Indium-Catalyzed Cycloisomerization of ω-Alkynyl-β-ketoesters into Six- to Fifteen-Membered Rings

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General. All reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under a positive pressure of argon or nitrogen. Air- and moisture-sensitive liquids or solutions were transferred via a syringe or teflon cannula. Analytical thin-layer chromatography was performed on a glass plate pre-coated with 0.25-mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light (UV) and/or by immersion in an acidic solution of p-anisaldehyde followed by heating on a hot plate. Flash column chromatography was performed as described by Still et al.,\(^1\) employing Kanto Silica gel 60 (spherical, neutral, 140–325 mesh).

Materials. Commercial reagents were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used either distilled or recrystallized before use. Toluene was distilled over CaH\(_2\). Anhydrous acetonitrile was purchased from Kanto Co., and was kept in the presence of MS3A. The water content of the solvent was confirmed with a Karl-Fischer moisture titrator to be less than 20 ppm. Anhydrous ethereal solvents (stabilizer-free) were purchased from WAKO Pure Chemical and purified by a solvent purification system (GlassContour).\(^2\) TBAF stands for tetrabutylammonium fluoride.

Instrumentation. Melting points are uncorrected. \(^1\)H NMR and \(^13\)C NMR spectra were measured on JEOL ECA-500 or ECX 400 spectrometer and reported in parts per million from tetramethylsilane. \(^1\)H NMR spectra in CDCl\(_3\) were referenced internally to tetramethylsilane as a standard, and \(^13\)C spectra to the solvent resonance (CDCl\(_3\) 77.0 ppm, toluene-\(d_8\) 20.4 ppm (methyl group)). IR spectra recorded on a React IR 1000 Reaction Analysis System equipped with DuraSample IR (ASI Applied System) were reported in cm\(^{-1}\). GCMS analysis was performed on a Shimadzu PARVUM2 equipped with glass capillary column Rtx\(^\circledast\)-5MS. High resolution mass spectra (HRMS) were taken with JEOL Accu TOF JMS-T100LC. X-ray diffraction study was carried out on a Rigaku MERCURY CCD system.

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Preparation of Starting Materials

Compounds 1s–5s were prepared by the reaction of dianion of β-dicarbonyl compounds with the corresponding alkyl halide according to the method reported by Malacria. 

Scheme S1. Synthesis of ω-alkynyl β-ketoesters (1s–5s).

Ethyl 3-oxooct-7-ynoate (1s)

Colorless oil; 1H NMR (500 MHz, CDCl3) δ 1.28 (t, J = 6.9 Hz, 3H), 1.80–1.85 (m, 2H), 1.97 (t, J = 2.3 Hz, 1H), 2.25 (dt, J = 2.3, 6.9 Hz, 2H), 2.71 (t, J = 6.9 Hz, 2H), 3.46 (s, 2H), 4.20 (q, J = 6.9 Hz, 2H) (enol form: 2.34 (t, J = 6.9 Hz, 2H), 5.01 (s, 1H), 12.01 (s, 1H)); 13C NMR (CDCl3, 125 MHz) δ 14.1, 17.6, 21.9, 41.3, 49.4, 61.4, 69.2, 83.3, 167.1, 202.1; FTIR (neat) (cm−1) 3311, 2957, 1732, 1714, 1425, 1409, 1309, 1247, 1171, 1054, 1005, 882; Anal. Calcd for C10H14O3: C, 65.91; H, 7.74. Found C, 65.64; H, 7.52.

Methyl 3-oxonon-8-ynoate (2s)

A colorless oil; 1H NMR (CDCl3) δ 1.51–1.58 (m, 2H), 1.68–1.76 (m, 2H), 1.96 (t, J = 2.9 Hz, 1H), 2.21 (td, J = 6.9, 2.9 Hz, 2H), 2.58 (t, J = 7.5 Hz, 2H), 3.46 (s, 2H), 3.74 (s, 3H); 13C NMR (CDCl3, 125 MHz) δ 18.2, 22.4, 27.6, 42.4, 49.0, 52.4, 68.6, 83.9, 167.6, 202.1.

