Supporting Information

Cobalt Catalyzed Cycloisomerization of 1,6-Enynes and Allyl Propargyl Ethers.

Alain Ajamian and James L. Gleason*

Department of Chemistry, McGill University, 801 Sherbrooke Street West,
Montréal, QC, Canada, H3A 2K6.

Experimental Section

General Experimental. All reagents were commercial materials (Sigma-Aldrich, Lancaster, Strem Chemicals) and were used without further purification with the following exceptions. Benzene was distilled from sodium benzophenone ketyl. Toluene was distilled from calcium hydride. All substrates were dried via azeotropic distillation of water using dry toluene. All reactions were conducted with $\text{Co}_2(\text{CO})_8$ which had been freshly recrystallized from degassed hexanes. All reaction vessels were flame dried under vacuum prior to use. Chromatography was conducted using 230-400 mesh silica gel. GC analysis was conducted on an HP 6890 Series GC system using a HP-5 (Cross-linked 5% Ph-Me-Siloxane) column and a flame ionization detector. GC conditions: oven temperature = 120 °C for 5 min then increased 3 °C/min for 20 minutes; He carrier gas; 14 psi. NMR spectra were recorded at 200, 300 or 400 MHz for ^1H and 67.5, 75 or 100 MHz ^{13}C . High resolution mass spectras were obtained from Université de Sherbrooke, Sherbrooke, QC.

General procedure for the cobalt catalyzed cycloisomerization reaction (small scale):

3-(tert-butyldimethylsilyloxy)-4,4-dimethyl-1-trimethylsilyl-5-vinylcyclopentene (3). $\text{Co}_2(\text{CO})_8$ (11 mg, 0.030 mmol, 0.10 equiv) was added to a solution of 3-(tert-butyldimethylsilyloxy)-2,2-dimethyl-1-trimethylsilyl-hept-6-en-1-yne (**1**) (100 mg, 0.31 mmol, 1.0 equiv) in toluene (8 ml) at 23 °C and the reaction stirred for 30 min. $(\text{MeO})_3\text{P}$ (3 μl , 0.03 mmol, 0.10 equiv) was then added and the reaction heated at reflux for 5h. The reaction was then cooled to 23 °C and filtered through a pad of celite. The filtrate was concentrated and purified by chromatography on silica gel eluting with hexanes to afford a 97 mg mixture of the desired cycloisomerization product (**3**) and isomerized product (**4**) as a clear translucent oil (97%). This mixture was then treated with K_2CO_3 (4

mg, 0.030 mmol, 0.1 equiv) in methanol (2ml) for 1 h. The reaction was partitioned between hexanes (2 ml) and H₂O (2ml), the organic phase separated, dried over Na₂SO₄ and concentrated in vacuo. The resulting oil was purified by a silica gel plug, eluting with hexanes, to afford 91 mg of the known¹ cycloisomerization product (**3**) as a clear translucent oil (91%).

Cycloisomerization on 1.5 mmol scale.

(Co₂(CO)₈ (53 mg, 0.154 mmol, 0.10 equiv) was added to a solution of 3-(tert-butyldimethylsilyloxy)-2,2-dimethyl-1-trimethylsilyl-hept-6-en-1-yne (**1**) (500 mg, 1.54 mmol, 1.0 equiv) in toluene (8 ml) at 23 °C and the reaction stirred for 30 min. (MeO)₃P (18 µl, 0.154 mmol, 0.10 equiv) was then added and the reaction heated at reflux for 5h. The reaction was then cooled to 23 °C and filtered through a pad of celite. The filtrate was concentrated and purified by chromatography on silica gel eluting with hexanes to afford a 470 mg mixture of the desired cycloisomerization product (**3**) and isomerized product (**4**) as a clear translucent oil (94%). This mixture was then treated with K₂CO₃ (22 mg, 0.154 mmol, 0.1 equiv) in methanol (7ml) for 1 h. The reaction was partitioned between hexanes (10 ml) and H₂O (10ml), the organic phase separated, dried over Na₂SO₄ and concentrated in vacuo. The resulting oil was purified by a silica gel plug, eluting with hexanes, to afford 435 mg of the desired cycloisomerization product (**3**) as a clear translucent oil (87%).

NOTE: The K₂CO₃ in methanol treatment only applies to the mixture of (**3**) & (**4**) and may be omitted if the cycloisomerized product is readily separable from the isomerized enyne.

