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SUPPORTING INFORMATION

for

Direct and Straightforward Transfer of C1 Functionalized Synthons to Phosphorous Electrophiles for Accessing gem-P-Containing Methanes

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1. Instrumentation and General Analytical Methods

Melting Points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Bruker maXis 4G instrument (ESI-TOF, HRMS). ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 spectrometer 400MHz (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F, 162 MHz for ^{31}P, 76 MHz for ^{77}Se, 149 MHz for ^{119}Sn) at 297 K using a directly detecting broadband observe (BBFO) probe. The center of the (residual) solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^{1}H in $CDCl_3$), δ 77.00 ppm (^{13}C in $CDCl_3$). Spin-spin coupling constants (*J*) are given in Hz.

In nearly all cases, full and unambiguous assignment of all resonances could be performed by combined application of standard NMR techniques, such as APT, HSQC, HMBC, COSY and NOESY experiments.

All the reactions were carried out under inert atmosphere of Argon. THF was distilled over Na/benzophenone. Other chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar and TCI Europe. Solutions were evaporated under reduced pressure with a rotary evaporator. MeLi-LiBr ethereal solution (2.2 M) was purchased from Acros and titrated before the use. The derivatization of hydrocodone (Scheme 4 – *path b*) required special attention due to the narcotic properties of the drug.

TLC was carried out on aluminium sheets precoated with silica gel $60F^{254}$ (Merchery-Nagel, Merk); the spots were visualised under UV light (λ=254 nm) and/or $KMnO_4$ (aq.) was used as revealing system.

2. General Procedures

General Procedure for homologation of different phosphorous electrophiles (General Procedure 1)

To a cooled (-78 °C) solution of the suitable electrophile (R_nPX_n/R_nOPX_n, 1.0 equiv) in dry THF, the proper dihalomethane (2.0 equiv) was added under Argon. After 2 min, an ethereal solution of MeLi-LiBr (1.8 equiv, 2.2 M) was added dropwise, using a syringe pump (flow: 0.200 mL/min). The resulting solution was stirred for one hour at -78 °C. A satured solution of NH_4Cl was added (2 mL/mmol substrate), then was extracted with Et_2O (2 x 5 mL) and washed with water (5 mL) and brine (10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and, after removal of the solvent under reduced pressure, the so-obtained crude mixture was subjected to chromatography silica gel to afford pure compounds.

General Procedure for the preparation of lithium dihalocarbenoids and its subsequent addition to different phosphorous electrophiles (General Procedure 2)

Preparation of LDA.

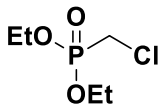
To a solution of distilled *N,N*-diisopropylamine (DIPA, 1.8 equiv) in anhydrous THF, MeLi-LiBr (2.2 M, 1.8 equiv) was added dropwise at 0 °C under Argon. The reaction was stirred for 30 minutes in order to generate lithium diisopropylamide (LDA).

Dihalomethylation

To a cooled (-78 °C) solution of the suitable electrophile (R_nPX_n/R_nOPX_n, 1.0 equiv) in dry THF, the proper dihalomethane (2.0 equiv) was added under Argon. After 2 min, LDA (1.8 equiv) was added dropwise, using a syringe pump (flow: 0.200 mL/min). The resulting solution was stirred for one hour at -78 °C. A satured solution of NH_4Cl was added (2 mL/mmol substrate), then was extracted with Et_2O (2 x 5 mL) and washed with water (5 mL) and brine (10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and, after removal of the solvent under reduced pressure, the so-obtained crude mixture was subjected to chromatography silica gel to afford pure compounds.

3. Spectral and Characterization Data

Diethyl (chloromethyl)phosphonate (2)[1]



By following General Procedure 1, starting from diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv), chloroiodomethane (0.353 g, 2.0 mmol, 2.0 equiv), MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv) in dry THF (3 mL), **2** was obtained in 89% yield (0.166 g) as colourless oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.20 (m, 4H, $C\underline{H}_2CH_3$), 3.53 (d, *J* = 6.6 Hz, 2H, CH_2Cl), 1.35 (m, 6H, CH_3).

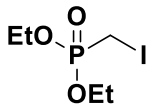
^{13}C NMR (100 MHz, $CDCl_3$) δ: 63.37 (d, *J* = 6.5 Hz, $\underline{C}H_2CH_3$), 33.34 (d, *J* = 159.9 Hz, CH_2Cl), 16.37 (d, *J* = 5.8 Hz, CH_3).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 18.71 (m).

HRMS (ESI), *m/z*: calcd. for $C_5H_{12}ClO_3NaP^+$: 209.0105 $[M+Na]^+$; found 209.0109.

Scaling-up of the reaction (20 mmol) - By following General Procedure 1, starting from diethyl phosphorochloridate (3.450 g, 20.0 mmol, 1.0 equiv), chloroiodomethane (7.055 g, 40.0 mmol, 2.0 equiv), MeLi-LiBr complex (16.4 mL of 2.2M, 36.0 mmol, 1.8 equiv) in dry THF (30 mL), **2** was obtained in 89% yield (3.320 g) as colourless oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4). *Spectroscopic and spectrometric data match with those reported for the 1.0 mmol scale reaction.*

Diethyl (iodomethyl)phosphonate (3)[2]



By following General Procedure 1, starting from diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv), diiodomethane (0.536 g, 2.0 mmol, 2.0 equiv), MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv) in dry THF (3 mL), **3** was obtained in 84% yield (0.233 g) as pale oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.17 (m, 4H, $C\underline{H}_2CH_3$), 3.02 (d, 2H, CH_2I), 1.34 (dt, J^d = 0.6, Hz J^t = 7.1 Hz, 6H, CH_3).

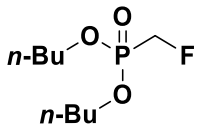
^{13}C NMR (100 MHz, $CDCl_3$) δ: 63.39 (d, *J* = 6.5 Hz, $\underline{C}H_2CH_3$), 16.32 (d, *J* = 6.0 Hz, CH_3), -14.43 (d, *J* = 156.0 Hz, CH_2I).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 20.20 (m).

HRMS (ESI), *m/z*: calcd. for $C_5H_{12}IO_3NaP^+$: 300.9461 $[M+Na]^+$; found 300.9456.

Scaling-up of the reaction (20 mmol) - By following General Procedure 1, starting from diethyl phosphorochloridate (3.450 g, 20.0 mmol, 1.0 equiv), diiodomethane (10.714 g, 40.0 mmol, 2.0 equiv), MeLi-LiBr complex (16.4 mL of 2.2M, 36.0 mmol, 1.8 equiv) in dry THF (30 mL), **3** was obtained in 84% yield (4.671 g) as pale oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).
Spectroscopic and spectrometric data match with those reported for the 1.0 mmol scale reaction.

Dibutyl (fluoromethyl)phosphonate (4)[3]



By following General Procedure 1, starting from dibutyl phosphorochloridate (0.201 g, 1.0 mmol, 1.0 equiv), fluoroiodomethane (0.320 g, 2.0 mmol, 2.0 equiv) and MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv) in dry THF:Et_2O 50:50 (6 mL), **4** was obtained in 86% yield (0.194 g) as a colorless oil after flash column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

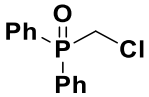
^{1}H NMR (400 MHz, C_6D_6) δ: 4.34 (dd, $^2J^{H,F}$ = 47.1 Hz, $^2J^{H,P}$ = 4.7 Hz, 1H, CH_2F), 3.93 (m, 4H, $C\underline{H}_2CH_2CH_2CH_3$), 1.40 (m, 4H, $CH_2C\underline{H}_2CH_2CH_3$), 1.19 (m, 4H, $CH_2CH_2C\underline{H}_2CH_3$), 0.74 (t, *J* = 7.3 Hz, 6H, CH_3).

^{13}C NMR (100 MHz, C_6D_6) δ: 76.80 (dd, $^2J^{C,F}$ = 181.0 Hz, $^2J^{C,P}$ = 168.5 Hz, CH_2F), 66.28 (d, $^2J^{C,P}$ = 6.3 Hz, $\underline{C}H_2CH_2CH_2CH_3$), 32.78 (d, $^3J^{C,P}$ = 5.6 Hz, $CH_2\underline{C}H_2CH_2CH_3$), 18.86 (s, $CH_2CH_2\underline{C}H_2CH_3$), 13.60 (s, CH_3).

^{19}F-NMR (376 MHz, C_6D_6) δ: - 248.56 (dt, d: $^2J^{PF}$ = 61.9 Hz, t: $^2J^{FH}$ = 47.1 Hz).

HRMS (ESI), *m/z*: calcd. for $C_9H_{20}FO_3NaP^+$: 249.1026 $[M+Na]^+$; found 249.1029.

(Chloromomethyl)(diphenyl)phosphine oxide (5)[4]



By following General Procedure 1, starting from diphenylphosphinic chloride (0.237 g, 1.0 mmol, 1.0 equiv), chloroiodomethane (0.353 g, 2.0 mmol, 2.0 equiv), MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv) in dry THF (3 mL), **5** was obtained in 90% yield (0.226 g) as colourless oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 7:3).

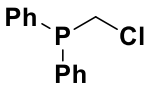
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (m, 4H, Ph H-2,6), 7.59 (m, 2H, Ph H-4), 7.51 (m, 4H, Ph H-3,5), 4.04 (d, *J* = 6.6 Hz, 2H, CH_2Cl).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 132.64 (d, *J* = 2.8 Hz, Ph C-4), 131.54 (d, *J* = 9.4 Hz, Ph C-2,6), 129.63 (d, *J* = 104.4 Hz, Ph C-1), 128.75 (d, *J* = 12.2 Hz, Ph C-3,5), 37.64 (d, *J* = 72.2 Hz, CH_2Cl).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 28.39 (s).

HRMS (ESI), *m/z*: calcd. for $C_{13}H_{12}ClONaP^+$: 273.0207 $[M+Na]^+$; found 273.0210.

(Chloromethyl)(diphenyl)phosphine (6)[5]



By following General Procedure 1, starting from diphenylphosphinous chloride (0.221 g, 1.0 mmol, 1.0 equiv), chloroiodomethane (0.353 g, 2.0 mmol, 2.0 equiv), MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv) in dry THF (3 mL), **6** was obtained in 80% yield (0.188 g) as colourless oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

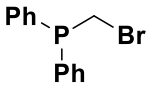
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (m, 4H, Ph H-2,6), 7.58 (m, 2H, Ph H-4), 7.50 (m, 4H, Ph H-3,5), 4.04 (d, *J* = 6.6 Hz, 2H, CH_2Cl).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 132.60 (d, *J* = 2.8 Hz, Ph C-4), 131.49 (d, *J* = 9.4 Hz, Ph C-2,6), 129.57 (d, *J* = 104.4 Hz, Ph C-1), 128.70 (d, *J* = 12.2 Hz, Ph C-3,5), 37.60 (d, *J* = 72.2 Hz, CH_2Cl).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 28.52 (m).

HRMS (ESI), *m/z*:calcd. for $C_{13}H_{12}ClNaP^+$: 257.0257 $[M+Na]^+$; found 257.0262.

(Bromomethyl)(diphenyl)phosphine (7)



By following General Procedure 1, starting from diphenylphosphinous chloride (0.221 g, 1.0 mmol, 1.0 equiv), bromoiodomethane (0.442 g, 2.0 mmol, 2.0 equiv), MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv) in dry THF (3 mL), **7** was obtained in 83% yield (0.232 g) as pale oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

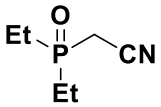
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (m, 4H, Ph H-2,6), 7.59 (m, 2H, Ph H-4), 7.52 (m, 4H, Ph H-3,5), 3.81 (d, *J* = 5.8 Hz, 2H, CH_2Br).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 132.59 (d, *J* = 2.8 Hz, Ph C-4), 131.49 (d, *J* = 9.4 Hz, Ph C-2,6), 130.03 (d, *J* = 104.9 Hz, Ph C-1), 128.77 (d, *J* = 12.2 Hz, Ph C-3,5), 23.47 (d, *J* = 69.7 Hz, CH_2Br).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 27.11 (m).

HRMS (ESI), *m/z*: calcd. for $C_{13}H_{12}BrNaP^+$: 300.9752 $[M+Na]^+$; found 300.9755.

(Diethylphosphosphino)acetonitrile (8)



Commercially available dry acetonitrile (0.082 g, 2.0 mmol, 2.0 equiv) was dissolved in 3 mL of dry THF under argon. To this solution MeLi-LiBr (0.82 mL of 2.2 M, 1.8 mmol, 1.8 equiv) was added drop wise at -78 °C and the mixture stirred for 30 min for the generation of lithioacetonitrile.

Diethylphosphinic chloride (0.141 g, 1.0 mmol, 1.0 equiv) dissolved in 3 mL of dry THF was added dropwise to the prepared lithioacetonitrile at the same temperature and allowed to react for 60 min. The reaction was quenched with aqueous NH_4Cl and allowed to stand at -78 °C for 10 min before warming at r.t. The resulting organic phase was exhaustively extracted 3 times with Et_2O, washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The reaction provided 0.132 g (91% yield) of **8** as a colorless oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 7.5:2.5).

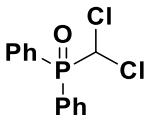
^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.22 (m, 4H, $C\underline{H}_2CH_3$), 2.85 (dd, *J* = 20.9 Hz, *J* = 0.9 Hz, 2H, CH_2CN), 1.36 (m, 6H, CH_3)

^{13}C NMR (100 MHz, $CDCl_3$) δ: 112.57 (d, *J* = 11.3 Hz, CN), 63.84 (d, *J* = 6.5 Hz, $\underline{C}H_2CH_3$), 16.41 (d, *J* = 143.9 Hz, $\underline{C}H_2CN$) 16.22 (d, *J* = 5.9 Hz, CH_3)

^{31}P NMR (162 MHz, $CDCl_3$) δ: 14.32 (m)

HRMS (ESI), *m/z*: calcd. for $C_6H_{12}NNaP^+$: 152.0600 $[M+Na]^+$; found 152.0605.

(Dichloromethyl)(diphenyl)phosphine oxide (9)[6]



By following General Procedure 2, starting from the corresponding diphenylphosphinic chloride (0.237g, 1.0 mmol, 1.0 equiv), dichloromethane (0.170 g, 2.0 mmol, 2.0 equiv), LDA [1.8 equiv in THF solution (5 mL) – generated from *N,N*-di-*i*-propylamine (0.202 g, 1.8 mmol, 1.8 equiv) and MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv)]. The reaction provided 0.251 g (88% yield) of **9** as a colourless oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 5:5).

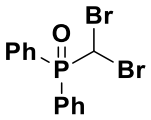
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (m, 4H, Ph H-2,6), 7.62 (m, 2H, Ph H-4), 7.53 (m, 4H, Ph H-3,5), 6.20 (m, 1H, $CHCl_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.11 (d, *J* = 2.9 Hz, Ph C-4), 132.41 (d, *J* = 9.2 Hz, Ph C-2,6), 128.67 (d, *J* = 12.4 Hz, Ph C-3,5), 127.26 (d, *J* = 106.4 Hz, Ph C-1), 64.98 (d, *J* = 70.9 Hz, $CHCl_2$).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 30.37 (m).

HRMS (ESI), *m/z*: calcd. for $C_{13}H_{11}Cl_2ONaP^+$: 306.9817 $[M+Na]^+$; found 306.9813.

(Dibromomethyl)(diphenyl)phosphine oxide (10)



By following General Procedure 2, starting from the corresponding diphenylphosphinic chloride(0.237g, 1.0 mmol, 1.0 equiv), dibromomethane (0.348 g, 2.0 mmol, 2.0 equiv), LDA [1.8 equiv in THF solution (5 mL) – generated from *N,N*-di-*i*-propylamine (0.202 g, 1.8 mmol, 1.8 equiv) and MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv)]. The reaction provided 0.314 g (84% yield) of **10** as a pale oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 7:3).

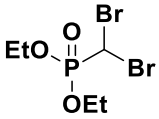
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (m, 4H, Ph H-2,6), 7.63 (m, 2H, Ph H-4), 7.54 (m, 4H, Ph H-3,5), 6.04 (d, *J* = 1.1 Hz, 1H, $CHBr_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.02 (d, *J* = 2.8 Hz, Ph C-4), 132.42 (d, *J* = 9.1 Hz, Ph C-2,6), 128.69 (d, *J* = 12.4 Hz, Ph C-3,5), 127.82 (d, *J* = 107.3 Hz, Ph C-1), 35.28 (d, *J* = 61.0 Hz, $CHBr_2$).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 28.78 (m).

HRMS (ESI), *m/z*: calcd. for $C_{13}H_{11}Br_2ONaP^+$: 394.8806 $[M+Na]^+$; found 394.8809.

Diethyl (dibromomethyl)phosphonate (11)[7]



By following General Procedure 2, starting from the corresponding diethyl phosphorochloridate (0.173g, 1.0 mmol, 1.0 equiv), dibromomethane (0.348 g, 2.0 mmol, 2.0 equiv), LDA [1.8 equiv in THF solution (5 mL) – generated from *N,N*-di-*i*-propylamine (0.202 g, 1.8 mmol, 1.8 equiv)and MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv)]. The reaction provided 0.248 g (80% yield) of **11** as a pale oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

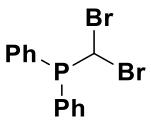
^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.49 (d, *J* = 1.8 Hz, 1H, $CHBr_2$), 4.32 (m, 4H, CH_2), 1.39 (dt, J^d = 0.7 Hz, J^t = 7.0 Hz, 6H, CH_3)

^{13}C NMR (100 MHz, $CDCl_3$) δ: 65.43 (d, *J* = 6.9 Hz, 1H, CH_2), 28.09 (d, *J* = 169.7 Hz, 4H, $CHBr_2$), 16.39 (d, *J* = 6.0 Hz, CH_3)

^{31}P NMR (162 MHz, $CDCl_3$) δ: 9.99(m)

HRMS (ESI), *m/z*: calcd. for $C_5H_{11}Br_2O_3NaP^+$: 330.8705 $[M+Na]^+$; found 330.8701.

(Dibromomethyl)(diphenyl)phosphine (12)



By following General Procedure 2, starting from the corresponding diphenylphosphinous chloride (0.221g, 1.0 mmol, 1.0 equiv), dibromomethane (0.348 g, 2.0 mmol, 2.0 equiv), LDA [1.8 equiv in THF solution (5 mL) – generated from *N,N*-di-*i*-propylamine (0.202 g, 1.8 mmol, 1.8 equiv) and MeLi-LiBr complex (0.82 mL of 2.2M, 1.8 mmol, 1.8 equiv)]. The reaction provided 0.283 g (79% yield) of **12** as a pale oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

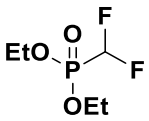
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (m, 4H, Ph H-2,6), 7.63 (m, 2H, Ph H-4), 7.53 (m, 4H, Ph H-3,5), 6.04 (m, 1H, $CHBr_2$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.01 (d, *J* = 2.9 Hz, Ph C-4), 132.41 (d, *J* = 9.1 Hz, Ph C-2,6), 128.68 (d, *J* = 12.4 Hz, Ph C-3,5), 127.83 (d, *J* = 107.2 Hz, Ph C-1), 35.29 (d, *J* = 60.9 Hz, $CHBr_2$).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 28.78 (m).

HRMS (ESI), *m/z*: calcd. for $C_{13}H_{11}Br_2NaP^+$: 378.8857 $[M+Na]^+$; found 378.8860.

Diethyl (difluoromomethyl)phosphonate (13)[8]



To a solution of diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) in dry THF (3 mL) cooled at 0 °C, difluoromethyltrimethylsilane (0.248 g, 2.0 mmol, 2.0 equiv) was added under Argon atmosphere. Then, potassium *tert*-pentoxide 0.9 M in toluene (2.0 mL, 1.8 mmol, 1.8 equiv) was added *via* syringe pump (0.20 mL/min) at 0 °C during a period of 15 min. The reaction mixture was further stirred to reach rt within 4 h. Subsequently, saturated (*aq.*) NH_4Cl (3 mL) was added to the mixture and the organic phase was extracted with diethyl ether (3 x 3 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Compound **13** was obtained as a colourless oil 86% (0.162 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.90 (dt, J^d = 26.9 Hz, J^t = 48.7 Hz, 1H, CHF_2), 4.28 (m, 4H, CH_2), 1.38 (t, *J*= 7.1 Hz, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 111.39 (dt, d: $^1J^{PC}$ = 213.3 Hz, t: $^1J^{FC}$ = 258.0 Hz, CHF_2), 64.48 (d, *J* = 6.5 Hz, CH_2), 16.36 (d, *J* = 5.3 Hz, CH_3).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 4.90 (m, $^2J^{PF}$ = 91.2 Hz, $^2J^{PH}$ = 26.9 Hz, $^3J^{PH}$ = 8.2 Hz).

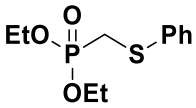
^{19}F-NMR (376 MHz, $CDCl_3$) δ: - 135.23 (dd, $^2J^{PF}$ = 91.2 Hz, $^2J^{FH}$ = 48.7 Hz).

HRMS (ESI), *m/z*: calcd. for $C_5H_{11}F_2O_3NaP^+$: 211.0306 $[M+Na]^+$; found 211.0303.

Scaling-up of the reaction (20 mmol) - To a solution of diethyl phosphorochloridate (3.450 g, 20.0 mmol, 1.0 equiv) in dry THF (30 mL) cooled at 0 °C, difluoromethyltrimethylsilane (4.968 g, 40.0 mmol, 2.0 equiv) was added under Argon atmosphere. Then, potassium *tert*-pentoxide 0.9 M in toluene (40 mL, 36.0 mmol, 1.8 equiv) was added *via* syringe pump (0.20 mL/min) at 0 °C during a period of 15 min. The reaction mixture was further stirred to reach rt within 4 h. Subsequently, saturated (*aq.*) NH_4Cl (30 mL) was added

to the mixture and the organic phase was extracted with diethyl ether (3 x 30 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Compound **13** was obtained as a colourless oil 86% (3.235 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).
Spectroscopic and spectrometric data match with those reported for the 1.0 mmol scale reaction.

Diethyl [(phenylsulfanyl)methyl]phosphonate (14)[9]



Thioanisole (248 mg, 0.23 mL, 2.0 mmol, 2.0 equiv) was added to a solution of DABCO (224 mg, 0.2 mL, 2.0 mmol, 2.0 equiv) at 0 °C in THF (1 M concentration) while stirring under Argon atmosphere. Then *n*-butyllithium (0.72 mL, 1.8 mmol, 1.8 equiv, 2.5 M) was added dropwise and the mixture stirred for 1.5 hours at the same temperature. A 0.5 M solution of diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) in dry THF was added and the mixture was stirred at 0 °C for 1.5 hours and quenched with aqueous NH_4Cl. Subsequently, the reaction mixture was allowed to reach rt and extracted three times with Et_2O, washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Compound **14** was obtained as a pale oil 87% (0.226 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 5:5).

