2nd Revised

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 CaH_2 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 ^{13}C 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 JEOL-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 F_{254}.

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/cm^2, 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 $MgSO_4$ (s) and concentrated under reduced pressure. Purification of the crude products by use of silica gel column chromatography with a mixture of $CHCl_3$ and hexanes (1:1 in volume) as the eluant gave the desired ketone.

2-Hydroxymethyl-4-(trimethylsilyl)cyclopentan-1-one (2)[1]: ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 $C_9H_{18}O_2Si$ (M$^+$) 186.1076, found 186.1082.

2,2-Dihydroxymethyl-4-(trimethylsilyl)cyclopentan-1-one (3)[1]: ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) 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 $C_{10}H_{20}O_3Si$ (M$^+$) 216.1182, found 216.1169.

2-Hydroxymethyl-5-(trimethylsilyl)cyclohexan-1-one (5)[1]: ^{1}H NMR ($CDCl_3$) δ –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), 2.78 (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 ($CDCl_3$) δ –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 $C_{10}H_{20}O_2Si$ (M^+) 200.1232, found 200.1231.

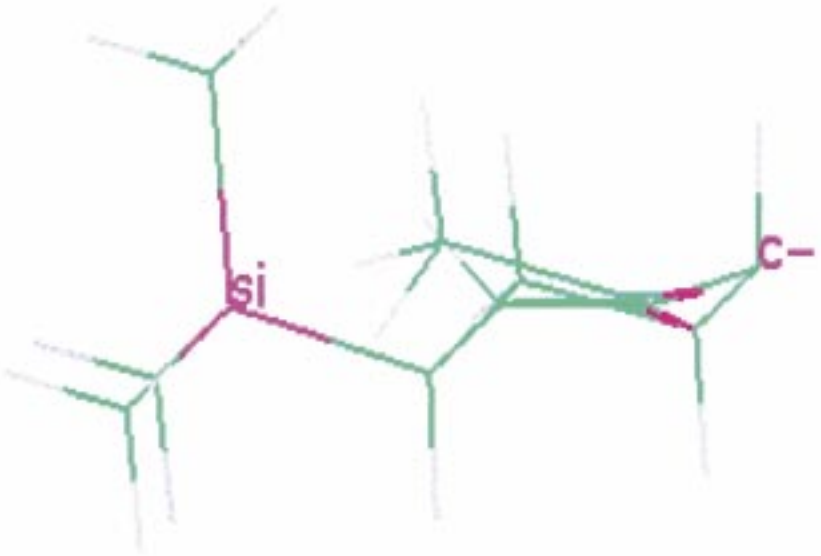
2,2-Dihydroxymethyl-5-(trimethylsilyl)cyclohexan-1-one (6)[1]: ^{1}H NMR ($CDCl_3$) δ –0.01 (s, 9 H), 0.94–1.18 (m, 1 H), 1.28–1.98 (m, 4 H), 2.23–2.25 (m, 2 H), 3.15 (br s, 2 H), 3.71 (dd, J = 11.6, 3.4 Hz, 1 H), 3.83 (dd, J = 11.6, 7.3 Hz, 1 H), 3.93 (dd, J = 11.6, 7.3 Hz, 1 H), 4.11 (dd, J = 11.6, 3.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ –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 $C_{11}H_{22}O_3Si$ (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.

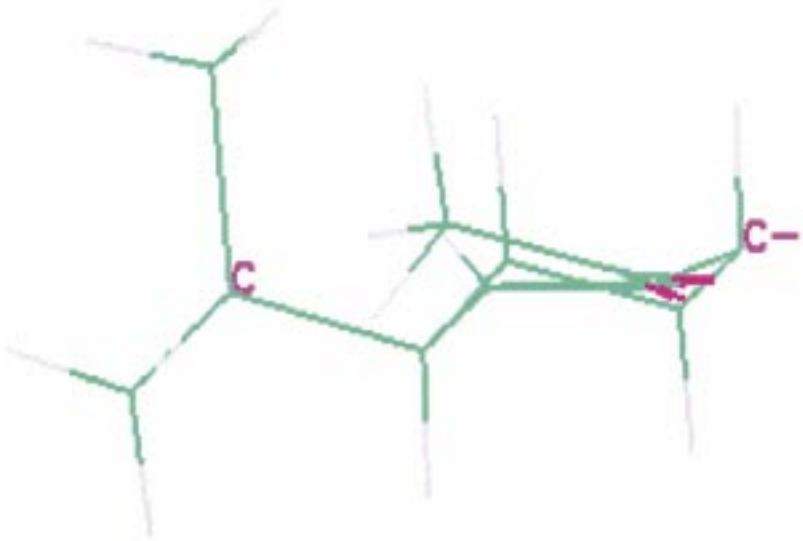
Reference

(1) Lin, L. C.; Li, Y. C.; Lin, C. C.; Hwu, J. R. *J. Chem. Soc., Chem. Commun.* **1996**, 509–510.

(2) Carey, F. A.; Sundberg, R. J. In *Advanced Organic Chemistry*, 3rd ed.; Plenum: New York, 1990; Part A, Chapter 3, p 167.



A



B