Supporting Information

Hydration of Terminal Alkynes Catalyzed by Water-Soluble Cobalt Porphyrin Complexes

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1. General Comments

^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECA-600 (600 MHz for ^{1}H, 150 MHz for ^{13}C), a JEOL ECA-500 (500 MHz for ^{1}H, 125 MHz for ^{13}C), or a JEOL GSX (270 MHz for ^{1}H) at 27 °C. Chemical shifts are reported as δ in ppm and are internally referenced to tetramethylsilane (TMS, 0.0 ppm for ^{1}H) or $CDCl_3$ (77.06 ppm for ^{13}C) and calculated relative to TMS. The following abbreviations are used: s = singlet, d = doublet, t = triplet, bs = broad singlet, dt = double triplet, ddd = double double doublet, ddt = double double triplet, and m = multiplet). High-resolution mass spectra (HRMS) were obtained from JEOL JMS (EI or FAB). Low-resolution mass spectra (LRMS) were obtained from Agilent 5973 MSD (EI). IR spectra were recorded on a FT-IR6100 (JASCO) at 25 °C. UV spectra were recorded on a UV–2450 (SHIMADZU).

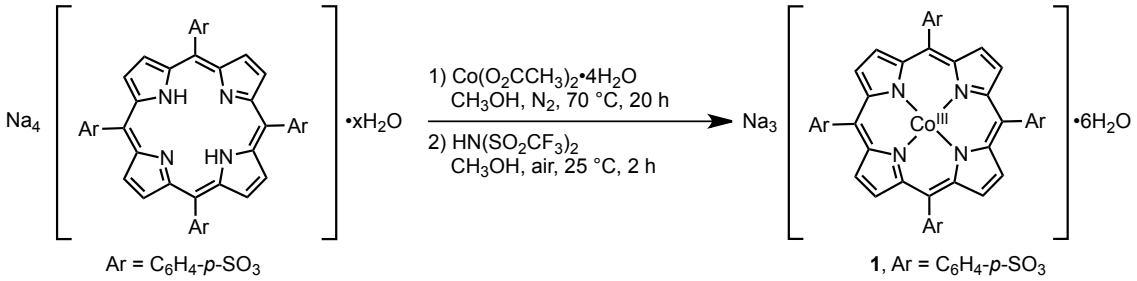
2. Materials

1-Decyne (**2a**), 1,8-nonadiyne (**2b**), 4-*t*-butylphenylacetylene (**2i**), 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)ethynylbenzene (**2l**) and 5-hexyne-1-ol were purchased from Wako Chemicals. 10-Undecyne-1-ol, 10-undecynoic acid, and *N*,*N*-dimethyl-4-aminopyridine (DMAP) were purchased from TCI. Phenylacetylene (**2h**), 4-ethynyl benzonitrile (**2m**), 1-ethynyl-4-nitrobenzene (**2n**), and 5,10,15,20-tetraphenyl-21*H*,23*H*- porphine-*p*,*p*′,*p*′′,*p*′′′-tetrasulfonic acid, tetrasodium salt [$Na_4(H_2TPPS)$], imidazole, trityl chloride (TrCl), boron trifluoride diethyl etherate, L-phenylalanine methyl ester hydrochloride, and *N*-(3-Dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDAC) were

purchased from Aldrich. Anhydrous methanol (water content: <50 ppm), anhydrous diethyl ether (water content: <50 ppm), anhydrous dichloromethane (water content: <10 ppm), anhydrous tetrahydrofuran (water content: <10 ppm), anhydrous toluene (water content: <10 ppm), cobalt(II) dichloride hexahydrate, cobalt(II) acetate tetrahydrate, trifluoro-*N*-[(trifluoromethyl)sulfonyl]methanesulfonamide ($HNTf_2$), *tert*-butyldimethylsilyl chloride (TBDMSCl), sodium hydride (60% dispersion in mineral oil), and allylbromide were purchased from Kanto Chemicals. *tert*-Butyldiphenyl(hex-5-yn-1-yloxy)silane (**2c**) [1], hex-5-ynyl benzoate (**2f**) [2], *N*-(4-ethynylphenyl)acetamide (**2j**)[3], and 1-iodo-4-ethynylbenzene (**2k**)[4] were prepared according to the literature procedures.[1–4]

3. Synthesis of 1 and 2

Tetrakis(*p*-sulfonatophenyl)porphyrin cobalt(III) trisodium salt hexahydrate (1)



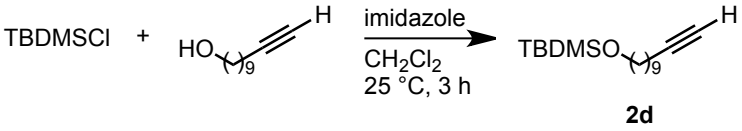
To a 500 mL Schlenk flask equipped with a stirring bar, 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine-*p*,*p*′,*p*′′,*p*′′′-tetrasulfonic acid, tetrasodium

[1] Baldwin, J. E.; Romeril, S. P.; Lee, V.; Claridge, T. D. W.; *Org. Lett*. **2001**, *3*, 1145–1148.
[2] Chan, W.-K.; Ho, C.-M.; Wong, M.-K.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 14796–14797.
[3] Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C.; Terlizzi, R. *Eur. J. Org. Chem.* **2004**, 3447–3458.
[4] Goeb, S.; Ziessel, R. *Org. Lett*. **2007**, *9*, 737–740.

salt hydrate [550.1 mg, 0.54 mmol (calculated as anhydrate)], cobalt acetate tetrahydrate (141.5 mg, 0.57 mmol), and dry CH_3OH (150 mL) were added under a N_2 atmosphere. The mixture was stirred at 70 °C for 20 h, cooled to 25 °C, and concentrated to around 30 mL under reduced pressure. Dry Et_2O (400 mL) was added to the mixture under a N_2 atmosphere. After an orange precipitate was generated, the supernatant was removed. The dissolution–reprecipitation process using dry CH_3OH and dry Et_2O was repeated two more times to afford tetrakis(*p*-sulfonatophenyl)porphyrin cobalt(II) tetrasodium salt as a orange solid. After this crude product was placed in a 300 mL recovery flask equipped with a stirring bar, dry CH_3OH (160 mL) and $HNTf_2$ (811.7 mg, 2.9 mmol) were added to the flask. The mixture was stirred under air at 25°C for 2 h, and was concentrated to around 20 mL under reduced pressure. Addition of dry Et_2O (200 mL) induced a formation of a purple precipitate, and the supernatant was removed after centrifugation. The dissolution–reprecipitation process was repeated two more times. The purple precipitate was dried under reduced pressure, and was dissolved in pure water (60 mL). The solution was dialyzed for 2 days (SPECTRUM CE, MWCO: 500–1000). The solution was concentrated to around 5 mL under reduced pressure, and passed through ion exchange resin (Dowex 50W×2 200–400, in Na^+ form). The solution was concentrated, and dried under reduced pressure (0.08 mmHg) at 80 °C for 9 h to afford **1** (374.2 mg, 60% in two steps, hexahydrate) as a purple solid: mp >400 °C; ^{1}H NMR (500 MHz, CD_3OD) δ 8.26–8.48 (m, 16H), 9.34−9.37 (m, 8H); $^{13}C\{^1H\}$ NMR (125 MHz, CD_3OD) δ 120.8, 125.9, 135.2, 136.4, 144.1, 145.5, 146.6; UV-vis (CH_3OH) λ_{max}, nm (ε, $M^{-1}cm^{-1}$) 426.5 (1.92×10^5), 539.0 (1.37×10^4); elemental analysis calcd for [$C_{44}H_{36}CoN_4Na_3O_{18}S_4$]: C, 45.36; H, 3.11; N, 4.81, found: C, 46.33;

H, 3.33; N, 4.83.