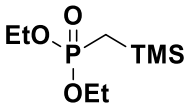
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (m, 2H, Ph H-2,6), 7.30 (m, 2H, Ph H-3,5), 7.22 (m, 1H, Ph H-4), 4.13 (m, 4H, $C\underline{H}_2CH_3$), 3.20 (d, *J* = 14.1 Hz, 2H, PCH_2S), 1.30 (t, *J* = 7.1, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 135.57 (d, *J* = 5.6 Hz, Ph C-1), 129.62 (s, Ph C-6,2), 128.99 (s, Ph C-3,5), 126.80 (s, Ph C-4), 62.73 (d, *J* = 6.6 Hz, $\underline{C}H_2CH_3$), 28.52 (d, *J* = 148.4 Hz, PCH_2S), 16.35 (d, *J* = 6.0 Hz, CH_3).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 22.94 (m).

HRMS (ESI), *m/z*: calcd. for $C_{11}H_{17}O_3PSNa^+$: 283.0528 $[M+Na]^+$; found 283.0532.

Diethyl [(trimethylsilyl)methyl]phosphonate (15)[10]



Diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) was solubilized in THF (3 mL) and the solution was allowed to reach -78 °C. Afterwards, a 1.0 M solution of (trimethylsilyl)methyllithium (1.8 mL, 1.8 mmol, 1.8 equiv) in pentane was added dropwise and the reaction was stirred for 1 h at -78 °C. Subsequently, the reaction mixture was quenched with aqueous NH_4Cl and extracted three times with Et_2O, washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Derivative **15** was obtained as a colourless oil 85% (0.190 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 5:5).

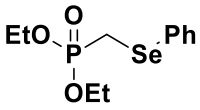
^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.04 (m, 4H, $C\underline{H}_2CH_3$), 1.29 (t, *J* = 7.1 Hz, 6H, CH_3), 1.13 (d, *J* = 22.0 Hz, 2H, PCH_2Si), 0.14 (s, 9H, $SiCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 60.98 (d, *J* = 6.4 Hz, $\underline{C}H_2CH_3$), 16.38 (d, *J* = 6.6 Hz, CH_3), 14.63 (d, *J* =128.4 Hz, PCH_2Si) -0.38 (d, *J* = 3.8 Hz, $SiCH_3$).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 33.03 (m).

HRMS (ESI), *m/z*: calcd. for $C_8H_{21}O_3PNaSi^+$: 247.0890 $[M+Na]^+$; found 247.0885.

Diethyl [(phenylselanyl)methyl]phosphonate (16)[11]



To a solution of 1,1'-(methylenediselanyl)dibenzene (0.650 g, 2.0 mmol, 2.0 equiv) in dry Et_2O (5 mL) at -78 °C under argon was added dropwise a 1.6 M solution of *n*-BuLi in hexanes (1.1 mL, 1.8 mmol, 1.8 equiv) and the reaction mixture was stirred at -78 °C for 1 hour. Afterwards, a solution of diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) in dry Et_2O (3 mL) was added and the mixture was stirred at -78 °C for 1 hour. Then it was quenched with sat. aqueous NH_4Cl and stirred at room temperature. The mixture was exhaustively extracted with Et_2O, the combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Compound **16** was obtained as a colourless oil 89% (0.273 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (m, 2H, Ph H-2,6), 7.25 (m, 3H, Ph H-3,4,5), 4.11 (m, 4H, $C\underline{H}_2CH_3$), 3.04 (d, *J* = 12.5 Hz, 2H, PCH_2Se), 1.28 (t, *J* = 7.1, 6H, CH_3).

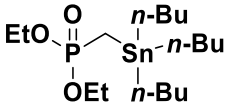
^{13}C NMR (100 MHz, $CDCl_3$) δ: 132.75 (m, Ph C-2,6), 129.82 (d, *J* = 4.2 Hz, Ph C-1), 129.11 (s, Ph C-3,5), 127.54 (s, Ph C-4), 62.63 (d, *J* = 6.6 Hz, $\underline{C}H_2CH_3$), 18.96 (d, *J* = 149.8 Hz, PCH_2Se), 16.30 (d, *J* = 6.1 Hz, CH_3).

^{77}Se NMR (76 MHz, $CDCl_3$) δ: 257.46 (m).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 24.64 (m).

HRMS (ESI), *m/z*: calcd. for $C_{11}H_{17}O_3PSeNa^+$: 330.9973 $[M+Na]^+$; found 330.9970.

Diethyl [(tributylstannyl)methyl]phosphonate (17)[12]



To a solution of tributyl(iodomethyl)stannane (0.862 g, 2.0 mmol, 2.0 equiv) in dry Et_2O (5 mL) at -78 °C under argon was added dropwise a 1.6 M solution of *n*-BuLi in hexanes (1.1 mL, 1.8 mmol, 1.8 equiv) and the reaction mixture was stirred at -78 °C for 1 hour. Afterwards, a solution of diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) in dry Et_2O (3 mL) was added and the mixture was stirred at -78 °C for 1 hour. Then it was quenched with sat. aqueous NH_4Cl and stirred at room temperature. The mixture was exhaustively extracted with Et_2O, the combined organic phases were dried over Na_2SO_4 and the solvent

was removed under reduced pressure. Compound **17** was obtained as a colourless oil 80% (0.353 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.03 (m, 4H, $POCH_2CH_3$), 1.50 (m, 6H, $SnCH_2CH_2CH_2CH_3$), 1.31 (m, 6H, $SnCH_2CH_2CH_2CH_3$), 1.29 (t, *J* = 7.1 Hz, 6H, $POCH_2CH_3$), 1.03 (d, *J* = 17.7 Hz, 2H, PCH_2Sn), 1.00 (m, 6H, $SnCH_2CH_2CH_2CH_3$), 0.89 (t, 9H, $SnCH_2CH_2CH_2CH_3$).

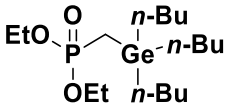
^{13}C NMR (100 MHz, $CDCl_3$) δ: 60.94 (d, *J* = 6.2 Hz, $POCH_2CH_3$), 28.81 (s, $SnCH_2CH_2CH_2CH_3$), 27.23 (s, $SnCH_2CH_2CH_2CH_3$), 16.46 (d, *J* = 6.6 Hz, $POCH_2CH_3$), 13.65 (s, $SnCH_2CH_2CH_2CH_3$), 10.54 (d, *J* = 2.0 Hz, $SnCH_2CH_2CH_2CH_3$), 3.49 (d, *J* = 134.9 Hz, PCH_2Sn).

^{119}Sn NMR (149 MHz, $CDCl_3$) δ: -8.85 (d, *J* = 61.0 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 38.00 (m).

HRMS (ESI), *m/z*: calcd. for $C_{17}H_{39}O_3PSnNa^+$: 465.1551 $[M+Na]^+$; found 465.1554.

Diethyl [(tributylgermyl)methyl]phosphonate (18)



To a solution of tributyl(iodomethyl)germane (0.770 g, 2.0 mmol, 2.0 equiv) in dry Et_2O (5 mL) at -78 °C under argon was added dropwise a 1.6 M solution of *n*-BuLi in hexanes (1.1 mL, 1.8 mmol, 1.8 equiv) and the reaction mixture was stirred at -78 °C for 1 hour. Afterwards, a solution of diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) in dry Et_2O (3 mL) was added and the mixture was stirred at -78 °C for 1 hour. Then it was quenched with sat. aqueous NH_4Cl and stirred at room temperature. The mixture was exhaustively extracted with Et_2O, the combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Compound **17** was obtained as a colourless oil 80% (0.353 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4). Compound **18** was obtained as a colourless oil 83% (0.328 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

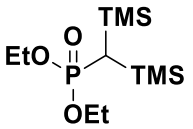
^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.12-3.97 (m, 4H, $POCH_2CH_3$), 1.34 (m, 6H, $GeCH_2CH_2CH_2CH_3$), 1.34 (m, 6H, $GeCH_2CH_2CH_2CH_3$), 1.30 (t, *J* = 7.0 Hz, 6H, $POCH_2CH_3$), 1.11 (d, *J* = 19.6 Hz, 2H, PCH_2Ge), 0.89 (m, 6H, $GeCH_2CH_2CH_2CH_3$), 0.89 (m, 9H, $GeCH_2CH_2CH_2CH_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 60.92 (d, *J* = 6.4 Hz, $POCH_2CH_3$), 27.07 (m, $GeCH_2CH_2CH_2CH_3$), 26.43 (m, $GeCH_2CH_2CH_2CH_3$), 16.43 (d, *J* = 6.6 Hz, $POCH_2CH_3$), 13.72 (m, $GeCH_2CH_2CH_2CH_3$), 13.63 (d, *J* = 3.2 Hz, $GeCH_2CH_2CH_2CH_3$), 8.88 (d, *J* = 134.0 Hz, PCH_2Ge).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 35.32 (m).

HRMS (ESI), *m/z*: calcd. for $C_{17}H_{39}GeO_3NaP^+$: 419.1741 $[M+Na]^+$; found 419.1745.

Diethyl [bis(trimethylsilyl)methyl]phosphonate (19)[13]



To a solution of bis(trimethylsilyl)methane (0.321 g, 0.43 mL, 2.0 mmol, 2.0 equiv) in THF (5 mL), the preformed LDA [generated from *N,N*-di-*i*-propylamine and MeLi-LiBr at 0 °C in THF, 1.8 equiv] was added under Argon via syringe pump (0.2 mL /min rate) at -78 °C and the solution was stirred for 30 minutes. Afterwards, diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) was added and the reaction was stirred for a further hour at – 78 °C. Subsequently, it was quenched with aqueous saturated NH_4Cl solution. The resulting organic phase was extracted 3 times with Et_2O, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Compound **19** was obtained as a colourless oil 85% (0.252 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

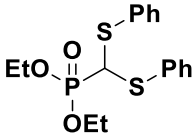
^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.03 (m, 4H, $C\underline{H}_2CH_3$), 1.29 (t, *J* = 7.1 Hz, 6H, CH_3), 0.65 (d, *J* = 25.1 Hz, 1H, CH), 0.19 (s, 18H, $SiCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 60.77 (d, *J* = 6.9 Hz, $\underline{C}H_2CH_3$), 16.60 (d, *J* = 108.2 Hz, CH), 16.40 (d, *J* = 6.9 Hz, CH_3), 1.42 (d, *J* = 3.5 Hz, $SiCH_3$).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 34.23 (m).

HRMS (ESI), *m/z*: calcd. for $C_{11}H_{29}O_3PNaSi_2^+$: 319.1285 $[M+Na]^+$; found 319.1281.

Diethyl [bis(phenylsulfanyl)methyl]phosphonate (20)[14]



To a solution of 1,1'-(methylenedisulfanediyl)dibenzene (0.465 g, 0.4 mL, 2.0 mmol, 2.0 equiv) in dry THF, a 1.6 M solution of *n*-BuLi in hexanes (1.1 mL, 1.8 mmol, 1.8 equiv) was added under Argon dropwise at -78 °C and the reaction was stirred for 30 minutes. Afterwards, diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) was added and the mixture was stirred for a further hour at -78 °C. Subsequently, it was quenched with aqueous saturated NH_4Cl solution. The resulting organic phase was extracted 3 times with Et_2O, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Compound **20** was obtained as a colourless oil 89% (0.328 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 5:5).

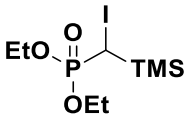
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (m, 2H, Ph H-2,6), 7.29 (m, 2H, Ph H-3,5), 7.27 (m, 1H, Ph H-4), 4.42 (d, *J* = 16.4 Hz, 1H, PCH), 4.14-4.30 (m, 4H, $C\underline{H}_2CH_3$), 1.32 (dt, J^d = 0.6, J^t = 7.1, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.63 (d, *J* = 5.9 Hz, Ph C-1), 133.11 (s, Ph C-6,2), 128.93 (s, Ph C-3,5), 128.31 (s, Ph C-4), 63.88 (d, *J* = 7.0 Hz, $\underline{C}H_2CH_3$), 53.61 (d, *J* = 152.9 Hz, PCHS), 16.40 (d, *J* = 6.0 Hz, CH_3).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 18.59 (m).

HRMS (ESI), *m/z*: calcd. for $C_{17}H_{21}O_3PS_2Na^+$: 391.0562 $[M+Na]^+$; found 391.0565.

Diethyl [iodo(trimethylsilyl)methyl]phosphonate (21)



To a solution of (iodomethyl)trimethylsilane (0.428 g, 0.3 mL, 2.0 mmol, 2.0 equiv) in THF (5 mL), the preformed LDA [generated from *N,N*-di-*i*-propylamine and MeLi-LiBr at 0 °C in THF, 1.8 equiv] was added under Argon via syringe pump (0.2 mL /min rate) at -78 °C and the solution was stirred for 30 minutes. Afterwards, diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) was added and the reaction was stirred for a further hour at – 78 °C. Subsequently, it was quenched with aqueous saturated NH_4Cl solution. The resulting organic phase was extracted 3 times with Et_2O, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Compound **21** was obtained as a yellow oil 78% (0.273 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 6:4).

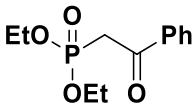
^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.15 (m, 4H, $C\underline{H}_2CH_3$), 2.76 (d, *J* = 16.9 Hz 1H, CHI), 1.33 (t, *J* = 7.1 Hz, 6H, CH_3), 0.27 (s, 9H, $SiCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 63.24, (d, *J* = 7.0 Hz, $\underline{C}H_2CH_3$), 62.83 (d, *J* = 6.6 Hz, $\underline{C}H_2CH_3$), 16.32, (d, *J* = 6.3 Hz, CH_3), 16.29 (d, *J* = 6.4 Hz, CH_3), - 0.69 (d, *J* =129.9 Hz, CHI), - 0.69 (d, *J* =2.4 Hz, $SiCH_3$).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 25.03 (brs).

HRMS (ESI), *m/z*: calcd. for $C_8H_{20}IO_3PSiNa^+$: 372.9856 $[M+Na]^+$; found 372.9859.

Diethyl (2-oxo-2-phenylethyl)phosphonate (22)[15]



Diethyl phosphorochloridate (0.173 g, 1.0 mmol, 1.0 equiv) was dissolved in dry THF (3 mL) and chloroiodomethane (0.353 g, 2.0 mmol, 2.0 equiv) was added at -78 °C under Argon. Subsequently, MeLi-LiBr complex (0.82 mL of 2.2 M, 1.8 mmol, 1.8 equiv) was added dropwise and the reaction was stirred for 1 hour in order to obtain diethyl (chloromethyl)phosphonate (2). Afterwards, this was added dropwise to a suspension of Li metal (0.035 g, 5.0 mmol, 5.0 equiv) and naphthalene (0.013 g, 0.1 mmol, 0.1 equiv) in THF (1 mL), stirred for 10 minutes at -78 °C under Argon. After 10 minutes a THF solution of *N*-methoxy-*N*-methylbenzamide (0.157 g, 0.95 mmol, 0.95 equiv) was added and the reaction was stirred for further two hours. Subsequently, it was quenched with aqueous saturated NH_4Cl solution. The resulting organic phase was extracted 3 times with Et_2O, washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Compound **22** was obtained as a colourless oil 81% (0.207 g) after column chromatography on silica gel (*n*-hexane:ethyl acetate 5:5).

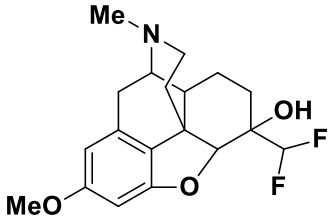
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (m, 2H, Ph H-2,6), 7.58 (m, 1H, Ph H-4), 7.47(m, 2H, Ph H-3,5), 4.12 (m, 4H, $C\underline{H}_2CH_3$), 3.62 (d, *J* = 22.7 Hz, 2H, PCH_2), 1.27 (t, *J* = 7.1, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.91 (d, *J* = 6.6 Hz, CO), 136.51 (d, *J* = 2.0 Hz, Ph C-1), 133.61 (s, Ph C-4), 129.00 (s, Ph C-2,6), 128.56 (s, Ph C-3,5), 62.59 (d, *J* = 6.5 Hz, $\underline{C}H_2CH_3$), 38.47 (d, *J* = 129.9 Hz, PCH_2), 16.19 (d, *J* = 6.4 Hz, CH_3).

^{31}P NMR (162 MHz, $CDCl_3$) δ: 19.87 (m).

HRMS (ESI), *m/z*: calcd. for $C_{12}H_{17}O_4NaP^+$: 279.0757 $[M+Na]^+$; found 279.0752.

6-(Difluoromethyl)-3-methoxy-17-methyl-4,5-epoxymorphinan-6-ol (23)



To a solution of diethyl (difluoromethyl)phosphonate **13** (0.16 mL, 1.00 mmol, 1.5 equiv) in THF (5 mL) cooled at -78 °C, a solution of LDA [generated from diisopropylamine (0.14 mL, 1.0 mmol, 1. 5equiv), *n*-butyllithium 2.5 M in hexanes (0.4 mL, 1.5 equiv) in THF (2 mL) at 0 °C, 30 min] in THF (5 mL) was added dropwise over during 5 min. The mixture was stirred at-78 °C under Argon for 40 min. Then, a solution of dihydrocodeinone (200 mg, 0.67 mmol, 1.0 equiv) in THF (5 mL) was added. After 15 min, a solution of potassium *tert*-pentoxide 0.9 M (1.1 mL, 1.00 mmol, 1.5 equiv) was added and the reaction was heated to 80 °C overnight. The reaction was cooled at room temperature, quenched by the addition of distilled water (20 mL) and extracted with dichloromethane (3 × 5 mL). The organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered and, concentrated under reduced pressure (bath: rt). The crude was purified via column chromatography on neutral aluminium oxide grade IV (dichloromethane/methanol, 98:2 *v*/*v*) to afford the corresponding pure compound **23** in 78% yield (183 mg) as pale yellow oil.

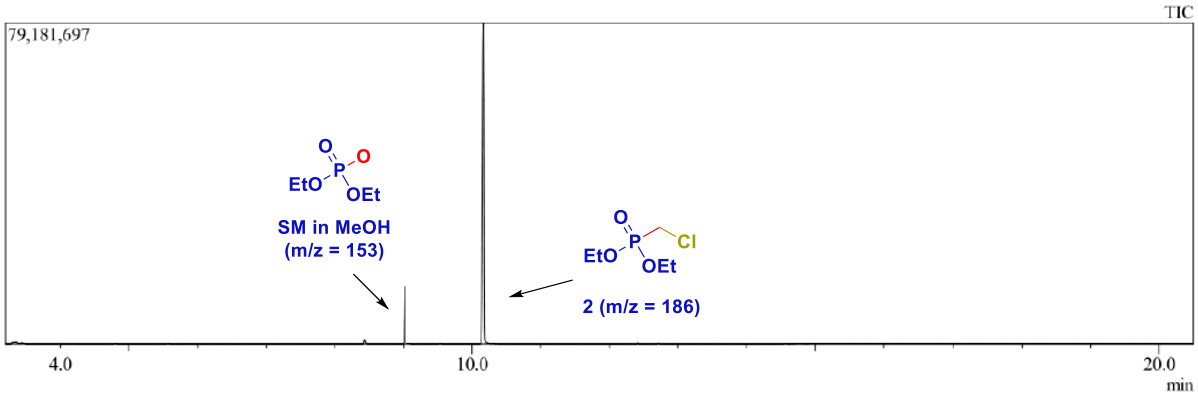
^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.73 (d, 1H, $^3J_{H,H}$ = 8.2 Hz, Ph H-2), 6.67 (m, 1H, Ph H-1), 5.50 (t, 1H, $^2J_{H,F}$ = 56.2 Hz, CHF_2), 4.69 (s, 1H, H-5), 3.87 (s, 3H, OCH_3), 3.13 (m, 1H, H-9), 3.03 (d, 1H, $^2J_{H,H}$ = 18.4 Hz, H-10), 2.56 (m, 1H, H-16), 2.42 (s, 3H, NCH_3), 2.37 (dd, 1H, $^2J_{H,H}$ = 18.4 Hz, $^3J_{H,H}$ = 5.4 Hz, H-10), 2.25 (m, 1H, H-16), 2.23 (m, 1H, H-14), 1.93 (m, 1H, H-15), 1.78 (m, 1H, H-7), 1.70 (m, 1H, H-15), 1.44 (m, 1H, H-7), 1.39 (m, 1H, H-8), 1.25 (m, 1H, H-8), OH not found.

^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2 (1C, Ph C-4), 141.8 (1C, Ph C-3), 129.5 (1C, Ph C-12), 126.1 (1C, Ph C-11), 119.7 (1C, Ph C-1), 116.9 (t, 1C, $^1J_{C,F}$ = 249.4 Hz, CHF_2), 113.5 (1C, Ph C-2), 86.3 (1C, C-5), 72.7 (t, 1C, $^2J_{C,F}$ = 20.6 Hz, C-6), 59.6 (1C, C-9), 56.3 (1C, OCH_3), 47.2 (1C, C-16), 43.1 (1C, C-14), 42.8 (1C, NCH_3), 42.6 (1C, C-13), 37.0 (1C, C-15), 28.0 (1C, C-7), 20.1 (1C, C-10), 18.8 (1C, C-8).

^{19}F NMR (376 MHz, C_6D_6) δ: -134.6 (dd, $^2J_{H,F}$= 56.2 Hz, $^2J_{F,F}$ = 282.5 Hz, CHF_2), -131.7 (dd, $^2J_{H,F}$ = 56.2 Hz, $^2J_{F,F}$ = 282.5 Hz, CHF_2).

HRMS, *m/z*: calcd. for $C_{19}H_{23}F_2NO_3H^+$: 352.1719 $[M+H]^+$; found: 352.1717.

