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New Journal of Chemistry RSCPublishing

COMMUNICATION

One-pot and highly regio-selective 1, 3-dipole cycloaddition of azomethine ylide generated in situ to tetraethyl vinylidenebisphosphonate (VBP) catalyzed by cerium(IV) oxide

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1. General Information

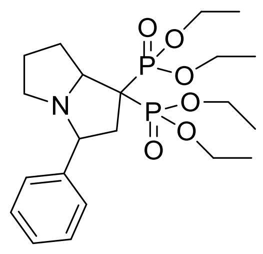
All compounds were fully characterized by spectroscopic data.The NMR spectra were recorded on a Bruker Avance III (^{1}H: 400 MHz, ^{13}C: 100.6 MHz), ^{31}P NMR spectra were recorded with a Bruker Avance III spectrometer at 162MHz(external standard 85% H_3PO_4), chemical shifts (δ) are expressed in ppm, and J values are given in Hz, and $CDCl_3$ were used as solvents. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF254. EI-MS (70eV): esquire HCT-Agilent 1200 mass spectrometer. IR spectra were recorded on a Thermo Scientific Nicolet 6700 Fourier IR spectrometer (ATIR) in KBr pellet. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (300–400 mesh). Tetraethyl vinylidenebisphosphonate (VBP) were prepared according to the literature[1]. Other materials were purchased from Aladdin-reagent Corporation Limited.

2. General Procedure

To a stirred solution of VBP (1 mmol, 0.3g) with benzaldehyde (1.2mmol) and L-proline (1.5mmol, 0.17 g) in toluene (2 mL) were added CeO_2 (5%mmol, 0.05mmol, 0.0086 g). The mixture was heated at 80°C and the progress of the reaction was monitored by TLC. As the reaction completed, silica gel (0.5 g) was added to the reaction mixture and the desired product was separated and purified by column chromatography on silica gel using petroleum ether(60-90)/ethyl acetate(1/2-1/5 v/v) as eluents.

The products were further identified by NMR, MS and IR, being in good agreement with the assigned structures.

Tetraethyl (3-phenylhexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate) (1)



Yellow oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.25-1.28 (m, 12H), 1.87-1.93 (m, 2H), 2.01-2.03 (m, 1H), 2.27-2.3 (m, 1H), 2.52-2.62 (2H), 2.73-2.85 (2H), 4.04-4.18 (10H), 7.15-7.16 (1H), 7.21-7.24 (2H), 7.32-7.34 (2H).

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^{31}P NMR ($CDCl_3/H_3PO_4$, 162.0 MHz): δ (ppm) = 24.77 & 25.62.

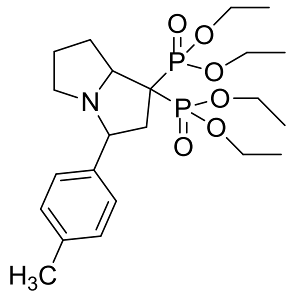
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 16.23 (P-O-C-$\underline{C}H_3$), 16.29 (P-O-C-$\underline{C}H_3$), 16.34 (P-O-C-$\underline{C}H_3$), 16.40 (P-O-C-$\underline{C}H_3$), 28.31($\underline{C}H_2$), 28.60 (t, J = 6.4 Hz, P-C-C-$\underline{C}H_2$), 43.52 (t, J = 4.79Hz, P-C-C-N-$\underline{C}H_2$), 48.89 (t, J = 141.7 Hz, P-$\underline{C}$-P), 52.07, 62.63 (P-O-$\underline{C}H_2$), 62.71 (P-O-$\underline{C}H_2$), 62.80 (P-O-$\underline{C}H_2$), 63.05 (d, J = 6.76Hz, P-O-$\underline{C}H_2$), 68.45 (d, J = 10.08Hz, P-C-C-$\underline{C}H$), 69.43, 126.84, 126.91, 128.16, 143.28.

IR: 1240.45 (P=O), 1067.68 (P-O-C)

MS calcd for 460.20 (MH^+), found: 460.3.

Yield: 68%.

Tetraethyl (3-(p-tolyl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate) (2)



Yellow oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.23-1.31 (m, 12H), 1.82-1.91 (m, 2H), 1.99-2.01 (m, 1H), 2.23 (s, 3H), 2.30-2.34 (m, 1H), 2.43-2.61 (2H), 2.67-2.84 (2H), 3.96-4.27 (10H), 7.02-7.04 (2H), 7.20-7.22 (2H).

^{31}P NMR ($CDCl_3/H_3PO_4$, 162.0 MHz): δ (ppm) = 24.74 & 25.80.

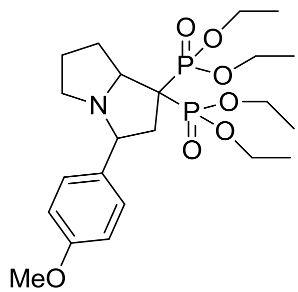
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 16.22 (P-O-C-$\underline{C}H_3$), 16.28 (P-O-C-$\underline{C}H_3$), 16.32 (P-O-C-$\underline{C}H_3$), 16.38 (P-O-C-$\underline{C}H_3$), 20.88 ($\underline{C}H_3$), 28.25($\underline{C}H_2$), 28.58 (t, J = 6.3 Hz, P-C-C-$\underline{C}H_2$), 43.45 (t, J = 4.4Hz, P-C-C-N-$\underline{C}H_2$), 48.76 (t, J = 136.1 Hz, P-$\underline{C}$-P), 51.99, 62.39 (P-O-$\underline{C}H_2$), 62.47 (P-O-$\underline{C}H_2$), 62.58 (P-O-$\underline{C}H_2$), 63.06 (d, J = 6.9Hz, P-O-$\underline{C}H_2$), 68.28 (d, J = 9.4Hz, P-C-C-$\underline{C}H$), 69.31, 126.78, 128.85, 136.43, 140.11.

IR ν: 1244.17 (P=O), 1061.20 (P-O-C)

MS calcd for 474.22 (MH^+), found: 474.4; MS calcd for 496.20 (MNa^+), found: 496.4.

Yield: 70%.

Tetraethyl(3-(4-methoxyphenyl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate)(3)



Yellow oil

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^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.27-1.38 (m, 12H), 1.68-1.76 (m, 2H), 1.89-2.08 (m, 2H), 2.33-2.34 (m, 1H), 2.54-2.61 (1H), 2.73-2.88 (2H), 3.78 (s, 3H),4.03-4.24 (10H), 6.81-6.85 (2H), 7.29-7.32 (2H).

^{31}P NMR ($CDCl_3/H_3PO_4$, 162.0 MHz): δ (ppm) = 24.74 & 25.75.

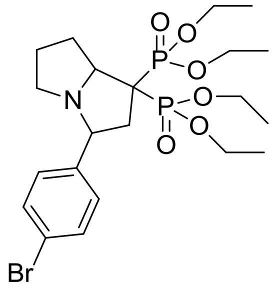
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 16.44 (P-O-C-$\underline{C}H_3$), 16.47 (P-O-C-$\underline{C}H_3$), 16.49 (P-O-C-$\underline{C}H_3$), 16.52 (P-O-C-$\underline{C}H_3$), 28.34($\underline{C}H_2$), 28.77 (d, J = 4.5 Hz, P-C-C-$\underline{C}H_2$), 43.51 (t, J = 4.8Hz, P-C-C-N-$\underline{C}H_2$), 48.88 (t, J = 136.4 Hz, P-$\underline{C}$-P), 52.13, 55.27 ($\underline{C}H_3$), 62.66 (P-O-$\underline{C}H_2$), 62.75 (P-O-$\underline{C}H_2$), 62.84 (P-O-$\underline{C}H_2$), 63.30 (d, J = 6.7Hz, P-O-$\underline{C}H_2$), 68.21 (d, J = 9.5Hz, P-C-C-$\underline{C}$H), 69.38, 113.78, 128.18, 135.00, 158.86.

IR: 1246.21 (P=O), 1033.38 (P-O-C)

MS calcd for 490.21 (MH^+), found: 490.4; MS calcd for 512.19 (MNa^+), found: 512.4.

Yield: 55%.

Tetraethyl (3-(4-bromophenyl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate)(4)



Brown oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.23-1.31 (m, 12H), 1.86-1.91 (m, 2H), 1.94-2.02 (m, 2H), 2.25-2.29 (m, 1H), 2.45-2.51 (m,1H), 2.74-2.82 (m, 2H), 3.96-4.23 (m, 10H), 7.19-7.22 (m, 2H), 7.31-7.34 (m, 2H).

^{31}P NMR ($CDCl_3/H_3PO_4$, 162.0 MHz): δ (ppm) = 24.57 & 25.59.

