Enhanced Diastereoselectivity In Asymmetric Crotylation Reactions using Propargylic Dicobalt Hexacarbonyl Complexes

Meng Sui and James S. Panek*
Department of Chemistry and Center for Streamlines Synthesis
Metcalf Center for Science and Engineering
Boston University
Boston, Massachusetts 02215

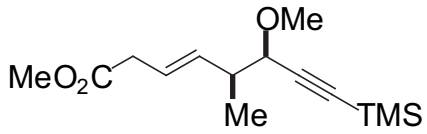
Supporting Information

General Information

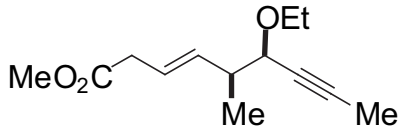
^{1}H- and ^{13}C- NMR were taken in $CDCl_3$ at 400 MHz and 75.0 MHz respectively unless specified otherwise. Chemical shifts are reported in parts per million using the solvent resonance internal standard (chloroform 7.24 and 77.0 ppm, unless specified otherwise). Data are reported as follows: chemical shift, multiplicity (app = apparent, par obsc = partially obsured, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, abq = ab quartet), integration, and coupling constant. Ratios of diastereomers (dr) were determined by ^{1}H-NMR (400 MHz) operating at a signal/noise ratio of >200:1. Infrared Resonance spectra were recorded on a Nicolet Impace 400 FT-IR spectrophotometer. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm, and are reported as $[\alpha]_D$ (concentration in grams/100 mL solvent). High-resolution mass spectra (HRMS) were obtained on a Fingan MAT-90 spectrometer on the Boston University Mass Spectrometer Laboratory. Mythylene chloride (CH_2Cl_2) and $BF_3 \bullet OEt_2$ were freshly distilled under nitrogen from CaH_2. All other reagents were used as supplied. All reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted. Analytical thin layer

chromatography was performed on Whatman Reagent silica gel 60-A plates. Flash chromatography was performed on E. Merck silica gel 230-400 mesh.

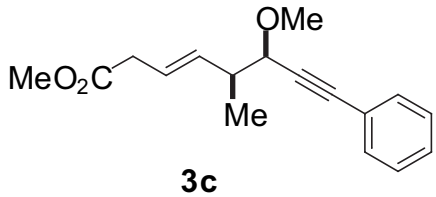
Spectral data



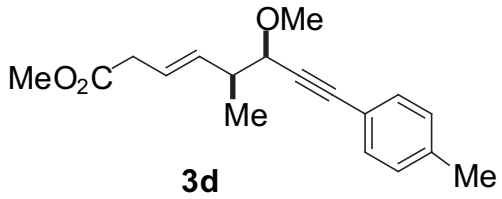
3a **(*5S, 6R*)-methyl-3*E*-5-methyl-6-methoxy-8-trimethylsilyl-7 octynoate (3a)**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 5.61 (m, 2H), 3.78 (d, 1H, *J* = 4.9 Hz), 3.70 (s, 3H), 3.37 (s, 3H), 3.06 (m, 2H), 2.49 (m, 2H), 1.07 (d, 3H, *J* = 6.9 Hz), 0.16 (s, 9H). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.3, 135.2, 122.6, 102.9, 91.8, 75.9, 56.7, 51.7, 41.3, 38.0, 15. 9, -0.1 (3C). IR (neat): 2959, 1741 cm^{-1}. HRMS (EI): calcd. For $C_{14}H_{24}O_3Si$ 268.1495, found 268.1497. $[\alpha]_D$ = +40.6° (C = 0.66, CH_2Cl_2).



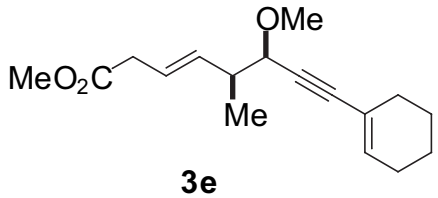
3b **(*5S, 6R*)-methyl-3*E*-5-methyl-6-ethoxy-7nonynoate (3b)**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 5.63 (m, 2H), 3.81 (m, 1H), 3.73 (m, 1H), 3.66 (s, 3H), 3.39 (m, 1H), 3.07 (d, 2H, *J* = 5.94 Hz), 2.45 (m, 1H), 1.83 (d, 3H, *J* = 2.3 Hz), 1.17 (t, 3H, *J* = 6.92 Hz), 1.06 (d, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.5, 135.7, 122.3, 82.4, 77.4, 73.8, 64.3, 51.7, 41.5, 38.1, 16.0, 15.0, 3.6. IR (neat): 2924, 1734 cm^{-1}. HRMS (EI): calcd. For $C_{13}H_{20}O_3$ 224.1412, found 224.1423. $[\alpha]_D$ = +4.9° (C = 0.485, CH_2Cl_2).