4. GC-MS Study



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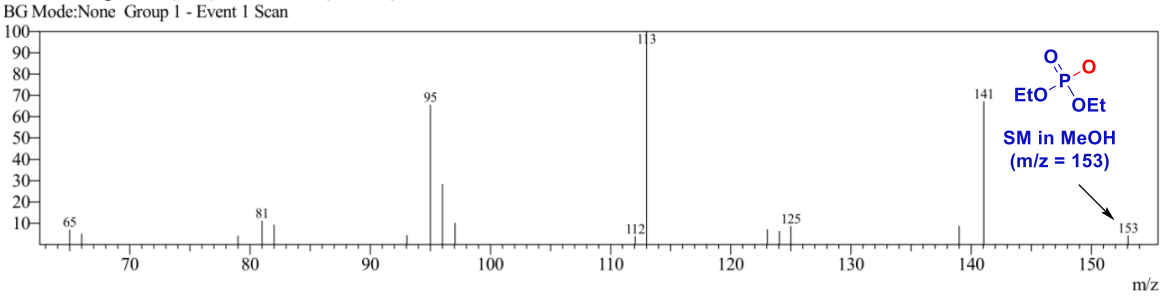
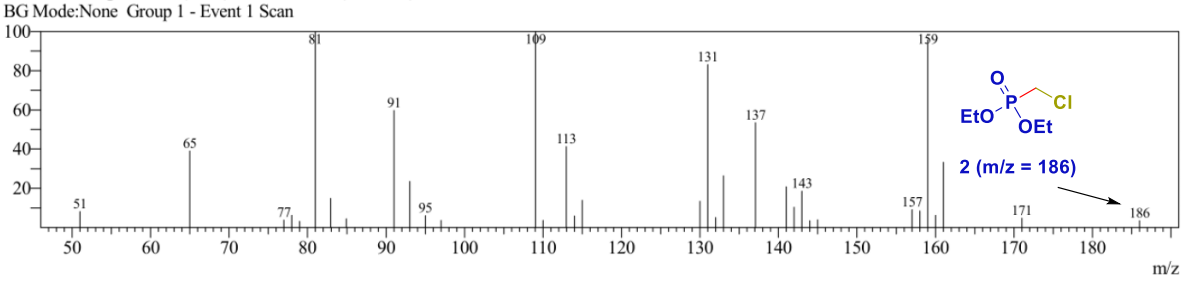
BG Mode:None Group 1 - Event 1 Scan

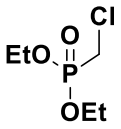


Line#:2 R.Time:10.160(Scan#:1393)
MassPeaks:34
RawMode:Single 10.160(1393) BasePeak:109(8396120)
BG Mode:None Group 1 - Event 1 Scan

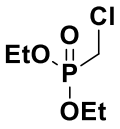


5. Copies of ^{1}H- and ^{13}C-NMR spectra

Diethyl (chloromethyl)phosphonate (2)

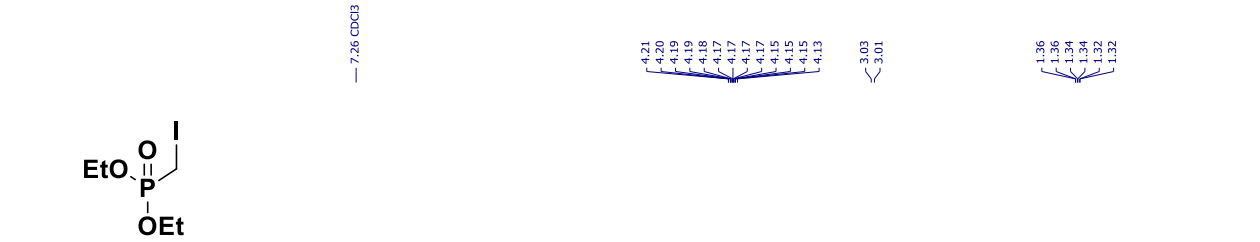


(^{1}H-NMR, 400 MHz, $CDCl_3$)

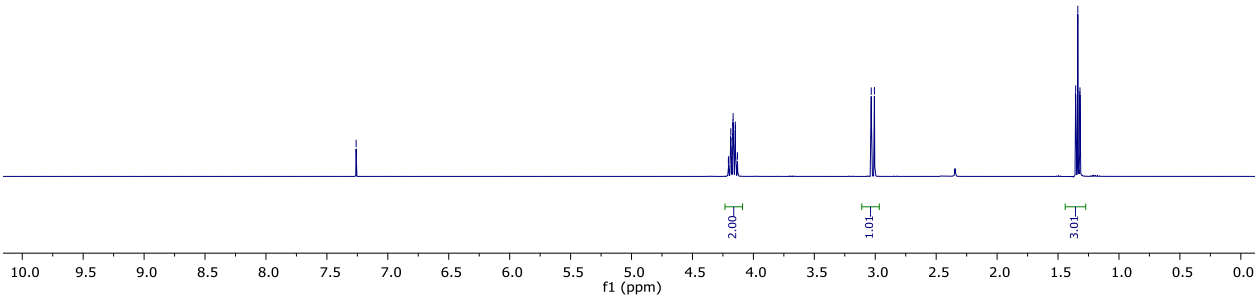


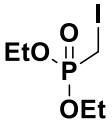
(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl (iodomethyl)phosphonate (3)



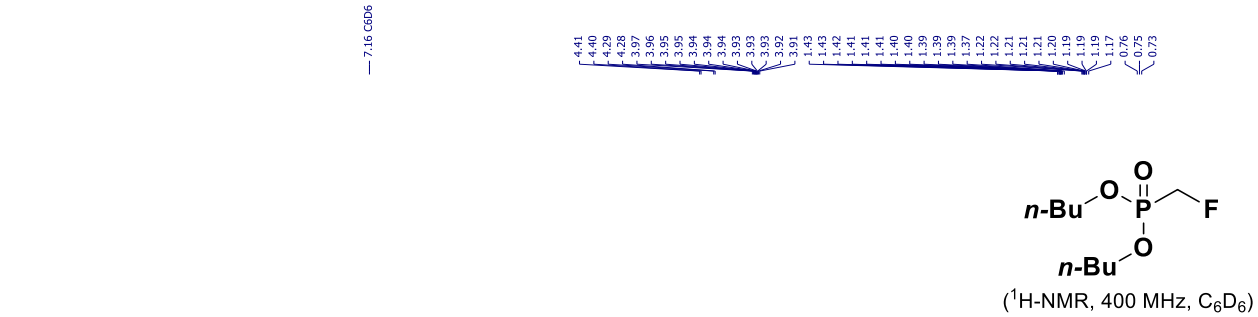
(^{1}H-NMR, 400 MHz, $CDCl_3$)



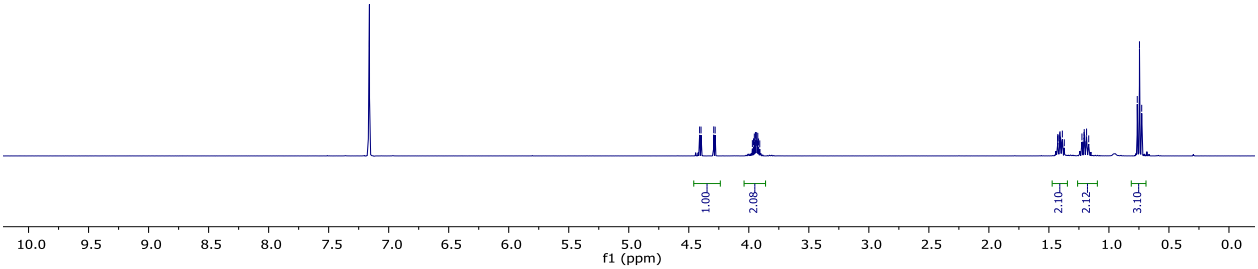


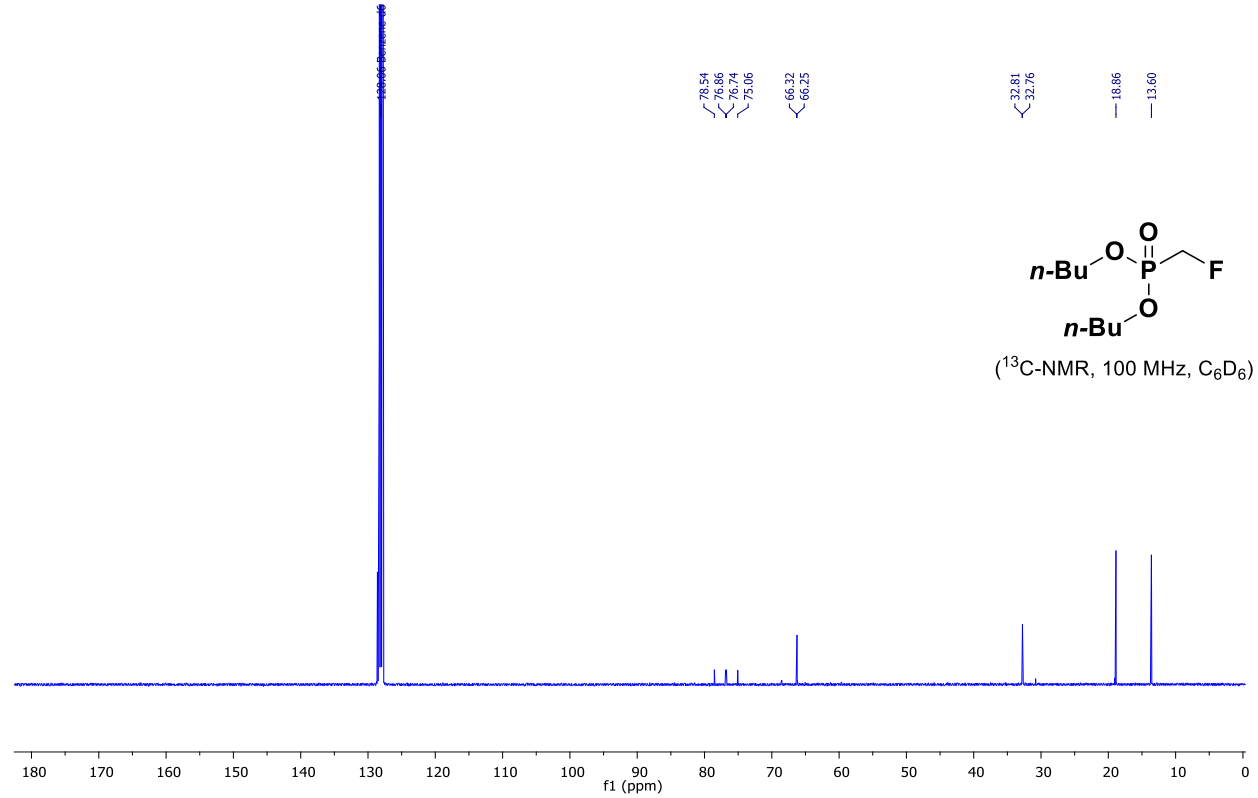
(^{13}C-NMR, 100 MHz, $CDCl_3$)

Dibutyl (fluoromethyl)phosphonate (4)



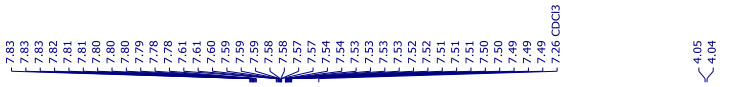
(^{1}H-NMR, 400 MHz, C_6D_6)

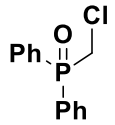




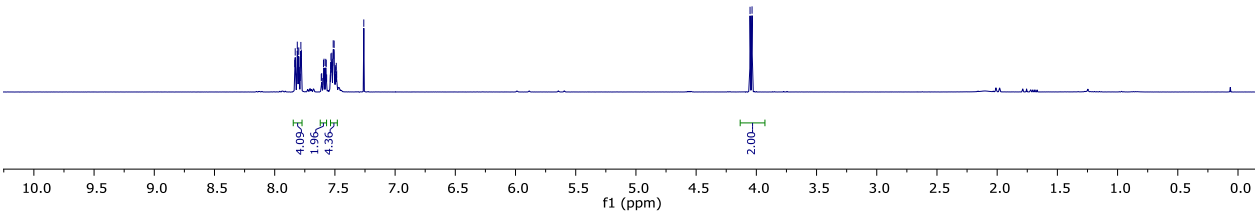
(^{13}C-NMR, 100 MHz, C_6D_6)

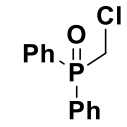
(Chloromomethyl)(diphenyl)phosphine oxide (5)



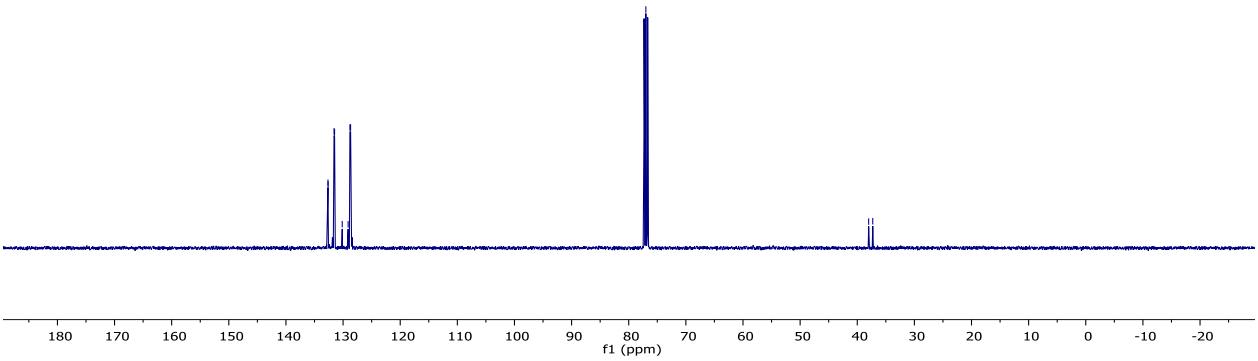


(^{1}H-NMR, 400 MHz, $CDCl_3$)

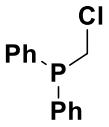




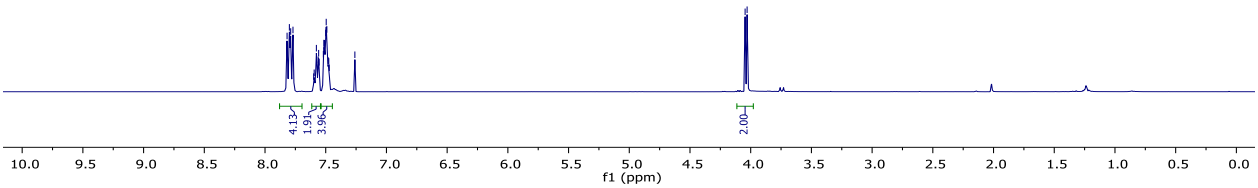
(^{13}C-NMR, 100 MHz, $CDCl_3$)

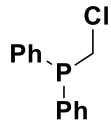


(Chloromethyl)(diphenyl)phosphine (6)

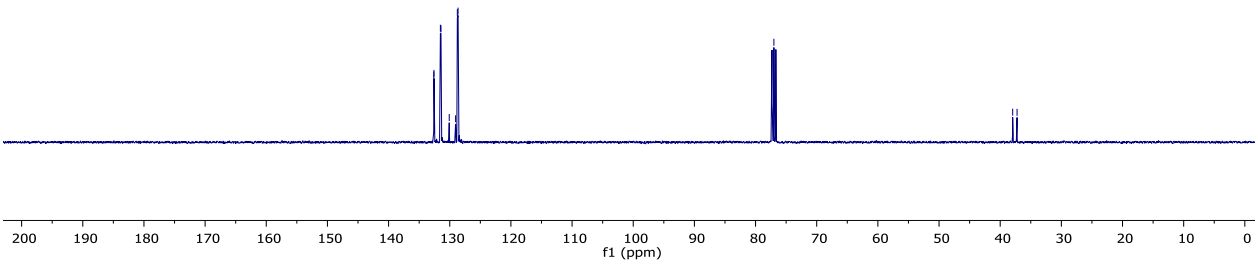


(^{1}H-NMR, 400 MHz, $CDCl_3$)

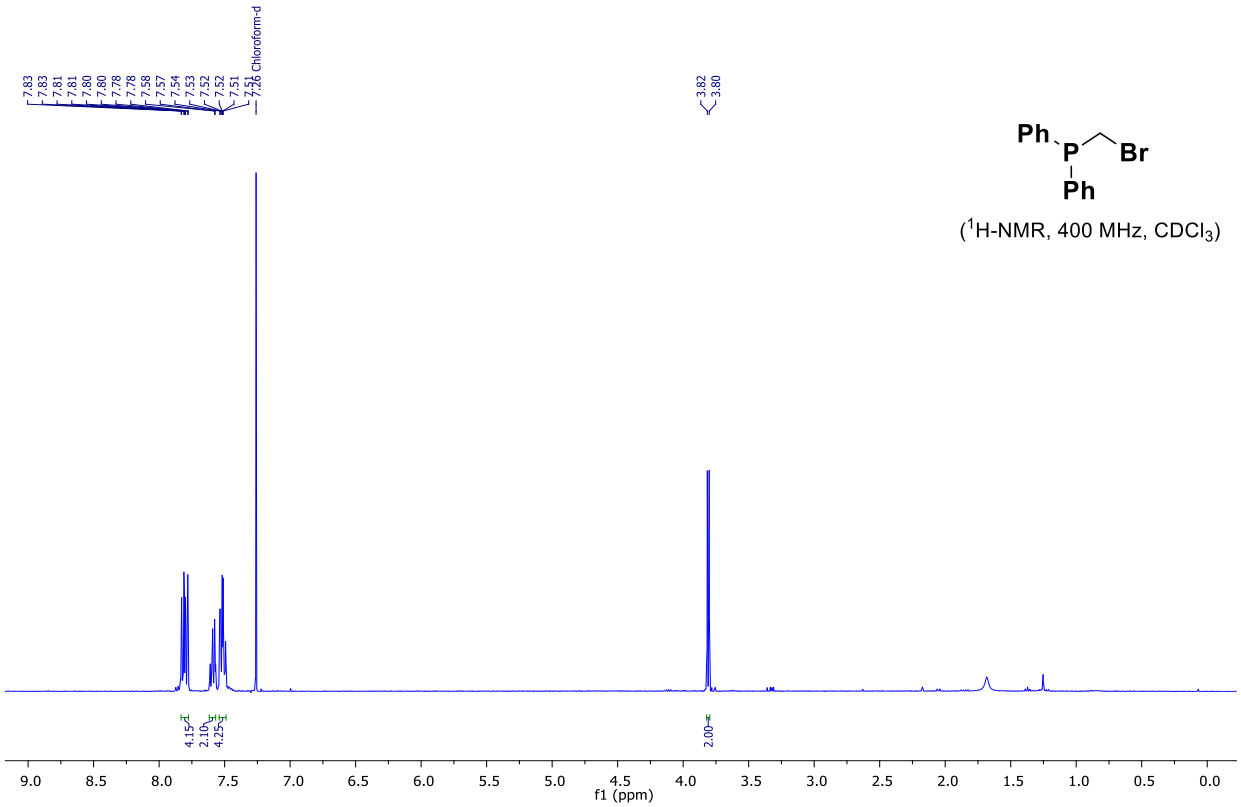




(^{13}C-NMR, 100 MHz, $CDCl_3$)

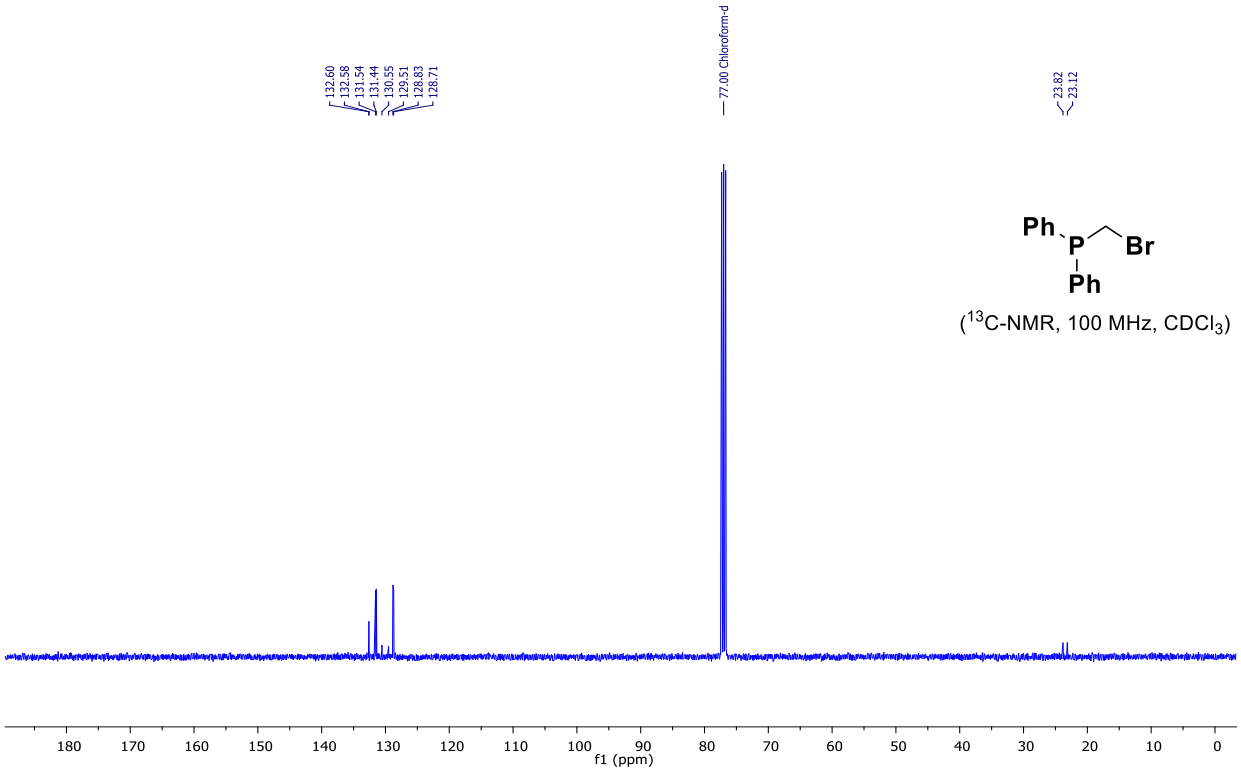


(Bromomethyl)(diphenyl)phosphine (7)



Ph, P, Br, Ph

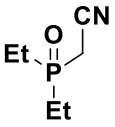
(^{1}H-NMR, 400 MHz, $CDCl_3$)



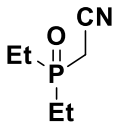
Ph, P, Br, Ph

(^{13}C-NMR, 100 MHz, $CDCl_3$)

(Diethylphosphosphino)acetonitrile (8)

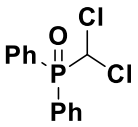


(^{1}H-NMR, 400 MHz, $CDCl_3$)

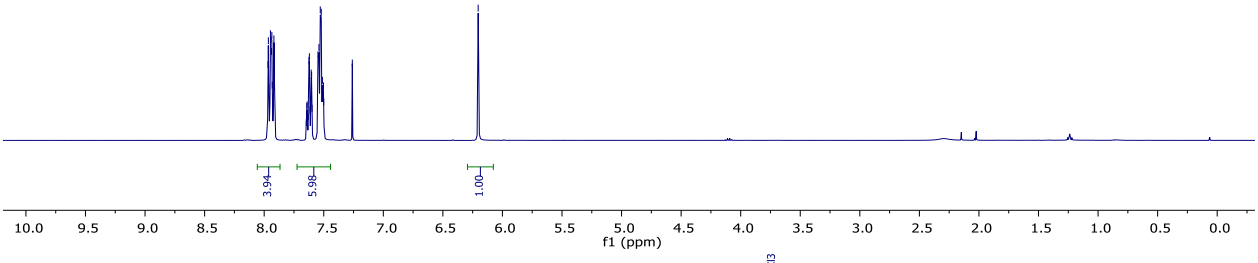


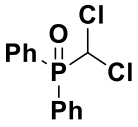
(^{13}C-NMR, 100 MHz, $CDCl_3$)

(Dichloromethyl)(diphenyl)phosphine oxide (9)

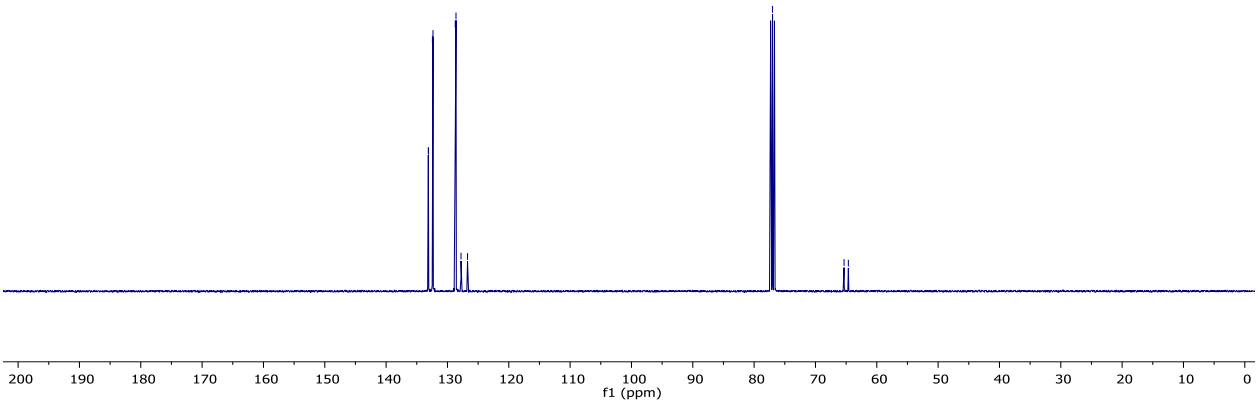


(^{1}H-NMR, 400 MHz, $CDCl_3$)