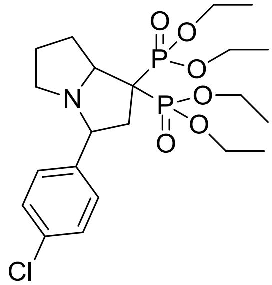
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 16.19 (P-O-C-$\underline{C}H_3$), 16.24 (P-O-C-$\underline{C}H_3$), 16.30 (P-O-C-$\underline{C}H_3$), 16.37 (P-O-C-$\underline{C}H_3$), 28.38($\underline{C}H_2$), 28.49 (t, J = 6.0 Hz, P-C-C-$\underline{C}H_2$), 43.53 (t, J = 4.3Hz, P-C-C-N-$\underline{C}H_2$), 48.80 (t, J = 136.2 Hz, P-$\underline{C}$-P), 52.00, 62.42 (P-O-$\underline{C}H_2$), 62.49 (P-O-$\underline{C}H_2$), 62.58 (P-O-$\underline{C}H_2$), 63.05 (d, J = 6.9Hz, P-O-$\underline{C}H_2$), 67.81 (d, J = 9.7Hz, P-C-C-$\underline{C}$H), 69.42, 120.42, 128.55, 131.16, 142.51.

IR: 1242.92 (P=O), 1063.22 (P-O-C)

MS calcd for 438.11 (MH^+), found: 538.3; MS calcd for 560.09 (MNa^+), found: 560.3.

Yield: 45%.

Tetraethyl (3-(4-chlorophenyl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate)(6)



Black oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.25-1.32 (m, 12H), 1.87-1.96 (m, 2H), 2.00-2.92 (m, 1H), 2.26-2.30 (m,1H), 2.46-2.58 (m, 2H), 2.74-2.84 (m, 2H), 4.01-4.20 (m, 10H), 7.17-7.19 (d, 2H, J = 8.4Hz), 7.26-7.28 (d, 2H, J = 8.2Hz).

^{31}P NMR ($CDCl_3/H_3PO_4$, 162.0 MHz): δ (ppm) = 24.58 & 25.51.

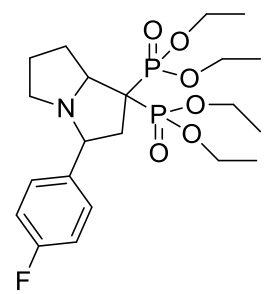
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 16.34 (P-O-C-$\underline{C}H_3$), 16.40 (P-O-C-$\underline{C}H_3$), 16.46 (P-O-C-$\underline{C}H_3$), 16.52 (P-O-C-$\underline{C}H_3$), 28.53($\underline{C}H_2$), 28.67 (t, J = 4.4 Hz, P-C-C-$\underline{C}H_2$), 43.62 (t, J = 4.3Hz, P-C-C-N-$\underline{C}H_2$), 48.80 (t, J = 136.2 Hz, P-$\underline{C}$-P), 52.00, 62.65 (P-O-$\underline{C}H_2$), 62.71 (P-O-$\underline{C}H_2$), 62.78 (P-O-$\underline{C}H_2$), 63.27 (d, J = 6.9Hz, P-O-$\underline{C}H_2$), 67.95 (d, J = 9.8Hz, P-C-C-$\underline{C}H$), 69.54, 128.37, 128.40, 132.57, 141.87.

MS calcd for 438.11 (MH^+), found: 538.3; MS calcd for 560.09 (MNa^+), found: 560.3.

IR: 1241.32 (P=O), 1072.74 (P-O-C)

Yield: 45%.

Tetraethyl (3-(4-fluorophenyl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate)(7)



Yellow oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.25-1.31 (m, 12H), 1.86-1.91 (m, 2H), 1.99-2.02 (m, 1H), 2.26-2.31 (m,1H), 2.48-2.52 (m, 2H), 2.71-2.82 (m, 2H), 3.99-4.21 (m, 10H), 6.17-6.91(t, 2H, J = 2.2Hz), 7.27-7.30 (m, 2H).

^{31}P NMR ($CDCl_3/H_3PO_4$, 162.0 MHz): δ (ppm) = 24.69 & 25.67.

^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 15.26 (P-O-C-$\underline{C}H_3$), 15.32 (P-O-C-$\underline{C}H_3$), 15.37 (P-O-C-$\underline{C}H_3$), 15.43 (P-O-C-$\underline{C}H_3$), 27.40($\underline{C}H_2$), 27.62 (t, J = 6.2 Hz, P-C-C-$\underline{C}H_2$), 42.72 (t, J = 4.1Hz, P-C-C-N-$\underline{C}H_2$), 47.88 (t, J = 136.2 Hz, P-$\underline{C}$-P), 51.05, 61.46 (P-O-$\underline{C}H_2$), 61.55 (P-O-$\underline{C}H_2$), 61.62 (P-O-$\underline{C}H_2$), 62.11 (d, J = 6.8Hz, P-O-$\underline{C}H_2$), 66.84 (d, J = 9.8Hz, P-C-C-$\underline{C}H$), 68.42, 113.92 (d, J = 21.1Hz, F-C-$\underline{C}H$), 127.35 (d, J = 7.9 Hz, F-C-

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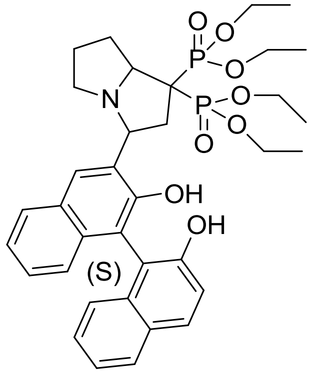
C-CH), 138.01, 160.86 (d, J = 244.3Hz, F-C).

IR: 1241.95 (P=O), 1059.55(P-O-C)

MS calcd for 478.19 (MH^+), found: 478.5.

Yield: 60%.

Tetraethyl (3-(2,2'-dihydroxy-[1,1'-(S)-binaphthalen]-3-yl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate) (8)



Yellowish oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.10-1.46 (m, 12H), 1.84-1.95 (m, 1H), 2.00-2.03 (m, 1H), 2.14-2.20 (m,1H), 2.35-2.48 (m, 1H), 2.75-2.81 (m, 1H), 2.84-2.96 (m, 2H), 3.05-3.10 (m, 1H), 4.05-4.35 (m, 9H), 4.56-4.61 (m, 1H), 7.09-7.23(m, 4H), 7.25-7.30 (m, 2H), 7.35 (d, 1H, J = 8.84Hz), 7.66 (s, 1H), 7.76 (d, 2H, J = 7.76Hz), 7.83 (d, 1H, J = 8.12Hz), 7.86 (d, 1H, J = 8.92Hz).

^{31}P NMR ($CDCl_3$/H_3PO_4, 162.0 MHz): δ (ppm) = 23.67.

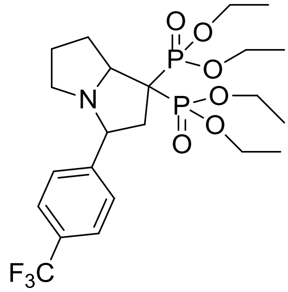
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 15.26 (P-O-C-CH_3), 15.32 (P-O-C-CH_3), 15.37 (P-O-C-CH_3), 15.43 (P-O-C-CH_3), 28.40(CH_2), 28.72, 42.38, 49.80 (t, J = 136.9 Hz, P-C-P), 51.96, 63.29 (P-O-CH_2), 63.38 (P-O-CH_2), 63.45 (P-O-CH_2), 63.70 (d, J = 5.9Hz, P-O-CH_2), 68.97, 70.12, 113.22, 115.55, 117.70, 123.10, 123.49, 124.35, 125.29, 125.89, 126.14, 127.00, 127.85, 128.08, 128.16, 129.10, 129.33, 129.71, 133.59, 133.98, 151.26, 155.40.

IR: 1251.60 (P=O), 1041.23(P-O-C)

MS calcd for 668.25 (MH^+), found: 668.4; MS calcd for 690.24 (MNa^+), found: 690.3

Yield: 30%.

Tetraethyl (3-(4-(trifluoromethyl)phenyl)hexahydro-1H-pyrrolizine-1,1-diyl)bis(phosphonate) (9)



Yellow oil

^{1}H NMR ($CDCl_3$, 400 MHz): δ(ppm) = 1.17-1.28 (m, 12H), 1.83-1.88 (m, 2H), 1.97-1.99 (m, 1H), 2.24-2.28 (m, 1H), 2.45-2.47 (m, 2H), 2.76-2.79 (m, 2H), 4.02-4.18 (m, 10H), 7.41 (s, 4H).

