

Supporting Information

Title

**Radical Cascade Reaction with 1,4-Dienes and 1,4-Enynes using 2-(Iodomethyl)cyclopropane-1,1-dicarboxylate as a Homoallyl Radical Precursor:
One-step Synthesis of Bicyclo[3.3.0]octane Derivatives.**

Authored by

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Supporting Information Available. Experimental procedures and characterization data for products **3a-3d**, **2e-2g**, **5h**. This material is available free of charge via Internet at <http://pubs.acs.org>.

Experimental Section

Melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. In ^1H and ^{13}C NMR spectra, chemical shifts were expressed in δ (ppm) downfield from CHCl_3 (7.26 ppm) and CDCl_3 (77.0 ppm), respectively. Mass spectra were recorded by electron impact or chemical ionization. Column chromatography was performed on silica gel (75-150 μm). Medium-pressure liquid chromatography (MPLC) was performed on a 30 X 4 cm i. d. prepacked column (silica gel, 50 μm) with a UV detector.

Preparation of dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (1) through $\text{Ti}(\text{OR})_4$ -mediated iodocarbocyclization:¹ Under Ar atmosphere, to a solution of dimethyl allylmalonate (344 mg, 2 mmol) in CH_2Cl_2 (12 mL) was added $\text{Ti}(\text{O}i\text{-Bu})_4$ (0.8 mL, 2 mmol). After being stirred for 10 min, I_2 (608 mg, 2.4 mmol) and CuO (192 mg, 2.4 mmol) were successively added, and then the mixture was stirred for 4 h. The mixture was poured into 10 % HCl , and the products were extracted with ether. The ether extracts were washed with aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, dried over MgSO_4 , and evaporated to dryness. Purification of the residue by column chromatography (hexane/ AcOEt = 9) gave **1** (584 mg, 98 %). NMR data of **1** coincided with that reported in our previous paper.²

Preparation of dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (1) through Beckwith's method:³ Under Ar atmosphere, to a solution of dimethyl allylmalonate (861 mg, 5 mmol) in THF (15 mL) was added to NaH (240 mg, 6 mmol) at 0 $^\circ\text{C}$. After being stirred for 10 min, I_2 (1.27 g, 5 mmol) was successively added, and then the mixture was refluxed for 4 h. The mixture was poured into aqueous NH_4Cl solution and the products were extracted with ether. The ether extracts were washed with aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, dried over MgSO_4 , and evaporated to dryness. Purification of the residue by column chromatography (hexane/ AcOEt = 9) gave **1** (994 mg, 67 %). NMR data of **1** coincided with that reported in our previous paper.²

General procedure of radical iodine atom transfer cascade reaction of 1 with 1,4-dienes.

Under Ar atmosphere, to a solution of dimethyl 2-iodomethylcyclopropane-1,1-dicarboxylate **1** (149 mg, 0.5 mmol), 1,4-pentadiene (0.10 mL, 1.0 mmol) and Yb(OTf)₃ (310 mg, 0.5 mmol) in CH₂Cl₂ (4 mL) was added Et₃B (0.5 mL, 1M hexane solution) at -15 °C. 20 mL of dry air was subsequently introduced with a syringe. After being stirred for 1 h at -15 °C, the mixture was poured into aqueous NH₄Cl solution and extracted with Et₂O. The Et₂O extracts were washed with brine, dried over MgSO₄, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 30) gave an inseparable mixture of *exo*-**2a** and *endo*-**2a** (*exo/endo* = 2.7). To the mixture (*exo*-**2a** and *endo*-**2a**) in DMF (4 mL) was added DBU (0.09 mL, 0.6 mmol). After being stirred for 2 h at 80 °C, the mixture was poured into aqueous NH₄Cl solution and extracted with Et₂O. The Et₂O extracts were washed with brine, dried over MgSO₄, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 30) gave **3a** (93 mg, total 78 %).

