Dichloromethane as an Unusual Methylene Equivalent. A New Entry of Highly Nucleophilic and Selective Titanium-Methylene-Complexes for Ester Methylenation

Tu-Hsin Yan*, Ching-Ting Chien, Chia-Chung Tsai, Kuo-Wei Lin, and Yen-Hsien Wu
Department of Chemistry, National Chung-Hsing University, Taichung 400, Taiwan, Republic of China
E-mail: thyan@mail.nchu.edu.tw

Supporting Information

General Information. Dichloromethane was distilled from P_2O_5 prior to use. Commercially available esters were used as received (Lancaster, Acros, Aldrich, Tedia, RDH). Titanium tetrachloride was purchased from Fluka Chemie AG. Magnesium powder (ca 50 mesh) was purchased from Lancaster Synthesis Ltd. Esters **1b**,¹ **1c-1e**,² and **1g-1p**² were prepared according to the reported procedures. Flash chromatography was performed on neutral (Macherey Nagel) or basic aluminum oxide (Merck, 90-active basic). All reactions were carried out under an atmosphere of N_2 . 1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 MHz spectrometer at ambient temperature. High-resolution mass spectra were determined on a Jeol JMS-HX 110 spectrometer.

¹Stork, G.; Landesman, H. K. *J. Am. Chem. Soc.* **1956**, 78, 5128.

²Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, 17, 522.

General procedure for the methylenation of esters **1a-1e**, **1g-1l**, and **1p**:

A solution of ester **1** (1 mmol) in 2 mL of THF was added by syringe to a suspension consisting of Mg (192 mg, 8 mmol), $TiCl_4$ (379 mg, 0.21 mL, 2 mmol), and CH_2Cl_2 (5 mL) at room temperature. After being stirred for 1 h, the resulting black slurry was cooled to 0 °C, then carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried, evaporated, and purified by chromatography on basic aluminum oxide (elution with 100:3:1 hexane-ethyl acetate- NEt_3).

Procedure for the methylenation of esters **1f**:

To a 0 °C suspension consisting of Mg (192 mg, 8 mmol), TiCl₄ (379 mg, 0.21 mL, 2 mmol), and toluene (5 mL) was added dry THF (4 mL) over a 1-min period. After the initial exotherm had ceased, the cooling bath was removed. A solution of ester **1f** (1 mmol) in CH₂Cl₂ (5 mL) and THF (1 mL) was added. The reaction mixture was stirred for 1 h at room temperature. Standard workup and purification gave **2f**.

General procedure for methylenation of esters **1m-1o**:

Methylenation of benzyl 2,5-cyclohexadiene-1-carboxylate **1n**: At 0 °C, ester **1n** (214 mg, 1 mmol) in CH₂Cl₂ (2 mL) and THF (2 mL) was added to a suspension consisting of Mg (192 mg, 8 mmol) and TiCl₄ (2 mmol, 0.5 M in CH₂Cl₂, 4 mL). After the initial exotherm had ceased, the cooling bath was removed. The black slurry was stirred for 1 h, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried, evaporated, and purified by chromatography on basic aluminum oxide (elution with 100:3:1 hexane-ethyl acetate-NEt₃) to give vinyl ether **2n** (191 mg, 90% yield) as a colorless oil.

Methyl [2-(2methylenecyclohexyl)ethyl]vinyl ether 2b: As described above, 184 mg (1 mmol) of **1b** and Mg/TiCl₄/CH₂Cl₂/THF gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 166 mg (92%) of **2b** as a colorless oil: ¹H NMR (400 MHz, C₆D₆) δ 4.74 and 4.71 (2s, 2 H, H₂C=C), 3.97 (d, *J* = 1.2 Hz, 1 H, HC=C-O), 3.85 (d, *J* = 1.2 Hz, 1 H, HC=C-O), 3.23 (s, 3 H, H₃C-O), 5.63 (dt, *J* = 10, 2.8 Hz, 1 H, HC=CH), 4.41 (bs, 1 H, HC-O), 4.00 and 4.02 (2s, 2 H, H₂C=C-O), 3.38 (s, 2 H, =C-H₂C-Ph), 2.24-1.92 (m, 5 H), 1.69-1.21 (m, 8 H); ¹³C NMR (75.5 MHz, C₆D₆) δ 164.84, 152.31, 106.34, 80.34, 54.38, 42.93, 34.84, 34.11, 33.41, 30.28, 29.09, 24.33; high-resolution MS *m/e* Calcd for C₁₂H₂₀O: 180.1521. Found: 180.1514.

