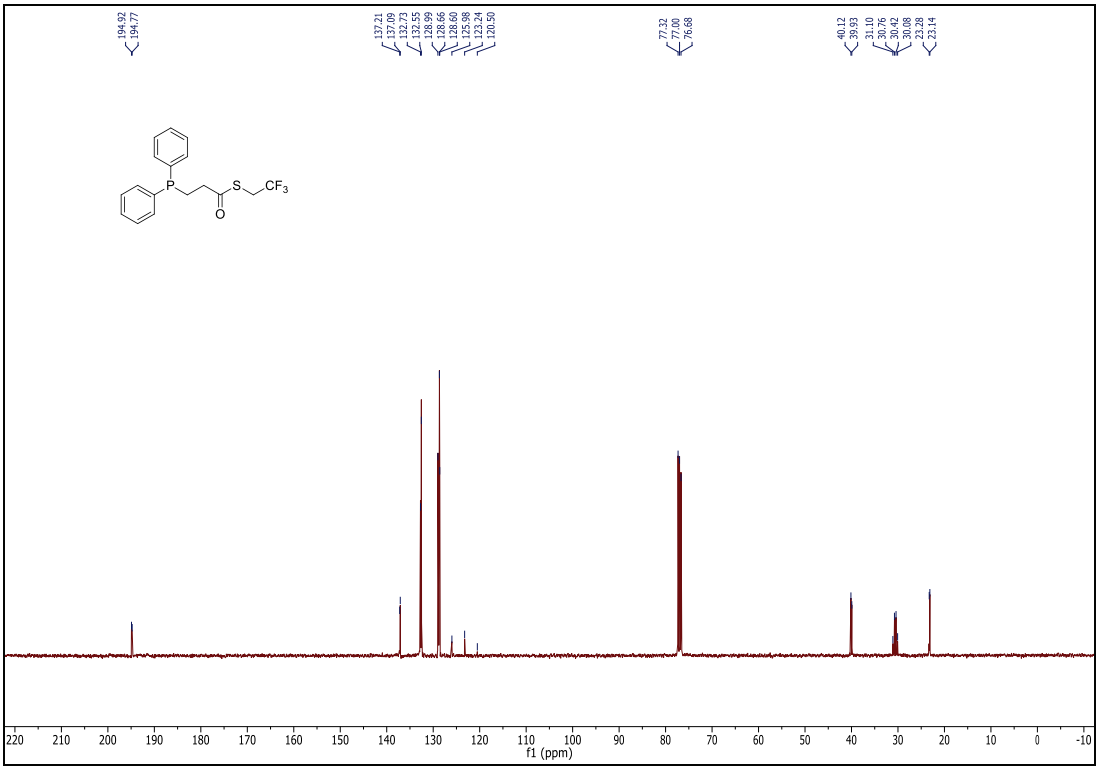
3-Pyridyl 3-(diphenylphosphino)propanoate



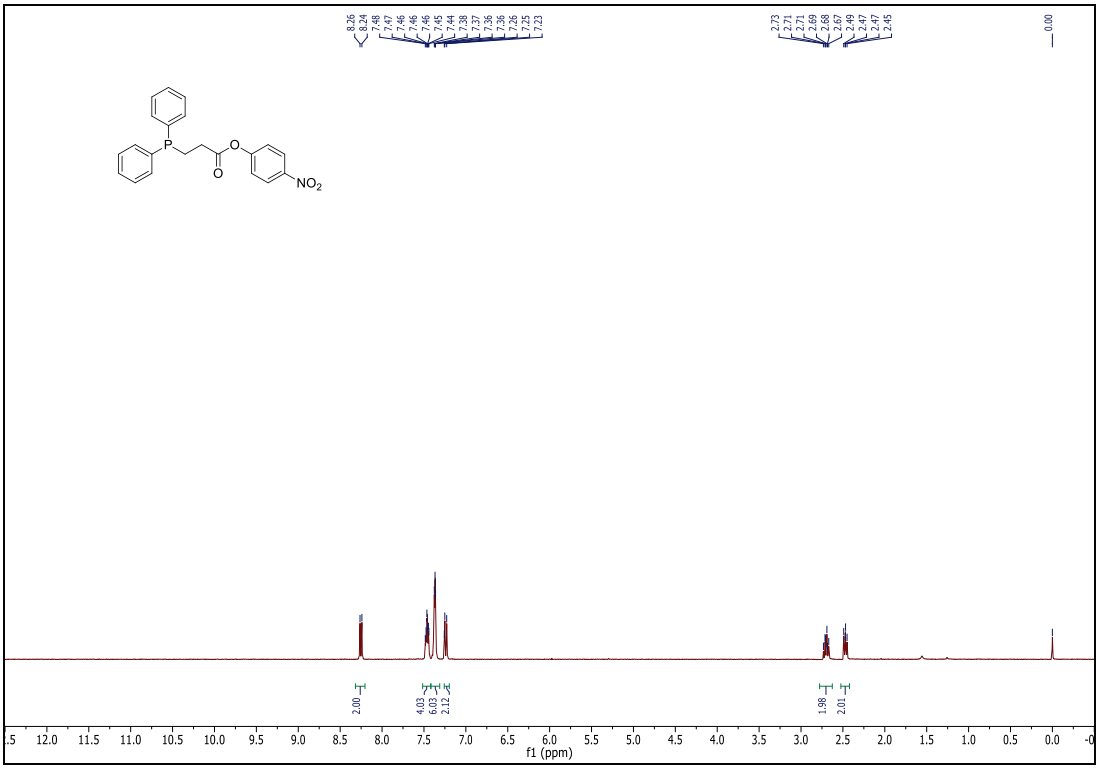


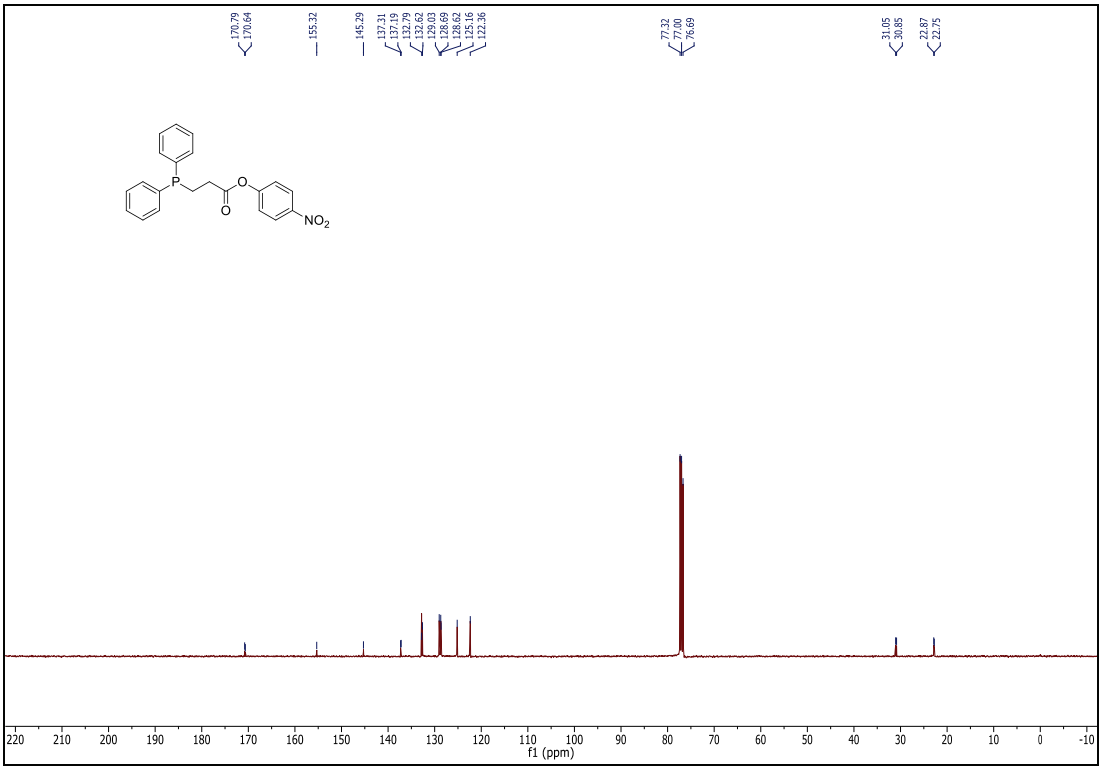
S-2,2,2-Trifluoroethyl 3-(diphenylphosphino) propanethioate



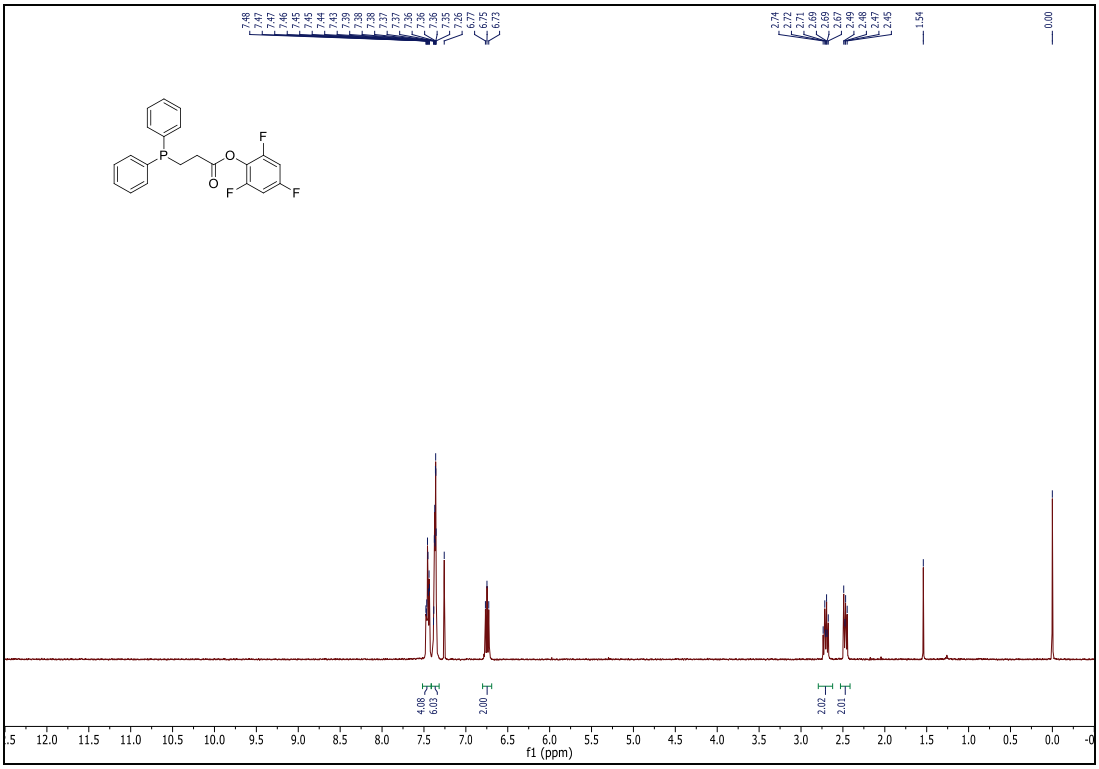


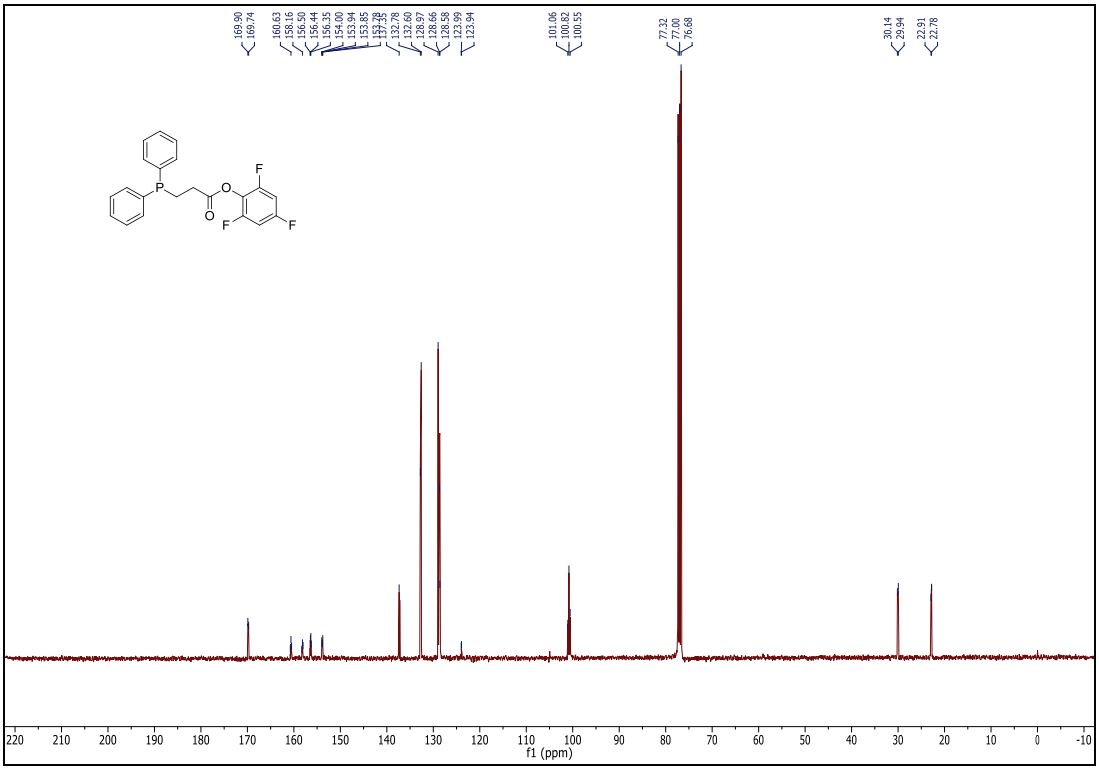
4-Nitrophenyl 3-(diphenylphosphino)propanoate



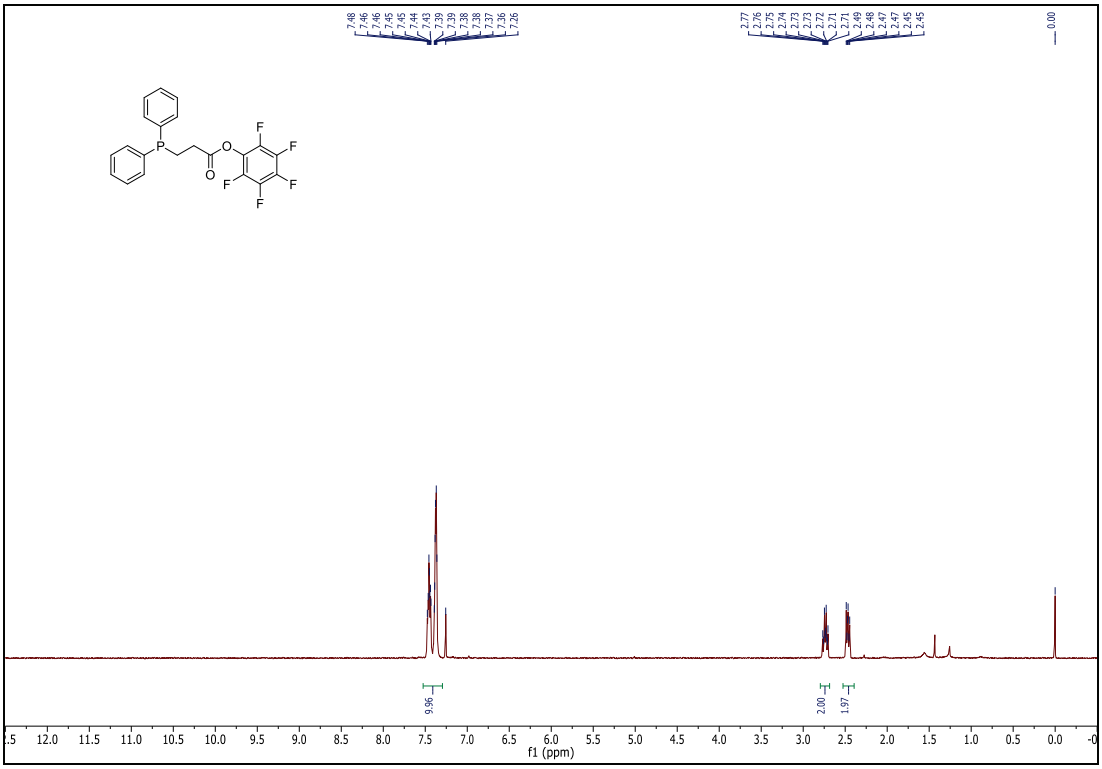


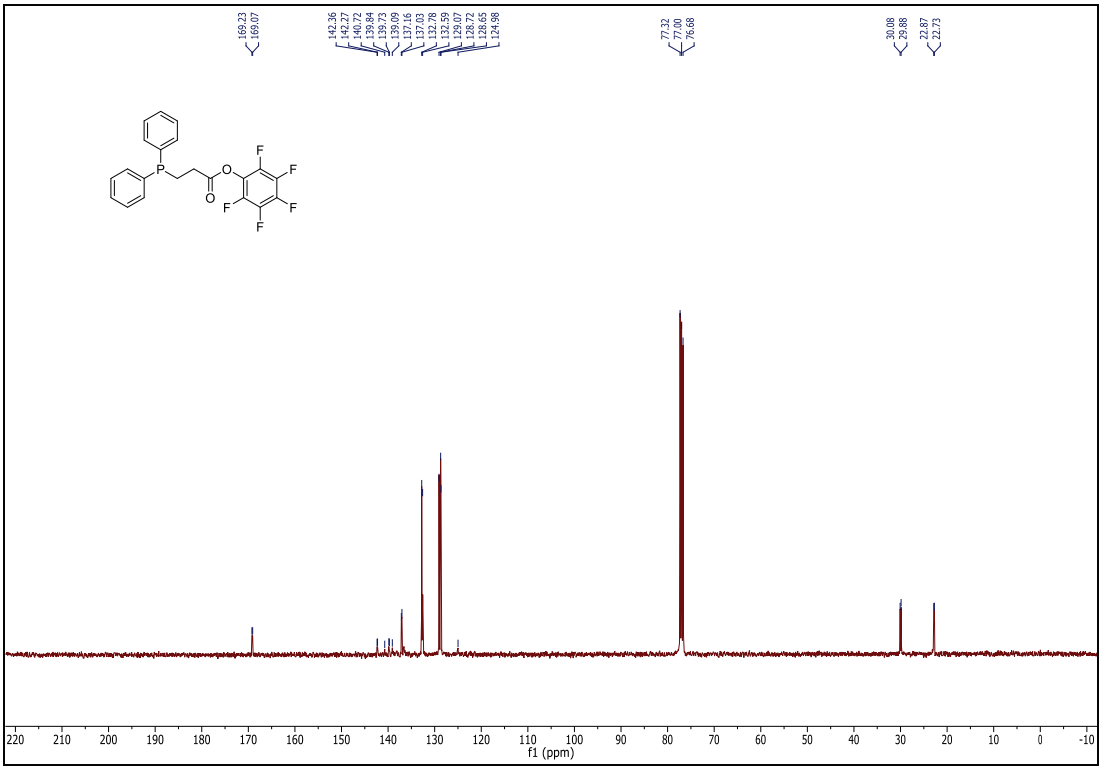
2,4,6-Trifluorophenyl 3-(diphenylphosphino)propanoate



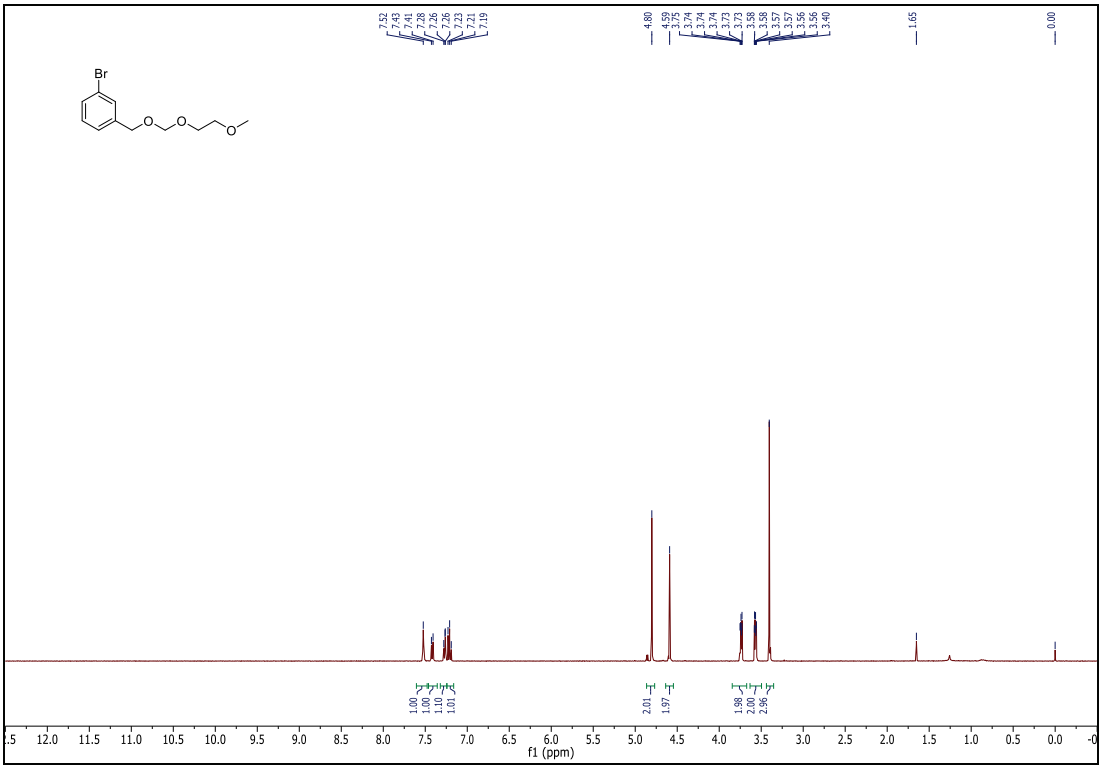


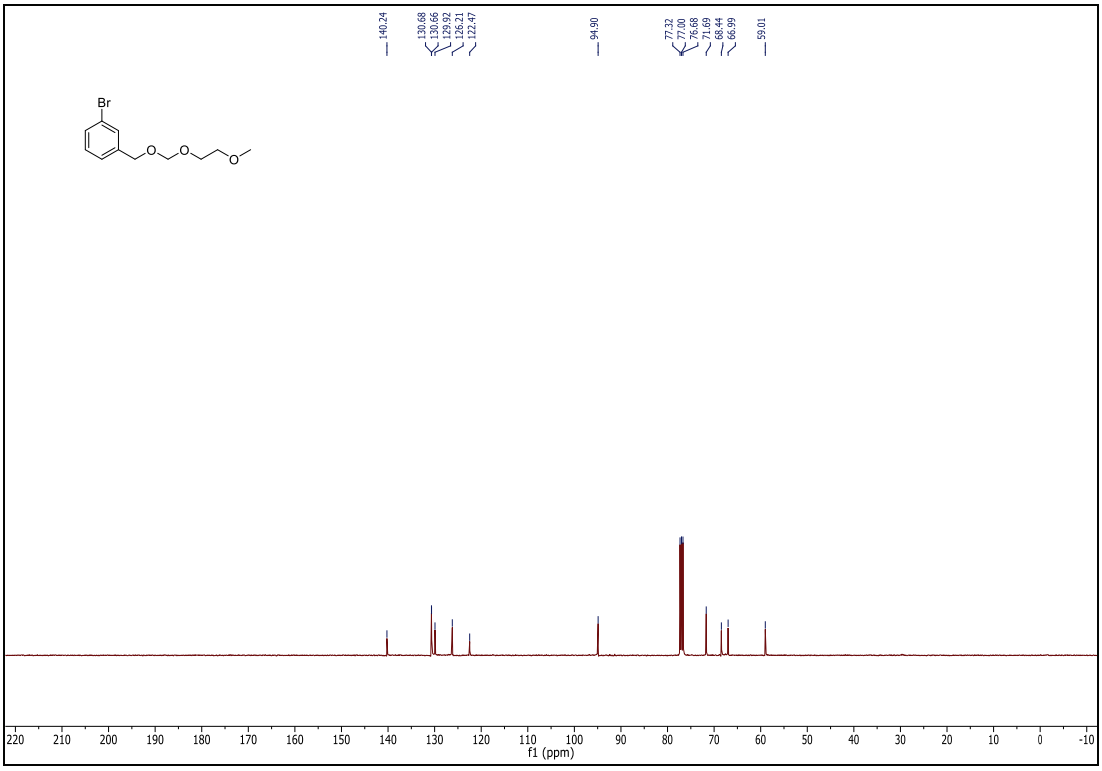
Pentafluorophenyl 3-(diphenylphosphino)propanoate



