Hydroboration of Unsaturated Phosphonic Esters: Synthesis of Boronophosphonates and Trisubstituted Vinylphosphonates

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Supporting Information

Preparation of Phosphonoalkenes

1.Preparation of 1a:

Vinylphosponic acid (108 mg, 1mmol) was placed in a dry flask and trimethylsilylcyanid(109 mg, 1.1 mmol)was added in a room temperature. The mixture was stirred for 30 min. Dichloromethane (1 ml), DMF (0.1 ml) was added and oxallyl chloride (127 mg, 2mmol) was added dropwise during a period of 10 min. After the stirring for 1h at ambient temperature, the volatile components were removed under reduced pressure. Ethanol (1 ml) was added with a stirring. Then the excess of ethanol was evaporated and residue **1a** was distilled. ^{1}HNMR (CDCl$_3$): δ=1.27 (t, 6H), 4.05 (q, 4H), 5.91-6.09 (m, 2H), 6.17-6.30 (dd, 1H). ^{13}C (CDCl$_3$): δ=16.45, 63.02, 125.92, 136.79(d).
^{31}P(CDCl$_3$): δ=17.52.

2. Common procedure for preparation of 1 b-d:

Sodium (230 mg, 10mmol) was added in a small portions to the solution of diethylphosphite (1.370 g, 10mmol) in dry THF (20 ml). When sodium reacted completely, the mixture was cooled to -70^{0}C and alkenylbromide (10mmol) was added at this temperature. The reaction mixture was allowed to warm to room temperature and stirred overnight. Then water (20 ml) was added and product was extracted with ethyl acetate (2 x 100ml). The organic layer was dried with sodium sulfate and evaporated. The residue liquid was distilled under high pressure.

NMR data of 1 b-d:

1b: ^{1}HNMR (CDCl$_3$):δ= 1.22-1.35 (t, 4H), 2,55-2.65 (dd), 4.05 (q, 4H), 5.91-6.09 (m, 2H), 6.17-6.30 (dd, 1H).
^{13}C (CDCl$_3$)δ=16.49, 31.0-32.85 (d, J_{cp} =213Hz), 61.97, 120.05, 127. 62-127.77 (d). ^{31}P(CDCl$_3$):δ=26.47.

1c: ^{1}HNMR (CDCl$_3$):δ =1.36 (t,1H), 1.72 (m,2H), 2.26-2.33 (m, 2H), 4.05 (q,4H), 4.93-5.04 (t, 2H), 5.80 (m, 1H). ^{13}C (CDCl$_3$):δ=16.49, 25.15-27.05 (d, J_{cp}= 142Hz), 33.77, 62.00, 117.23, 135.04.
^{31}P(CDCl$_3$):δ=28.05.

1d: ^{1}HNMR (CDCl$_3$):δ=1.27 (t, 6H), 1.62-1.67 (m, 4H), 2.08 (t, 2H), 4,035 (q, 4H), 4,97 (t, 2H), 5.68-5.79 (m, 1H). ^{13}C (CDCl$_3$):δ=16.50, 21.75, 24.13-26.01 (d, J_{cp}=140Hz), 34.40, 61.37, 115.67, 137.34.
^{31}P(CDCl$_3$):δ=30.66.

3. Preparation of 1e:

A 2.5 molar solution of n-butyllithium in hexane (2.4 ml, 6 mmol) was placed in a three necked flask equipped with a stirrer, an addition funnel, and a low temperature thermometer. An equal volume of THF (20 ml) was added to the cooled solution. Diethylchloromethylphosphonate (940 mg, 5 mmol)in THF (5ml) was added at $–75^0$ to $–70^0$. After 10min, allylbromide (432 ml, 5mmol) in THF was added at $–75^0$. The reaction mixture was stirred for 20 min at $–70^0$ and then allowed to warm to room temperature. Stirring was continued at room temperature for 8 h, water (10 ml) was added and the product was extracted by ethyl acetate (2 x 50 ml). The combined organic layers are dried with sodium sulfate, the solvent was removed under reduced pressure and the product was purified by vacuum distillation. ^{1}HNMR ($CDCl_3$):δ= 1.30 (t, 6H), 2.51-2.93 (m, 2H), 3.72 (dt, 1H), 4.13 (q, 4H), 5.10 (dd, 2H), 5.84 (m, 1H), ^{13}C ($CDCl_3$):δ= 16.33, 36.49, 52.22-50.32 (d, J_{cp}=142Hz), 63.64, 118, 50, 132.91.^{31}P($CDCl_3$):δ=19.71.