^{31}P NMR ($CDCl_3$/H_3PO_4, 162.0 MHz): δ (ppm) = 24.51 & 25.41.

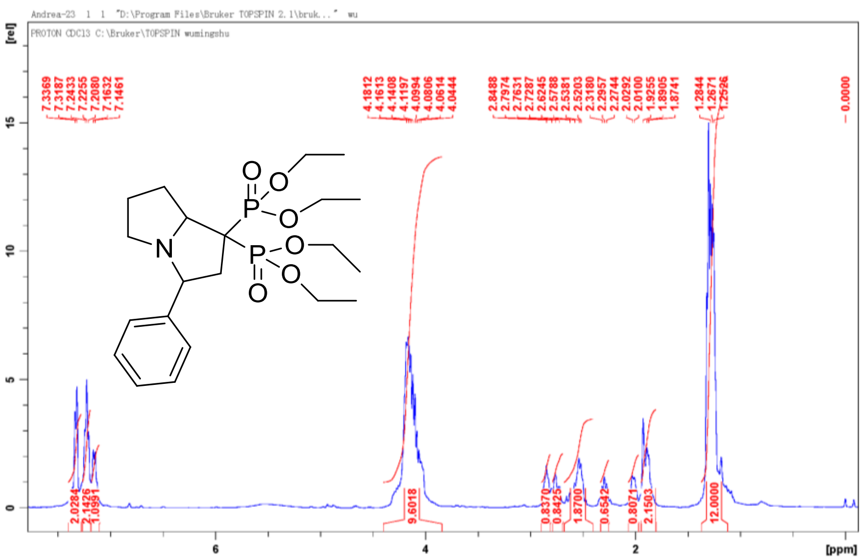
^{13}C NMR ($CDCl_3$, 100.6 MHz): δ(ppm) = 16.06 (P-O-C-$\underline{C}H_3$), 16.12 (P-O-C-$\underline{C}H_3$), 16.15 (P-O-C-$\underline{C}H_3$), 16.19 (P-O-C-$\underline{C}H_3$), 28.44($\underline{C}H_2$), 28.49, 43.71, 49.01 (t, J = 134.5 Hz, P-$\underline{C}$-P), 52.07, 62.31 (P-O-$\underline{C}H_2$), 62.37 (P-O-$\underline{C}H_2$), 62.44 (P-O-$\underline{C}H_2$), 62.99 (d, J = 6.7Hz, P-O-$\underline{C}H_2$), 67.94 (d, J = 10.0Hz, P-C-C-$\underline{C}H$), 69.62, 124.09 (d, J = 271.8Hz, F-$\underline{C}$), 124.95 (d, J = 3.6 Hz, F-C-C-$\underline{C}H$), 126.99, 128.74 (q, J = 32.0Hz, F-C-$\underline{C}$), 148.05.

MS calcd for 528.19 (MH^+), found: 528.5.

Yield: 55%.

1. Gao, J.; Liu, J.; Qiu, Y.; Chu, X.; Qiao, Y.; Li, D., *BBA - General Subjects.* **2013,** *1830* (6), 3635-3642.

^{1}H NMR of **1**



^{31}P NMR of **1**

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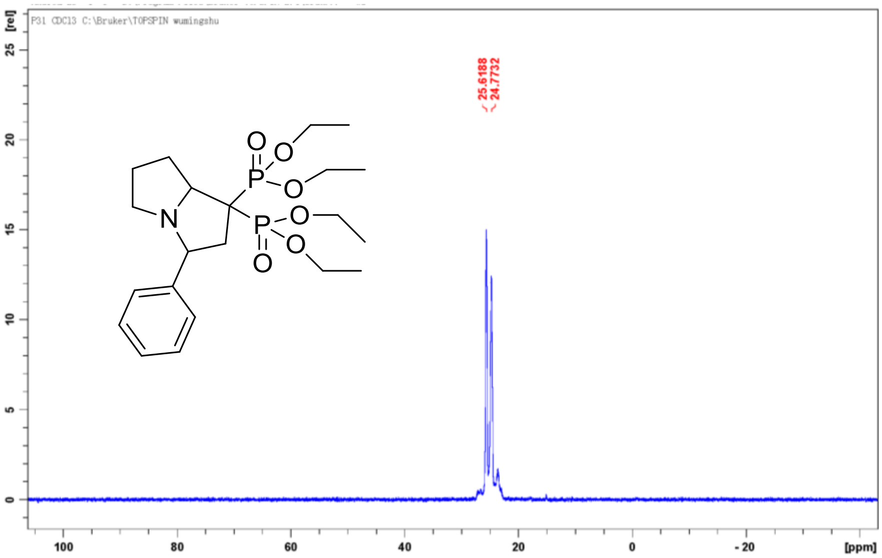
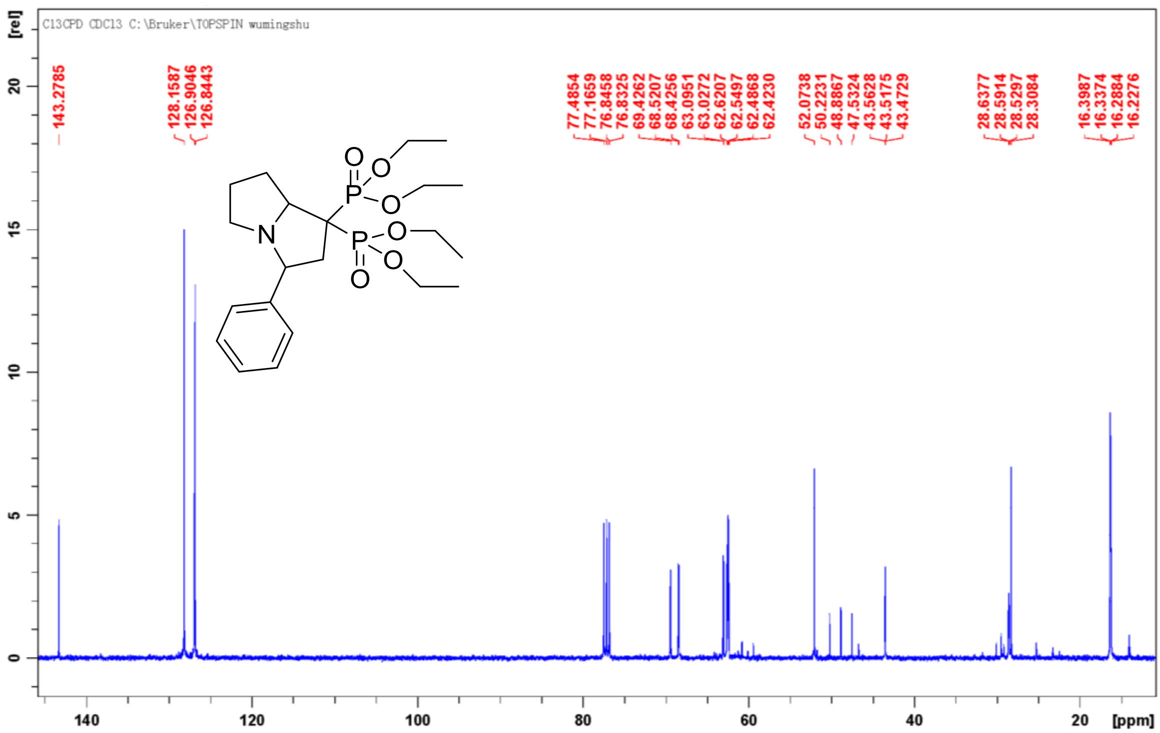
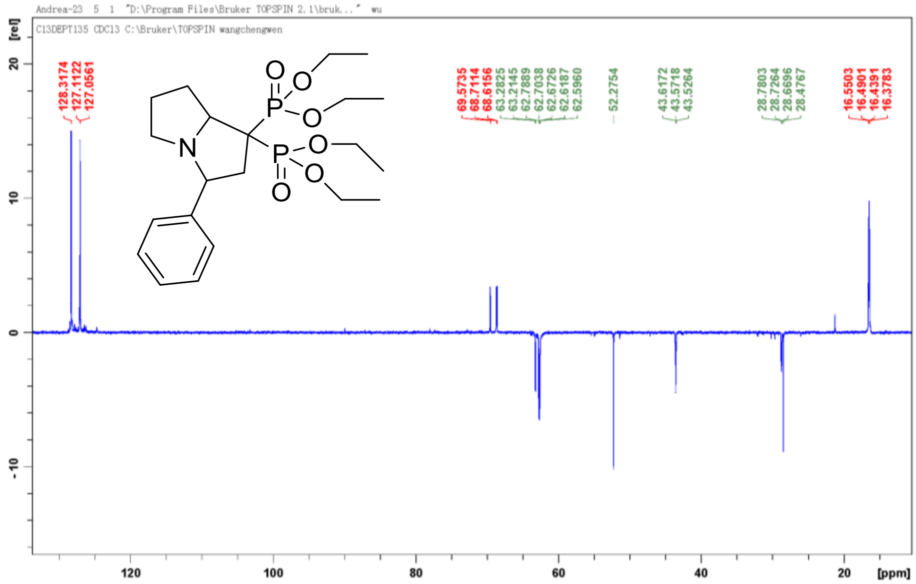