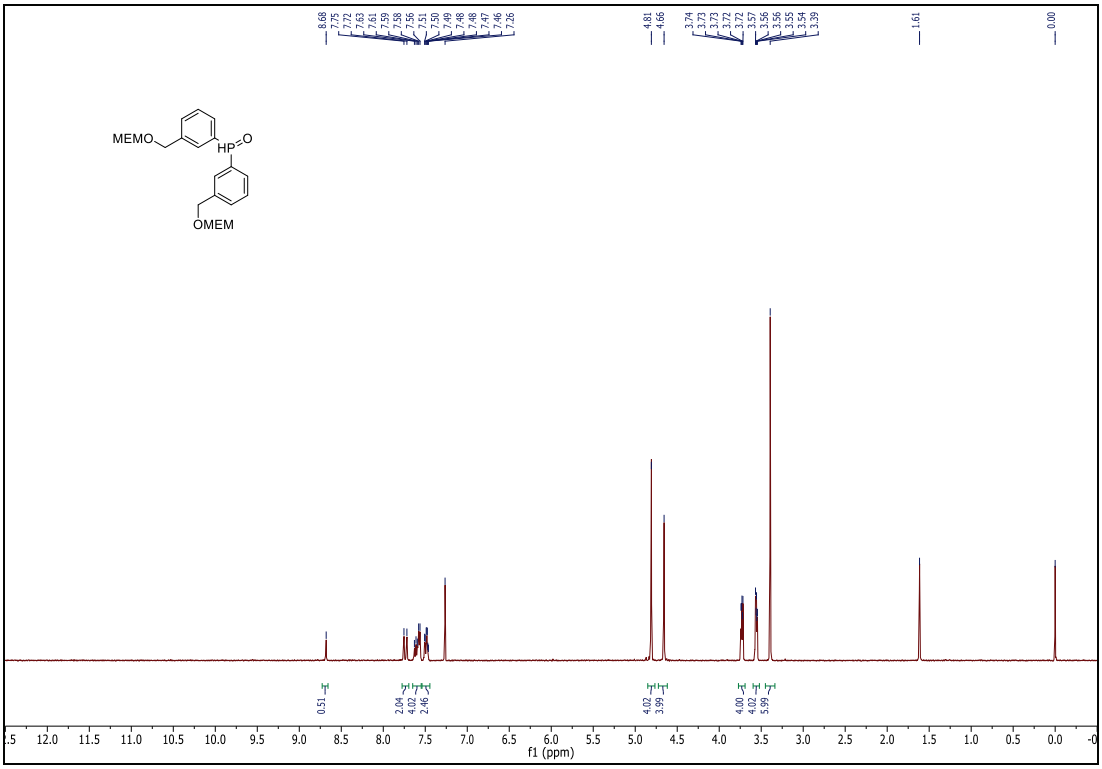


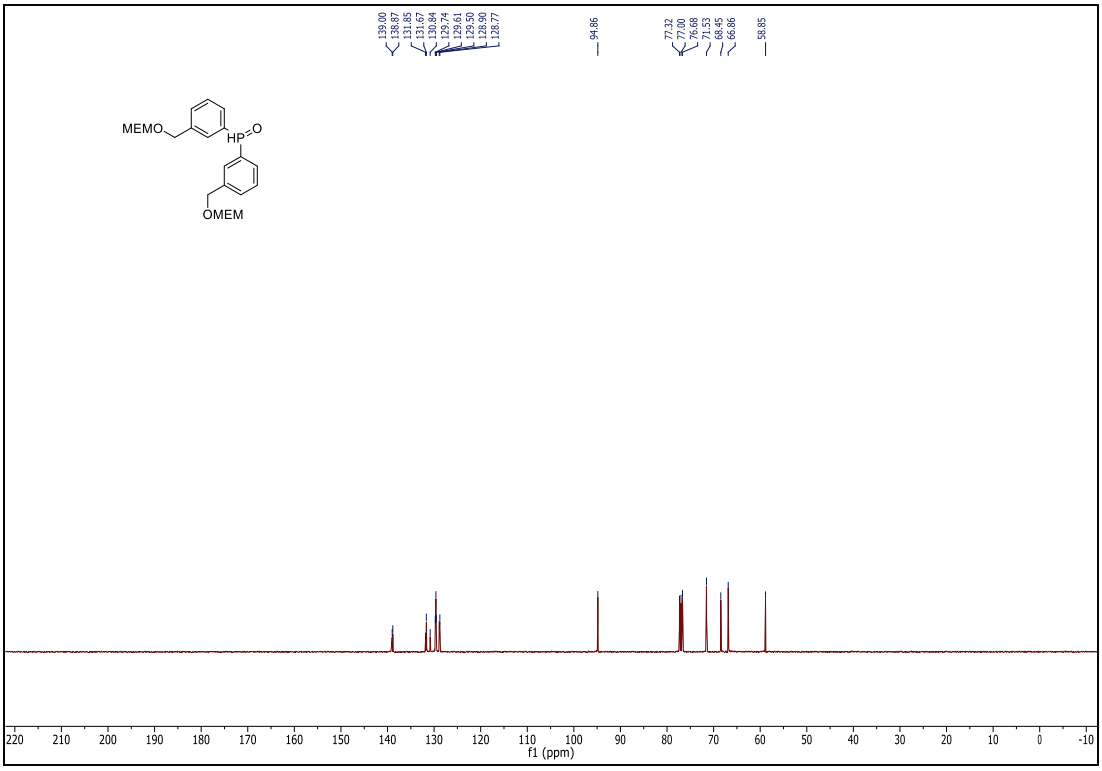
1-Bromo-3-[(2-methoxyethoxy)methoxy]methyl]benzene



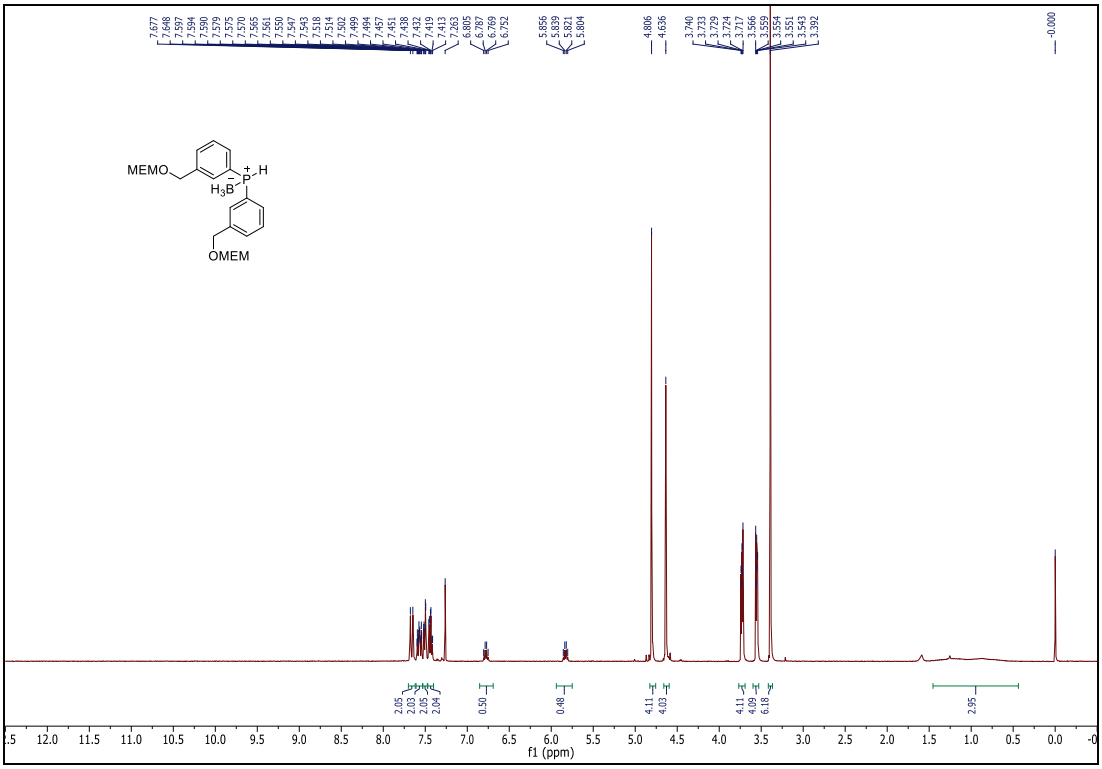


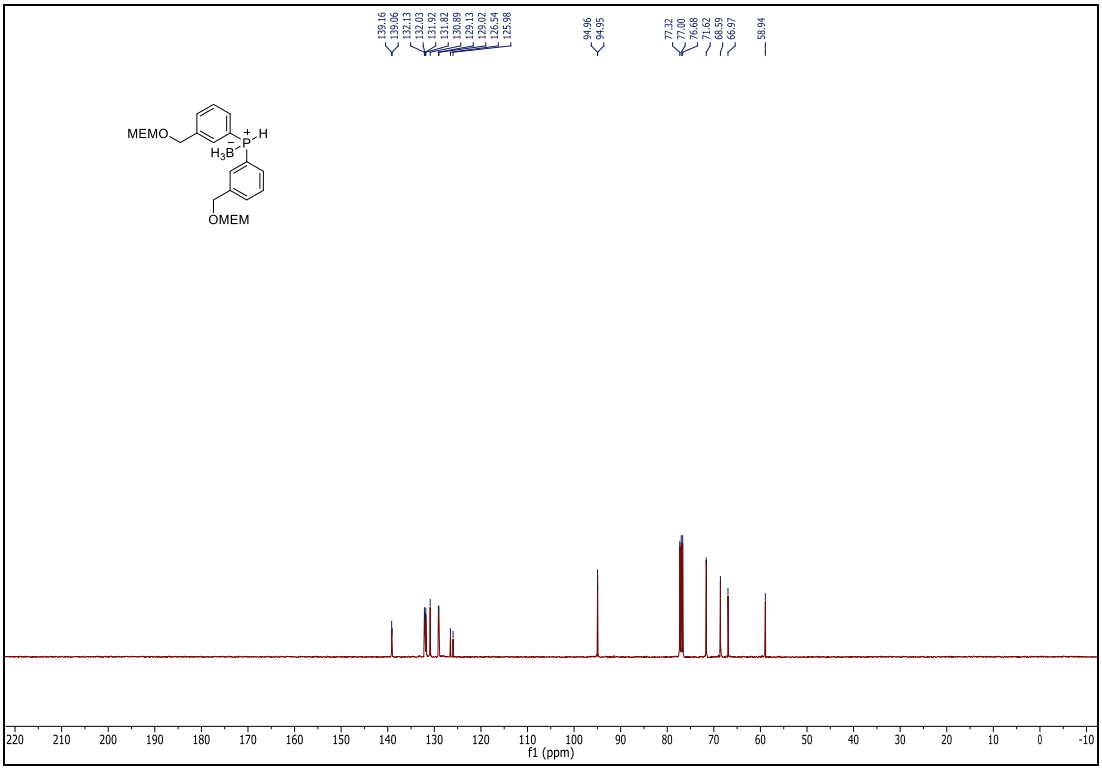
Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine oxide



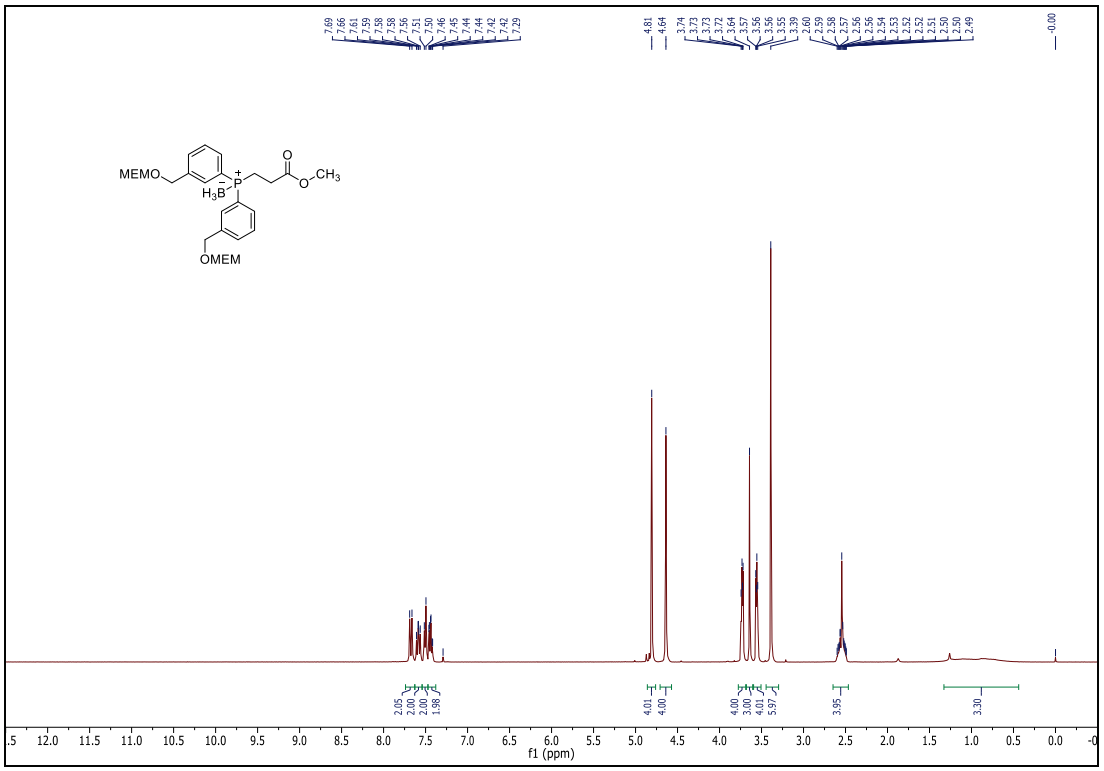


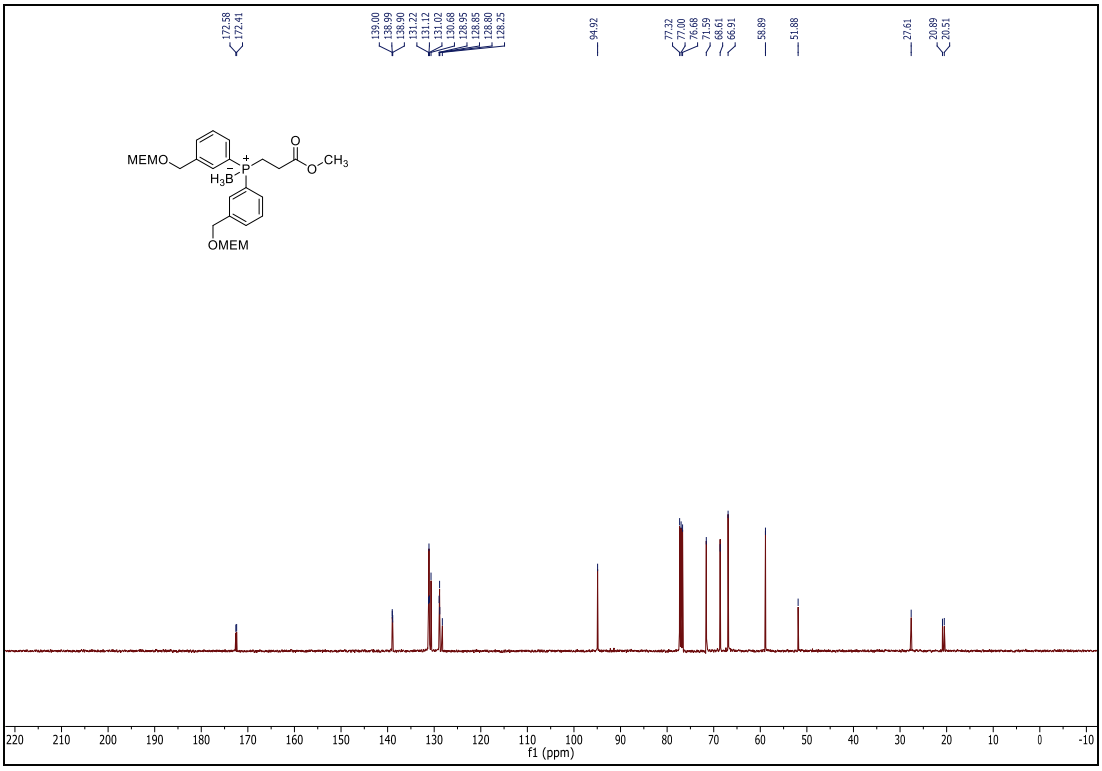
Borane bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphine complex



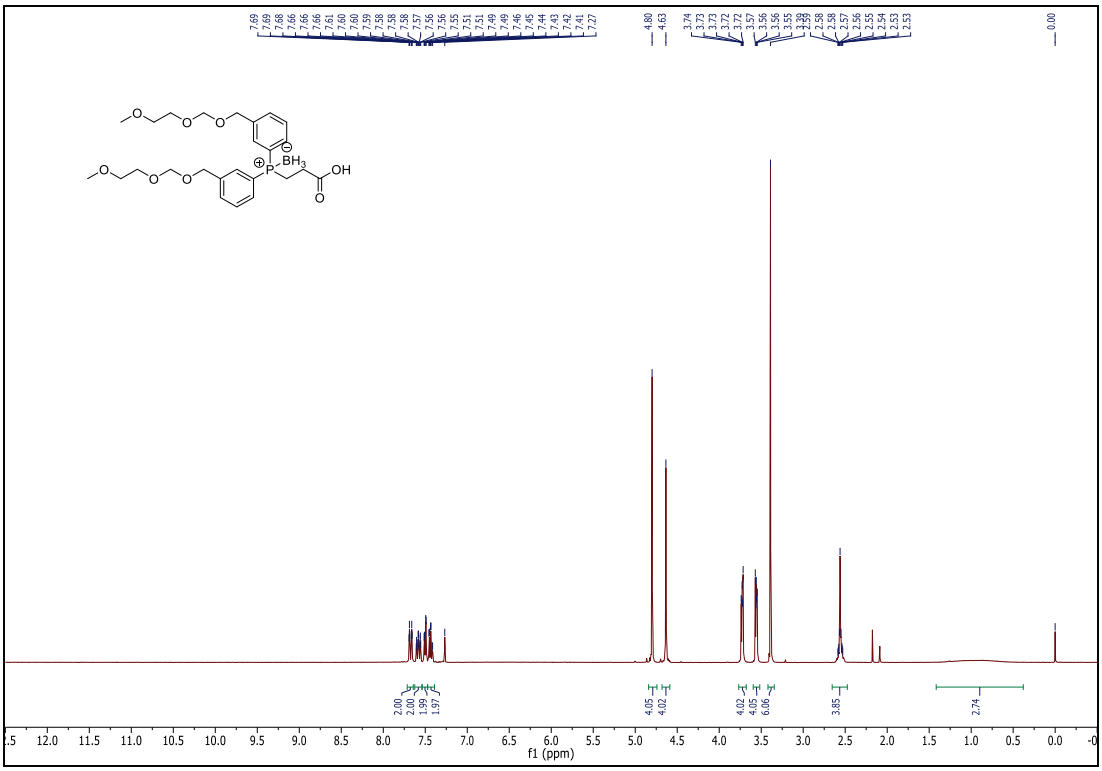


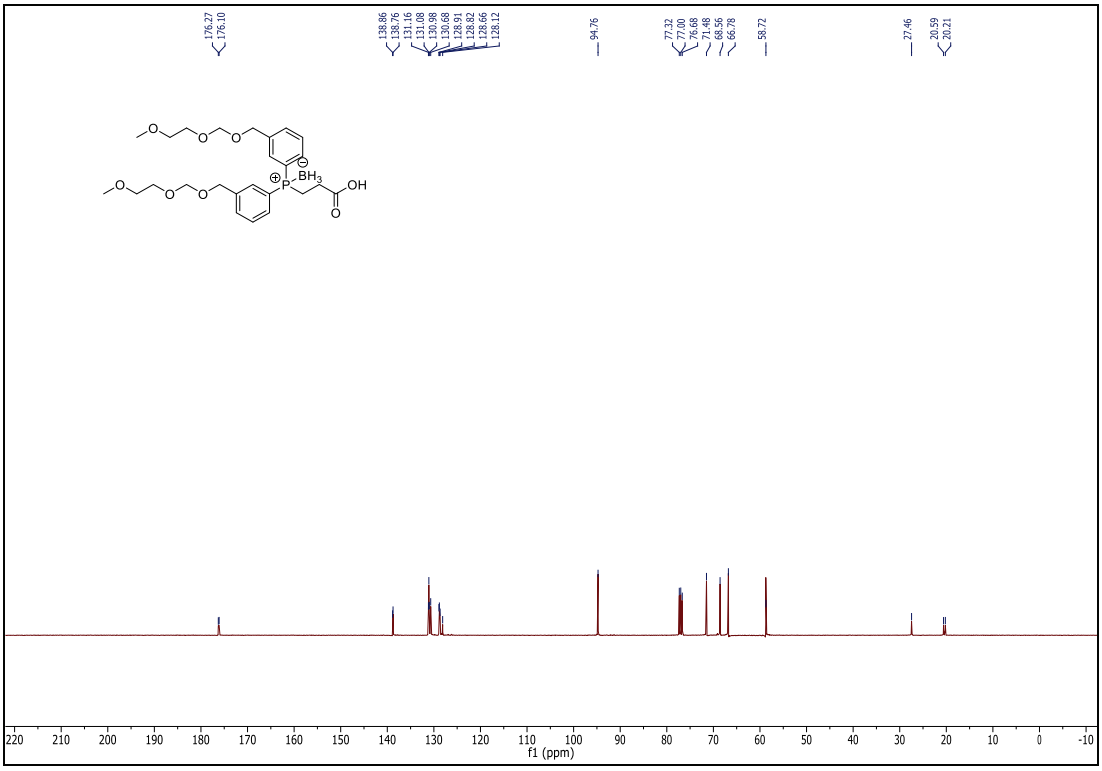
Borane methyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoate complex



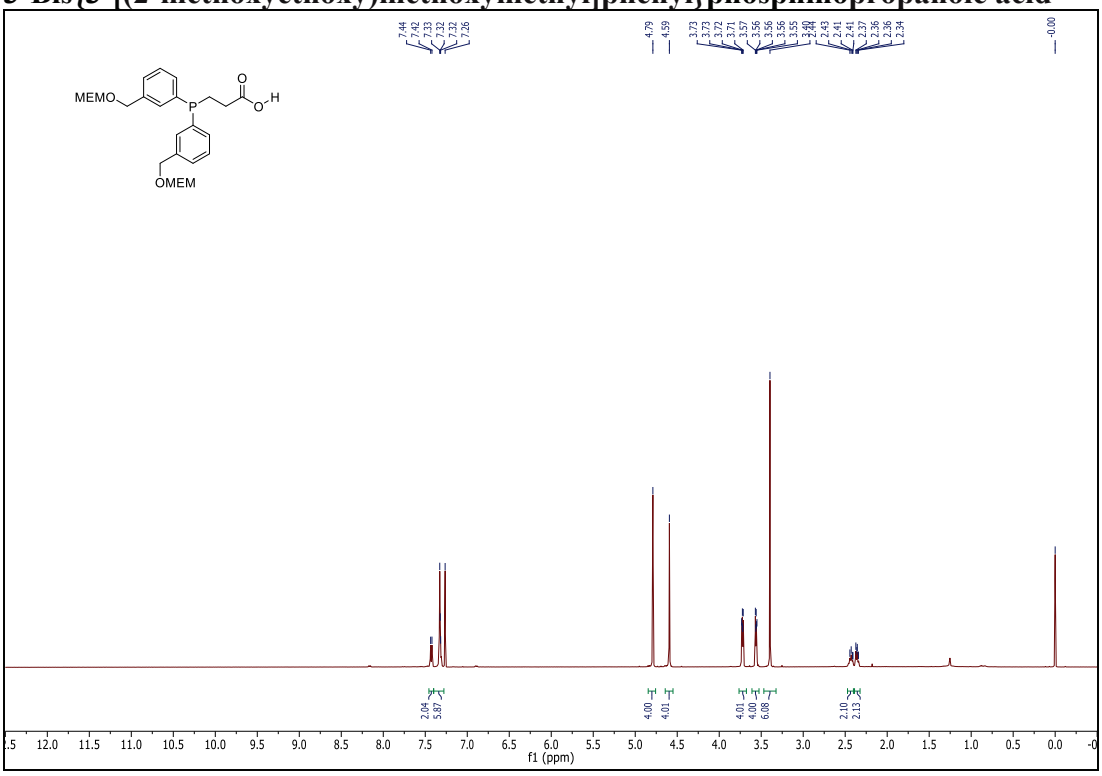


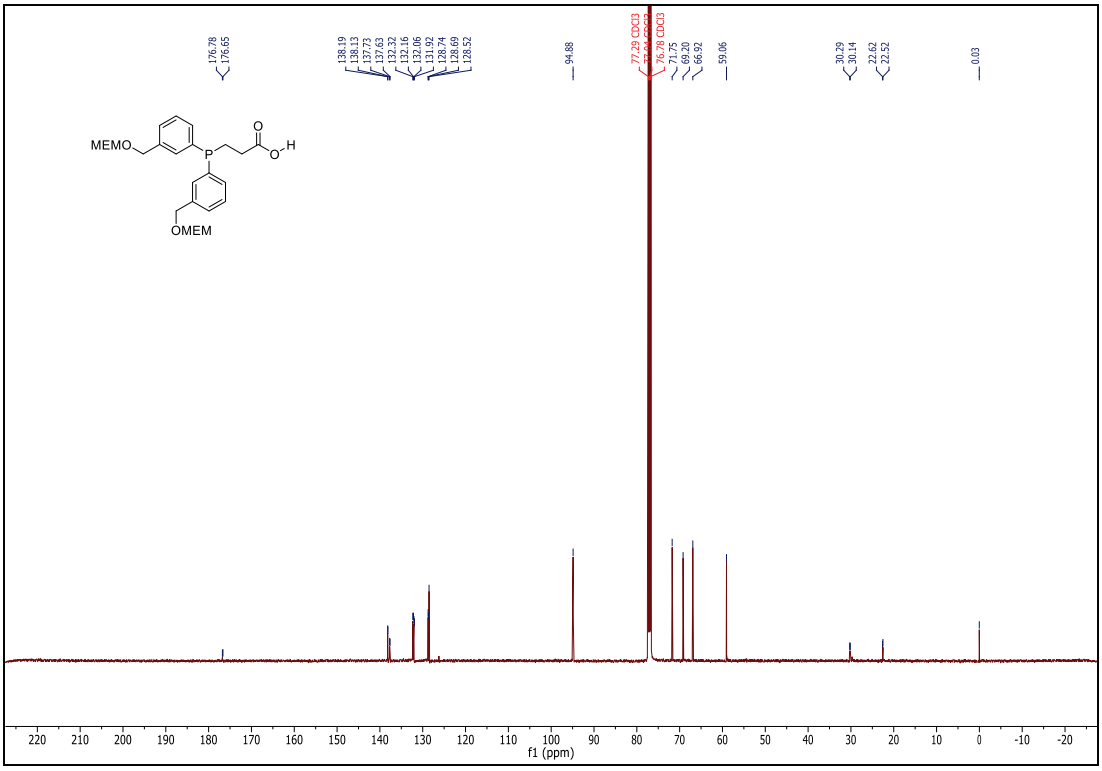
Borane 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid complex



