Supporting Information

Iron-Catalyzed Carbometalation of Propargylic and Homopropargylic alcohols

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Method and Materials

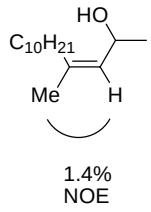
General. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly purified solvents. Solvents were purified using solvent purification columns purchased from Glass Contour, Laguna Beach, CA. All reactions were monitored by thin-layer chromatography with E. Merck silica gel 60 F254 pre-coated plates (0.25 mm). Gas chromatography (GC) was performed on an HP 6890N autosampling GC with an HP-5 capillary column and equipped with a FID detector. Flash chromatography was performed with indicated solvents using silica gel (particle size 0.032-0.063 μm) purchased from Sorbent Technologies.^{1}H and ^{13}C NMR spectra were recorded on Varian Inova-400 or Mercury-300 spectrometer. Chemical shift are reported relative to internal chloroform or methanol ($CDCl_3$: ^{1}H, δ = 7.27, ^{13}C, δ = 77.26 and CD_3OD: ^{1}H, δ = 3.31, ^{13}C, δ = 49.15). Coupling constants are in Hz and are reported as d (doublet), t (triplet), q (quartet), sep (septet). For signals having multiple coupling patterns, the coupling constant are listed in the same order as the pattern (e.g. dt, J = 2.0, 4.0; 2.0 is the coupling constant for the doublet and 4.0 is for the coupling constant for the triplet). Infrared spectra were recorded on a Perkin- Elmer 1000 series FTIR. Low-resolution mass spectra were acquired on a Shimadzu QP5000 GC/MS using the indicated ionization method. HPLC analyses were carried out on a Shimadzu LC-2010A system. Optical rotations were measured on a Rudolph Research Analytical Autopol® IV Polarimeter

Materials

All propargylic alcohols and homopropargylic alcohols were prepared by addition of alkynes to aldehydes except otherwise noted. CH_3MgBr and EtMgBr were titrated before use. $Fe(acac)_3$ and $Fe(ehx)_3$ were used as received from SigmaAldrich and Alfa Aesar, respectively.

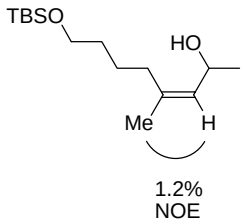
General procedure for carbomagnesiation reactions (Table 2). Grignard reagent (5 equiv) was added to Fe salt, +/- ligand (1 equiv to Fe; see below), alkyne and solvent at –78 ^{o}C. The resulting black mixture was warmed to 0 ^{o}C and stirred for 7h at this temperature. After cooling to –78 ^{o}C, aqueous ammonium chloride and diluted with ether were added. The organic layer was separated and the aqueous layer was extracted with ether. Triethyl amine[1] (3 mL) was added to the combined organic phases, and they were dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel. Reagent amounts, purification conditions and characterization data are provided below for all entries in Table 2.

Characterization data for synthetic new compounds and reaction details.



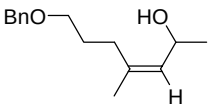
(*Z*)-4-Methyltetradec-3-en-2-ol (Table 2, entry 1):

CH_3MgBr (0.67 mL, 2.0 mmol); $Fe(ehx)_3$ (0.069 mL, 0.080 mmol); DPPE (32 mg, 0.080 mmol); tetradec-3-yn-2-ol (84 mg, 0.40 mmol); THF (5.0 mL). Chromatography (5.0% EtOAc in hexane) provided 67 mg (75% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.89 (t, *J* = 6.8, 3H), 1.23 (d, *J* = 6.0, 3H), 1.27 (br. s, 14H), 1.27-1.43 (m, 2H), 1.70 (s, 3H), 2.00-2.20 (m, 2H), 4.58 (dq, *J* = 8.8, 6.0, 1H), 5.20 (d, *J* = 8.8, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 22.9, 23.6, 24.0, 28.6, 29.6, 29.8 (x2), 32.1, 32.4, 64.6, 129.8, 138.7. FTIR (thin film) 3364, 2924, 1622cm^{-1}. MS (EI) 226 $[M]^+$.



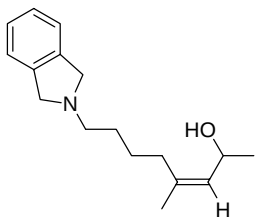
(*Z*)-8-(tert-Butyldimethylsilyloxy)-4-methyloct-3-en-2-ol (Table 2, entry 2):