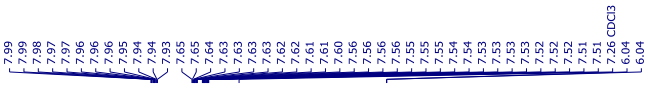


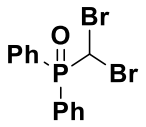


(^{13}C-NMR, 100 MHz, $CDCl_3$)

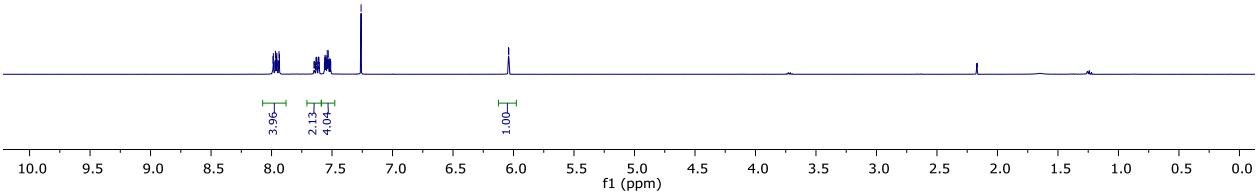


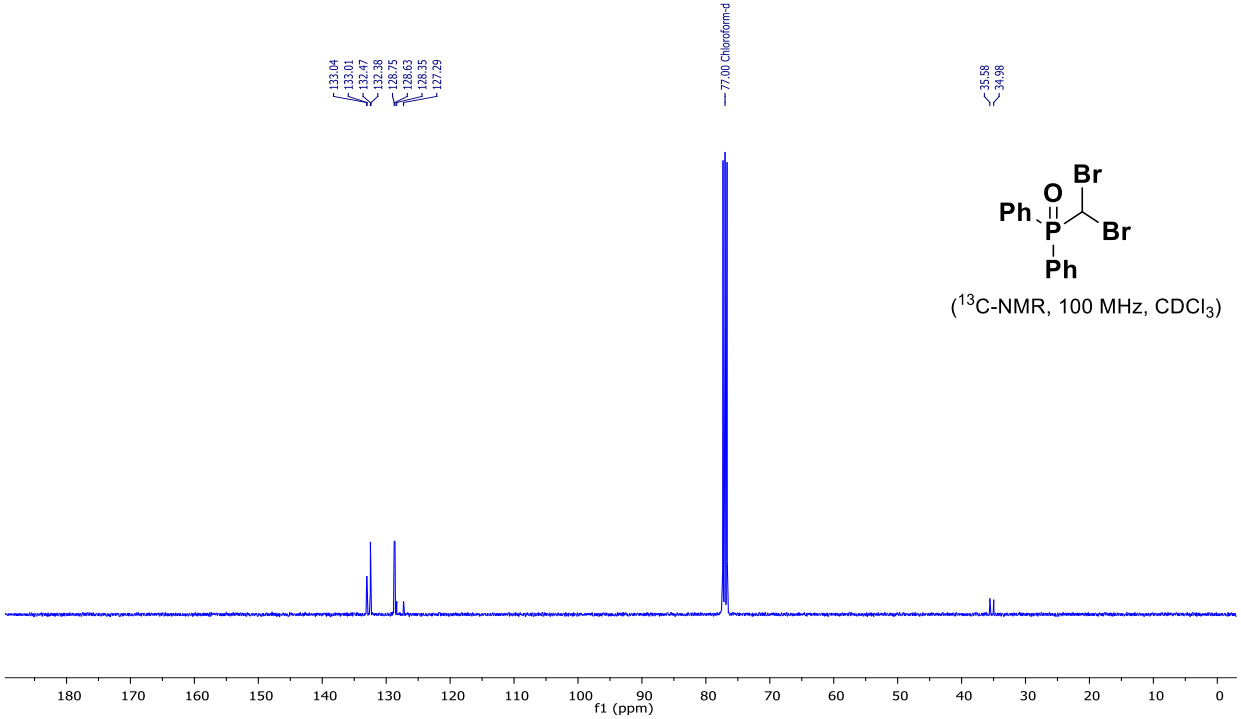
(Dibromomethyl)(diphenyl)phosphine oxide (10)





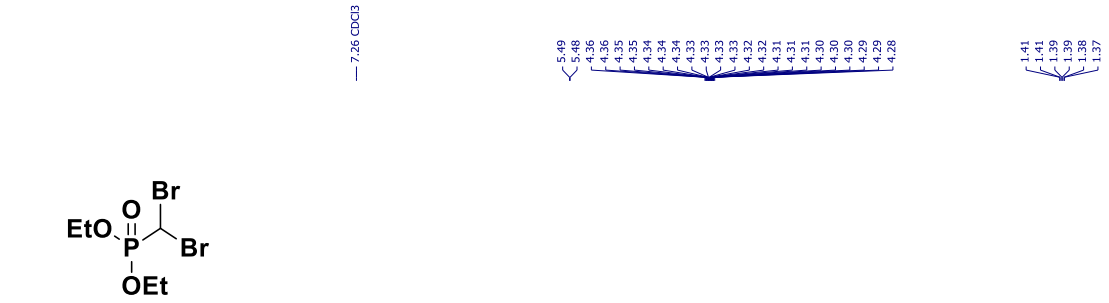
(^{1}H-NMR, 400 MHz, $CDCl_3$)



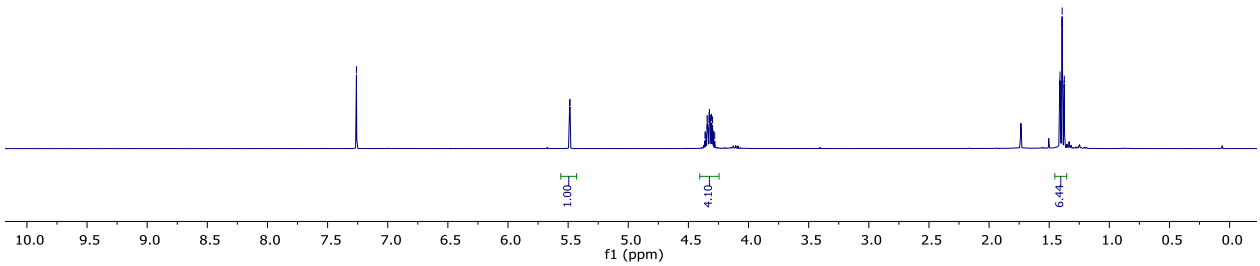


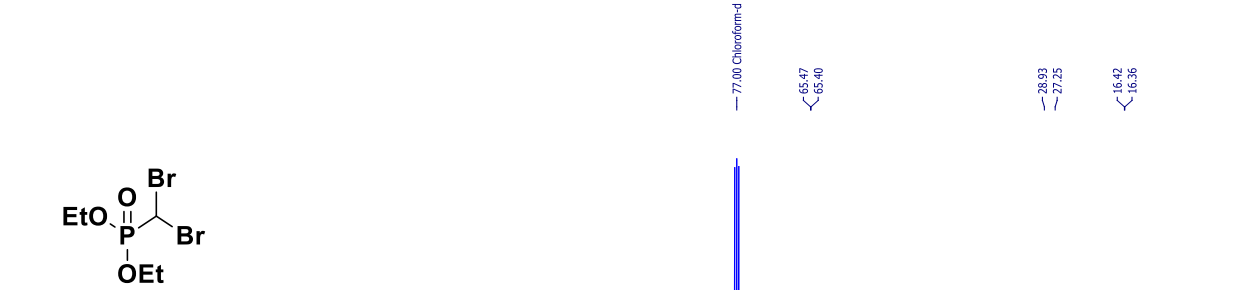
(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl (dibromomethyl)phosphonate (11)



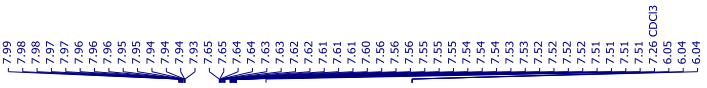
(^{1}H-NMR, 400 MHz, $CDCl_3$)

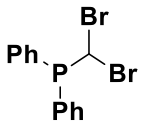




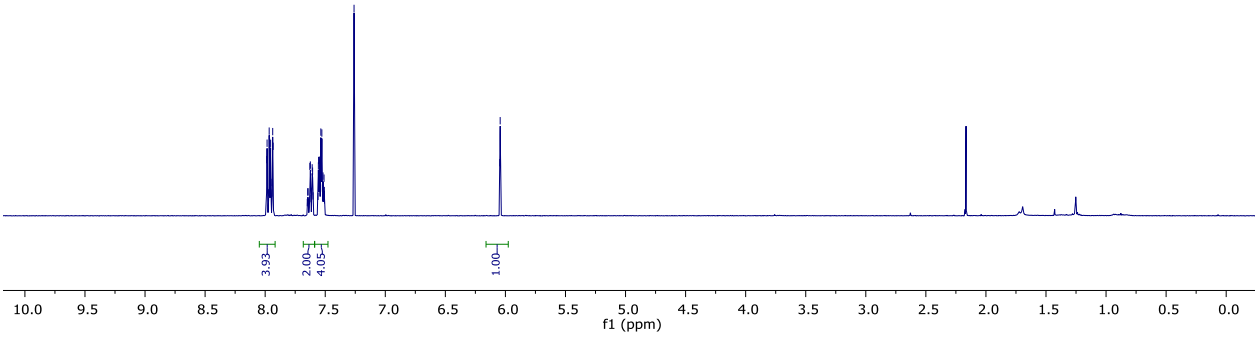
(^{13}C-NMR, 100 MHz, $CDCl_3$)

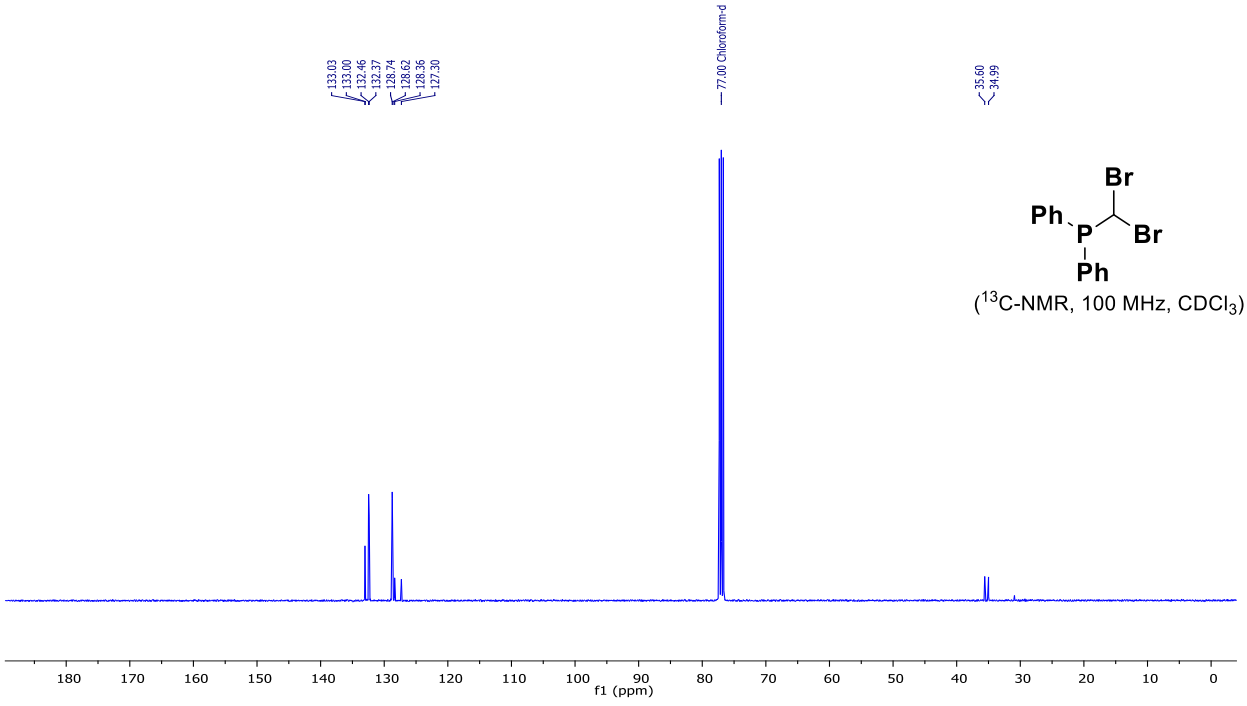
(Dibromomethyl)(diphenyl)phosphine (12)





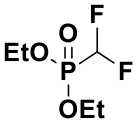
(^{1}H-NMR, 400 MHz, $CDCl_3$)





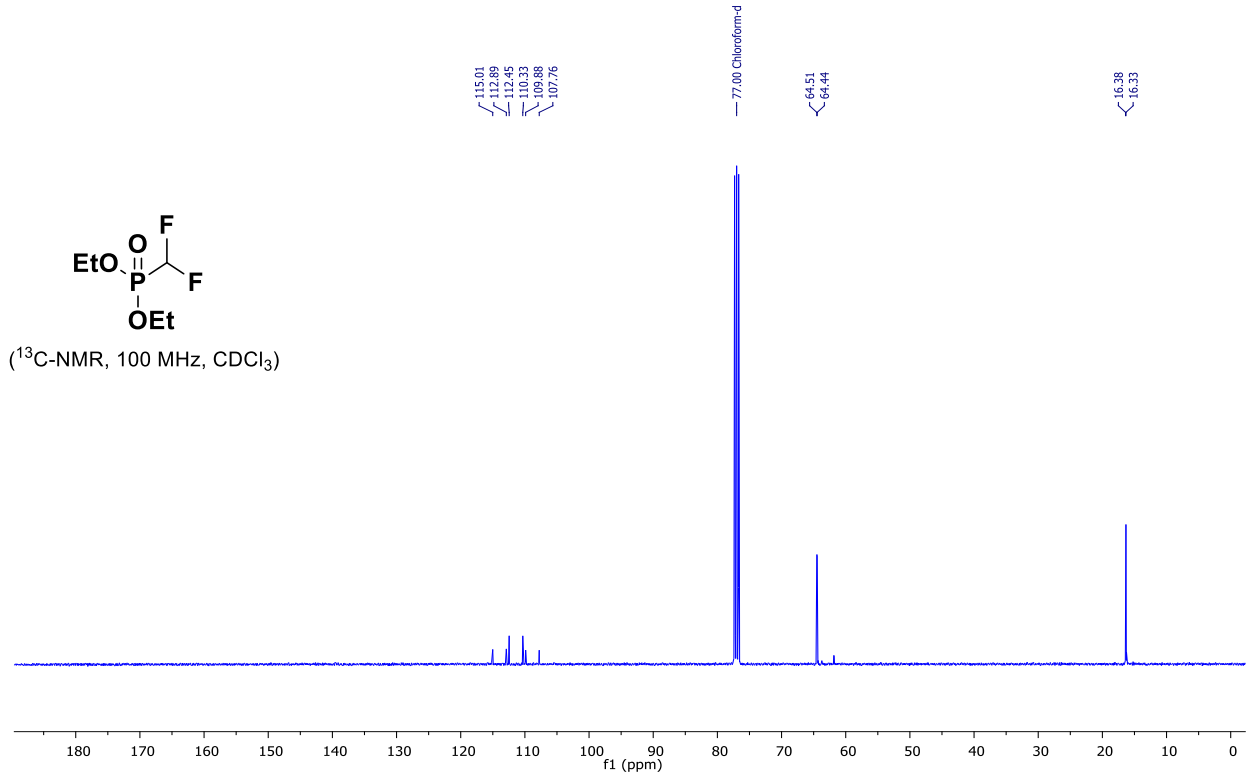
(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl (difluoromomethyl)phosphonate (13)

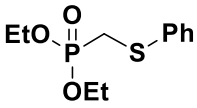


(^{1}H-NMR, 400 MHz, $CDCl_3$)

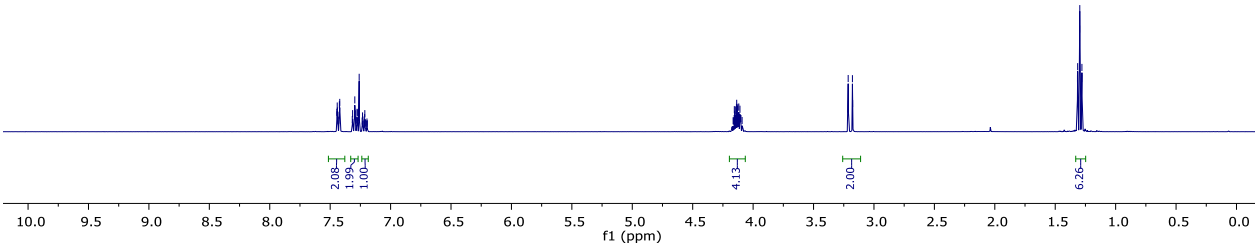
(^{13}C-NMR, 100 MHz, $CDCl_3$)

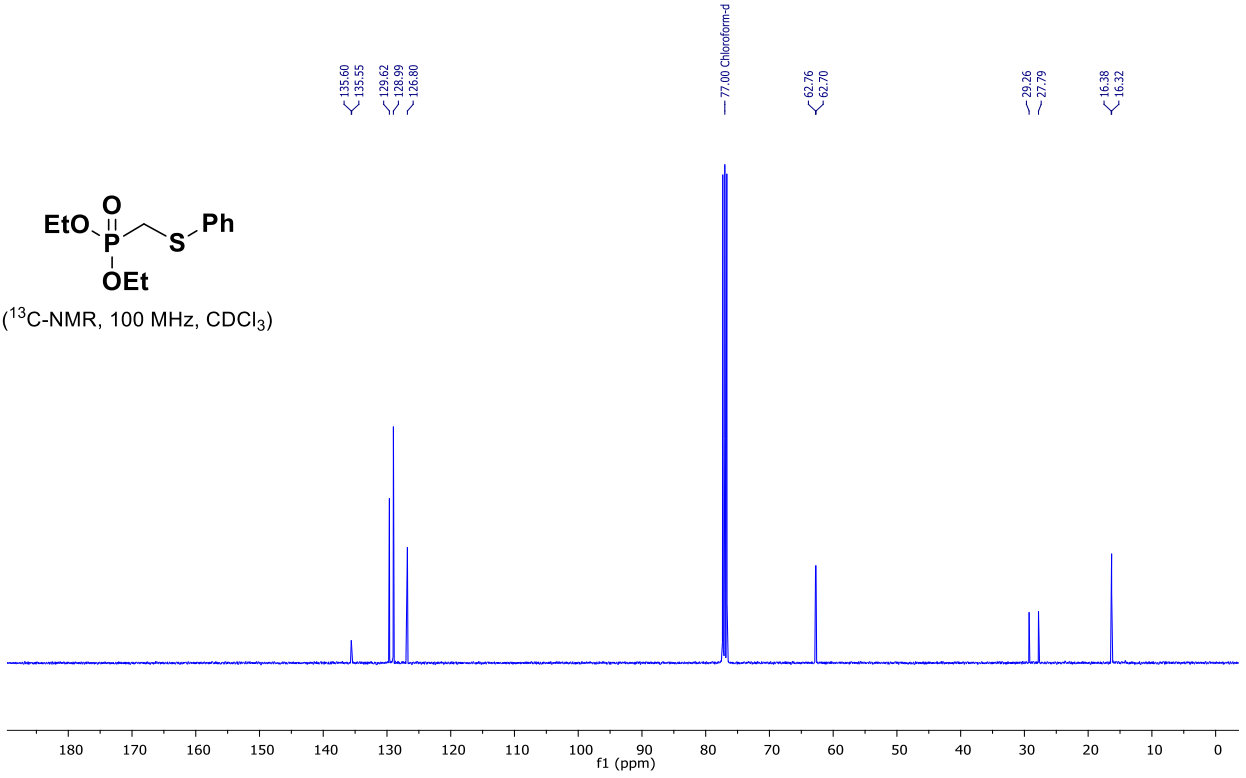


Diethyl [(phenylsulfanyl)methyl]phosphonate (14)



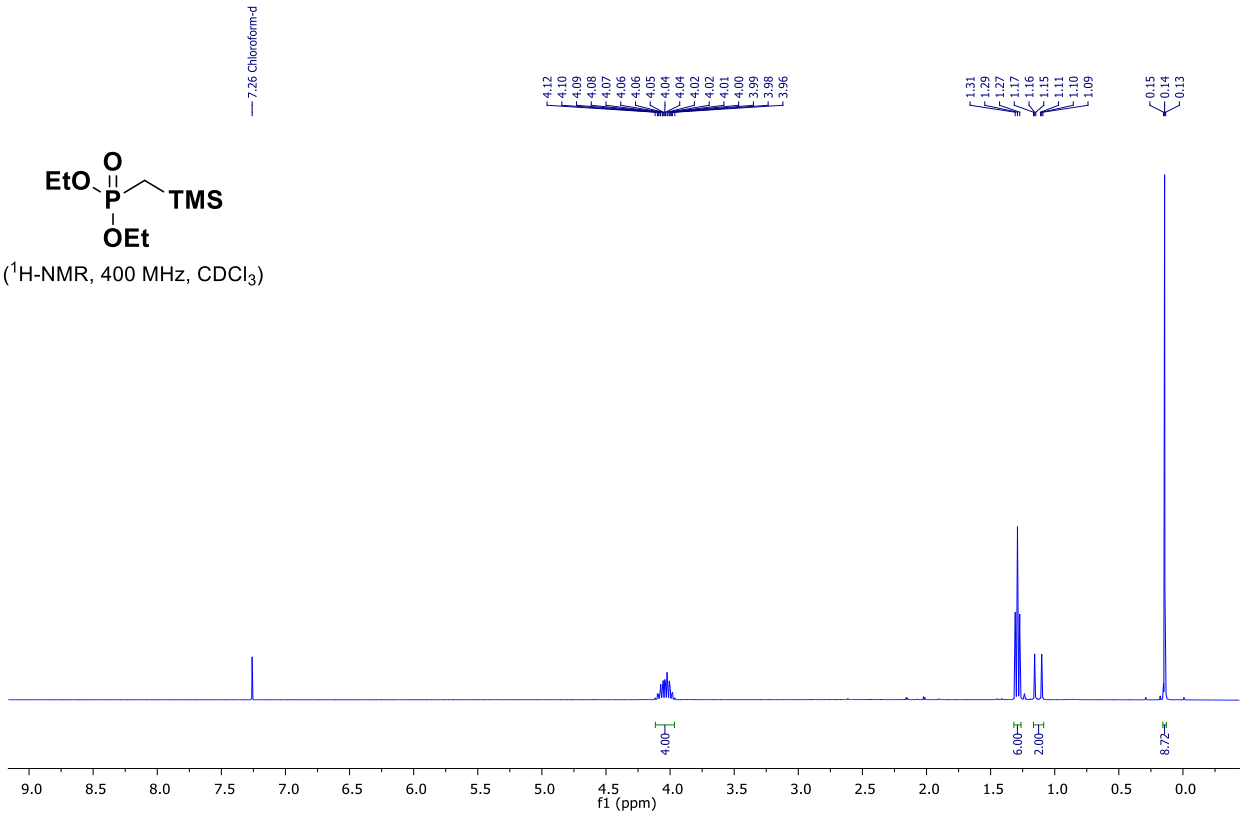
(^{1}H-NMR, 400 MHz, $CDCl_3$)



