Phosphine-Triggered Complete Chemo-Switch: from Efficient Aldehyde-Alkyne-Amine Coupling to Efficient Aldehyde-Alkyne Coupling in Water

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Supporting information

All experiments were carried out in air, unless otherwise stated. Flash column chromatography was performed over SORBENT silica gel 30-60 μ m. ^1H NMR and ^{13}C NMR spectra were acquired by Varian 400 MHz and 100 MHz, or 300 MHz and 75 MHz, respectively, and referenced to the internal solvent signals. IR spectra were recorded by ABB Bomem MB100 interferometer. MS data were obtained by KRATOS MS25RFA Mass Spectrometer. HRMS were performed at McGill University.

Cy_3PAgCl ¹, Ph_3PAgX ($\text{X}=\text{Cl}$, Br and I)², and $[\text{AgC}\equiv\text{CPh}]_4$ ³ were prepared by the reported methods.

Typical procedure (entry 1, Table 2):

Cy_3PAgCl (0.0105g, 0.025 mmol, 5 mol%) was mixed with 2 mL distilled water, 0.11 mL of phenylacetylene (1mmol, 2 equivalent) and 17 μL of $i\text{-Pr}_2\text{NEt}$ (0.1 mmol, 20 mol%). The mixture was stirred at room temperature until all solid disappeared. Benzaldehyde (0.0503g, 0.5 mmol), was added and stirred at room temperature for 5 min, and then stirred at 70 $^\circ\text{C}$ for one day. The reaction was stopped and extracted with ether (3 $\times$ 5 mL). The extraction was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column (15:1 hexanes and EtOAc). Compound **3a** was obtained in 69% of yield (0.0714g).

The reaction using silver acetylide 4 as substrate (entry 3, Scheme 2):

Silver acetylide **4** (20.9mg, 0.10 mmol) and Cy_3P (0.11 mmol, 31.0mg) were mixed with 1 mL of dichloromethane under a nitrogen atmosphere. The mixture was stirred at room temperature for 10 min to give a colorless clear solution. The solvent was removed with a nitrogen flow, and the residue was dried under vacuum. Cyclohexanecarboxaldehyde

(0.112 g, 1.0 mmol) was added and stirred for 5 min and 1 mL of water was introduced into the mixture and stirred overnight at 35°C. The reaction was stopped and extracted with ether (3×5 mL). The extraction was dried with Na₂SO₄ and then concentrated under reduced pressure. The residue and mesitylene (0.05 mmol, 6.95 μL, as internal standard) were dissolved in 1 mL of CDCl₃, and then analyzed by ¹H NMR to obtain the yield.

1,3-Diphenyl-prop-2-yn-1-ol (3a) CA registry Number: [159113-62-9] ¹H NMR (CDCl₃, 400MHz, ppm) δ 7.63-7.30 (m, 10H), 5.70 (d, *J* = 6 Hz, 1H), 2.29 (d, *J* = 6 Hz, 1H); ¹³C NMR (CDCl₃, 100MHz, ppm) δ 140.8, 132.0, 128.9, 128.8, 128.7, 128.5, 127.0, 122.6, 88.9, 87.0, 65.5.

1-(4-Chloro-phenyl)-3-phenyl-prop-2-yn-1-ol (3b) CA registry Number: [102990-14-7] ¹H NMR (CDCl₃, 400MHz, ppm) δ 7.51 (dd, *J* = 7.2, 1.6 Hz, 2H), 7.45-7.43 (m, 2H), 7.34-7.27 (m, 5H), 5.64 (s, 1H), 2.64 (s, 1H); ¹³C NMR (CDCl₃, 100MHz, ppm) δ 139.2, 134.4, 132.0, 129.00, 128.98, 128.6, 128.3, 122.3, 88.5, 87.3, 64.7.

1-(2-Chloro-phenyl)-3-phenyl-prop-2-yn-1-ol (3c) CA registry Number: [191403-26-6] ¹H NMR (CDCl₃, 400MHz, ppm) δ 7.82 (d, *J* = 6.4 Hz, 1H), 7.47-7.24 (m, 8H), 6.04 (s,

1H), 2.71 (bs, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 138.1, 133.0, 132.0, 130.0, 129.9, 128.9, 128.7, 128.5, 127.5, 122.5, 87.9, 87.0, 62.8.