202.3; FTIR (cm⁻¹) 3294, 2957, 1746, 1716, 1436, 1409, 1320, 1252, 1171, 1054, 1005; Anal. Calcd. for C₁₀H₁₄O₃: C, 65.91; H, 7.74. Found C, 65.82; H, 7.83.

Methyl 3-oxodec-9-ynoate (3s)

A colorless oil; ¹H NMR (CDCl₃) δ 1.39–1.46 (m, 2H), 1.51–1.57 (m, 2H), 1.60–1.65 (m, 2H), 1.95 (t, J = 2.3 Hz, 1H), 2.20 (dt, J = 2.3, 6.9 Hz, 2H), 2.56 (t, J = 7.5 Hz, 2H), 3.46 (s, 2H), 3.74 (s, 3H) (enol form: 3.73 (s, 1H), 5.00 (s, 1H), 12.02 (s, 1H), keto/enol = 92/8); ¹³C NMR (CDCl₃, 125 MHz) δ 18.2, 22.8, 27.9, 28.0, 42.8, 49.0, 52.3, 68.3, 84.2, 167.6, 202.5; FTIR (neat) (cm⁻¹) 3301, 2943, 1746, 1715, 1436, 1324, 1243, 1167, 1009; Anal. Calcd for C₁₁H₁₆O₃: C, 67.32; H, 8.22. Found C, 67.18; H, 8.43.

Ethyl 3-oxoundeca-10-ynoate (4s)

A pale yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 1.26–1.35 (m, 5H, including 1.28, t, J = 7.2 Hz, 3H), 1.37–1.47 (m, 2H), 1.47–1.56 (m, 2H), 1.56–1.65 (m, 2H), 1.94 (t, J = 2.3 Hz, 1H), 2.18 (dt, J = 2.3, 6.9 Hz, 2H), 2.55 (t, J = 7.2 Hz, 2H), 3.43 (s, 2H), 4.20 (q, J = 7.3 Hz, 2H) (enol form: 4.97 (s, 1H), 12.1 (s, 1H)); ¹³C NMR (125 MHz, CDCl₃) δ 14.1, 18.3, 23.2, 26.0, 28.2, 28.36, 28.41, 42.9, 49.3, 61.3, 68.2, 84.5, 167.2, 202.8 (two of the methylene carbons are overlapped with each other); FTIR (neat) (cm⁻¹) 3289, 2982, 2937, 2860, 2116, 1744, 1717, 1647, 1628, 1368, 1315, 1237, 1163, 1030, 645; Anal. Calcd for C₁₃H₂₀O₃: C, 69.61; H, 8.99. Found: C, 69.70; H, 9.11.

Methyl 3-oxo-heptadec-16-ynoate (5s)

Colorless crystals; mp = 56.9–57.9 °C; ¹H NMR (500 MHz, CDCl₃) δ 1.23–1.33 (brs, 16H), 1.33–1.43 (m, 2H), 1.48–1.56 (m, 2H), 1.94 (t, J = 2.6 Hz, 1H), 2.18 (dt, J = 2.7,
7.2 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H), 3.44 (s, 2H), 3.74 (s, 3H) (enol form: 3.73 (s, 3H), 4.99 (s, 1H), 12.02 (s, 1H)); \(^1\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 18.4, 23.4, 28.5, 28.7, 29.0, 29.1, 29.3, 29.37, 29.44, 29.5, 43.1, 49.0, 52.3, 68.0, 84.8, 167.7, 202.8 (two of the alkyl carbons are overlapped); FTIR (KBr) (cm\(^{-1}\)) 3259, 2934, 2918, 2848, 2360, 2345, 1742, 1705, 1471, 1328, 1318, 1258, 1164, 1089, 1085, 1009, 718, 701, 675, 659; Anal. Calcd for C\(_{18}\)H\(_{30}\)O\(_3\): C, 73.43; H, 10.27. Found: C, 73.32; H, 10.49.