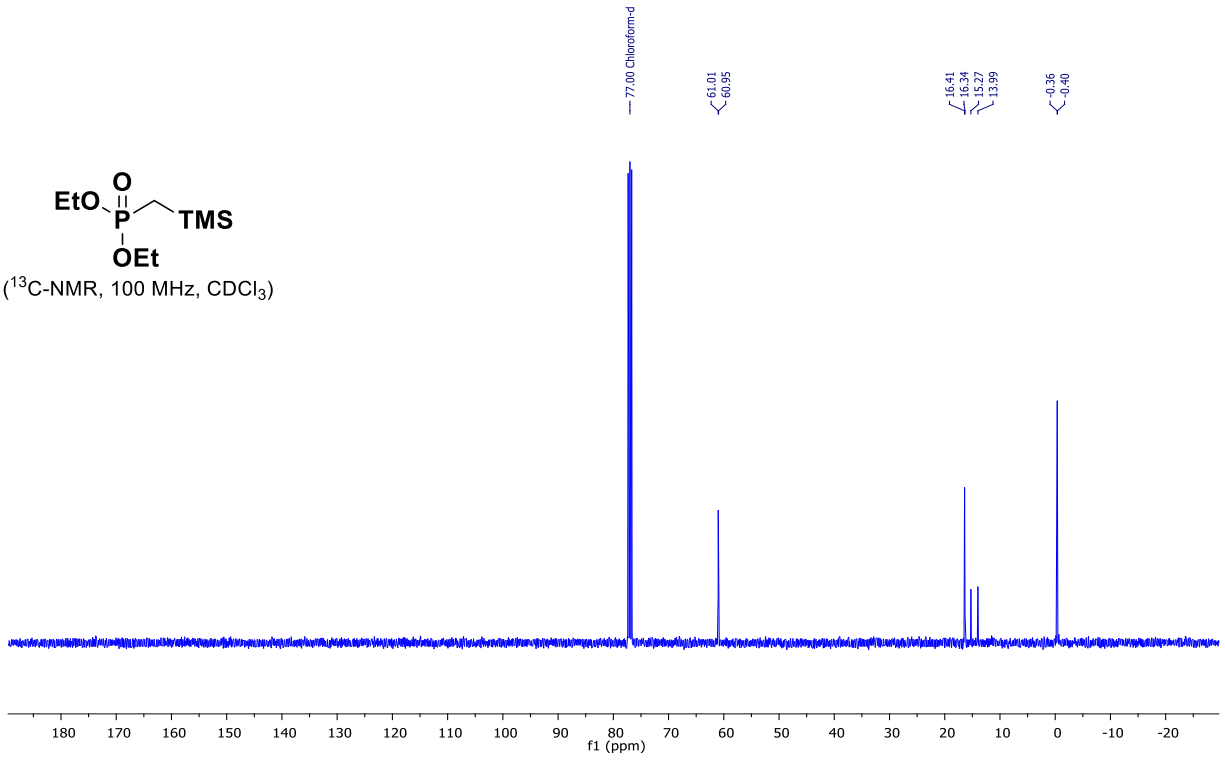


(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl [(trimethylsilyl)methyl]phosphonate (15)

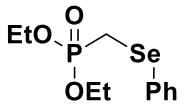


(^{1}H-NMR, 400 MHz, $CDCl_3$)

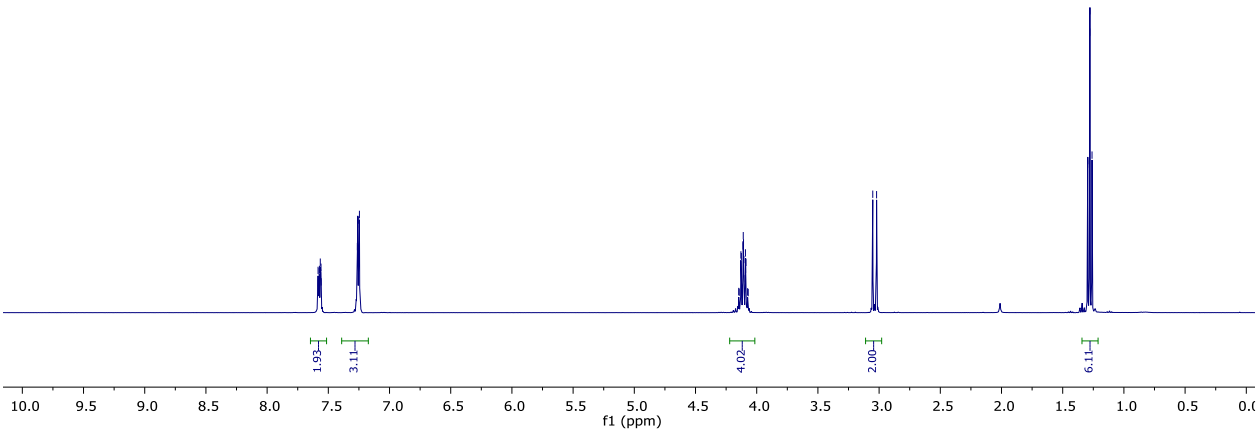


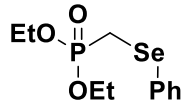
(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl [(phenylselanyl)methyl]phosphonate (16)

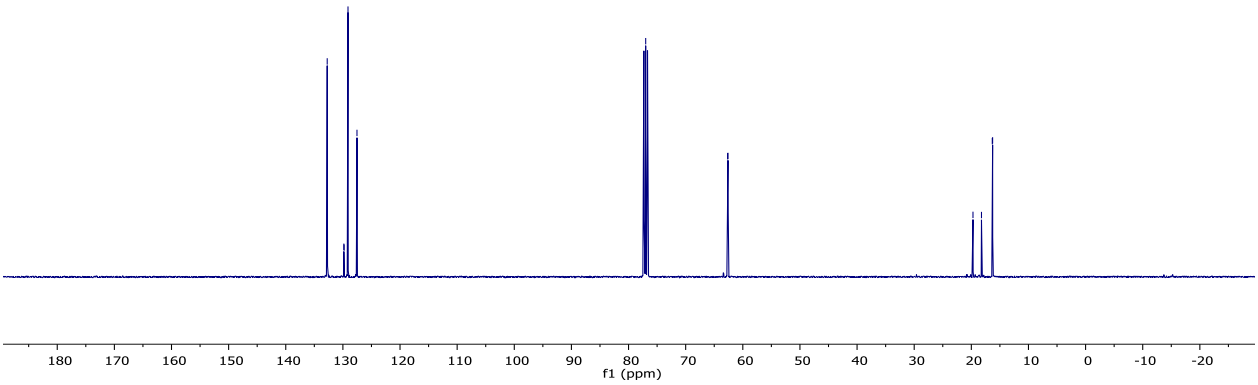


(^{1}H-NMR, 400 MHz, $CDCl_3$)

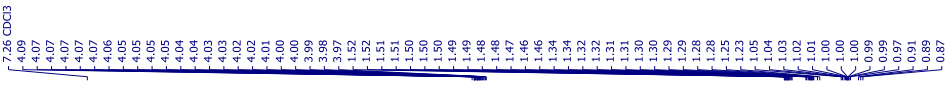


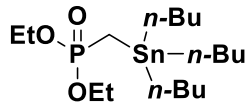


(^{13}C-NMR, 100 MHz, $CDCl_3$)

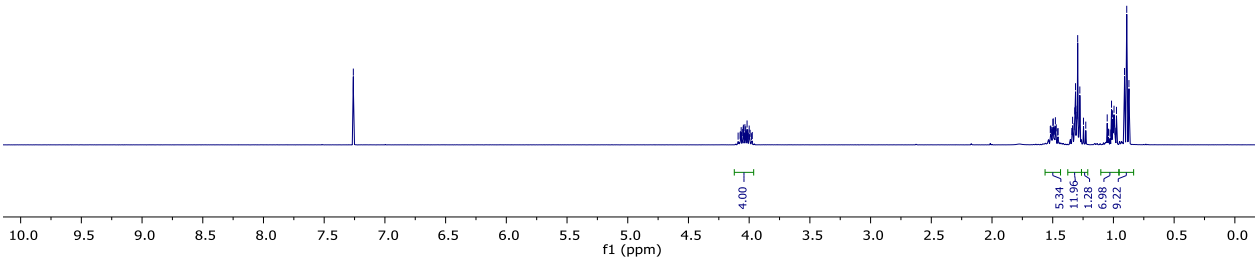


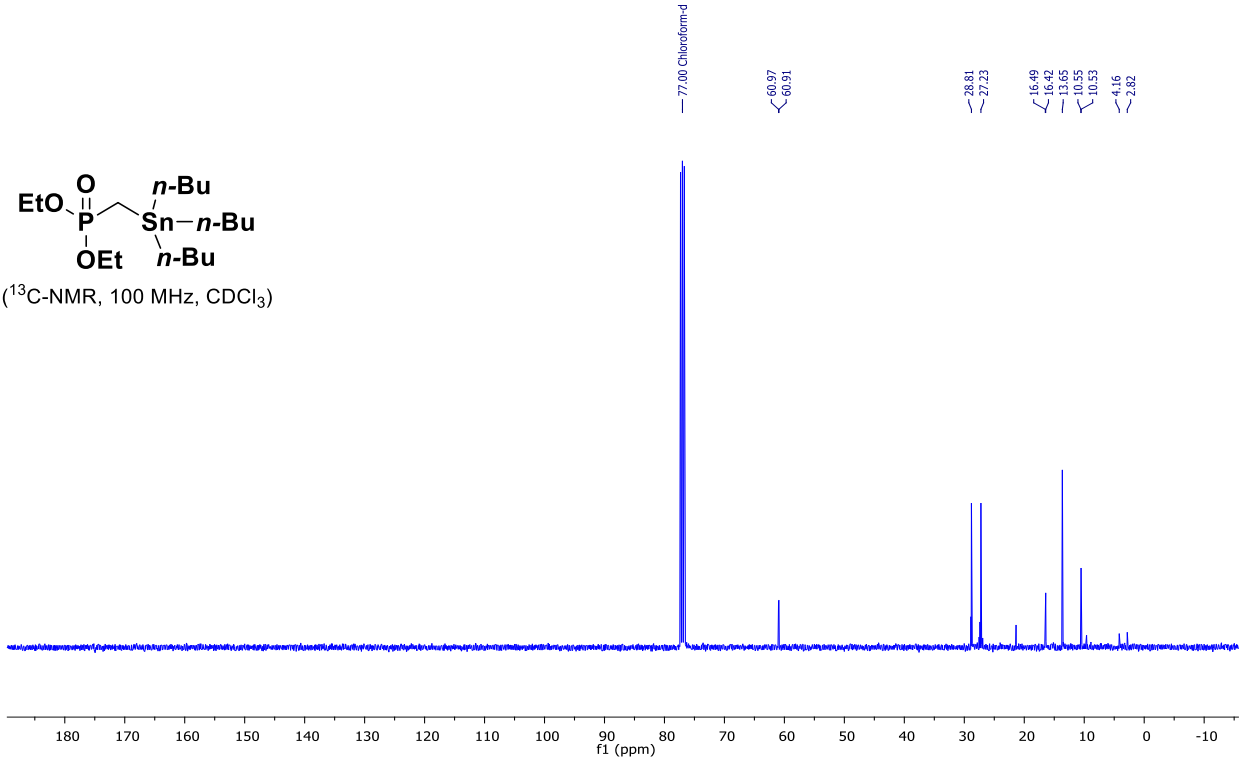
Diethyl [(tributylstannyl)methyl]phosphonate (17)





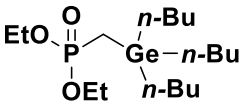
(^{1}H-NMR, 400 MHz, $CDCl_3$)



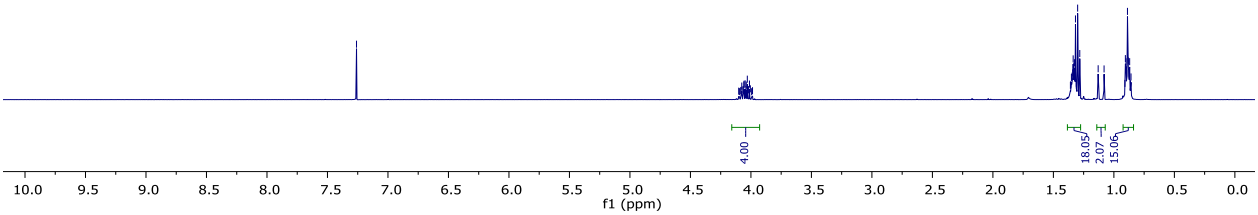


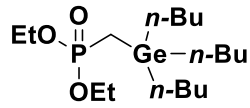
(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl [(tributylgermyl)methyl]phosphonate (18)



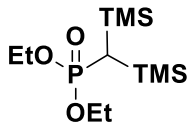
(^{1}H-NMR, 400 MHz, $CDCl_3$)



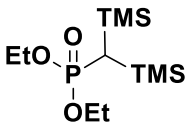


(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl [bis(trimethylsilyl)methyl]phosphonate (19)

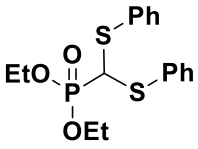


(^{1}H-NMR, 400 MHz, $CDCl_3$)

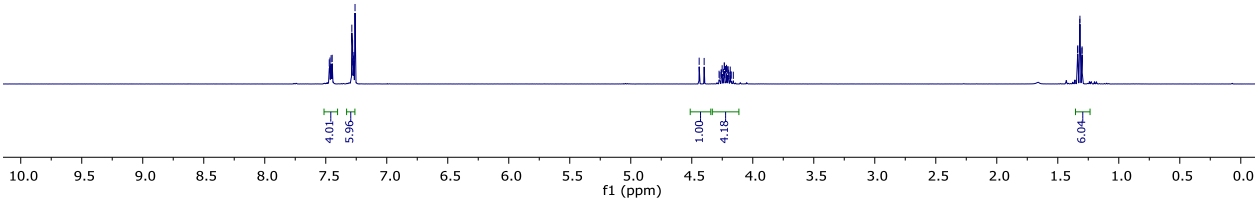


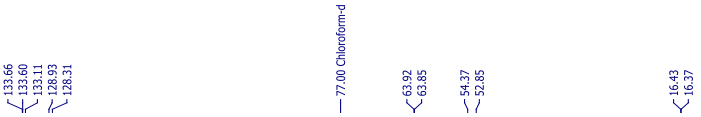
(^{13}C-NMR, 100 MHz, $CDCl_3$)

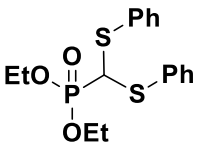
Diethyl [bis(phenylsulfanyl)methyl]phosphonate (20)



(^{1}H-NMR, 400 MHz, $CDCl_3$)

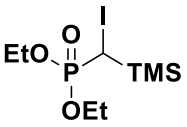




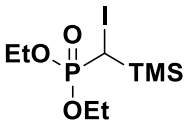


(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl [iodo(trimethylsilyl)methyl]phosphonate (21)

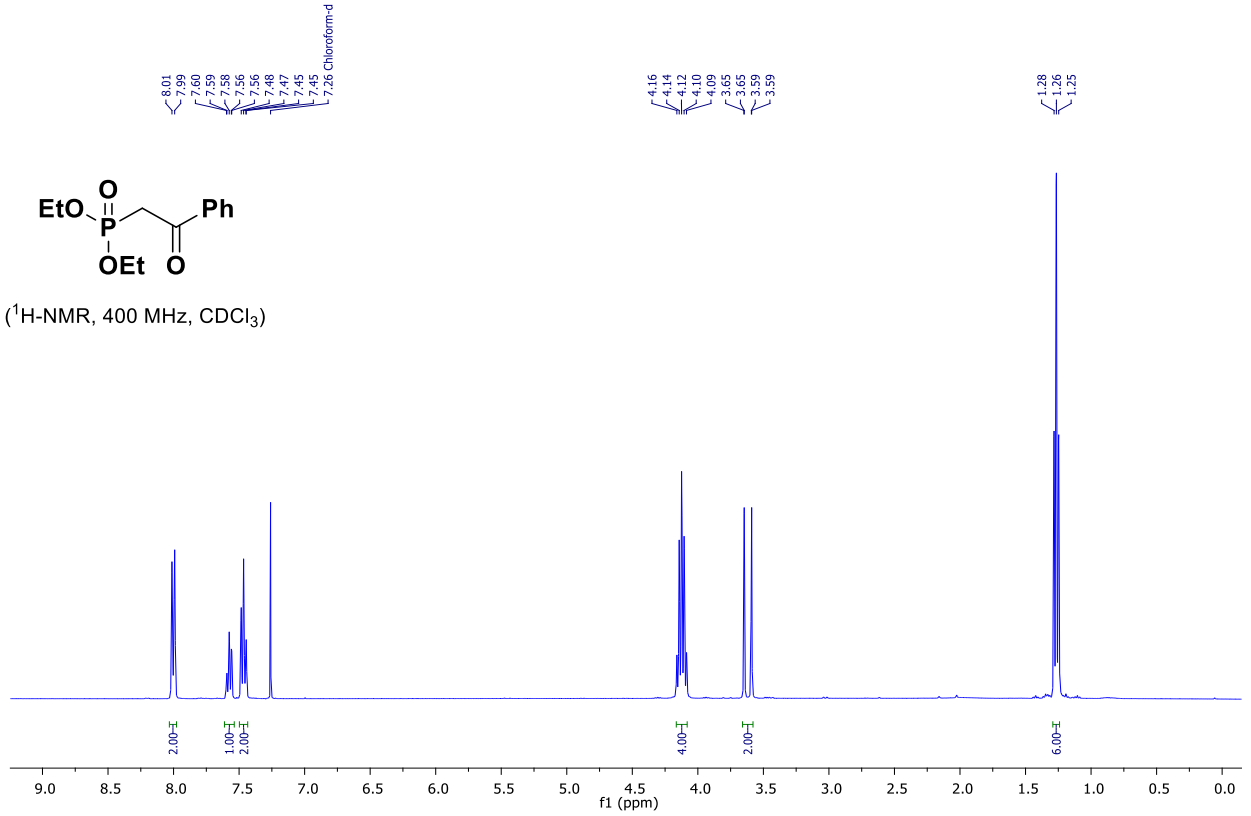


(^{1}H-NMR, 400 MHz, $CDCl_3$)

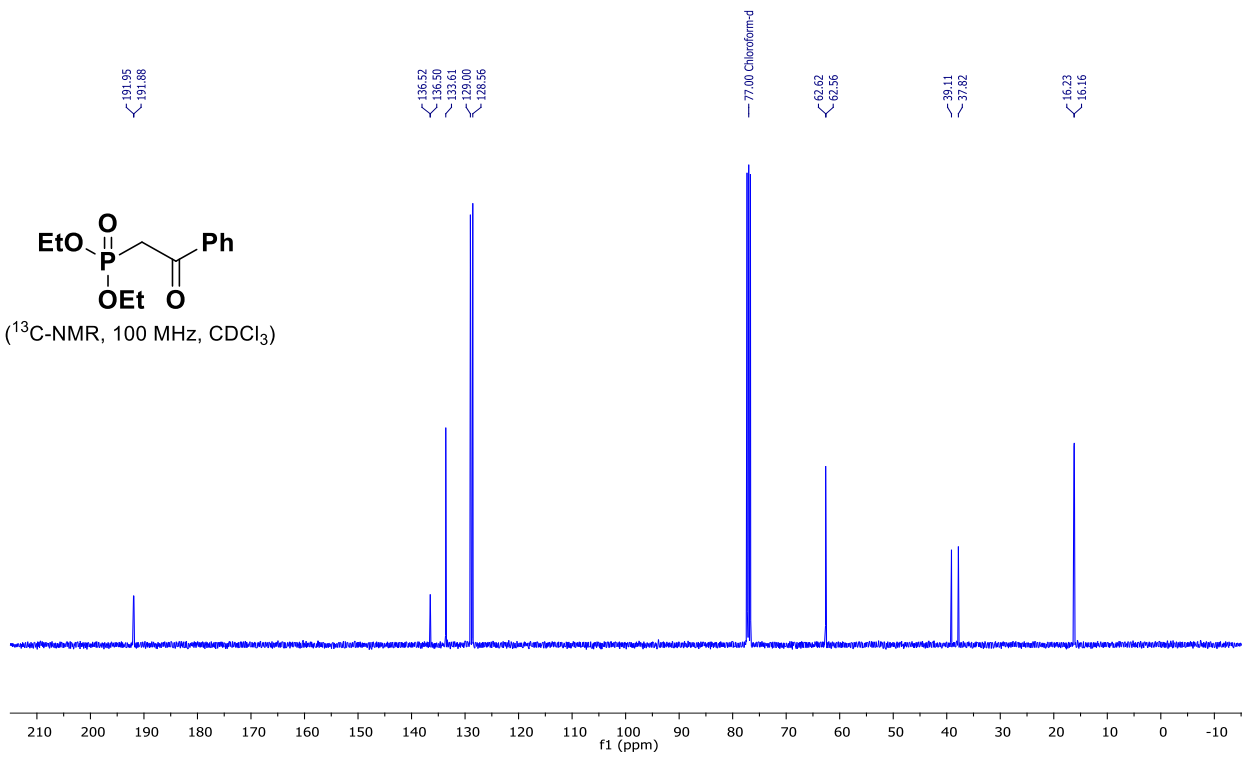


(^{13}C-NMR, 100 MHz, $CDCl_3$)

Diethyl (2-oxo-2-phenylethyl)phosphonate (22)

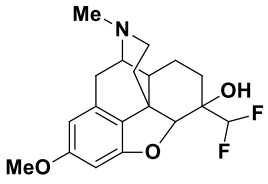


(^{1}H-NMR, 400 MHz, $CDCl_3$)

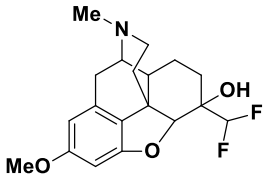


(^{13}C-NMR, 100 MHz, $CDCl_3$)

6-(Difluoromethyl)-3-methoxy-17-methyl-4,5-epoxymorphinan-6-ol (23)



