Supporting information

Zinc-Mediated Ring-Expansion and Chain Extension Reaction of β -Keto Esters

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General Methods. All reactions were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring. Dichloromethane was dried and freshly distilled from calcium hydride under nitrogen atmosphere. ^1H NMR (300MHz) and ^{13}C NMR (75MHz) spectra were recorded on a spectrometer operating at 300 MHz or 75 MHz, respectively, with tetramethylsilane (TMS) as an internal standard. Column chromatography was performed on silica gel (10~40 mesh) and analytical TLC on silica gel 60-F₂₅₄ was detected by fluorescence. High resolution mass spectra were obtained with a micromass GCT TOF mass spectrometer.

β -Keto esters **17**, **19**, **21**, **25**, and **31** were purchased from commercial sources and used as received. β -Keto esters **1**, **3**, **5**, **7**, **9**, **11**, **13**, **15** and **33** were prepared through application of the procedure of B. A. Marples and C. J. Li,¹ Compound **23** was prepared according to the procedure of E. J. Roskamp,² and compounds **27** and **29** were prepared through application of the procedure of S. Masamune.³ Characterization data of the purified products **2**,⁴ **4**,⁴ **6**,⁵ **8**,⁶ **10**,⁵ **12**,⁵ **14**,⁵ **16**,⁵ **18**,⁷ **20**,⁷ **22**,⁷ **24**,⁷ **26**,⁸ **28**,⁷ and **32**⁹ were shown to be consistent to the literature values.

General Procedure for Chain Extension and Ring Expansion of β -keto ester with $\text{CF}_3\text{COOZnCH}_2\text{I}$

To a solution of ZnEt_2 (90 μL , 0.9 mmol, 3 eq) in 3 mL CH_2Cl_2 at 0°C was added dropwise CF_3COOH (70 μL , 0.9 mmol, 3 eq) slowly via syringe under N_2 . After stirring for 30 min at 0°C , methylene iodide (75 μL , 0.9 mmol, 3 eq) was added dropwise with stirring. The suspension was stirred for 30 min, and β -keto ester (0.3 mmol) was added rapidly by syringe. The mixture was stirred at room temperature until TLC indicated mostly complete consumption of the starting β -keto ester. The reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O (10 mL $\times$ 3). The combined organic extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure to an oil residue. The desired product was isolated by silica gel chromatography.

5-Ethoxycarbonyl-1,2-benzo-3-oxocycloheptenone⁴ (2): oil (83%); ^1H NMR (300MHz, CDCl_3): δ = 7.63 (dd, 1H, J = 7.6, 1.5 Hz), 7.37 (td, 1H, J = 7.5, 1.5 Hz), 7.25 (td, 1H, J = 7.5, 1.2 Hz), 7.14 (d, 1H, J = 7.5 Hz), 4.15 (q, 2H, J = 7.2 Hz), 3.05-2.75 (m, 5H), 2.22 (m, 1H), 2.12-1.98 (m, 1H), 1.15 (t, 3H, J = 7.2 Hz). ^{13}C NMR (75MHz, CDCl_3): δ = 202.9, 174.3, 140.8, 138.2, 132.6, 129.8, 128.8, 127.0, 61.0, 42.8, 38.3, 31.2, 28.6, 14.2.

5-Ethoxycarbonyl-1,2-benzo-3-oxocyclooctenone⁴ (4): oil (75%); ^1H NMR (300MHz, CDCl_3): δ = 7.76 (dd, 1H, J = 7.8, 1.2 Hz), 7.39 (td, 1H, J = 7.2, 1.5 Hz), 7.27 (td, 1H, J = 7.2, 0.9 Hz), 7.15 (d, 1H, J = 7.5 Hz), 4.15 (q, 2H, J = 7.2 Hz), 3.40 (dd, 1H, J = 13.8, 9.9 Hz), 3.27 (m, 1H), 3.02-2.86 (m, 3H), 1.89 (m, 1H), 1.78-1.60 (m, 3H), 1.23 (t, 3H, J = 7.2 Hz). ^{13}C NMR (75MHz, CDCl_3): δ = 203.7, 174.2, 140.0, 139.2, 132.4, 131.4, 128.7, 126.7, 60.9, 44.9, 40.8, 34.4, 27.1, 25.2, 14.3.

5-Ethoxycarbonyl-1,2-benzo-3-oxocyclohexenone⁵ (6): oil (46%); ^1H NMR (300MHz, CDCl_3): δ = 8.03 (dd, 1H, J = 7.8, 1.2 Hz), 7.51 (td, 1H, J = 7.2, 1.5 Hz), 7.35 (t, 1H, J = 7.5 Hz), 7.27 (d, 1H, J = 7.8 Hz), 4.10 (q, 2H, J = 7.2 Hz), 3.26-3.14 (m, 3H), 2.95 (m, 1H), 2.84 (m, 1H), 1.25 (t, 3H, J = 7.2 Hz). ^{13}C NMR (75MHz, CDCl_3): δ = 195.9, 173.2, 141.7, 133.9, 132.1, 129.1, 128.9, 127.3, 61.1, 40.9, 40.4, 32.18, 14.2.