CH_3MgBr (0.67 mL, 2.0 mmol); $Fe(ehx)_3$ (0.069 mL, 0.080 mmol); DPPE (32 mg, 0.080 mmol); 8-(*tert*-butyldimethylsilyloxy) oct-3-yn-2-ol (103 mg, 0.40 mmol); THF (5.0 mL) Chromatography (5.0% EtOAc in hexane) provided 87 mg (80% yield) of colorless oil. ^1H NMR ($CDCl_3$) = 0.05 (s, 6H), 0.89 (s, 9H), 1.22 (d, J = 6.4, 3H), 1.41-1.57 (m, 4H), 1.69 (d, J = 1.2, 3H), 2.06 (dd, J = 8.8, 6.0, 1H), 2.14 (dd, J = 8.4, 13.2, 1H), 3.61, (t, J = 6.0, 2H), 4.56 (dq, J = 8.8, 6.0, 1H), 5.21 (d, J = 8.8, 1H). ^{13}C NMR ($CDCl_3$) = -5.06, 18.6, 23.5, 24.0, 24.7, 26.2, 321, 32.8, 63.1, 64.6, 130.1, 138.3. FTIR (thin film) 3344, 2955, 2859, 2930, 1667cm^{-1}. MS (EI) 215 $[M-^tBu]^+$.



(*Z*)-7-(Benzyloxy)-4-methylhept-3-en-2-ol (Table 2, entry 3):

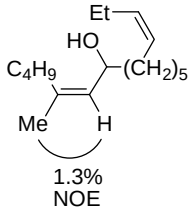
CH_3MgBr (0.67 mL, 2.0 mmol); $Fe(ehx)_3$ (0.10 mL, 0.12 mmol); DPPE (48 mg, 0.12 mmol); 7-(benzyloxy)hept-3-yn-2-ol (87 mg, 0.40 mmol); THF (5.0 mL); Chromatography (20% EtOAc in hexane) provided 66 mg (70% yield) of colorless oil. ^1H NMR ($CDCl_3$) = 1.22 (d, J = 6.0, 3H), 1.71 (s, 3H), 1.70-1.77 (m, 2H), 2.15 (dt, J = 13.6, 6.8, 1H), 2.90 (dt, J = 13.6, 8.0, 1H), 3.40-3.50 (m, 2H), 4.51 (s, 2H), 4.58 (dq, J = 8.4, 6.0 1H), 5.27 (d, J = 8.4, 1H), 7.30-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) = 23.3, 23.8, 27.8, 28.5, 64.1, 69.3, 72.9, 127.9 (x 2), 128.7, 131.0, 137.4, 138.5. FTIR (thin film) 3401, 3030, 1667, 1101cm^{-1}. MS (EI) 216 $[M-H_2O]^+$.



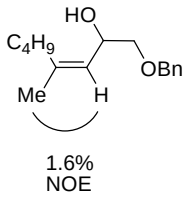
(*Z*)-8-(Isoindolin-2-yl)-4-methyloct-3-en-2-ol (Table 2, entry 4):

CH_3MgBr (0.67 mL, 2.0 mmol); $Fe(acac)_3$ (28 mg, 0.080 mmol); DPPE (32 mg, 0.080 mmol); 8-(isoindolin-2-yl)oct-3-yn-2-ol (97

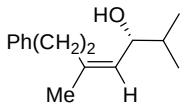
mg, 0.40 mmol); THF (5.0 mL); Chromatography (33% EtOAc in hexane) provided 81 mg (78% yield) of yellow oil. ^{1}H NMR ($CDCl_3$) = 1.22 (d, *J* = 6.0, 3H), 1.41-1.68 (m, 4H), 1.72 (d, *J* = 1.5, 3H), 1.84-2.04 (m, 2H), 2.06-2.30 (m, 2H), 2.72 (dt, *J* = 2.4, 6.9, 2H), 3.92 (s, 4H), 4.57 (qd, *J* = 6.3, 9.0, 1H), 5.23 (dd, *J* = 0.6, 9.0, 1H), 7.19 (br. s, 4H). ^{13}C NMR ($CDCl_3$) = 23.6, 24.1, 26.0, 28.7, 32.0, 56.1, 59.3, 64.4, 122.5, 126.9, 130.5, 137.8, 140.2. FTIR (thin film) 3378, 2933, 2789, 1675 cm^{-1}. MS (EI) 241 $[M\text{-}H_2O]^+$.



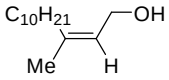
(*5Z, 13Z*)-5-Methylhexadeca-5, 13-dien-7-ol (Table 2, entry 5): CH_3MgBr (0.83 mL, 2.5 mmol); $Fe(acac)_3$ (53 mg, 0.15 mmol); DPPE (60 mg, 0.15 mmol); (*Z*)-hexadec-13-en-5-yn-7-ol (118 mg, 0.50 mmol); THF (5.0 mL); Chromatography (5.0% EtOAc in hexane) provided 107 mg (85% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.91 (t, *J* = 7.2, 3H), 0.95 (t, *J* = 7.6, 3H), 1.24-1.44 (m, 12H), 1.71 (d, *J* = 1.2, 3H), 2.00-2.11 (m, 6H), 4.34 (dt, *J* = 8.8, 6.4, 1H), 5.15 (d, *J* = 8.8, 1H), 5.28-5.39 (m, 2H). ^{13}C NMR ($CDCl_3$) = 14.2, 14.6, 20.7, 22.9, 23.6, 25.6, 27.2, 29.4, 29.9, 30.8, 32.2, 38.0, 68.4, 128.8, 129.4, 131.8, 139.5. FTIR (thin film) 3340, 3006, 1667 cm^{-1}. MS (EI) 252 $[M]^+$.



