Phenylboronic Acid as Efficient and Eco-Friendly Catalyst for the One-Pot Three-Component Synthesis of α-Aminophosphonates Under Solvent Free-Conditions

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Experimental

General information

All commercial materials were used as received without further purification. Melting points were registered in a Fisher-Johns apparatus and are uncorrected. Flash chromatography was performed using 230-400 mesh Silica Flash 60® silica gel. Thin layer chromatography was performed with pre-coated TLC sheets of silica gel (60 F254, Merck). NMR spectra were recorded in a Varian System instrument (400 MHz for 1H, and 100 MHz for 13C) and a Mercury instrument (81 MHz for 31P) and calibrated with CDCl3 as solvent and TMS as internal standard signal. Chemical shifts (δ) are reported in parts per million. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, bs = broad singlet, q = quartet and m = multiplet. Coupling constants (J) are given in Hz. High resolution FAB+ and CI+ mass spectra (HRMS) were obtained in a JEOL HRMSStation JHRMS-700.

General procedure for the one-pot three-component reaction of carbonyl compounds with benzylamine and dimethyl phosphite catalyzed with PhB(OH)2.

In a typical experiment, to a mixture of aldehyde or ketone (2.5 mmol) and benzylamine (2.5 mmol) was added PhB(OH)2 (10 mol%). The reaction mixture was stirred at room temperature for 15 min. After this time, dimethyl phosphite (2.6 mmol) was added and the reaction mixture was stirred at 50 °C for specific period of time (see Tables 1 and 2), and the progress of the reaction was monitored by TLC. The crude was purified by flash chromatography with AcOEt:Hex (70:30), obtaining the pure α-aminophosphonates.

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2.3. Spectroscopy-spectrometry data for the reaction products

Spectroscopic data for the products 1a [1], 1b [2], 1h [3], 2a [3], 2g [4] and 2h [5] are described in the literature.

1c: White solid; m.p. 55-57 ºC; 1H NMR (400 MHz, CDCl3) δ: 2.20 (bs, 1H, NH); 3.55 (d, JHP = 10.8 Hz, 3H, (CH3O)2P); 3.74 (d, JHP = 10.4 Hz, 3H, (CH3O)2P); 3.80 (system AB, J = 13.2 Hz, 2H, CH2Ph); 3.89 (s, 3H, CH3O); 3.90 (s, 3H, CH3O); 3.98 (d, JHP = 19.6 Hz, 1H, CHP); 6.86-7.00 (m, 3H, HAr); 7.23-7.33 (m, 5H, HAr). 13C NMR (100 MHz, CDCl3) δ: 51.3 (d, JCP = 16.7 Hz, CH2Ph); 53.5 (d, JCP = 6.1 Hz (CH3O)2P); 53.8 (d, JCP = 7.5 Hz (CH3O)2P); 56.1 (CH3O); 56.2 (CH3O); 59.1 (d, JCP = 154.7 Hz, CHP); 111.5; 111.9; 121.4 (d, JCP = 7.6 Hz); 127.3; 128.0; 128.5; 128.6; 139.5; 149.2; 149.5. 31P NMR (80 MHz, CDCl3) δ: 27.03. HRMS [FAB+] : Calcd C18H25NO5P: 366.1470; found: 366.1467.

1d: Yellow liquid; 1H NMR (400 MHz, CDCl3) δ: 2.20 (bs, 1H, NH); 3.51 (d, JHP = 10.4 Hz, 3H, (CH3O)2P); 3.56 (system AB, J = 13.2 Hz, 1H, CH2Ph); 3.74 (d, JHP = 10.4 Hz, 3H, (CH3O)2P); 3.80 (system AB, J = 13.2 Hz, 1H, CH2Ph); 3.78 (d, JHP = 10.8 Hz, 3H, (CH3O)2P); 3.80 (s, 3H, OCH3); 4.68 (d, JHP = 21.1 Hz, 1H, CHP); 6.90 (d, JHH = 8.4 Hz, 1H, HAr); 7.01 (t, JHH = 7.2 Hz, 1H, HAr); 7.20-7.31 (m, 6H, HAr); 7.53-7.56 (m, 1H, HAr). 13C NMR (100 MHz, CDCl3) δ: 51.6 (d, JCP = 16.8 Hz, CH2Ph); 51.7 (d, JCP = 156.6 Hz, CHP); 53.4 (d, JCP = 6.5 Hz (CH3O)2P); 53.9 (d, JCP = 6.6 Hz (CH3O)2P); 55.8 (CH3O); 111.0 (d, JCP = 2.2 Hz); 121.2 (d, JCP = 3.0 Hz); 124.4; 127.2; 128.4; 128.6; 129.0 (d, JCP = 5.6 Hz); 129.1 (d, JCP = 3.0 Hz); 139.8; 158.0 (d, JCP = 7.3 Hz). 31P NMR (80 MHz, CDCl3) δ: 27.66. HRMS [FAB+] : Calcd C17H23NO4P: 336.1365; found: 336.1378.