4. Preparation of 1f:

Acrolein (2.8 ml, 40 mmol) and diethylphosphite (5.48 ml, 40 mmol) were mixed in an Ehrlenmeyer flask and 20 g of basic Al_2O_3 was added and the mixture was allowed to stand at room temperature for 2 h. Then CH_2Cl_2 was added to extract the 1-hydroxyallylphosphonate. It was purified by distillation. 1.94 g (10mmol) of product dissolved in pyridine (5 ml) and acetic anhydride (3.09 g, 30 mmol) was added to solution. Reaction was stirred overnight at room temperature. Then it was treated with 10 ml of HCl and extracted with ethyl acetate (2 x 100 ml). The organic layer washed with sodium bicarbonate (10 ml), and dried on sodium sulfate. Evaporation under reduced pressure and distillation of residue gave **1f** as a colorless oil. ^{1}HNMR ($CDCl_3$):δ= 1.30 (t, 6H), 2.14 (s, 3H), 4.15 (q,4H), 5.32-5.43 (td, 2H), 5.64-5.71 (dd, 1H), 5.88 (m, 1H). ^{13}C ($CDCl_3$):δ= 16.29, 20.64, 24.66, 63.04, 68.05-70.23 (d, J_{cp}=163Hz), 118.9, 129.22, 168.96. ^{31}P($CDCl_3$):δ= 16.13.

5. Preparation of 1g

1-hydroxyallylphosphonate was obtained according to procedure described above. 1.94 g (10 mmol) of it was dissolved in DMF (5 ml). Solution of DMPAP (100 mg, 0.8 mmol) and imidazole (1.02 g, 15 mmol) in DMF(10 ml) was added followed by solution of TBDMSCl (2.27 g, 15 mmol) in 5 ml DMF. Reaction was stirred at room temperature overnight. Then sodium carbonate was added and product was extracted by ethyl acetate. Organic phase was dried and evaporated to obtain colorless oil that was distilled on high vacuum. ^{1}HNMR ($CDCl_3$):δ=0.06 (s, 3H), 0.10 (s, 3H), 0.92 (s, 9H), 1.26 (t, 6H), 4.15 (q, 4H), 4.53-4.60 (dd, 1H), 5.25-5.30 (dd, 2H), 5.40-5.47 (dd, 1H), 5.96-6.04 (m, 1H). ^{13}C ($CDCl_3$):δ= -4.85, -3.30, 16.75, 18.44, 25.84, 63.04, 69.74-71.94 (d, J_{cp}=164Hz), 115.51, 133.61. ^{31}P($CDCl_3$):δ=18.60.

6. Preparation of 1h

Mg (2.400 g, 10 mmol) was placed in a dry three necked flask equipped with condenser and additional funnel. Dry ether (75 ml) and followed by solution of allylbromide (864 ml, 10 mmol) in ether (50 ml) were added. The reaction mixture was heated for a 1h and then solution of $ClP(O)(OPh)_2$ (10 mmol) in ether (50 ml) was added. The reaction was refluxed overnight, then it was cooled and water (50 ml) was added. The organic layer was dried on sodium sulfate, ether was removed by evaporating and residue was distilled. ^{1}HNMR ($CDCl_3$):δ= 2.80-3.07 (dd, 2H), 5.27 (m, 1H), 5.78-6.02 (m, 2H), 6.78-6.86 (m, 10H). ^{13}C ($CDCl_3$):δ=30.90-32.76 (d, J_{cp}=139Hz), 115.77, 118.50, 119.79, 120.40, 120.89, 150.76, 152.84. ^{31}P($CDCl_3$):δ=19.01.

Typical procedure for hydroboration of 1 a-h:

Pinacolborane (2 eq) was added to the phosphonoalkene neat at room temperature and reaction mixture was stirred at 70^0C for 1h (method A) or at 110^0C for 5h (method B) . The excess of pinacolborane was distilled under reduced pressure and residue was chromatographed on silica gel (80:20 chloroform:ethyl acetate).

NMR data of 2a-g

2a: ^{1}HNMR
($CDCl_3$):δ=1.12 (m, 2H), 1.24 (s , 12H), 1.2–1.3 (m , 2H), 1.28–1.31 (t, 6H), 4.02–4.07 (q, 4H).^{13}C($CDCl_3$):δ =9.50(br),16.27,24.31, 24.46, 61.33, 82.81. ^{31}P($CDCl_3$):δ= 33.67. ^{11}B($CDCl_3$):δ=33.75.