(3aR, 6aS)-Dimethyl 5-methylenehexahydro-2,2-(1H)-pentalenedicarboxylate (3a). **3a**: colorless oil; IR (neat) 1737 cm⁻¹; ¹H-NMR (CDCl₃) δ: 4.82 (2H, m), 3.71 (3H, s), 3.69 (3H, s), 2.38-2.64 (6H, m), 2.01 (2H, d, *J* = 15.0 Hz), 1.75 (2H, dd, *J* = 7.0, 12.5 Hz); ¹³C-NMR (CDCl₃) δ: 172.6, 172.2, 151.1, 107.0, 61.7, 52.6, 52.5, 41.8, 40.8, 39.1; MS (*m/z*) 238 (M⁺); Anal. Calcd for C₁₃H₁₈O₄: C, 65.53; H, 7.61. Found: C, 65.44; H, 7.64.

(3aR, 6aS)-Dimethyl 6-methyl-5-methylenehexahydro-2,2-(1H)-pentalenedicarboxylate (3b). **2b** was prepared from **1** (149 mg, 0.5 mmol) and 3-methyl-1,4-pentadiene (0.12 mL, 1.0 mmol) in accordance with the general procedure. The subsequent treatment with DBU in CH₃CN, work-up and purification of the residue by column chromatography (hexane/AcOEt = 30) gave the mixture of *exo*-**3b** and *endo*-**3b** (53 mg, total 42 %) in a ratio of *exo/endo* = 2.8. *exo*-**3b**: colorless oil; IR (neat) 1737 cm⁻¹; ¹H-NMR (CDCl₃) δ: 4.77 (1H, quint, *J* = 1.5 Hz), 4.73 (1H, quint, *J* = 1.5 Hz), 3.72 (3H, s), 3.70 (3H, s), 2.47-2.64 (4H, m), 2.05-2.23 (2H, m), 1.80-1.98 (2H, m), 1.61 (1H, m), 1.04 (3H, d, *J* = 6.7 Hz); ¹³C-NMR (CDCl₃) δ: 172.7, 172.4, 157.0, 105.0, 62.1, 52.5, 51.1, 45.0, 40.9, 40.7, 39.5, 37.7, 35.1, 18.5. MS (*m/z*) 252 (M⁺); Anal. Calcd for C₁₄H₂₀O₄: C, 66.65; H, 7.99. Found: C, 66.40; H, 8.02.

(3a*R*, 6a*S*)-Dimethyl 5-ethylidenehexahydro-2,2-(1*H*)-pentalenedicarboxylate (3c). **2c** was prepared from **1** (149 mg, 0.5 mmol) and 1,4-hexadiene (0.12 mL, 1.0 mmol) in accordance with the general procedure. The subsequent treatment with DBU in DMF, work-up and the purification of the residue by column chromatography (hexane/AcOEt = 30) gave **3c** (95 mg, total 75 %). **3c**: colorless oil; IR (neat) 1737 cm⁻¹; ¹H-NMR (CDCl₃) δ: 5.28 (1H, m), 3.72 (3H, s), 3.69 (3H, s), 2.24-2.64 (6H, m), 2.04 (2H, t, *J* = 16.8 Hz), 1.72-1.83 (2H, m), 1.56 (3H, d, *J* = 6.6 Hz); ¹³C-NMR (CDCl₃) δ: 172.8, 172.4, 142.1, 116.1, 61.8, 52.5 (OMe x 2), 42.3, 41.8, 41.0, 40.4, 39.3, 34.0, 14.6; MS (*m/z*) 252 (M⁺); Anal. Calcd for C₁₄H₂₀O₄: C, 66.65; H, 7.99. Found: C, 66.62; H, 8.01.