1e: Yellow liquid; 1H NMR (400 MHz, CDCl3) δ: 3.47 (d, JHP = 10.4 Hz, 3H, (CH3O)2P); 3.53 (system AB, J = 13.2 Hz, 1H, CH2Ph); 3.78 (d, JHP = 20.8 Hz, 1H, CHP); 6.75-6.86 (m, 2H, HAr); 7.16-7.25 (m, 3H, HAr); 7.26-7.33 (m, 4H, HAr). 13C NMR (100 MHz, CDCl3) δ: 51.0 (d, JCP = 18.0 Hz, CH2Ph); 53.7 (d, JCP = 6.7 Hz, (CH3O)2P); 54.1 (d, JCP = 6.9 Hz (CH3O)2P); 58.8 (d, JCP = 155.0 Hz CHP); 114.9 (d, JCP = 5.1 Hz); 115.8 (d, JCP = 2.9 Hz); 120.4 (d, JCP = 7.9 Hz); 127.1; 128.3; 128.4; 129.6 (d, JCP = 1.8 Hz); 136.3 (d, JCP = 2.8 Hz); 139.1; 157.6 (d, JCP = 2.8 Hz). 31P NMR (80 MHz, CDCl3) δ: 27.19. HRMS [FAB+] : Calcd C16H21NO4P: 322.1208; found: 322.1219.

1f: Yellow liquid; 1H NMR (400 MHz, CDCl3) δ: 2.30 (bs, 1H, NH); 3.52 (system AB, J = 13.6 Hz, 1H, CH2Ph); 3.59 (d, JHP = 10.8 Hz, 3H, (CH3O)2P); 3.73 (d, JHP = 10.4 Hz, 3H, (CH3O)2P); 3.79 (system AB, J = 13.6 Hz, 1H, CH2Ph); 4.03 (d, JHP = 20.0 Hz, 1H, CHP); 7.22-7.38 (m, 9H, HAr). 13C
NMR (100 MHz, CDCl₃) δ: 51.3 (d, J = 16.7 Hz, CH₂Ph); 53.7 (d, J_Cp = 7.6 Hz, (CH₃O)₂P); 54.0 (d, J_Cp = 6.0 Hz, (CH₃O)₂P); 58.7 (d, J_Cp = 154.7 Hz, CHP); 127.5; 128.5; 128.7; 129.0; 130.1 (d, J_Cp = 6.1 Hz); 134.0 (d, J_Cp = 4.5 Hz); 134.2 (d, J_Cp = 4.5 Hz); 139.0. ³¹P NMR (80 MHz, CDCl₃) δ: 26.20.


1g: Yellow liquid. ¹H NMR (400 MHz, CDCl₃) δ: 2.06 (bs, 1H, NH); 3.51 (d, J_HP = 10.4 Hz, 3H, (CH₃O)₂P); 3.66 (system AB, J = 13.2 Hz, 1H, CH₂Ph); 3.78 (d, J_HP = 10.4 Hz, 3H, (CH₃O)₂P); 3.86 (system AB, J = 13.2 Hz, 1H, CH₂Ph); 4.40 (d, J_HP = 18.4 Hz, 1H, CHP); 7.09-7.38 (m, 9H, HAr); 7.66 (d, J_HH = 2.0 Hz, 1H, HAr); 9.1 (bs, NH). ¹³C NMR (100 MHz, CDCl₃) δ: 51.5 (d, J_CP = 16.7 Hz, CH₂Ph); 51.6 (d, J_CP = 162.3 Hz, CHP); 53.6 (d, J_CP = 7.6 Hz, (CH₃O)₂P); 53.9 (d, J_CP = 7.6 Hz, (CH₃O)₂P); 109.7; 111.7; 119.5; 119.9; 122.3; 124.7 (d, J_Cp = 7.6 Hz); 127.0; 127.3; 128.5; 128.6; 136.5; 139.7. ³¹P NMR (80 MHz, CDCl₃) δ: 27.89. HRMS [FAB⁺]: Calcd. for C₁₈H₂₂N₂O₃P: 345.1368; found: 345.1369.