**Scheme S2.** Preparation of substrate 6s.

A mixture of 2-bromophenethyl bromide (12.5 g, 47 mmol), trimethylsilylacetylene (10 mL, 70 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (3.3 g, 4.7 mmol), and CuI (2.0 g, 10 mmol) in 80 mL of diisopropylamine was stirred at 100 °C for 18 h. The resulting mixture was cooled to RT and filtered through a pad of silica gel with an elution of hexane. Filtrate was concentrated in vacuo to afford crude product. Flash column chromatography (silica gel, hexane 100%) of the crude product gave 12.4 g of the product as a mixture of the title compound and the starting material (85/15 by GCMS analysis). This mixture was used in the next step without further purification.
**Ethyl 3-oxo-6-(2-trimethylsilylethynylphenyl)hexanoate**

To a suspension of sodium hydride (1.54 g, 63% in oil, 40 mmol) was added a solution of ethyl acetoacetate (5.4 g, 40 mmol) in 20 mL of THF dropwise at 0 °C for 30 min. After stirring for 30 min, BuLi (1.60 M solution, 25 mL, 40 mmol) was added then stirred for 30 min at 0 °C. A mixture of 2-bromophenethyl bromide and HMPA was added to the orange solution of the dianion, and the cooling bath was removed. After stirred at 50 °C for 6 h, 100 mL of saturated aqueous NH₄Cl and extracted with Et₂O (100 mL, 3 times). Combined organic layer was washed with water (50 mL) and brine (50 mL) successively and dried over Na₂SO₄. After filtration, the filtrate was concentrated in vacuo to afford a crude product. Flash column chromatography (silica gel, hexane/Et₂O = 85/15) of the crude product gave the title compound (1.20 g, 3.6 mmol, 9%).

**Ethyl 6-(2-ethynylphenyl)-3-oxohexanoate (6s)**

To a solution of ethyl 3-oxo-6-(2-trimethylsilylethynylphenyl)hexanoate (1.15 g, 3.5 mmol) in 5 mL of THF was added a solution of TBAF in THF (4 mL, 1.0 M, 4...
mmol) at RT. After stirred for 15 min, the mixture was filtered through the pad of Florisil. The filtrate was concentrated in vacuo to obtain a crude product. Flash column chromatography (silica gel, hexane/Et₂O = 85/15) of the crude product gave the titled compound (0.50 g, 1.9 mmol, 54%).

¹H NMR (400 MHz, CDCl₃) δ 1.27 (t, J = 7.2 Hz, 3H), 1.97 (m, 2H), 2.57 (t, J = 7.6 Hz, 2H), 2.82 (t, J = 7.6 Hz, 2H), 3.25 (s, 1H), 3.43 (s, 2H), 4.18 (q, J = 7.2 Hz, 2H), 7.14–7.19 (m, 2H), 7.27 (t, J = 8.0 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 14.1, 24.1, 33.2, 42.1, 49.3, 61.3, 80.8, 82.2, 121.6, 126.0, 128.9, 129.0, 132.9, 144.0, 167.2, 202.5; FTIR (neat) (cm⁻¹) 3284, 2937, 1738, 1713, 1646, 1482, 1367, 1233, 1028, 758; Anal. Calcd for C₁₆H₁₉O₃: C, 74.39; H, 7.02. Found C, 74.18; H, 6.97.

**Scheme S3.** Preparation of substrate 7s

3-(2-Bromophenyl)propan-1-ol (CAS: 52221-92-8)

To a suspension of LiAlH₄ (6.2 g, 0.16 mol) in Et₂O (ca. 100 mL) was added a solution of 3-(2-bromophenyl)propionic acid (25 g, 0.11 mol) in THF (ca. 200 mL) dropwise via dropping funnel over 45 min. Then the reaction mixture was warmed to 75 °C and refluxed for 1 h. After cooling the solution to 0 °C, ca. 40 mL of AcOEt, ca. 200 g of ice, and ca. 250 mL of 5 M HCl was added slowly to the reaction mixture
successively. The mixture was extracted three times with Et₂O. Combined organic layer was dried over MgSO₄ and evaporated under reduced pressure. Chromatographic separation of the crude mixture was carried out by silica gel (CH₂Cl₂ only to CH₂Cl₂/MeOH = 20/1) to afford a mixture of 3-(2-bromophenyl)propan-1-ol (64 mmol, 59% yield) and 3-phenylpropan-1-ol (25 mmol). This mixture was used for the next reaction without further purification.