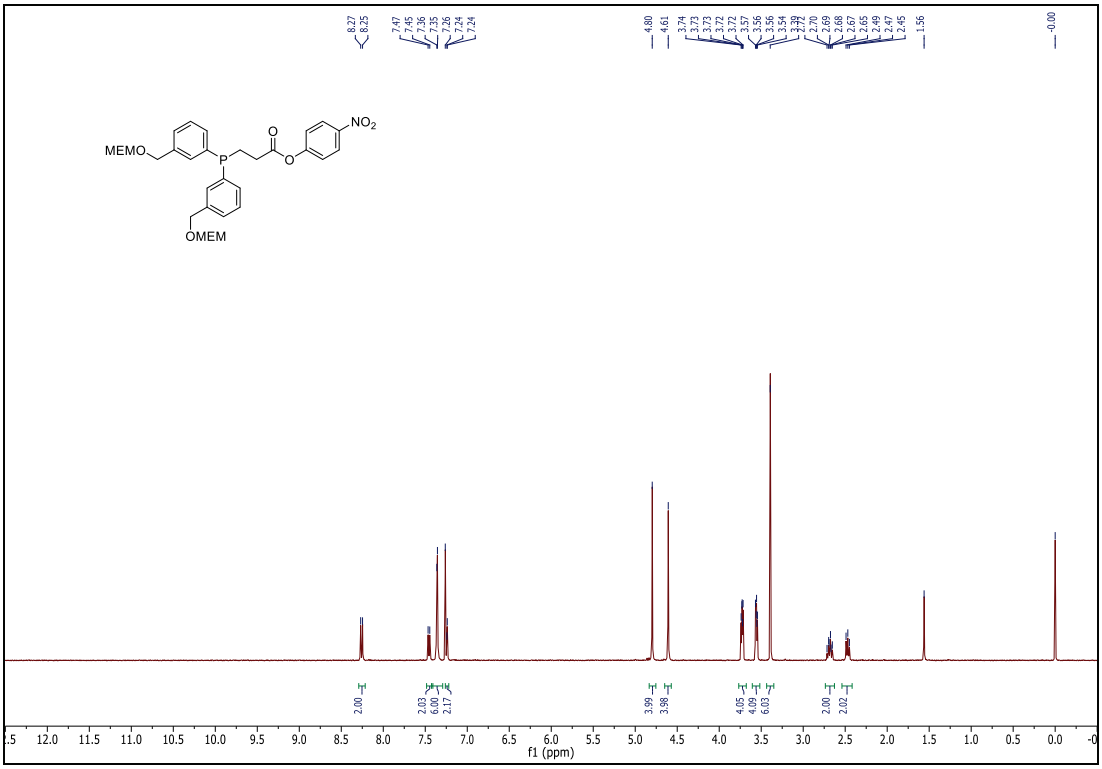


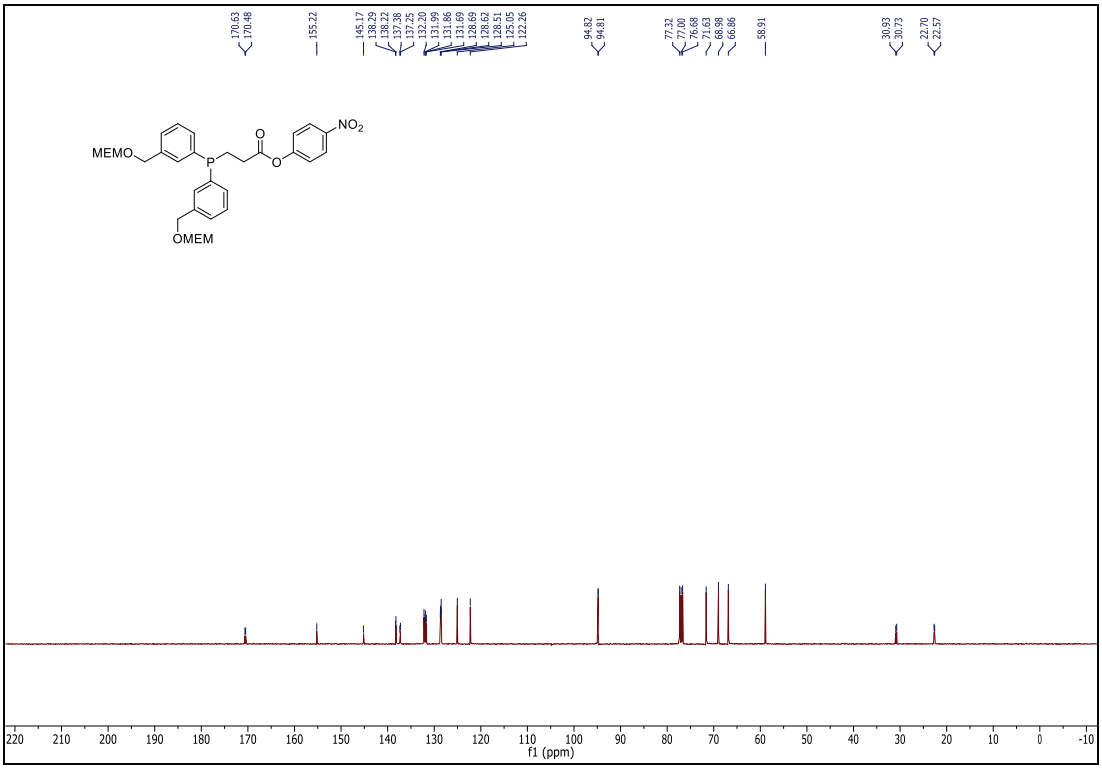
3-Bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanoic acid



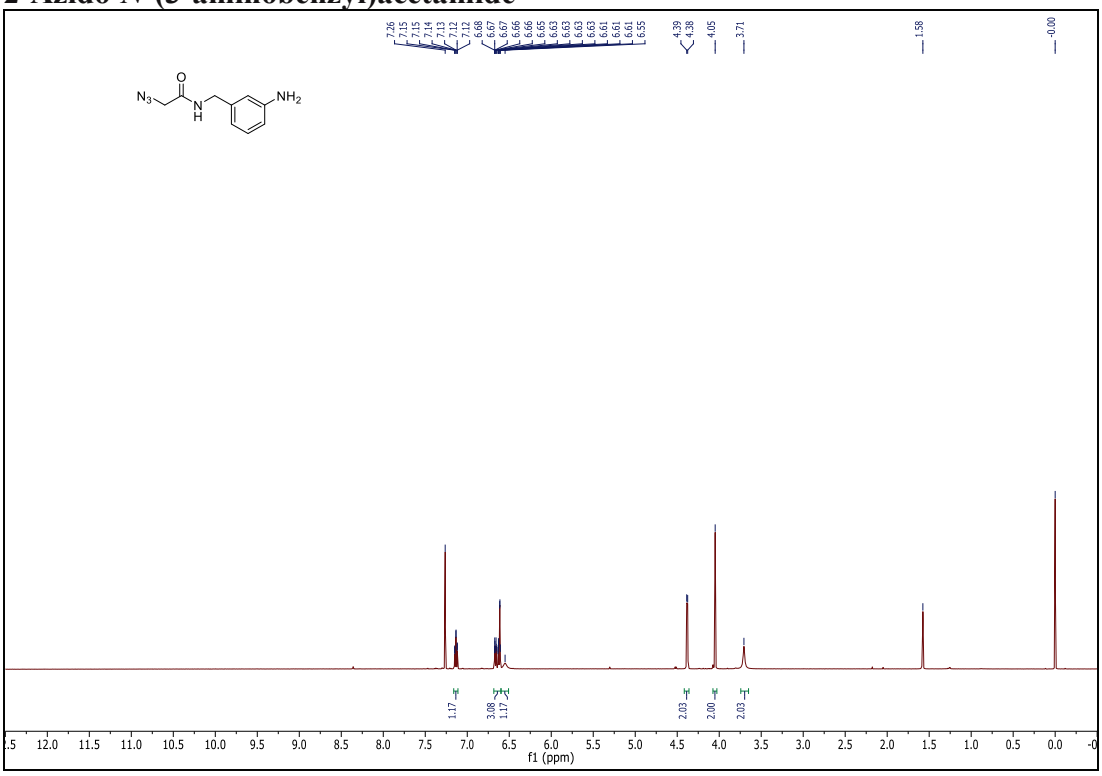


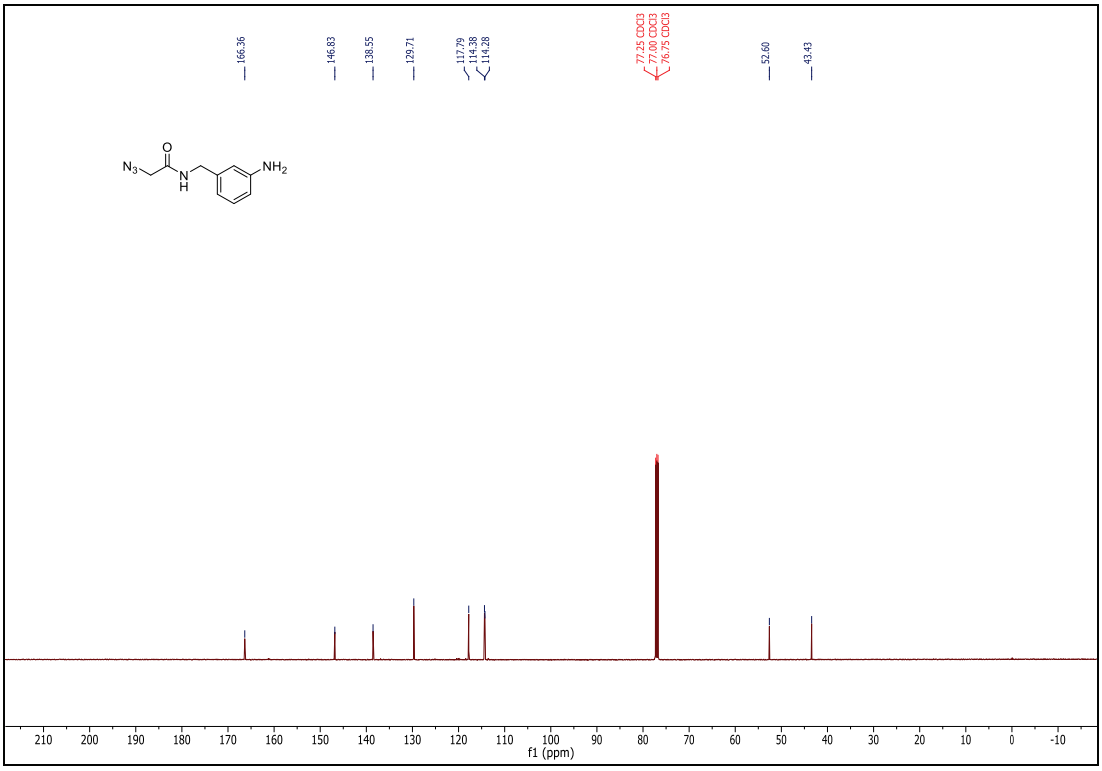
4-Nitrophenyl 3-bis{3-[(2-methoxyethoxy)methoxymethyl]phenyl}phosphinopropanate



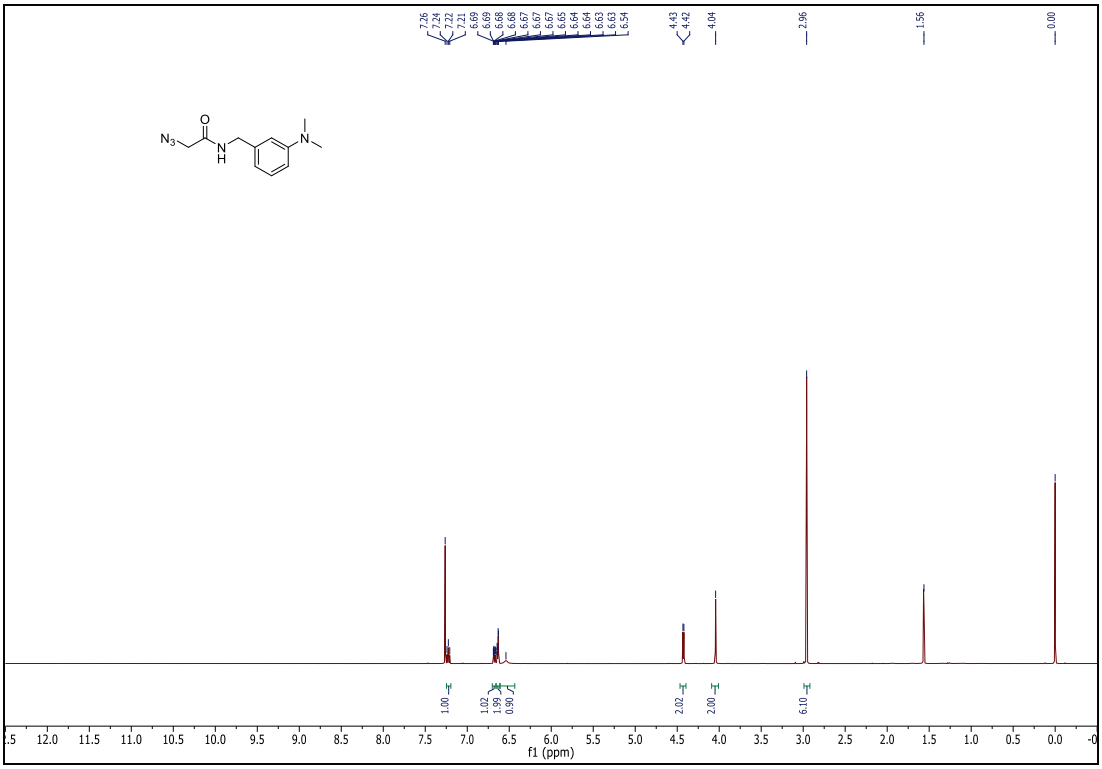


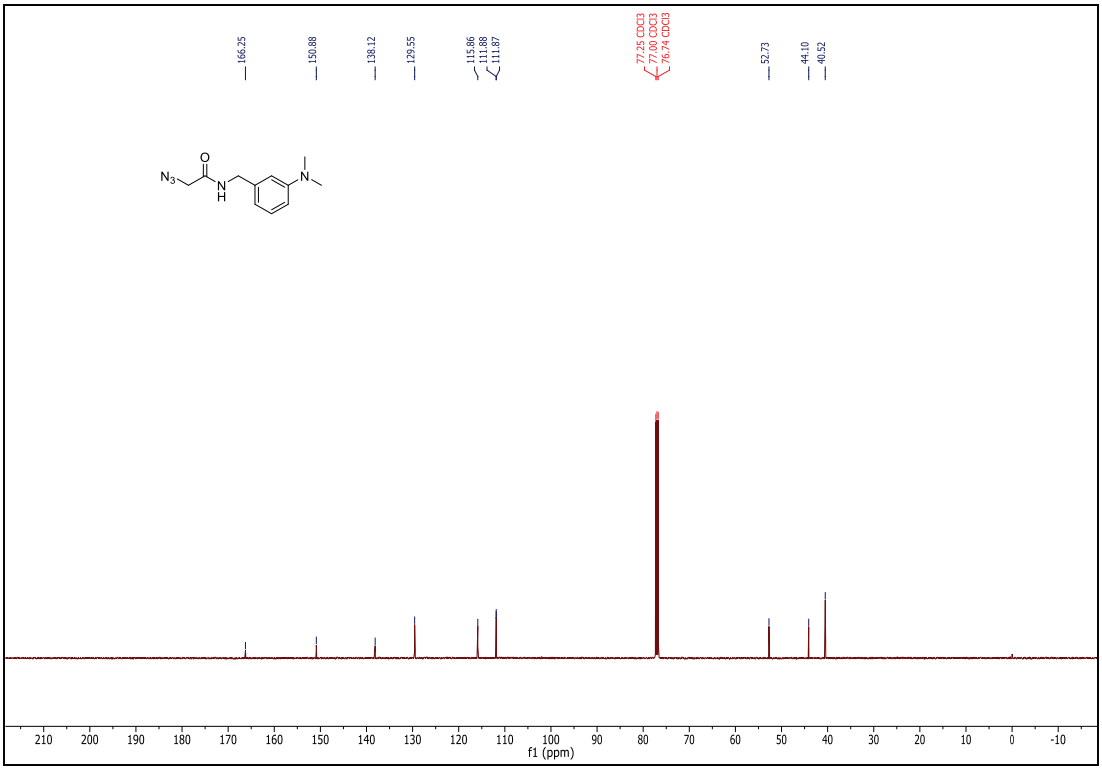
2-Azido-*N*-(3-aminobenzyl)acetamide



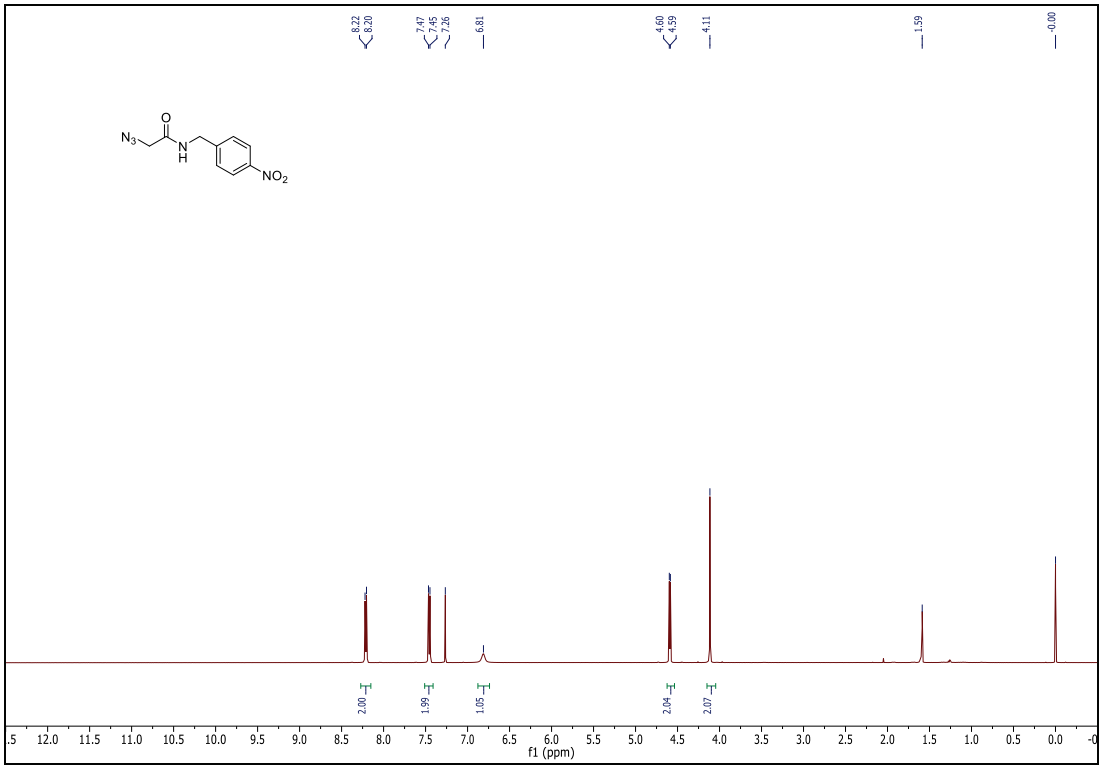


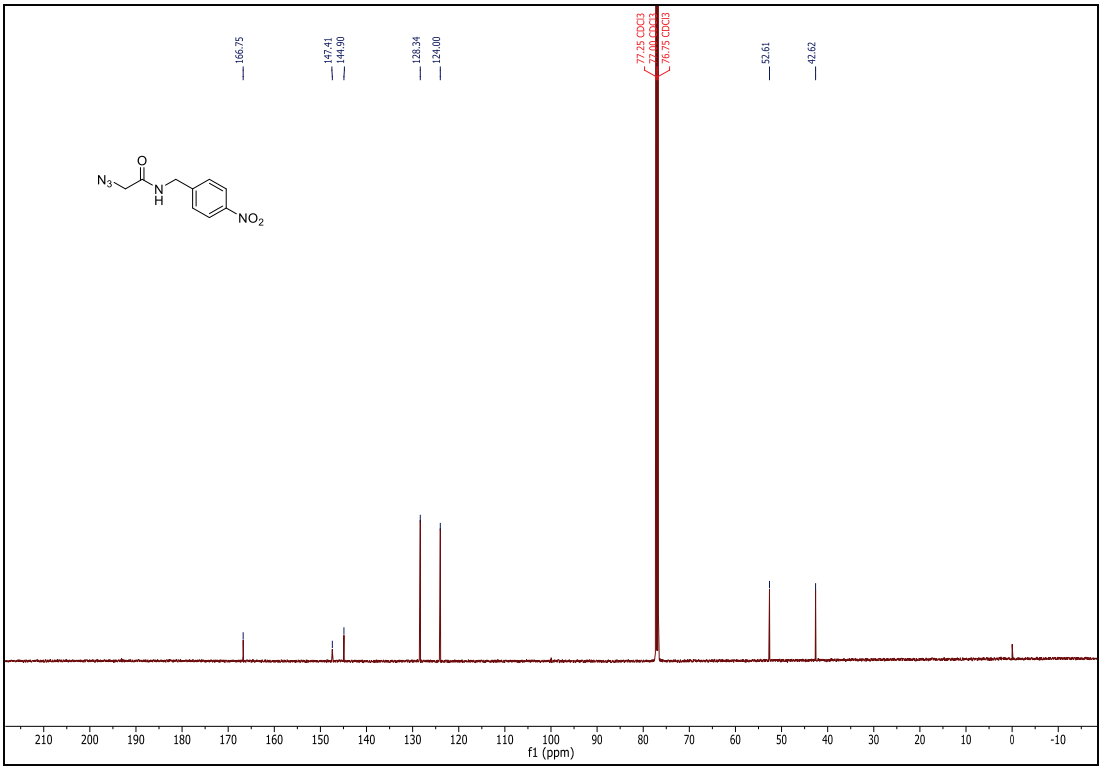
2-Azido-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide



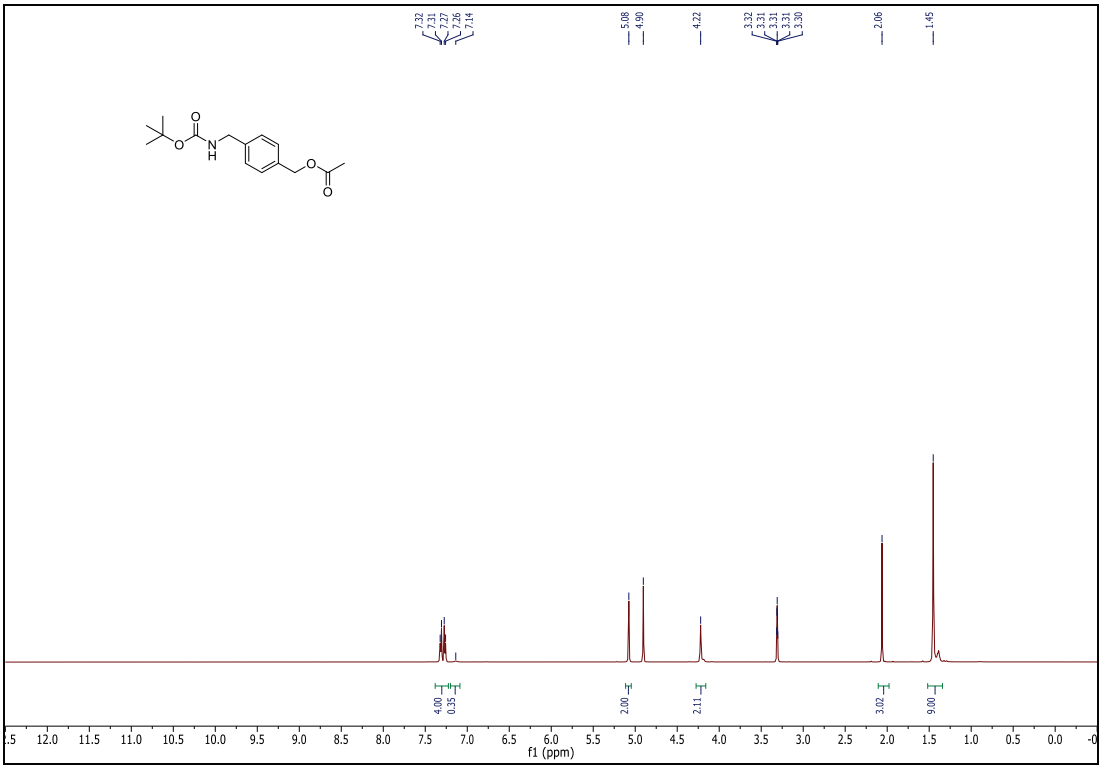


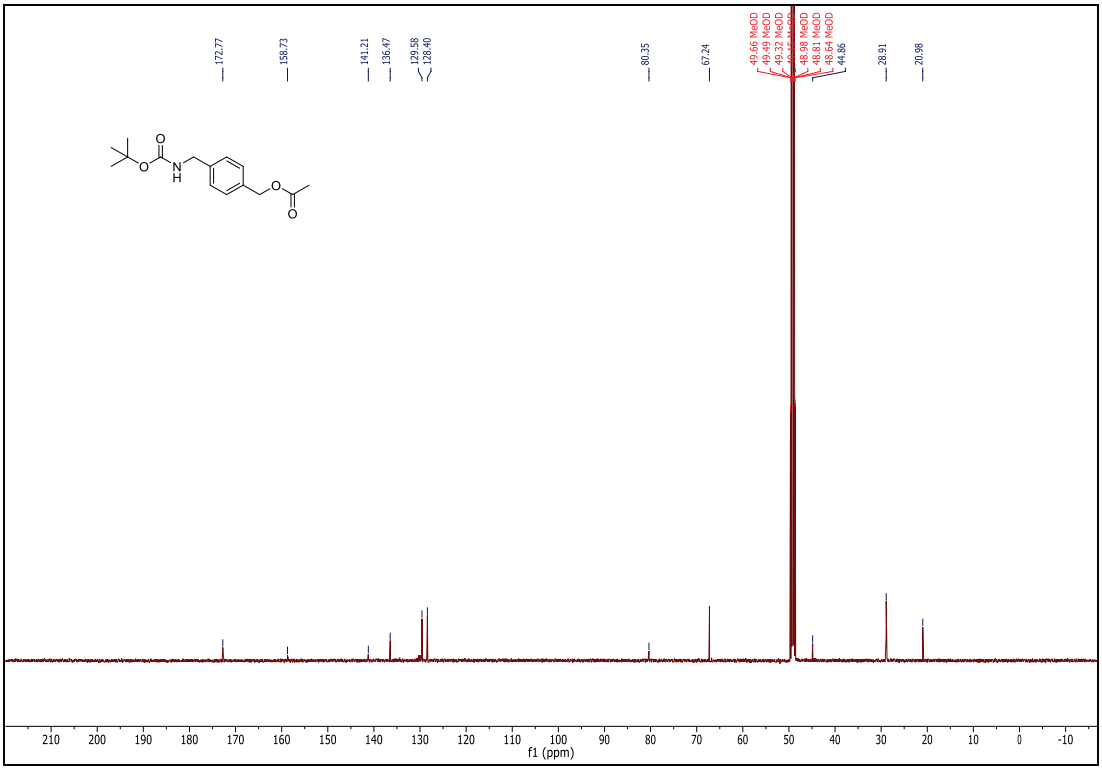
2-Azido-*N*-(4-nitrobenzyl)acetamide



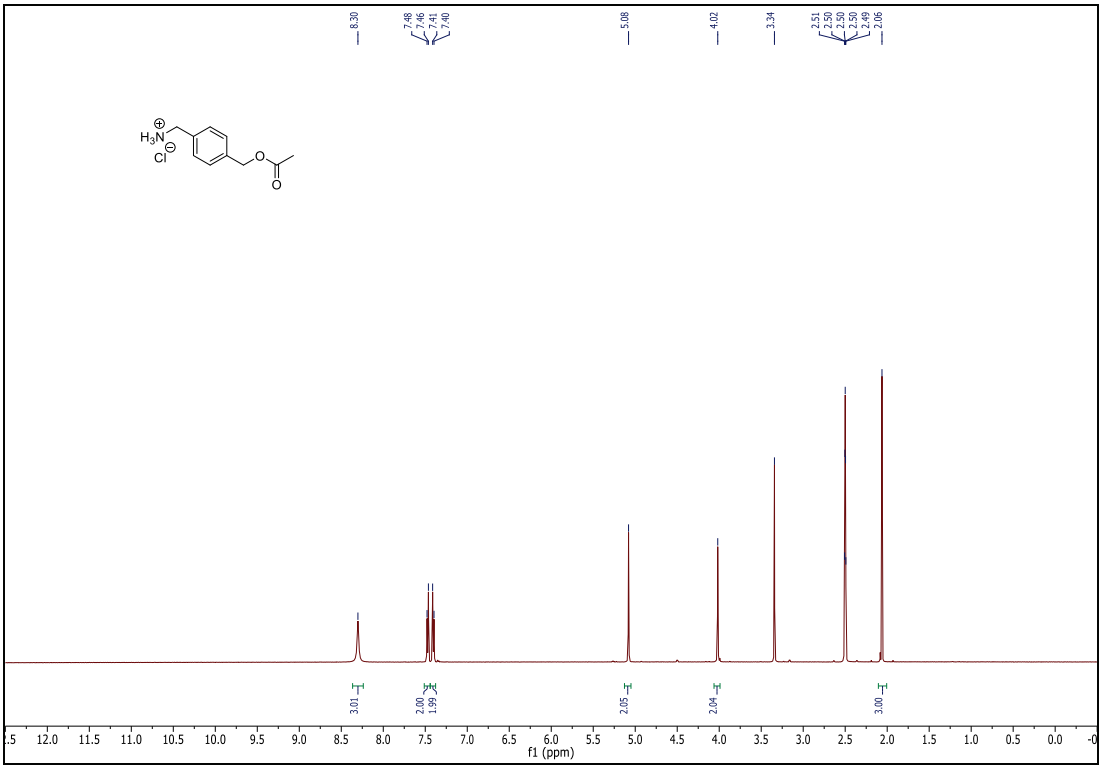


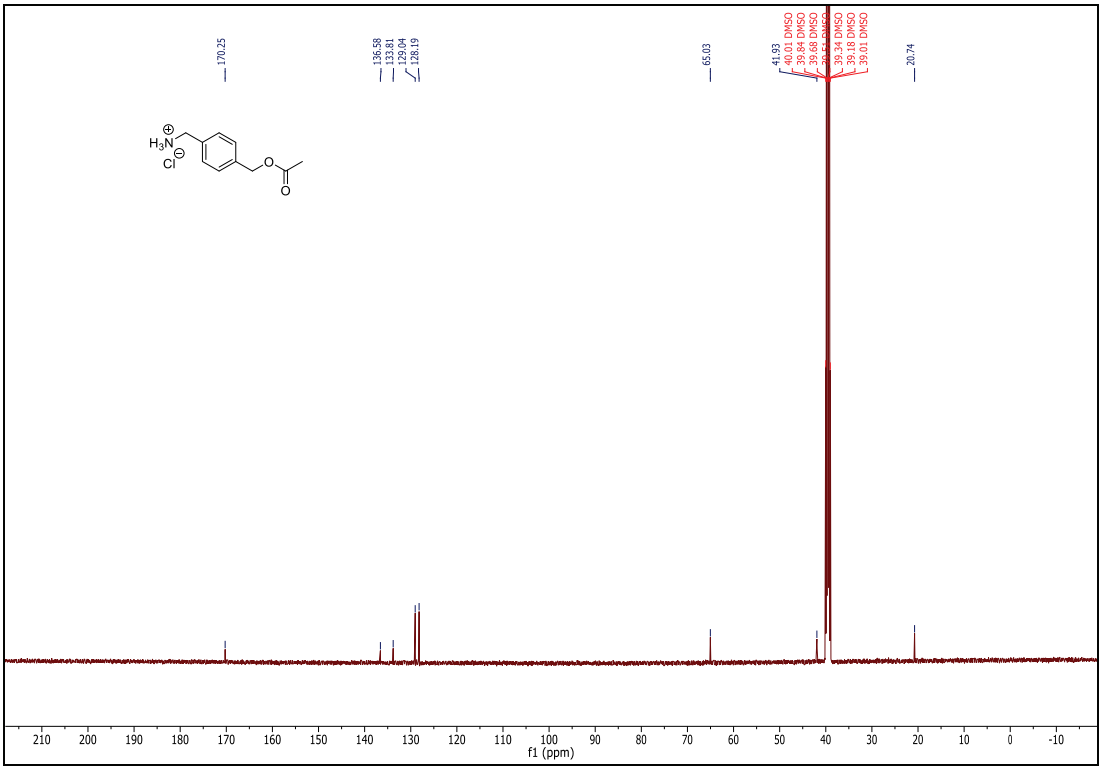
4-(*tert*-Butoxycarbonylaminomethyl)benzyl acetate



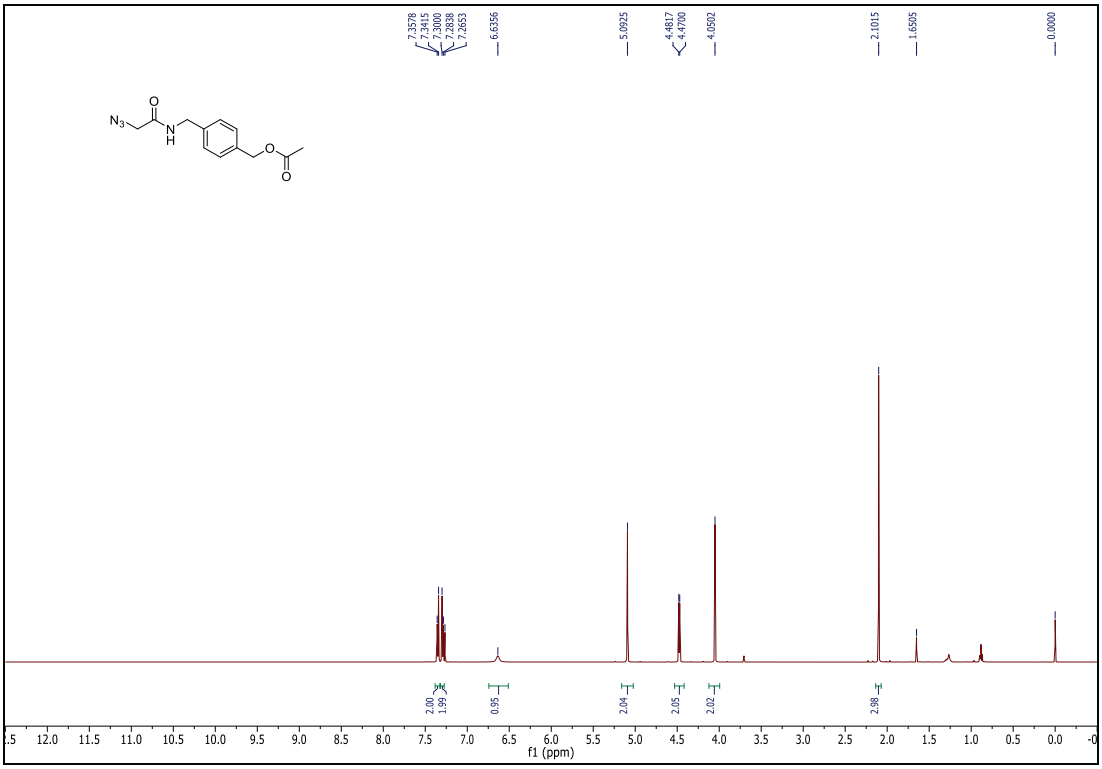


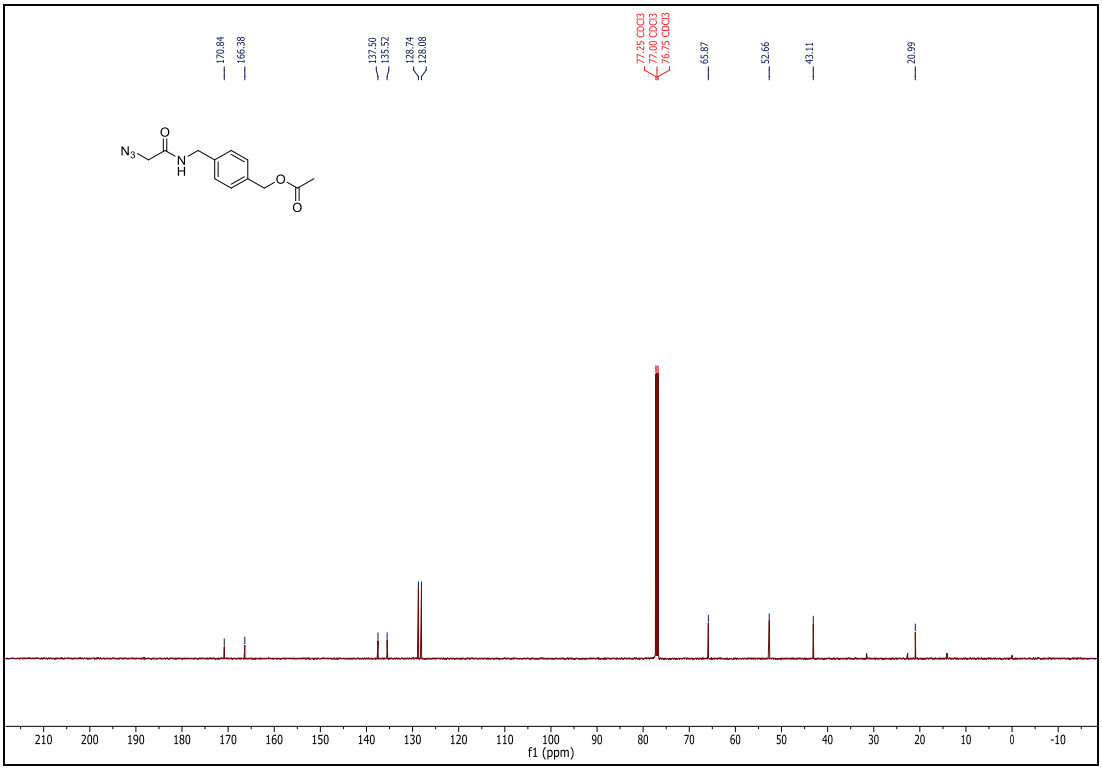
4-(Aminomethyl)benzyl acetate hydrochloride



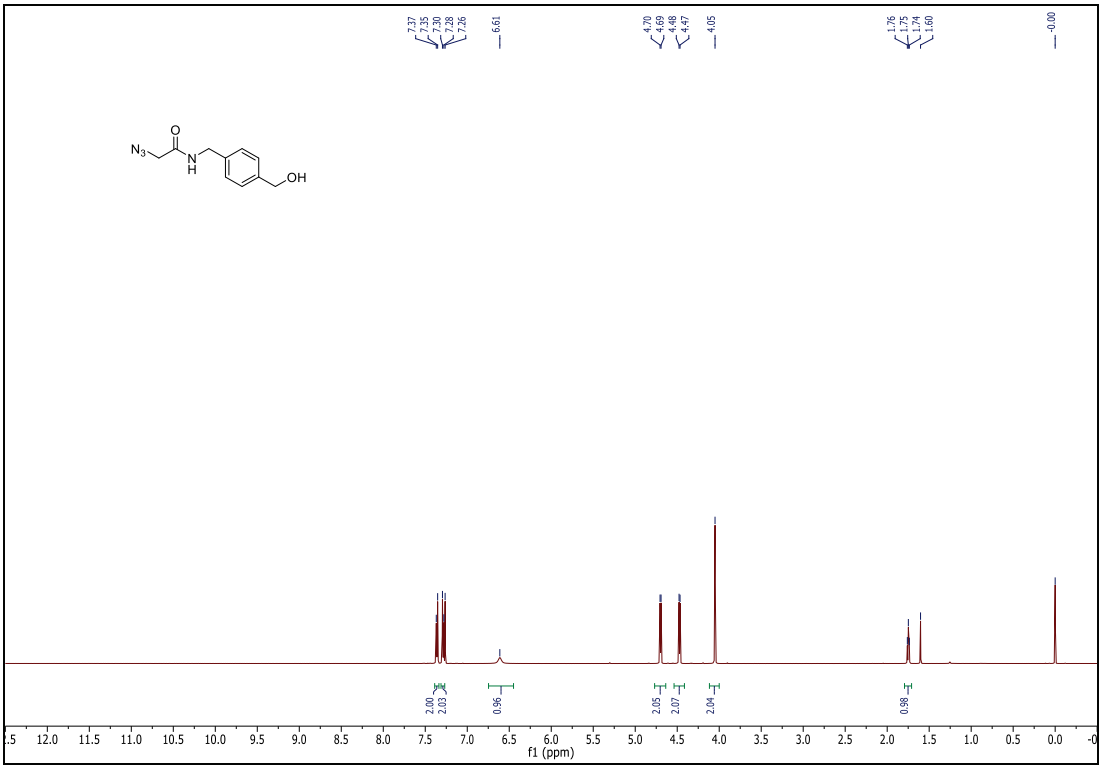


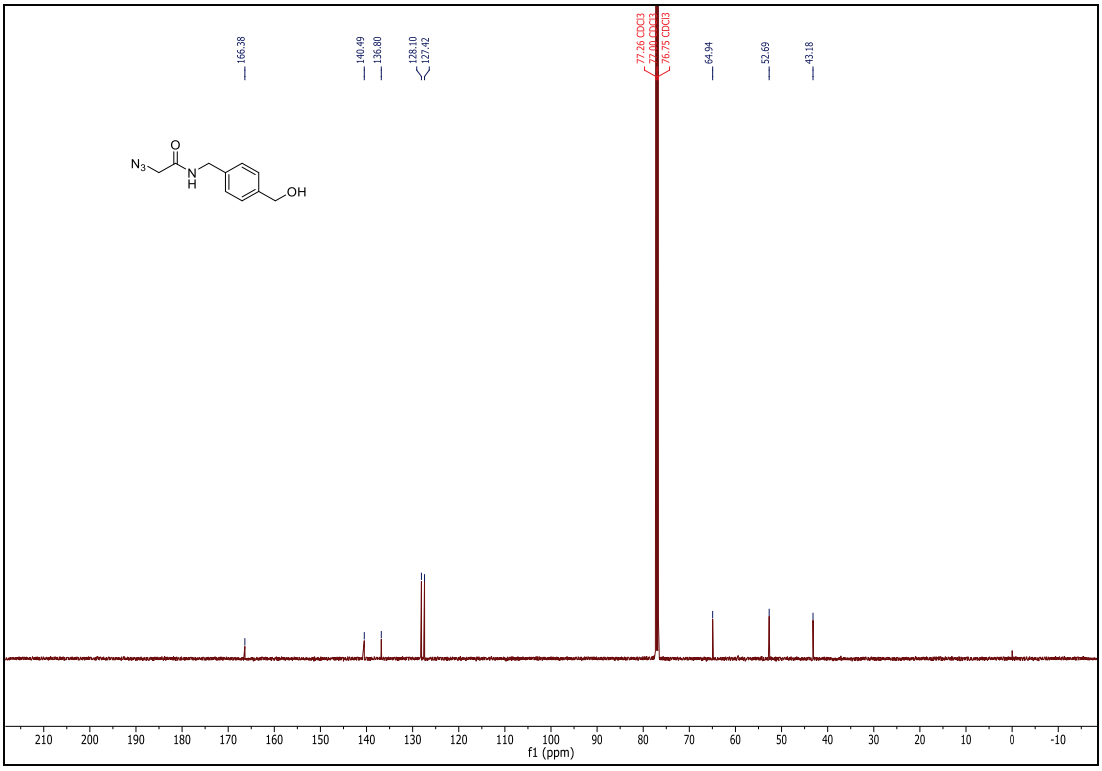
2-Azido-*N*-[4-(acetyloxymethyl)benzyl]acetamide



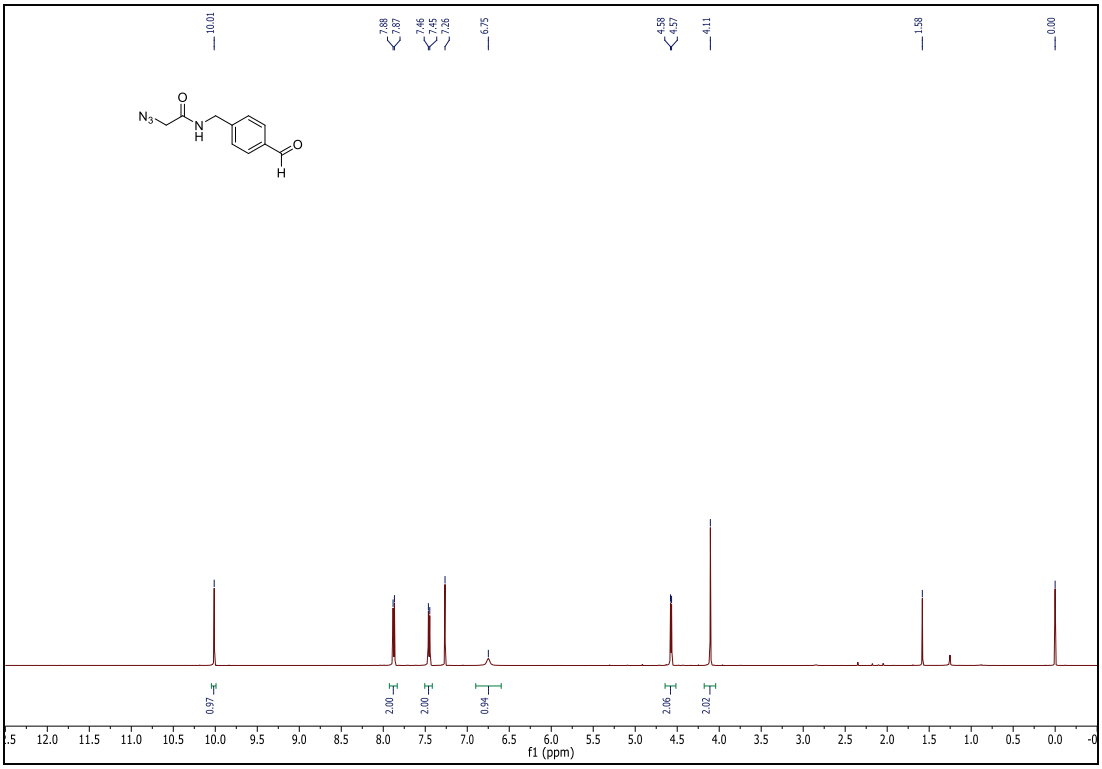


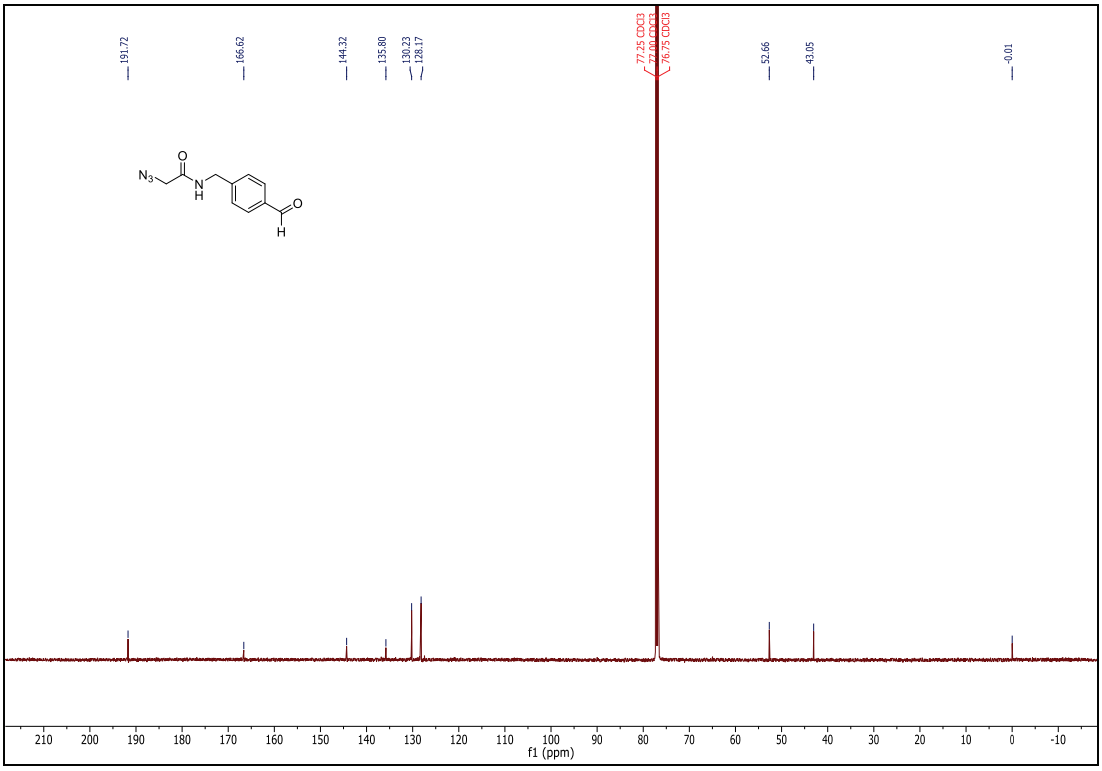
2-Azido-*N*-[4-(hydroxymethyl)benzyl]acetamide