3c **(*5S, 6R*)-methyl-3*E*-5-methyl-6-methoxy-8-phenyl-7-octynoate (3c)**: H NMR ($CDCl_3$, 400 MHz) (ppm) 7.42 (m, 2H), 7.29(m, 3H), 5.68 (m, 2H), 4.02 (d, 1H, *J* = 5.27 Hz), 3.63 (s, 3H), 3.452 (s, 3H), 3.08 (m, 2H), 2.60 (m, 1H), 1.14 (d, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.3, 135.3, 134.2, 131.7 (2C), 128.2 (2C), 122.8, 122.1, 87.0, 86.6, 76.1, 56.9, 51.7, 41.6, 38.1, 16.1. IR (neat): 2931, 2225, 1739 cm^{-1}. HRMS (EI): calcd. For $C_{17}H_{20}O_3$ 272.1412, found 272.1406. $[\alpha]_D$ = +44.9° (C = 0.575, CH_2Cl_2).

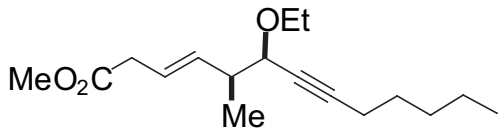


3d **(*5S, 6R*)-methyl-3*E*-5-methyl-6-methoxy-8-(3-methylphenyl)-7-octynoate (3d)**: ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.31(d, 2H, *J* = 7.9 Hz), 7.10 (d, 2H, *J* = 7.9 Hz), 5.68 (m, 2H), 4.01 (d, 1H, *J* = 5.3 Hz), 3.64 (s, 3H), 3.44 (s, 3H), 3.08 (m, 2H), 2.60 (m, 1H), 3.33 (s, 3H), 1.14 (d, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.3, 138.4, 135.4, 131.6 (2C), 129.0 (2C), 122.7, 119.7, 87.2, 85.8, 76.0, 56.8, 51.7, 41.6, 38.0, 21.4, 16.1. IR (neat): 2952, 2228,1739 cm^{-1}. HRMS (EI): calcd. For $C_{18}H_{22}O_3$ 286.1569, found 286.1558. $[\alpha]_D$ = +42.1° (C = 0.61, CH_2Cl_2).



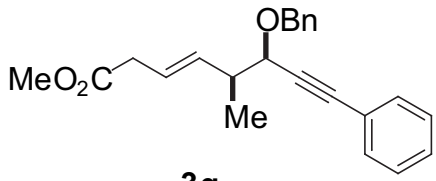
3e

(*5S, 6R*)-methyl-3*E*-5-methyl-6-methoxy-8-(1-cyclohexene)-7-octynoate (3e): ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 6.09 (m, 1H), 5.63 (m, 2H), 3.91 (d, 1H, *J* = 5.27 Hz), 3.66 (s, 3H), 3.38 (s, 3H), 3.06 (m, 2H), 2.51 (m, 1H), 2.07 (m, 4H), 1.58 (m, 4H), 1.77 (d, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.4, 135.5, 135.0, 122.5, 120.3, 88.9, 83.7, 76.0, 56.7, 51.7, 41.6, 38.0, 29.3, 25.6, 22.3, 21.5, 16.1. IR (neat): 2930, 1741 cm^{-1}. HRMS (EI): calcd. For $C_{17}H_{24}O_3$ 276.1725, found 276.1775. $[\alpha]_D$ = +32.0° (C = 0.56, CH_2Cl_2).