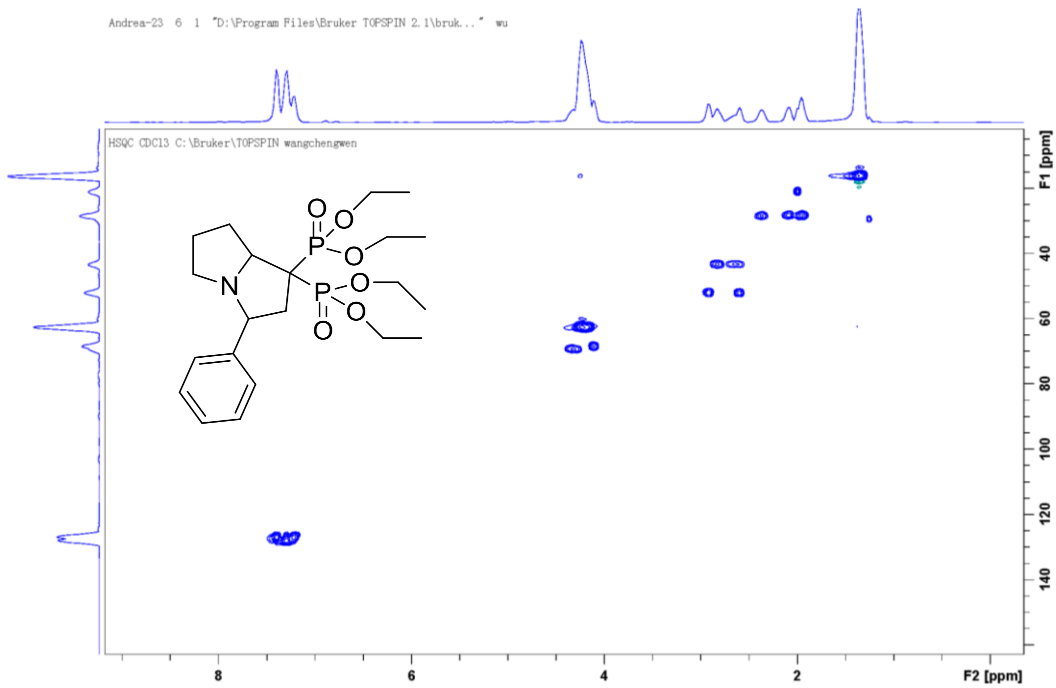
^{13}C NMR of **1**



^{13}CDEPT of **1**



HSQC of **1**



HMBC of **1**

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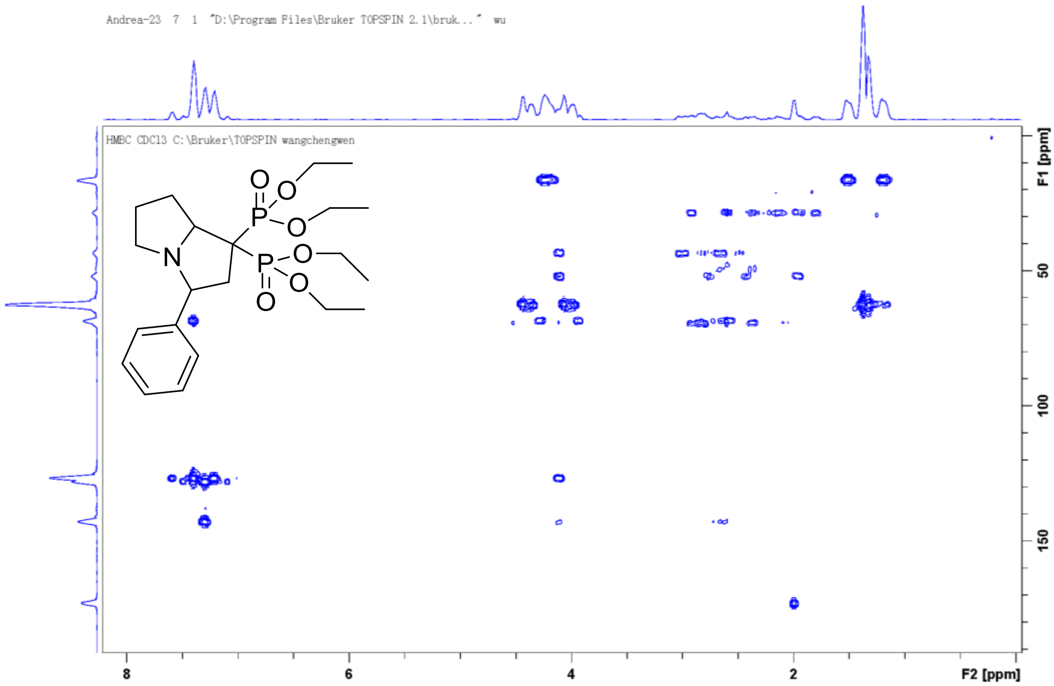
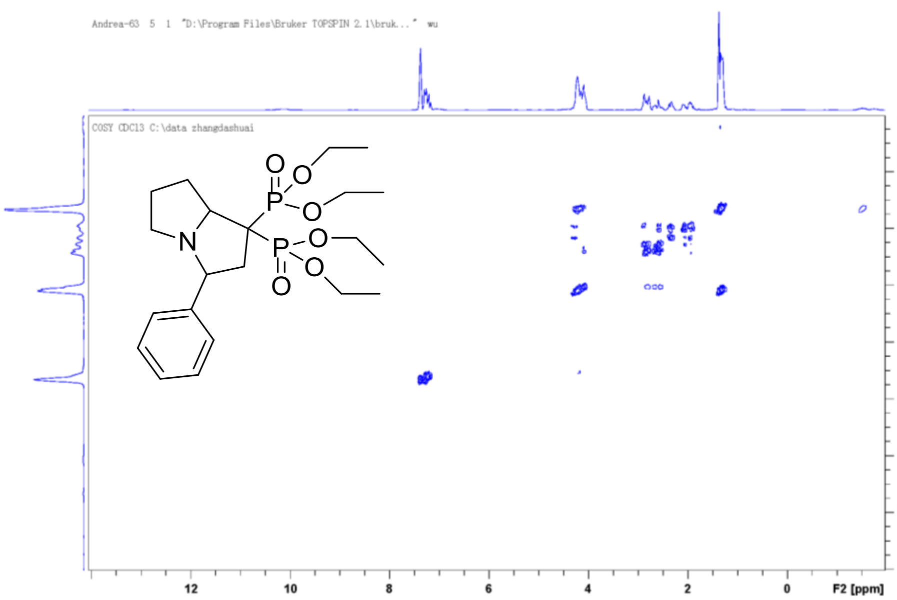
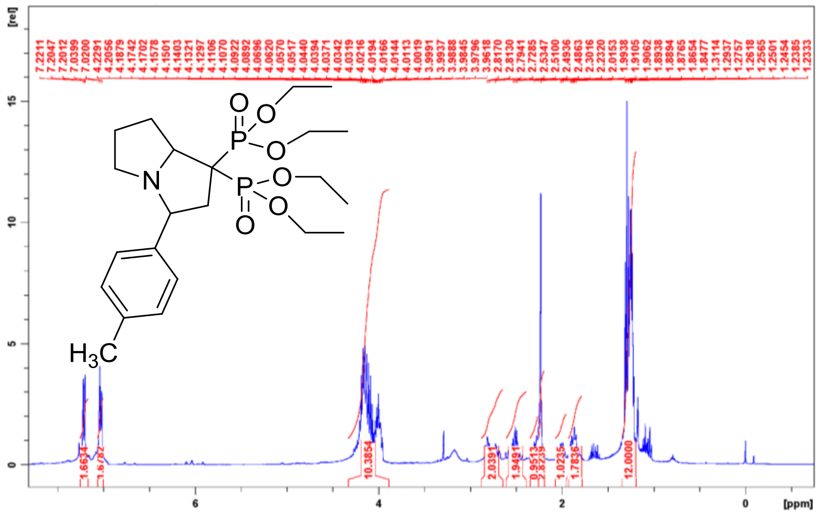


