Facile S_N2' Coupling Reactions of Wittig Reagents with Dimethyl

Bromomethylfumarate: Synthesis of Enes, Dienes and Related Natural Products

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Experimental: General Description

Melting points are uncorrected. The ^1H NMR spectra were recorded on 200 MHz NMR spectrometer using TMS as an internal standard. The ^{13}C NMR spectra were recorded on 200 NMR spectrometer (50 MHz), 400 NMR spectrometer (100 MHz) and 500 NMR spectrometer (125 MHz). The IR spectra were recorded on an FT-IR spectrometer. Column chromatographic separations were carried out on silica gel (60-120 mesh). Commercially available citraconic anhydride, triphenyl phosphine, benzyl bromide, 2-nitrobenzyl bromide, 4-nitrobenzyl bromide, 4-methoxybenzyl bromide, 3,5-dimethoxybenzyl bromide, 3,4-dimethoxybenzyl bromide, 2-chlorobenzyl bromide, 3-chlorobenzyl bromide, 2-fluorobenzyl bromide, allyl bromide, 5-iodo-[1,3]dioxole, 4-iodo-1,2-dimethoxybenzene, methyl bromide, $\text{Pd}(\text{OAc})_2$, Cy_2NH , iodobenzene, *n*-BuLi (1.50 M) and *N*-Bromosuccinimide were used. The LiAlH_4 dried THF was used.

Spectral and analytical data for compounds **3b**, **3d**, **3e**, **3f**, **5b**, **5d**, **5e**, **5f** and **5i**.

The compounds **3b** and **3d-f** were prepared similarly using the procedure described for the preparation of **3a** in the experimental section.

(E)-Dimethyl 2-(4-methoxybenzylidene)-3-methylenesuccinate (3b). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain major product **3b** (64%) and minor product **5b** (11%) as thick oils. ^1H NMR (CDCl_3 , 200 MHz) δ 3.75 (s, 3H), 3.79 (s, 3H), 3.82 (s, 3H), 5.73 (d, $J = 2$ Hz, 1H), 6.53 (d, $J = 2$ Hz, 1H), 6.85 (d, $J = 8$ Hz, 2H), 7.42 (d, $J = 10$ Hz, 2H), 7.76 (s, 1H); ^{13}C NMR (CDCl_3 , 50 MHz) δ 52.2, 52.3, 55.3, 114.0, 125.9, 126.9, 130.5, 132.0, 136.4, 141.4, 160.6, 166.6, 167.5; IR (CHCl_3) ν_{max} 1711, 1605, 1512 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_5$: C, 65.21; H, 5.84. Found: C, 65.17; H, 5.65.

(E)-Dimethyl 2-(3,5-dimethoxybenzylidene)-3-methylenesuccinate (3d). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain major product **3d** (64%) and minor product **5d** (11%) as thick oils. ^1H NMR (CDCl_3 , 200 MHz) δ 3.74 (s, 3H), 3.75 (s, 6H), 3.80 (s, 3H), 5.72 (d, $J = 2$ Hz, 1H), 6.42 (t, $J = 2$ Hz, 1H), 6.51 (d, $J = 2$ Hz, 1H), 6.58 (d, $J = 2$ Hz, 2H), 7.73 (s, 1H); ^{13}C NMR (CDCl_3 , 50 MHz) δ 52.2, 52.3, 55.2, 101.8, 107.9, 128.8, 130.5, 136.1, 136.2, 141.8, 160.6, 166.3, 167.0; IR (CHCl_3) ν_{max} 1717, 1593, 1437 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_6$: C, 62.74; H, 5.92. Found: C, 62.70; H, 5.89.

(E)-Dimethyl 2-(2-chlorobenzylidene)-3-methylenesuccinate (3e). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain major product **3e** (66%) and minor product **5e** (12%) as thick oils. ^1H NMR

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(CDCl₃, 200 MHz) δ 3.76 (s, 3H), 3.83 (s, 3H), 5.54 (d, J = 2 Hz, 1H), 6.33 (d, J = 2 Hz, 1H), 7.10-7.30 (m, 3H), 7.35-7.43 (m, 1H), 7.94 (s, 1H); ¹³C NMR (CDCl₃, 50 MHz) δ 52.2, 52.4, 126.6, 129.5, 130.0, 130.3, 130.7, 131.4, 133.7, 134.4, 135.6, 139.0, 166.3, 166.5; IR (CHCl₃) $\nu_{\max}$ 1717, 1643, 1624, 1437 cm⁻¹. Anal. Calcd for C₁₄H₁₃ClO₄: C, 59.90; H, 4.67; Cl, 12.63. Found: C, 60.01; H, 4.88; Cl, 12.57.