1H NMR (500 MHz, CDCl₃) δ 1.86-1.94 (m, 2H, overlapped with the peak of 3-phenyl-1-propionic acid), 2.84 (t, J = 7.5 Hz, 2H), 3.71 (t, J = 6.3 Hz, 2H), 7.03–7.09 (m, 1H), 7.17–7.31 (m, 2H, overlapped with the peak of 3-phenylpropan-1-ol), 7.53 (d, J = 7.5 Hz, 1H); 13C NMR (125 MHz, CDCl₃) δ 32.4, 32.7, 62.3, 124.4, 127.5, 127.6, 130.4, 132.8, 141.8.

1-Bromo-3-(2-bromophenyl)propane (CAS: 1075-28-1)

To a solution of the mixture of 3-(2-bromophenyl)propan-1-ol and 3-phenylpropan-1-ol (total 17 g, 64 mmol and 25 mmol each) in CH₂Cl₂ was added MsCl (8.3 mL, 0.11 mol) and Et₃N (15 mL, 0.11 mol) at 0 °C and the reaction mixture was stirred for 1 h. To the reaction mixture was added H₂O and the crude compound was extracted three times with CH₂Cl₂ and filtered through a paper filter. The crude solution was evaporated in vacuo. To the crude compound was added LiBr (15 g, 0.18 mmol) and acetone (ca. 200 mL). After refluxing for 8.5 h, the reaction mixture was cooled to RT and acetone was evaporated in vacuo. To the crude mixture was added water and CH₂Cl₂, and the aqueous layer was extracted three times with CH₂Cl₂. The organic layer was filtered through a paper filter and the solvent was evaporated in vacuo to obtain a 79/21 mixture of the title compound and 1-bromo-3-phenylpropane (containing a small amount of an unidentified compound) after silica gel column chromatography (hexane) (total 19 g, 68 mmol, 83%). This mixture was used directly to the next reaction without further purification.

1H NMR (500 MHz, CDCl₃) δ 2.15–2.23 (m, 2H, overlapped with the peak of 1-bromo-3-phenylpropane), 2.91 (t, J = 7.5 Hz, 2H), 3.43 (t, J = 6.9 Hz, 2H), 7.06–7.11 (m, 1H), 7.18–7.32 (m, 2H, overlapped with the peak of 1-bromo-3-phenylpropane), 7.54 (d, J = 8.0 Hz, 1H).
1-Bromo-3-[2-(trimethylsilylethynyl)phenyl]propane

To a solution of the mixture of 1-bromo-3-(2-bromophenyl)propane (58 mmol) and 1-bromo-3-phenylpropane (16 mmol) (total 19 g) in diisopropylamine (ca. 120 mL) was added trimethylsilylacetylene (12 mL, 87 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (4.1 g, 5.8 mmol), and CuI (2.2 g, 12 mmol) and heated to 100 °C. After the reaction mixture was stirred for 10 h at this temperature, the solvent was evaporated in vacuo and filtered through a pad of Celite. The title compound was purified by silica gel column chromatography and distillation to obtain colorless oil (bp 97–99 °C) (11 g, 37 mmol, 64%).

R\(_f\) = 0.36 (hexane); ^1H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 0.26 (s, 9H), 2.22 (quint, \(J = 7.2\) Hz, 2H), 2.94 (t, \(J = 6.9\) Hz, 2H), 3.41 (t, \(J = 6.3\) Hz, 2H), 7.15 (dt, \(J = 1.5, 7.5\) Hz, 1H), 7.19–7.27 (m, 2H), 7.44 (dd, \(J = 1.4, 8.0\) Hz, 1H); ^13C NMR (125 MHz, CDCl\(_3\)) \(\delta\) –0.01, 33.1 (Two alkyl carbons are overlapped), 33.3, 98.3, 103.5, 122.6, 126.1, 128.7, 129.1, 132.6, 143.1; FTIR (neat) (cm\(^{-1}\)) 3068, 3019, 2959, 2899, 2859, 2360, 2156, 1483, 1448, 1249, 869, 843, 759; Anal. Calcd for C\(_{14}\)H\(_{19}\)BrSi: C, 56.94; H, 6.49. Found: C, 57.13; H, 6.55.