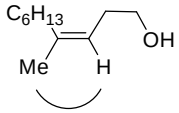
(*Z*)-1-(Benzyloxy)-4-methyloct-3-en-2-ol (Table 2, entry 6): CH_3MgBr (0.83 mL, 2.5 mmol); $Fe(acac)_3$ (27 mg, 0.075 mmol); 1-(benzyloxy)oct-3-yn-2-ol (116 mg, 0.50 mmol); THF (5.0 mL); Chromatography (10 % EtOAc in hexane) provided 100 mg (81% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.90 (t, *J* = 6.9, 3H), 1.26-1.42 (m, 4H), 1.72 (d, *J* = 1.5, 3H), 2.00-2.12 (m, 2H), 3.36 (appr. t, *J* = 9.0, 1H), 3.45 (dd, *J* = 3.3, 9.6, 1H), 4.56-4.63 (m, 3H), 5.13 (d, *J* = 9.0, 1H), 7.30-7.37 (m, 5H). ^{13}C NMR ($CDCl_3$) = 14.2, 22.9, 23.7, 30.8, 32.5, 67.5, 73.5, 74.6, 123.3, 128.0, 128.7, 138.2, 142.0. FTIR (thin film) 3433, 3064, 3031, 2859, 1668 cm^{-1}. MS (EI) 248 $[M]^+$.



(*R, Z*)-2, 5-Dimethyl-7-phenylhept-4-en-3-ol (Table 2, entry 7): CH_3MgBr (0.83 mL, 2.5 mmol); $Fe(acac)_3$ (53 mg, 0.15 mmol); (R)-2-methyl-7-phenylhept-4-yn-3-ol[2] (101 mg, 0.50 mmol, 99% ee); THF (5.0 mL); Chromatography (5.0 % EtOAc in hexane) provided 66 mg (61% yield) of colorless oil. 99% ee as determined by HPLC analysis (Chiralcel OD-H, 2.0 % ^{i}PrOH in hexane, 210 nm). $[\alpha]_D^{20}$ = -7.3 (*c* = 0.22, $CHCl_3$). ^{1}H NMR ($CDCl_3$) = 0.75 (br. s, 1H), 0.79 (d, *J* = 6.8, 3H), 0.89 (d, *J* = 6.8, 3H), 1.52-1.60 (o, J = 6.8, 1H), 1.82 (d, J = 0.8, 3H), 2.35 (td, J = 7.2, 13.2, 1H), 2.48 (td, J = 8.0, 13.2, 1H), 2.68-2.80 (m, 2H), 3.81 (dd, J = 6.8, 9.2, 1H), 5.20 (d, J = 9.2, 1H), 7.20-7.33 (m, 5H). ^{13}C NMR ($CDCl_3$) = 18.4, 18.6, 23.6, 34.1, 34.4, 34.5, 73.3, 126.3, 128.2, 128.6, 128.8, 138.2, 142.1. FTIR (thin film) 3582, 3391, 3063, 1666, 1603 cm^{-1}. MS (EI) 175 $[M\text{-}C_3H_7]^+$.

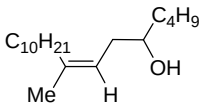


(*Z*)-3-Methyltridec-2-en-1-ol (Table 2, entry 8): CH_3MgBr (0.67 mL, 2.0 mmol); $Fe(ehx)_3$ (0.1 mL, 0.12 mmol); DPPE (60 mg, 0.12 mmol); 2-tridecyn-1-ol[3] (78 mg, 0.40 mmol); THF (5.0 mL); Chromatography on silica gel (3.0% EtOAc in hexane) provided 68 mg (80% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.89 (t, *J* = 6.8, 3H), 1.27-1.42 (m, 16H), 1.74 (d, *J* = 0.4, 3H), 2.07 (t, *J* = 8.0, 2H), 4.13 (d, *J* = 7.2, 2H), 5.42 (t, *J* = 7.2, 1H). ^{13}C NMR ($CDCl_3$) = 14.4, 22.9, 23.7, 28.6, 29.6, 29.8, 29.9, 32.1 (x 2), 59.4, 124.1, 140.9. FTIR (thin film) 3330, 2924, 2854, 1667 cm^{-1}. MS (EI) 212 $[M]^+$.



