**Phosphine-catalyzed Hydration and Hydroalkoxylation of Activated Olefins:
Use of a Strong Nucleophile to Generate a Strong Base**

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Supporting Information

General Procedures. Unless otherwise noted, reactions and manipulations were performed at ambient temperature. Glassware was dried overnight at 150 °C or flame dried under vacuum immediately prior to use. All NMR spectra were obtained at ambient temperature using Bruker AMX-300, AMX-400, or DRX-500 spectrometers. ¹H NMR chemical shifts (δ) are reported in parts per million (ppm) downfield of TMS and are referenced relative to residual protiated solvent. ¹³C NMR chemical shifts (δ) are reported in ppm relative to the carbon resonance of the deuterated solvent. Infrared (IR) spectra were recorded as a thin film between NaCl plates.

Materials. Unless otherwise noted, reagents were purchased from commercial suppliers and used without further purification. Diethyl ether was distilled from sodium/benzophenone ketyl under N₂ prior to use. Deuterated solvents (Cambridge Isotope Laboratories) were used without further purification. Trimethylphosphine was stored over sodium under vacuum.

van't Hoff plot. A solution of methyl vinyl ketone (0.006 mL, 0.08 mmol) and *p*-methoxy phenol (0.06 g, 0.5 mmol) in CD₃CN (0.3 mL) was subjected to three freeze-pump-thaw cycles, following which PMe₃ (0.005 mmol) was added via vacuum transfer. 1,3,5-Tribromobenzene was used as an internal standard. Variable temperature ¹H NMR

single-scan experiments were recorded on a Bruker DRX-500 spectrometer. Probe temperature was calibrated with an ethylene glycol standard.

T (K)	325.6	331.8	337.0	342.9	348.8	354.3
K	0.31	0.28	0.25	0.21	0.20	0.17

General procedure for the initiation of hydration and hydroalkoxylation reactions. A solution of substrate (10 mmol) in alcohol (10 mL) was subjected to three freeze-pump-thaw cycles, following which PMe_3 (0.5 mmol) was added via vacuum transfer. The flask was sealed and left for the time indicated. For each reaction, see individual work-up procedures below.

5-Hydroxyhexan-3-one. After 20 h at ambient temperature, the solution was filtered through a pad of silica and concentrated under reduced pressure. Chromatography (2:1 hexane:EtOAc) afforded spectroscopically pure product as a yellow oil (0.891 g, 77%). Spectral data match literature values¹: ¹H NMR (CDCl₃, 500 MHz) δ 3.98 (m, 1H), 3.49 (br s, 1H), 2.33 (d, 2H, *J* = 6.4 Hz), 2.24 (q, 2H, *J* = 7.3 Hz), 0.95 (d, 3H, *J* = 6.4 Hz), 0.80 (t, 3H, *J* = 7.3 Hz) ppm; ¹³C{¹H} NMR (CDCl₃, 125 MHz) δ 211.9, 63.7, 50.3, 36.5, 22.5, 7.3 ppm; IR (film) 3455 (br s), 2973 (s), 1710 (s), 1376 (m), 1121 (m), 1022 (m), 938 (m) cm⁻¹.

5-Methoxyhexan-3-one. After 24 h at ambient temperature, the solution was filtered through a pad of silica and concentrated under reduced pressure. Chromatography (1:1 pentane:EtOAc) afforded spectroscopically pure product as a yellow oil (0.965 g, 85%). Spectral data match literature values²: ¹H NMR (CDCl₃, 300 MHz) δ 3.65 (sextet, 1H, *J* = 6.6 Hz), 3.15 (s, 3H), 2.55 (dd, 1H, *J* = 8.4, 7.4 Hz), 2.2-2.4 (m, 3H), 1.01 (d, 3H, 6.6 Hz), 0.89 (t, 3H, *J* = 7.2) ppm; ¹³C{¹H} NMR (CDCl₃, 75 MHz) δ 211.5, 74.9, 57.9, 51.0, 38.6, 20.9, 9.2 ppm; IR (film) 2936 (br s), 1713 (s), 1376 (m), 1135 (m), 1092 (m) cm⁻¹.