Ethyl 3-oxo-7-[2-(trimethylsilylethynyl)phenyl]heptanoate

To a solution of NaH (1.4 g, 37 mmol, 63% in oil) in THF (ca. 40 mL) was added ethyl 3-oxo-butanoate dropwise via dropping funnel at 0 °C. During the addition, gas evolution was observed. After the reaction mixture was stirred for 20 min at this temperature, n-BuLi (24 mL of 1.55 M in hexane, 37 mmol) was added to the reaction mixture. The mixture was kept stirring for 45 min at 0 °C. To the reaction mixture was added a solution of 1-bromo-3-[2-(trimethylsilylethynyl)phenyl]propane (11 g, 37 mmol) and HMPA (13 mL, 74 mmol) in THF (ca. 10 mL). The reaction mixture was
stirred for 3 h at 0 °C, 2 h at RT, and 2 h at 50 °C. The reaction was quenched with saturated aqueous NH₄Cl. The crude product was extracted three times with CH₂Cl₂ and filtered through a paper filter. The crude mixture was purified by silica gel column chromatography (hexane/AcOEt = 7/1 to 5/1) to obtain the title compound (7.7 g, 22 mmol, 61%) (keto/enol = 88/12) as a colorless oil.

Rₛ = 0.21 (hexane/AcOEt = 10:1); ¹H NMR (500 MHz, CDCl₃) δ 0.26 (s, 9H), 1.27 (t, J = 7.3 Hz, 3H), 1.61–1.72 (m, 4H), 2.54–2.59 (m, 2H), 2.72–2.82 (m, 2H), 3.42 (s, 2H), 4.18 (q, J=7.3 Hz), 7.12 (dt, J = 1.4, 7.6 Hz, 1H), 7.16 (brd, J = 6.9 Hz, 1H), 7.23 (dt, J = 1.4, 7.6 Hz, 1H), (enol form: 4.97 (s, 1H), 12.10 (s, 1H)); ¹³C NMR (125 MHz, CDCl₃) δ 0.0, 14.1, 23.3, 29.8, 34.3, 42.9, 49.3, 61.3, 97.8, 103.9, 122.4, 125.7, 128.6, 128.7, 132.5, 144.6, 167.2, 202.6; FTIR (neat) (cm⁻¹) 3064, 2956, 2861, 2375, 2347, 2321, 2155, 1744, 1718, 1250, 868, 843, 759; Anal. Calcd for C₁₇H₂₀O₃: C, 69.72; H, 8.19. Found: C, 69.69; H, 8.27.

**Ethyl 3-oxo-7-(2-ethynlyphenyl)heptanoate (7s)**

![Image of chemical structure](ethyl_3-oxo-7-(2-ethynlyphenyl)heptanoate)

To a solution of ethyl 3-oxo-7-[2-(trimethylsilylethynyl)phenyl]heptanoate (7.6 g, 22 mmol) in THF was added TBAF (23 mL of 1.0 M in THF, 23 mmol) and stirred for 1 h at RT. Evaporation of THF and successive silica gel column chromatography (hexane/AcOEt = 5 to AcOEt only) gave the title compound (5.9 g, 22 mmol, 98%) (keto/enol = 93/7) as a pale yellow oil.