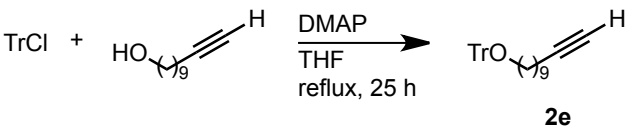
tert-Butyldimethyl(undec-10-yn-1-yloxy)silane (2d)



2d

To a solution of *tert*-butyldimethylsilyl chloride (4.52 g, 30.0 mmol) and imidazole (4.08 g, 59.9 mmol) in dry CH_2Cl_2 (30 mL) was added 10-undecyne-1-ol (3.0 mL, 15.6 mmol) at 25 °C under a N_2 atmosphere. The mixture was stirred at 25 °C for 3 h. The reaction was quenched with water (50 mL). After the mixture was extracted with CH_2Cl_2 (3 × 50 mL), the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (2% ethyl acetate in *n*-hexane) to afford **2d** (4.24 g, 96%) as a colorless oil: IR (neat) 3314, 2930, 2857, 1097 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.89 (s, 9H), 1.27–1.41 (m, 10H), 1.49−1.60 (m, 4H), 1.93 (t, J = 2.8 Hz, 1H), 2.17 (dt, J = 2.8, 7.6 Hz, 2H), 3.59 (t, J = 6.8 Hz, 2H) ; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ –5.3, 18.4, 25.8, 26.0, 28.5, 28.7, 29.0, 29.4, 29.5, 32.9, 63.3, 68.0, 84.8; HRMS (FAB) calcd for $[C_{17}H_{35}OSi^+]$ ($[MH^+]$) 283.2457; found 283.2463.

[(Undec-10-yn-1-yloxy)methanetriyl]tribenzene (2e)

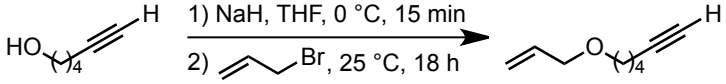


2e

To a solution of trityl chloride (6.70 g, 24 mmol) and 4-(dimethylamino)pyridine (3.67

g, 30 mmol) in dry THF (50 mL) was added 10-undecyne-1-ol (3.80 mL, 20 mmol) at 25 °C under a N_2 atmosphere. The mixture was refluxed for 25 h, and was cooled to 25 °C. The reaction was quenched with water (50 mL). After the mixture was extracted with ethyl acetate (3 × 60 mL), the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (2% ethyl acetate in *n*-hexane) to afford **2e** (6.69 g, 82%) as a colorless oil: IR (neat) 3306, 2930, 2856, 1071 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.20–1.42 (m, 10H), 1.45–1.54 (m, 2H), 1.58–1.67 (m, 2H), 1.86 (t, J = 2.8 Hz, 1H), 2.12 (dt, J = 2.8, 6.9 Hz, 2H), 3.06 (t, J = 6.9 Hz, 2H), 7.12–7.30 (m, 9H), 7.41–7.52 (m, 6H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 18.4, 26.2, 28.5, 28.7, 29.0, 29.4(2C), 30.0, 63.6, 68.0, 84.7, 86.3, 126.8, 127.6, 128.7 , 144.5; HRMS (ESI) calcd for $[C_{30}H_{34}NaO^+]$ ($[MNa^+]$) 433.2507; found 433.2516.

1-Allyalkoxy-5-hexyne (2g)

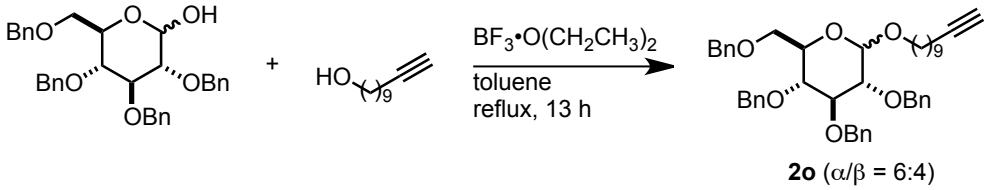


2g

To a stirring suspension of NaH (144 mg, 6.0 mmol) in THF (30 mL) at 0 ºC was slowly added 5-hexyl-1-ol (552 μL, 5.0 mmol). After the mixture was stirred for 15 min at 0 ºC, 3-bromo-1-propene (418 μL, 4.8 mmol) was slowly added to the mixture, and the mixture was stirred for 18 h at 25 °C. The reaction was quenched with sat. aq. NH_4Cl, the layers were separated, and the aqueous phase was extracted with diethyl ether. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The products was purified by SiO_2 column

chromatography (*n*-hexane only) to give **2g** (300 mg, 43%) as a colorless oil: IR (neat) 3300, 2116, 1647, 1107, 996, 915 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.70–1.60 (m, 4H), 1.94 (s, 1H), 2.19 (dt, J = 2.0, 6.8 Hz, 2H), 3.44 (t, J = 6.2 Hz, 2H), 3.95 (ddd, J = 1.2, 1.6, 5.6 Hz, 2H), 5.11 (ddt, J = 1.2, 1.7, 10.4 Hz, 1H), 5.22 (ddt, J = 1.6, 1.7, 17.2 Hz, 1H), 5.86 (ddt, J = 5.6, 10.4, 17.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 18.1, 25.1, 28.6, 68.3, 69.6, 71.7, 84.1, 116.6, 134.9; HRMS (EI) calcd for [$C_9H_{14}O^+$] ([M^+]) 138.1045; found 138.1049. These data are consistent with the literature values.[5]

(2*R*,3*R*,4*S*,5*R*)-3,4,5-Tris(benzyloxy)-2-[(benzyloxy)methyl]-6-(undec-10-yn-1-yloxy)tetrahydro-2*H*-pyran [2o]



2o (α/β = 6:4)

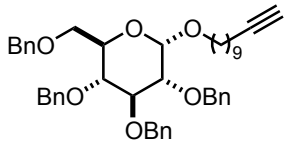
In a 100 mL two-necked flask equipped with a stirring bar and a condenser, tetrabenzyl D-glucose (2.44 g, 4.5 mmol), 10-undecyne-1-ol (5.0 mL, 26.1 mmol), and $BF_3{\cdot}OEt_2$ (170 μL, 1.38 mmol) were dissolved in toluene (30 mL). The mixture was refluxed for 13 h, and cooled to 25 °C. The mixture was evaporated, and the residue was purified by silica gel column chromatography (11% ethyl acetate in *n*-hexane) to afford **2o** (2.50 g, 80%, a mixture of isomers, α/β = 6:4[6]) as a colorless oil.

The α,β-mixture was purified by MPLC (Isolera One, Biotage, Ltd.; silica gel

[5] Granados-Focil, S.; Woudenberg, R. C.; Yavuzcetin, O.; Tuominen, M. T.; Coughlin, E. B. *Macromolecules* **2007**, *40*, 8708–8713.
[6] Vankaylapati, H.; Singh, G.; Tranoy, I. *Tetrahedron*: *Asymmetry* **2001**, *12*, 1373−1381.

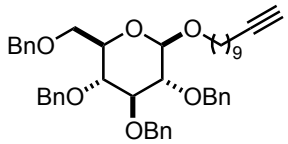
column, Biotage® SNAP Cartridge KP-Sil 50 g; eluent, diethyl ether/hexane 1:16–1:1 in 20 minute; flow rate, 50 mL/min.) to afford each isomer of **2o** in α (α/β = 99:1) and β (α/β = 7:93) forms.