1-trimethylsilylhept-6-en-1-yn-3-ol. A 2.77 M solution of n-BuLi in hexanes (2.1ml, 1.2 equiv) was added to a solution of trimethylsilylacetylene (0.80 ml, 5.7 mmol 1.2 equiv) in THF (20 ml) at –78 °C and the reaction stirred for 30 min. 4-pentenal (0.40 ml, 4.7 mmol, 1.0 equiv) was then added dropwise at –78 °C and the reaction allowed to warm to 0 °C over 1h. The reaction was quenched by the addition of sat. NH₄Cl solution. The aqueous phase was separated and extracted with Et₂O (2 x 5ml). The combined organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo. The light yellow oil was purified by chromatography on silica gel eluting with 10% ethyl acetate in hexanes to afford 805 mg of the desired enyne as a clear translucent oil (93 %). ¹H NMR (CDCl₃)

¹ Dolaine, R; Gleason, J. L. *Org. Lett.* **2000**, 2, 1753.

δ 5.85 (m, 1H), 5.07 (d_{obs}, 1H, J = 17 Hz), 5.00 (d_{obs}, 1H, J = 10 Hz), 4.39 (t_{obs}, 1H, J = 6.3 Hz), 2.24 (q_{obs}, 2H, J = 7.8, 14.5 Hz), 1.82 (m, 3H), 0.19 (s, 9H). ¹³C NMR (CDCl₃) δ 137.8, 115.5, 106.7, 89.9, 62.7, 37.1, 29.8, 0.37. HRMS (EI) m/z 181.1052 (M⁺, C₁₀H₁₇OSi requires 181.1049).

3-(tert-butyldimethylsilyloxy)-1-trimethylsilylhept-6-en-1-yne (5). Imidazole (67 mg, 0.90 mmol, 1.2 equiv) was added to a solution of TBSCl (136 mg, 0.90 mmol, 1.2 equiv) and 1-trimethylsilyl-hept-6-en-1-yn-3-ol (150 mg, 0.80 mmol, 1.0 equiv) in DMF (1.5 ml) at 23 °C and the reaction stirred for 12 h. The reaction was then partitioned between sat. NH₄Cl solution (6 ml) and hexanes (6 ml). The organic layer was washed with H₂O (2 x 5ml) and brine (5 ml). The organic layer was then dried over Na₂SO₄ and concentrated in vacuo. The oil was purified by chromatography on silica gel eluting with 2% ethyl acetate in hexanes to afford 236 mg of the desired TBS ether (**7**) as a clear translucent oil (97 %). ¹H NMR (CDCl₃) δ 5.83 (m, 1H), 5.04 (d_{obs}, 1H, J = 17 Hz), 4.97 (d_{obs}, 1H, J = 10 Hz), 4.35 (t_{obs}, 1H, J = 6.74 Hz) 2.19 (m, 2H), 1.76 (m, 2H), 0.92 (s, 9H), 0.17 (s, 9H), 0.15 (s 3H), 0.12 (s, 3H). ¹³C NMR (CDCl₃) δ 138.2, 115.1, 107.8, 88.9, 63.0, 37.9, 29.9, 26.2, 18.7, 0.27, -3.9, -4.5. HRMS (EI) m/z 281.1760 (M – CH₃⁺, C₁₅H₂₉OSi₂ requires 281.1757).

3-(tert-butyldimethylsilyloxy)-1-trimethylsilyl-5-vinylcyclopentene (6). Prepared as described for **3**. ¹H NMR (CDCl₃) δ 5.94 (s, 1H), 5.54 (m, 1H), 5.05-4.88 (m, 3H), 3.55 (m, 1H), 1.96 (m, 2H), 0.92 (s, 9H), 0.17 (s, 3H), 0.09 (s, 12H). ¹³C NMR (CDCl₃) δ 144.7, 142.9, 113.7, 79.3, 53.2, 42.9, 30.7, 26.4, 18.8, -0.7, -4.1. HRMS (EI) m/z 296.1988 (M⁺, C₁₆H₃₂OSi₂ requires 296.1992).

***trans*-1-(2,2-dibromoethenyl)-2-allyl-cyclohexane.** CBr₄ (738 mg, 2.2 mmol, 1.5 equiv) was added in one portion to a solution of Ph₃P (1.2 g, 4.4 mmol, 3.0 equiv) in CH₂Cl₂ (2 ml) at 0 °C and the reaction stirred for 15 min. The reaction was then cooled to -78 °C and a solution of *trans*-1-carboxaldehyde-2-allyl-cyclohexane² in CH₂Cl₂ (15 ml) was cannulated into the reaction dropwise at -78 °C and the reaction stirred for 9h. The reaction was quenched by the addition sat. NH₄Cl solution. The aqueous phase was separated and extracted with Et₂O (2 x 10ml). The organic phases were combined, dried over Na₂SO₄ and concentrated in vacuo. The brownish oil was purified by chromatography on silica gel eluting with hexanes to afford 369 mg of the desired dibromo compound as a clear translucent oil (81 %). ¹H NMR (CDCl₃) δ 6.19 (d, 1H, J = 9.78 Hz), 5.74 (m, 1H), 5.00 (m, 2H), 2.22 (m, 1H), 2.07 (m, 2H), 1.88-0.92 (m, 9H). ¹³C NMR (CDCl₃) δ 143.5, 136.8, 116.4, 88.1, 48.1, 41.9, 39.4, 31.8, 31.5, 26.3, 26.0. HRMS (EI) m/z 305.9623 (M⁺, C₁₁H₁₆Br₂ requires 305.9619).

