Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

The First Efficient Oxidative Cyclization of 1,6-Dienes. A Highly Diastereoselective Entry to Substituted Tetrahydropyranes.

Stefanie Roth and Christian B. W. Stark*

Dipl.-Chem. S. Roth, Jr.-Prof. Dr. C. B. W. Stark
Freie Universität Berlin
Institut für Chemie und Biochemie
Takustraße 3, 14195 Berlin (Deutschland)
Fax: (+49)30-838-55367
E-mail: stark@chemie.fu-berlin.de

Experimental

Materials and methods. All reagents were used as purchased from commercial suppliers. Solvents were purified by conventional methods prior to use. Column chromatography: Merck silica gel 60, 0.040-0.063 mm (230-400 mesh). TLC: pre-coated aluminium sheets, Merck silica gel 60, F_{254}; detection by UV or by cerium/molybdenum solution [phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), concd. H_2SO_4 (60 ml), H_2O (940 ml)]. ^1H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ with a Bruker AC 500. Chemical shifts δ are given relative to TMS as internal standard or relative to the resonance of the solvent (^1H: $CDCl_3$, δ= 7.24 ppm; ^{13}C: $CDCl_3$, δ= 77.0 ppm). Mass spectra were recorded with a Varian MAT 771, MAT 112 S. FT-IR spectra were recorded with a Nicolet 5 SXC with DTGS detector.

Preparation of sodium periodate on wet silica

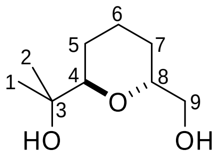
5.14 g (24.0 mmol) sodium periodate are suspended in 12 ml of water. Under magnetic stirring the mixture is heated to 70°C in a 100 ml flask. To this slightly cloudy solution is added 20 g silica in one go (at 70°C). The flask is removed from the heating bath fitted with a stopper and swirled until a fine homogenous powder has developed. The final concentration of solid supported periodate is 0.64 mmol/g.

General procedure for the oxidative cyclization of 1,6-dienes

0.05 mmol of a $RuCl_3$ stock solution (0.50 ml, 0.10 M) are dissolved in a solvent mixture of 15 ml ethylacetate and 15 ml of acetonitrile at 0 °C. 4.00 mmol $NaIO_4$ on wet silica (6.12 g, 1.53 mmol) are added after 5 minutes stirring. After the colour changes to bright yellow, 1.00 mmol of substrate is added dropwise via syringe. The reaction progress is monitored by TLC. After complete conversion of the starting material, 3 ml of *iso*-propanol (excess) are added. The reaction mixture is allowed to warm up to room temperature and stirred for another 5 minutes. The solids are filtered off and washed successively with ethylacetate and methanol. The filtrate is concentrated in vacuo and the resulting crude product is purified by column chromatography.

Reductive work up: In case where an aldehyde byproduct is formed, a reductive work up procedure is suggested. Therefore, the crude product is dissolved in 10 ml methanol and two spatula tips of sodium borohydride are added carefully. After 30 minutes stirring at room temperature the solvent is evaporated and the crude product is purified by column chromatography over silica gel.

***trans*-2-(6-Hydroxymethyl-tetrahydro-pyran-2-yl)-propan-2-ol**



reaction time: 25 min.

column chromatography: ethylacetate and hexane (4 : 1).

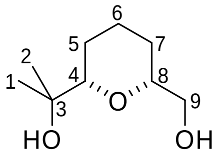
yield: 85 %, colourless oil.

^{1}H NMR (500 MHz): δ = 3.97 (dd, ^{3}J = 9.6 Hz, ^{2}J = 16.2 Hz, 2 H, H-9), 3.71 (s, 2 H, OH), 3.32 (dd, ^{3}J = 11.8, 2.1 Hz, 1 H, H-4), 3.27 (td , ^{3}J = 9.6, 9.6 Hz, 1 H, H-8), 1.34 - 1.68 (m, 5 H, H-5$_{\text{äq}}$, H-6, H-7), 1.20 (ddd, ^{3}J = 11.8, 4.0 Hz, ^{2}J = 24.3 Hz, 1 H, H-5$_{ax}$), 1.08 (s, 3 H, H-1), 1.07 ppm (s, 3 H, H-2); ^{13}C NMR (125 MHz): δ = 76.0 (s, C-4), 73.8 (s, C-8), 72.4 (s, C-3), 60.4 (s, C-9), 25.8 (s, C-1), 25.8 (s, C-2), 25.0 (s, C-7), 23.3 (s, C-5), 19.1 ppm (s, C-6); MS (EI, 50 °C): m/z = 159 (3