(3a*R*, 6a*S*)-Dimethyl 3a-methyl-5-methylenehexahydro-2,2-(1*H*)-pentalenedicarboxylate (3d). **2d** was prepared from **1** (149 mg, 0.5 mmol) and 2-methyl-1,4-pentadiene (0.12 mL, 1.0 mmol) in accordance with the general procedure. The subsequent treatment with DBU in DMF, work-up and the purification of the residue by column chromatography (hexane/AcOEt = 30) gave **3d** (64 mg, total 51 %). **3d**: colorless oil; IR (neat) 1737 cm⁻¹; ¹H-NMR (CDCl₃) δ: 4.82 (2H, m), 3.73 (3H, s), 3.70 (3H, s), 2.56 (1H, ddd, *J* = 1.0, 7.2, 13.4 Hz), 2.50 (1H, m), 2.07-2.34 (6H, m), 1.85 (1H, dd, *J* = 9.1, 13.4 Hz), 1.06 (3H, s); ¹³C-NMR (CDCl₃) δ: 173.1, 172.7, 151.3, 107.1, 60.6, 52.6 (OMe x 2), 50.0, 49.8, 47.3, 46.8, 40.8, 37.6, 27.3; MS (*m/z*) 252 (M⁺); Anal. Calcd for C₁₄H₂₀O₄: C, 66.65; H, 7.99. Found: C, 66.66; H, 8.03.

General procedure of radical iodine atom transfer cascade reaction of 1 with 1,4-enynes. Under Ar atmosphere, to a solution of dimethyl 2-iodomethylcyclopropane-1,1-dicarboxylate **1** (149 mg, 0.5 mmol), 1-undecene-4-yne (150 mg, 1.0 mmol) and Yb(OTf)₃ (310 mg, 0.5 mmol) in CH₂Cl₂ (4 mL) was added Et₃B (0.5 mL, 1M hexane solution) at -15 °C. 20 mL of dry air was subsequently introduced with a syringe. After being stirred for 1 h at -15 °C, the mixture was poured into aqueous NH₄Cl solution and extracted with Et₂O. The Et₂O extracts were washed with brine, dried over MgSO₄, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 30) gave **2e** (166 mg, 74 %).

(3a*R*, 6a*S*)-Dimethyl 5-(1-iodoheptylidene)hexahydro-2,2-(1*H*)-pentalenedicarboxylate (2e). **2e**: colorless oil; IR (neat) 1738 cm⁻¹; ¹H-NMR (CDCl₃) δ: 3.71 (3H, s), 3.70 (3H, s), 2.72 (1H, m), 2.44-2.59 (5H, m), 2.37 (2H, t, *J* = 7.2 Hz), 2.19-2.27 (2H, m), 1.87-1.97 (2H, m), 1.46

(2H, m), 1.21-1.34 (6H, m), 0.87 (3H, t, $J = 6.8$ Hz); ^{13}C -NMR (CDCl_3) δ : 172.8, 172.5, 147.2, 98.8, 61.7, 52.7 (OMe x 2), 46.4, 44.9, 42.2, 41.7, 40.2, 40.2, 36.3, 31.7, 29.2, 28.0, 22.6, 14.0; MS (m/z) 448 (M^+); Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{IO}_4$: C, 50.90; H, 6.52. Found: C, 51.05; H, 6.57.

(3aR, 6aS)-Dimethyl 5-[iodo(phenyl)methylene]hexahydro-2,2-(1H)-pentalenedicarboxylate (2f). **2f** was prepared from **1** (149 mg, 0.5 mmol) and 1-phenyl-4-pentene-yne (142 mg, 1.0 mmol) in accordance with the general procedure. Purification of the residue by column chromatography (hexane/AcOEt = 30) gave **2f** (156 mg, 71 %). **2f**: colorless oil; IR (neat) 1734 cm^{-1} ; ^1H -NMR (CDCl_3) δ : 7.27-7.30 (4H, m), 7.21 (1H, m), 3.73 (3H, s), 3.72 (3H, s), 2.37-2.80 (7H, m), 2.20 (1H, dd, $J = 2.7, 16.9$ Hz), 2.03 (1H, dd, $J = 6.4, 13.4$ Hz), 1.86 (1H, dd, $J = 6.4, 13.4$ Hz); ^{13}C -NMR (CDCl_3) δ : 172.5, 172.3, 151.0, 143.7, 128.7, 128.0, 127.4, 90.5, 61.6, 52.6 (OMe x 2), 46.9, 44.9, 42.0, 40.4, 40.0, 37.8; MS (m/z) 440 (M^+); Anal. Calcd for $\text{C}_{19}\text{H}_{21}\text{IO}_4$: C, 51.83; H, 4.81. Found: C, 51.59; H, 4.84.