5-Benzyloxyhexan-3-one. 4-hexen-3-one (1.24 mL, 10 mmol) and benzyl alcohol (5.17 mL, 50 mmol) were added to CH₃CN (5 mL). PMe₃ (0.5 mmol) was added as described above. After 16 h at 45 °C, the solution was filtered through a pad of silica and concentrated under reduced pressure. Chromatography (4:1 hexane:EtOAc) afforded spectroscopically pure product as a yellow oil (1.309 g, 63%). Spectral data match literature values³: ¹H NMR (CDCl₃, 300 MHz) δ 7.2-7.4 (m, 5H), 4.56 (d, 1H, *J* = 11.7 Hz), 4.44 (d, 1H, *J* = 11.7 Hz), 4.05 (sextet, 1H, *J* = 6.6 Hz), 2.78 (dd, 1H, *J* = 8.1, 7.5

Hz), 2.4-2.5 (m, 3H), 1.23 (d, 3H, $J = 6$ Hz), 1.04 (t, 3H, $J = 7.2$ Hz) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 75 MHz) δ 210.2, 138.7, 128.53, 127.9, 127.7, 72.0, 71.1, 49.8, 37.3, 20.1, 7.8 ppm; IR (film) 2974 (br s), 1712 (s), 1454 (m), 1375 (m), 1095 (m), 1063 (m), 738 (m), 698 (m) cm^{-1} .

4-Methoxybutan-2-one. After 1 h at ambient temperature, the solution was filtered through a pad of silica and concentrated under reduced pressure to afford spectroscopically pure product as a pale yellow oil (0.681 g, 56%). Spectral data match literature values⁴: ^1H NMR (CDCl_3 , 300 MHz) δ 3.51 (t, 2H, $J = 6.3$ Hz), 3.22 (s, 3H), 2.56 (t, 2H, $J = 6.3$ Hz), 2.11 (s, 3H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 75 MHz) δ 207.0, 67.4, 58.7, 43.5, 30.3 ppm; IR (film) 2890 (br s), 1718 (s), 1359 (m), 1118 (s), 919 (m), 733 (m) cm^{-1} .

4-Isopropoxybutan-2-one. Methyl vinyl ketone (0.80 mL, 10 mmol) and 2-propanol (3.8 mL, 50 mmol) were added to CH_3CN (10 mL). PMe_3 (0.5 mmol) was added as described above. After 1 h at ambient temperature, the solution was filtered through a plug of silica and concentrated under reduced pressure to afford spectroscopically pure product as a clear yellow oil (1.074 g, 83%). Spectral data match literature values⁴: ^1H NMR (CDCl_3 , 500 MHz) δ 3.63 (t, 2H, $J = 6$ Hz), 3.53 (septet, 1H, $J = 6.1$ Hz), 2.63 (t, 2H, $J = 6$ Hz), 2.15 (s, 3H), 1.10 (d, 6H, $J = 6.1$ Hz) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 125 MHz) δ 207.7, 71.7, 63.0, 44.0, 30.5, 21.9 ppm; IR (film) 2971 (br s), 1711 (s), 1368 (m), 1129 (m), 1080 (m), 734 (w) cm^{-1} .

4-Phenoxybutan-2-one. Methyl vinyl ketone (0.83 mL, 10 mmol) and phenol (9.4 g, 100 mmol) were added to CH_3CN (10 mL). PMe_3 (0.5 mmol) was added as described above. After 16 h at 45 $^\circ\text{C}$, the solution was filtered through a plug of silica

and concentrated under reduced pressure. The resulting solution was diluted with Et₂O and unreacted phenol was extracted with 2 M NaOH. The aqueous layer was extracted with 100 mL Et₂O (3x) and the combined organic layers were dried with Na₂SO₄ and concentrated under reduced pressure to afford the product as a clear brown oil (0.982 g, 59%). Spectral data match literature values⁵: ¹H NMR (CDCl₃, 300 MHz) δ 6.8-7.2 (m, 5H), 4.24 (t, 2H, *J* = 6.3 Hz), 2.91 (t, 2H, *J* = 6.3 Hz), 2.25 (s, 3H) ppm; ¹³C{¹H} NMR (CDCl₃, 75 MHz) δ 206.4, 158.4, 129.5, 120.9, 114.4, 62.6, 42.9, 30.4 ppm; IR (film) 3041 (br w), 1713 (s), 1599 (s), 1498 (s), 1245 (s), 1059 (m), 755 (m), 693 (m) cm⁻¹.