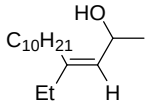
(*Z*)-4-Methyldec-3-en-1-ol (Table 2, entry 9): CH_3MgBr (0.83 mL, 2.5 mmol); $Fe(acac)_3$ (35 mg, 0.10 mmol); 3-decyne-1-ol (77 mg, 0.50 mmol); toluene (5.0 mL); Chromatography on silica gel (10% EtOAc in hexane) provided 64 mg (75% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.88 (t, *J* = 6.4, 3H), 1.27- 1.38 (m, 8H), 1.71 (s, 3H), 2.04 (t, *J* =

7.2, 2H), 2.27 (q, J = 6.8, 2H), 3.61 (t, J = 6.4, 2H), 5.11 (t, J = 7.2, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 22.9, 23.8, 28.3, 29.5, 31.6, 32.0, 32.1, 62.9, 120.4, 139.7. FTIR (thin film) 3330, 2928, 2958 cm^{-1}. MS (EI) 170 $[M]^+$.



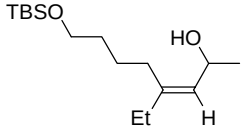
(*Z*)-8-Mmethyloctadec-7-en-5-ol (Table 2, entry 10):

CH_3MgBr (0.67 mL, 2.0 mmol); $Fe(acac)_3$ (28 mg, 0.080 mmol); octadec-7-yn-5-ol (115 mg, 0.40 mmol); toluene (5.0 mL); Chromatograph on silica gel (2.0% EtOAc in hexane) provided 84 mg (74% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.89 (t, J = 6.8, 3H), 0.92(t, J = 6.8, 3H), 1.22-1.50 (m, 22H), 1.97-2.10 (m, 2H), 2.16 (t, J = 7.6, 2H), 3.58 (m, 1H), 5.16 (t, J = 7.2, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 14.4, 22.9, 23.0, 23.9, 28.2, 28.3, 29.6, 29.8, 29.9, 32.1, 32.2, 36.2, 36.8, 72.0, 120.6, 139.8. FTIR (thin film) 3340, 2956, 2925, 2854 cm^{-1}. MS (EI) 283 $[M+H]^+$.



(*Z*)-4-Ethyltetradec-3-en-2-ol (Table 2, entry 11):

EtMgBr (0.63 mL, 2.0 mmol); $Fe(acac)_3$ (28 mg, 0.080 mmol); tetradec-3-yn-2-ol (84 mg, 0.40 mmol); THF (5.0 mL) and NMP (0.10 mL); Chromatography on silica gel (3.0% EtOAc in hexane) provided 68 mg (70% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.87 (t, J = 6.4, 3H), 0.99 (t, J = 7.2, 3H), 1.22-1.40 (m, 16H), 2.00 (dq, J = 0.8, 7.6, 2H), 1.98-2.14 (m, 2H), 4.58 (qd, J = 6.0, 8.8, 1H), 5.16 (d, J = 8.8, 1H). ^{13}C NMR ($CDCl_3$) = 13.1, 14.7, 23.3, 24.5, 29.5, 29.8, 29.9, 30.1, 30.2, 30.4, 31.3, 32.5, 65.0, 128.2, 144.5. FTIR (thin film) 3334, 2925, 2854, 2963 cm^{-1}. MS (EI) 240 $[M]^+$.

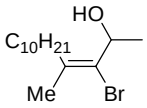


(*Z*)-8-(*tert*-Butyldimethylsilyloxy)-4-ethyloct-3-en-2-ol (Table 2, entry 12):

EtMgBr (0.63 mL, 2.0 mmol); $Fe(acac)_3$ (28 mg, 0.080 mmol); 8-(*tert*-butyldimethylsilyloxy)oct-3-yn-2-ol (103 mg, 0.40 mmol); THF (5.0 mL) and NMP (0.10 mL); Chromatography on silica gel (5.0% EtOAc in hexane) to provide 85 mg (74% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.05 (s, 6H), 0.89 (s, 9H), 1.00 (t, *J* = 7.2, 3H), 1.24 (d, *J* = 6.4, 3H), 1.18-1.52 (m, 4H), 2.01 (qd, *J* = 7.2, 1.2, 2H), 2.00-2.17 (m, 2H), 3.62 (t, *J* = 6.0, 2H), 4.59 (qd, *J* = 6.4, 8.8, 1H), 5.19 (d, *J* = 8.8, 1H). ^{13}C NMR ($CDCl_3$) = -5.1, 12.7, 18.6, 24.1, 25.3, 26.2, 29.4, 30.7, 33.0, 63.1, 64.6, 128.2, 143.8. FTIR (thin film) 3350, 2859, 1665 cm^{-1}. MS (EI) 229 $[M-^tBu]^+$.