1-(3-Chloro-phenyl)-3-phenyl-prop-2-yn-1-ol (3d) CA registry Number: [59931-63-4]

^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.57 (d, $J = 0.8$, 1H), 7.45-7.42 (m, 3H), 7.31-7.27 (m, 5H), 5.62 (s, 1H), 2.64 (s, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 142.7, 134.7, 132.0, 130.1, 129.0, 128.7, 128.6, 127.1, 125.1, 122.3, 88.3, 87.4, 64.3.

1-(2-Fluoro-phenyl)-3-phenyl-prop-2-yn-1-ol (3e) CA registry Number: [245322-87-6]

^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.75 (dt, $J = 1.6, 7.5$ Hz, 1H), 7.50-7.07 (m, 8H), 5.99 (s, 1H), 2.82 (s, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 160.4 (d, $J = 246.5$ Hz), 132.0, 130.4 (d, $J = 8.3$ Hz), 128.9, 128.7 (d, $J = 3.8$ Hz), 128.5, 128.1 (d, $J = 13$ Hz), 124.6 (d, $J = 3.8$ Hz), 122.5, 115.9 (d, $J = 20.6$), 88.0, 86.9, 59.9 (d, $J = 5.4$ Hz).

1-(4-Fluoro-phenyl)-3-phenyl-prop-2-yn-1-ol (3f) CA registry Number: [142739-41-1]

^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.61-7.57 (m, 2H), 7.47-7.46 (m, 2H), 7.34-7.31 (m, 3H), 7.10-7.06 (m, 2H), 5.68 (d, $J = 6$ Hz, 1H), 2.57 (d, $J = 6$ Hz, 1H); ^{13}C NMR (CDCl_3 ,

100MHz, ppm) δ 162.8 (d, J = 244.6 Hz), 136.7 (d, J = 3.8 Hz), 131.9, 128.9, 128.9 (d = 8.4 Hz), 128.6, 122.4, 115.7 (d, J = 21.4 Hz), 88.8, 87.2, 64.8.

1-(2-Bromo-phenyl)-3-phenyl-prop-2-yn-1-ol (3g) CA registry Number: [134419-85-5]

^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.85 (dd, J = 1.2, 7.2 Hz, 1H), 7.60-7.18 (m, 8H), 6.02 (s, 1H), 2.69 (s, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 139.7, 133.3, 132.0, 130.2, 128.9, 128.5, 128.1, 123.0, 122.5, 88.0, 87.1, 65.1.

1-(4-Bromo-phenyl)-3-phenyl-prop-2-yn-1-ol (3h) CA registry Number: [142739-40-0]

^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.53-7.45 (m, 1H), 7.33-7.31 (m, 3H), 5.65 (d, J = 3.6 Hz, 1H), 2.58 (d, J = 3.6 Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 139.8, 132.0, 131.9, 129.0, 128.6, 128.6, 122.6, 122.3, 88.5, 87.3, 64.8.

3-Phenyl-1-(2-trifluoromethyl-phenyl)-prop-2-yn-1-ol(3i)⁴ ^1H NMR (CDCl_3 , 400MHz, ppm) δ 8.09 (d, J = 8 Hz, 1H), 7.69-7.61 (m, 2H), 7.47-7.43 (m, 3H), 7.34-7.31 (m, 3H), 6.10 (d, J = 4.8 Hz, 1H), 2.71 (d, J = 4.8 Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 139.5, 132.8, 131.9, 129.3, 128.9, 128.7, 128.5, 127.4 (q, J = 30.5 Hz), 126.0 (q, J = 5.4 Hz), 124.4 (q, J = 272 Hz), 122.4, 88.5, 87.0, 61.4 (q, J = 3.1 Hz).

