

Supporting Information for

A systematic study on the Z-enoate assisted Meyer-Schuster rearrangement

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General procedure:

To a solution of the *z*-enoate-propargylic alcohol¹ (1equi.) and the arene (5 equiv.) in dichloromethane (5 mL / 0.2 mmol, 0.04 M) under nitrogen atmosphere was added an acid (1.3 equi.). The reaction tube was stirred either at prescribed temperature (0 °C or 55 °C or higher temperature) for 1-8 h. After completion of the reaction (by TLC analysis), saturated NaHCO₃, and DCM were added to reaction mixture and extracted with DCM. The combined organic layer was washed with the brine, dried (MgSO₄) and solvent was evaporated under reduced pressure. The crude material was purified by flash column chromatography using hexane-ethyl acetate mixture as eluent to yield the corresponding α -OMs or α -OTs or α -Cl-enone derivatives and arene trapped products.

Ethyl 6-methyl-5-(methylsulfonyloxy)-4-oxohept-5-enoate (12)

¹H NMR (400 MHz, CDCl₃): δ = 4.12 (q, *J* = 7.2 Hz, 2 H), 3.19 (s, 3 H), 2.99 (t, *J* = 6.7 Hz, 2 H), 2.64 (t, *J* = 6.5 Hz, 2 H), 2.15 (s, 3 H), 2.01 (s, 3 H) and 1.25 (t, *J* = 7.2 Hz, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 194.9, 172.9, 142.4, 139.8, 60.8, 38.6, 35.4, 28.3, 21.8, 20.6 and 14.3 ppm.

IR (neat): 2980, 2936, 1735 (C=O), 1699 (C=O), 1625, 1408, 1358, 1348, 1200, 1107, 968 and 821 cm⁻¹.

HR ESI-MS: [C₁₁H₁₉O₆S]⁺ = [M+H]⁺ requires 279.0897; found 297.0894.

TLC: R_f = 0.4 (3:1, Hex/EtOAc)

Ethyl 6-methyl-4-oxo-5-(tosyloxy)hept-5-enoate (21)

¹H NMR (400 MHz, CDCl₃): δ = 7.80 (d, *J* = 8.4 Hz, 2 H), 7.25 (d, *J* = 8.2 Hz, 2 H), 4.12 (q, *J* = 7.2 Hz, 2 H), 2.93 (t, *J* = 6.8 Hz, 2 H), 2.58 (t, *J* = 6.6 Hz, 2 H), 3.07 (s, 3 H), 2.47 (s, 3 H), 1.99 (s, 3 H) and 1.25 (t, *J* = 7.2 Hz, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 195.8, 172.8, 145.9, 141.3, 140.2, 132.7, 130.1, 128.7, 60.7, 35.2, 28.4, 21.9, 20.7, 20.2 and 14.3 ppm.

IR (neat): 2980, 2936, 2927, 2858, 1731 (C=O), 1698 (C=O), 1626, 1607, 1598, 1444, 1395, 1377, 1373, 1191, 1178, 1089, 997 and 812 cm^{-1} .

HR ESI-MS: $[\text{C}_{17}\text{H}_{23}\text{O}_6\text{S}]^+ = [\text{M}+\text{H}]^+$ requires 355.1210; found 355.1206.

TLC: $R_f = 0.4$ (4:1, Hex/EtOAc).

M. P.; 93-97 °C.

Ethyl 5-chloro-6-methyl-4-oxohept-5-enoate (22)

^1H NMR (400 MHz, CDCl_3): $\delta = 4.14$ (q, $J = 7.1$ Hz, 2 H), 3.08 (t, $J = 6.6$ Hz, 2 H), 2.60 (t, $J = 6.6$ Hz, 2 H), 2.13 (s, 3 H), 2.02 (s, 3 H) and 1.26 (t, $J = 7.2$ Hz, 3 H) ppm

^{13}C NMR (100 MHz, CDCl_3): $\delta = 196.4, 172.9, 145.8, 125.6, 60.7, 36.3, 28.6, 24.7, 22.8$ and 14.3 ppm.

IR (neat): 2965, 2926, 2875, 2854, 1736 (C=O), 1691 (C=O), 1596, 1493, 1461, 1375, 1340, 1268, 1188, 1061, 965 and 819 cm^{-1} .