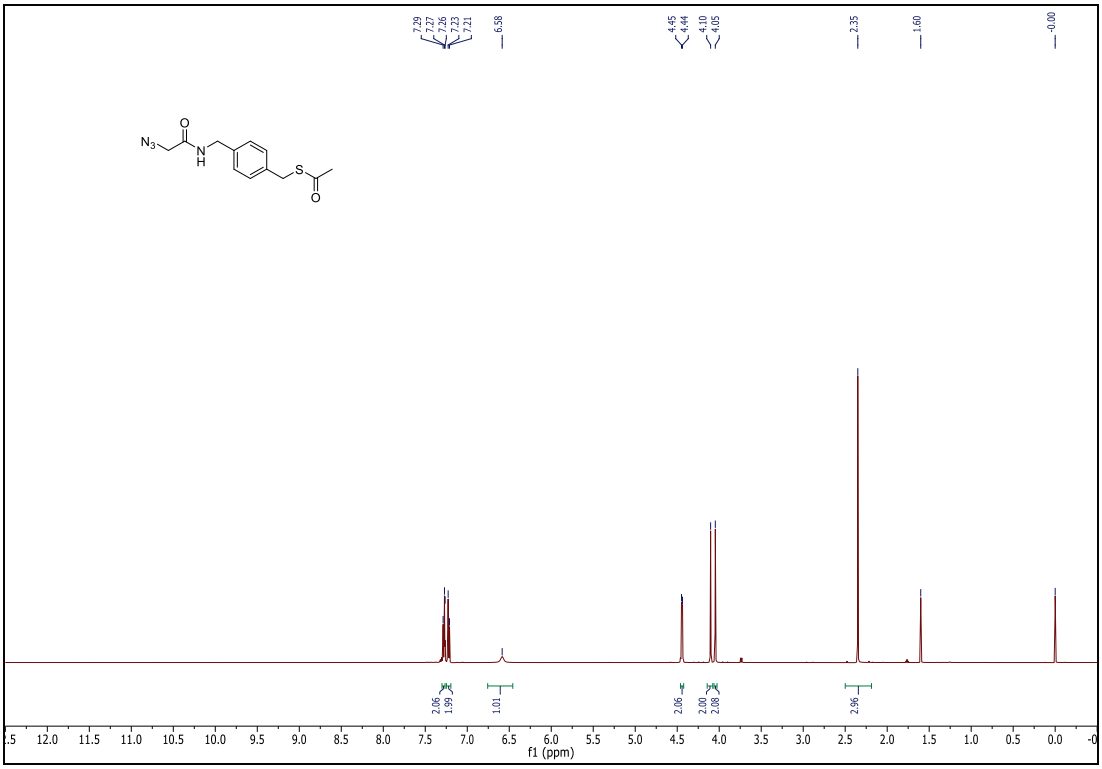


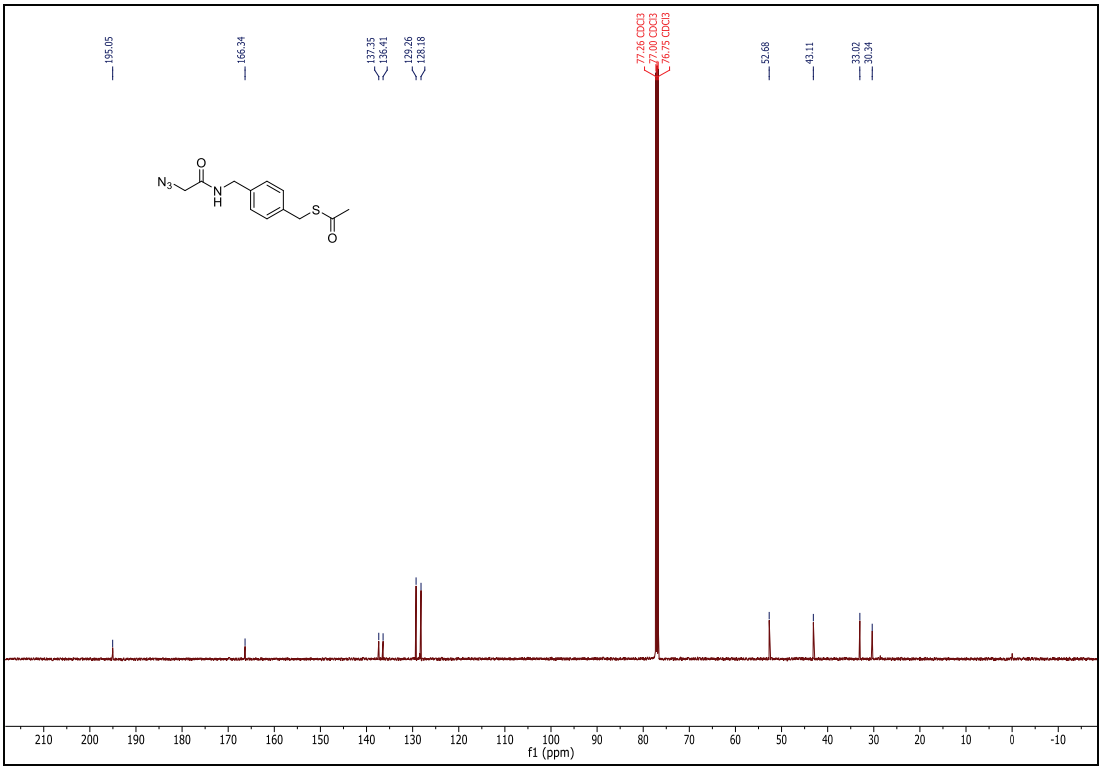
2-Azido-*N*-(4-formylbenyl)acetamide



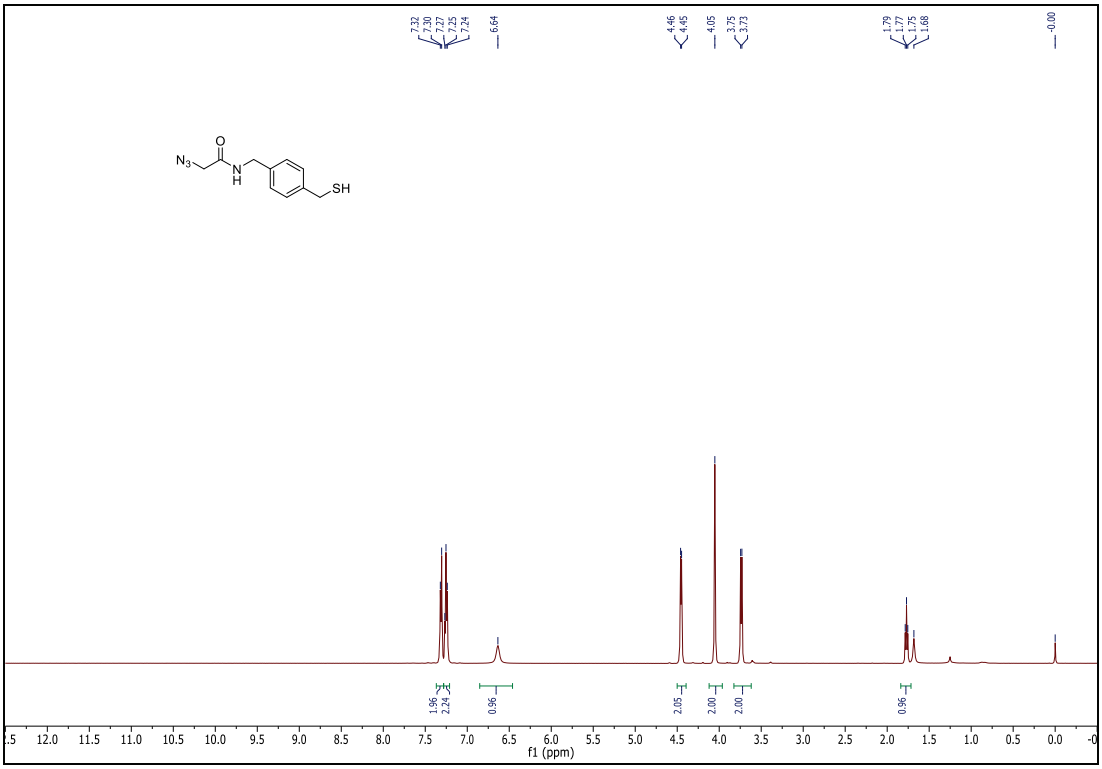


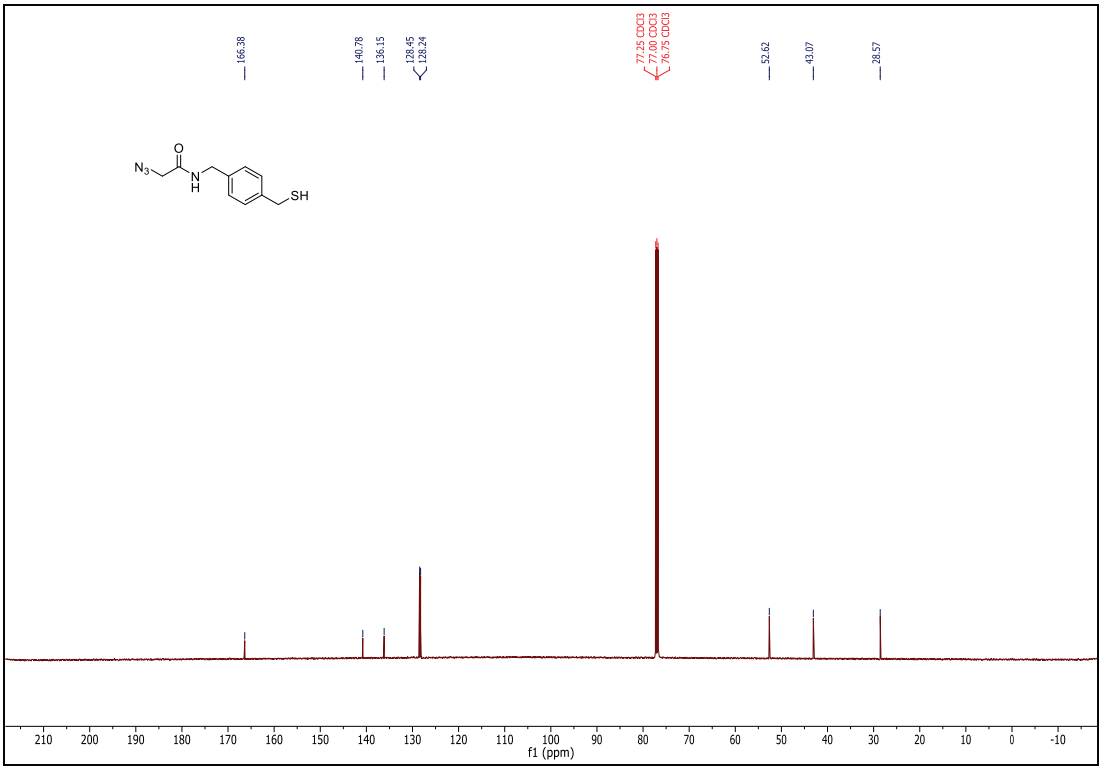
2-Azido-*N*-[4-(acetylmercaptomethyl)benzyl]acetamide



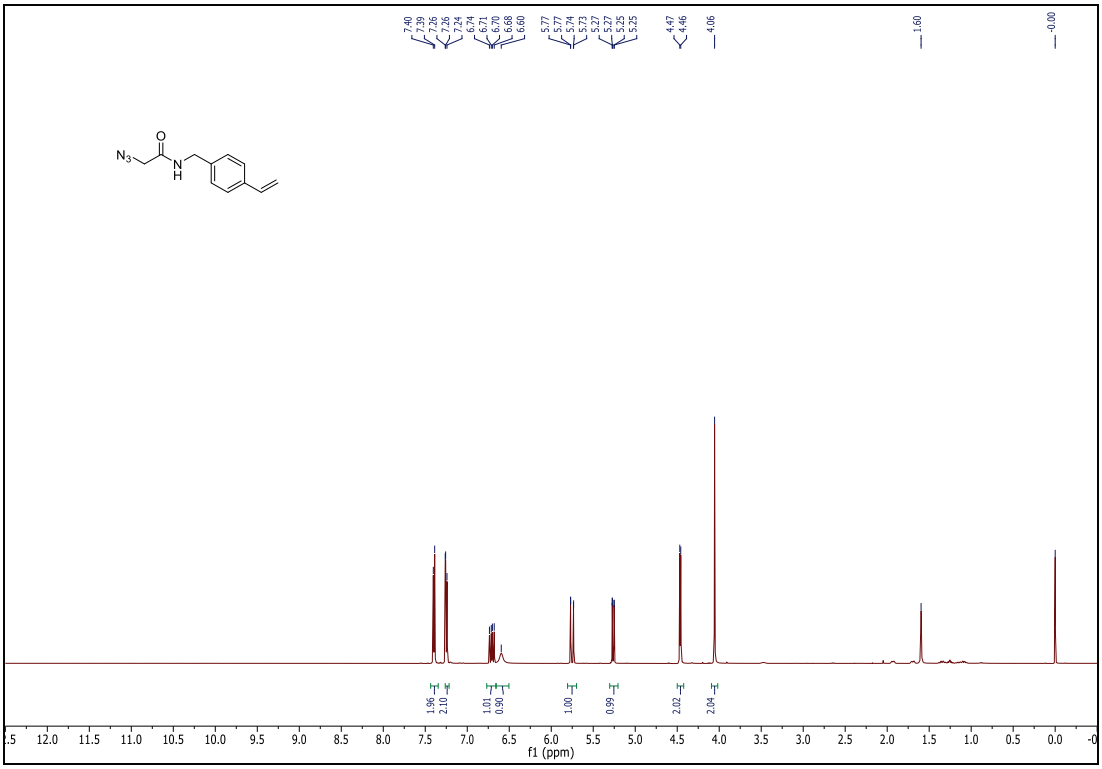


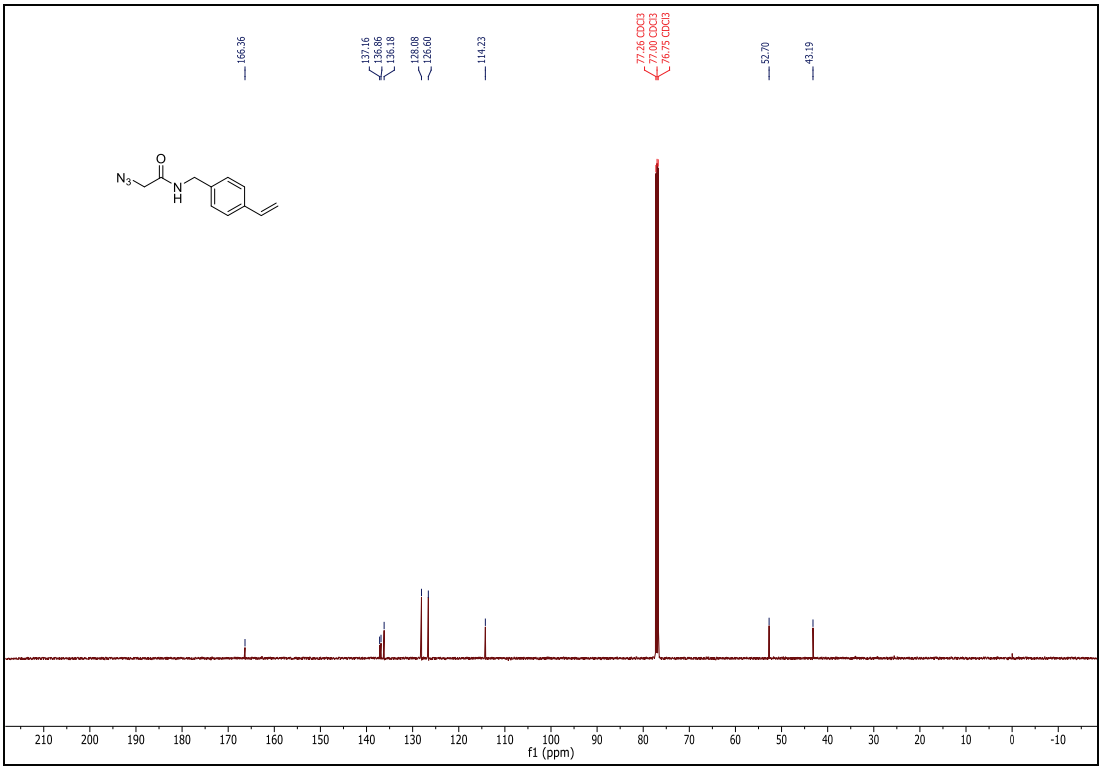
2-Azido-*N*-[4-(mercaptomethyl)benzyl]acetamide