%, [M – CH_3]$^+$), 156 (1 %, [M – H_2O]$^+$), 143 (38 %, [M – CH_3O]$^+$), 125 (29 %, [M – CH_3O – H_2O]$^+$), 115 (17 %, [M – CH_3O - CO]$^+$), 107 (11 %, [M – CH_3O – H_2O – H_2O]$^+$), 97 (41 %, [M – C_3H_7O – H_2O]$^+$), 85 (51 %, [M – C_3H_7O - CH_3O]$^+$), 69 (34 %, [C_4H_5O]$^+$), 59 (53 %, [C_3H_7O]$^+$), 55 (38 %, [C_4H_7]$^+$), 43 (100 %, [CH_3O]$^+$); HRMS: calculated for $C_8H_{15}O_3$ ([M]$^+$): m/z = 159,102, found: 159,103; IR (KBr): $\bar{\nu} =$ 3385, 2936, 2869, 1462, 1444, 1382, 1363, 1157, 1105, 1049, 908, 877 cm^{-1}; EA: for $C_8H_{16}O_3$, calculated: C: 62,04 %, H: 10,41 %, found: C: 61,59 %, H: 10,29 %.

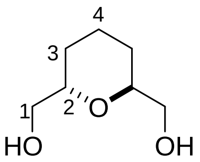
***cis*-2-(6-Hydroxymethyl-tetrahydro-pyran-2-yl)-propan-2-ol**

(**Note**: This compound has been prepared independently for comparison. This *cis*-isomer is not available by oxidative cyclisation.)



^{1}H NMR (500 MHz): δ = 3.50 (m, 2 H, H-4, H-8), 3.16 (dd, ^3J = 11.6 Hz, ^2J = 2.1 Hz, 2 H, H-9), 1.86 (m, 1 H, H-5a), 1.16-1.74 (m, 5 H, H-5b, H-6, H-7), 1.14 (s, 3 H, CH_3), 1.11 ppm (s, 3 H, CH_3); ^{13}C NMR (125 MHz): δ = 84.0, 78.5, 72.1, 66.2, 26.9, 26.2, 25.6, 23.7, 22.9 ppm. All other data are identical to the *trans*-isomer (vide infra).

(6-Hydroxymethyl-tetrahydro-pyran-2-yl)-methanol



reaction time: 10 min.

column chromatography: ethylacetate and hexane (4 : 1).

yield: 53 %.

^{1}H NMR (500 MHz): δ = 4.54 (s, 2 H, OH), 3.71 (m, 2 H, H-2), 3.63 (dd, ^3J = 9.2 Hz, ^2J = 11.6 Hz, 2 H, H-1a), 3.24 (dd, ^3J = 3.0 Hz, ^2J = 11.6 Hz, 2 H, H-1b) , 1.42 (m, 4 H, H-3), 1.17 ppm (m, 2 H, H-4); ^{13}C NMR (127,5 MHz): δ = 71.7 (C-1), 62.9 (C-2), 25.9 (C-3), 18.3 ppm (C-4); MS (pos. FAB, CH_2Cl_2 / m-NO_2-benzylic alcohol): m/z = 169 (17 %, $[M + Na]^+$), 147 (100 %, $[M+H]^+$), 128 (8 %, $[M - H_2O]^+$), 115 (15 %, $[M - CH_3O]^+$); HRMS: calculated for $C_7H_{12}O_2$ ($[M - H_2O]^+$): m/z = 128,084, found: 128,084; IR (KBr): $\bar{\nu} =$3370, 2937, 2870, 1664, 1443, 1102, 1043, 878, 775 cm^{-1}.

The *cis*-isomer of this compound has been described previously, cf.: A. C. Cope, A. Fournier Jr., *J. Am. Chem. Soc*. **1957**, *79*, 3896-3899; J. B. Jones, R. S. Hinks, *Can. J. Chem*. **1987**, *65*, 704-707.