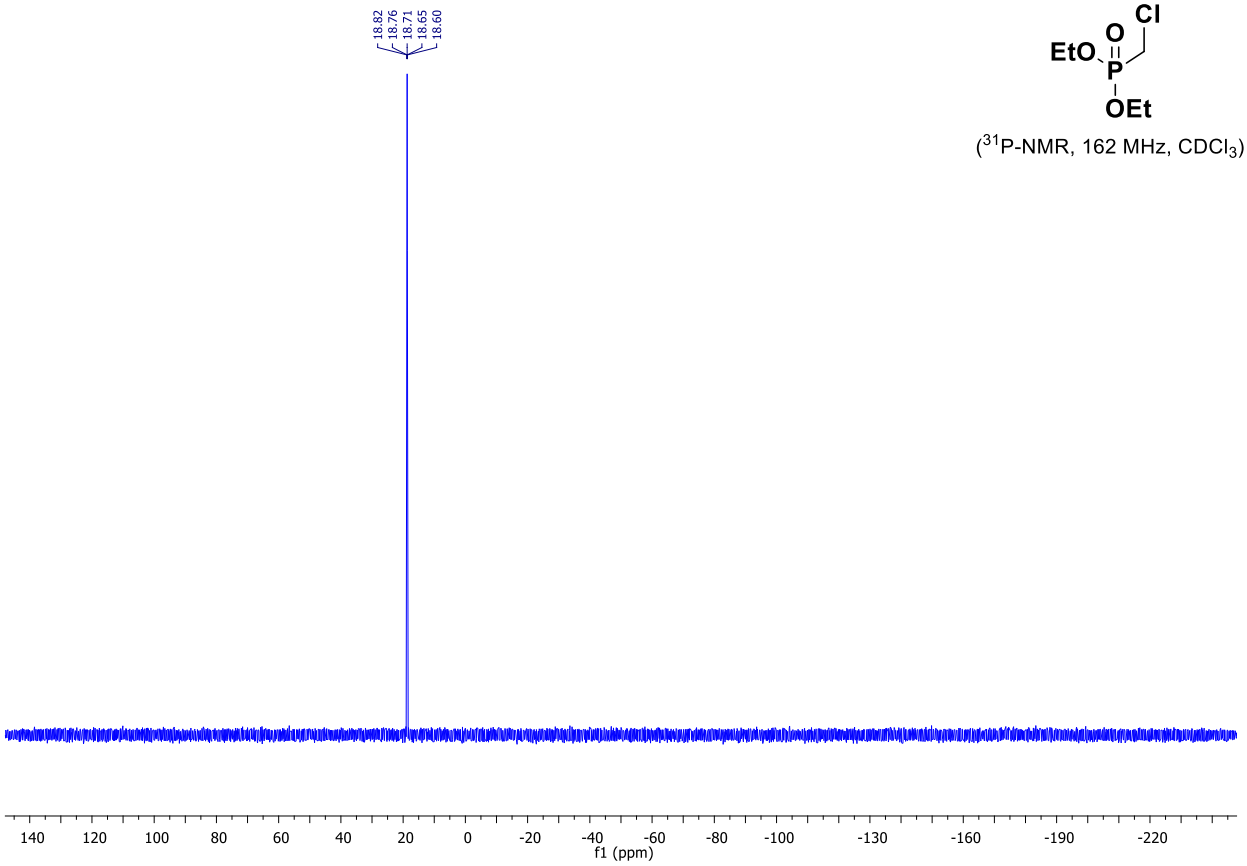
^{1}H-NMR, 400MHz, $CDCl_3$



^{13}C-NMR, 100MHz, $CDCl_3$

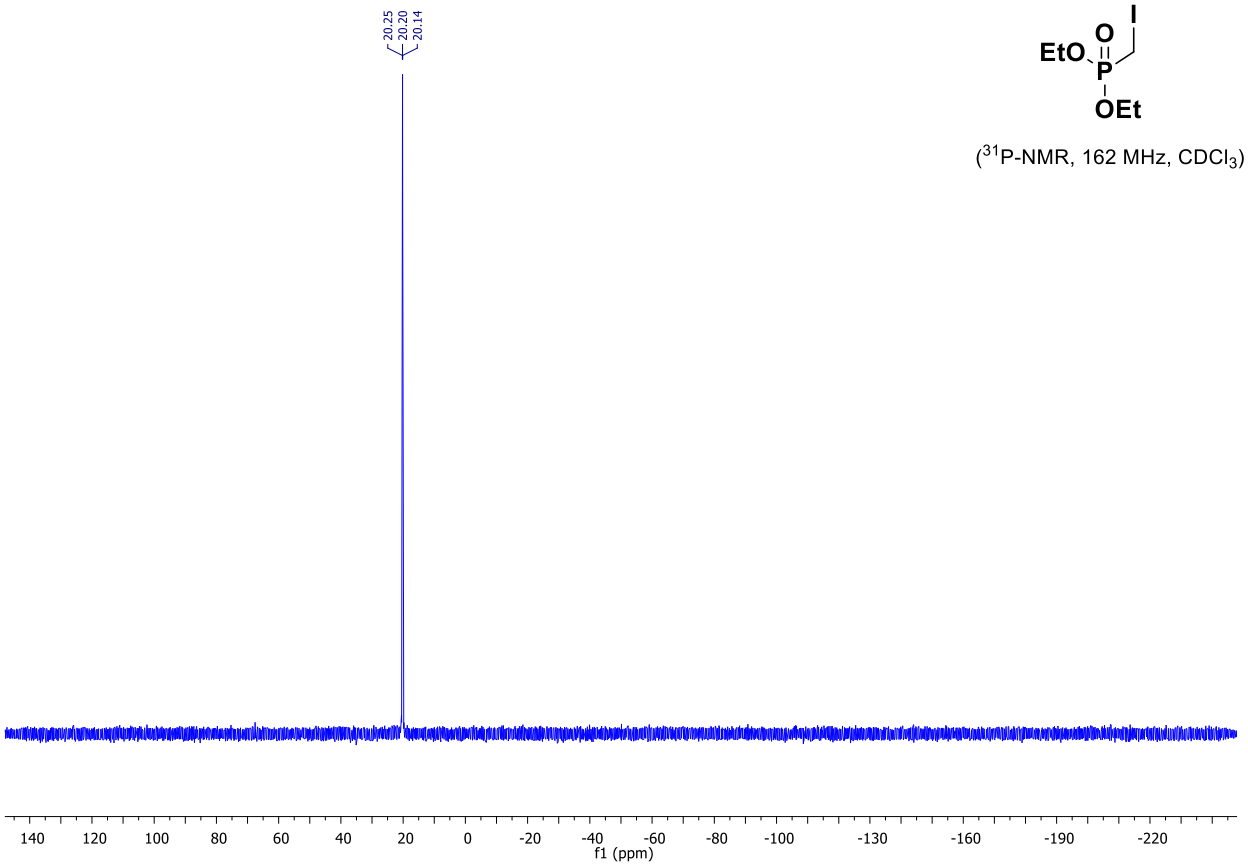
6. Copies of ^{31}P-NMR spectra

Diethyl (chloromethyl)phosphonate (2)



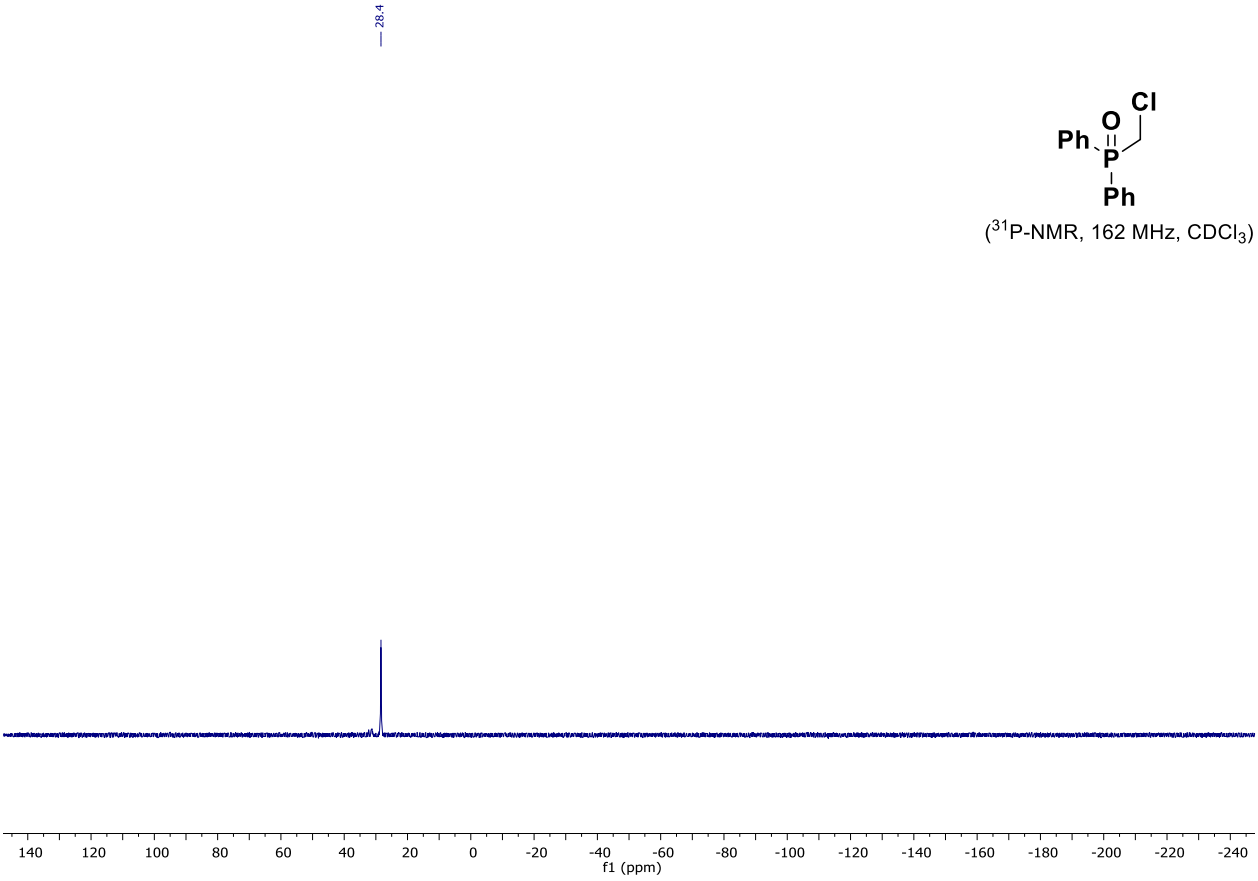
(^{31}P-NMR, 162 MHz, $CDCl_3$)

Diethyl (iodomethyl)phosphonate (3)



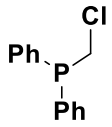
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Chloromomethyl)(diphenyl)phosphine oxide (5)



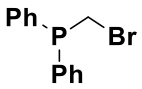
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Chloromethyl)(diphenyl)phosphine (6)



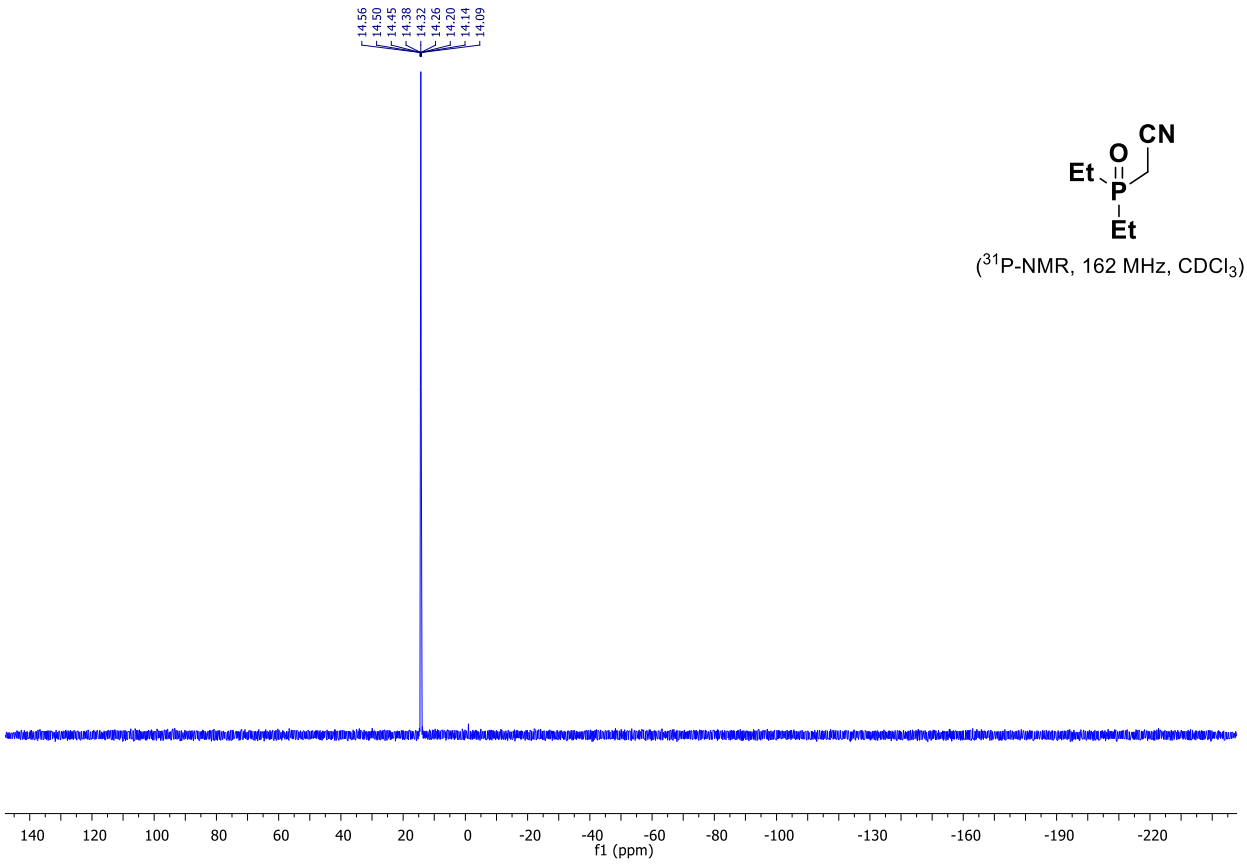
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Bromomethyl)(diphenyl)phosphine (7)



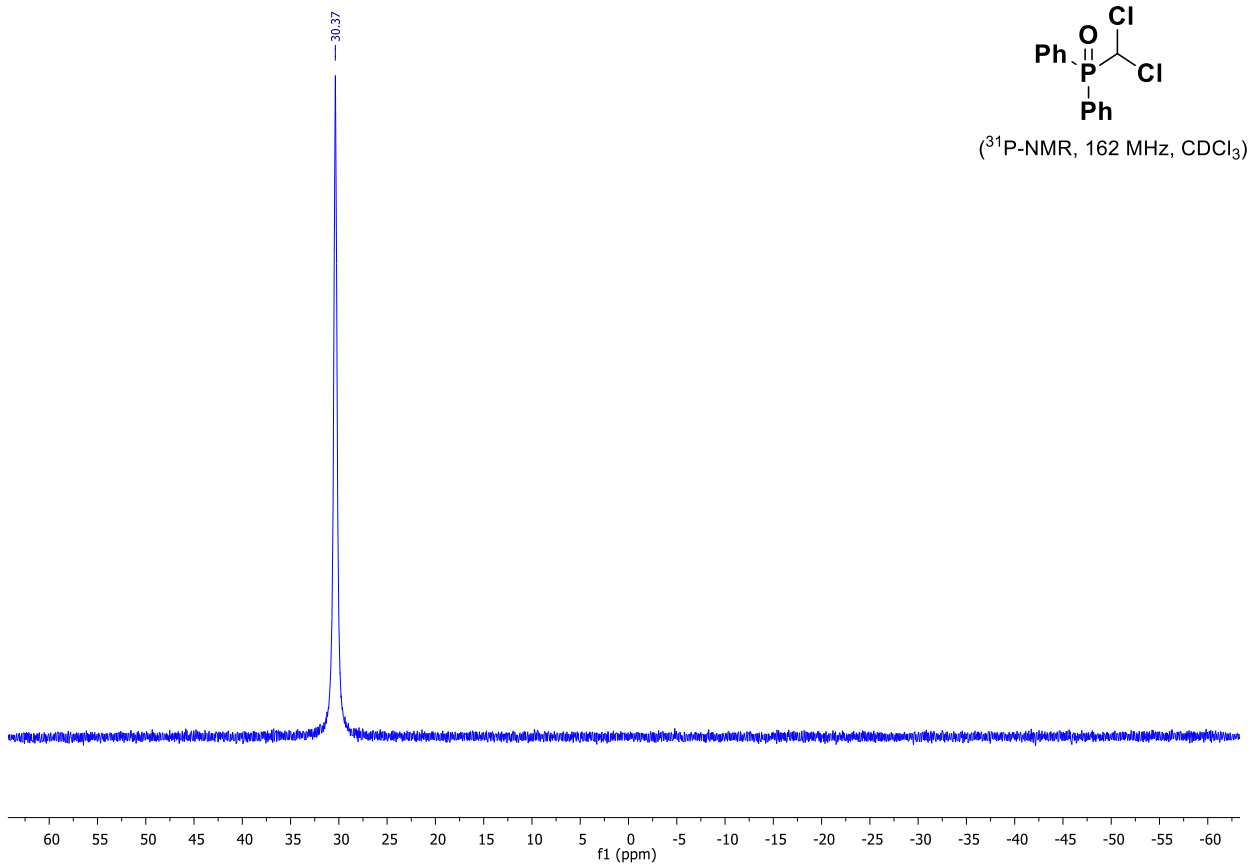
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Diethylphosphosphino)acetonitrile (8)



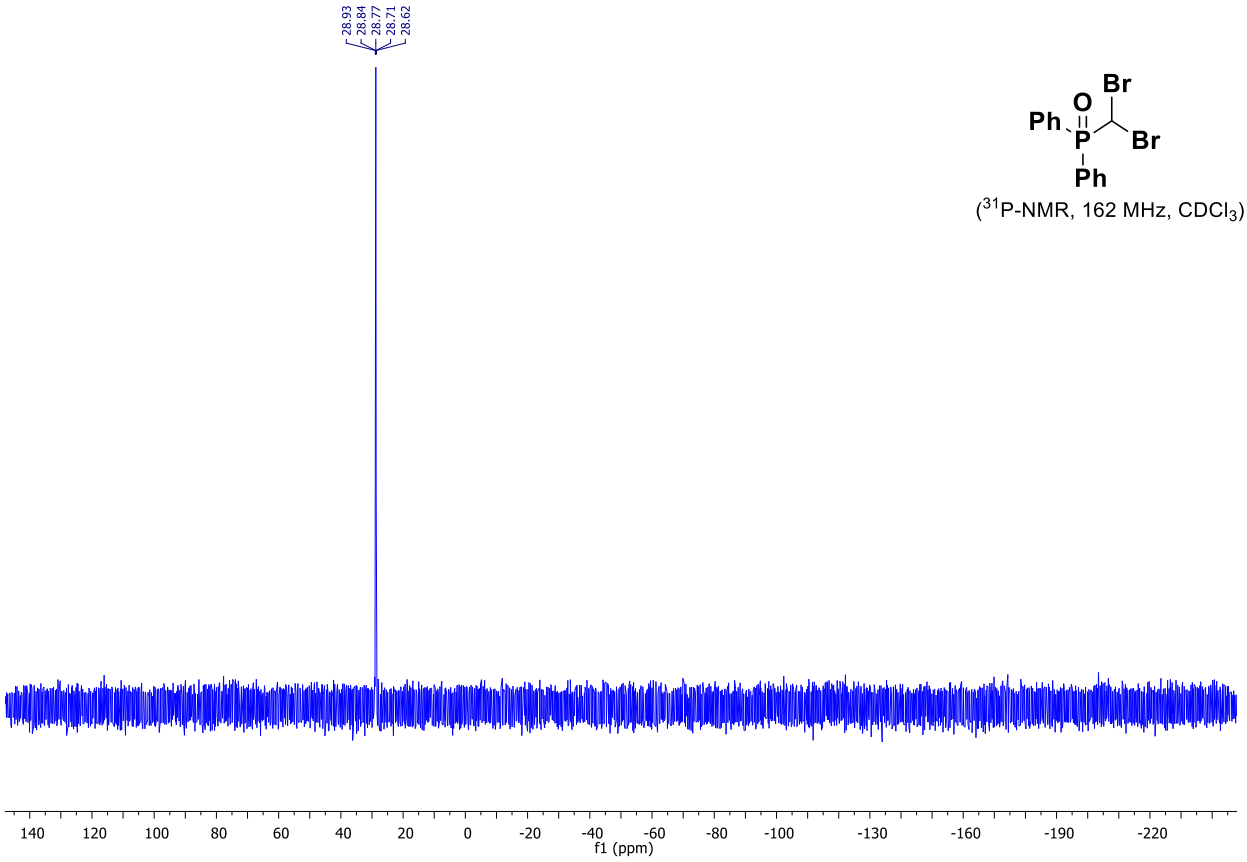
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Dichloromethyl)(diphenyl)phosphine oxide (9)



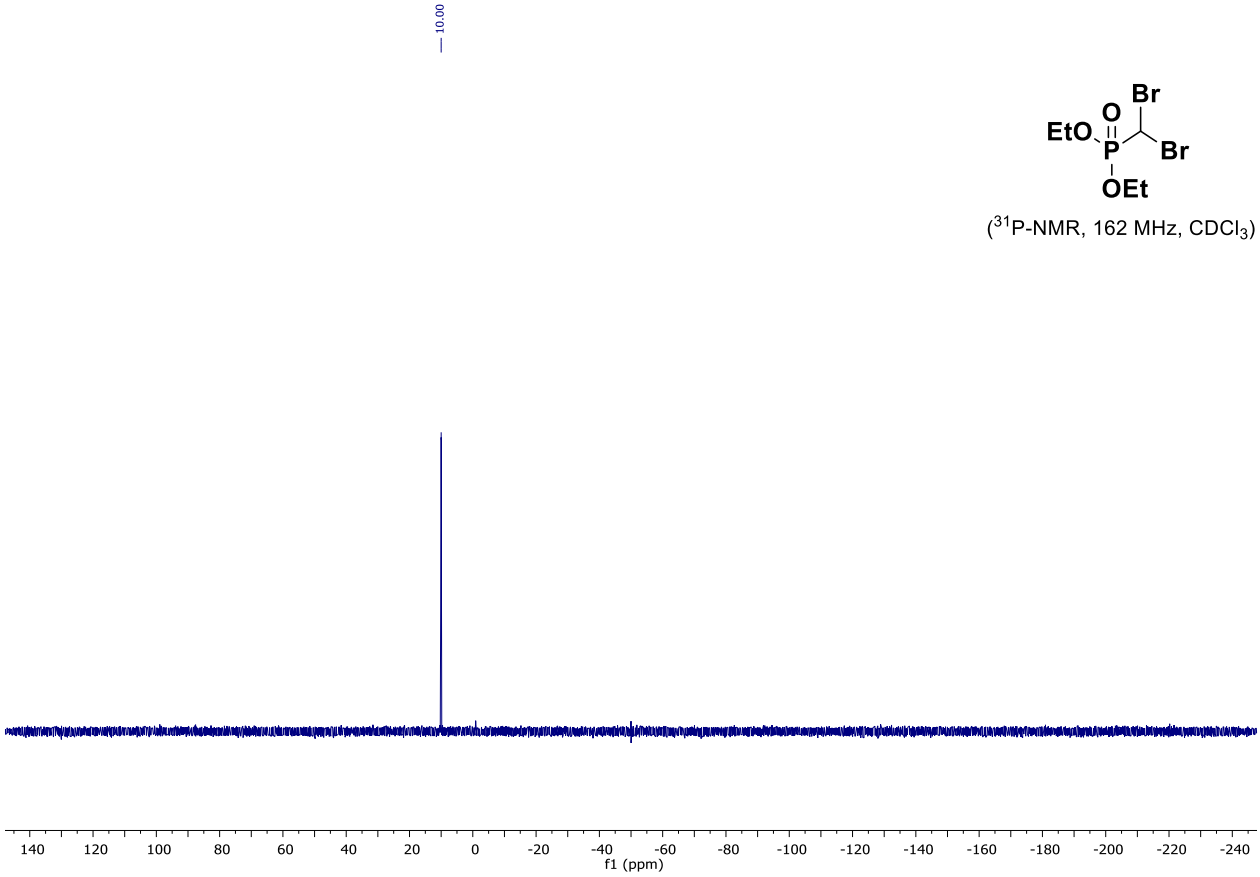
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Dibromomethyl)(diphenyl)phosphine oxide (10)