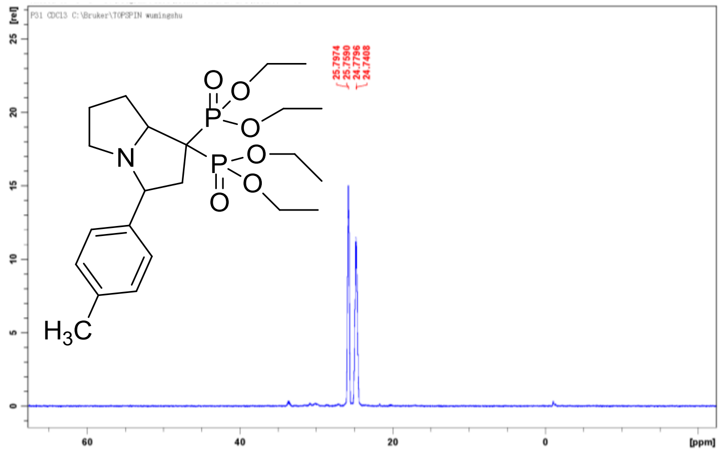
^{1}H-^{1}H COSY of **1**



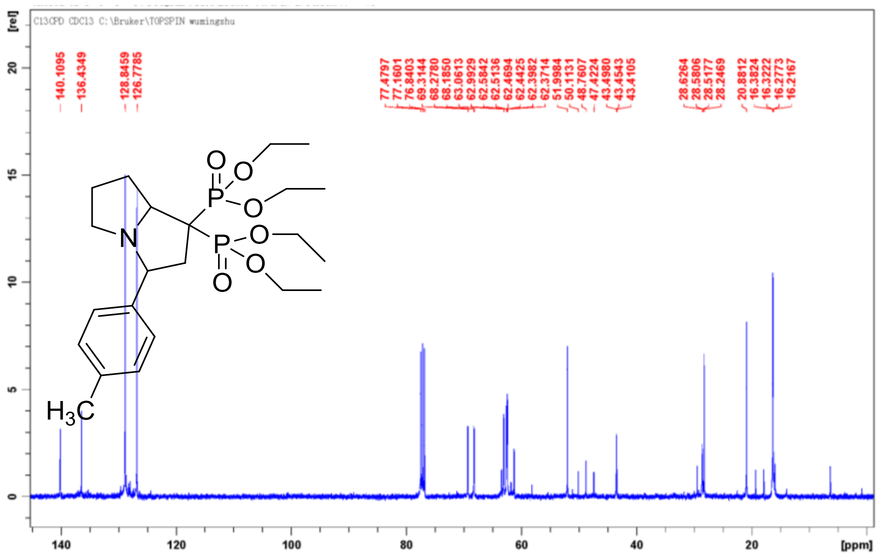
^{1}H NMR of **2**



^{31}P NMR of **2**



^{13}C NMR of **2**



^{1}H NMR of **3**

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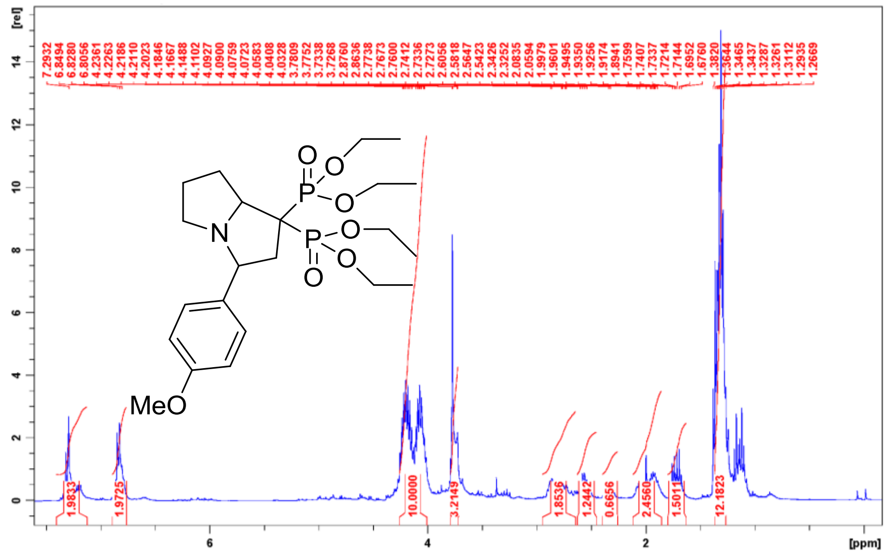
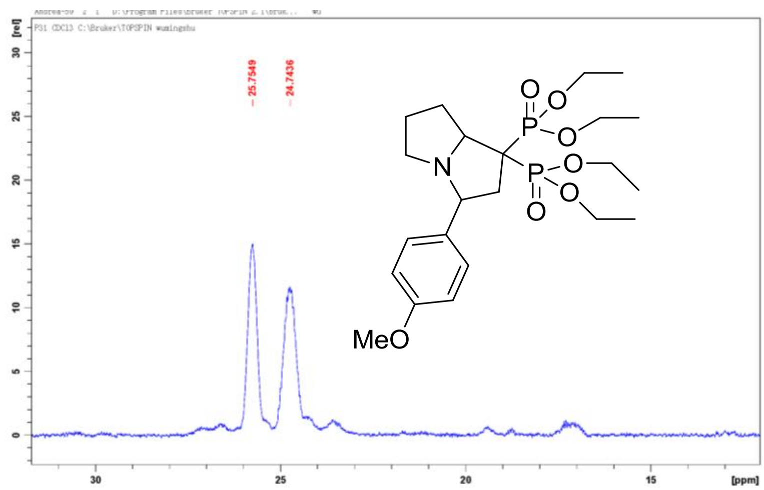
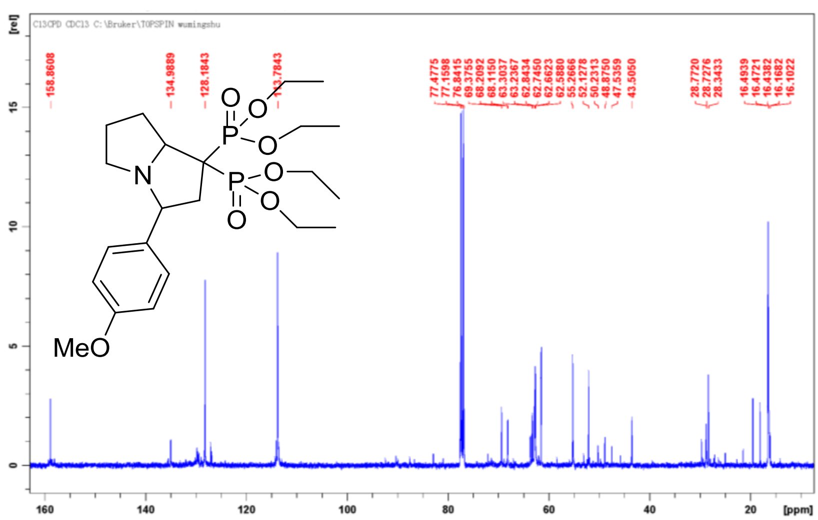