Rₛ = 0.19 (hexane/AcOEt = 5/1); ¹H NMR (500 MHz, CDCl₃) δ 1.27 (t, J = 7.2 Hz, 3H), 1.61–1.72 (m, 4H), 2.58 (distorted t, J = 6.9 Hz, 2H), 2.80 (distorted t, J = 7.2 Hz, 2H), 3.25 (s, 1H), 3.42 (s, 2H), 4.19 (q, J = 7.1 Hz, 2H), 7.15 (dt, J = 1.4, 7.6 Hz, 1H), 7.12 (brd, J = 6.9 Hz), 7.26 (brdt, J = 1.4, 6.9 Hz), 7.46 (dd, J = 1.4, 7.6 Hz, 1H) (enol form: 4.98 (s, 1H), 12.10 (s, 1H)); ¹³C NMR (125 MHz, CDCl₃) δ 14.1, 23.1, 29.8, 34.1, 42.8, 49.3, 61.3, 80.6, 82.3, 121.4, 125.8, 128.7, 128.9, 132.9, 144.7, 167.2, 202.7; FTIR (neat) (cm⁻¹) 3288, 3064, 2982, 2939, 2862, 2366, 2346, 2323, 1743, 1717, 1313, 1238, 1173, 1027, 761; Anal. Calcd for C₁₇H₂₆O₃: C, 74.97; H, 7.40. Found: C, 75.14; H, 7.49.
Scheme S4. Preparation of substrate 8s

2-(2-Bromophenyl)ethane-1-ol (CAS: 1074-16-4)

To a suspension of LiAlH₄ (17.6 g, 464 mmol) in Et₂O (ca. 750 mL) was added a solution of 3-(2-bromophenyl)acetic acid (100 g, 464 mmol) in Et₂O (ca. 350 mL) dropwise via dropping funnel. Then the reaction mixture was refluxed for 40 min. After cooling the solution to 0 °C, Celite and THF was added to the reaction mixture. To the mixture was added 18 mL of H₂O slowly. Then 18 mL of 15% aqueous NaOH and 54 mL of H₂O was added successively. The crude mixture was filtered through a glass filter and concentrated in vacuo. The NMR spectrum of the crude mixture showed a quantitative formation of the title compound (95.3 g). This material was used for the next reaction without further purification.

^1H NMR (500 MHz, CDCl₃) δ 1.64 (brs, 1H), 3.03 (t, J = 6.9 Hz, 2H), 3.88 (t, J = 6.9 Hz, 2H), 7.07–7.12 (m, 1H), 7.23–7.30 (m, 2H), 7.55 (d, J = 7.5 Hz, 1H); ^13C NMR (125 MHz, CDCl₃) δ 39.3, 62.0, 124.7, 127.4, 128.2, 131.2, 132.9, 137.8.

To a solution of the crude mixture of 2-(2-bromophenyl)ethan-1-ol (95.3 g, assumed as 464 mmol) in CH₂Cl₂ (ca. 500 mL) was added imidazole (34.8 g, 472
mmol) and chlorotriisopropylsilane (100 mL, 472 mmol) and stirred at RT for 1.5 h. To the reaction mixture was added H₂O and the aqueous layer was extracted three times with CH₂Cl₂. Combined organic layer was filtered through a paper filter and evaporated under reduced pressure. NMR spectrum of the crude mixture showed a quantitative formation of the titled compound (168 g). This material was used for the next reaction without further purification.

¹H NMR (500 MHz, CDCl₃) δ 0.99–1.11 (m, 21H), 3.01 (t, J = 6.9 Hz, 2H), 3.89 (t, J = 7.2 Hz, 2H), 7.06 (dt, J = 1.7, 7.8 Hz, 1H), 7.21 (dt, J = 1.1, 7.5 Hz, 1H), 7.29 (dd, J = 1.7, 8.0 Hz, 1H), 7.52 (dd, J = 1.2, 8.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 12.0, 18.0, 39.7, 62.7, 124.6, 127.1, 127.9, 131.7, 132.6, 138.5.