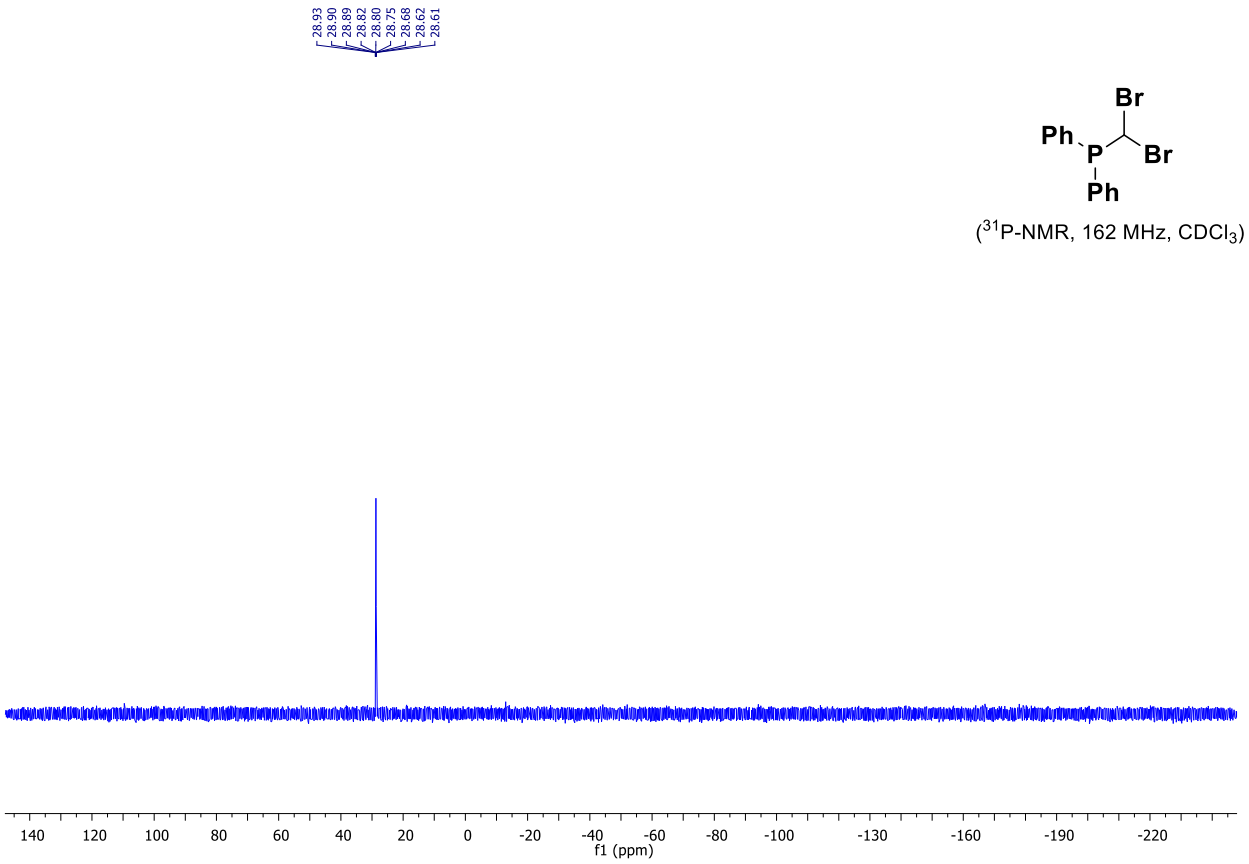
(^{31}P-NMR, 162 MHz, $CDCl_3$)

Diethyl (dibromomethyl)phosphonate (11)



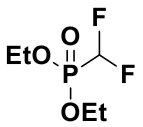
(^{31}P-NMR, 162 MHz, $CDCl_3$)

(Dibromomethyl)(diphenyl)phosphine (12)

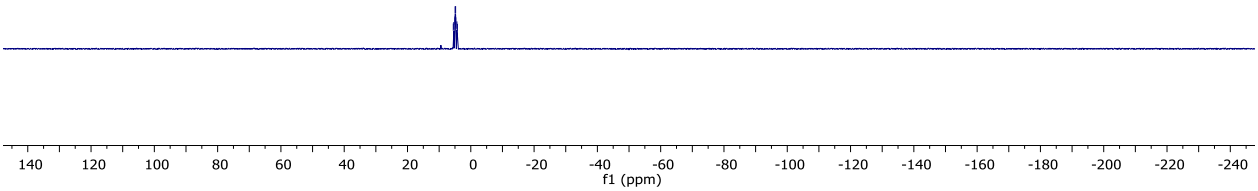


(^{31}P-NMR, 162 MHz, $CDCl_3$)

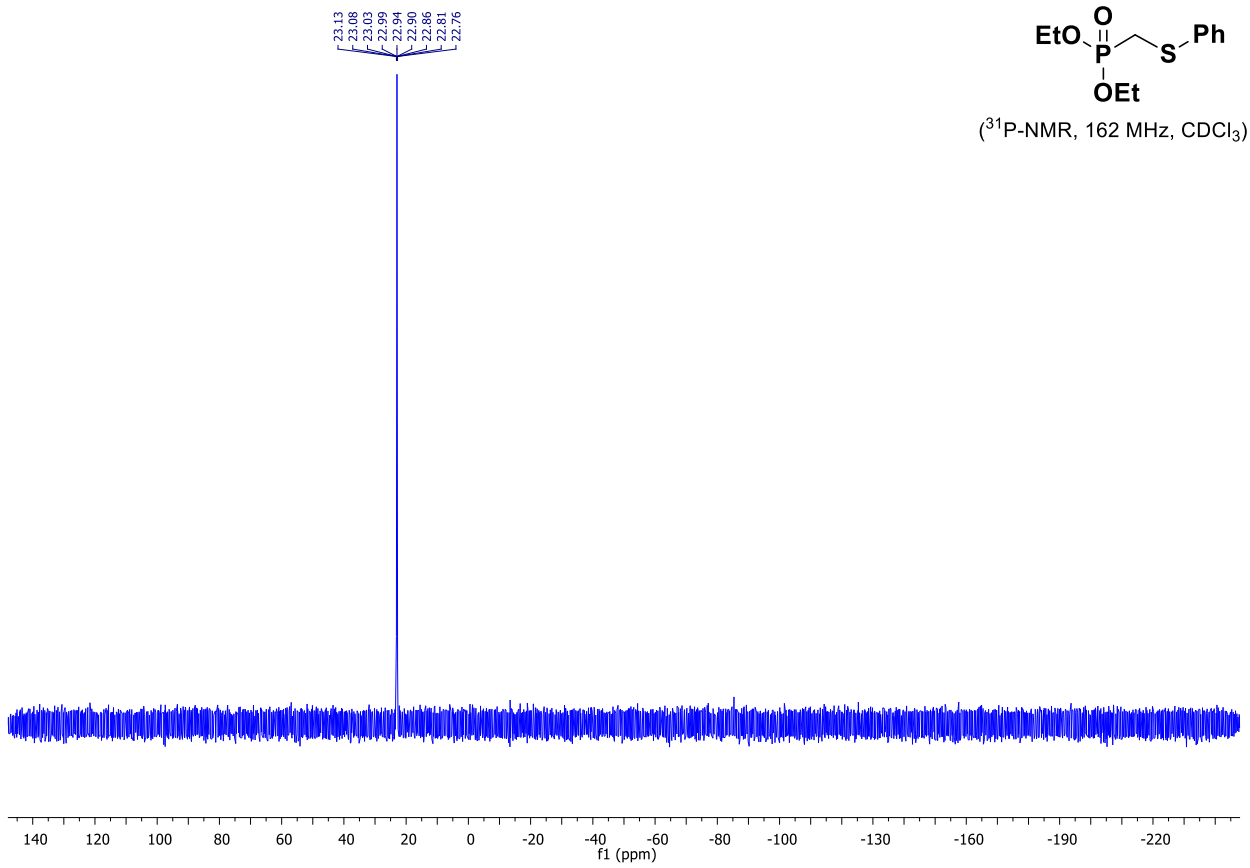
Diethyl (difluoromomethyl)phosphonate (13)



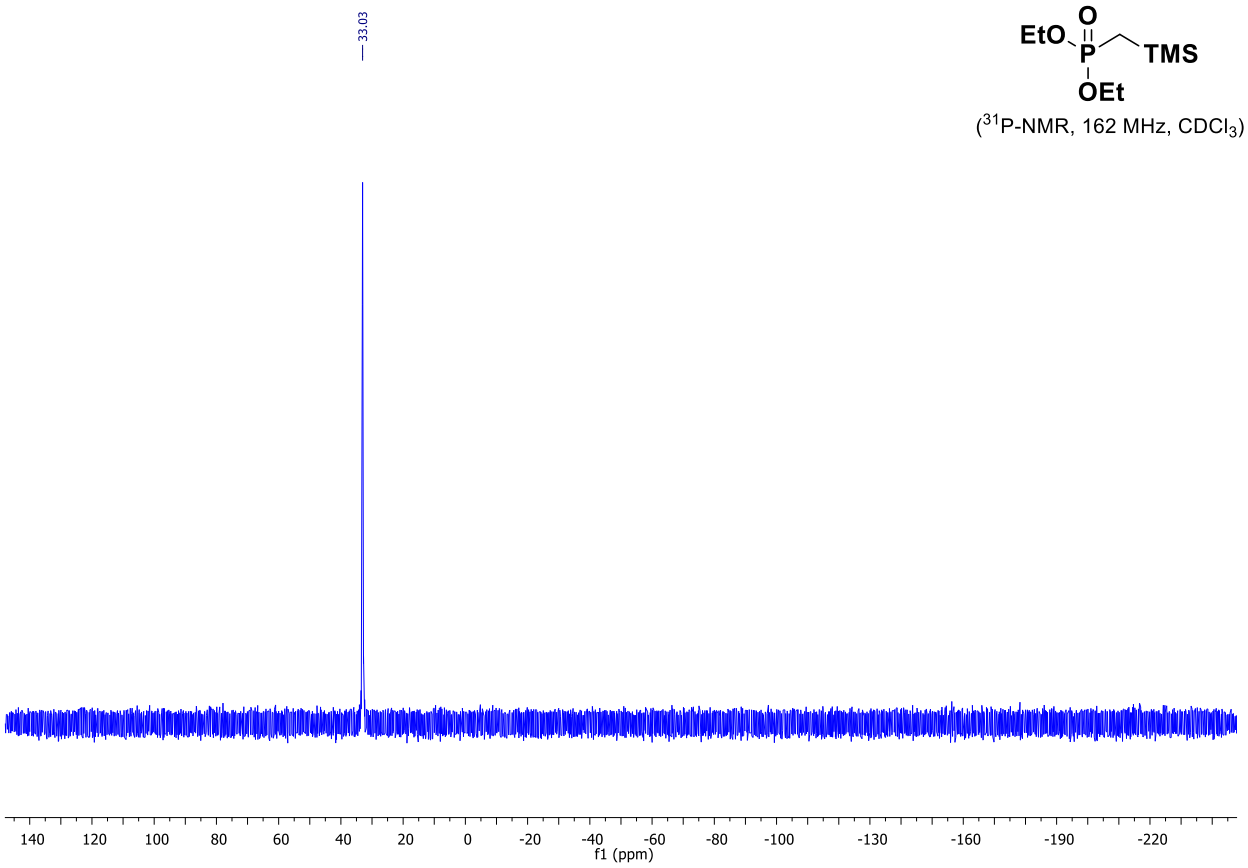
(^{31}P-NMR, 162 MHz, $CDCl_3$)



Diethyl [(phenylsulfanyl)methyl]phosphonate (14)

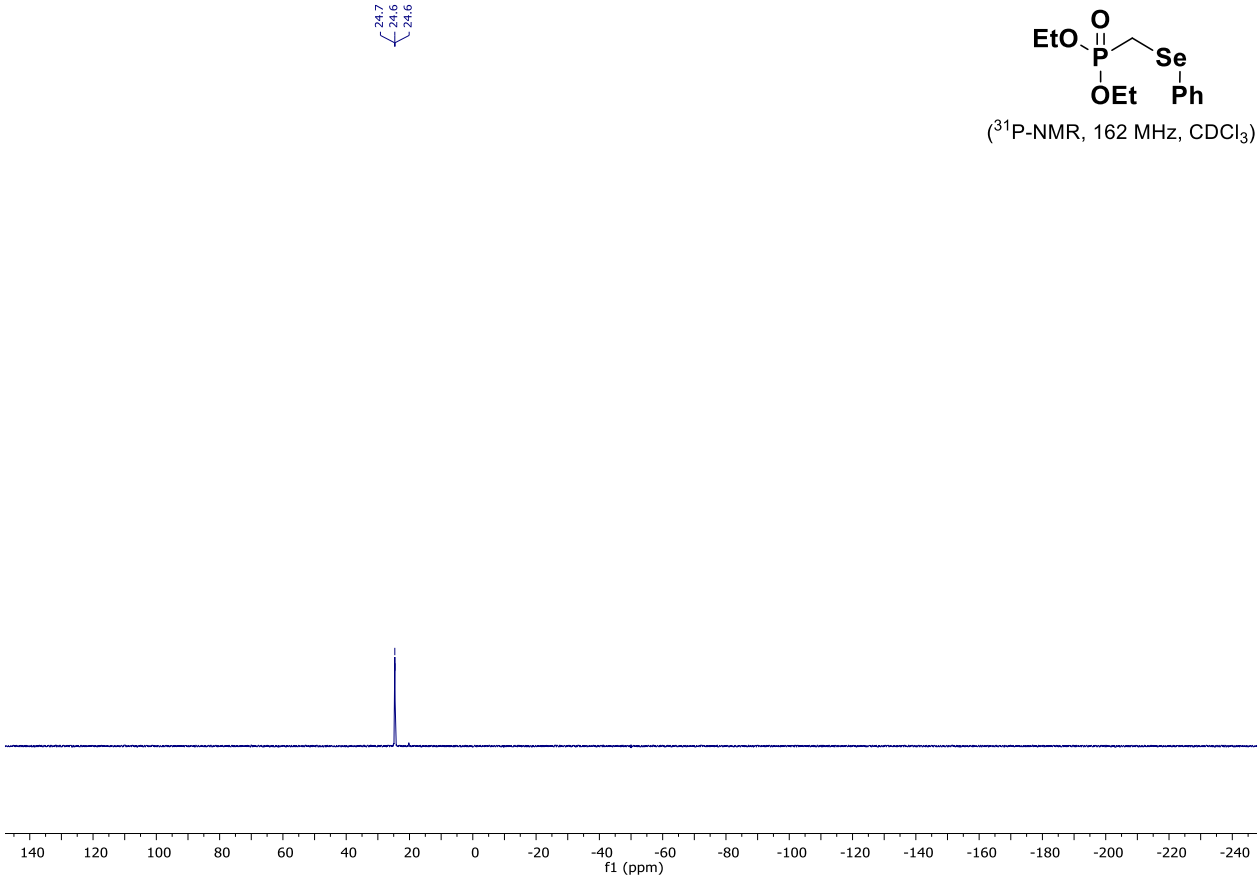


Diethyl [(trimethylsilyl)methyl]phosphonate (15)



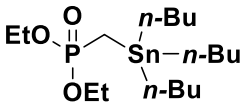
(^{31}P-NMR, 162 MHz, $CDCl_3$)

Diethyl [(phenylselanyl)methyl]phosphonate (16)

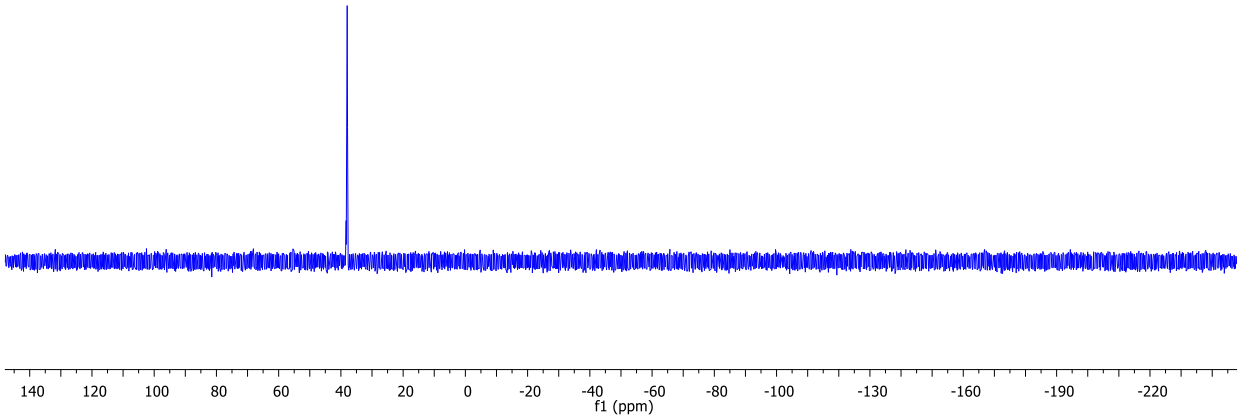


(^{31}P-NMR, 162 MHz, $CDCl_3$)

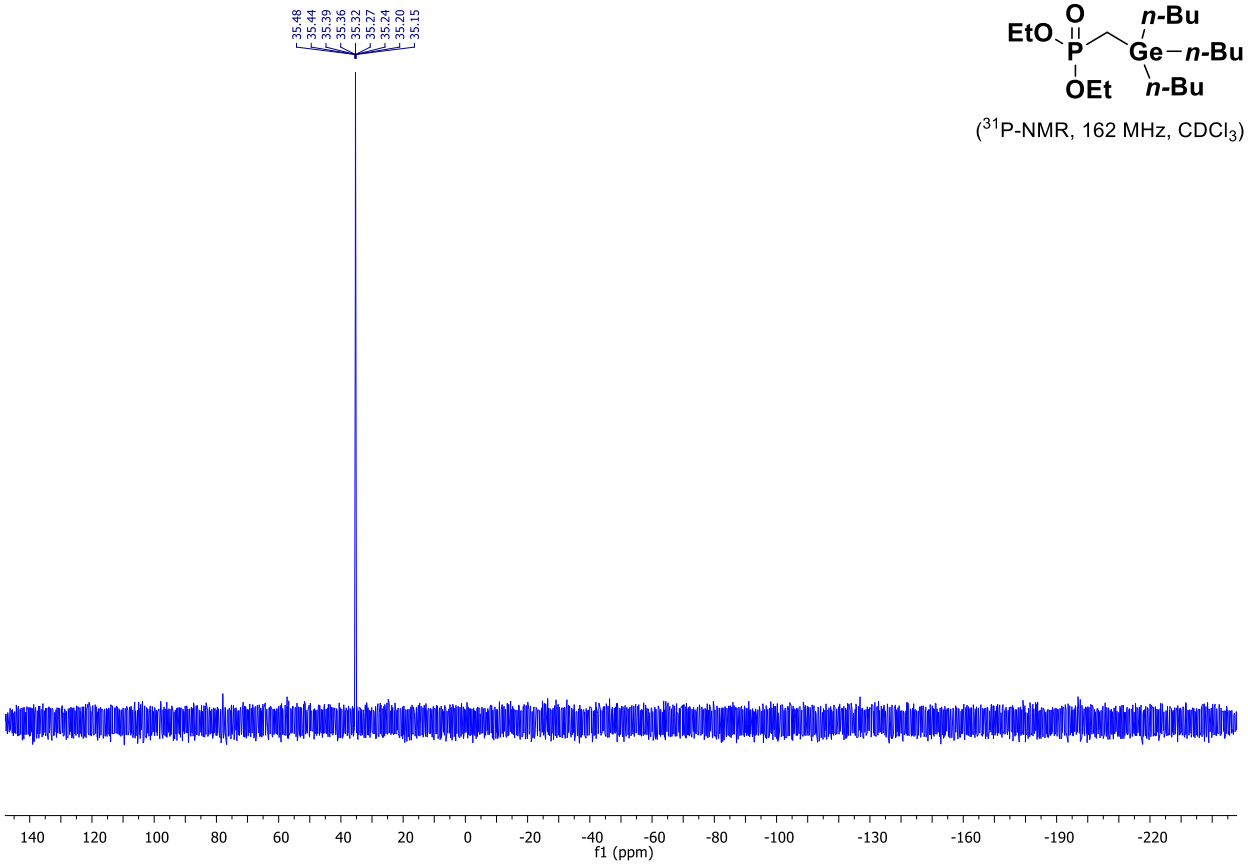
Diethyl [(tributylstannyl)methyl]phosphonate (17)



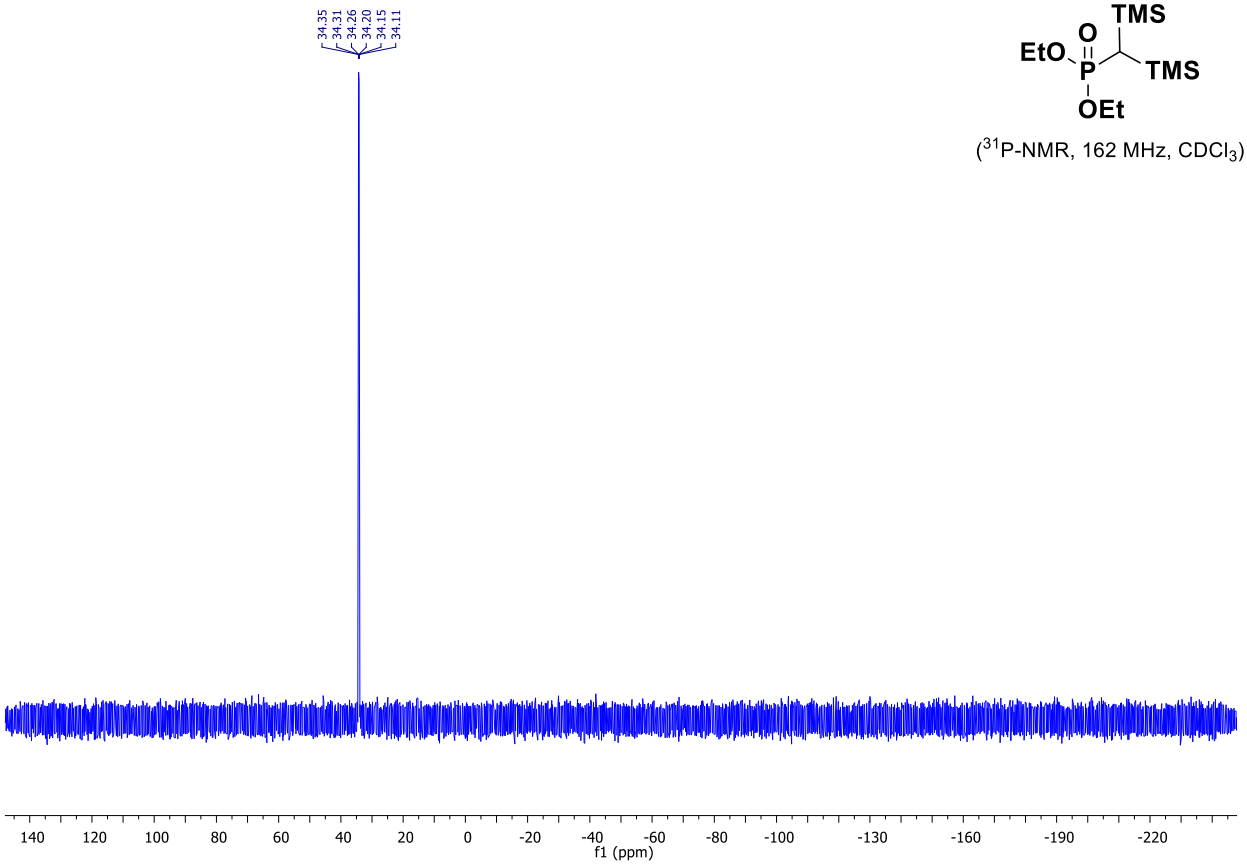
(^{31}P-NMR, 162 MHz, $CDCl_3$)