2oα



Colorless oil; IR (ATR) 3294, 2924, 2858, 1065 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.23–1.41 (m, 10H), 1.47–1.54 (m, 2H), 1.57–1.67 (m, 2H), 1.93 (t, *J* = 2.8 Hz, 1H), 2.16 (dt, *J* = 2.8, 7.6 Hz, 2H), 3.38–3.44 (m, 1H), 3.55 (dd, *J* = 3.4, 9.6 Hz, 1H), 3.60–3.66 (m, 3H), 3.72 (dd, *J* = 3.4, 10.3 Hz, 1H), 3.76–3.80 (m, 1H), 3.99 (t, *J* = 9.7 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.60 (d, *J* = 12.4 Hz, 1H), 4.65 (d, *J* = 11.7 Hz, 1H), 4.74–4.85 (m, 4H), 4.99 (d, *J* = 10.3 Hz, 1H), 7.11–7.15 (m, 2H), 7.22–7.37 (m, 18H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 18.3, 26.1, 28.4, 28.7, 29.0, 29.3(2C), 68.1(2C), 68.5, 73.0, 73.4, 75.0, 75.6, 77.7, 80.1, 82.1, 84.7, 96.8, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 137.9, 138.2, 138.3, 138.9; HRMS (ESI) calcd for $[C_{45}H_{54}NaO_6^+]$ ($[MNa^+]$) 713.3813; found 713.3818.

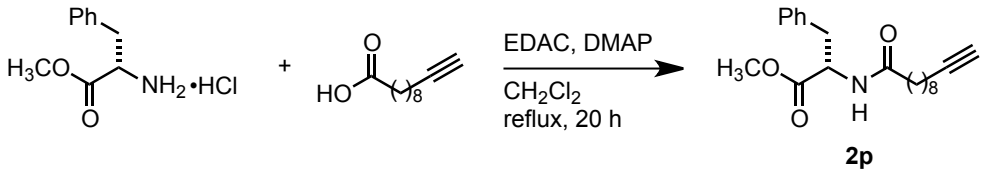
2oβ



Colorless oil; IR (ATR) 3294, 2927, 2858, 1068 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.24–1.44 (m, 10H), 1.47–1.53 (m, 2H), 1.60–1.69 (m, 2H), 1.93 (t, *J* = 2.8 Hz, 1H), 2.16 (dt, *J* = 2.8, 6.8 Hz, 2H), 3.42–3.49 (m, 2H), 3.50–3.59 (m, 2H), 3.61–3.69 (m, 2H), 3.74 (d, *J* = 11.0 Hz, 1H), 3.93–3.99 (m, 1H), 4.38 (d, *J* = 8.3 Hz, 1H), 4.51–4.57 (m,

2H), 4.61 (d, J = 12.4 Hz, 1H), 4.71 (d, J = 11.0 Hz, 1H), 4.78 (d, J = 11.0 Hz, 1H), 4.81 (d, J = 11.0 Hz, 1H), 4.92 (d, J = 11.0 Hz, 1H), 4.95 (d, J = 11.0 Hz, 1H), 7.14–7.17 (m, 2H), 7.24–7.36 (m, 18H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 18.4, 26.2, 28.5, 28.7, 29.0, 29.4(2C),29.8, 68.1, 69.0, 70.1, 73.5, 74.8, 74.9, 75.0, 75.7, 78.0, 82.3, 84.7, 84.8, 103.6, 127.6, 127.6, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 138.1, 138.2, 138.5, 138.6; HRMS (ESI) calcd for $[C_{45}H_{54}NaO_6^+]$ ($[MNa^+]$) 713.3813; found 713.3814.

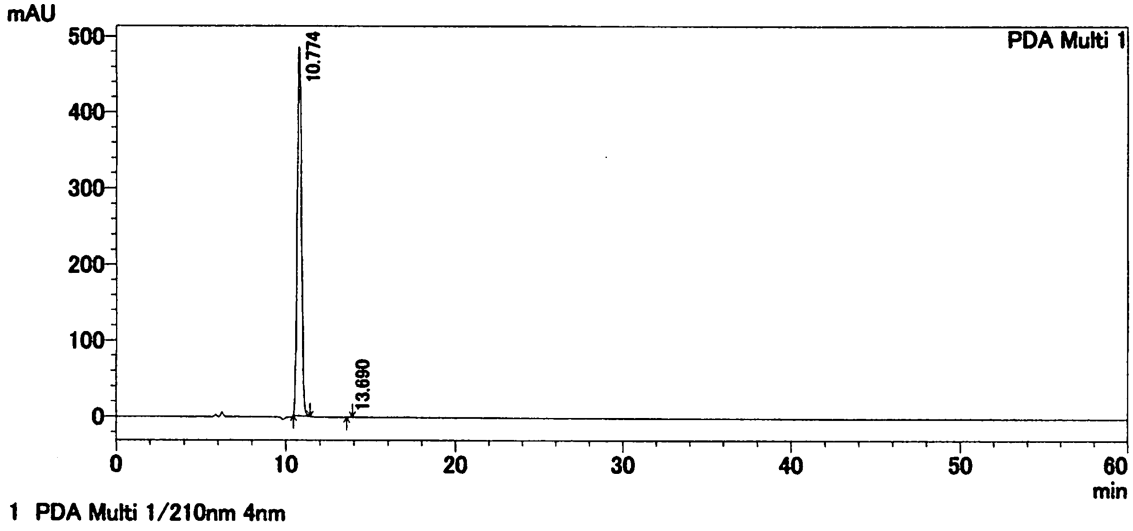
(*R*)-Methyl 3-phenyl-2-(undec-10-ynamido)propanoate (2p)



2p

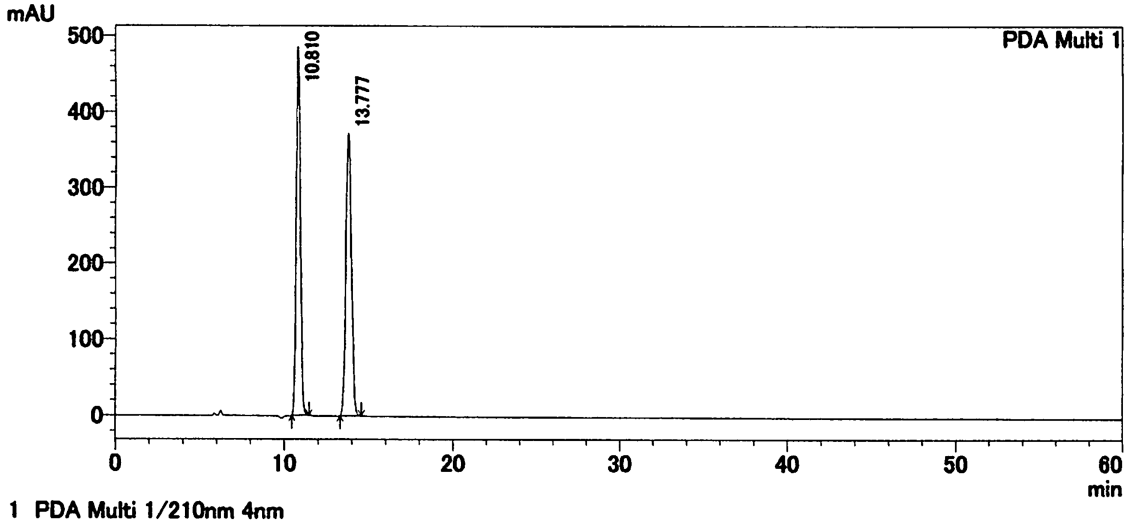
In a 50 mL two-necked flask equipped with a stirring bar and a condenser, undecynoic acid (397 mg, 2.2 mmol), L-phenylalanine methyl ester hydrochloride (474 mg, 2.2 mmol), EDAC (441 mg, 2.3 mmol), and DMAP (489 mg, 4.0 mmol) were dissolved in dry CH_2Cl_2 (8 mL). The mixture was refluxed for 20 h, and cooled to 25 °C. The reaction was quenched with water (20 mL). After the mixture was extracted with CH_2Cl_2 (3 × 20 mL), the combined organic phases were washed with sat. aq $NaHCO_3$ (10 mL) and brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (25% ethyl acetate in *n*-hexane) to afford **2p** (614.7 mg, 86%) as a colorless oil; IR (neat) 3292, 2931, 1747, 1650 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.24–1.40 (m, 8H), 1.48–1.60 (m, 4H), 1.93 (t, J = 2.8 Hz, 1H), 2.14–2.19 (m, 4H), 3.07 (dd, J = 6.2, 13.8 Hz, 1H), 3.15 (dd, J = 6.2, 13.8 Hz, 1H), 3.72 (s, 3H), 4.89 (ddd, J = 6.2, 6.2, 7.6 Hz, 1H), 5.96 (d, J = 7.6 Hz, 1H), 7.09 (d, J = 6.9 Hz, 2H), 7.22–7.30 (m, 3H); $^{13}C\{^{1}H\}$ NMR (150