(E)-Dimethyl 2-(3-chlorobenzylidene)-3-methylenesuccinate (3f). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain major product **3f** (62%) and minor product **5f** (13%) as thick oils. ¹H NMR (CDCl₃, 200 MHz) δ 3.77 (s, 3H), 3.81 (s, 3H), 5.67 (d, J = 2 Hz, 1H), 6.49 (d, J = 2 Hz, 1H), 7.23-7.30 (m, 3H), 7.35-7.40 (m, 1H), 7.73 (s, 1H); ¹³C NMR (CDCl₃, 50 MHz) δ 52.3, 52.4, 127.8, 129.2, 129.7 (2 carbons), 129.9, 130.9, 134.3, 135.6, 136.1, 140.1, 166.2, 166.8; IR (CHCl₃) $\nu_{\max}$ 1728, 1630, 1599, 1574, 1437 cm⁻¹. Anal. Calcd for C₁₄H₁₃ClO₄: C, 59.90; H, 4.67; Cl, 12.63. Found: C, 59.67; H, 4.62; Cl, 12.78.

The compounds **5b**, **5d-f** and **5i** were prepared similarly using the procedure described for the preparation of **5a** in the experimental section.

Dimethyl 2-(4-methoxybenzyl)-3-methylenesuccinate (5b). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain major product **5b** (55%) and minor product **3b** (20%) as thick oils. ¹H NMR (CDCl₃, 200 MHz) δ 2.91 (dd, J = 14 & 8 Hz, 1H), 3.18 (dd, J = 14 & 8 Hz, 1H), 3.63 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 3.70-3.83 (m, 1H), 5.68 (s, 1H), 6.31 (s, 1H), 6.81 (d, J = 8 Hz, 2H), 7.08 (d, J = 8 Hz, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 36.6, 49.0, 52.0, 52.1, 55.1, 113.7, 127.4, 129.9, 130.8, 137.7, 158.2, 166.4, 173.1; IR (CHCl₃) $\nu_{\max}$ 1732, 1715, 1630, 1612, 1514 cm⁻¹. Anal. Calcd for C₁₅H₁₈O₅: C, 64.74; H, 6.52. Found: C, 64.85; H, 6.68.

Dimethyl 2-(3,5-dimethoxybenzyl)-3-methylenesuccinate (5d). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain major product **5d** (58%) and minor product **3d** (17%) as thick oils. ¹H NMR (CDCl₃, 200 MHz) δ 2.90 (dd, J = 14 & 8 Hz, 1H), 3.20 (dd, J = 14 & 8 Hz, 1H), 3.65 (s, 3H), 3.76 (s, 9H), 3.80 (dd, J = 14 & 8 Hz, 1H), 5.69 (s, 1H), 6.31 (bs, 4H); ¹³C NMR (CDCl₃, 125 MHz) δ 37.6, 48.5, 52.1 (2 carbons), 55.2, 98.5, 106.9, 127.5, 137.6, 141.1, 160.7, 166.4, 172.9; IR (CHCl₃) $\nu_{\max}$ 1732, 1717, 1597 cm⁻¹. Anal. Calcd for C₁₆H₂₀O₆: C, 62.33; H, 6.54. Found: C, 62.42; H, 6.61.

Dimethyl 2-(2-chlorobenzyl)-3-methylenesuccinate (5e). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an

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eluent to obtain major product **5e** (60%) and minor product **3e** (18%) as thick oils. ^1H NMR (CDCl_3 , 200 MHz) δ 3.11 (dd, $J = 14$ & 8 Hz, 1H), 3.39 (dd, $J = 14$ & 8 Hz, 1H), 3.64 (s, 3H), 3.74 (s, 3H), 3.90 (t, $J = 8$ Hz, 1H), 5.61 (s, 1H), 6.26 (s, 1H), 7.05-7.20 (m, 3H), 7.25-7.38 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 35.0, 47.0, 52.0 (2 carbons), 126.6, 127.9, 128.0, 129.5, 131.5, 134.2, 136.4, 137.6, 166.1, 172.6; IR (CHCl_3) ν_{max} 1734, 1717, 1636, 1630 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{ClO}_4$: C, 59.48; H, 5.35; Cl, 12.54. Found: C, 59.38; H, 5.41; Cl, 12.47.

