Supporting Information

β-Destabilizing Effect of Silicon in Regioselective Hydroxymethylation of β-Silylcycloalkanone Enol Acetates by Electrochemical Method

Jih Ru Hwu,*†‡ Shwu-Chen Tsay,† Lung Ching Lin,§ and Lu Lin Chueh§

†Organosilicon and Synthesis Laboratory, Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan 11529, Republic of China; ‡Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 30043, Republic of China; and §Department of Chemistry, National Taiwan University, Taipei, Taiwan 10671, Republic of China

Experimental Section

General. Reagents were purchased from Aldrich or Fisher Chemical Co. Dry ether was obtained by distillation from the sodium kettle of benzophenone and hexanes were distilled over CaH₂ under nitrogen. Absolute methanol was purchased from Merck and used as received.

Infrared (IR) spectra were recorded on a Perkin–Elmer 983G spectrophotometer. Proton NMR spectra were obtained on a Bruker AM-300WB or AC-300 (300 MHz) spectrometer and ¹³C NMR spectra were performed on a Bruker AM-300WB or AC-300 (75 MHz) spectrometer. Mass spectra were carried out on a JEOL JMS-300 mass spectrometer and high resolution mass spectra
(HRMS) were performed on a JEOI-HX110 high performance mass spectrometer. Purification by column chromatography was carried out by use of Merck reagent silica gel 60 (particle size 230–400 mesh). Thin-layer chromatography was carried out on aluminum sheets (20 cm × 20 cm) coated with a 1-mm thick layer of silica gel/Kieselguhr F254.

**Standard Procedure for Hydroxymethylation of β-Silyl Enol Acetates.** To an anhydrous methanolic solution (25 mL) containing β-silyl enol acetates (50.0 mmol) were added 1.5 or 2.5 equivalents of NaOMe (75.0 or 125 mmol). The reaction was passed electricity of 2.0–4.0 F/mol at a constant current of 0.10 A (0.20 A/cm², terminal voltage 20 V) in an undivided cell equipped with two platinum electrodes. After enol acetates were consumed completely at room temperature, the reaction mixture was worked up with 0.50 N of aqueous HCl (30 mL) and then the aqueous solution was extracted with ether (100 mL × 3). The combined etheral layers were dried over MgSO₄ (s) and concentrated under reduced pressure. Purification of the crude products by use of silica gel column chromatography with a mixture of CHCl₃ and hexanes (1:1 in volume) as the eluant gave the desired ketone.

**2-Hydroxymethyl-4-(trimethylsilyl)cyclopentan-1-one (2)⁴:** ¹H NMR (CDCl₃) δ 0.03 (s, 9 H), 1.14–1.17 (m, 1 H), 1.61–2.40 (m, 5 H), 2.87 (br s, 1 H), 3.61 (dd, J = 11.6, 7.3 Hz, 1 H), 3.83 (dd, J = 11.6, 3.4 Hz, 1 H); ¹³C NMR (CDCl₃) δ −2.95, 22.95, 25.66, 39.05, 52.41, 62.26, 224.20; IR (neat) 3432 (s), 1733 (s), 1249 (s), 842 (s) cm⁻¹; MS m/z 186 (M⁺), 153, 147, 75, 73; HRMS calcd for C₅H₁₈O₂Si (M⁺) 186.1076, found 186.1082.

**2,2-Dihydroxymethyl-4-(trimethylsilyl)cyclopentan-1-one (3)⁴:** ¹H NMR (CDCl₃) δ −0.01 (s, 9 H), 1.33–1.35 (m, 1 H), 1.62–2.04 (m, 2 H), 2.20–2.24 (m, 2 H), 2.94 (br s, 2 H), 3.59–3.71 (m, 4 H); ¹³C NMR (CDCl₃) δ −3.52, 19.49, 30.40, 40.80, 55.95, 63.29, 65.41, 223.59; IR (neat) 3410 (s), 1723 (s), 1249 (s), 842 (s) cm⁻¹; MS m/z 216 (M⁺), 153, 147, 75, 73; HRMS calcd for C₁₀H₂₀O₃Si (M⁺) 216.1182, found 216.1169.
2-Hydroxymethyl-5-(trimethylsilyl)cyclohexan-1-one (5): $^1$H NMR (CDCl$_3$) $\delta$ -0.03 (s, 9 H), 0.94–1.16 (m, 1 H), 1.44–1.98 (m, 4 H), 2.08–2.50 (m, 3 H), 2.75 (br s, 1 H), 3.58 (dd, $J = 11.6$, 7.3 Hz, 1 H), 3.70 (dd, $J = 11.6$, 3.4 Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ -1.86, 26.70, 29.74, 30.16, 42.26, 53.69, 61.74, 216.32; IR (neat) 3471 (s), 1691 (s), 1249 (s), 842 (s) cm$^{-1}$; MS $m/z$ 200 (M$^+$), 153, 147, 75, 73; HRMS calcd for C$_{10}$H$_{20}$O$_2$Si (M$^+$) 200.1232, found 200.1231.

2,2-Dihydroxymethyl-5-(trimethylsilyl)cyclohexan-1-one (6): $^1$H NMR (CDCl$_3$) $\delta$ -0.01 (s, 9 H), 0.94–1.18 (m, 1 H), 1.28–1.98 (m, 4 H), 2.23–2.25 (m, 2 H), 3.15 (br s, 2 H), 3.71 (dd, $J = 11.6$, 3.4 Hz, 1 H), 3.83 (dd, $J = 11.6$, 7.3 Hz, 1 H), 3.93 (dd, $J = 11.6$, 7.3 Hz, 1 H), 4.11 (dd, $J = 11.6$, 3.4 Hz, 1 H); $^{13}$C NMR (CDCl$_3$) $\delta$ -3.75, 21.68, 28.47, 33.60, 40.03, 54.22, 59.67, 67.29, 217.32; IR (KBr) 3356 (s), 1702 (s), 1249 (s), 842 (s) cm$^{-1}$; MS $m/z$ 230 (M$^+$), 153, 147, 75, 73; HRMS calcd for C$_{11}$H$_{22}$O$_3$Si (M$^+$) 230.1338, found 230.1339.

Computations. Computations and graphic molecular modeling of the allylic anions of 3-(trimethylsilyl)cyclohexan-1-one enol acetate (4) and 3-(i-propyl)cyclohexan-1-one enol acetate were performed on a Silicon Graphics IRIS CRIMSON/Elan workstation. The programs Builder was used for the construction of organic species. The program Discover was used for energy calculation. The energies for different conformations were computed with the consistent valence forcefield. Our analysis indicates that no significant torsional effect$^2$ would result from the difference between the C–Si and the C–C bonds (the former is about 20% longer). The most stable conformational isomers of 7 (i.e., A) and its isopropyl derivative (i.e., B) are shown on the next page.

Reference