(1-Benzylvinyl) phenyl ether 2e: As described above, 212 mg (1 mmol) of **1e** and Mg/TiCl₄/CH₂Cl₂/THF gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) gave **2e** (191 mg, 90%) as a colorless oil: ¹H NMR (400 MHz, C₆D₆) δ 7.26-6.83 (m, 10 H), 4.11 (s, 2 H, H₂C=C), 3.44 (s, 2 H, =C-H₂C-Ph); ¹³C NMR (75.5 MHz, C₆D₆) δ 163.00, 155.95, 138.39, 129.77, 129.37, 128.64, 126.75, 124.20, 121.22, 90.25, 40.97; high-resolution MS *m/e* Calcd for C₁₅H₁₄O: 210.1045. Found: 210.1053.

3,4-Dihydro-2-methylene-2H-1-benzopyran 2f: As described above, 150 mg (1 mmol) of **1f** and Mg/TiCl₄/CH₂Cl₂/THF gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 121 mg (82%) of **2f** as a colorless oil: ¹H NMR (400 MHz, C₆D₆) δ 6.99-6.93 (m, 2 H), 6.80-6.74 (m, 2 H), 4.71 and 3.99 (2s, 2 H,

$H_2C=C$), 2.30 (t, $J = 6.4$ Hz, 2 H, H_2C-Ph), 2.09 (t, $J = 6.4$ Hz, 2 H, $H_2C-C=$); ^{13}C NMR (75.5 MHz, C_6D_6) δ 156.46, 153.63, 128.94, 125.80, 122.99, 121.41, 116.47, 89.60, 26.53, 25.33; high-resolution MS m/e Calcd for $C_9H_8O_2$: 148.0524. Found: 148.0531.

(1-Benzylvinyl) 2-cyclohexenyl ether 2g: As described above, 216 mg (1 mmol) of **1g** and $Mg/TiCl_4/CH_2Cl_2/THF$ gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) gave **2g** (161 mg, 75%) as a colorless oil: 1H NMR (400 MHz, C_6D_6) δ 7.25-7.04 (m, 5 H, C_6H_5), 5.85 (dd, $J = 10$, 2.4 Hz, 1 H, $HC=CH$), 5.63 (dt, $J = 10$, 2.8 Hz, 1 H, $HC=CH$), 4.41 (bs, 1 H, $HC-O$), 4.00 and 4.02 (2s, 2 H, $H_2C=C-O$), 3.38 (s, 2 H, $=C-H_2C-Ph$), 1.76-1.48 (m, 5 H), 1.32-1.22 (m, 1 H); ^{13}C NMR (75.5 MHz, C_6D_6) δ 161.11, 139.21, 130.99, 129.32, 128.43, 126.92, 126.42, 83.17, 70.12, 42.43, 28.17, 25.21, 19.41; high-resolution MS m/e Calcd for $C_{15}H_{18}O$: 214.1352. Found: 214.1358.

2-Cyclohexenyl phenyl ether 2k: As described above, 212 mg (1 mmol) of **1k** and $Mg/TiCl_4/CH_2Cl_2/THF$ gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 164 mg (78%) of **2k** as a colorless oil: 1H NMR (400 MHz, C_6D_6) δ 7.76-7.74 (m, 2 H), 7.14-7.07 (m, 3 H), 5.95 (dd, $J = 10$, 2.4 Hz, 1 H, $HC=CH$), 5.71 (dt, $J = 10$, 2.8 Hz, 1 H, $HC=CH$), 4.75 (d, $J = 2.4$ Hz, 1 H, $HC=C-O$), 4.56 (bs, 1 H, $HC-O$), 4.21 (d, $J = 2.4$ Hz, 1 H, $HC=C-O$), 1.89-1.60 (m, 5 H), 1.36-1.30 (m, 1 H); ^{13}C NMR (75.5 MHz, C_6D_6) δ 158.89, 137.74, 131.31, 128.54, 128.29, 126.81, 126.03, 83.27, 70.46, 28.31, 25.31, 19.46; high-resolution MS m/e Calcd for $C_{15}H_{14}O$: 210.1045. Found: 210.1053.