MHz, $CDCl_3$) δ 18.3, 25.4, 28.3, 28.5, 28.8, 29.0, 29.1, 36.4, 37.8, 52.2, 52.8, 68.0, 84.6, 127.0, 128.4, 129.1, 135.8, 172.1, 172.5; HRMS (FAB) calcd for [$C_{21}H_{30}NO_3^+$] ([MH^+]) 344.2220; found 344.2231. HPLC (Daicel Chiralcel OD-H, hexane/2-propanol 80:20, 0.50 mL/min) t_R 10.8 min.



HPLC chart of 2p

Enantiomer of **2p** (*ent*-**2p**) was prepared similarly using D-phenylalanine methyl ester hydrochloride. A racemic mixture of **2p** and *ent*-**2p** was analyzed by HPLC [Daicel Chiralcel OD-H, hexane/2-propanol 80:20, 0.50 mL/min, t_R = 10.8 min (*R*), 13.8 min (*S*)].



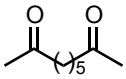
HPLC chart of a racemic mixture of 2p and *ent*-2p

4. Hydration of Terminal Alkynes 2 to Methyl Ketones 3

A Representative Procedure for Hydration of Terminal Alkynes: Decan-2-one (3a, Table 1, Entry 15)

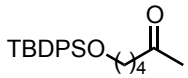
A mixture of alkyne **2a** (5.0 mmol, 691.0 mg), H_2O (22 mmol, 0.40 mL), **1** in CH_3OH (15 μmol, 8 mM, 1.88 mL), $HNTf_2$ in CH_3OH (15 μmol, 12 mM, 1.25 mL), and CH_3OH (1.88 mL) was heated at 80 °C for 12 h under air in a closed J. Young tube. The progress of the reaction was checked using TLC and GC. After the tube was cooled to 25 °C, *n*-hexane and water was added to the mixture. The layers were separated, and the aqueous phase was extracted with *n*-hexane. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by distillation (3.75 mmHg, 140 °C) to give **3a** as a colorless oil (749.0 mg, 96%): IR (neat) 1719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3H), 1.20–1.38 (m, 10H), 1.50–1.66 (m, 2H), 2.14 (s, 3H), 2.42 (t, J = 7.5 Hz, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 14.0, 22.6, 23.8, 29.1, 29.2, 29.3, 29.8, 31.8, 43.8, 209.3; LRMS (EI) *m/z*: 156 (M^+).

2,8-Nonanedione (3b)



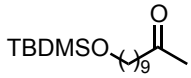
White solid, purified by recrystalization (from *n*-hexane); IR (neat) 1713, 1701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.22–1.28 (m, 2H), 1.53–1.60 (m, 4H), 2.13 (s, 6H), 2.44 (t, J = 7.5 Hz, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 23.3, 28.4, 29.8, 43.3, 208.8; HRMS (FAB) calcd for [$C_9H_{16}CsO_2^+$] ([MCs^+]) 289.0199; found 289.0212.

6-*tert*-Butyldiphenylsilyloxy-2-hexanone (3c)



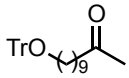
Colorless oil, purified by column chromatography on silica gel (5% ethyl acetate in *n*-hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.50–1.68 (m, 4H), 2.11 (s, 3H), 2.41 (t, J = 7.5 Hz, 2H), 3.68 (t, J = 6.3 Hz, 2H), 7.35−7.50 (m, 6H), 7.60–7.68 (m, 4H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 19.3, 20.4, 27.0, 29.9, 32.0, 43.5, 63.6, 127.7, 129.7, 134.1. 135.7, 209.1. LRMS (EI) *m/z*: 239 [Si(*t*-C_4H_9)(C_6H_5)$_2^+$].

11-[(*tert*-Butyldimethylsilyl)oxy]undecan-2-one (3d)



Colorless oil, purified by column chromatography on silica gel (5% ethyl acetate in *n*-hexane); IR (neat) 2929, 2856, 1719 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.89 (s, 9H), 1.25–1.34 (m, 10H), 1.48–1.60 (m, 4H), 2.12 (s, 3H), 2.41 (t, J = 7.6 Hz, 2H), 3.59 (t, J = 6.2 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ –5.5, 18.2, 23.7, 25.6, 25.8, 29.0, 29.2(2C), 29.3, 29.6, 32.7, 43.6, 63.0, 208.6; HRMS (ESI) calcd for [$C_{17}H_{37}O_2Si^+$] ([MH^+]) 301.2563; found 301.2583.

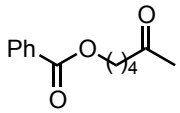
11-(Trityloxy)undecan-2-one (3e)



Colorless oil, purified by column chromatography on silica gel (5% ethyl acetate in *n*-hexane); IR (neat) 2929, 2854, 1717 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16–1.43 (m, 10H), 1.45–1.65 (m, 4H), 2.00 (s, 3H), 2.31 (t, J = 7.8 Hz, 2H), 3.06 (t, J = 6.4 Hz, 2H), 7.06–7.28 (m, 9H), 7.44 (t, J = 7.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 23.5, 26.0, 28.9, 29.1(2C), 29.2, 29.5, 29.8, 43.4, 63.3, 86.0, 126.5, 127.4, 128.4,

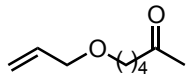
144.0, 208.5; HRMS (ESI) calcd for [$C_{30}H_{36}NaO_2^+$] ([MNa^+]) 451.2613; found 451.2626.

5-Oxohexyl benzoate (3f)



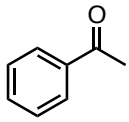
Colorless oil; IR (neat) 1718, 1274 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.65–1.80 (m, 4H), 2.14 (s, 3H), 2.44 (t, J = 6.9 Hz, 2H), 2.52 (t, J = 6.8 Hz, 2H), 4.32 (t, J = 6.2 Hz 2H), 7.35–7.60 (m, 3H), 8.02−8.04 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 20.1, 28.1, 29.8, 42.9, 64.4, 128.3, 129.4, 130.2, 132.8, 166.5, 208.3; HRMS (FAB) calcd for [$C_{13}H_{17}O_2^+$] ([MH^+]) 221.1178; found 221.1184.

1-(1-Propen-2-oxy)-5-heptanone (3g)



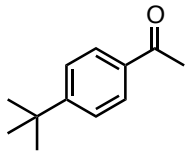
Colorless oil, purified by distillation (3.75 mmHg, 130 °C); IR (neat) 1718, 1106 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.60–1.70 (m, 4H) 2.13 (s, 3H), 2.46 (t, J = 6.8 Hz, 2H), 3.43 (t, J = 6.2 Hz, 2H), 3.95 (ddd, J = 1.3, 1.6, 5.7 Hz, 2H), 5.14 (ddt, J = 1.3, 1.7, 10.4 Hz, 1H), 5.23 (ddt, J = 1.6, 1.6, 17.2 Hz, 1H), 5.88 (ddt, J = 5.7, 10.4, 17.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 20.5, 29.1, 29.8, 43.4, 69.9, 71.7, 116.7, 134.9, 208.8; HRMS (FAB) calcd for [$C_9H_{17}O_2^+$] ([MH^+]) 157.1229; found 157.1229.