1i: Yellow liquid. ¹H NMR (400 MHz, CDCl₃) δ: 0.76 (d, J_HH = 6.4 Hz, 3H, CH₃); 0.91 (d, J_HH = 7.2 Hz, 3H, CH₃); 1.48-1.55 (m, 2H, CH₂); 1.60 (bs, 1H, NH); 1.84-1.88 (m, 1H, CH); 2.93-2.99 (m, 1H, CHP); 3.79 (d, J_HP = 10.8 Hz, 3H, (CH₃O)₂P); 3.80 (d, J_HP = 10.0 Hz, 3H, (CH₃O)₂P); 3.86 (system AB, J = 13.2 Hz, 1H, CH₂Ph); 4.00 (system AB, J = 13.2 Hz, 1H, CH₂Ph); 7.23-7.35 (m, 5H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 21.5 (CH₃); 23.6 (CH₃); 35.4 (d, J_CP = 7.3 Hz, C(CH₃)₃); 52.1 (d, J_CP = 6.6 Hz, (CH₃O)₂P); 52.8 (d, J_CP = 7.3 Hz, (CH₃O)₂P); 55.4 (d, J_CP = 2.2 Hz, CH₂Ph); 64.5 (d, J_CP = 138.5 Hz, CHP); 127.3; 128.5; 128.6; 140.3. ³¹P NMR (80 MHz, CDCl₃) δ: 31.99. HRMS [FAB⁺]: Calcd. C₁₄H₂₅NO₅P: 286.1572; found: 286.1565.

1j: Yellow liquid. ¹H NMR (400 MHz, CDCl₃) δ: 1.06 (s, 9H, (CH₃)₃C); 1.7 (bs, 1H, NH); 2.57 (d, J_HP = 15.6 Hz, 1H, CHP); 3.76 (d, J_HP = 10.4 Hz, 3H, (CH₃O)₂P); 3.78 (system AB, J = 12.4 Hz, 1H, CH₂Ph); 3.79 (d, J_HP = 10.8 Hz, 3H, (CH₃O)₂P); 4.05 (system AB, J = 12.4 Hz, 1H, CH₂Ph); 7.23-7.38 (m, 5H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 27.7 (d, J_Cp = 6.5 Hz, (CH₃)₂C); 35.4 (d, J_Cp = 7.3 Hz, C(CH₃)₃); 52.1 (d, J_CP = 6.6 Hz, (CH₃O)₂P); 52.8 (d, J_CP = 7.3 Hz, (CH₃O)₂P); 55.4 (d, J_CP = 2.2 Hz, CH₂Ph); 64.5 (d, J_CP = 138.5 Hz, CHP); 127.3; 128.5; 128.6; 140.4. ³¹P NMR (80 MHz, CDCl₃) δ: 31.99. HRMS [FAB⁺]: Calcd. C₁₄H₂₅NO₅P: 286.1572; found: 286.1565.

1k: Yellow liquid. ¹H NMR (400 MHz, CDCl₃) δ: 1.88 (bs, 1H, NH); 3.67-3.82 (m, 8H, (CH₃O)₂P, CHP, and CH₂Ph); 3.97 (system AB, J = 13.4 Hz, 1H, CH₂Ph); 6.12-6.17 (m, 1H, CH); 6.62 (d, J_HH = 16.0 Hz, 1H, CH); 7.26-7.41 (m, 10H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 51.5 (d, J_Cp = 16.1 Hz,
CH₂Ph); 53.7 (d, J_CP = 6.6 Hz, (CH₃O)₂P); 53.9 (d, J_CP = 7.3 Hz, (CH₃O)₂P); 57.7 (d, J_CP = 155.1 Hz, CHP); 124.1 (d, J_CP = 6.6 Hz, CH); 126.8; 127.4; 128.2; 128.5; 128.7; 128.8; 134.9 (d, J_CP = 14.0 Hz, CH); 136.5; 139.5. ³¹P NMR (80 MHz, CDCl₃) δ: 27.06. HRMS [FAB⁺]: Calcd C₁₈H₂₃NO₃P: 332.1416; found: 332.1420.