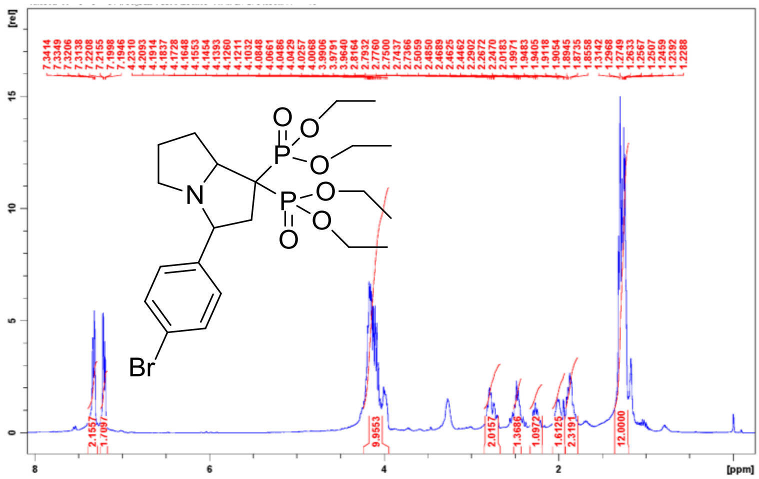
^{31}P NMR of **3**



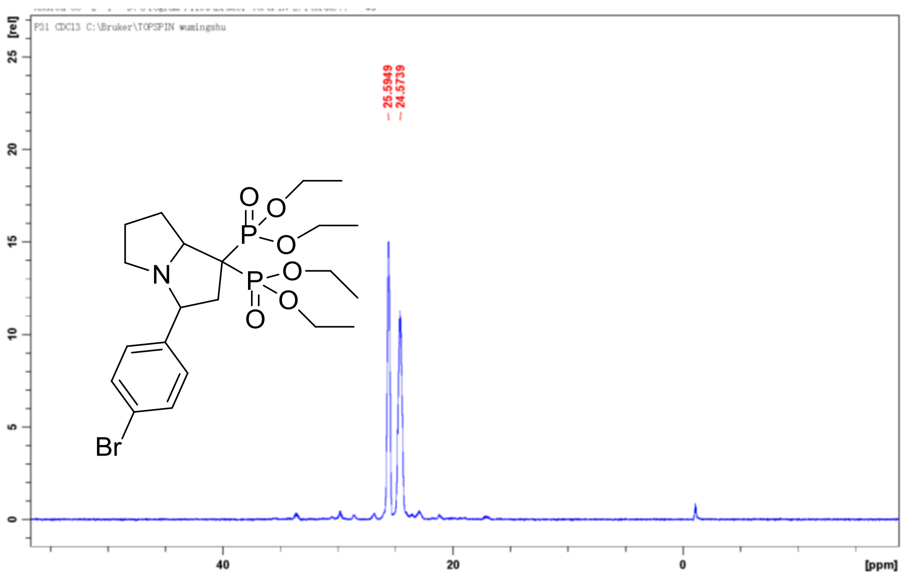
^{13}C NMR of **3**



^{1}H NMR of **4**



^{31}P NMR of **4**



^{13}C NMR of **4**

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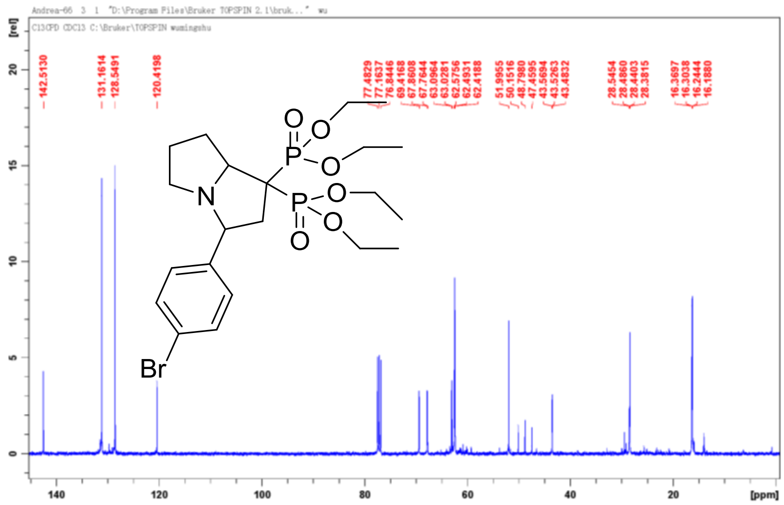
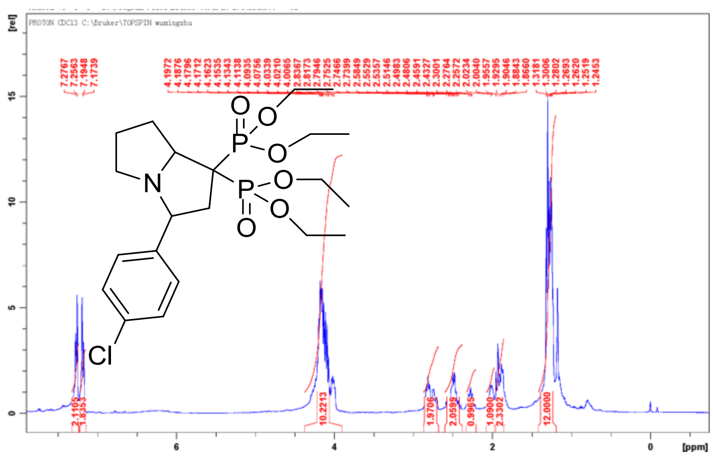
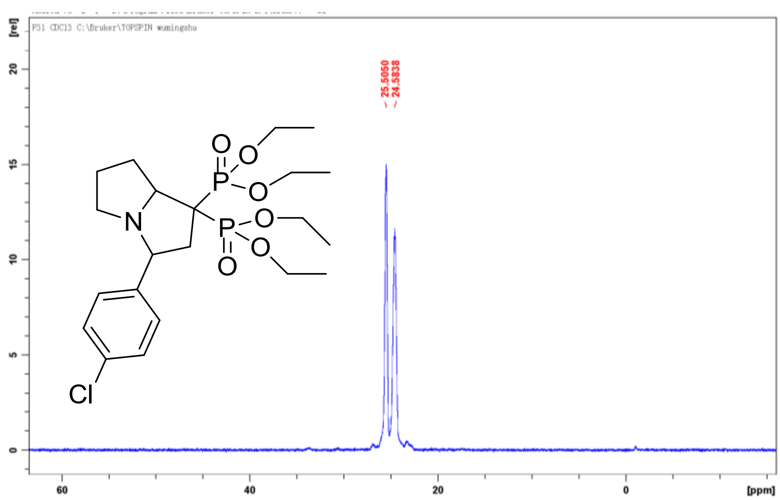


^{1}H NMR of **6**



^{31}P NMR of **6**



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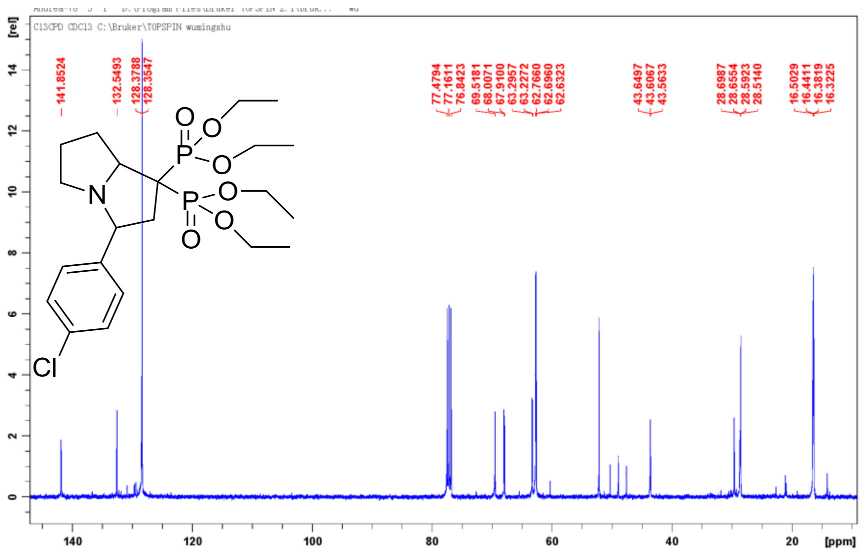
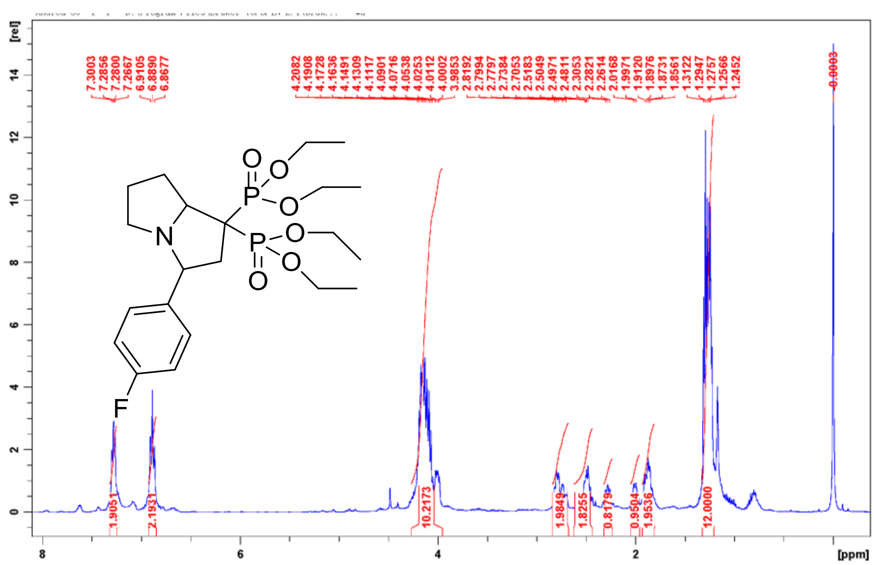
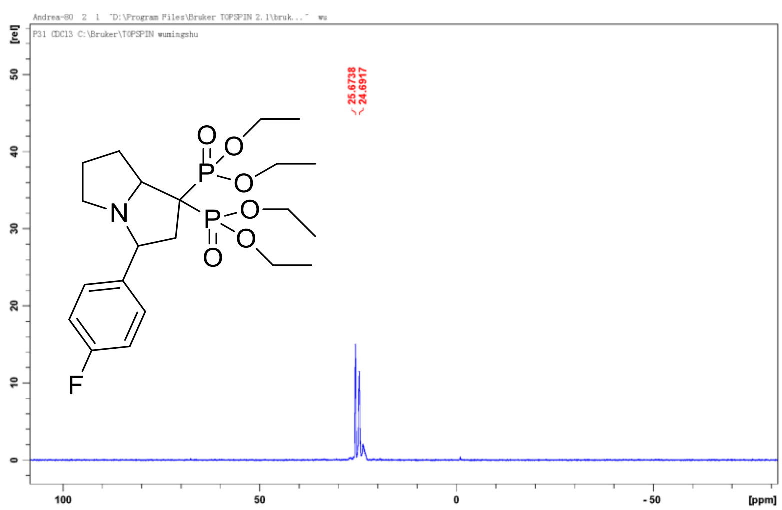