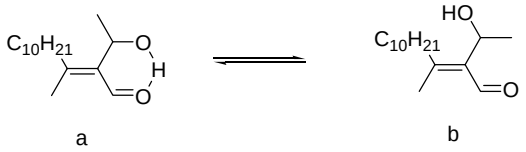
Synthesis of tetrasubstituted olefins. Scheme 2

(*E*)-3-Bromo-4-methyltetradec-3-en-2-ol (Scheme 2):



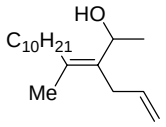
CH_3MgBr (0.67 mL, 2.0 mmol) was added drop-wise to a black solution of $Fe(ehx)_3$ (0.050 mL, 0.060 mmol) and tetradec-3-yn-2-ol (84 mg, 0.40 mmol) in THF (5.0 mL) at –78 ^{o}C. The resulting brown mixture was stirred at 0 ^{o}C for 7h and then cooled to –78 ^{o}C. A solution of anhydrous $ZnCl_2$ (273 mg, 2.0 mmol) in THF (2.0 mL) was added and the mixture was warmed up to 0 ^{o}C for 10 min. After that, the mixture was cooled to -78 ^{o}C and a solution of NBS (391 mg, 2.2 mmol) in THF (4.0 mL) was added. After 2h at -78 ^{o}C, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. Triethyl amine (3 mL) was added to the combined organic phases, and they were dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel (3% EtOAc in hexane) to provide 77mg (65% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.88 (t, *J* = 6.8, 3H), 1.32 (d, *J* = 6.4, 3H), 1.26 (br. s, 14H), 1.37-1.45 (m, 2H), 1.88 (s, 3H), 1.91-1.93 (m, 1H), 2.16 (ddd, *J* = 5.6, 9.2, 13.2, 1H), 2.25 (ddd, *J* = 8.4, 9.2, 13.2, 1H), 4.70 (q, *J* = 6.0, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 22.9,

23.5, 24.1, 28.7, 29.5, 29.7, 29.8 (x 2), 32.1, 35.3, 66.6, 129.0, 136.5. FTIR (thin film) 3369, 2925, 2854, 1639 cm^{-1}. MS (EI) 304 $[M]^+$.



(*E*)-2-(1-Hydroxyethyl)-3-methyltridec-2-enal (Scheme 2):

CH_3MgBr (0.67 mL, 2.0 mmol) was added drop-wise to a black solution of $Fe(ehx)_3$ (0.050 mL, 0.060 mmol) and tetradec-3-yn-2-ol (84 mg, 0.40 mmol) in THF (5.0 mL) at –78 ^oC. The resulting brown mixture was stirred at 0 ^oC for 7h and then cooled to –78 ^oC. Neat DMF (0.30 mL, 4.0 mmol) was added and the reaction mixture was warmed up to 0 ^oC and stirred overnight. The reaction was quenched by adding aqueous ammonium chloride and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. Triethyl amine (3 mL) was added to the combined organic phases, and they were dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel (5.0 % EtOAc in hexane) to provide 51 mg (50 % yield) of colorless oil. ^1H NMR ($CDCl_3$) = 0.89 (t, *J* = 6.9, 3H), 1.20-1.60 (m, 19H), 1.98 (s, Me-b), 2.19 (s, 3H, Me-a), 2.24 (dt, *J* = 2.4, 8.1, 2H), 2.54 (appr. t, *J* = 6.6, allylic methylene-b), 4.69 (dq, *J* = 1.8, 6.3, 1H), 10.1 (d, *J* = 2.1, 1H), 10.05 (d, *J* = 2.4, H_bCO). ^{13}C NMR ($CDCl_3$) = 14.3, 18.3, 21.2(b), 22.9, 23.2(b), 23.7, 28.2, 29.5, 29.6, 29.7, 29.8, 30.1, 32.1, 33.8(b), 36.6, 67.0, 67.4(b), 138.0, 160.6, 193.2(b), 194.0. FTIR (thin film) 3457, 2926, 1652, 1620 cm^{-1}. MS (EI) 236 $[M-H_2O]^+$.

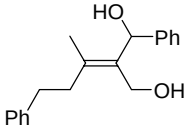


(*Z*)-3-Allyl-4-methyltetradec-3-en-2-ol (Scheme 2):

CH_3MgBr (0.67 mL, 2.0 mmol) was added drop-wise to a black solution of $Fe(ehx)_3$ (0.050 mL, 0.060 mmol) and tetradec-3-yn-2-ol (84 mg, 0.40 mmol) in THF (5.0 mL) at – 78 ^oC. The resulting brown mixture was warmed up to 0 ^oC and stirred for 7h and then cooled to –20 ^oC. A solution of $CuCN{\cdot}2LiCl$ (0.40

mmol) in THF (2.0 mL) was added and stirred for 10 min then neat allyl bromide (0.35 mL, 4.0 mmol) was added. After 3h at – 20 ^{o}C, the reaction mixture was quenched by adding aqueous ammonium chloride and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. Triethyl amine (3 mL) was added to the combined organic phases, and they were dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel (5.0 % EtOAc in hexane) to provide 65 mg (61 % yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.88 (t, *J* = 6.4 3H), 1.21 (d, *J* = 6.4, 3H), 1.27-1.40 (m, 16H), 1.64 (s, 3H), 2.00-2.05 (m,1H), 2.07-2.16 (m, 1H), 2.88 (dq, *J* = 6.4, 16.4, 2H), 4.88 (q, *J* = 6.4, 1H), 4.98 (s, 1H), 4.99 (dd, *J* = 1.6, 25.6, 1H), 5.86 (tq, *J* = 5.6, 11.2, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 19.3, 22.0, 22.9, 29.3, 29.6, 29.8, 29.9, 30.0, 30.8, 32.1, 34.0, 67.4, 114.4, 132.5, 134.3, 138.1. FTIR (thin film) 3343, 3077, 2925, 1635cm^{-1}. MS (EI) 248 $[M-H_2O]^{+}$.

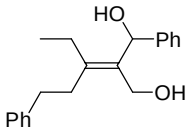
(*E*)-1-Phenyl-2-(4-phenylbutan-2-ylidene)propane-1,3-diol



(Scheme 2, **8**):

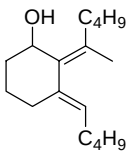
CH_3MgBr (1.17 mL, 3.5 mmol) was added drop-wise to a black solution of $Fe(ehx)_3$ (0.095 mL, 0.11mmol) and 5-phenylpent-2-yn-1-ol[4] (112 mg, 0.70 mmol) in THF (7.0 mL) at –78 ^{o}C. The resulting mixture was warmed up to 0 ^{o}C and stirred for 7h. The reaction mixture was cooled to –78 ^{o}C, neat benzaldehyde (0.57 mL, 5.6 mmol) was added and then the mixture was allowed to warm up to 4 ^{o}C overnight. The reaction was quenched by adding aqueous ammonium chloride and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. Triethyl amine (3 mL) was added to the combined organic phases, and they were dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel (30% EtOAc in hexane) to provide 105 mg (51 % yield) of a colorless oil. ^{1}H NMR (CD_3OD) = 1.92 (s, 3H), 2.38-2.47 (m, 1H), 2.61-2.87 (m, 3H), 3.76 (d, *J* = 11.7, 1H), 4.00 (d, *J* = 11.7, 1H), 5.77 (s, 1H), 7.13-7.29 (m,

10H). ^{13}C NMR (CD_3OD) = 18.9, 35.8, 38.2, 59.1, 73.5, 127.0, 127.1, 127.9, 129.2, 129.5, 129.8, 136.0, 138.0, 143.2, 145.0. FTIR (thin film) 3352, 3084, 3061, 3026, 2929 cm^{-1}. MS (EI) 264 $[M-H_2O]^+$.



(*E*)-1-Phenyl-2-(1-phenylpentan-3-ylidene)propane-1,3-diol (Scheme 2, **9**):

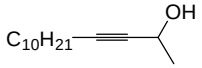
EtMgBr (1.1 mL, 3.5 mmol) was added drop-wise to a black solution of $Fe(ehx)_3$ (0.12 mL, 0.14 mmol) and 5-phenylpent-2-yn-1-ol[4] (112 mg, 0.70 mmol) in THF (7.0 mL) at –78 ^{o}C. The resulting mixture was stirred at 0 ^{o}C for 7h. The reaction mixture was cooled to –78 ^{o}C, neat benzaldehyde (0.57 mL, 5.6 mmol) was added and then the mixture was allowed to warm up to 4 ^{o}C overnight. The reaction was quenched by adding aqueous ammonium chloride and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. Triethyl amine (3 mL) was added to the combined organic phases, and they were dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel (20 % EtOAc in hexane) to provide 106 mg (52 % yield) of a colorless oil. ^{1}H NMR ($CDCl_3$) = 1.16 (t, J = 7.6, 3H), 1.46 (t, J = 6.4, 1H), 2.35 (q, J = 7.2, 2H), 2.47-2.59 (m, 2H), 2.72-2.84 (m, 2H), 3.25 (d, J = 6.0, 1H), 3.78 (dd, J = 5.6, 12.0, 1H), 4.10 (dd, J = 5.2, 12.0, 1H), 5.83 (d, J = 6.0, 1H), 7.18-7.34 m, 10H). ^{13}C NMR ($CDCl_3$) = 14.1, 25.2, 33.9, 35.4, 59.7, 73.0, 125.8, 126.4, 127.1, 128.5, 128.6, 128.9, 133.8, 141.7, 143.0, 143.5. FTIR (thin film) 3346, 3026, 2965, 1601 cm^{-1}. MS (EI) 278 $[M-H_2O]^+$.