HR ESI-MS: $[\text{C}_{10}\text{H}_{16}\text{ClO}_3]^+ = [\text{M}+\text{H}]^+$ requires 219.0782; found 219.0779

TLC: $R_f = 0.4$ (18:1, Hex/EtOAc).

Ethyl 5-(4-hydroxyphenyl)-6-methyl-4-oxohept-5-enoate (13)

The hydroxyester¹ (40 mg, 0.22 mmol), phenol (77 mg, 0.82 mmol), in DCM (4 mL), and MsOH (27.4 mg, 0.02 mmol, 0.29 ml of 1.4 M in DCM) were stirred for 24 h at 0 °C to RT. Purification by flash column chromatography (8:1 hexanes:EtOAc) gave the 1,4-keto-ester **13** (18 mg, 0.065 mmol, 30%) as a pale yellow oil and α -OMs-enone **12** (22 mg, 0.08 mmol, 36%) as a pale yellow oil.

^1H NMR (400 MHz, CDCl_3): $\delta = 7.30$ -7.37 (m, 2 H), 7.00 (t, $J = 7.3$ Hz, 1 H), 6.89 (d, $J = 7.8$ Hz, 1 H), 4.09 (q, $J = 7.1$ Hz, 2 H), 2.75 (t, $J = 6.6$ Hz, 2 H), 2.49 (t, $J = 6.6$ Hz, 2 H), 2.22 (s, 3 H), 1.781 (s, 3 H) and 1.22 (t, $J = 7.1$ Hz, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 197.7, 173.0, 157.5, 143.0, 139.6, 130.1, 122.1, 114.7, 60.6, 35.1, 28.0, 20.7, 20.1 and 14.3 ppm.

IR (neat): 2952, 2854, 1734 (OC=O), 1699 (C=O), 1611, 1548, 1514, 1442, 1364, 1312, 1281, 1155, 1105, 1054, 954 and 817 cm⁻¹.

HR ESI-MS: [C₁₆H₂₀O₄Na]⁺ = [M+Na]⁺ requires 299.1254; found 299.1258

TLC: R_f = 0.4 (8:1, Hex/EtOAc).

Ethyl 5-(2,3-dimethoxyphenyl)-6-methyl-4-oxohept-5-enoate (15)

The hydroxyester (40 mg, 0.22 mmol), 1,2-dimethoxybenzene (113 mg, 0.82 mmol), in DCM (4 mL), and MsOH (27.4 mg, 0.02 mmol, 0.29 ml of 1.4 M in DCM) were stirred for 5 h at 0 °C to RT. Purification by flash column chromatography (6:1 hexanes:EtOAc) gave the 1,4-keto-ester **15** (24 mg, 0.075 mmol, 34%) as a pale yellow oil and α -OMs-enone **12** (33 mg, 0.12 mmol, 54%) as a pale yellow oil.

¹H NMR (500 MHz, CDCl₃): δ = 6.87 (d, J = 8.2 Hz, 1 H), 6.71 (dd, J = 8.2 & 1.8 Hz, 1 H), 6.67 (m, 1 H), 4.09 (q, J = 7.1 Hz, 2 H), 3.89 (s, 3 H), 3.86 (s, 3 H), 2.57 (t, J = 6.6 Hz, 2 H), 2.49 (t, J = 6.3 Hz, 2 H), 2.02 (s, 3 H), 1.68 (s, 3 H) and 1.23 (t, J = 7.1 Hz, 3 H) ppm.

¹³C NMR (125 MHz, CDCl₃): δ = 203.1, 173.1, 149.0, 148.3, 143.3, 137.9, 131.1, 122.3, 112.8, 111.3, 60.6, 56.0, 55.9, 37.4, 28.4, 23.6, 22.4 and 14.3 ppm.

IR (neat): 2923, 2853, 1734 (OC=O), 1687 (C=O), 1618, 1568, 1514, 1445, 1374, 1312, 1282, 1153, 1112, 1034, 957 and 813 cm⁻¹.

HR ESI-MS: [C₁₈H₂₄O₅Na]⁺ = [M+Na]⁺ requires 343.1516; found 343.1516

TLC: R_f = 0.4 (6:1, Hex/EtOAc).