2b: ^{1}HNMR ($CDCl_3$):δ=0.85 (t, 2H), 1.60-1.77 (m, 4H), 1.29 (t, 6H), 1.20 (s, 12H), 4.02-4.08 (m, 4H). ^{13}C ($CDCl_3$):δ = 12.58 (br), 16.67-17.44 (d), 25.011, 27.25, 29.09, 61.54, 83.27.
^{31}P($CDCl_3$):δ=30.45. ^{11}B($CDCl_3$):δ=33.06

2c: ^{1}HNMR (CDCl$_3$):δ= 0.80(t, 2H), 1.20 (s, 12H), 1.35 (t, 6H), 1.51 (t, 2H), 1.65 (m, 2H), 1.75 (m, 2H), 4.10 (q, 4H). ^{13}C (CDCl$_3$):δ=10.84 (br), 16.39, 24.56, 24.57, 25.02, 24.77, 61.31, 82.97. ^{31}P(CDCl$_3$):δ=32.62.
^{11}B(CDCl$_3$):δ=34.25

2d: ^{1}HNMR (CDCl$_3$):δ=0.80 (t, 2H), 1.4-1.7 (m, 6H), 1.29 (t, 6H), 1.20 (s, 12H), 4.02-4.08 (q, 4H).
^{13}C (CDCl$_3$):δ=10.05 (br), 16.38, 22.11, 23.44, 24.56, 24.70, 41.33, 82.99.
^{31}P(CDCl$_3$):δ=32.80
^{11}B(CDCl$_3$):δ=34.34

2e: ^{1}HNMR (CDCl$_3$):δ =0.75-0.83 (t, 2H), 1.22 (s, 12H), 1.81 (m, 2H), 2.04 (m, 2H), 1.34 (t, 6H), 3.84 (td, 1H), 4.17-4.26 (q, 4H).
^{13}C (CDCl$_3$):δ= 10.22,16.35, 21.20, 24.99, 34.26, 52.3 (d, J=210 Hz), 63.49, 83.28.
^{31}P(CDCl$_3$):δ=20.64
^{11}B(CDCl$_3$):δ=33.62

2f: ^{1}HNMR (CDCl$_3$):δ=0.85 (t, 2H), 1.25 (s, 12H), 1.33 (t, 6H), 1.74 (m, 4H), 2.12 (s, 3H), 4.15 (q, 4H), 5.22 (dt, 1H).
^{13}C (CDCl$_3$):δ=9.05, 16.65, 20.94, 24.21, 25.03, 29.91, 62.81, 69.55 (d, J_{cp}= 221 Hz), 83.47.
^{31}P(CDCl$_3$):δ=30.86
^{11}B(CDCl$_3$):δ=33.88

2g ^{1}HNMR (CDCl$_3$):δ=0.07(s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.95 (t, 2H), 1.25 (s, 12H), 1.31 (t, 6H), 1.7-1.9 (m, 2H), 3.88 (m, 1H), 4.05-4.17 (q, 4H).
^{13}C (CDCl$_3$):δ=4.69, 8.5 (br), 16.55, 24.64, 25.75, 24.94, 62.14, 670.64(d, J=234 Hz), 83.10.
^{31}P(CDCl$_3$):δ=24.02. ^{11}B(CDCl$_3$):δ=34.01.

<u>Preparation of 3:</u>

n-BuLi (31.25 ml of 1.6M solution in hexane, 50 mmol)was added to solution of alkyne (50 mmol) in dry diethyl ether (100 ml) at –78^{0}C. The mixture was stirred for 15 minutes and then it was added at -78^{0}C to the solution of diethylchlorophosphate (7.19 ml, 50 mmol) in diethyl ether(100 ml) ,previously cooled to –78^{0}C. Reaction mixture was allowed to warm to room temperature and it was stirred for 3h. 1N HCl was added . The organic phase was separated, dried on sodium sulfate and solvent was removed in vacuo. The residue was distilled to obtain **3** as colorless liquids, in ~95 % yield.