2b: Yellow liquid; ¹H NMR (400 MHz, CDCl₃) δ: 1.02 (t, J_HH = 7.2 Hz, 3H, CH₃); 2.07-2.21 (m, 2H, CH₂CH₂ and NH); 2.40-2.50 (m, 1H, CH₂CH₃); 3.51 (d, J_HP = 10.0 Hz, 3H, (CH₃O)₂P); 3.70 (system AB, J = 13.2 Hz, 1H, CH₂Ph); 3.72 (d, J_HP = 10.4 Hz, 3H, (CH₃O)₂P); 3.76 system AB, J = 12.8 Hz, 1H, CH₂Ph); 7.24-7.45 (m, 8H, HAr); 7.70-7.73 (m, 2H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 7.9 (d, J_CP = 6.1 Hz, CH₃); 27.3 (CH₂); 46.7 (d, J_CP = 9.1 Hz, CH₂Ph); 53.2 (d, J_CP = 7.6 Hz, (CH₃O)₂P); 53.5 (d, J_CP = 6.0 Hz, (CH₃O)₂P); 64.4 (d, J_CP = 142.6 Hz, CHP); 127.1; 127.3 (d, J_CP = 3.1 Hz); 128.1; 128.2; 128.3; 128.5; 139.0; 140.8. ³¹P NMR (80 MHz, CDCl₃) δ: 29.92. HRMS [FAB⁺]: Calcd. for C₁₈H₂₅NO₃P: 334.1572; found: 334.1581.

2d: Yellow liquid; ¹H NMR (400 MHz, CDCl₃) δ: 1.80-1.87 (m, 1H, CH₂); 2.09-2.25 (m, 2H, CH₂); 2.32-2.43 (m, 1H, CH₂); 2.78-2.85 (m, 2H, CH₂); 3.45 (d, J_HP = 10.0 Hz, 3H, (CH₃O)₂P); 3.51 (system AB, J = 12.0 Hz, 1H, CH₂Ph); 3.70 (system AB, J = 12.4 Hz, 1H, CH₂Ph); 3.75 (d, J_HH = 10.8 Hz, 3H, (CH₃O)₂P); 7.13-7.33 (m, 8H, HAr); 7.76-7.80 (m, 1H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 20.3 (d, J_CP = 3.1 Hz, CH₂); 30.2 (CH₂); 30.4 (CH₂); 47.0 (d, J_CP = 12.1 Hz, CH₂Ph); 53.7 (d, J_CP = 7.6 Hz, (CH₃O)₂P); 54.1 (d, J_CP = 7.6 Hz, (CH₃O)₂P); 60.2 (d, J_CP = 148.7 Hz, CHP); 126.2 (d, J_CP = 3.0 Hz); 127.1, 127.7 (d, J_CP = 3.0 Hz); 128.4; 128.5; 128.8 (d, J_CP = 4.6); 128.9; 129.6; 139.8 (d, J_CP = 6.1 Hz); 140.6. ³¹P NMR (80 MHz, CDCl₃) δ: 30.52. HRMS [FAB⁺]: Calcd. for C₁₉H₂₅NO₃P: 346.1572; found: 346.1568.