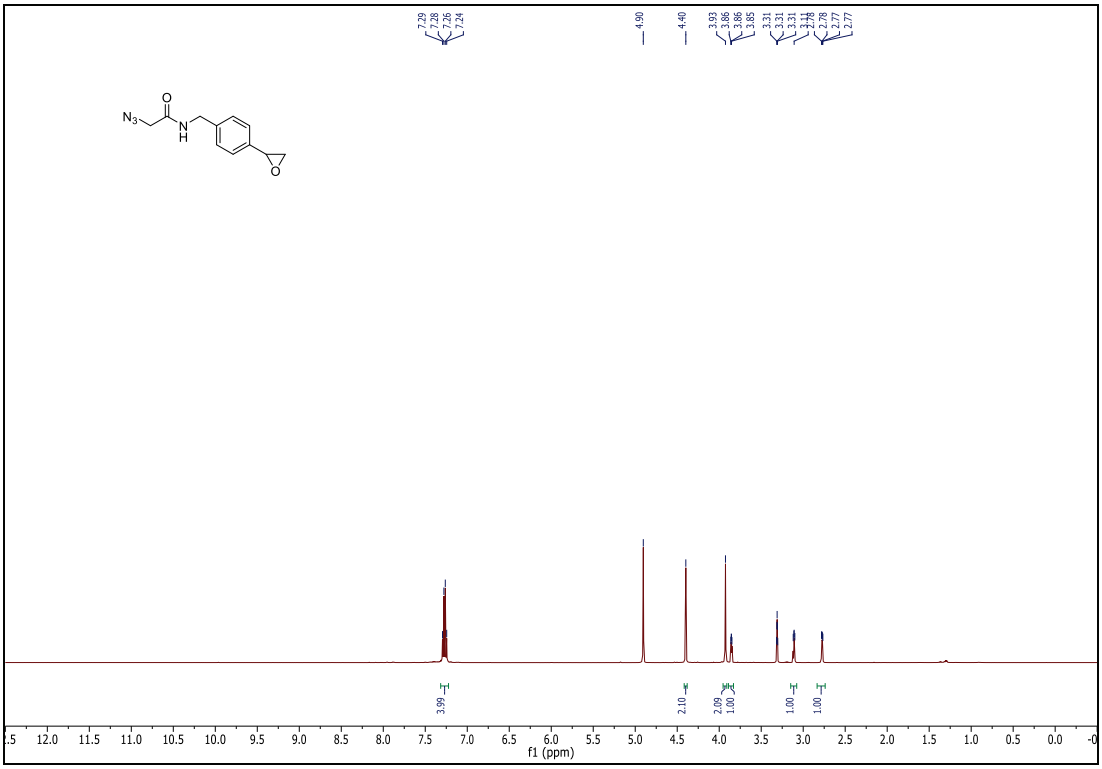


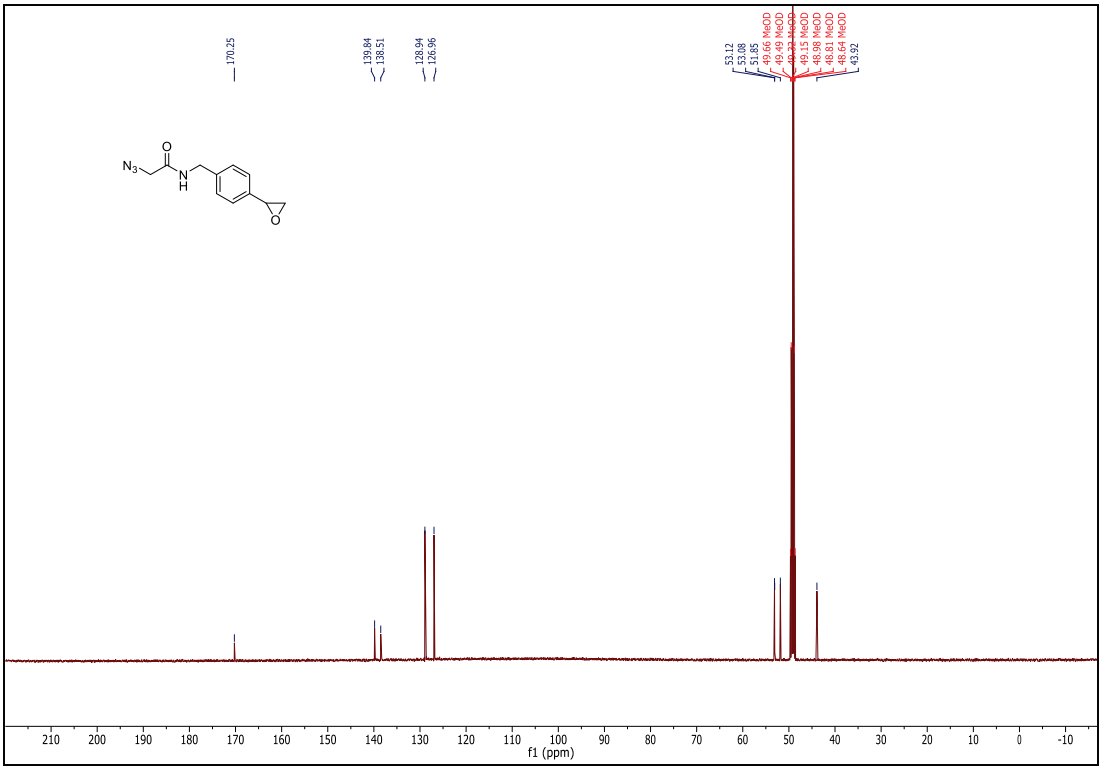
2-Azido-*N*-(4-vinylbenzyl)acetamide



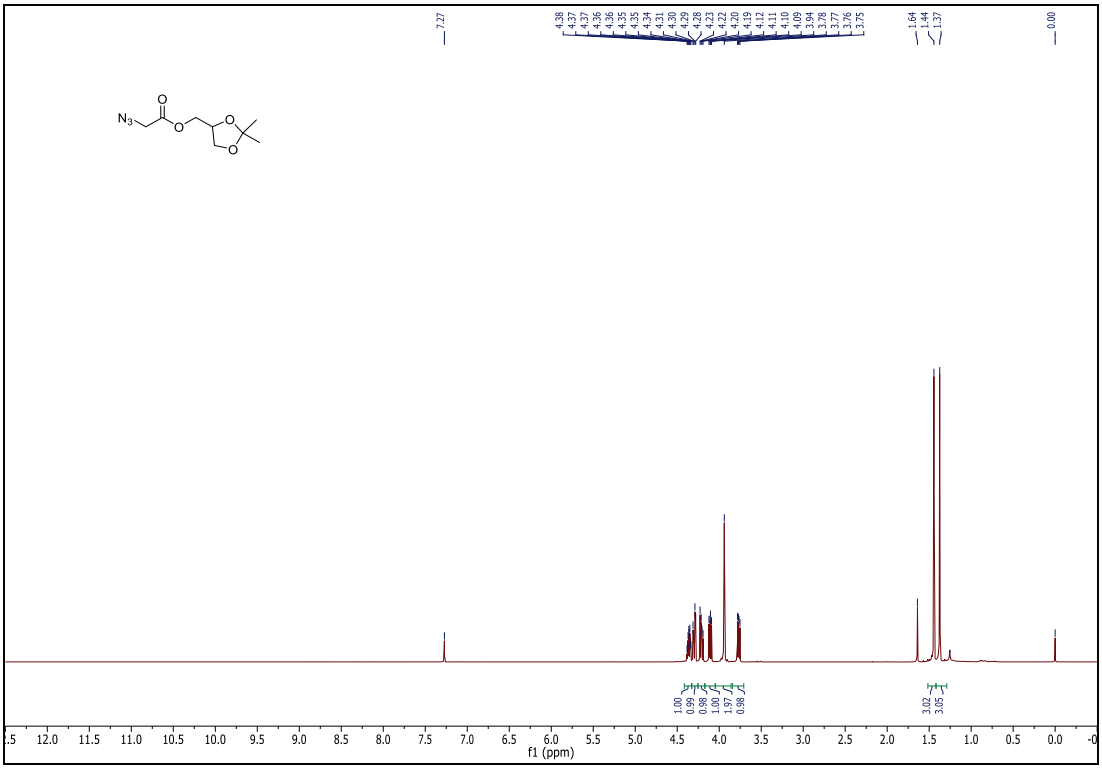


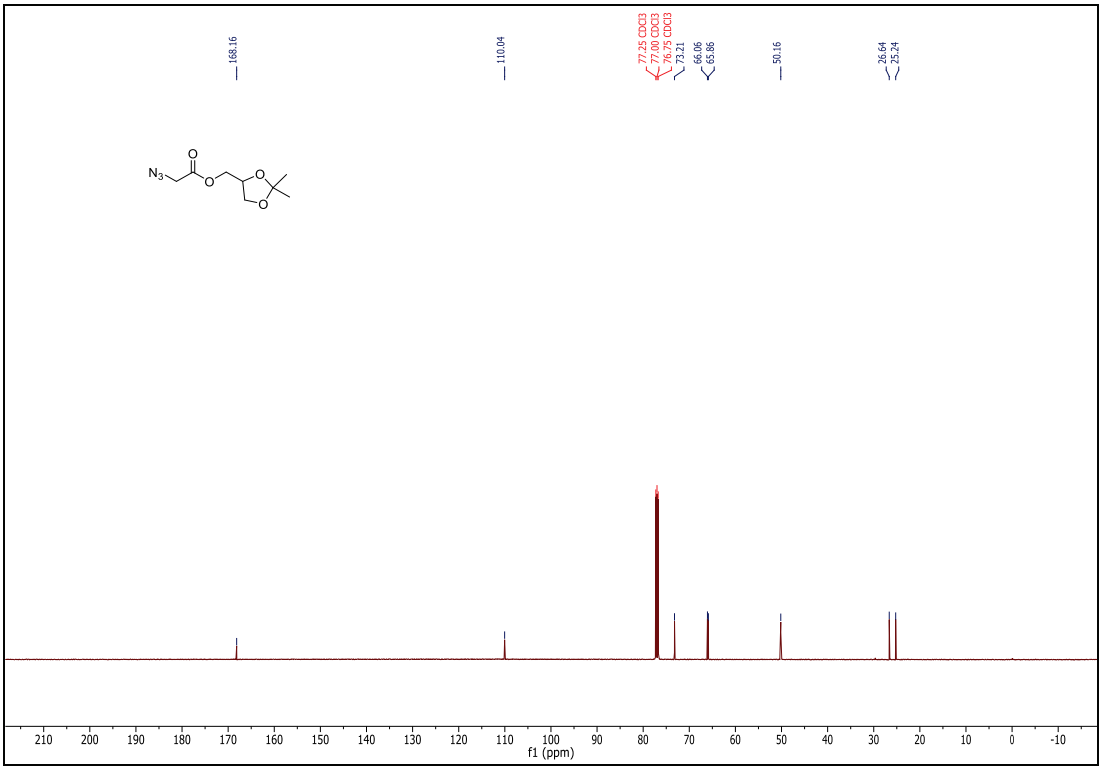
2-Azido-*N*-(4-oxiranylbenzyl)acetamide



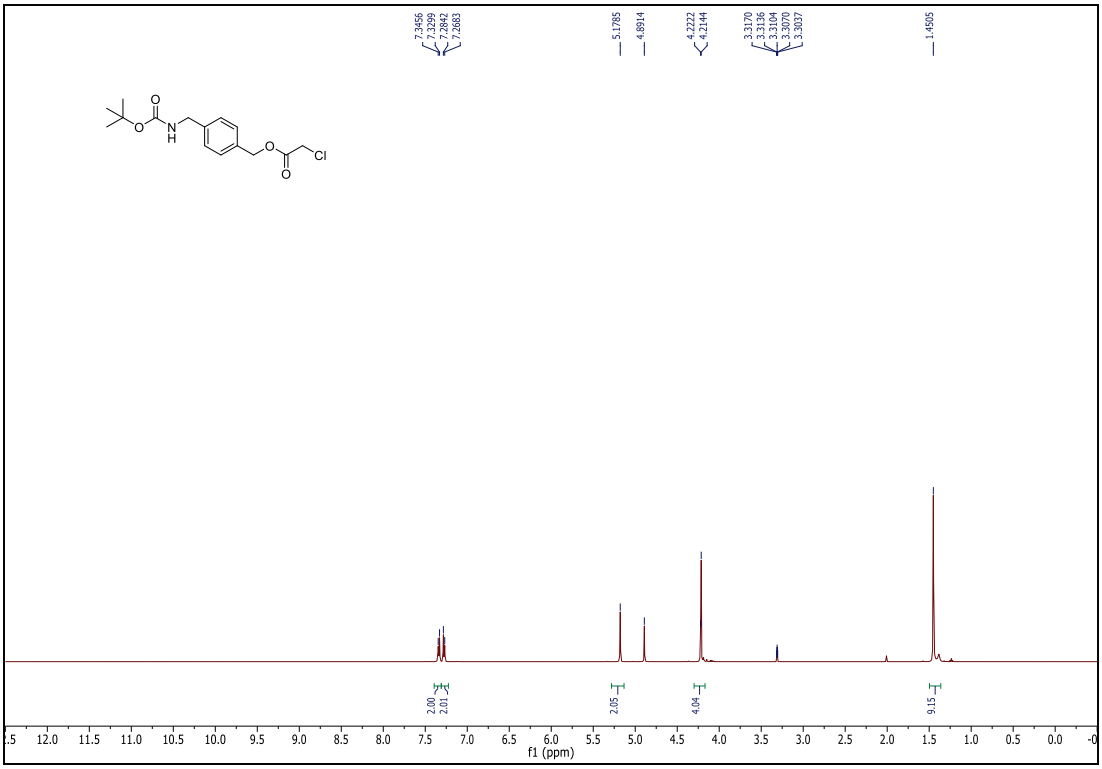


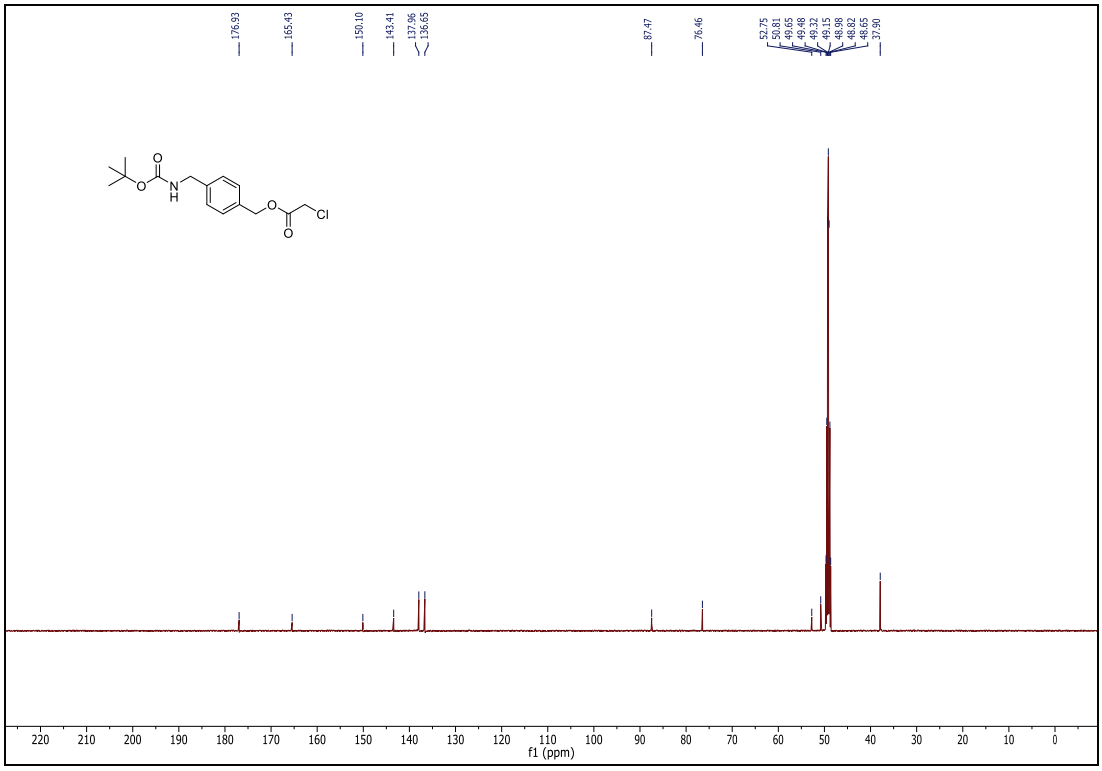
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-azidoacetate



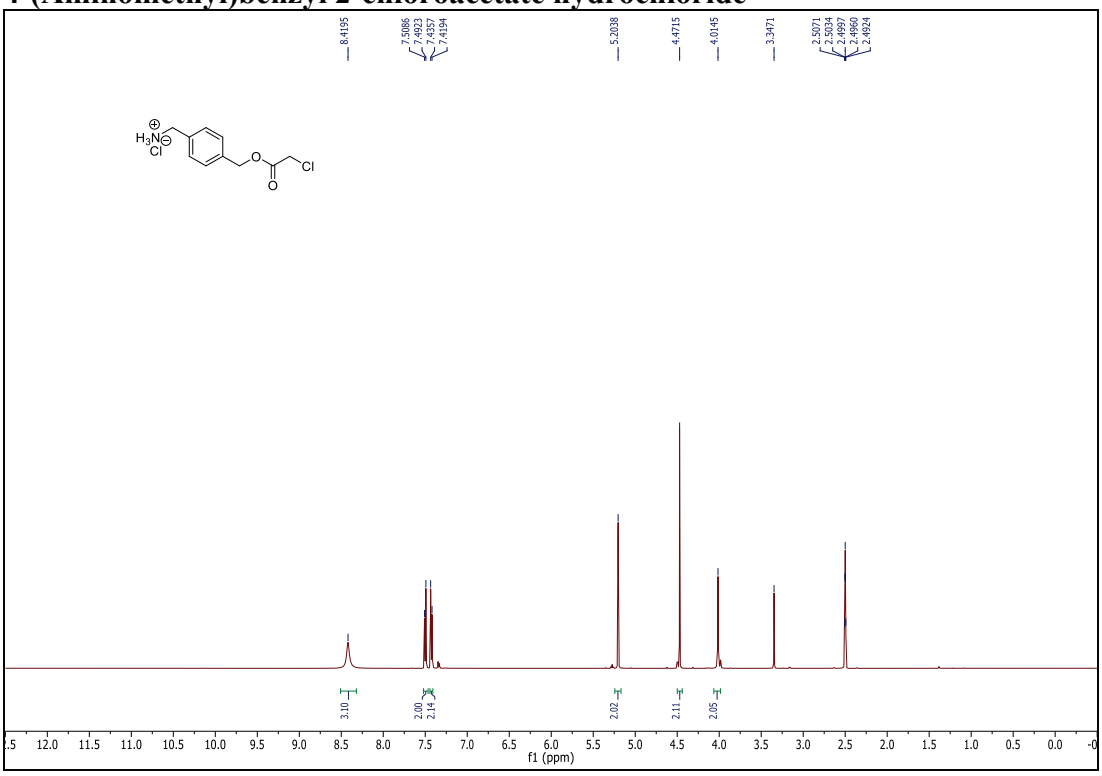


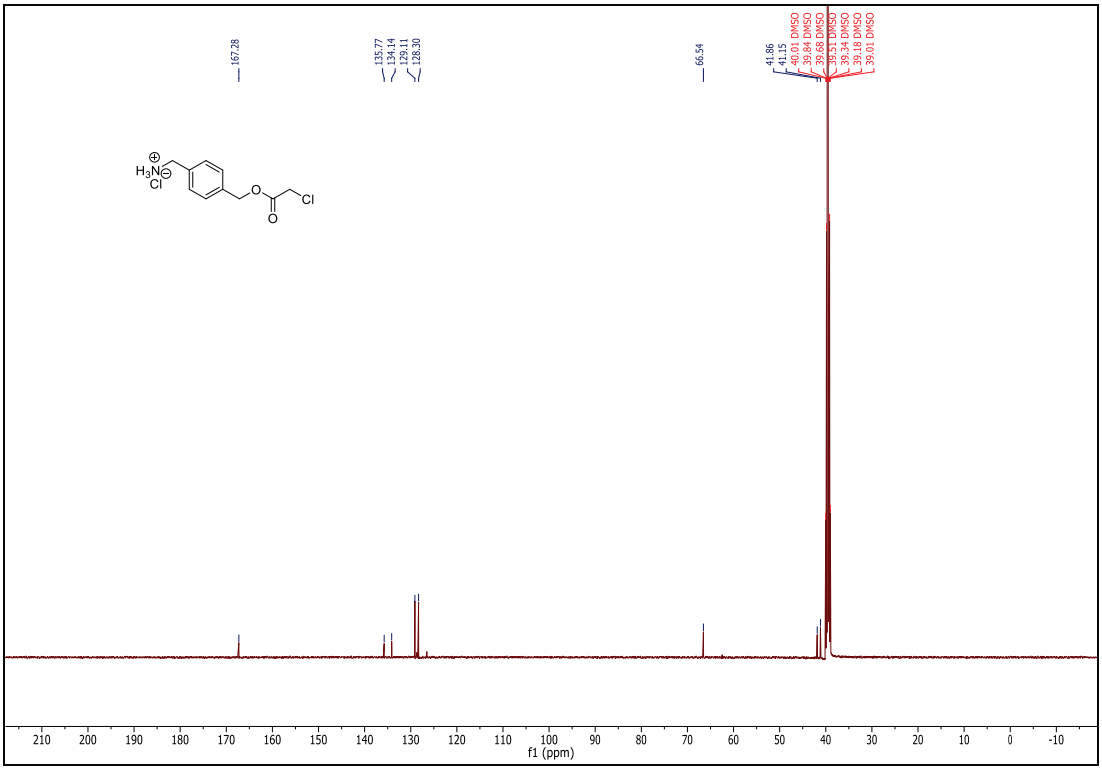
4-(*tert*-Butoxycarbonylaminomethyl)benzyl 2-chloroacetate



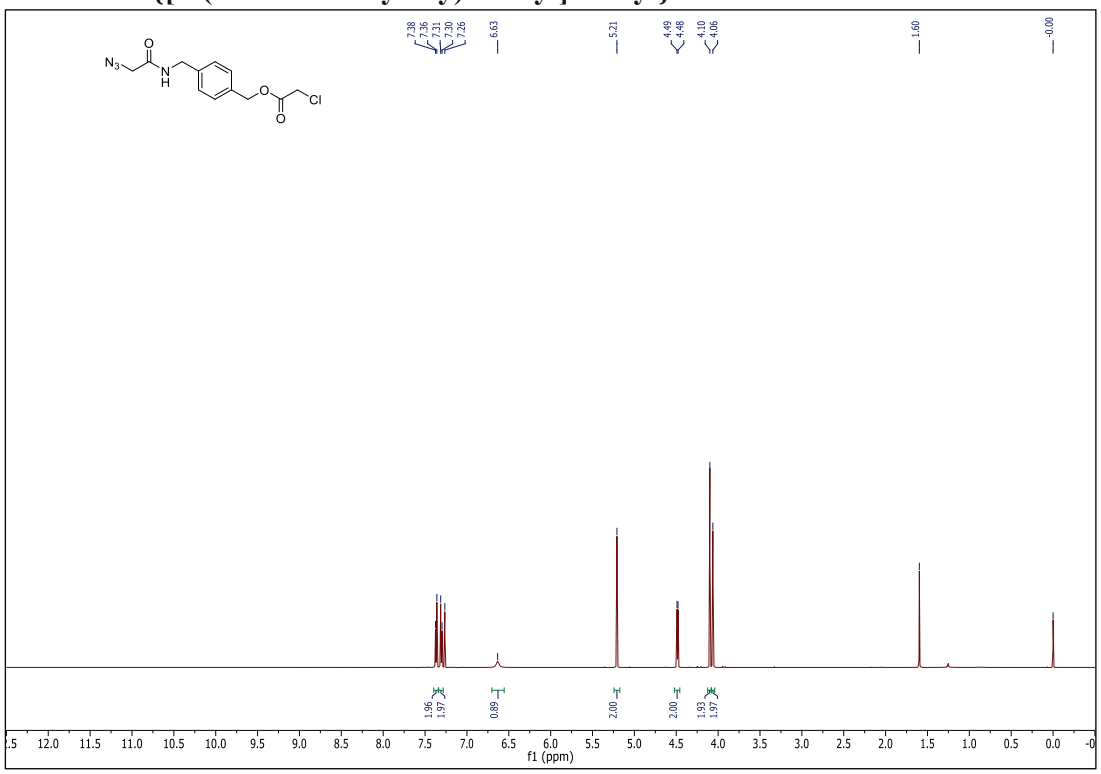


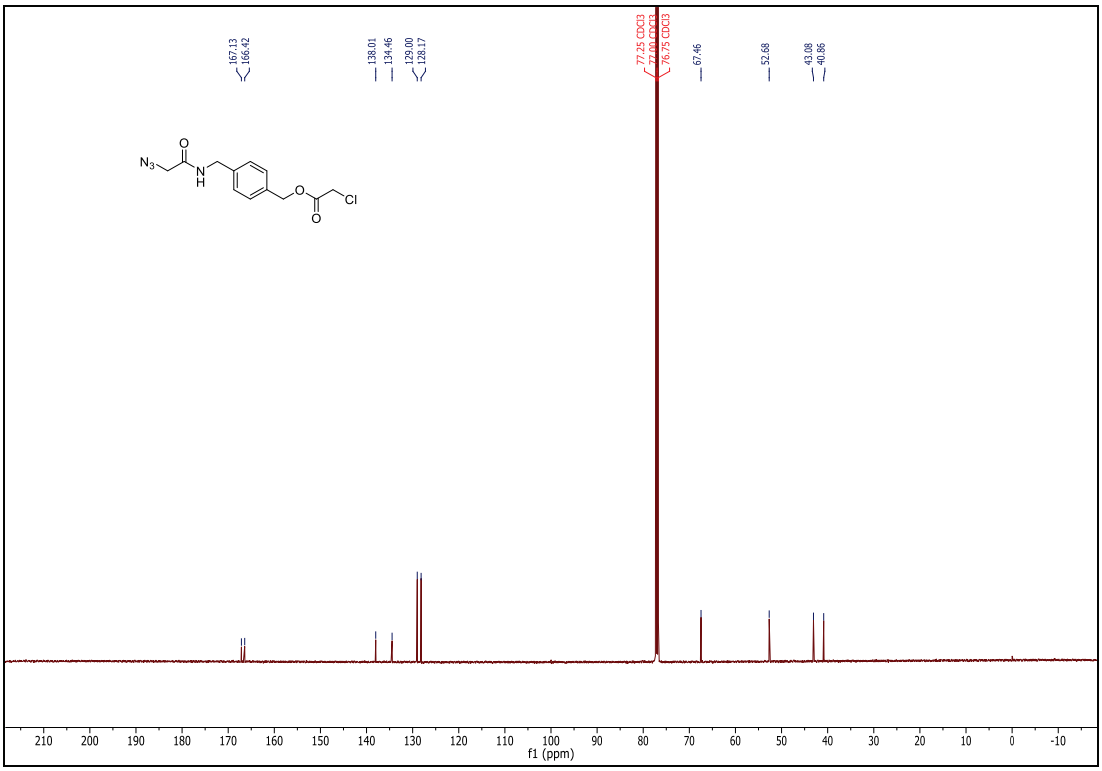
4-(Aminomethyl)benzyl 2-chloroacetate hydrochloride



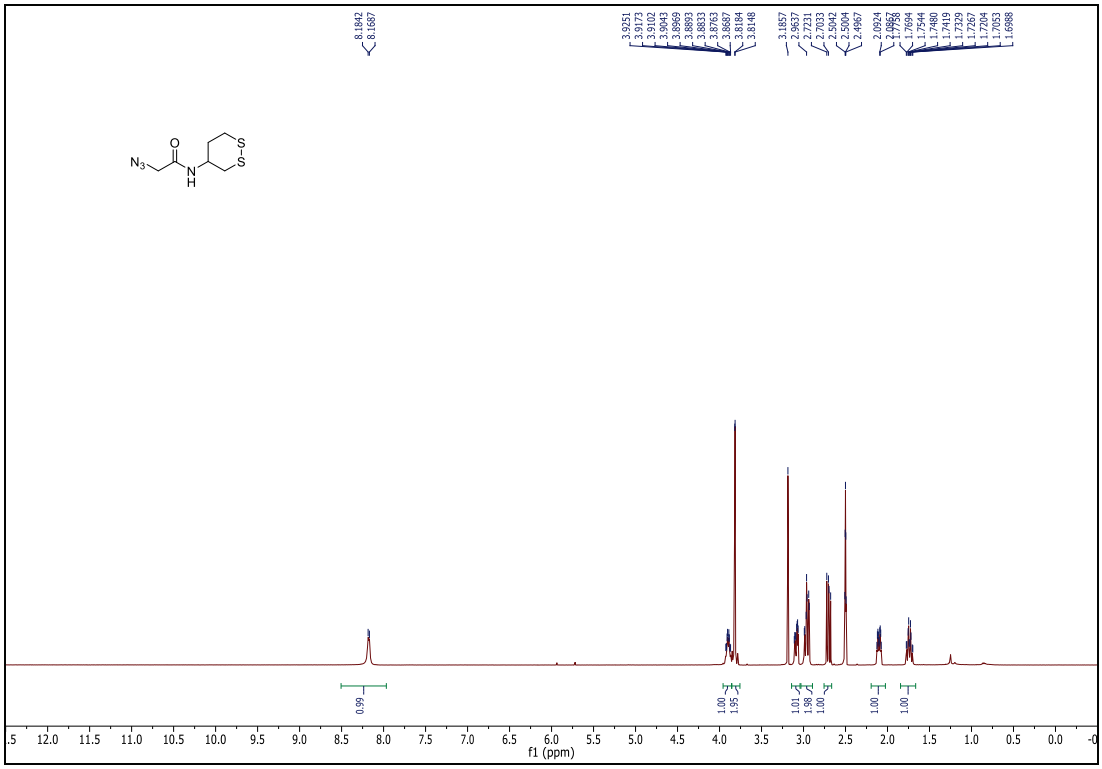


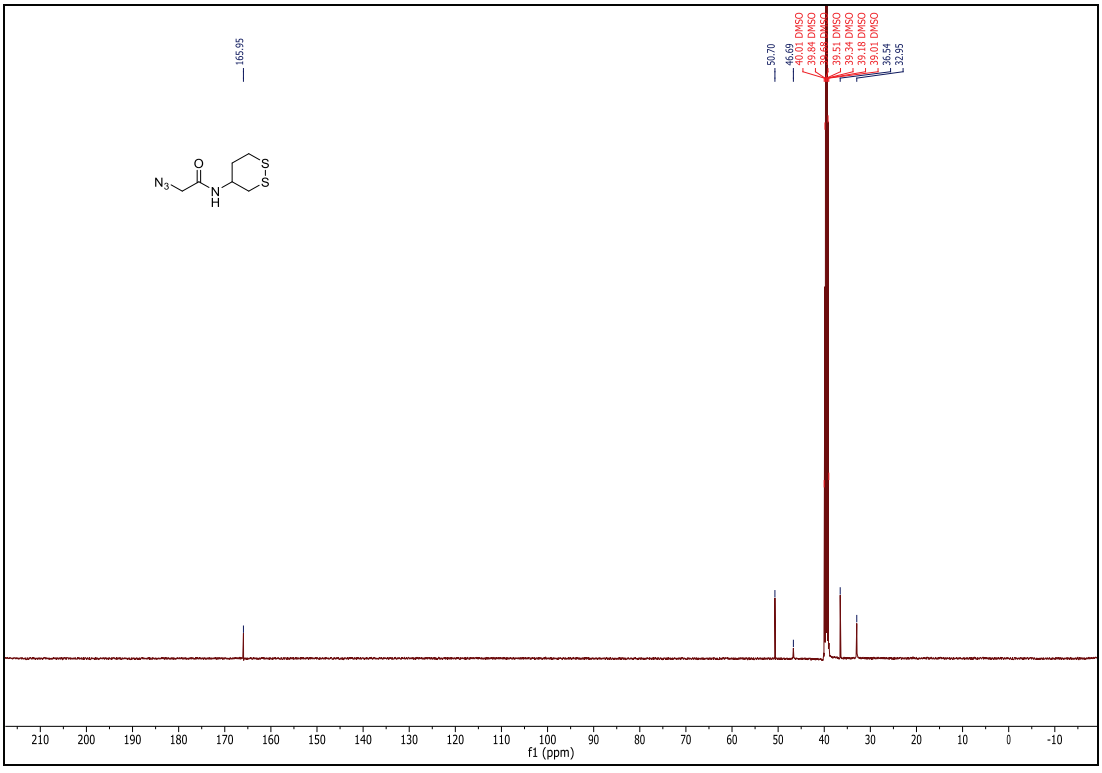
2-Azido-*N*-{[4-(2-chloroacetyloxy)methyl]benzyl}acetamide