1-(2-Trifluoromethyl-phenyl)-non-2-yn-1-ol (3i') IR (liquid film): $\nu_{\max}$ 3350, 2961, 2931, 2858, 2282, 2231, 1608, 1585, 1457, 1379, 1317, 1167, 1126, 1060, 1038, 1009, 958 cm^{-1} ; ^1H NMR (CDCl_3 , 400MHz, ppm) δ 8.00 (d, $J = 7.6$ Hz, 1H), 7.64-7.60 (m, 2H), 7.42 (t, $J = 7.6$ Hz, 1H), 5.84 (m, 1H), 2.44 (d, $J = 4.8$ Hz, 1H), 2.24 (td, $J = 2, 7.2$ Hz, 2H), 1.52 (m, 2H), 1.39-1.27 (m, 6H), 0.89 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 140.2, 132.6, 129.2, 128.4, 127.3 (q, $J = 30.4$ Hz), 125.8 (q, $J = 6.1$ Hz), 124.4 (q, $J = 272$ Hz), 88.2, 79.9, 61.0 (q, $J = 3.1$ Hz), 31.7, 28.9, 28.8, 23.0, 19.2, 14.4; MS (EI) m/z (%) 284 (M^+), 253, 227, 207, 193, 173 (100), 155, 145, 127, 96, 67; HRMS calcd for $\text{C}_{16}\text{H}_{19}\text{F}_3\text{O}$: 284.1388; found: 284.1383.

3-Phenyl-1-(4-trifluoromethyl-phenyl)-prop-2-yn-1-ol (3j) CA registry Number: [443287-60-6] ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.74 (d, $J = 8.4$ Hz, 2H), 7.66 (d, $J = 12.4$ Hz, 2H), 7.47-7.46 (m, 2H), 7.36-7.31 (m, 3H), 5.75 (d, $J = 5.2$ Hz, 1H), 2.53 (d, $J = 5.2$ Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 144.5, 132.0, 130.7 (q, $J = 32$ Hz), 129.1, 128.6, 127.2, 125.8 (q, $J = 3.8$ Hz), 124.2 (q, $J = 270$ Hz), 88.2, 87.6, 64.8.

1-Naphthalen-1-yl-3-phenyl-prop-2-yn-1-ol (3k) CA registry Number: [672959-14-7]

^1H NMR (CDCl_3 , 400MHz, ppm) δ 8.39 (d, J = 8.4 Hz, 1H), 7.95-7.86 (m, 3H), 7.59-7.49 (m, 5H), 7.34-7.32 (m, 3H), 6.36 (d, J = 5.6 Hz, 1H), 2.57 (d, J = 5.6 Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 135.9, 134.3, 132.0, 130.8, 129.6, 129.0, 128.8, 128.5, 126.7, 126.1, 125.5, 124.9, 124.2, 122.7, 88.9, 87.6, 63.8.

1-(2,5-Dimethoxy-phenyl)-3-phenyl-prop-2-yn-1-ol (3l) IR (KBr): ν_{max} 3312, 3078, 2937, 2953, 2916, 2834, 2061, 1610, 1573, 1505, 1489, 1331, 1227, 1148, 1044, 1021, 806, 756, 700, 689 cm^{-1} ; ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.49-7.46 (m, 2H), 7.31-7.25 (m, 4H), 6.85 (m, 2H), 5.90 (d, J = 6.0 Hz, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.24 (d, J = 6.0 Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 153.9, 151.1, 132.0, 130.1, 128.6, 128.4, 122.9, 114.3, 114.3, 112.4, 88.6, 86.4, 62.0, 56.6, 56.1; MS (EI) m/z (%) 268 (M^+), 252, 237, 194, 166, 151, 123, 102 (100), 76, 51; HRMS calcd for $\text{C}_{17}\text{H}_{16}\text{O}_3$: 268.1099; found: 268.1097

3-Phenyl-1-o-tolyl-prop-2-yn-1-ol (3m) CA registry Number: [479213-83-7] ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.75 (m, 1H), 7.50-7.47 (m, 2H), 7.35-7.22 (m, 6H), 5.85 (d, J = 6 Hz, 1H), 2.52 (s, 3H), 2.48 (d, J = 6 Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 138.6, 136.2, 131.9, 131.0, 128.8, 128.7, 128.5, 126.8, 126.5, 122.8, 88.9, 86.8, 63.3, 19.5.