(2*Z*,3*E*)-2-(Hexan-2-ylidene)-3-pentylidenecyclohexanol (Scheme 2, **10**):

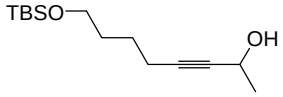
CH_3MgBr (0.83 mL, 2.5 mmol) was added drop-wise to a red solution of $Fe(acac)_3$ (53 mg, 0.15mmol), CuBr (21 mg, 0.15 mmol),

tributyl phosphine (0.075 mL, 0.30 mmol) and hexadeca-5,11-diyn-7-ol (113 mg, 0.48 mmol) in THF (7.0 mL) at –78 ^{o}C. The resulting brown mixture was stirred at rt for 4h and became a deep brown mixture at the end of reaction. After cooling to 0 ^{o}C, the reaction mixture was quenched with aqueous ammonium chloride and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic phases were dried over Na_2SO_4, concentrated and purified by flash chromatograph on silica gel (3.0 % EtOAc in hexane) to provide 84 mg (70% yield) of colorless oil. ^{1}H NMR ($CDCl_3$) = 0.89-0.94 (m, 6H), 1.27-2.21 (m, 18H), 1.71 (s, 3H), 2.60-2.70 (m, 1H), 4.74 (t, *J* = 3.0, 1H), 5.16 (t, *J* = 7.2, 1H). ^{13}C NMR ($CDCl_3$) = 14.2, 14.3, 20.2, 22.0, 22.6, 23.0, 27.5, 29.6, 31.4, 32.4, 33.5, 34.5, 67.6, 129.7, 131.1, 136.4, 138.4. FTIR (thin film) 3431, 2929 cm^{-1}. MS (EI) 250 $[M]^{+}$.



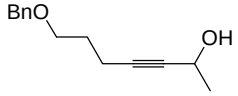
Tetradec-3-yn-2-ol:

^{1}H NMR ($CDCl_3$) = 0.89 (t, *J* = 6.8, 3H), 1.27 (br. s, 12H), 1.32-1.38 (m, 2H), 1.43 (d, *J* = 6.4, 3H), 1.49 (appr. p, *J* = 7.2, 2H), 1.91 (d, *J* = 3.2, 1H), 2.19 (dt, *J* = 2.0, 6.8, 2H), 4.51 (m, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 18.9, 22.9, 25.0, 28.9, 29.1, 29.4, 29.6, 29.7, 29.8, 32.1, 58.8, 82.4, 85.0. FTIR (thin film) 3335, 2924, 2855, 2248 cm^{-1}. MS (EI) 195 $[M\text{-}Me]^{+}$.



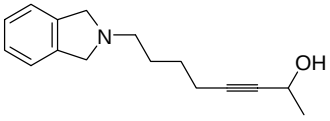
8-(*tert*-Butyldimethylsilyloxy)oct-3-yn-2-ol:

^{1}H NMR ($CDCl_3$) = 0.06 (s, 6H0, 0.9 (s, 9H), 1.43 (d, *J* = 6.4, 3H), 1.50-1.65 (m, 4H), 1.71 (d, *J* = 4.2, 1H), 2.23 (td, *J* = 6.8, 2.0, 2H), 3.63 (t, *J* = 6.4, 2H), 4.48-4.56 (tdq, *J* = 2.0, 6.4, 6.7, 1H). ^{13}C NMR ($CDCl_3$) = -5.1, 18.6, 18.7, 25.0, 25.3, 26.2, 32.1, 58.5, 62.9, 82.7, 84.7. FTIR (thin film) 3360, 2930, 2858, 2248 cm^{-1}. MS (EI) 241 $[M\text{-}Me]^{+}$.



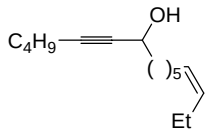
7-(Benzyloxy)hept-3-yn-2-ol:

^{1}H NMR ($CDCl_3$) = 1.40 (d, *J* = 6.3, 3H), 1.81 (appr. p, *J* = 6.3, 2H), 2.00 (br. s, 1H), 2.34 (dt, *J* = 1.8, 7.2, 2H), 3.56 (t, *J* = 6.3, 2H), 4.48 (tq, *J* = 1.8, 6.9, 1H), 4.52 (s, 2H), 7.29-7.36 (m, 5H). ^{13}C NMR ($CDCl_3$) = 15.7, 24.9, 28.9, 58.7, 68.8, 73.1, 82.8, 84.0, 127.8, 127.9, 128.6, 138.6. FTIR (thin film) 3401, 3030, 2863, 2212 cm^{-1}. MS (EI) 217 $[M-H]^+$.



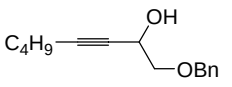
8-(Isoindolin-2-yl)oct-3-yn-2-ol:

^{1}H NMR ($CDCl_3$) = 1.35 (d, *J* = 6.3, 3H), 1.54-1.64 (m, 2H), 1.67-1.76 (m, 2H), 2.24 (dt, *J* = 1.8, 6.9, 2H), 2.73 (t, *J* = 7.2, 2H), 3.50 (br. s, 1H), 3.94 (s, 4H), 4.38 (tq, *J* = 1.8,6.9, 1H), 7.11 (s, 4H). ^{13}C NMR ($CDCl_3$) = 18.7, 24.9, 26.5, 28.0, 55.8, 58.2, 59.2, 83.3, 83.7, 122.4, 126.9, 140.2. FTIR (thin film) 3372, 3076, 2935, 2247, 1674 cm^{-1}. MS (EI) 242 $[M-H]^+$.