2e: Dark brown oil; ¹H NMR (400 MHz, CDCl₃) δ: 2.17 (bs, 1H, NH); 2.30-2.43 (m, 1H, CH₂); 2.59-2.70 (m, 1H, CH₂); 3.00-3.05 (m, 2H, CH₂); 3.52 (system AB, J = 12.8 Hz, 1H, CH₂Ph); 3.60 (d, J_HP = 10.4 Hz, 3H, (CH₃O)₂P); 3.70 (system AB, J = 12.4 Hz, 1H, CH₂Ph); 3.72 (d, J_HP = 10.4 Hz, 3H, (CH₃O)₂P); 7.20-7.33 (m, 8H, HAr); 7.49-7.52 (m, 1H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 30.6 (d, J_CP = 3.0 Hz, CH₂); 32.2 (CH₂); 46.9 (d, J_CP = 12.1 Hz, CH₂Ph); 53.6 (d, J_CP = 7.6 Hz, (CH₃O)₂P); 54.3 (d, J_CP = 6.0 Hz, (CH₃O)₂P); 69.7 (d, J_CP = 154.7 Hz, CHP); 125.1, 125.7 (d, J_CP = 3.0 Hz); 126.7; 127.1; 128.3; 128.5; 128.7; 140.2; 140.5; 145.0 (d, J_CP = 7.6 Hz). ³¹P NMR (80 MHz, CDCl₃) δ: 29.41. HRMS [FAB⁺]: Calcd. for C₁₈H₂₃NO₃P: 332.1416; found: 332.1431.
2f: Brown solid; m.p. 85-87 °C; ¹H NMR (400 MHz, CDCl₃) δ: 1.80 (bs, 1H, NH); 3.12 (dd, J = 16.4, 7.2 Hz, 2H, CH₂); 3.53 (dd, J = 16.4, 13.2 Hz, 2H, CH₂); 3.77 (d, Jₜₜ = 10.4 Hz, 3H, (CH₃O)₂P); 3.78 (d, Jₜₜ = 10.4 Hz, 3H, (CH₃O)₂P); 3.84 (s, 2H, CH₂Ph); 7.16-7.25 (m, 9H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 41.0 (d, Jₜₚ = 6.1 Hz, CH₂); 48.4 (d, Jₜₚ = 6.1 Hz, CH₂Ph); 53.4 (d, Jₜₚ = 6.0 Hz, (CH₃O)₂P); 64.3 (d, Jₜₚ = 156.3 Hz, CHP); 124.6; 127.0; 128.2; 128.4; 140.5; 140.6; 140.8. ³¹P NMR (80 MHz, CDCl₃) δ: 32.42. HRMS [FAB⁺]: Calcd. for C₁₈H₂₃NO₃P: 332.1416; found: 332.1431.

2i: Yellow liquid; ¹H NMR (400 MHz, CDCl₃) δ: 0.99 (t, Jₜₜ = 7.2 Hz, 3H, CH₃CH₂); 1.31, (d, Jₜₚ = 16.0 Hz, 3H, CH₃); 1.65-1.78 (m, 2H, CH₂CH₃ and NH); 1.81-1.91 (m, 1H, CH₂CH₃); 3.80 (d, Jₜₜ = 10.4 Hz, 3H, (CH₃O)₂P); 3.82 (d, Jₜₜ = 10.4 Hz, 3H, (CH₃O)₂P); 3.83 (system AB, J = 12.4 Hz, 1H, CH₂Ph); 3.90 (system AB, J = 12.4 Hz, 1H, CH₂Ph); 7.21-7.38 (m, 5H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 7.2 (d, Jₜₚ = 7.6 Hz, CH₃); 20.6 (CH₃); 27.4 (CH₂); 47.6 (CH₂Ph); 52.9 (d, Jₜₚ = 7.6 Hz, (CH₃O)₂P); 53.2 (d, Jₜₚ = 7.6 Hz, (CH₃O)₂P); 57.1 (d, Jₜₚ = 141.1 Hz, CP); 127.1; 128.4; 128.6; 141.2. ³¹P NMR (80 MHz, CDCl₃) δ: 34.32. HRMS [FAB⁺]: Calcd. for C₁₃H₂₃NO₃P: 272.1416; found: 272.1417.

2j: Yellow liquid; ¹H NMR (400 MHz, CDCl₃) δ: 0.99 (t, Jₜₜ = 8.0 Hz, 6H, CH₃CH₂); 1.71-1.85 (m, 5H, CH₂CH₃ and NH); 3.80 (d, Jₜₜ = 10.8 Hz, 6H, (CH₃O)₂P); 3.85 (s, 2H, CH₂Ph); 7.22-7.38 (m, 5H, HAr). ¹³C NMR (100 MHz, CDCl₃) δ: 7.7 (d, Jₜₚ = 6.1 Hz, CH₃); 25.8 (d, Jₜₚ = 4.5 Hz, CH₂); 47.3 (d, Jₜₚ = 3.0 Hz, (CH₃O)₂P); 52.7 (d, Jₜₚ = 9.1 Hz, CH₂Ph); 60.6 (d, Jₜₚ = 136.5 Hz, CHP); 127.0; 128.3; 128.5; 141.2. ³¹P NMR (80 MHz, CDCl₃) δ: 30.61. HRMS [FAB⁺]: Calcd. for C₁₄H₂₅NO₃P: 286.1572; found: 286.1575.

References: