Highly Efficient Access to Strained Bicyclic Ketals via Gold-catalyzed Cycloisomerization of Bis-homopropargylic Diols

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Supporting information

AuCl and AuCl₃ were purchased from Cortecnet. All manipulations were carried out under argon and Schlenk techniques for catalytic tests. Solvents were degassed by sparging with argon and/or exposure to vacuum. ¹H NMR and ¹³C NMR were recorded on a Bruker AV 300 instrument. All signals were expressed as ppm down field from Me₄Si for ¹H and ¹³C NMR used as an internal standard (δ). Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplicities. Mass spectrometry analyses (direct introduction by chemical ionization with ammoniac) were performed at the Ecole Nationale Supérieure de Chimie de Paris. High resolution mass spectra were performed on a Varian MAT311 instrument at the Ecole Normale Supérieure (Paris).

Standard procedure: a mixture of bis-homopropargylic diol, AuCl or AuCl₃ (2 mol%) in degassed methanol (0.5 molL⁻¹) was stirred under argon atmosphere at room temperature. After completion of the reaction, the mixture was filtered through a short pad of celite (EtOAc) and the solvents were evaporated under reduced pressure to give the corresponding ketal.

1-Methyl-4-[3'-phenylprop-2'-enyl]-2,6-dioxabicyclo[2.2.1]heptane **2a**

¹H-NMR (300 MHz, CDCl₃): δ 1.55 (s, 3H), 1.77 (s, 2H), 2.50 (d, *J*=7,53 Hz, 2H), 3.82 (m, 4H), 6.13 (td, *J*=7,53 Hz, *J*=15,66 Hz, 1H), 6.43 (d, *J*=15,66 Hz, 1H), 7.13-7.27 (m, 5H). ¹³C-NMR (75 MHz, CDCl₃): δ 17.9, 32.8, 44.2, 48.7, 75.8, 108.4, 117.8, 133.3. CI-MS (NH₃): *m/z* 231 [M+H]⁺. DCI/NH₃-HRMS Calculated for C₁₅H₁₉O₂: 231.1385. Found: 231.1388.

4-Benzyl-1-methyl-2,6-dioxabicyclo[2.2.1]heptane **2b**

¹H-NMR (300 MHz, CDCl₃): δ 1.51 (s, 3H), 1.70 (s, 2H), 2.87 (s, 2H), 3.74 (m, 4H), 7.00-7.40 (m, 5H). ¹³C-NMR (75 MHz, CDCl₃): δ 17.9, 35.2, 44.6, 49.9, 76.2, 108.3, 126.7, 128.5, 129.1, 137.3. CI-MS (NH₃): *m/z* 222 [M+NH₄]⁺, 205 [M+H]⁺. DCI/NH₃-HRMS Calcd for C₁₃H₁₇O₂: 205.1229. Found: 205.1235.

1-Methyl-4-phenyl-2,6-dioxabicyclo[2.2.1]heptane **2c**

¹H-NMR (300 MHz, CDCl₃): δ 1.67 (s, 3H), 2.20 (s, 2H), 4.10 (m, 4H), 7.15-7.40 (m, 5H). ¹³C-NMR (75 MHz, CDCl₃): δ 18.0, 44.4, 52.8, 77.6, 109.1, 126.4, 127.6, 128.8, 136.4. CI-MS (NH₃) *m/z* 208 [M+NH₄]⁺, 191 [M+H]⁺. DCI/NH₃-HRMS Calcd for C₁₂H₁₅O₂: 191.1072. Found: 191.1075.

4-*n*-Butyl-1-methyl-2,6-dioxabicyclo[2.2.1]heptane **2d**

¹H-NMR (400 MHz, CDCl₃): δ 0.88 (t, 3H, *J* = 6.7 Hz), 1.21-1.58 (m, 9H), 1.66 (s, 2H), 3.71-3.78 (m, 4H). ¹³C-NMR (75 MHz, C₆D₆): δ 13.8, 18.3, 23.5, 27.9, 28.2, 44.9, 49.0, 76.2, 108.3. CI-MS (NH₃) *m/z* 188 [M+NH₄]⁺, 171 [M+H]⁺. DCI/NH₃-HRMS Calculated for C₁₀H₁₉O₂: 171.1385. Found: 171.1387.

1-Methyl-4-[3'-phenylprop-2'-enyl]-2,6-dioxabicyclo[2.2.2]octane **2e**

¹H-NMR (400 MHz, CDCl₃): δ 1.20 (s, 3H), 1.63-1.97 (m, 6H), 3.72-3.82 (m, 4H), 5.96 (dt, 1H, *J* = 15.6, 7.5 Hz), 6.28 (d, 1H, *J* = 15.6 Hz), 7.13-7.27 (m, 5H). ¹³C-NMR (75 MHz, CDCl₃): δ 25.0, 28.0, 32.0, 32.8, 37.4, 76.8, 94.7, 123.8, 126.1, 127.4, 128.6, 133.3, 137.0. CI-MS (NH₃) *m/z* 262 [M+NH₄]⁺, 245 [M+H]⁺. DCI/NH₃-HRMS Calculated for C₁₆H₂₁O₂: 245.1542. Found: 245.1547.

1-Methyl-4-[prop-2'-enyl]-2,6-dioxabicyclo[2.2.2]octane **2f**

¹H-NMR (400 MHz, CDCl₃): δ 1.25 (s, 3H), 1.63-1.97 (m, 6H), 3.72-3.82 (m, 4H), 5.00 (dd, 1H, *J* = 16.8, 1.7 Hz), 5.04 (dd, 1H, *J* = 8.9, 1.7 Hz), 5.63 (ddt, 1H, *J* = 16.8, 8.9, 7.5 Hz). ¹³C-NMR (75 MHz, CDCl₃): δ 25.0, 27.9, 31.9, 32.0, 38.3, 72.7, 94.6, 118.2, 132.2. CI-MS (NH₃) *m/z* 169 [M+H]⁺. DCI/NH₃-HRMS Calculated for C₁₀H₁₇O₂: 169.1150. Found: 169.1231.

1-Methyl-4-[prop-2'-enyl]-2,6-dioxabicyclo[2.2.1]heptane **2g**

¹H-NMR (300 MHz, CDCl₃): δ 1.52 (s, 3H), 1.68 (s, 2H), 2.32 (d, *J* = 7.4 Hz, 2H), 3.74 (m, 4H), 4.95-5.15 (m, 2H), 5.60-5.85 (m, 1H). ¹³C-NMR (75 MHz, CDCl₃): δ 17.9, 32.8, 44.2, 48.7, 75.8, 108.4, 117.8, 133.3. CI-MS (NH₃) *m/z* 172 [M+NH₄]⁺, 155 [M+H]⁺. DCI/NH₃-HRMS Calcd for C₉H₁₅O₂: 155.1072. Found: 155.1069.

1-Methyl-4-[cyclohex-2'-enyl]-2,6-dioxabicyclo[2.2.1]heptane **2h**

¹H-NMR (400 MHz, CDCl₃): δ 1.29-1.98 (m, 11H), 2.40-2.50 (m, 1H), 3.74-3.85 (m, 4H), 5.51 (d, 1H, *J* = 10.2 Hz), 5.73-5.78 (m, 1H). ¹³C-NMR (75 MHz, CDCl₃): δ 17.9, 21.9, 24.9, 25.8, 35.3, 43.0, 52.5, 74.5, 75.3, 108.0, 127.0, 129.3. CI-MS (NH₃) *m/z* 195 [M+H]⁺. DCI/NH₃-HRMS Calculated for C₁₂H₁₉O₂: 195.1385. Found: 195.1390.

1-Methyl-4-[3'-methyl-but-2'-enyl]-2,6-dioxabicyclo[2.2.1]heptane **2i**

¹H-NMR (400 MHz, CDCl₃): δ 1.51 (s, 3H), 1.58 (s, 3H), 1.67 (s, 2H), 1.69 (s, 3H), 2.23 (d, 2H, *J* = 7.6 Hz), 3.70-3.76 (m, 4H), 5.06-5.12 (m, 1H). ¹³C-NMR (75 MHz, CDCl₃): δ 17.6, 17.9, 25.7, 26.5, 44.2, 49.6, 76.3, 108.4, 118.9, 134.4. CI-MS (NH₃) *m/z* 183 [M+H]⁺. DCI/NH₃-HRMS Calculated for C₁₁H₁₉O₂: 183.1385. Found: 183.1379.

3-hydroxymethyl-3-prop-2'-ynylpentane-1,4-diol **1j**
(2 diastereomers)

¹H-NMR (300 MHz, CDCl₃) δ 1.19-1.23 (m, 3H), 1.50-1.70 (m, 2H), 2.00 (m, 1H), 2.10-2.40 (m, 2H), 3.40-4.20 (m, 5H). ¹³C-NMR (75 MHz, CDCl₃) δ 16.6, 16.7, 20.7, 22.1, 28.7, 32.8, 33.5, 42.4, 42.7, 57.1, 57.2, 65.1, 65.6, 69.8, 70.2, 70.7, 80.0, 80.2. CI-MS (NH₃) *m/z* 190 [M+NH₄]⁺, 173 [M+H]⁺. DCI/NH₃-HRMS Calcd for C₉H₁₇O₃: 173.1178. Found: 173.1174.

4-[1'-hydroxyethyl]-1-methyl-2,7-dioxabicyclo[3.2.1]octane **2j**
(4 diastereomers)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 1.10-1.30 (m, 3H), 1.40 (m, 3H), 1.50-1.80 (m, 4H), 2.20 (s, 1H), 3.40-4.30 (m, 5H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 13.7, 17.7, 19.0, 19.6, 23.8, 24.2, 24.5, 27.5, 28.5, 29.3, 33.1, 42.2, 44.6, 44.7, 45.5, 46.4, 46.6, 48.3, 48.5, 59.8, 60.2, 60.4, 65.6, 66.0, 70.7, 71.5, 73.9, 75.9, 79.6, 80.5, 104.3, 104.9, 106.3, 106.5. CI-MS (NH_3) m/z 190 $[\text{M}+\text{NH}_4]^+$, 173 $[\text{M}+\text{H}]^+$. DCI/ NH_3 -HRMS Calculated for DCI/ NH_3 -HRMS Calcd for $\text{C}_9\text{H}_{17}\text{O}_3$: 173.1178. Found: 173.1175.