(3aR, 6aS)-Dimethyl 5-{2-[(*tert*-butyldiphenylsilyl)oxy]-1-iodoethylidene}hexahydro-2,2-(1H)-pentalenedicarboxylate (2g). **2g** was prepared from **1** (149 mg, 0.5 mmol) and 1-*tert*-butyldiphenylsiloxy-5-hexene-2-yne (335 mg, 1.0 mmol) in accordance with the general procedure. Purification of the residue by column chromatography (hexane/AcOEt = 30) gave **2g** (231 mg, 73 %). **2g**: colorless oil; IR (neat) 1736 cm^{-1} ; ^1H -NMR (CDCl_3) δ : 7.69-7.76 (4H, m), 7.35-7.48 (6H, m), 4.25 (2H, s), 3.72 (3H, s), 3.71 (3H, s), 2.46-2.65 (4H, m), 2.41 (1H, dd, $J = 7.4, 13.7$ Hz), 2.15-2.30 (2H, m), 1.90-2.02 (2H, m), 1.82 (1H, dd, $J = 7.0, 13.7$ Hz), 1.08 (9H, s); ^{13}C -NMR (CDCl_3) δ : 172.7, 172.4, 150.0, 135.7, 133.4, 129.7, 127.6, 97.3, 68.0, 68.0, 61.7, 52.7 (OMe x 2), 46.2, 44.9, 41.9, 40.0, 36.4, 26.8, 19.3; MS (m/z) 575 ($\text{M}^+ - t\text{-Bu}$); Anal. Calcd for $\text{C}_{30}\text{H}_{37}\text{IO}_5\text{Si}$: C, 56.96; H, 5.90. Found: C, 56.66; H, 5.91.

Dimethyl 3-(3-butenyl)-4-methylene-1,1-cyclopentenedicarboxylate (5h). **4h** was prepared from **1** (149 mg, 0.5 mmol) and 1,5-hexadiene (0.12 mL, 1.0 mmol) in accordance with the general procedure (using 1,4-diene). The subsequent treatment with DBU in DMF, work-up and the purification of the residue by column chromatography (hexane/AcOEt = 30) gave **5h** (85 mg, total 67 %). **5h**: colorless oil; IR (neat) 1738 cm^{-1} ; ^1H -NMR (CDCl_3) δ : 5.81 (1H, tdd, $J = 6.5, 10.2, 17.8$ Hz), 4.92-5.07 (3H, m), 4.83 (1H, q, $J = 2.3$ Hz), 3.73 (3H, s), 3.72 (3H, s), 3.03 (1H, brd, $J = 16.6$ Hz), 2.93 (1H, qd, $J = 2.2, 16.6$ Hz), 2.45-2.67 (2H, m), 1.98-2.22 (2H, m), 1.69-1.84

(2H, m), 1.37 (1H, m); ^{13}C -NMR (CDCl_3) δ :172.1 (C=O x 2), 151.8, 138.3, 114.6, 106.2, 58.2, 52.7 (OMe x 2), 41.7, 40.8, 39.7, 33.2, 31.6; MS (m/z) 193 ($\text{M}^+ - \text{CO}_2\text{Me}$); Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_4$: C, 66.65; H, 7.99. Found: C, 66.65; H, 8.04.

(References)

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