Methyl 1-(2,5-cyclohexadienyl)vinyl ether 2m: As described above, 138 mg (1 mmol) of **1m** and $Mg/TiCl_4/CH_2Cl_2/THF$ gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) gave **2m** (119 mg, 88%) as a colorless oil: 1H NMR (400 MHz, C_6D_6) δ 5.89-5.86 (m, 2 H, $(HC=C)_2CH$), 5.66-5.63 (m, 2 H, $(HC=C)_2CH_2$), 4.06 (d, $J = 1.6$ Hz, 1 H, $HC=C-O$), 3.88 (d, $J = 1.6$ Hz, 1 H, $HC=C-O$), 3.58-3.55 (m, 1 H, $HC-C=C$), 3.19 (s, 3 H, H_3C-O), 2.48-2.45 (m, 2 H, $H_2C-C=C$); ^{13}C NMR (75.5 MHz, C_6D_6) δ 166.64, 126.62, 124.78, 80.72, 54.60, 41.57, 26.17; high-resolution MS m/e Calcd for $C_9H_{12}O$: 136.0880. Found: 136.0884.

Benzyl 1-(2,5-cyclohexadienyl)vinyl ether 2n: As described above, 214 mg (1 mmol) of **1n** and $Mg/TiCl_4/CH_2Cl_2/THF$ gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 190 mg (90%) of **2n** as a colorless oil: 1H NMR (400 MHz, C_6D_6) δ 7.22-7.04 (m, 5 H, C_6H_5), 5.94-5.90 (m, 2 H, $(HC=C)_2CH$), 5.67-5.63 (m, 2 H, $(HC=C)_2CH_2$), 4.53 (s, 2 H, H_2C-O), 4.15 (d, $J = 1.6$ Hz, 1 H, $HC=C-O$), 4.00 (d, $J = 1.6$ Hz, 1 H, $HC=C-O$), 3.63-3.60 (m, 1 H, $HC-C=C$), 2.46-2.00 (m, 2 H, $H_2C-C=C$); ^{13}C NMR (75.5 MHz, C_6D_6) δ 165.43, 137.73, 128.69, 127.76, 127.56, 126.52, 124.90,

82.25, 69.59, 41.55, 26.21; high-resolution MS m/e Calcd for C₁₅H₁₆O: 212.1209. Found: 212.1205. Anal. Calcd for C₁₅H₁₆O: C, 84.87; H, 7.60. Found: C, 84.63; H, 7.66.

Isopropyl 1-(2,5-cyclohexadienyl)vinyl ether 2o: As described above, 166 mg (1 mmol) of **1o** and Mg/TiCl₄/CH₂Cl₂/THF gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) gave **2o** (142 mg, 87%) as a colorless oil: ¹H NMR (400 MHz, C₆D₆) δ 5.92-5.89 (m, 2 H, (HC=C)₂CH), 5.67-5.63 (m, 2 H, (HC=C)₂CH₂), 4.15 (d, *J* = 2.0 Hz, 1 H, HC=C-O), 4.04 (septet, *J* = 6.0 Hz, 1 H, HC(CH₃)₂), 3.92 (d, *J* = 2.0 Hz, 1 H, HC=C-O), 3.51-3.56 (m, 1 H, HC-C=C), 2.53-2.43 (m, 2 H, H₂C-C=C), 1.07 (d, *J* = 6.0 Hz, 6 H, (CH₃)₂C); ¹³C NMR (75.5 MHz, C₆D₆) δ 164.07, 126.84, 124.59, 81.58, 68.55, 41.83, 26.27, 21.53; high-resolution MS m/e Calcd for C₁₁H₁₆O: 164.1215. Found: 164.1208.

2-*t*-Butoxy-4-phenylbutene 2p: As described above, 206 mg (1 mmol) of **1p** and Mg/TiCl₄/CH₂Cl₂/THF gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 103 mg (50%) of **2p** as a colorless oil: ¹H NMR (400 MHz, C₆D₆) δ 7.15-7.04 (m, 5 H), 4.03 and 4.00 (2s, 2 H, H₂C=C), 2.81 (t, *J* = 8.0 Hz, 2 H, H₂C-Ph), 2.35 (t, *J* = 8.0 Hz, 2 H, H₂C-C=), 1.26 (s, 9 H, (H₃C)₃-C); ¹³C NMR (75.5 MHz, C₆D₆) δ 158.79, 142.22, 128.78, 128.58, 126.00, 87.01, 76.45, 39.54, 34.45, 28.28; high-resolution MS m/e Calcd for C₁₄H₂₀O: 204.1500. Found: 204.1507.