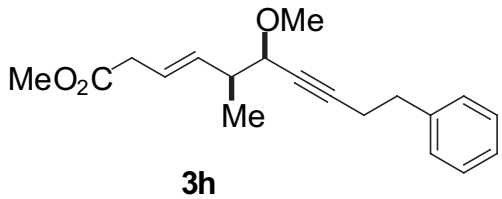
3f

(*5S, 6R*)-methyl-3*E*-5-methyl-6-ethoxy-7-tridecynoate (3f): ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 5.63 (m, 2H), 3.85 (m, 1H), 3.73 (m, 1H), 3.66 (s, 3H), 3.41(m, 1H), 3.06 (m, 2H), 2.46 (m, 1H), 2.19 (m, 2H), 1.49 (m, 2H), 1.30 (m, 4H), 1.18 (t, 3H, *J* = 7.25 Hz), 1.06 (d, 3H, *J* = 6.6 Hz), 0.88 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.4, 135.8, 122.2, 87.1, 77.9, 73.8, 64.2, 51.7, 41.6, 38.1, 31.0, 28.4, 22.1, 18.7, 16.1, 15.0, 14.0. IR (neat): 2932, 1743 cm^{-1}. HRMS (EI): calcd. For $C_{17}H_{28}O_3$ 280.4024, found 280.2021. $[\alpha]_D$ = +14.8° (C = 0.755, CH_2Cl_2).



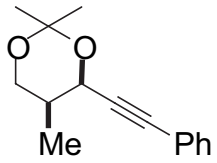
3g

(*5S, 6R*)-methyl-3*E*-5-methyl-6-benzyloxy-8-phenyl-7-octynoate (3g): ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.35 (m, 10H), 5.71(m, 2H), 4.87 (d, 1H, *J* =11.9 Hz), 4.58 (dd, 1H, *J* =11.9 Hz), 4.15 (d, 1H, *J* = 5.6 Hz), 3.64 (s, 3H), 3.09 (d, 2H, *J* = 5.9 Hz), 2.65 (m, 1H), 1.18 (d, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.3, 138.1, 135.5, 131.8, 128.3 (2C), 127.9, 127.6, 122.8, 122.7,87.1, 86.9, 73.3, 70.7, 51.6, 41.7, 38.1, 16.1. IR (neat): 2951, 1739 cm^{-1}. HRMS (EI): calcd. For $C_{23}H_{24}O_3$+H^+ 349.1725, found 349.1757. $[\alpha]_D$ = +78.9° (C = 0.79, CH_2Cl_2)



3h

(*5S, 6R*)-methyl-3*E*-5-methyl-6-methoxy-10-phenyl-7-decanoate (3h): ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.22 (m, 5H), 5.58 (m, 2H), 3.73 (m, 1H), 3.64 (s, 3H), 3.30 (s, 3H), 3.03 (m, 2H), 2.80 (t, 2H, *J* = 7.6 Hz), 2.51 (t, 2H, *J* = 7.6 Hz), 2.43 (m, 1H), 1.01(d, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 172.4, 140.6, 135.5, 128.4, 128.3, 126.3, 122.4, 86.7, 78.0, 75.8, 56.6, 51.7, 41.4, 38.0, 35.1, 20.8, 16.0. IR (neat): 2930, 1740 cm^{-1}. HRMS (EI): calcd. For $C_{19}H_{24}O_3$ 300.1725, found 300.1709. $[\alpha]_D$ = +26.6° (C = 0.58, CH_2Cl_2)



11 ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.45 (m, 2H), 7.28 (m, 3H), 5.12 (d, 1H, *J* = 3.63 Hz), 4.04 (dd, 1H, *J* = 3.14Hz, *J* = 11.70Hz), 3.69 (dd, 1H, *J* = 3.63Hz, *J* = 11.54Hz), 1.86 (m, 1H), 1.51 (s, 3H), 1.48 (s, 3H), 1.27 (d, 3H, *J* = 7.25Hz).

Ee Analysis: Attempts to perform the ee analysis directly on the crotylation products **3a-h** proved to be quite frustrating as HPLC conditions for their separation could not be defined. To solve this problem, ee determination was carried out using primary alcohol **10**, which was derived from **3g**. Accordingly, HPLC analysis of **3g** revealed an ee of 99% (chiral OD column, eluent n-hexane/2-propanol 97:3, flow rate 0.7 mL/min, 250×46 mm).