Ethyl 5-(2,4-dimethoxyphenyl)-6-methyl-4-oxohept-5-enoate (16)

The hydroxyester (30 mg, 0.16 mmol), 1,3-dimethoxybenzene (113 mg, 0.82 mmol), in DCM (3 mL), and MsOH (19.2 mg, 0.02 mmol, 0.14 ml of 1.4 M in DCM) were stirred for 4 h at 0 °C to RT. Purification by

flash column chromatography (6:1 hexanes:EtOAc) gave the 1,4-keto-ester **16** (35 mg, 0.11 mmol, 68%) as a pale yellow oil and α -OMs-enone **12** (6 mg, 0.02 mmol, 10%) as a pale yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.01 (d, J = 8.0 Hz, 1 H), 6.51-6.47 (m, 2 H), 4.11 (q, J = 7.1 Hz, 2 H), 3.83 (s, 3 H), 3.75 (s, 3 H), 2.51-2.45 (m, 4 H), 2.90 (s, 3 H), 1.64 (s, 3 H) and 1.23 (t, J = 7.1 Hz, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 202.3, 173.3, 160.8, 158.3, 145.9, 133.7, 132.4, 120.4, 104.6, 98.8, 60.5, 55.6, 55.5, 36.7, 28.6, 24.2, 22.6 and 14.3 ppm.

IR (neat): 2923, 2851, 1735 (OC=O), 1684 (C=O), 1608, 1578, 1504, 1443, 1372, 1302, 1272, 1155, 1114, 1033 and 800 cm⁻¹.

HR ESI-MS: [C₁₈NaH₂₄O₅]⁺ = [M+Na]⁺ requires 343.1516; found 343.1509

TLC: R_f = 0.4 (6:1, Hex/EtOAc).

Ethyl 6-methyl-4-oxo-5-(2,4,6-trimethoxyphenyl)hept-5-enoate (18)

The hydroxyester (30 mg, 0.16 mmol), 1,3,5-trimethoxybenzene (138 mg, 0.82 mmol), in DCM (3 mL), and MsOH (19.2 mg, 0.02 mmol, 0.14 ml of 1.4 M in DCM) were stirred for 6 h at 0 °C to RT.

Purification by flash column chromatography (4:1 hexanes:EtOAc) gave the 1,4-keto-ester **18** (42 mg, 0.12 mmol, 75%) as a pale yellow oil.

¹H NMR (500 MHz, CDCl₃): δ = 6.15 (s, 2 H), 4.08 (q, J = 7.0 Hz, 2 H), 3.84 (s, 3 H), 3.75 (s, 6 H), 2.45 (s, 4 H), 2.14 (s, 3 H), 1.56 (s, 3 H) and 1.22 (t, J = 7.0 Hz, 3 H) ppm.

¹³C NMR (125 MHz, CDCl₃): δ = 201.8, 173.5, 161.3, 158.8, 148.2, 128.4, 109.0, 90.6, 60.4, 55.8, 55.4, 36.2, 28.7, 24.3, 22.5 and 14.3 ppm.

IR (neat): 2932, 2844, 1734 (OC=O), 1689 (C=O), 1605, 1585, 1495, 1462, 1414, 1371, 1336, 1205, 1153, 1061, 952 and 813 cm⁻¹.

HR ESI-MS: [C₁₉H₂₆O₆Na]⁺ = [M+Na]⁺ requires 373.1622; found 373.1618

TLC: R_f = 0.4 (4:1, Hex/EtOAc).

Ethyl 6-methyl-4-oxo-5-(thiophen-2-yl)hept-5-enoate (20)

The hydroxyester (40 mg, 0.22 mmol), thiophene (69 mg, 0.82 mmol), in DCM (4 mL), and MsOH (27.4 mg, 0.02 mmol, 0.29 ml of 1.4 M in DCM) were stirred for 2 h at 0 °C to RT. Purification by flash column chromatography (9:1 hexanes:EtOAc) gave the 1,4-keto-ester **20** (23 mg, 0.086 mmol, 39%) as a pale yellow oil and α -OMs-enone **12** (24 mg, 0.086 mmol, 40%) as a pale yellow oil.