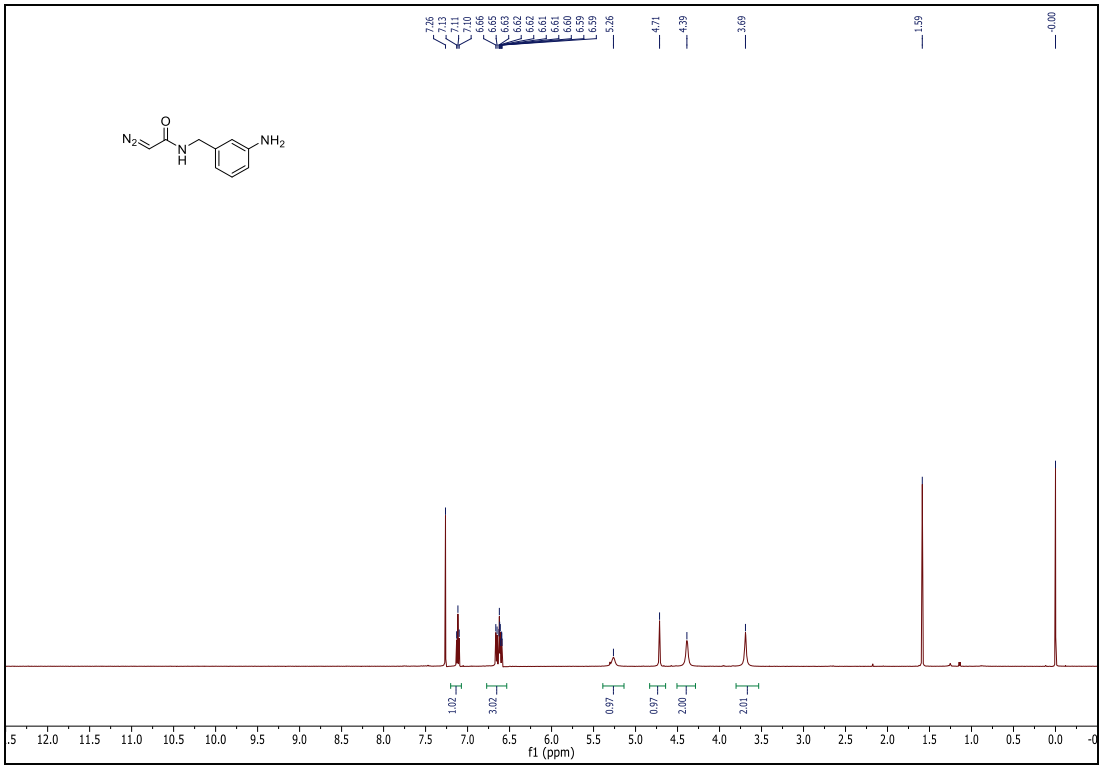


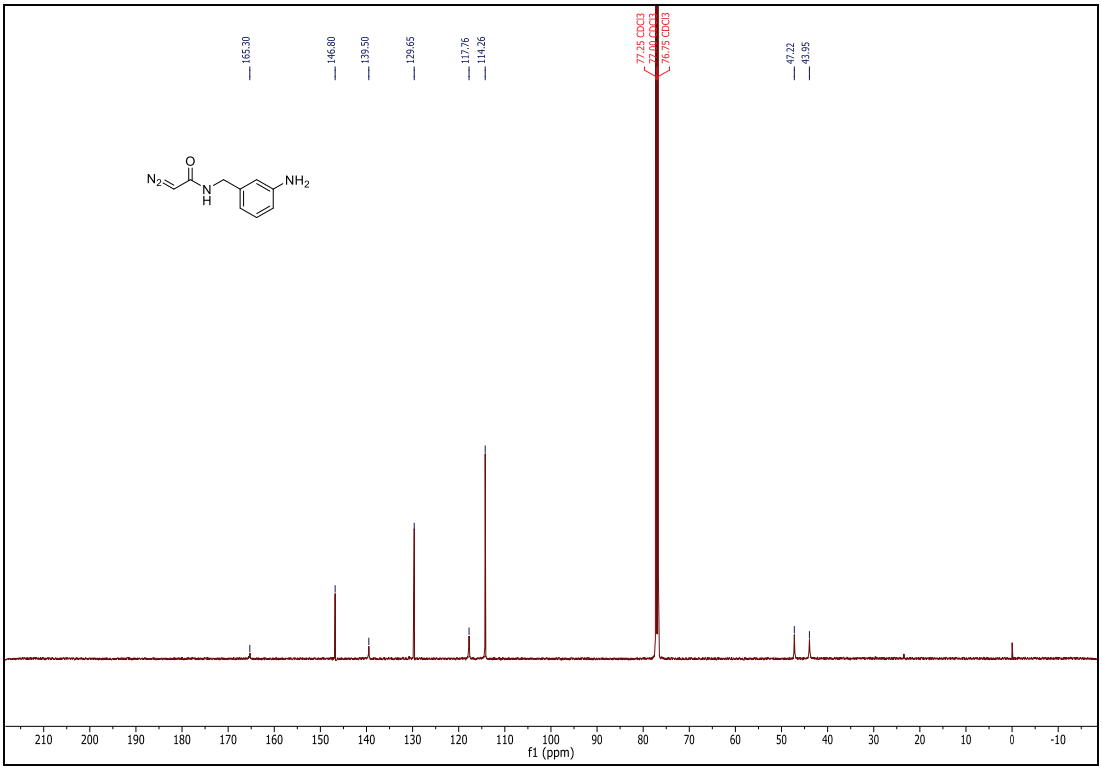
2-Azido-*N*-(3,4-dithianyl)acetamide



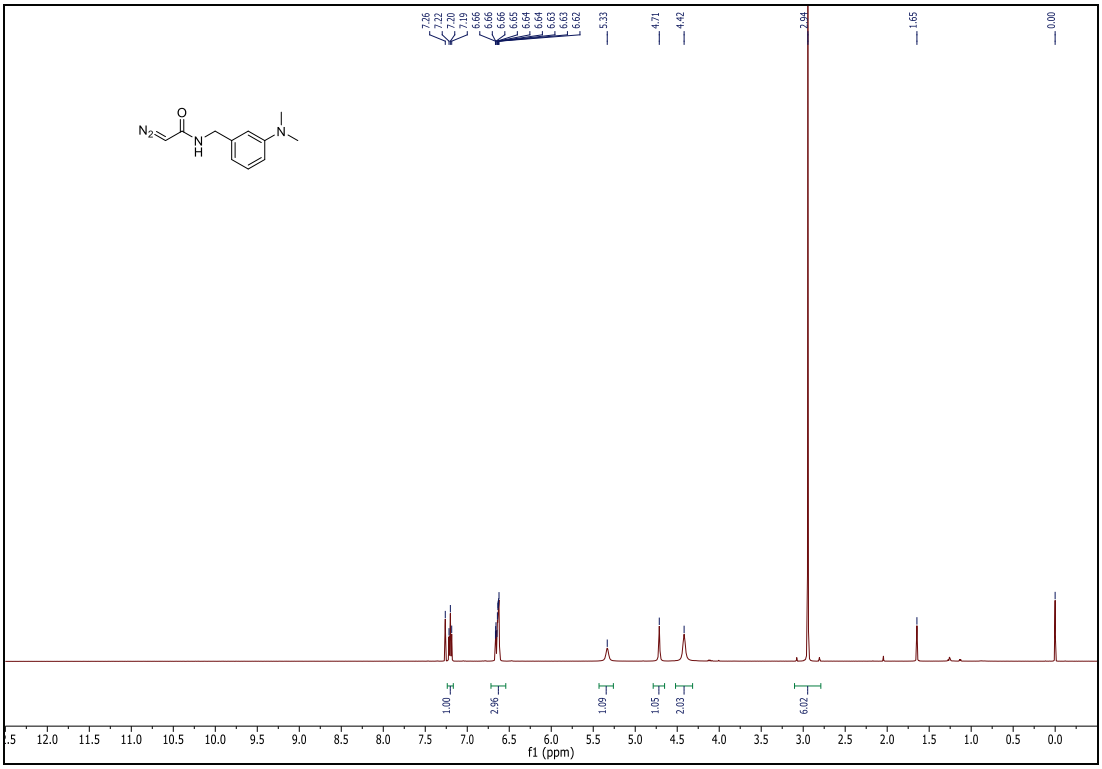


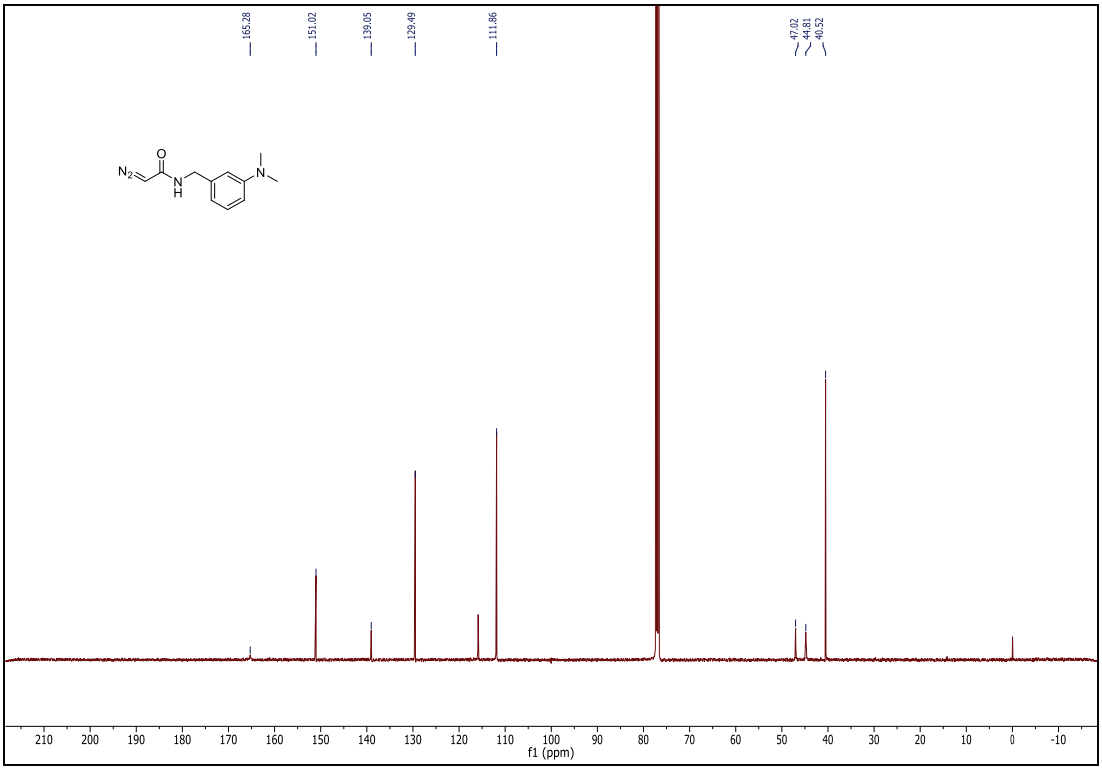
N-(3-Aminobenzyl)-2-diazoacetamide



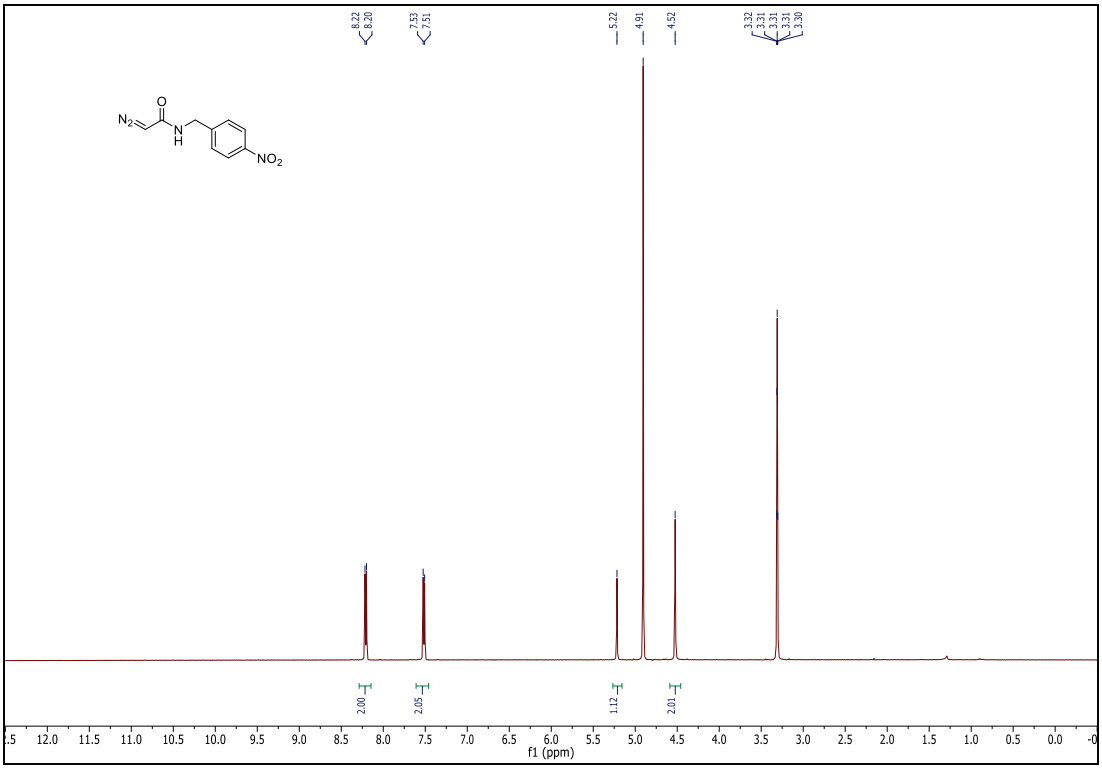


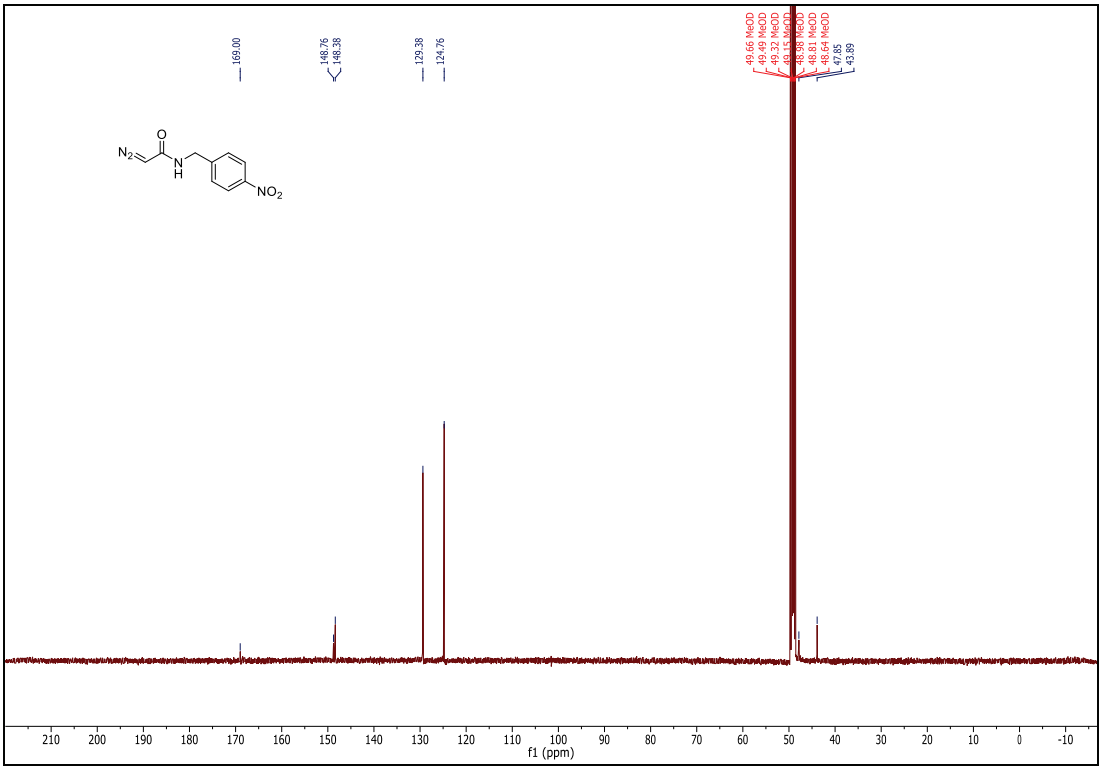
2-Diazo-*N*-[3-(*N*,*N*-dimethylamino)benzyl]acetamide



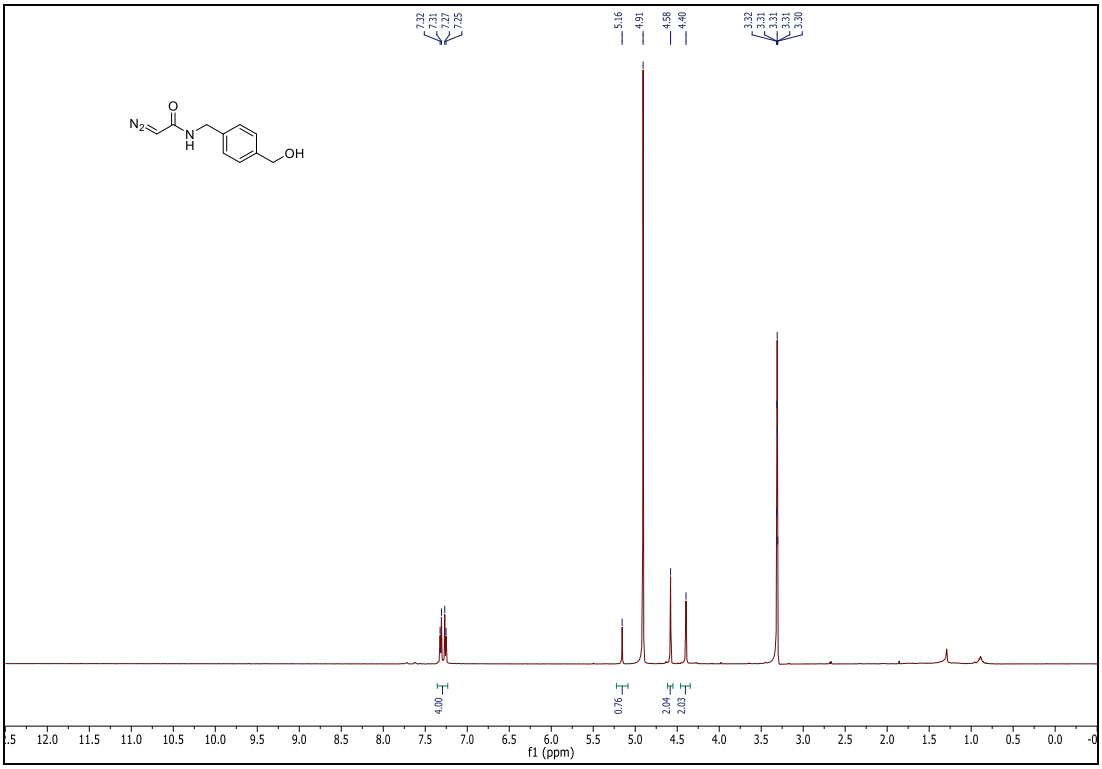


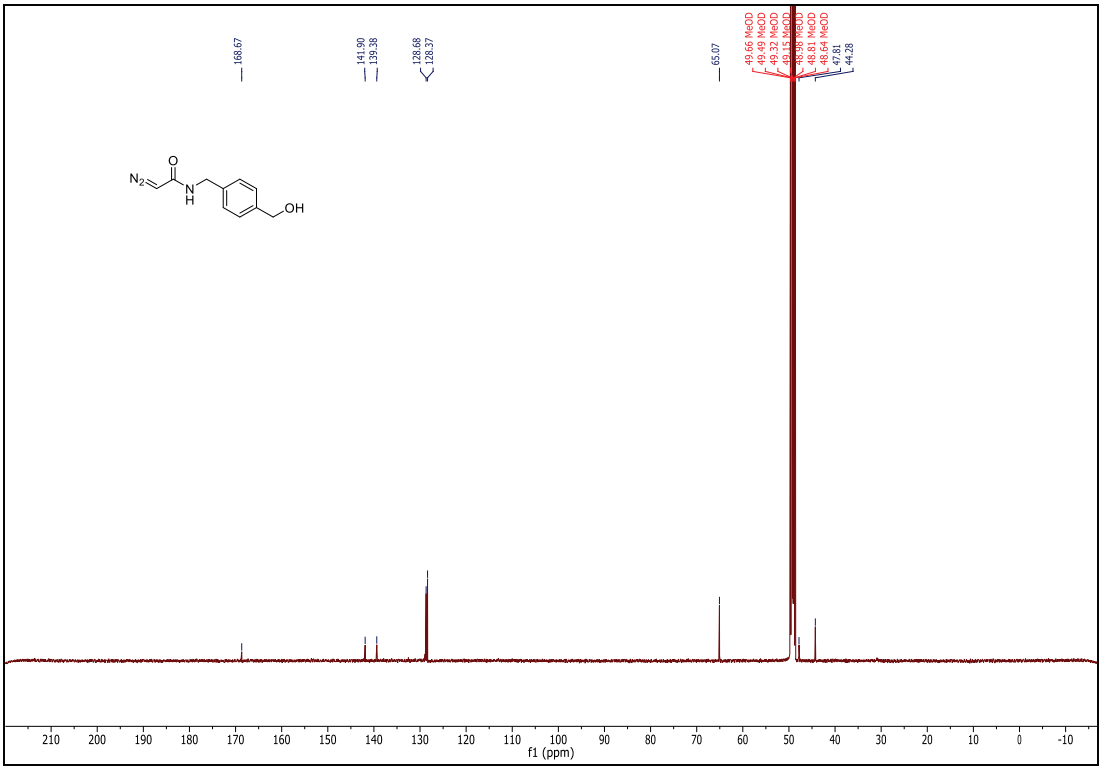
2-Diazo-*N*-(4-nitrobenzyl)acetamide



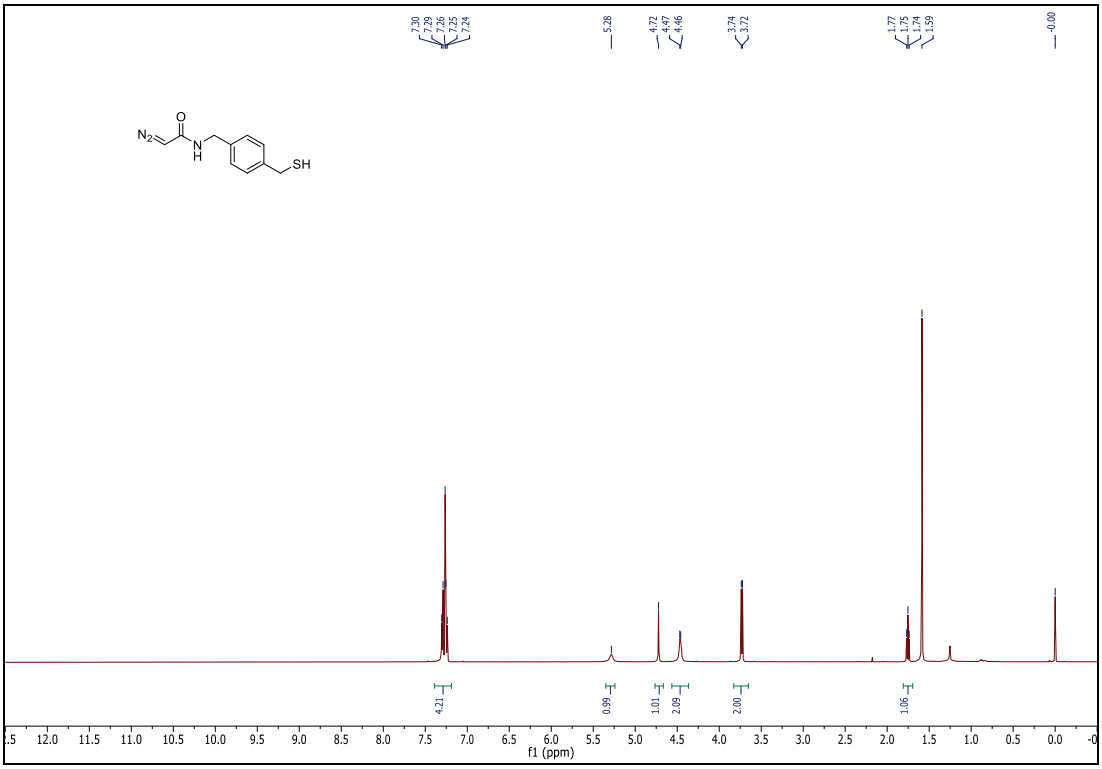


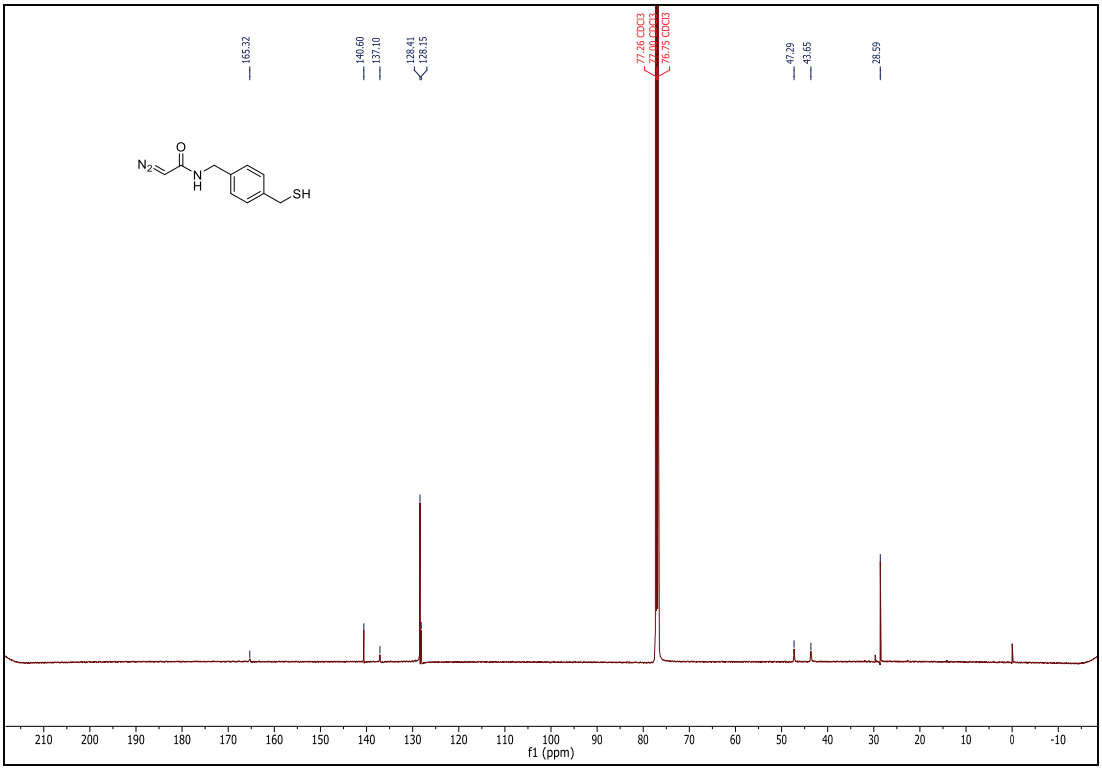
2-Diazo-*N*-[4-(hydroxymethyl)benzyl]acetamide