^{1}H NMR of **7**



^{31}P NMR of **7**



^{13}C NMR of **7**

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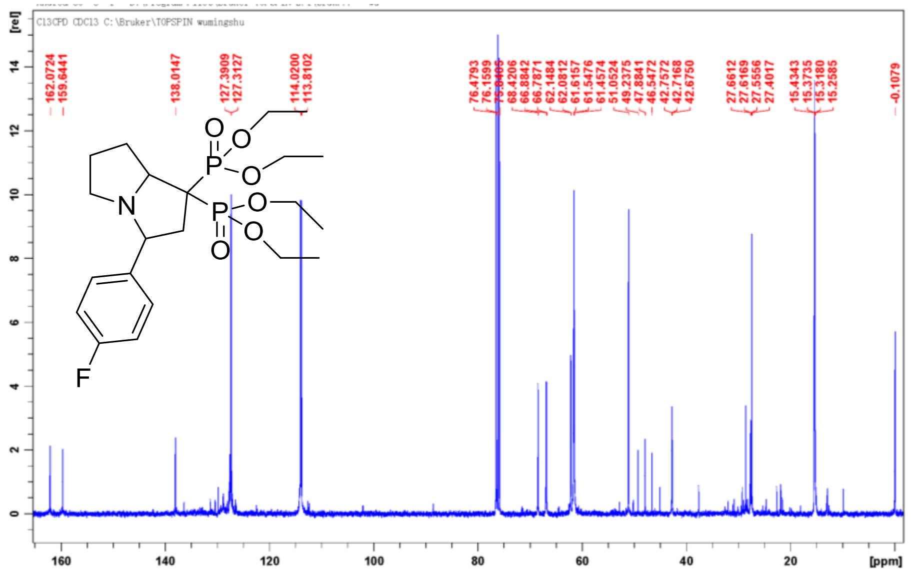
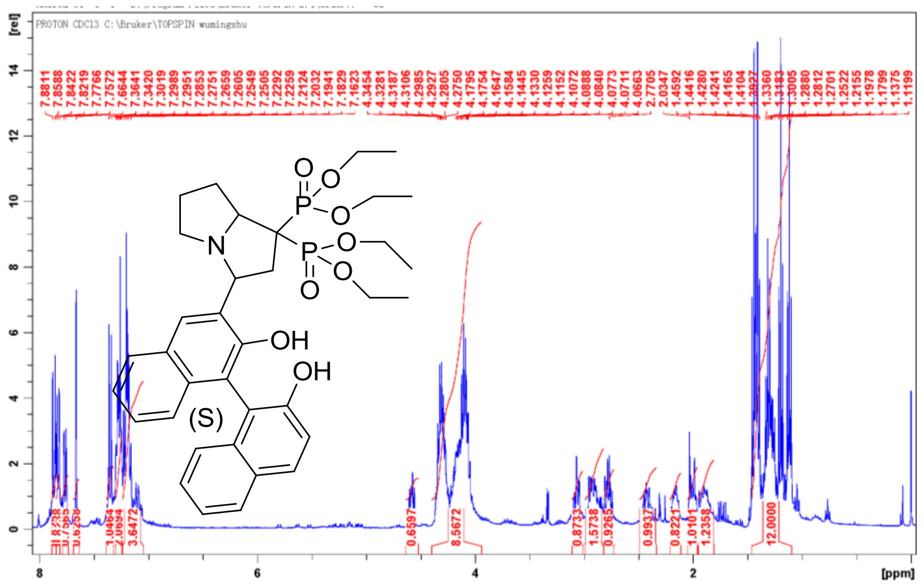


^{1}H NMR of **8**



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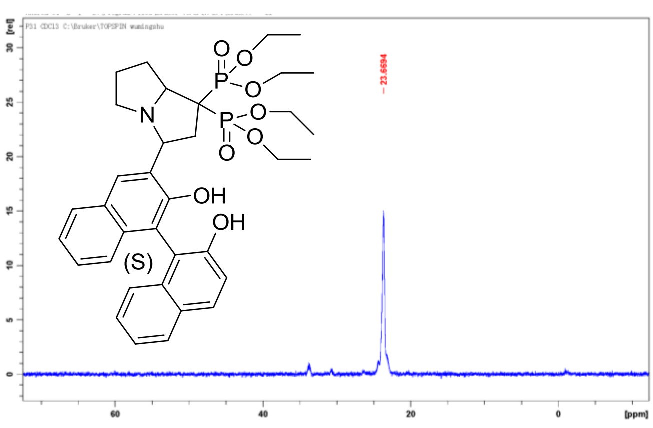

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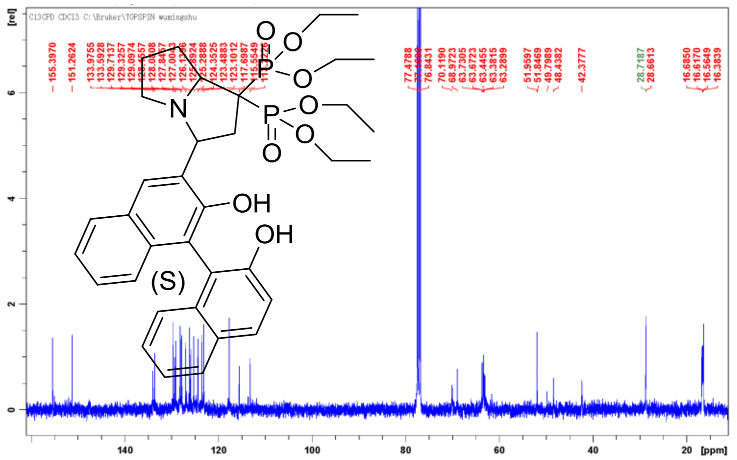
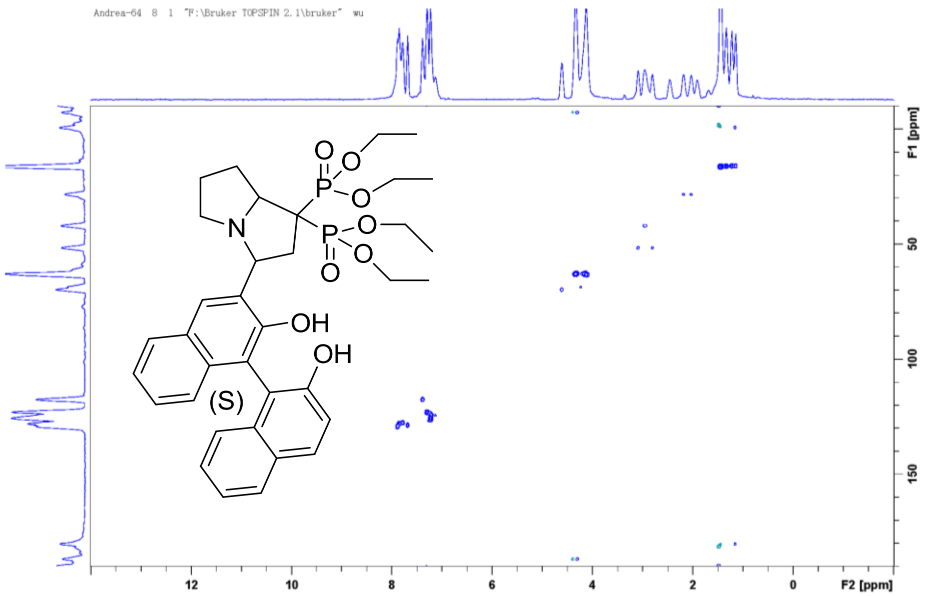
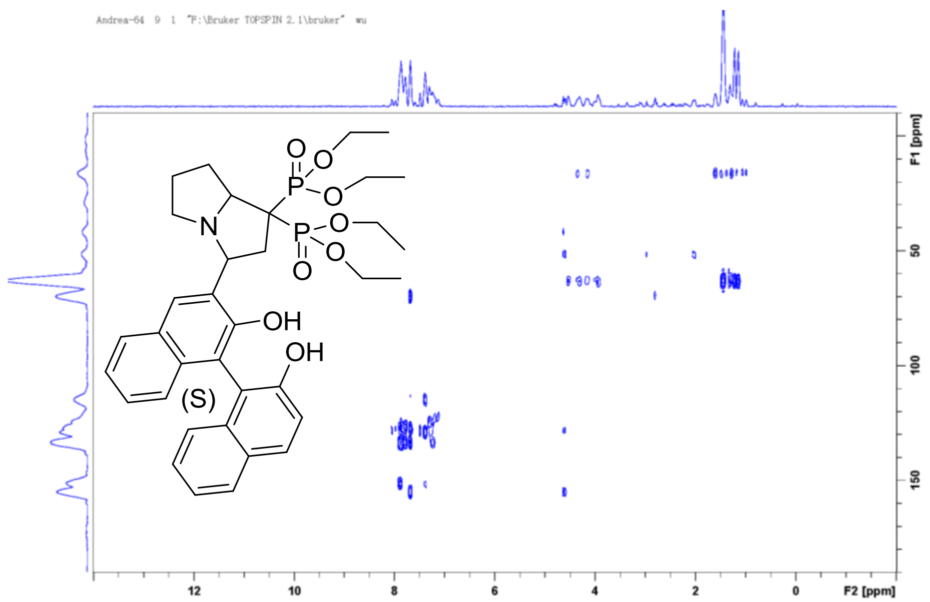