<u>NMR data of **3a**:</u>

^{1}H NMR (CDCl$_3$):δ = 0.88(t, 3H), 1.30(m, 2H), 1.33 (m, 2H),1.34 (t, 6H) 1.57 (m, 2H), 2.32 (t, 2H), 4.12 (q, 4H).
^{13}C NMR (CDCl$_3$):δ = 13.92, 16.21, 19.21, 22.12, 27.19, 30.99, 62.96, 102.99, 103.67.
^{31}P NMR (CDCl$_3$):δ = -7.58

<u>NMR data of **3b**:</u>

^{1}H NMR (CDCl$_3$):δ = 1.40 (t, 6H), 4.23 (q, 4H), 7.36 –7.56 (m, 5H).
^{13}C NMR (CDCl$_3$):δ = 16.21, 63.31, 80.41, 98.60, 119.52, 128.72, 130.87, 132.65.
^{31}P NMR (CDCl$_3$):δ = -7.55

<u>NMR data of **3c**:</u>

^{1}H NMR (CDCl$_3$): δ = 1.35 (t, 6H), 2.03 (t, 2H), 2.54 (m, 2H), 3.63 (t, 2H), 4.13 (q, 4H).
^{13}C NMR (CDCl$_3$): δ = 16.25, 24.91, 30.26, 43.28, 63.21, 100.59, 101.23.
^{31}P NMR (CDCl$_3$): δ = -8.133

<u>Hydroboration of 3:</u>

Compounds **3**(2 mmol) were dissolved in dry dichloromethane (1 ml) and added toa solution of pinacolborane (2.8 mmol) in dichloromethane (2 mmol) at –70^{0}C. The reaction mixture was stirred at room temperature overnight. Water (1 ml) was added at 0^{0}C. The organic layer was separated, and dried on sodium sulfate. The solvent was removed in vaccuo to obtain hydroboration products (70% – 90 % yields).

Suzuki coupling reaction of hydroboration products:

Solution of iodobenzene (113.3 μl, 1 mmol) in toluene (3 ml), $PdCl_2$ (10% mmol) and sodium methoxide (162 mg , 3 mmol) was placed to the flask equipped with condenser. The mixture was stirred at room temperature for 15 min. The product of hydroboration **3**(1.1 mmol) was dissolved in toluene (1 ml) and this solution was added to reaction flask . Mixture was refluxed for 2h. Then it was cooled to room temperature and treated with water. Ethyl acetate (15 ml) was added to extract the product. The organic layer was evaporated to dryness and residue was chromatographed on silica gel (40 % EtAc in PE) to obtain **4a-c** (30%- 40% yields).

NMR data of**4a**

^{1}H NMR ($CDCl_3$): δ = 0.83(t, 3H), 1.24(t. 6H), 1.33 (m, 2H),1.38 (m, 2H) 1.48 (m, 2H), 2.70 (t, 2H), 4.03 (q, 4H), 6.34-6.50 (dt, 1H), 7.28-7.32 (m, 5H).
^{13}C NMR ($CDCl_3$): δ = 14.24, 16.44, 22.76, 29.24, 30.84, 31.75 61.81, 127.38, 128.23, 128.58, 128.6, 130.18 - 130.51 (d, J_{cp} = 174 Hz), 140.36, 153.25 (d, J_{cp}= 8Hz).
^{31}P NMR ($CDCl_3$): δ =15.33

NMR data of **4b**:

^{1}H NMR ($CDCl_3$): δ = 1.13 (t, 6H), 3.87 (q, 4H), 7.26 –7.42 (m, 5H), 7.26-7.38 (m, 10H).
^{13}C NMR ($CDCl_3$): δ = 16.38, 62.98, 113.77 – 116.34 (d, J_{cp} = 193 Hz), 128.01-129.99 (8 carbons), 160.88 (d, J_{cp} = 3 Hz).
^{31}P NMR ($CDCl_3$): δ = 15.41

NMR data of **4c**:

^{1}H NMR ($CDCl_3$): δ = 1.33(t, 6H), 1.99 (t, 2H), 2.86 (t, 2H), 3.62 (t, 2H), 4.08 (q, 4H), 6.31 – 6.47 (dt, 1H) 7.30-7.32 (m, 5H).
^{13}C NMR ($CDCl_3$): δ = 16.44, 28.30, 32.55, 44.54, 62.00, 123.8-126.05 (d, J_{cp}=170 Hz), 127.62-128.54 (5 carbons), 150.42 (d, J = 11 Hz).
^{31}P NMR ($CDCl_3$): δ = 14.64.