¹H NMR (500 MHz, CDCl₃): δ = 7.32 (dd, J = 5.2 & 1.2 Hz, 1 H), 7.03 (dd, J = 5.2 & 3.4 Hz, 1 H), 6.84 (dd, J = 3.4 & 1.2 Hz, 1 H), 4.11 (q, J = 7.1 Hz, 2 H), 2.69 (t, J = 6.6 Hz, 2 H), 2.52 (t, J = 6.6 Hz, 2 H), 2.05 (s, 3 H), 1.81 (s, 3 H) and 1.23 (t, J = 7.1 Hz, 3 H) ppm.

¹³C NMR (125 MHz, CDCl₃): δ = 202.1, 173.0, 147.4, 139.1, 130.7, 127.9, 127.3, 126.4, 60.6, 37.1, 28.4, 24.0, 22.8 and 14.3 ppm.

IR (neat): 2932, 2853, 1735 (OC=O), 1697 (C=O), 1614, 1568, 1514, 1443, 1374, 1312, 1283, 1153, 1115, 1044, 954 and 819 cm⁻¹.

HR ESI-MS: [C₁₄H₁₉O₃S]⁺ = [M+Na]⁺ requires 267.1049; found 267.1042.

TLC: R_f = 0.4 (9:1, Hex/EtOAc).

5-(4-Chlorophenyl)-3-methylpent-1-yn-3-ol (S₁)

The ketone² (150 mg, 0.82 mmol), anhydrous THF (5 mL), ethynyl magnesium bromide (3.3 ml, 1.6 mmol, 0.5 M in THF) were stirred for 2 h at 0 °C. Purification by flash column chromatography (9:1 hexane:EtOAc) gave alcohol **S₁** (160 mg, 0.78 mmol, 95%) as a color less oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.24 (d, J = 8.4 Hz, 2 H), 7.15 (d, J = 8.4 Hz, 2 H), 2.85-2.80 (m, 2 H), 2.51 (s, 1 H), 2.04 (br s, 1H), 2.01-1.90 (m, 2 H) and 1.55 (s, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 140.4, 131.8, 129.9, 128.7, 87.3, 72.1, 68.0, 45.1, 30.6 and 30.2 ppm.

IR (neat): 3387, 3298, 2980, 2932, 2865, 1491, 1454, 1371, 1158, 1093, 1016, 907 and 661 cm^{-1} .

HR ESI-MS: $[\text{C}_{12}\text{H}_{13}\text{ClNaO}_3]^+ = [\text{M}+\text{Na}]^+$ requires 231.0547; found 231.0540

TLC: $R_f = 0.4$ (5:1, Hex/EtOAc)

(Z)-Ethyl 8-(4-chlorophenyl)-6-hydroxy-6-methyloct-2-en-4-ynoate (23)

Iodo-ester³ (223 mg, 0.99 mmol), alcohol **S**₁ (170 mg, 0.83 mmol), dry THF (8 mL), dry DIPA (2 mL), CuI (23.5 mg, 0.12 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (5.8 mg, 0.008 mmol) were stirred for 12 h at 0 °C to RT. Purification by flash column chromatography (4:1 hexane:EtOAc) gave the hydroxyester **23** (225 mg, 0.74 mmol, 89%) as a pale yellow oil.

¹H NMR (400 MHz, CDCl_3): $\delta = 7.25\text{--}7.22$ (m, 2 H), $7.18\text{--}7.16$ (m, 2 H), 6.16 (d, $J = 11.5$ Hz, 1 H), 6.12 (d, $J = 11.5$ Hz, 1 H), 4.22 (q, $J = 7.1$ Hz, 2 H), 2.94–2.83 (m, 2 H), 2.07–1.95 (m, 2 H), 1.71 (br s, 1H), 1.60 (s, 3 H) and 1.30 (t, $J = 7.1$ Hz, 3 H) ppm.

¹³C NMR (100 MHz, CDCl_3): $\delta = 164.7, 140.6, 131.7, 130.0, 129.2, 128.6, 122.6, 104.8, 80.9, 68.6, 60.6$ (C-OH), 45.2, 30.6, 30.0 and 14.4 ppm.

IR (neat): 3439 (OH), 2981, 2935, 2864, 1712 (C=O), 1610, 1491, 1410, 1386, 1188, 1091, 1020, 816 and 665 cm^{-1} .