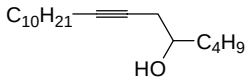
(*Z*)-Hexadec-13-en-5-yn-7-ol:

^{1}H NMR ($CDCl_3$) = 0.91 (t, *J* = 6.9, 3H), 0.96 (t, *J* = 7.5, 3H), 1.32-1.52 (m, 10H), 1.63-1.71 (m, 2H), 1.74 (d, *J* = 5.4, 1H), 1.99-2.09 (m, 4H), 2.21 (dt, *J* = 2.1, 6.6, 2H), 4.34 (tq, *J* = 2.1, 6.3, 1H), 5.27-5.43 (m, 2H). ^{13}C NMR ($CDCl_3$) = 13.8, 14.6, 18.6, 20.7, 22.1, 25.3, 27.2, 29.1, 29.9, 31.0, 38.4, 63.0 81.5, 85.7, 129.4, 131.9. FTIR (thin film) 3340, 2960, 2932, 1653cm^{-1}. MS (EI) 203 $[M-(H_2O + Me)]^+$.



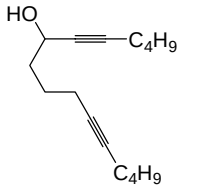
1-(Benzyloxy)oct-3-yn-2-ol:

^{1}H NMR ($CDCl_3$) = 0.91 (t, *J* = 7.2, 3H), 1.36-1.45 (m, 4H), 2.21 (dt, *J* = 1.8, 7.2, 2H), 2.52 (br. s, 1H), 3.54 (dd, *J* = 4.5, 9.9, 1H), 3.63 (dd, *J* = 3.6, 9.9, 1H), 4.50-4.6 (br. s, 1H), 4.61 (d, *J* = 2.1, 2H), 7.30-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) = 13.8, 18.6, 22.1, 30.8, 62.1, 73.6, 74.2, 77.8, 86.8, 128.0, 128.1, 128.7, 138.0. FTIR (thin film) 3418, 3031, 2863, 2236cm^{-1}. MS (EI) 232 $[M]^+$.



Octadec-7-yn-5-ol:

^{1}H NMR ($CDCl_3$) = 0.89 (t, *J* = 6.6, 3H), 0.91 (t, *J* = 7.2, 3H), 1.27-1.56 (m, 22H), 2.17 (tt, *J* = 2.4, 6.9, 2H), 2.27 (tdd, *J* = 2.4, 6.9, 16.2, 1H), 2.41 (tdd, *J* = 2.4, 4.5, 16.2, 1H), 3.69 (dq, *J* = 4.8, 6.6, 1H). ^{13}C NMR ($CDCl_3$) = 14.3, 14.4, 19.0, 22.9 (x 2), 28.0, 29.1, 29.2, 29.4, 29.6, 29.8 (x 2), 32.1, 36.2, 70.5, 76.3, 83.6. FTIR (thin film) 3360, 2926, 2855 cm^{-1}. MS (EI) 266 $[M]^+$.



Hexadeca-5, 11-diyn-7-ol:

^{1}H NMR ($CDCl_3$) = 0.89 (t, *J* = 7.2, 3H), 0.90 (t, *J* = 7.2, 3H), 1.34-1.51 (m, 8H), 1.62 (p, *J* = 7.2, 2H), 1.71-1.82 (m, 2H), 2.12-2.23 (m, 6H), 4.39 (q, *J* = 6.4, 1H). ^{13}C NMR ($CDCl_3$) = 13.8 (x2), 18.6 (x2), 18.7, 22.1, 25.0, 30.9, 31.4, 37.5, 62.5, 79.8, 80.9, 81.2, 85.8. FTIR (thin film) 3352, 2933, 2229, 1675 cm^{-1}. MS (EI) 233 $[M-H]^+$.

Notes and references:

1. Triethyl amine is used to remove 2-ethylhexanoic acid produced from $Fe(ehx)_3$ and it is not needed when $Fe(acac)_3$ is used as catalyst.
2. Boyall, D; Frantz, D. E.; Carreira, E. M. *Org. Lett.* **2002**, *4*, 2605-2606.
3. Miura, K; Wang, D; Matsumoto, Y; Hosomi, A. *Org. Lett.* **2005**, *7*, 503-505.
4. Khorana, N; Purohit, A; Herrick-Davis, K; Teitler, M; Glennon, R. A. *Bioorg. & Med. Chem.* **2003**, *11*, 717-722