1-(2-Methoxy-phenyl)-3-phenyl-prop-2-yn-1-ol (3n) CA registry Number: [245322-93-4] ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.66 (dd, $J = 1.6, 8$ Hz, 1H), 7.50-7.48 (m, 2H), 7.35-7.30 (m, 4H), 7.02 (dt, $J = 0.8, 7.6$ Hz, 1H), 6.93 (dd, $J = 0.8, 8$ Hz, 1H), 5.95 (d, $J = 6$ Hz, 1H), 3.92 (s, 3H), 3.17 (d, $J = 6$ Hz, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 157.0, 131.7, 129.9, 129.0, 128.6, 128.4, 128.2, 123.0, 121.1, 111.2, 88.7, 86.4, 62.0, 56.0.

1,5-Diphenyl-pent-1-en-4-yn-3-ol (3o) CA registry Number: [20496-89-3] ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.51-7.43 (m, 4H), 7.36-7.25 (m, 5H), 6.85 (d, $J = 15.6$ Hz, 1H), 6.40 (dd, $J = 15.6, 6$ Hz, 1H), 5.30 (bs, 1H), 2.23 (s, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 136.3, 132.2, 132.0, 128.8, 128.5, 128.3, 128.3, 127.0, 122.6, 88.2, 86.8, 63.8.

1-Phenyl-hept-1-yn-3-ol (3p) CA registry Number: [72206-40-7] ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.44-7.42 (m, 2H), 7.31-7.29 (m, 3H), 4.60 (m, 1H), 2.00 (d, $J = 5.6$ Hz, 1H), 1.85-1.79 (m, 2H), 1.56-1.39 (m, 4H), 0.95 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR

(CDCl₃, 100MHz, ppm) δ 131.9, 128.5, 128.5, 122.9, 90.5, 85.1, 63.4, 38.0, 27.8, 22.9, 14.5.

1-Cyclohexyl-3-phenyl-prop-2-yn-1-ol (3q) CA registry Number: [130708-23-5] ¹H NMR (CDCl₃, 400MHz, ppm) δ 7.45-7.42 (m, 2H), 7.31-7.29 (m, 3H), 4.38 (d, *J* = 6 Hz, 1H), 1.99-1.68 (m, 7H), 1.32-1.18 (m, 5H); ¹³C NMR (CDCl₃, 100MHz, ppm) δ 131.9, 128.5, 128.5, 123.0, 89.5, 86.0, 68.0, 44.7, 29.1, 28.7, 26.8, 26.4, 26.4.

3-Phenyl-prop-2-yn-1-ol (3r) CA registry Number: [1504-58-1] ¹H NMR (CDCl₃, 400MHz, ppm) δ 7.45-7.43 (m, 2H), 7.31-7.25 (m, 3H), 4.50 (s, 2H), 2.29 (s, 1H); ¹³C NMR (CDCl₃, 100MHz, ppm) δ 131.9, 128.7, 128.5, 122.8, 87.6, 85.9, 51.9.

(3-Phenyl-prop-2-ynyloxy)-methanol (3r') IR (liquid film): ν_{max} 3055, 3022, 2962, 2872, 2800, 1691, 1594, 1494, 1318, 1169, 1083, 1070, 954, 877, 810, 756, 694cm⁻¹; ¹H NMR (CDCl₃, 400MHz, ppm) δ 7.54 (d, *J* = 6.8 Hz, 2H), 7.32-7.29 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 5.42 (s, 2H), 5.32 (s, 1H), 4.58 (d, *J* = 1.2 Hz, 2H); ¹³C NMR (CDCl₃, 100MHz, ppm) δ 149.2, 135.7, 128.5, 127.6, 125.8, 98.4, 96.2, 68.5; MS (EI) *m/z* (%) 162 (M⁺), 131, 104 (100), 78, 63; HRMS calcd for C₁₀H₁₀O₂: 162.0681; found: 162.0677