Acetophenone (3h)



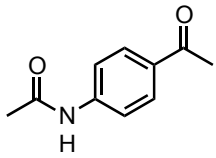
Colorless oil, purified by distillation (3.75 mmHg, 140 °C); IR (neat) 1684 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.60 (s, 3H), 7.40–7.59 (m, 3H), 7.92−8.01 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 26.5, 128.2, 128.5, 133.0, 137.0, 198.0; LRMS (EI) *m/z*: 120 (M^+).

4-*t*-Butylacetophenone (3i)



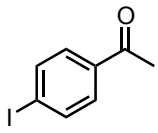
Colorless oil; IR (neat) 1678 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 9H), 2.58 (s, 3H), 7.40–7.50 (m, 2H), 7.90−8.00 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 26.5, 31.0, 35.0, 125.4, 128.2, 134.5, 156.7, 197.7; HRMS (FAB) calcd for [$C_{12}H_{16}NaO^+$] ([MNa^+]) 199.1093; found 199.1091.

***N*-Acetyl-4-acetoanilide (3j)**



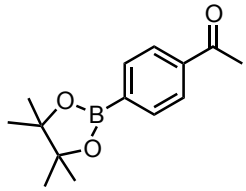
White solid; IR (neat) 3277, 1671 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.58 (s, 3H), 7.62−7.66 (m, 2H), 7.90−8.30 (m, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 24.8, 26.5, 118.8, 129.8, 132.8, 142.3, 168.6, 197.1; HRMS (EI) calcd for [$C_{10}H_{11}NO_2$] ([$M]^+$) 177.0790; found 177.0786.

4-Iodoacetophenone (3k)



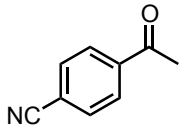
White solid; IR (neat) 1666 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58 (s, 3H), 7.65–7.84 (m, 4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 26.7, 101.3, 129.9, 136.5, 138.0, 197.4; HRMS (EI) calcd for $[C_8H_7IO]$ ($[M]^+$) 245.9542; found 245.9534.

1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethanone (3l)



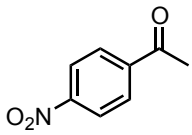
White solid; IR (neat) 2990, 1682 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.61 (s, 3H), 7.91 (m, 4H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 24.8, 26.6, 84.1, 127.2, 127.5, 164.8, 138.9, 198.3; HRMS (FAB) calcd for $[C_{14}H_{19}BO_3^+]$ ($[MH^+]$) 247.1506; found 247.1522.

4-Acetylbenzonitrile (3m)



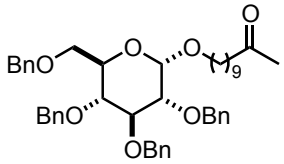
White solid; IR (neat) 1692 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.66 (s, 3H), 7.77−7.81 (m, 2H), 8.04−8.08 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 26.7, 116.3, 117.9, 128.6, 132.5, 139.8, 196.5; HRMS (FAB) calcd for $[C_9H_7CsNO^+]$ ($[MCs^+]$) 277.9577; found 277.9585.

4-Nitroacetophenone (3n)



White solid, purified by column chromatography on silica gel (50% CH_2Cl_2 in *n*-hexane); IR (neat) 1684, 1604, 1355, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.70 (s, 3H), 8.11−8.14 (m, 2H), 8.30−8.34 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 26.9, 123.8, 129.2, 141.3, 150.3, 196.3; HRMS (FAB) calcd for $[C_8H_7CsNO_3^+]$ ([MCs^+]) 297.9475; found 297.9476.

11-[[(2*S*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-[(benzyloxy)methyl]tetrahydro-2*H*-pyran-2-yl]oxy]undecan-2-one [3o(α/β = 99:1)]

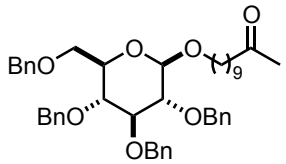


Pale yellow oil; IR (ATR) 2924, 2858, 1712, 1065 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22–1.40 (m, 10H), 1.50–1.69 (m, 4H), 2.11 (s, 3H), 2.40 (t, J = 7.8 Hz, 2H), 3.38–3.45 (m, 1H), 3.52–3.68 (m, 4H), 3.68–3.82 (m, 2H), 3.99 (t, J = 9.6 Hz, 1H), 4.47 (d, J = 11.9 Hz, 1H), 4.57–4.68 (m, 2H), 4.72–4.87 (m, 4H), 4.99 (d, J = 11.0 Hz, 1H), 7.10–7.17 (m, 2H), 7.19–7.40 (m, 18H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 23.8, 26.1, 29.2, 29.4, 29.8, 43.8, 68.2, 68.5, 70.1, 73.1, 73.5, 75.1, 75.7, 77.8, 80.1, 82.1, 96.9, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 138.0, 138.3, 138.4, 138.9, 209.3; HRMS (ESI) calcd for $[C_{45}H_{56}NaO_7^+]$ ([MNa^+]) 731.3918; found 731.3926.

The β isomer (**3o**β) was obtained and characterized by the hydration of **2o**(α/β = 6:4) followed by chromatographic separation using MPLC (Isolera One, Biotage, Ltd.; silica gel column, Biotage® SNAP Ultra 25 g; eluent, diethyl ether/hexane 1:16–1:1 in 27

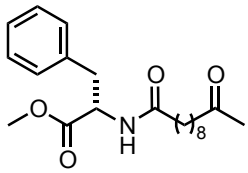
minute; flow rate, 25 mL/min.).

3oβ



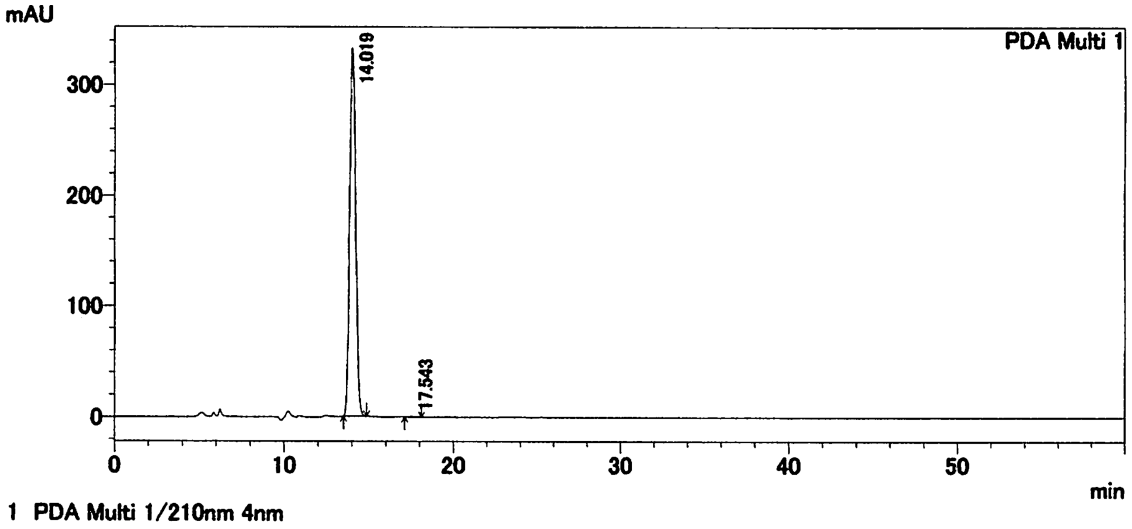
Colorless oil; IR (ATR) 2924, 2858, 1712, 1068 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.22–1.43 (m, 10H), 1.51–1.69 (m, 4H), 2.12 (s, 3H), 2.40 (t, J = 6.8 Hz, 2H), 3.42–3.49 (m, 2H), 3.49–3.60 (m, 2H), 3.60–3.70 (m, 2H), 3.74 (d, J = 11.0 Hz, 1H), 3.92–3.99 (m, 1H), 4.39 (d, J = 8.3 Hz, 1H), 4.51–4.63 (m, 3H), 4.71 (d, J = 11.0 Hz, 1H), 4.74–4.85 (m, 2H), 4.89–4.97 (m, 2H), 7.14–7.17 (m, 2H), 7.23–7.37 (m, 18H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 23.9, 26.2, 29.2, 29.4, 29.5, 29.8, 29.9, 43.9, 69.1, 70.2, 73.5, 74.8, 74.9, 75.1, 75.7, 78.0, 82.4, 84.8, 103.7, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.4, 138.2, 138.3, 138.6, 138.7; HRMS (ESI) calcd for [$C_{45}H_{56}NaO_7^+$] ([MNa^+]) 731.3918; found 731.3906.

