A Direct Preparation of 6-Methylene-2-cyclohexenones

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Received 10 June 2003; revised 5 February 2004

Abstract: The reaction of enol silyl ethers with Eschenmoser's salt, followed by methylation and elimination, provides ready access to 6-methylene-2-cyclohexenones.

Key words: Eschenmoser's salt, 6-methylene-2-cyclohexenones, enol silyl ethers

In the course of studying tandem reactions on dienones, we needed substituted 6-methylene cyclohexenones **1a**–**c**.[1] There are few literature reports of compounds of this class. Wiberg and coworkers prepared **1c** by the reaction of ketene with 1,4-bicyclo[2.2.0]hexene.[2] Reddy reported the preparation of **1b** as a by-product in a transition metal mediated rearrangement.[3]

Initially, we tried both the Gras methylenation reaction[4] and the McMurry methylenation reaction[5] with cyclohexenone. Although we had employed the latter reaction successfully with substituted cyclohexanones, neither reaction provided **1a**. We eventually discovered that the reaction of enol silyl ethers of cyclohexenone with Eschenmoser's salt[6] followed by methylation and elimination afforded good overall yields of the desired products. The overall yields from **3a**, **3b**,[7] and **3c** were 65%, 54% and 49%, respectively (Scheme 1).

Dienones **1a**–**c** can be prepared in a one-pot reaction from the corresponding enol silyl ethers.[8] The ready availability of these novel cross-conjugated dienones will make possible new pathways to complex bridged- and spiro systems.

General Experimental Procedure

To a cooled solution (0 °C) of Eschenmoser's salt (1.3 mmol) in CH_2Cl_2 (0.4 M solution) was added the silyl enol ether (1 mmol). After stirring for 24 h at r.t., the reaction mixture was diluted with CH_2Cl_2 (5 mL) and 1 N HCl (6 mL). After 10 min at r.t., a 2 N solution of NaOH was slowly added to the aqueous phase (until pH 14). The aqueous phase was extracted with CH_2Cl_2 (4×10 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give amine **2**, which was dissolved in anhyd MeOH (1 M solution). MeI (1.75mmol) was added slowly with stirring at 0 °C. The resulting solution was warmed to r.t. and stirred for 1 h to give the ammonium salt as a white precipitate. After removing the solvent and the excess MeI, the crude salt was dissolved in H_2O (10 mL) and Et_2O (10 mL). To the solution of salt was added $NaHCO_3$ (4.5 mmol) and the reaction was stirred vigorously for 2 h at r.t. The aqueous layer was extracted with Et_2O (3×20 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Further purification by short path column chromatography on silica gel (hexane–Et_2O = 10:1–5:1) gave compound **1** as a colorless volatile oil.

6-Methylene Cyclohexenone (1a)

R_f = 0.35 (hexane–Et_2O, 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.06 (dt, J = 10, 4 Hz, 1 H), 6.15 (d, J = 10 Hz, 1 H), 5.96 (d, J = 1.2 Hz, 1 H), 5.29 (d, J = 1.2 Hz, 1 H), 2.75 (t, J = 6.4 Hz, 2 H), 2.46 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.7, 150.7, 142.9, 130.5, 120.1, 31.0, 26.4.

HRMS (EI): m/z [M]$^+$ calcd for C_7H_8O: 108.0575; found: 108.0577.

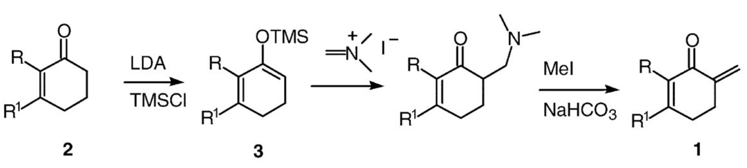
2-Methyl-6-methylene Cyclohexenone (1b)

R_f = 0.62 (hexane–Et_2O, 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (br s, 1 H), 5.95 (s, 1 H), 5.25 (d, J = 1.6 Hz, 1 H), 2.71 (t, J = 6.4 Hz, 2 H), 2.40 (dd, J = 4.4, 2 Hz, 2 H), 1.85 (d, J = 0.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.5, 145.8, 143.5, 136.9, 119.7, 31.7, 26.3, 16.4.

HRMS (EI): m/z [M]$^+$ calcd for $C_8H_{10}O$: 122.0732; found: 122.0773.



a: R = R^1 = H
b: R = Me, R^1 = H
c: R = H, R^1 = Me

Scheme 1

SYNTHESIS 2004, No. 11, pp 1737–1738
Advanced online publication: 22.07.2004
DOI: 10.1055/s-2004-829162; Art ID: M02803SS

3-Methyl-6-methylene Cyclohexenone (1c)
$R_f = 0.31$ (hexane–Et_2O, 2:1).

^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.01$ (br s, 1 H), 5.96 (d, $J = 1.6$ Hz, 1 H), 5.27 (d, $J = 1.2$ Hz, 1 H), 2.73 (tt, $J = 6.4, 1.6$ Hz, 2 H), 2.38 (t, $J = 6$ Hz, 2 H), 2.00 (d, $J = 0.4$ Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 188.8, 163.0, 142.3, 127.5, 119.1, 31.6, 31.0, 24.8$.

HRMS (EI): m/z calcd $[M]^+$ for $C_8H_{10}O$: 122.0732; found: 122.0773.

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