HR ESI-MS: $[\text{C}_{17}\text{H}_{19}\text{ClNaO}_3]^+ = [\text{M}+\text{Na}]^+$ requires 329.0915; found 329.0902

TLC: $R_f = 0.4$ (4:1, Hex/EtOAc)

Ethyl 8-(4-chlorophenyl)-6-methyl-5-(methylsulfonyloxy)-4-oxooct-5-enoate (25)

¹H NMR (400 MHz, CDCl_3): **Major isomer**: $\delta = 7.27\text{--}7.23$ (m, 2 H), $7.17\text{--}7.14$ (m, 2 H), 4.17–4.11 (m, 2 H), 3.15 (s, 3 H), 2.96–2.91 (m, 2 H), 2.82–2.71 (m, 4 H), 2.66–2.58 (m, 2 H), 1.93 (s, 3 H) and 1.27–1.23 (m, 3 H) ppm.

¹H NMR (400 MHz, CDCl₃): Minor: δ = 7.27-7.23 (m, 2 H), 7.17-7.14 (m, 2 H), 4.17-4.11 (m, 2 H), 3.19 (s, 3 H), 2.96-2.91 (m, 2 H), 2.82-2.71 (m, 4 H), 2.66-2.58 (m, 2 H), 2.15 (s, 3 H) and 1.27-1.23 (m, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 195.0, 194.8, 172.9, 172.8, 144.9, 140.2, 139.4, 132.1, 130.1, 129.9, 128.8, 128.7, 60.9, 60.8, 38.8, 38.5, 36.8, 35.6, 35.5, 35.2, 34.2, 32.8, 28.3, 28.2, 19.9, 18.7 and 14.3 ppm.

IR (neat): 2935, 2858, 1734 (OC=O), 1698 (C=O), 1611, 1563, 1524, 1442, 1384, 1322, 1293, 1152, 1115, 1054, 957 and 819 cm⁻¹.

HR ESI-MS: [C₁₈NaClH₂₃O₆S]⁺ = [M+Na]⁺ requires 425.0796; found 425.0791.

TLC: R_f = 0.4 (4:1, Hex/EtOAc).

Ethyl 4-(7-chloro-2-methyl-3,4-dihydronaphthalen-1-yl)-4-oxobutanoate (24)

¹H NMR (400 MHz, CDCl₃): δ = 7.11-7.05 (m, 2 H), 6.89 (d, J = 1.8 Hz, 1 H), 4.18 (q, J = 7.1 Hz, 2 H), 2.97 (t, J = 6.5 Hz, 2 H), 2.76 (t, J = 8.1 Hz, 2 H), 2.68 (t, J = 6.5 Hz, 2 H), 2.28 (t, J = 7.8 Hz, 2 H), 1.92 (s, 3 H) and 1.29 (t, J = 7.1 Hz, 3 H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 206.6, 172.7, 137.8, 134.9, 133.6, 133.0, 132.4, 128.9, 126.9, 123.6, 60.9, 40.0, 29.9, 28.1, 27.4, 20.8 and 14.4 ppm.

IR (neat): 2976, 2928, 2855, 1733 (OC=O), 1699 (C=O), 1595, 1483, 1433, 1399, 1372, 1262, 1206, 1158, 1098, 937 and 736 cm⁻¹.

HR ESI-MS: [C₁₇H₂₀ClO₃]⁺ = [M+H]⁺ requires 307.1095; found 307.1112

TLC: R_f = 0.4 (9:1, Hex/EtOAc)

References:

- 1 (a) P. Tharra and B. Baire, *Chem. Commun.* **2016**, 52, 12147. (b) P. Tharra and B. Baire, *Chem. Commun.* **2016**, 52, 14290. (c) P. Tharra and B. Baire, *Chem. –Eur. J.* **2017**, 23, 2014.
- 2 Sathyanarayana, P.; Ravi, O.; Muktapuram, P. R.; and Bathula, S. R. *Org. Biomol. Chem.* **2015**, 13, 9681.
- 3 Trost, B. M.; Papillon, J. P. N., and Nussbaumer, T. *J. Am. Chem. Soc.* **2005**, 127, 17921.