(*R*)-Methyl 2-(10-oxoundecanamido)-3-phenylpropanoate (3p)



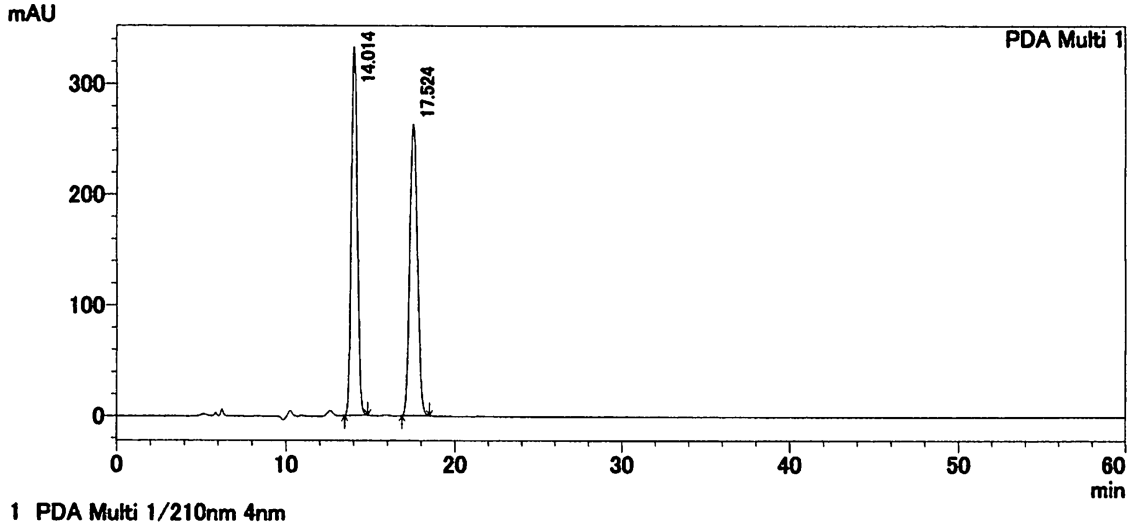
White solid, purified by recrystallization (from *n*-hexane); IR (neat) 3326, 2925, 1741, 1644 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20–1.39 (m, 8H), 1.50–1.66 (m, 4H), 2.07–2.23 (m, 5H), 2.41 (t, J = 7.8 Hz, 2H), 3.08 (dd, J = 6.0, 16.0 Hz, 1H), 3.14 (dd, J = 6.0, 16.0 Hz, 1H), 3.72 (s, 3H), 4.86–4.93 (ddd, J = 6.0, 6.0, 7.4 Hz, 1H), 5.93 (d, J = 7.4 Hz, 1H), 7.03–7.35 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 23.7, 25.4, 29.0, 29.1, 29.8, 36.4, 37.8, 43.7, 52.2, 52.8, 127.0, 128.5, 129.2, 135.9, 172.1, 172.5, 209.2;

HRMS (FAB) calcd for [$C_{21}H_{32}NO_4^+$] ([MH^+]) 362.2331; found 362.2329. HPLC (Daicel Chiralcel OD-H, hexane/2-propanol 80:20, 0.50 mL/min) t_R = 14.0 min.



HPLC chart of 3p

Enantiomer of **3p** was prepared by the hydration of the enantiomer of **2p**. A racemic mixture of **3p** and *ent*-**3p** was analyzed by HPLC [Daicel Chiralcel OD-H, hexane/2-propanol 80:20, 0.50 mL/min, t_R = 14.0 min (*R*), 17.5 min (*S*)].



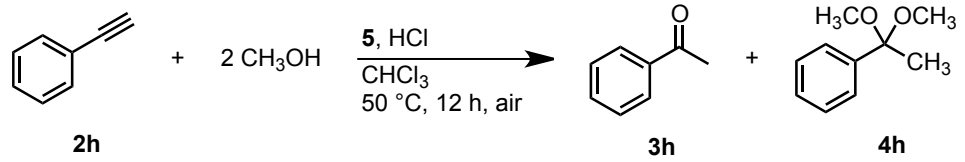
HPLC chart of a racemic mixture of 3p and *ent*-3p

Gram-Scale Hydration of 2b (Scheme 3)

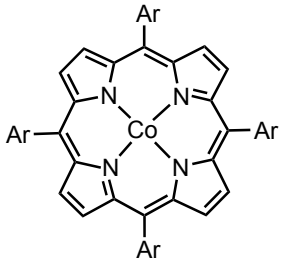
A mixture of **2b** (5.05 g, 6.32 mL, 42.0 mmol), **1** (0.251 mmol, 292.6 mg), $HNTf_2$ (0.126 mmol, 35.3 mg), H_2O (6.7 mL), and CH_3OH (42 mL) was heated at 80 °C for 12 h under air in a glass autoclave. After the autoclave was cooled to 25 °C, ethyl acetate and water was added to the mixture. The layers were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed several times with brine, dried over Na_2SO_4, and concentrated under reduced pressure. **3b** was obtained in 92% yield (6.03 g) as a pale yellow solid after recrystallization with *n*-hexane.

5. Tables

Table S1. Substituent Effect on the Aromatic Ring of Tetraaryl Porphyrins[a]



2h **3h** **4h**



5

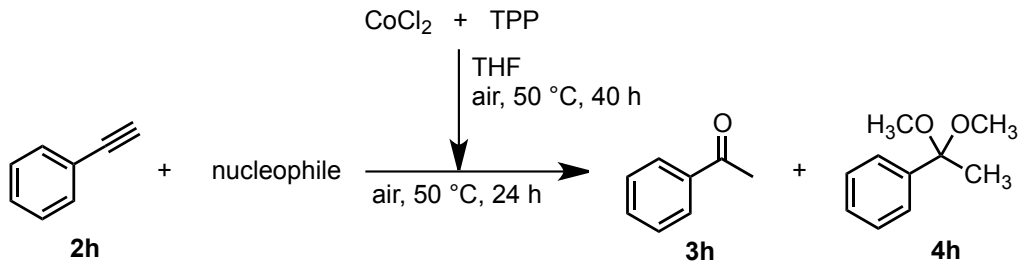
entry	Ar	yield of **3h** (%)[b]	yield of **4h** (%)[b]
1	C_6H_4-*p*-CO_2CH_3	4	90
2	C_6F_5	2	85
3	C_6H_4-*p*-SO_3Na	3	65
4	C_6H_5	4	63
5	C_6H_4-*p*-OH	2	19

[a]Molar ratio: **5**:HCl:**2h**: CH_3OH = 1:2:2000:22300. [**2h**]$_0$ = 1.82 M. [b]Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

Procedure for Table S1

A mixture of **2h** (2.0 mmol, 0.22 mL), 1,1,2,2-tetrachloroethane (50 μL), solution of HCl in CH_3OH (2.0 μmol, 10 mM, 0.2 mL), CH_3OH (22.3 mmol, 0.7 mL), and solution of **5** in $CHCl_3$ (1.0 μmol, 5.0 mM, 0.2 mL) was heated at 50 °C for 12 h under air in a closed J. Young tube. After the mixture was cooled to room temperature, an aliquot of the mixture was directly injected into a NMR tube, then yields of the products were determined by ^{1}H NMR.