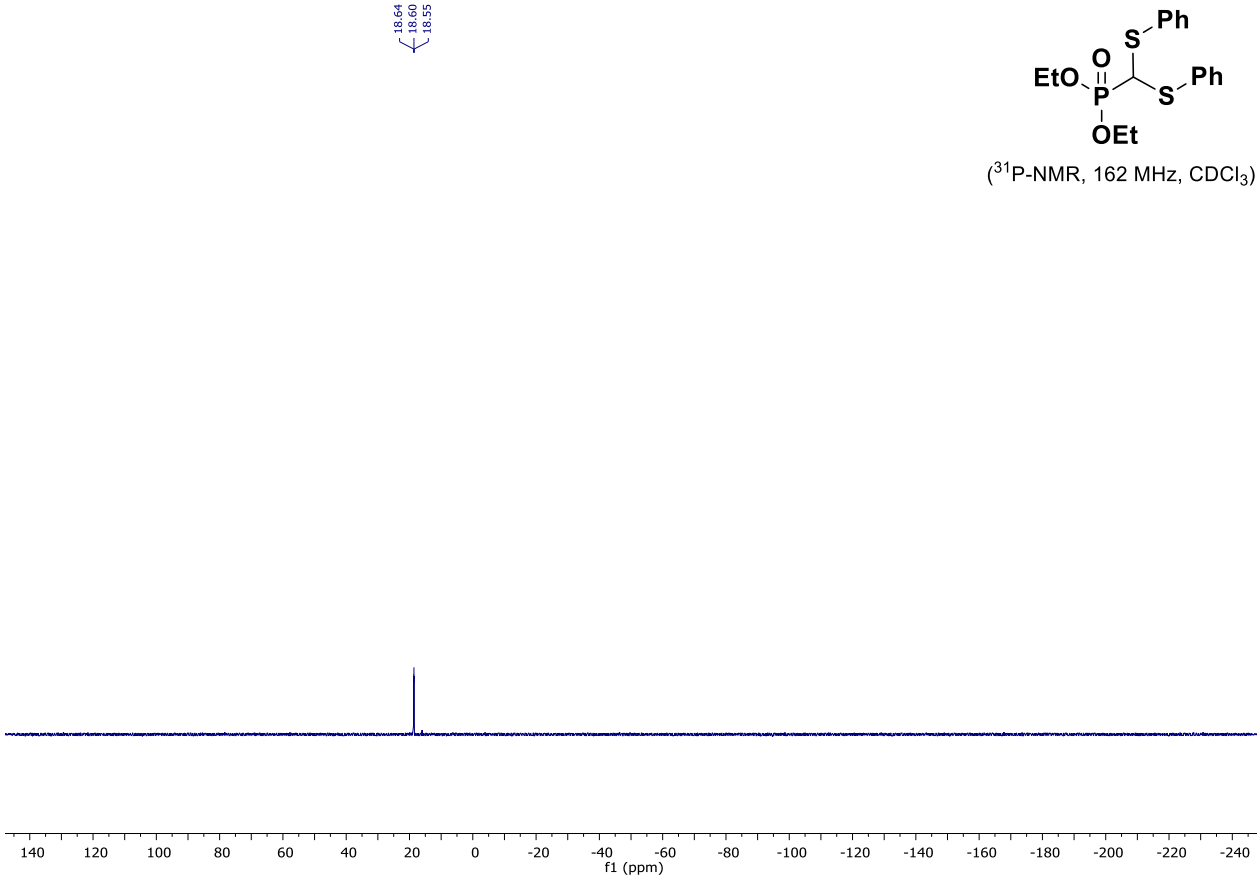
Diethyl [(tributylgermyl)methyl]phosphonate (18)



Diethyl [bis(trimethylsilyl)methyl]phosphonate (19)

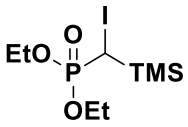


Diethyl [bis(phenylsulfanyl)methyl]phosphonate (20)



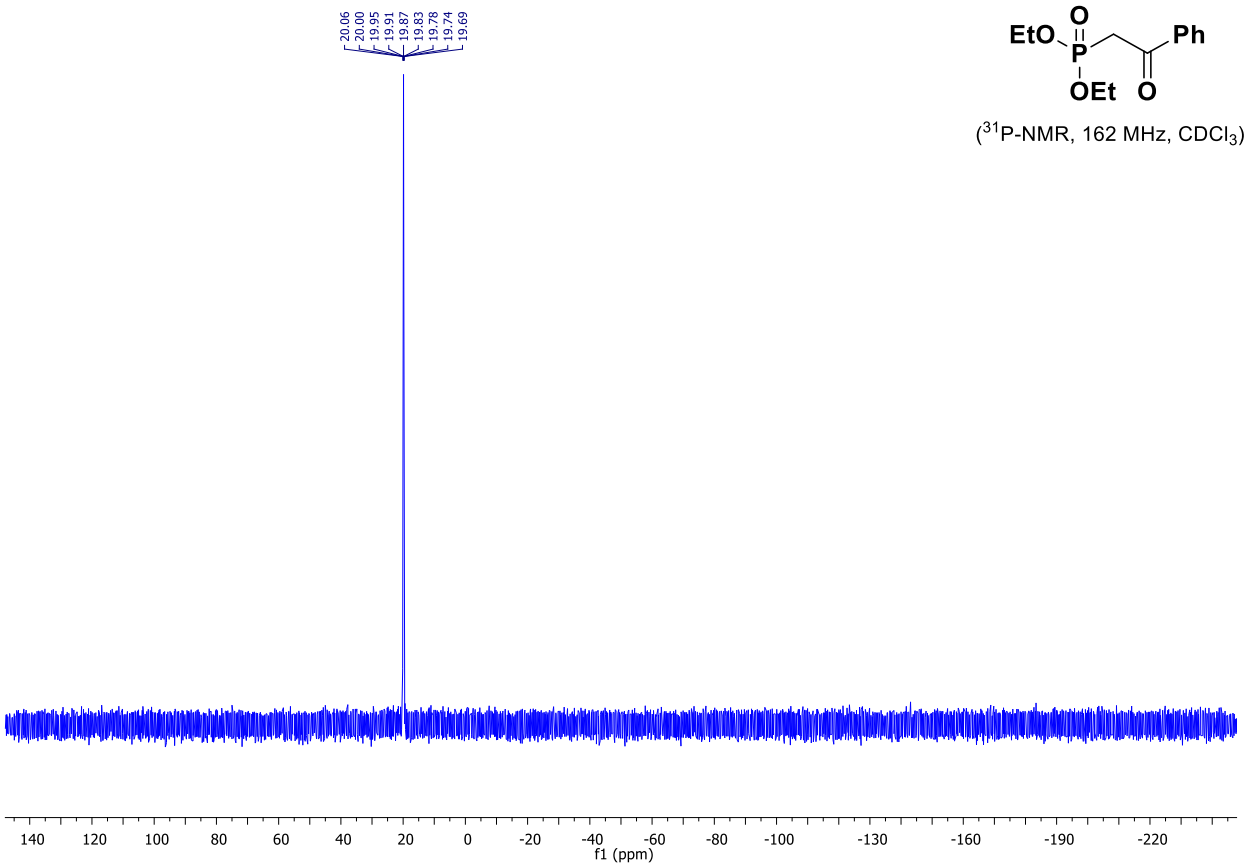
(^{31}P-NMR, 162 MHz, $CDCl_3$)

Diethyl [iodo(trimethylsilyl)methyl]phosphonate (21)



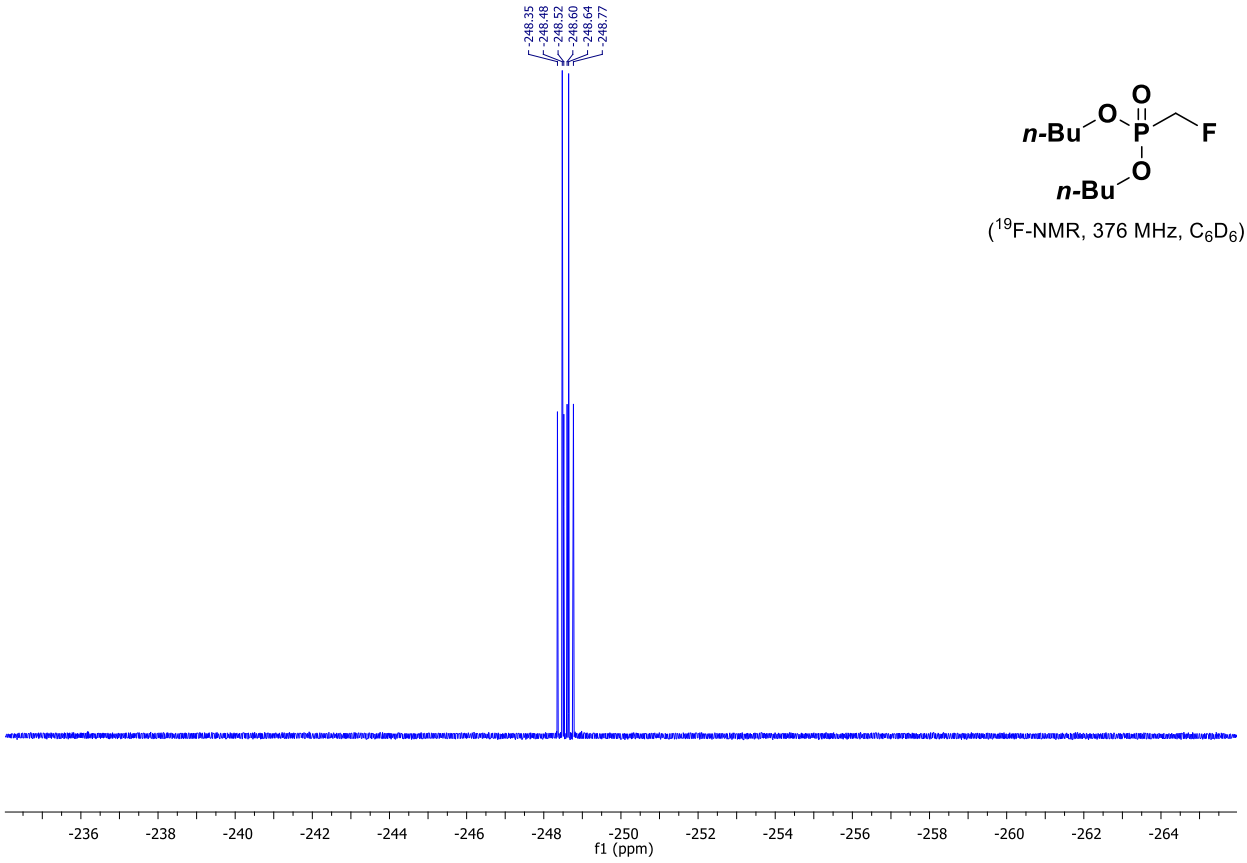
(^{31}P-NMR, 162 MHz, $CDCl_3$)

Diethyl (2-oxo-2-phenylethyl)phosphonate (22)



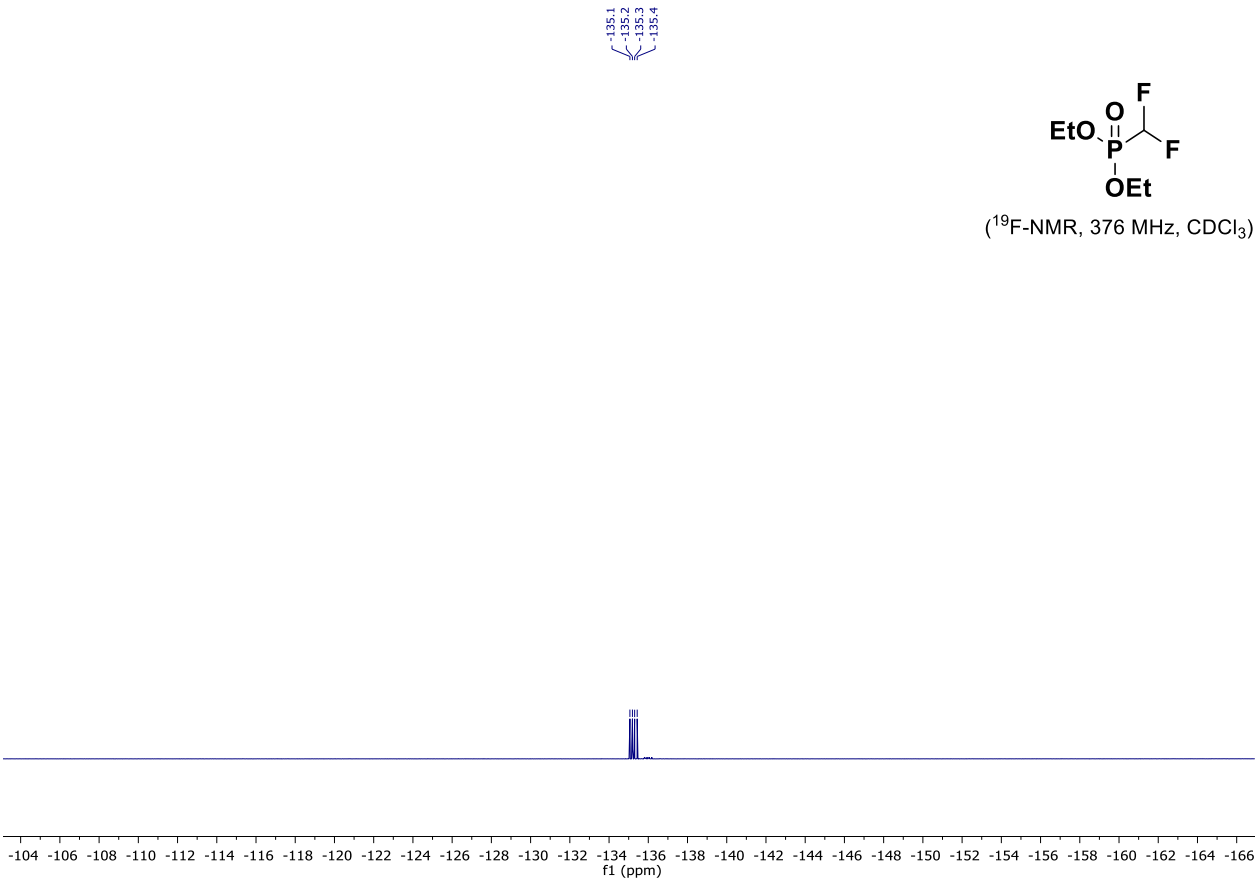
7. Copies of ^{19}F-NMR spectra

Dibutyl (fluoromethyl)phosphonate (4)



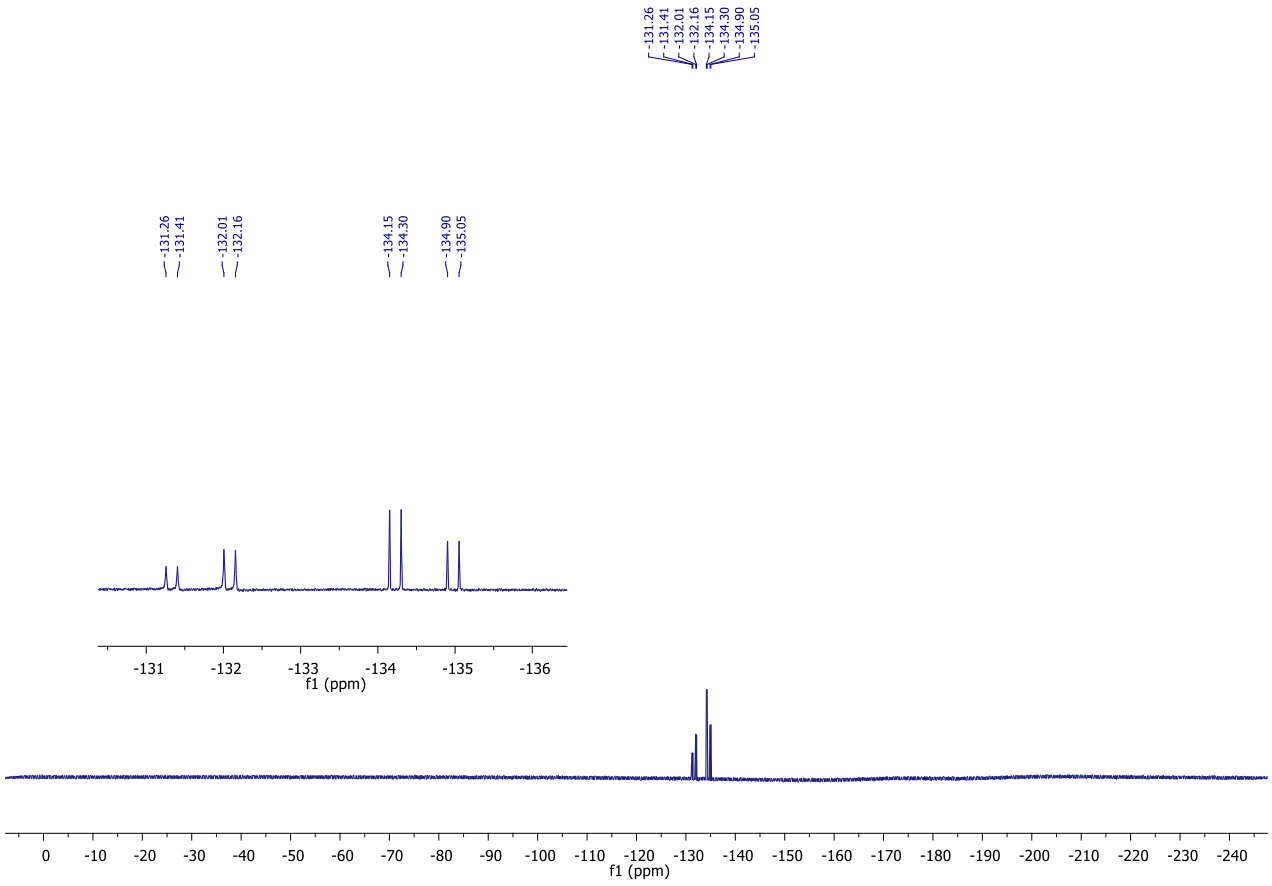
(^{19}F-NMR, 376 MHz, C_6D_6)

Diethyl (difluoromomethyl)phosphonate (13)



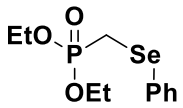
(^{19}F-NMR, 376 MHz, $CDCl_3$)

6-(Difluoromethyl)-3-methoxy-17-methyl-4,5-epoxymorphinan-6-ol (23)

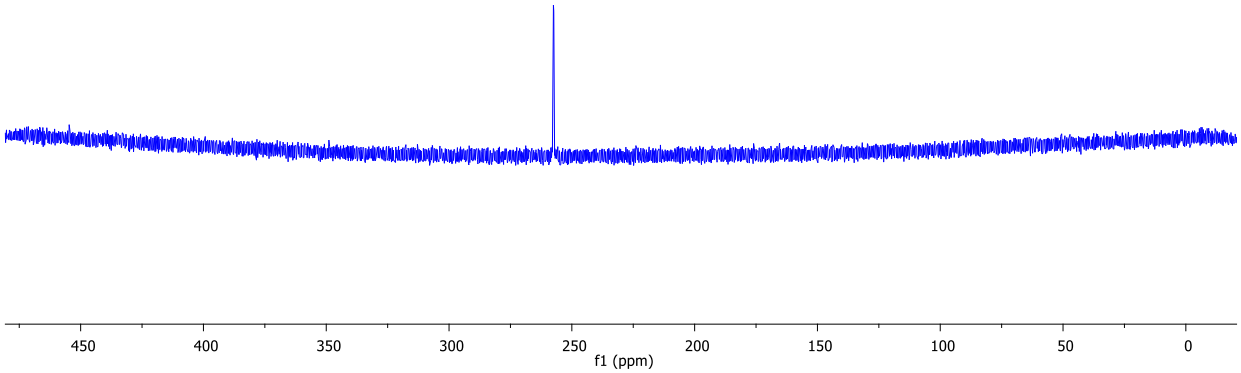


8. Copies of ^{77}Se-NMR spectra

Diethyl [(phenylselanyl)methyl]phosphonate (16)

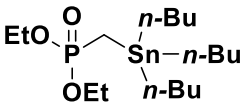


(^{77}Se-NMR, 76 MHz, $CDCl_3$)

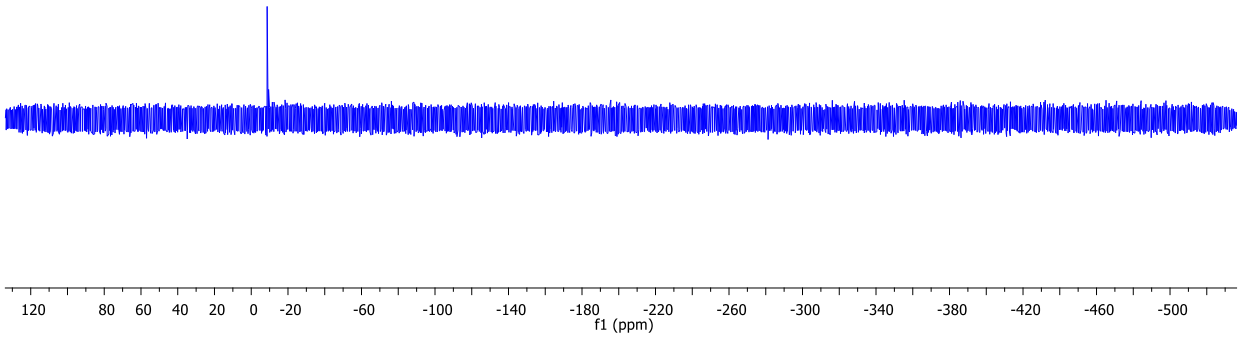


9. Copies of ^{119}Sn-NMR spectra

Diethyl [(tributylstannyl)methyl]phosphonate (17)



(^{119}Sn-NMR, 149 MHz, $CDCl_3$)



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