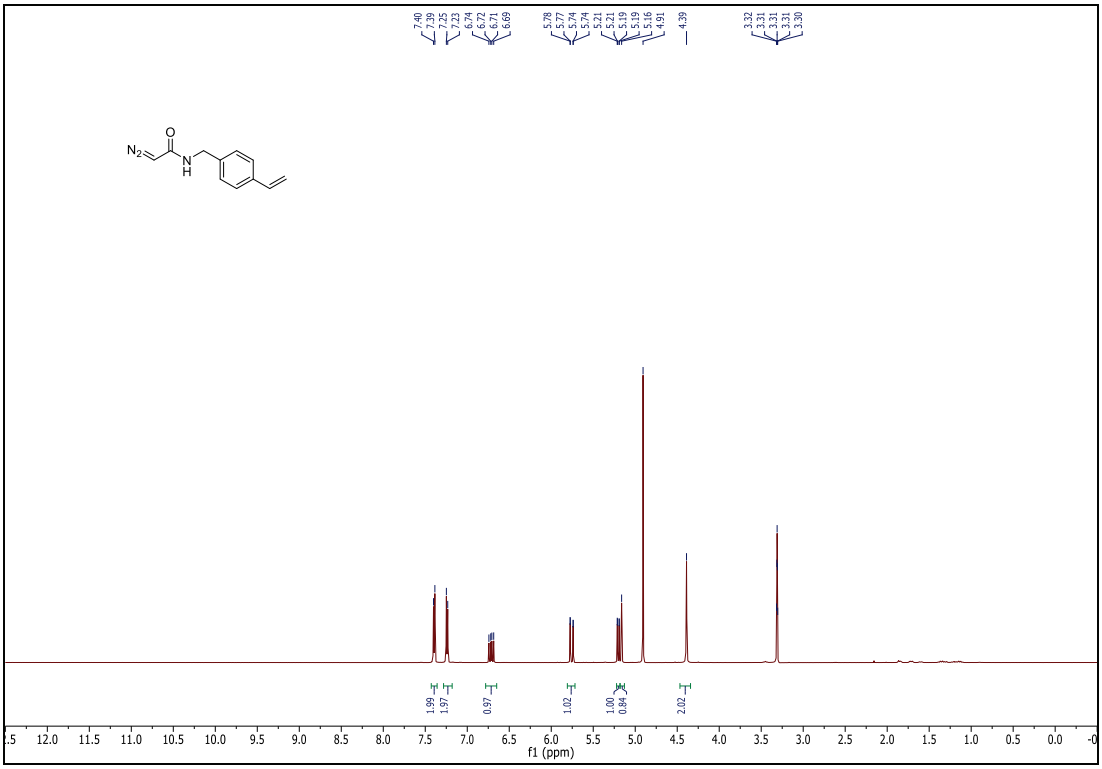


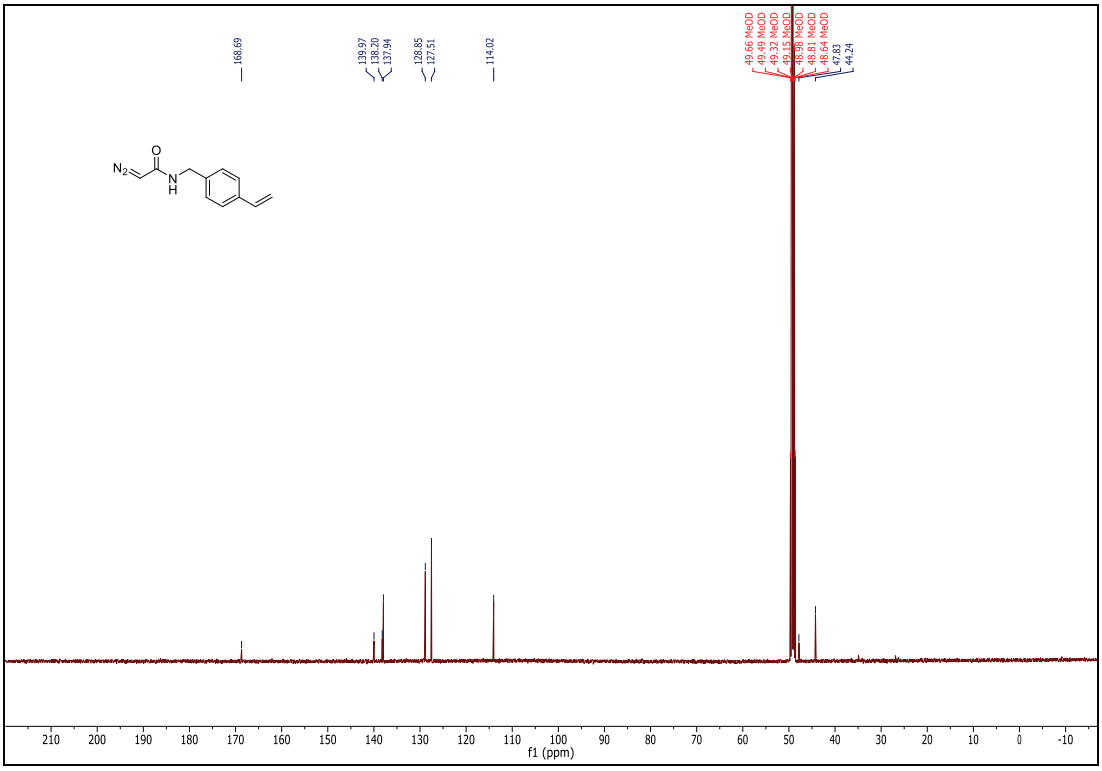
2-Diazo-*N*-[4-(mercaptomethyl)benzyl]acetamide



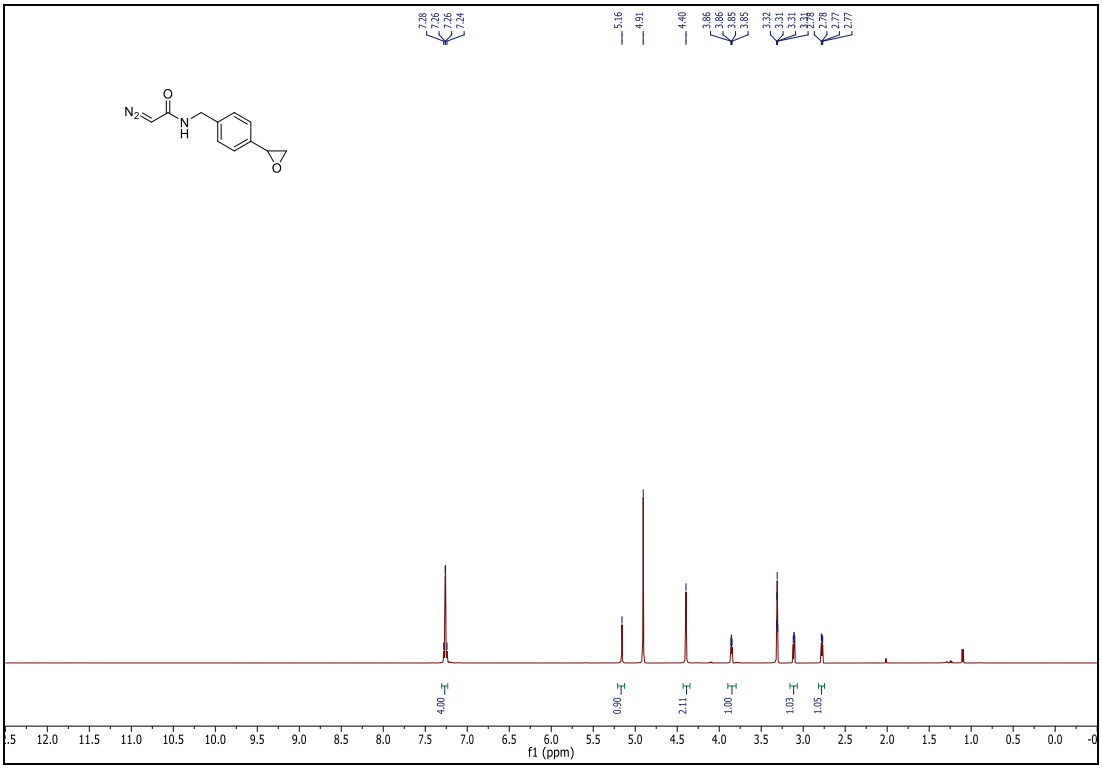


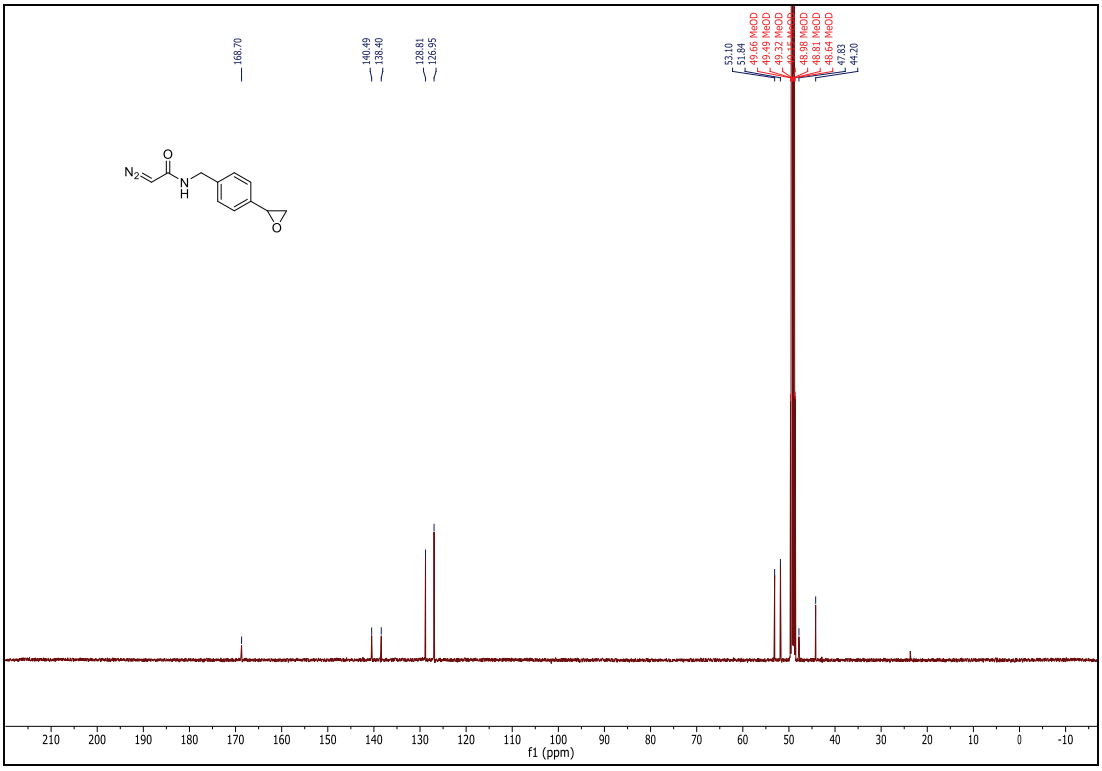
2-Diazo-*N*-(4-vinylbenzyl)acetamide



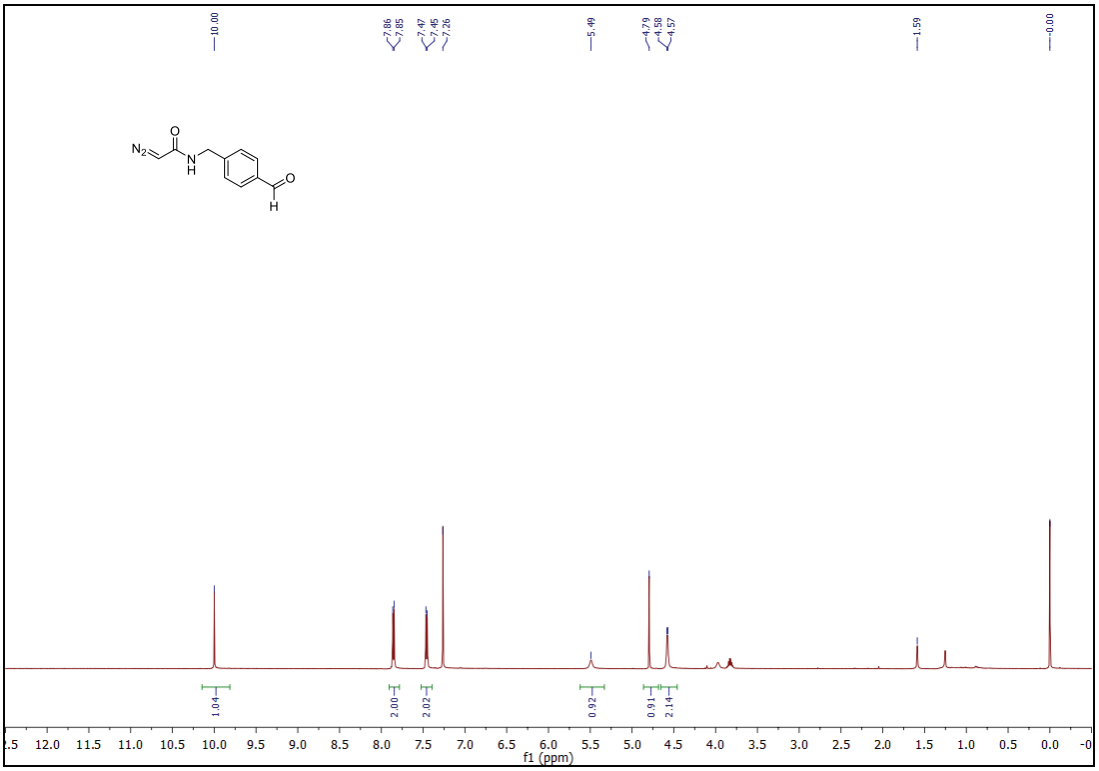


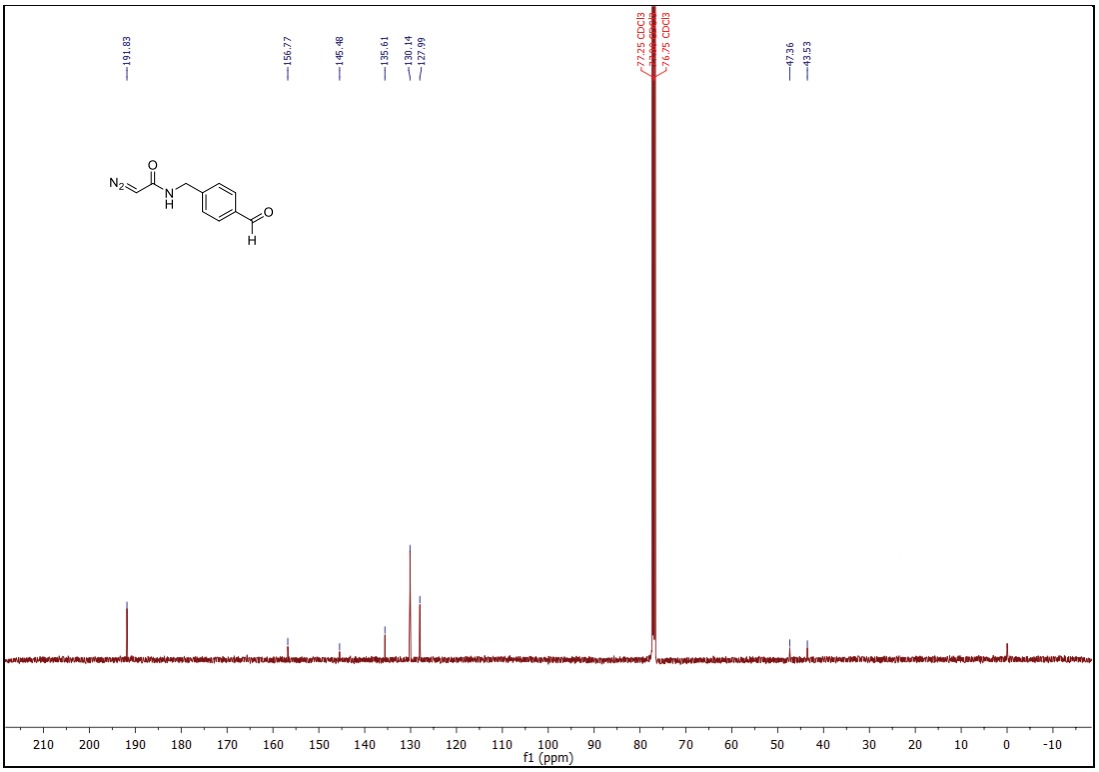
2-Diazo-*N*-(4-oxiranylbenzyl)acetamide



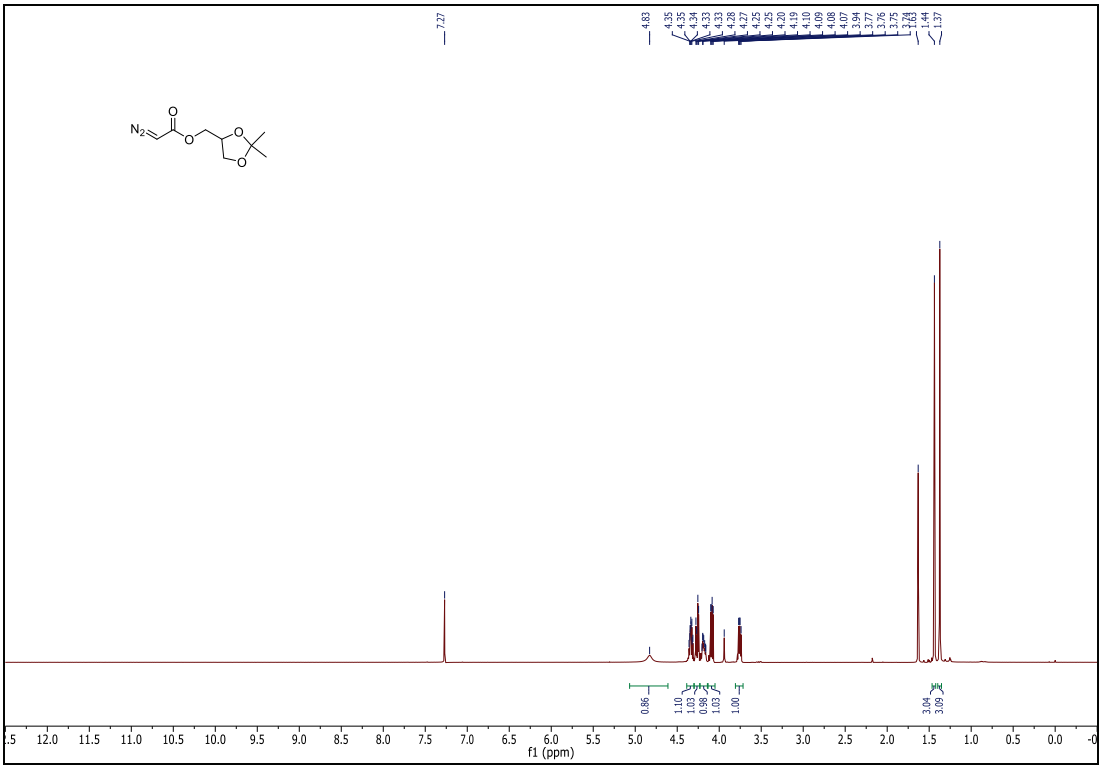


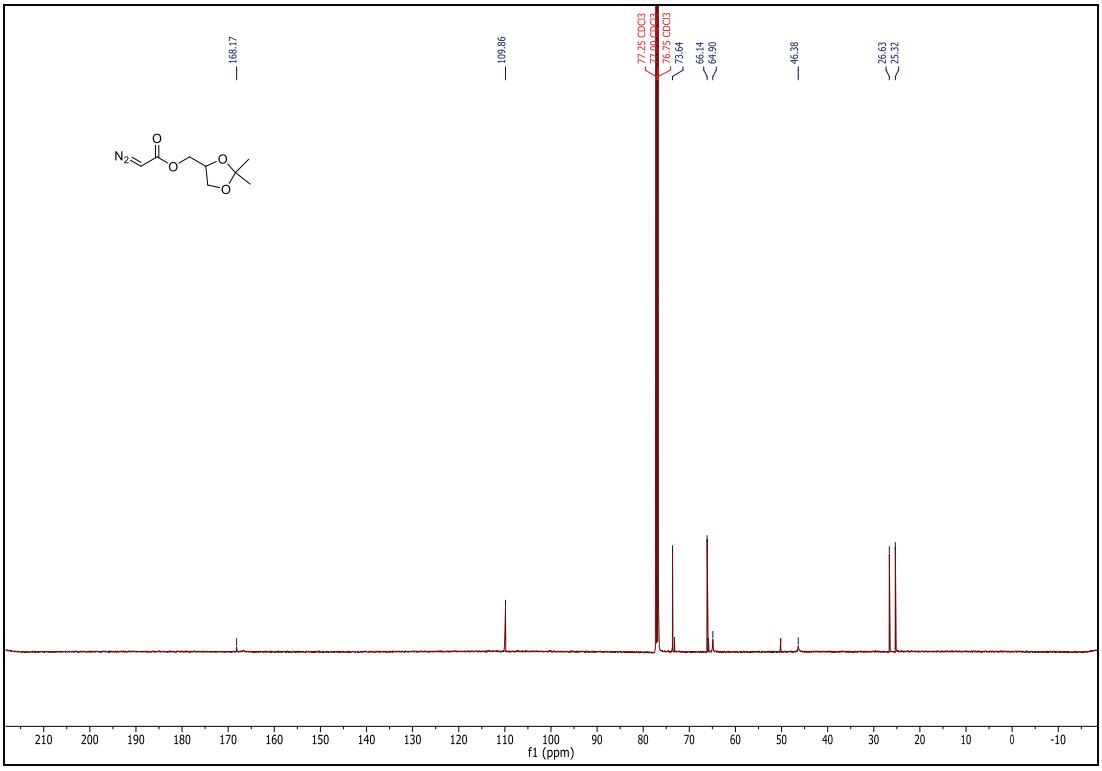
2-Diazo-*N*-(4-formylbenzyl)acetamide



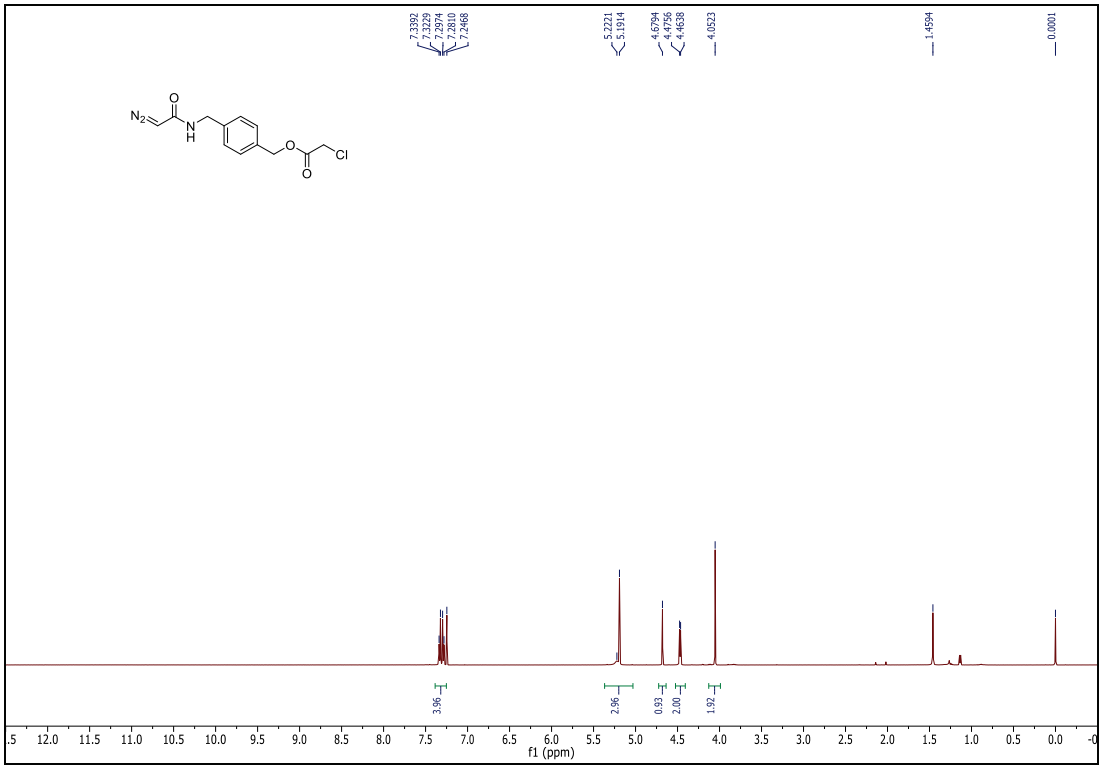


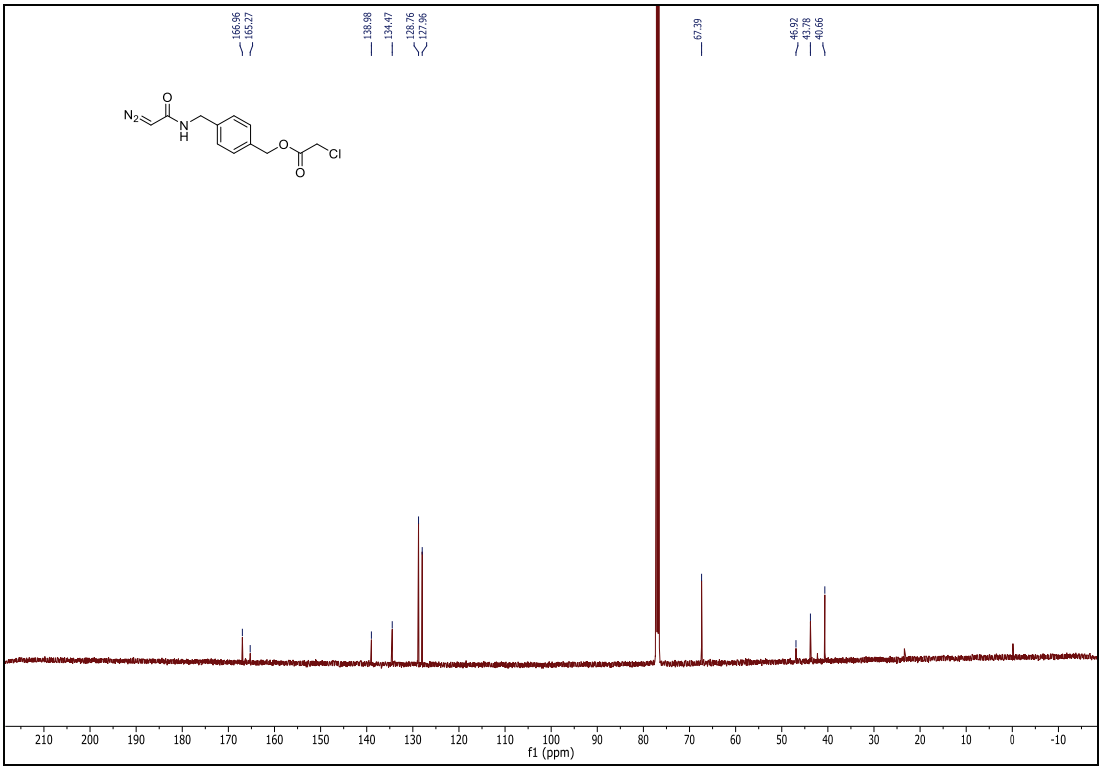
(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl 2-diazoacetate





N-{[4-(2-Chloroacetyloxy)methyl]benzyl}-2-diazoacetamide





2-Diazo-*N*-(3,4-dithianyl)acetamide