Ethyl 3-Oxocyclohexanecarboxylate⁶ (8): oil (20%); ¹H NMR (300MHz, CDCl₃): δ = 4.21 (q, 2H, *J* = 7.2 Hz), 3.33 (m, 1H), 2.56-2.53 (m, 2H), 2.34 (m, 2H), 2.07 (m, 2H), 1.78-1.72 (m, 2H), 1.22 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 209.4, 173.9, 61.0, 43.4, 43.3, 41.0, 27.9, 24.6, 14.3.

Ethyl 3-Oxocycloheptanecarboxylate⁵ (10): oil (67%); ¹H NMR (300MHz, CDCl₃): δ = 4.10 (q, 2H, *J* = 7.2 Hz), 2.70 (dd, 1H, *J* = 15.5, 11.0 Hz), 2.64-2.59 (m, 2H), 2.47-2.41 (m, 2H), 2.10 (m, 1H), 1.78-1.48 (m, 5H), 1.19 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 212.4, 174.7, 61.0, 45.7, 44.0, 41.4, 33.4, 28.4, 24.1, 14.3.

Ethyl 3-Oxocyclooctanecarboxylate⁵ (12): oil (88%); ¹H NMR (300MHz, CDCl₃): δ = 4.10 (q, 2H, *J* = 7.2 Hz), 2.94 (m, 1H), 2.80 (t, 1H, *J* = 13.2 Hz), 2.58 (m, 1H), 2.42 (m, 2H), 2.04-1.63 (m, 8H), 1.19 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 214.9, 174.7, 60.8, 43.2, 43.0, 42.8, 29.9, 27.4, 24.8, 23.4, 14.2.

Ethyl 3-Oxocyclononanecarboxylate⁵ (14): oil (72%); ¹H NMR (300MHz, CDCl₃): δ = 4.10 (q, 2H, *J* = 7.2 Hz), 2.90 (m, 1H), 2.75 (t, 1H, *J* = 13.6 Hz), 2.59 (dd, 2H, *J* = 13.8, 2.7 Hz), 2.40 (m, 2H), 1.72-2.88 (m, 4H), 1.54-1.38 (m, 5H), 1.20 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 215.3, 175.4, 60.8, 44.5, 43.9, 41.5, 29.5, 25.8, 25.7, 24.3, 23.1, 14.3.

Ethyl 3-Oxocyclotridecanecarboxylate⁵ (16): oil (70%); ¹H NMR (300MHz, CDCl₃): δ = 4.10 (q, 2H, *J* = 7.2 Hz), 3.0 (m, 1H), 2.75 (dd, 1H, *J* = 8.7, 16.8 Hz), 2.72 (dd, 1H, *J* = 3.3, 16.5 Hz), 2.55 (m, 1H), 2.35 (m, 1H), 1.80-1.39 (m, 18H), 1.20 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 210.2, 175.2, 60.5, 43.5, 42.4, 39.7, 29.5, 26.2, 26.0, 25.5, 24.6, 24.3, 23.6, 23.6, 14.2.

Ethyl 5-methyl-4-oxohexanoate⁷ (18): oil (90%); ¹H NMR (300MHz, CDCl₃): δ = 4.12 (q, 2H, *J* = 7.2 Hz), 2.77 (t, 2H, *J* = 6.6 Hz), 2.62 (m, 1H), 2.58 (t, 2H, *J* = 6.6 Hz), 2.51 (t, 3H, *J* = 7.2 Hz), 1.12 (d, 6H, *J* = 6.9 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 212.8, 174.9, 60.7, 40.9, 34.9, 28.1, 18.3, 14.3.

Methyl 5,5-dimethyl-4-oxohexanoate⁷ (20): oil (96%); ¹H NMR (300MHz, CDCl₃): δ = 3.6 (s, 3H), 2.75 (t, 2H, *J* = 6.5 Hz), 2.51 (t, 2H, *J* = 6.5 Hz), 1.11 (s, 9H). ¹³C NMR (75MHz, CDCl₃): δ = 214.2, 173.6, 51.8, 44.0, 31.6, 28.0, 26.6.

Ethyl 4-oxo-benzenebutanoate⁷ (22): oil (87%); ¹H NMR (300MHz, CDCl₃): δ = 8.0 (m, 2H), 7.6 (m, 1H), 7.5 (m, 2H), 4.15 (q, 2H, *J* = 7.2 Hz), 3.32 (t, 2H, *J* = 6.6 Hz), 2.76 (t, 2H, *J* = 6.6 Hz), 1.29 (q, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 198.3, 173.0, 136.7, 133.3, 128.8, 128.3, 60.8, 33.5, 28.4, 14.3.

Ethyl 4-oxo-6-phenylhexanoate⁷ (24): oil (77%); ¹H NMR (300MHz, CDCl₃): δ = 7.30-7.15 (m, 5H), 4.15 (q, 2H, *J* = 7.2 Hz), 2.95 (t, 2H, *J* = 7.1 Hz), 2.80 (t, 2H, *J* = 7.1 Hz), 2.70 (t, 2H, *J* = 6.5 Hz), 2.55 (t, 2H, *J* = 6.5 Hz), 1.2 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 208.0, 172.8, 140.9, 128.5, 128.3, 126.1, 60.6, 44.3, 37.2, 29.7, 28.0, 14.2.