***trans*-2-allyl-1-(trimethylsilylethynyl)-cyclohexane (11).** A 2.77 M solution of n-BuLi in hexanes (950 µl, 2.6 mmol, 2.2 equiv) was added to a solution of *trans*-1-(2,2-dibromovinyl)-2-allyl-cyclohexane (37 mg, 1.2 mmol, 1.0equiv) in Et₂O (6 ml) at -78 °C and the reaction stirred for 45 min. TMSCl (335 µl, 2.6 mmol, 2.2 equiv) was then added at -78 °C and the reaction allowed to warm to 0 °C over 1h. The reaction was quenched by the addition sat. NH₄Cl solution. The aqueous phase was separated and extracted with Et₂O (2 x 3ml). The combined organic phases were dried over Na₂SO₄ and concentrated in vacuo. The brownish-orange oil was purified by chromatography on silica gel eluting with hexanes to afford 187 mg of the desired 1,6-enyne as a clear translucent oil (71 %). ¹H NMR (CDCl₃) δ 5.81 (m, 1H), 5.01 (m, 2H), 2.56 (m, 1H), 2.05-0.84 (m, 11H), 0.16 (s, 9H). ¹³C NMR (CDCl₃) 137.0, 116.3, 111.0, 85.3, 42.3, 39.4, 36.3, 33.4, 31.2, 26.1, 0.7. HRMS (EI) m/z 220.1655 (M⁺, C₁₄H₂₄Si requires 220.1647)

² Tsuji, J.; Shimizu, I.; Kobayashi, Y. *Isr. J. Chem.* **1984**, 24, 153.

7-trimethylsilyl-8-vinyl-bicyclo[4.3.0.] non-6-ene (12). Prepared as described for **3**. ^1H NMR (CDCl_3) δ 6.12 (s, 1H), 5.64 (m, 1H), 5.00 (d_{obs} , 1H, $J = 17$ Hz), 4.94 (d_{obs} , 1H, 9.9 Hz), 3.19 (t_{obs} , 1H, $J = 8.2$), 2.19 (m, 1H), 2.01 (m, 1H), 1.79-0.87 (m, 8H), 0.08 (s, 9H). ^{13}C NMR (CDCl_3) δ 147.9, 146.8, 137.4, 114.8, 55.8, 53.8, 50.3, 31.0, 28.2, 27.2, 27.1, -0.5. HRMS (EI) m/z 220.1649 (M^+ , $\text{C}_{14}\text{H}_{24}\text{Si}$ requires 220.1647)

Isomerized Cyclohexylenyne (13). ^1H NMR (CDCl_3) δ 5.43 (m, 2H), 2.04-1.02 (m, 13 H), 0.134 (s, 9H). ^{13}C NMR (CDCl_3) δ 134.8, 125.7, 124.7, 111.4, 85.1, 46.0, 36.9, 33.1, 32.3, 30.7, 25.8, 0.7. HRMS (EI) m/z 220.1642 (M^+ , $\text{C}_{14}\text{H}_{24}\text{Si}$ requires 220.1647).

aaa_B8_p114

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p114

Pulse Sequence: s2pul

aa_B8_p37_addition

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

Pulse Sequence: s2pul

aaa_B8_p38

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p38_TBS

Pulse Sequence: s2pul

aaa_B8_p114

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p114

Pulse Sequence: s2pul

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p87

Pulse Sequence: s2pul

aa_B8_p94

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p94_OBcyclize

Pulse Sequence: s2pul

aaa_B8_p57

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p57_CF

Pulse Sequence: s2pul

aaa_B8_p58

Data Collected on: m400-mercury400
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p58_corey-fuchs2

Pulse Sequence: s2pul

aaa_B8_p60

Data Collected on: m300-mercury300
Archive directory: /export/home/AAA/vnmrsys/data
Sample directory:
File: aa_B8_p60_catcolumn

Pulse Sequence: s2pul