Table S2. Addition of Water or Methanol to 2h[a]



entry	nucleophile (equiv.)	yield of **3h** (%)[b]	yield of **4h** (%)[b]
1	CH_3OH (2)	2	2
2	CH_3OH (10)	34	2
3	H_2O (2)	<1	<1
4	H_2O (10)	<1	1

[a]Molar ratio: $CoCl_2$:TPP:**2h** = 1:1:400. [**2h**]$_0$ = 1.0 M. [b]Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. TPP = 5,10,15,20-tetraphenyl-21*H*,23*H*-porphyrin. THF = tetrahydrofuran.

Procedure for Table S2

A mixture of TPP (10 μmol, 6.1 mg), THF (2 mL), and solution of $CoCl_2$ in THF (10 μmol, 5.0 mM, 2 mL) was heated at 50 °C for 40 h under air in a closed J. Young tube. After the catalyst solution was cooled to room temperature, **2h** (4.0 mmol, 0.44 mL) and nucleophile was added and heated at 50 °C for 24 h under air. After the reaction, 1,1,2,2-tetrachloroethane was added to the mixture. An aliquot of the mixture was directly injected into a NMR tube, then yields of the products were determined by ^{1}H NMR.

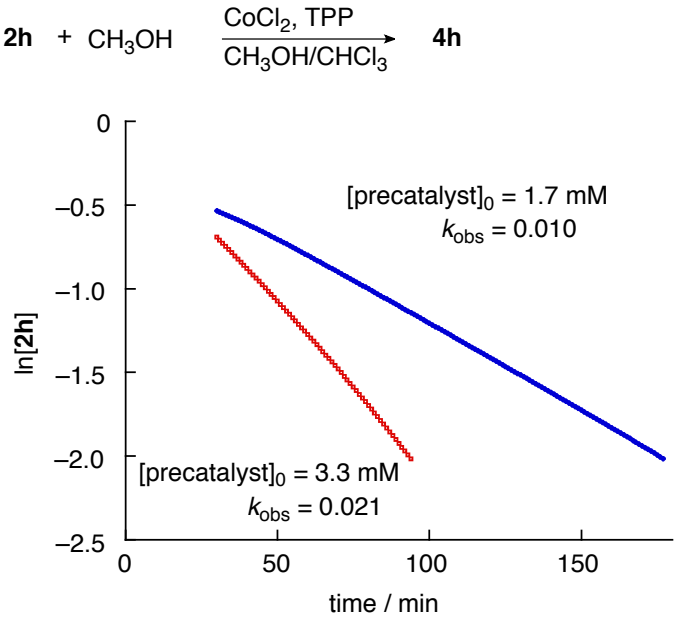
6. General Procedure for Kinetic Measurement Using Calorimeter

Reactions were performed using an Ominical SuperCRC reaction calorimeter. The instrument contains a differential scanning calorimeter (DSC), which compares the heat released or consumed in a sample vessel to a reference vessel. The reaction vessels were 16 mL borosilicate screw-thread vials fit with open-top black phenolic screw caps and white PTFE septa charged with PTFE stir bars. Sample volume did not exceed 3.5 mL. In a calorimetric experiment, **2h** and $CoCl_2$ was added to the reaction vessel with dry CH_3OH. The vessel containing the same amount of **2h** and CH_3OH was prepared as a reference vessel. The reaction vessel and reference vessel ware placed in the calorimeter and stirred until thermal equilibrium was reached. Two syringes containing 5 mM TPP solution in $CHCl_3$ and $CHCl_3$ were placed in the injection port of the reaction vessel and the reference vessel, respectively. These two syringes were allowed to thermally equilibrate (ca. 40 min). The reaction was initiated by injecting the solution to the reaction vessel and the reference vessel at the same time in order to remove the thermal difference. The temperature of DSC was monitored using internal thermometer in calorimeter and kept on 50–52 ºC. A raw data curve was produced by measuring the heat flow from the sample vessel every ten seconds during the reaction. After the reaction, the yields of the products were determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. A data curve was transformed into a square wave allowing for the response time of the instrument to be calculated using the WinCRC turbo software. The reaction rate, which is directly proportional to the heat flow, fraction conversion, and instantaneous concentration of reactants/products can all

be calculated from the data curve. Details of kinetic measurement using calorimeter are described in the literature.[7]

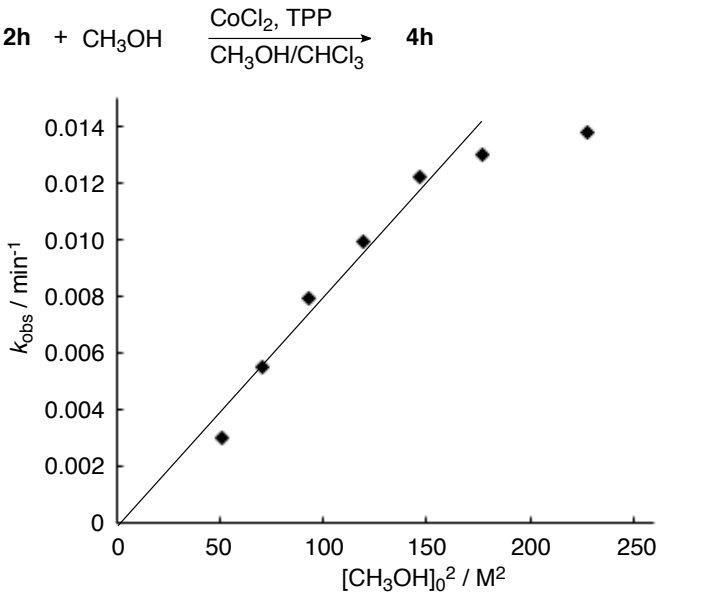
7. Figures

Figure S1. Determination of Reaction Order in [2h] and [precatalyst]



Conditions: $[\mathbf{2h}]_0$ = 0.67 M, $[CH_3OH]_0$ = 15 M, $[\text{precatalyst}]_0$ = $[CoCl_2]_0$ = $[TPP]_0$, T = 50 °C.