Ethyl 4-oxopentanoate⁸ (26): oil (81%); ¹H NMR (300MHz, CDCl₃): δ = 4.12 (q, 2H, *J* = 7.2 Hz), 2.76 (t, 2H, *J* = 6.4 Hz), 2.56 (t, 2H, *J* = 6.4 Hz), 2.20 (s, 3H), 1.26 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 206.8, 172.9, 60.8, 38.1, 30.0, 28.2, 14.3.

Ethyl 4-oxo-6-phenyl-5-hexenoate⁷ (28): oil (71%); ¹H NMR (300MHz, CDCl₃): δ = 7.6 (d, 1H, *J* = 16.2 Hz), 7.5 (m, 2H), 7.4 (m, 3H), 6.8 (d, 1H, *J* = 16.2 Hz), 4.15 (q, 2H, *J* = 7.2 Hz), 3.0 (t, 2H, *J* = 6.7 Hz), 2.7 (t, 2H, *J* = 6.7 Hz), 1.2 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 198.1, 172.9, 142.9, 134.5, 130.5, 129.0, 128.5, 125.9, 60.6, 35.3, 28.2, 14.2.

Ethyl 6-Cyclopropyl-4-oxohexanoate (30): oil (70%); IR (neat, cm⁻¹) 3077, 2984, 2927, 1736, 1448, 1411, 1373, 1350, 1194, 1095, 1017. ¹H NMR (300MHz, CDCl₃): δ = 4.15 (q, 2H, *J* = 7.2 Hz), 2.75 (t, 2H, *J* = 6.5 Hz), 2.60-2.51 (m, 4H), 1.5 (q, 2H, *J* = 7.3 Hz), 1.2 (t, 3H, *J* = 7.2 Hz), 0.68 (m, 1H), 0.5-0.35 (m, 2H), 0.01 (dd, 2H, *J* = 10.2, 5.4Hz). ¹³C NMR (75MHz, CDCl₃): δ = 209.2, 173.0, 60.7, 42.9, 37.3, 29.1, 28.1, 14.3, 10.6, 4.6. HRMS (EI) calcd for C₁₁H₁₈O₃: 198.1257 [M]⁺. Found: 198.1256.

Ethyl 2-methyl-4-oxopentanoate⁹ (32): oil (36%); ¹H NMR (300MHz, CDCl₃): δ = 4.15 (q, 2H, *J* = 7.2 Hz), 2.94 (m, 2H), 2.46 (m, 1H), 2.16 (s, 3H), 1.26 (t, 3H, *J* = 7.2 Hz), 1.15 (d, 3H, *J* = 6.8 Hz). ¹³C NMR (75MHz, CDCl₃): δ = 206.7, 175.8, 60.6, 46.6, 34.8, 30.1, 17.1, 14.2.

Two Examples of Ring Expansion and Chain Extension of β-keto ester (3 mmol)

5-Ethoxycarbonyl-1,2-benzo-3-oxocycloheptenone (2): To a solution of ZnEt₂ (0.90 mL, 9 mmol, 3 eq) in 8 mL CH₂Cl₂ at 0°C was added dropwise CF₃COOH (0.70 mL, 9 mmol, 3 eq) slowly via syringe under N₂. After stirring for 30 min at 0°C, CH₂I₂ (0.75 mL, 9 mmol, 3 eq) was added dropwise with stirring. The suspension was stirred for 30 min, and then 5-ethoxycarbonyl-1,2-benzo-2-oxocyclohexenone (650 mg, 3 mmol) in 1 mL of CH₂Cl₂ was added rapidly by syringe. The mixture was stirred at room temperature for 8 h, quenched with saturated aqueous NH₄Cl and extracted with Et₂O (10 mL × 3). The combined organic extracts was washed with brine, dried over MgSO₄ and concentrated under reduced pressure to an oil residue. The desired product (562 mg, 81%) was isolated by flash silica gel column chromatography.

Ethyl 4-oxo-benzenbutanoate (22): To a solution of ZnEt₂ (0.90 mL, 9 mmol, 3 eq) in 8 mL CH₂Cl₂ at 0°C was added dropwise CF₃COOH (0.70 mL, 9 mmol, 3 eq) slowly via syringe under N₂. After stirring for 30 min at 0°C, CH₂I₂ (0.75 mL, 9 mmol, 3 eq) was added dropwise with stirring. The suspension was stirred for 30 min, and ethyl benzoylacetate (580 mg, 3 mmol) was added rapidly by syringe. The mixture was stirred at room temperature 8 h. The reaction was quenched with saturated aqueous NH₄Cl and extracted with Et₂O (10 mL × 3). The combined organic extracts was washed with brine, dried over MgSO₄ and concentrated under reduced pressure to an oil residue. The desired product was isolated by flash silica gel column chromatography and gave ethyl 4-oxo-benzenbutanoate (22) (525 mg, 85%).

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