HSQC of **8**



HMBC of **8**



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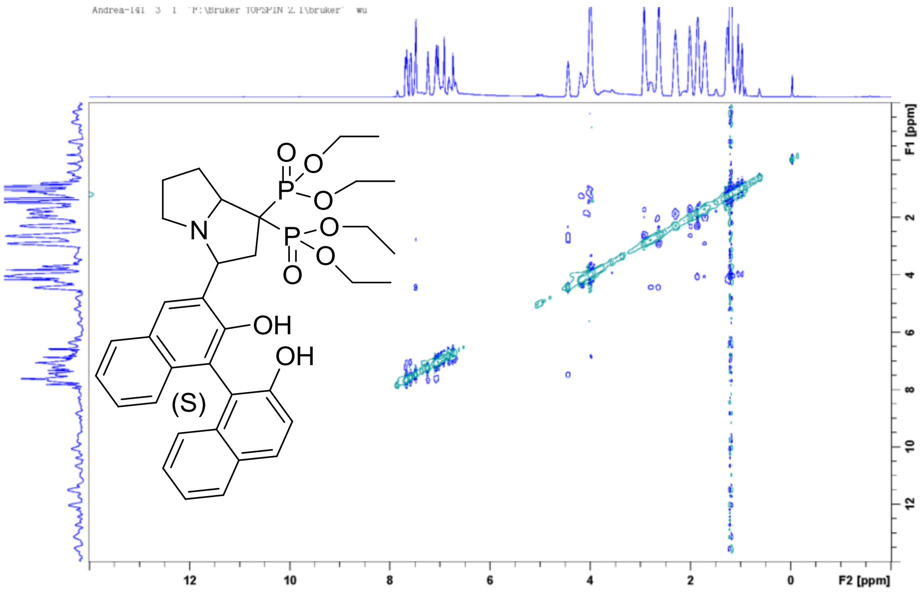
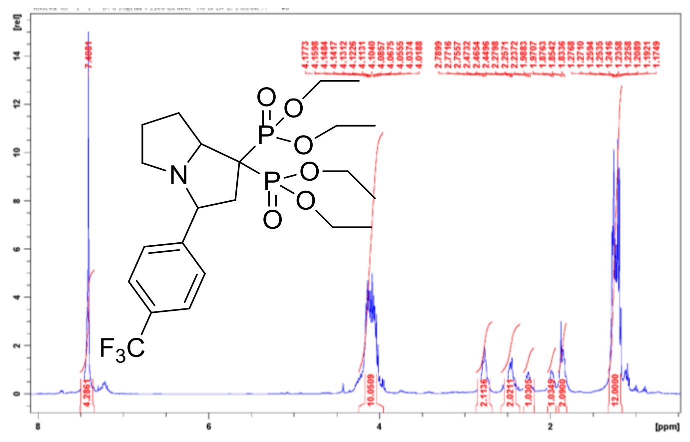
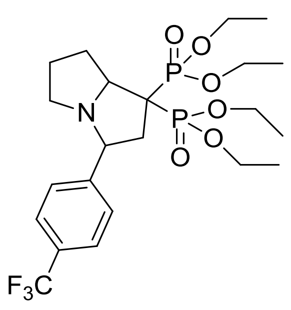
ROESY of **8**

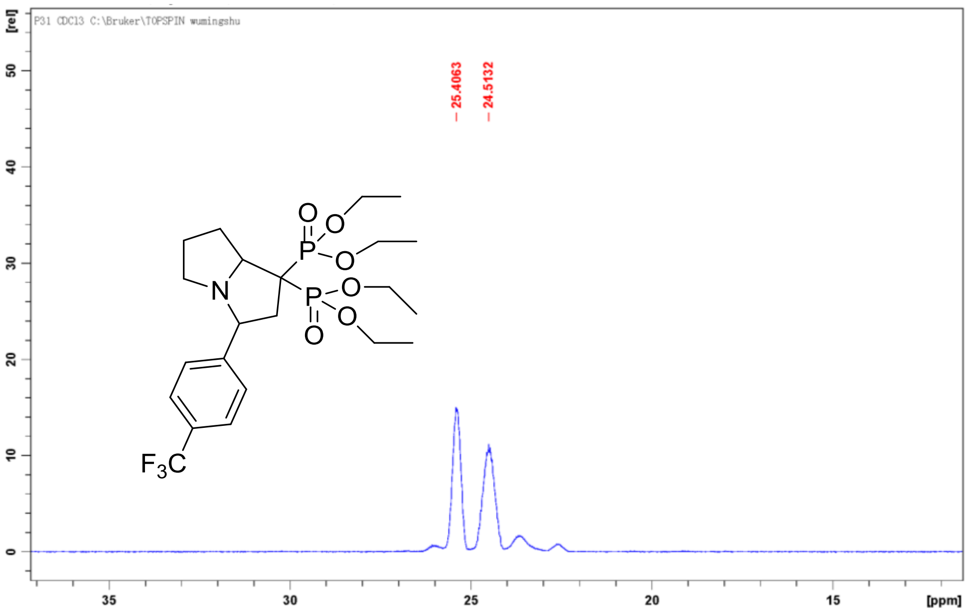


^{1}H NMR of **9**



^{31}P NMR of **9**





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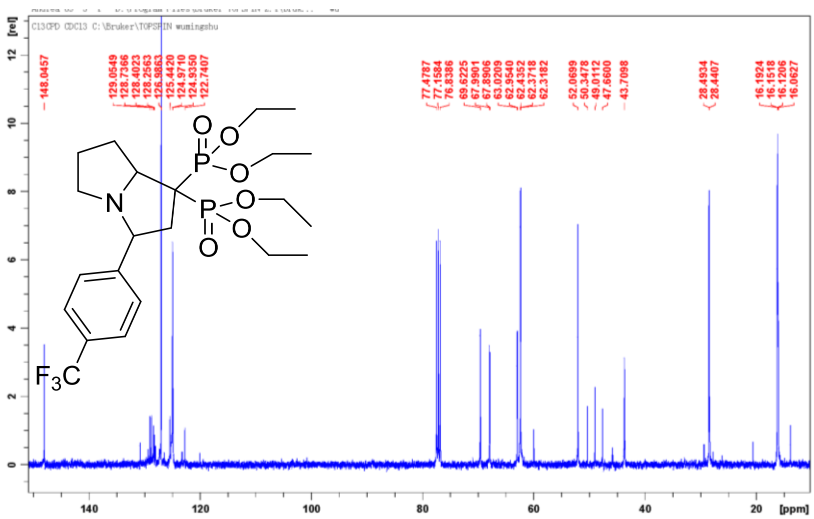

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