Methyl 3-methoxybutyrate. After 36 h at 45 °C, the solution was filtered through a plug of silica and concentrated under reduced pressure. Chromatography (4:1 hexane:EtOAc) afforded spectroscopically pure product as a yellow oil (1.035 g, 71%). Spectral data match literature values⁶: ¹H NMR (CDCl₃, 300 MHz) δ 3.58 – 3.72 (m, 1H), 3.57 (s, 3H), 3.21 (s, 3H), 2.45 (dd, 1H, *J* = 7.2, 6.6 Hz), 2.25 (dd, 1H, *J* = 7.2, 6.6 Hz), 1.08 (d, 3H, *J* = 6.2 Hz) ppm; ¹³C{¹H} NMR (CDCl₃, 75 MHz) δ 171.8, 73.5, 56.2, 51.5, 41.4, 19.0 ppm; IR (film) 2976 (br s), 1742 (s), 1439 (m), 1378 (m), 1302 (m), 1172 (m), 1087 (m), 917 (m), 735 (m) cm⁻¹.

3-Methoxypropionitrile. After 4 h at ambient temperature, the solution was filtered through a pad of silica and concentrated under reduced pressure to afford spectroscopically pure product as a clear oil (0.670 g, 79%). Spectral data match literature values⁷: ¹H NMR (CDCl₃, 400 MHz) δ 3.53 (t, 2H, *J* = 8.3 Hz), 3.34 (s, 3H), 2.57 (t, 2H, *J* = 8.3 Hz) ppm; ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 117.37, 66.3, 57.8, 17.7 ppm; IR (film) 2902 (br s), 2251 (m), 1711 (w), 1461 (m), 1385 (m), 1191 (m), 1119 (s), 1000 (m), 821 (w), 735 (w) cm⁻¹.

Trimethyl-(1-methyl-3-oxopentyl)-phosphonium chloride. A 50-mL bomb was charged with 4-hexen-3-one (1.7 mL, 15 mmol) and Et₂O (5 mL). PMe₃ (0.52 mL, 5.0 mmol) was added via syringe. Ethereal HCl (5 mL, 1.0 M) was added via syringe to the resulting cloudy brown solution, causing the immediate precipitation of a white solid. Et₂O and volatile materials were removed in vacuo to afford the desired salt contaminated with a small inseparable amount of trimethylphosphonium chloride. ¹H NMR (CD₃CN, 500 MHz) δ 2.95-3.05 (m, 1H, CH₂COEt), 2.88-2.95 (m, 1H, PCHCH₃), 2.70 (dt, 1H, *J* = 18, 8.4 Hz, CH₂COEt), 2.53 (dq, 1H, *J* = 18, 7 Hz, CH₂CH₃), 2.46 (dq, 1H, *J* = 18, 7 Hz, CH₂CH₃), 1.88 (d, 9H, *J* = 14.3 Hz, P(CH₃)₃), 1.17 (dd, 3H, *J* = 18.5, 7.3 Hz, PCHCH₃), 1.00 (t, 3H, 7 Hz, CH₂CH₃) ppm; ¹³C{¹H} NMR (CD₃CN, 100 MHz) δ 208.9 (C=O), 42.2 (CH₂COEt), 36.5 (CH₂CH₃), 24.2 (d, *J*_{P-C} = 50.5 Hz, Me₃PCH), 13.4 (d, *J*_{P-C} = 2.3 Hz, PCHCH₃), 7.8 (CH₂CH₃), 7.1 (d, *J*_{P-C} = 53.5 Hz, P(CH₃)₃) ppm; ³¹P{¹H} NMR (CD₃CN, 162 MHz) 33.3 ppm; IR (CH₃CN) 2983 (s), 2917 (s), 1718 (s), 1304 (m), 973 (s) cm⁻¹; HRMS (FAB+) calc. for [C₉H₂₀OP]⁺ 175.125179, found 175.125440.

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