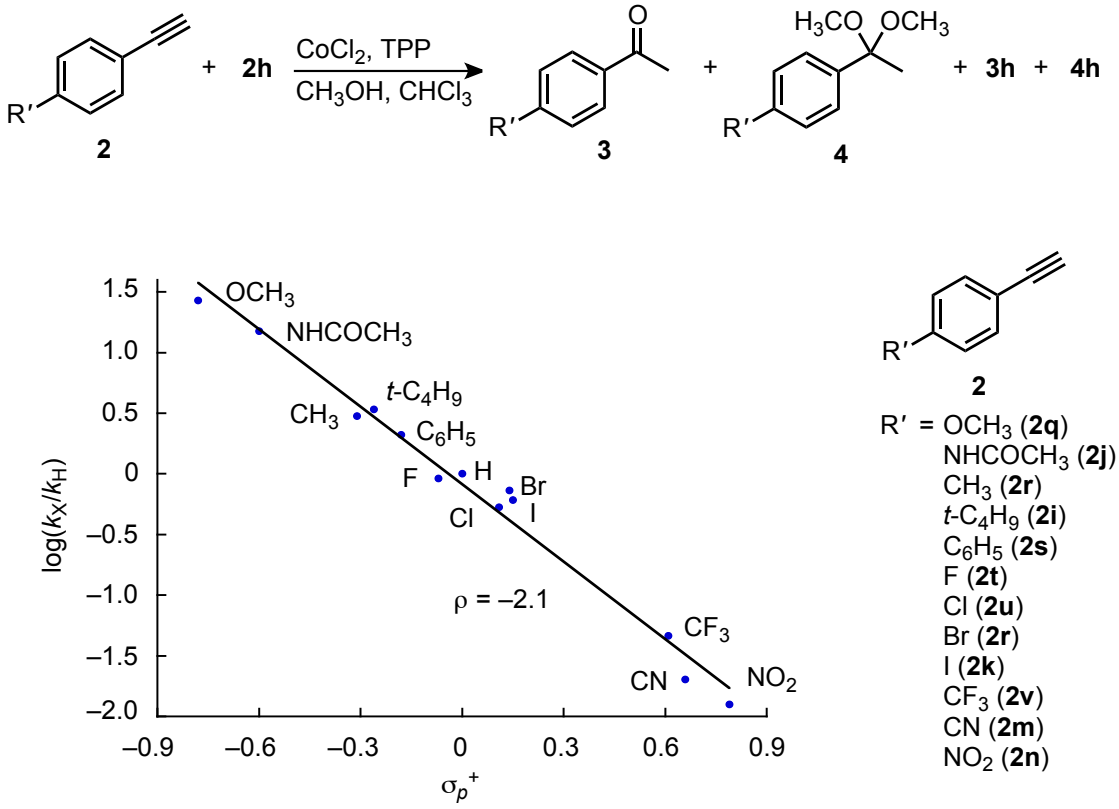
Figure S2. Determination of Reaction Order in [CH_3OH]



Conditions: $[\mathbf{2h}]_0$ = 1.0 M, $[CoCl_2]_0$ = $[TPP]_0$ = 2.5 mM, T = 50 °C.

[7] Blackmond, D. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 4302 – 4320.

Figure S3. Hammett Plot Analysis



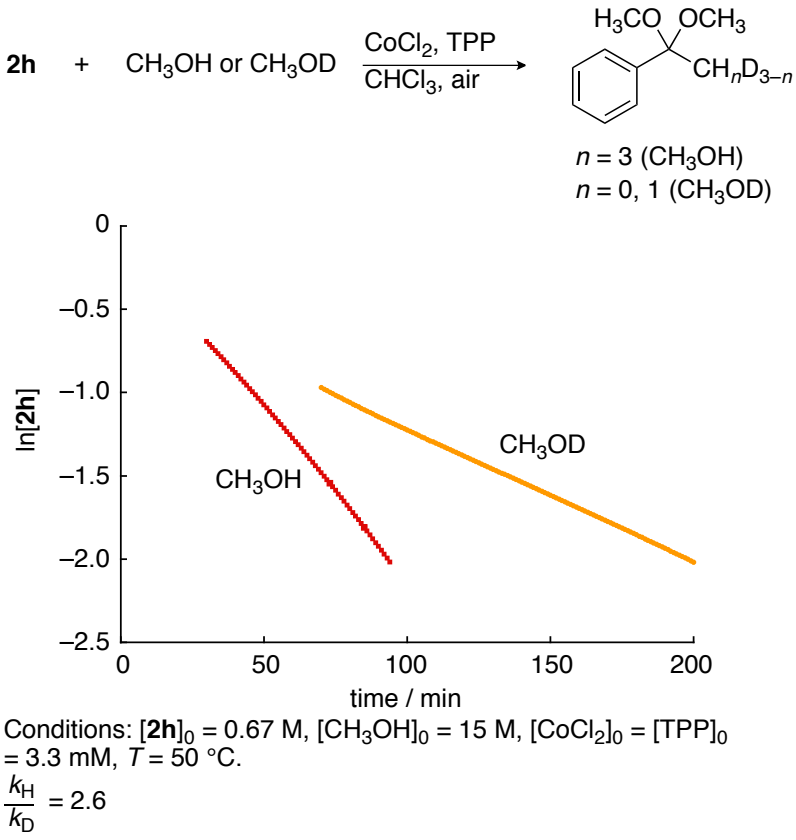
Conditions: $[\mathbf{2}]_0 = [\mathbf{2h}]_0 = 0.17$ mM, $[CH_3OH]_0 = 15$ M, $[\text{catalyst}]_0 = [CoCl_2]_0 = [TPP]_0$, $T = 50$ °C. Unless otherwise noted, reaction rate was measured using **2h** as an internal reference. Reaction rate for **2v**, **2n**, and **2m** were calibrated using **2r**, **2v**, and **2m**, respectively.

Procedure for Figure S3

A mixture of **2h** (0.22 mL, 2.0 mmol), **2** (0.5 mmol), CH_3OH (0.78 mL), $CoCl_2$ (5.0 mM in CH_3OH, 1mL, 5.0 μmol) and TPP (5.0 mM in $CHCl_3$, 1.0 mL, 5.0 μmol) was heated at 50 °C under air in the closed glass tube. The yields of **4h**, **4q**, **4j**, **4r**, **4i**, **4s**, **4t**, **4u**, **4r**, **4k**, **4v**, **4m**, and **4n** were determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard based on the signals at 1.54 ppm (s, 3H), 1.53 ppm (s, 3H), 1.53 ppm (s, 3H), 1.52 ppm (s, 3H), 1.59 ppm (s, 3H), 1.59 ppm (s, 3H), 1.53 ppm (s, 3H), 1.52 ppm (s, 3H), 1.52 ppm (s, 3H), 1.51 ppm (s, 3H), 1.55 ppm (s, 3H), 1.55 ppm (s, 3H), and 1.53 ppm (s, 3H), respectively. The yields of **3h**, **3q**, **3j**, **3r**, **3i**, **3s**, **3t**, **3u**, **3r, 3k**, **3v**, **3m**, and **3n** were determined based on the signals at

2.60 ppm (s, 3H), 2.57 ppm (s, 3H), 2.42 ppm (s, 3H), 2.59 ppm (s, 3H), 2.67 ppm (s, 3H), 2.67 ppm (s, 3H), 2.61 ppm (s, 3H), 2.61 ppm (s, 3H), 2.60 ppm (s, 3H), 2.60 ppm (s, 3H), 2.67 ppm (s, 3H), 2.67 ppm (s, 3H), and 2.71 ppm (s, 3H), respectively.

Figure S4. Kinetic Isotope Effect



Conditions: $[\mathbf{2h}]_0$ = 0.67 M, $[CH_3OH]_0$ = 15 M, $[CoCl_2]_0$ = $[TPP]_0$ = 3.3 mM, T = 50 °C.

$\frac{k_H}{k_D}$ = 2.6

Procedure for Figure S4

According to the general procedure on kinetic measurement using calorimeter, **1a** (0.22 mL, 2.0 mmol) and CH_3OD (0.78 mL) were charged both in the reaction vessel and the reference vessel. $CoCl_2$ (10 mM in CH_3OD, 1mL, 10 μmol) and CH_3OD (1.0 mL) were added to the reaction vessel and the reference vessel respectively, and the reaction was started by adding TPP (10 mM in $CHCl_3$, 1.0 mL, 10 μmol) and $CHCl_3$ (1.0 mL) to the reaction vessel and the reference vessel, respectively. After the kinetic measurement, ^1H

NMR and GCMS analysis of the reaction mixture indicated consumption of **1a** (100 %), and the presence of (2,2-D_2)**2a**, (2,2,2-D_3)**2a**, (2,2-D_2)**3a**, and (2,2,2-D_3)**3a**.