Dimethyl 2-(3-chlorobenzyl)-3-methylenesuccinate (5f). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain major product **5f** (55%) and minor product **3f** (20%) as thick oils. ^1H NMR (CDCl_3 , 200 MHz) δ 2.93 (dd, $J = 14$ & 6 Hz, 1H), 3.22 (dd, $J = 14$ & 8 Hz, 1H), 3.64 (s, 3H), 3.77 (s, 3H), 3.70-3.85 (m, 1H), 5.67 (s, 1H), 6.32 (s, 1H), 7.00-7.10 (m, 1H), 7.10-7.30 (m, 3H); ^{13}C NMR (CDCl_3 , 50 MHz) δ 37.0, 48.6, 52.1, 52.2, 126.7, 127.2, 127.7, 129.0, 129.6, 134.0, 137.4, 140.8, 166.2, 172.6; IR (CHCl_3) ν_{max} 1736, 1719, 1636, 1618 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{ClO}_4$: C, 59.48; H, 5.35; Cl, 12.54. Found: C, 59.55; H, 5.23; Cl, 12.67.

Dimethyl 2-methylene-3-(2-nitrobenzyl) succinate (5i). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain **5i** (85%) as a thick oil. ^1H NMR (CDCl_3 , 200 MHz) δ 3.27 (dd, $J = 14$ & 8 Hz, 1H), 3.63 (dd, $J = 14$ & 8 Hz, 1H), 3.64 (s, 3H), 3.74 (s, 3H), 3.89 (dd, $J = 14$ & 8 Hz, 1H), 5.62 (s, 1H), 6.29 (s, 1H), 7.29 (d, $J = 8$ Hz, 1H), 7.37 (t, $J = 8$ Hz, 1H), 7.50 (t, $J = 8$ Hz, 1H), 7.94 (d, $J = 8$ Hz, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 34.4, 47.9, 52.2 (2 carbons), 124.9, 127.8, 128.3, 132.8, 133.0, 133.8, 137.5, 149.5, 166.1, 172.4; IR (CHCl_3) ν_{max} 1740, 1720, 1630, 1611 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{NO}_6$: C, 57.33; H, 5.16; N, 4.78. Found: C, 57.24; H, 5.08; N, 4.85.

SI-6

CDCl₃ / 200 MHz

SI-7

CDCl₃ / 50 MHz

CDCl₃ / 50 MHz

SI-8

CDCl₃ / 200 MHz

SI-9

CDCl₃ / 125 MHz

CDCl₃ / 200 MHz

SI-10

CDCl₃ / 50 MHz

SI-11

CDCl₃ / 200 MHz

CDCl₃ / 50 MHz

SI-12

CDCl₃ / 50 MHz

CDCl₃ / 200 MHz

SI-13

CDCl₃ / 50 MHz

CDCl₃ / 50 MHz

SI-14

CDCl₃ / 50 MHz

SI-15

SI-16

CDCl₃ / 200 MHz

SI-17

CDCl₃ / 50 MHz

Chloroform-d

CDCl₃ / 200 MHz

SI-18

CDCl₃ / 50 MHz

SI-19

CDCl₃ / 200 MHz

CDCl₃ / 100 MHz

SI-20

CDCl₃ / 100 MHz

CDCl₃ / 200 MHz

SI-21

CDCl₃ / 125 MHz

SI-22

SI-23

CDCl₃ / 50 MHz

CDCl₃ / 200 MHz

SI-24

CDCl₃ / 125 MHz

SI-25

CDCl₃ / 200 MHz

SI-26

CDCl₃ / 100 MHz

Chloroform-d

CDCl₃ / 200 MHz

SI-27

CDCl₃ / 50 MHz

SI-28

CDCl₃ / 200 MHz

SI-29

CDCl₃ / 50 MHz

CDCl₃ / 200 MHz

SI-30

CDCl₃ / 125 MHz

SI-31

CDCl₃ / 200 MHz

SI-32

CDCl₃ / 125 MHz

SI-33

CDCl₃ / 50 MHz

SI-34

CDCl₃ / 200 MHz

SI-35

SI-36

CDCl₃ / 50 MHz

SI-37

SI-38

CDCl₃ / 50 MHz

148.51
147.59
147.50
147.33

142.34

131.44

129.56

128.79

122.47

121.12

111.80

110.79

108.38

108.08

101.18

CDCl₃ / 50 MHz