1-(4-Hydroxymethyl-phenyl)-3-phenyl-prop-2-yn-1-ol (3s) IR (KBr): $\nu_{\max}$ 3295, 3169, 2967, 2932, 2869, 2238, 1489, 1422, 1286, 1207, 1037, 1009, 962, 855, 779, 749, 683 cm^{-1} ; ^1H NMR (CDCl_3 , 400MHz, ppm) δ 7.69 (d, $J = 7.6$ Hz, 2H), 7.59-7.30 (m, 7H), 5.69 (d, $J = 6$ Hz, 1H), 4.71 (d, $J = 4.8$ Hz, 2H), 2.50 (d, $J = 6$ Hz, 1H), 1.85 (bs, 1H); ^{13}C NMR (CDCl_3 , 100MHz, ppm) δ 141.3, 140.3, 131.9, 128.8, 128.5, 127.4, 127.2, 122.5, 88.9, 87.0, 65.3, 65.2; MS (EI) m/z (%) 238 (M^+), 222, 207, 191, 179, 136, 129, 102 (100), 89, 77; HRMS calcd for $\text{C}_{16}\text{H}_{14}\text{O}_2$: 238.0994; found: 238.0989.

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 - 2 Teo, B.-K.; Calabrese, J. C. *Inorg. Chem.* **1976**, 15, 2467
 - 3 Teo, B. K.; Xu, Y. H.; Zhong, B. Y.; He, Y. K.; Chen, H. Y.; Qian, W.; Deng, Y. J.; Zou, Y. H. *Inorg. Chem.* **2001**, 40, 6794
 - 4 Takita, R.; Fukuta, Y.; Tsuji, R.; Ohshima, T.; Shibasaki, M. *Org. Lett.* **2005**, 7, 1363 and its supporting information

yxq-3-126

Data Collected on: m400-mercury400
Archive directory: /export/home/xyao/vnmrsys/data
Sample directory:
File: PROTON

Pulse Sequence: s2pu1

Solvent: CDCl3
Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6410.3 Hz
2 repetitions
OBSERVE H1, 400.1245662 MHz
DATA PROCESSING
FT size 32768
Total time 0 min

¹³C OBSERVE

Data Collected on: m400-mercury400
Archive directory: /export/home/xyao/vnmrsys/data
Sample directory:
File: CARBON

Pulse Sequence: s2pu1

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.199 sec
Width 25125.6 Hz
16512 repetitions
OBSERVE C13, 100.6113782 MHz
DECOUPLE H1, 400.1266027 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 63 hr, 35 min

220 200 180 160 140 120 100 80 60 40 20 0 ppm

yxq-3-110

Data Collected on: m400-mercury400
Archive directory: /export/home/xyao/vnmrsys/data
Sample directory:
File: PROTON

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.998 sec

Width 6410.3 Hz

Single scan

OBSERVE H1, 400.1245662 MHz

DATA PROCESSING

FT size 32768

Total time 0 min

yxq-3-110

Data Collected on:
Archive directory:
Sample directory:
File: PROTON

yxq-3-110

Data Collected on:
Archive directory:
Sample directory:
File: PROTON

yxq-3-129

Data Collected on: m400-mercury400
Archive directory: /export/home/xyao/vnmrsys/data
Sample directory:
File: PROTON

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 25.0 C / 298.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.998 sec

Width 6410.3 Hz

4 repetitions

OBSERVE H1, 400.1245662 MHz

DATA PROCESSING

FT size 32768

Total time 0 min

yxq-3-129

Data Collected on: m400-mercury400

Archive directory: /export/home/xyao/vnmrsys/data

Sample directory:

File: CARBON

Pulse Sequence: s2pu1

Solvent: CDCl3

Temp. 23.0 C / 296.1 K

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.199 sec

Width 25125.6 Hz

18368 repetitions

OBSERVE C13, 100.6113782 MHz

DECOUPLE H1, 400.1266027 MHz

Power 34 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

FT size 65536

Total time 63 hr, 35 min

yxq-3-129

Data Collected on

Archive directory

Sample directory:

File: CARBON

yxq-3-129

Data Collected on

Archive directory

Sample directory:

File: CARBON