2-(2-Triisopropylsilyloxyethyl)phenylboronic acid

To a solution of the crude mixture of 2-(2-bromophenyl)-1-triisopropylsilyloxethane (168 g, assumed as 464 mmol if pure) in THF (ca. 500 mL) was added BuLi (299 mL of 1.57 M in hexane, 469 mmol) at –78 °C over 1 h and stirred for 45 min at this temperature. Then, triisopropoxyborane (89.3 mL, 475 mmol) was added to the reaction mixture at –78 °C. The cooling bath was removed after the addition, and the reaction mixture was stirred at RT for 2 h. Then, the reaction mixture was cooled to 0 °C. To the reaction mixture was added 2M HCl to quench the reaction. The crude mixture was washed with aqueous HCl repeatedly until hydrolysis of the boronic acid ester was completed. The separated aqueous layer was extracted three times with Et₂O. The combined organic layer was washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by recrystallization (hexane / Et₂O) to obtain 77.4 g (240 mmol, 52% yield) of the title compound as colorless crystals.

Mp = 76–77 °C; ¹H NMR (500 MHz, CDCl₃) δ 0.91 (d, J = 7.5 Hz, 18H), 0.95–1.07 (m, 3H), 3.00 (t, J = 5.4 Hz, 2H), 4.04 (t, J = 5.4 Hz, 2H), 7.17 (d, J = 7.5 Hz, 1H), 7.22 (dt, J = 1.2, 7.7 Hz, 1H), 7.35 (dt, J = 1.5, 7.7 Hz, 1H), 7.68 (dd, J = 1.7, 7.5 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 11.7, 17.5, 38.3, 66.4, 125.8, 128.9, 130.1, 133.8, 143.6; IR (neat) (cm⁻¹) 3366, 3231, 2945, 2868, 1741, 1077, 1034, 1015, 911, 884, 737, 679.
2-[(2'-Ethynylphenyl)phenyl]ethanol

To a solution of 2-(2-triisopropylsilyloxyethyl)phenylboronic acid (40.0 g, 124 mmol), Pd(PPh₃)₄ (6.52 g, 5.64 mmol), and Ba(OH)₂·8H₂O (89.0 g, 282 mmol) in DME 200 mL and H₂O 30 mL was added 1-bromo-2-trimethylsilylalkynylbenzene (28.6 g, 113 mmol) and stirred at 80 °C for 10 h. After cooling the reaction mixture to 0 °C, 1N HCl was added to quench the reaction. The separated aqueous layer was extracted three times with Et₂O. Combined organic layer was washed brine, filtered through a pad of silica gel, and concentrated under reduced pressure. To the crude mixture was added 100 mL of THF and TBAF (140 mL of 1.0 M in THF, 140 mmol) successively. After stirring for 2 h at RT, the reaction was quenched by adding saturated aqueous NH₄Cl. The aqueous layer was extracted three times Et₂O. Combined organic layer was washed with brine, dried over MgSO₄, and evaporated under reduced pressure. The title compound was purified by silica gel column chromatography (hexane/AcOEt = 2/1 to 1 and CH₂Cl₂/MeOH = 100/1 to 20/1) to obtain the product in 66% yield (16.5 g, 74.0 mmol) including small amount of unidentified compound. This material was directly used for the next reaction without further purification because of its instability.

Rₛ = 0.28 (hexane/AcOEt = 2/1); ᵃ¹H NMR (500 MHz, CDCl₃) δ 1.33 (brs, 1H), 2.77 (dd, J = 5.8, 6.9 Hz, 2H), 2.91 (s, 1H), 3.63 (brt, J = 6.6 Hz, 2H), 7.18–7.36 (m, 6H), 7.39 (dt, J = 1.3, 7.5 Hz, 1H), 7.59 (dd, J = 1.4, 7.7 Hz, 1H); ᵃ¹³C NMR (125 MHz, CDCl₃) δ 36.5, 63.0, 80.4, 82.5, 121.8, 126.1, 127.2, 127.9, 128.6, 129.6, 129.8, 130.2, 132.9, 136.1, 140.8, 144.4.

2-[(2'-Ethynylphenyl)phenyl]acetaldehyde

To a solution of oxalyl chloride (6.98 mL, 82.4 mmol) in CH₂Cl₂ (200 mL) was added DMSO (11.7 mL, 165 mmol), which was dissolved in CH₂Cl₂ (40 mL), at –78 °C over 15 min. Then, 2-[(2'-ethynylpheneyl)phenyl]ethanol (16.7 g, 75.0 mmol)
in 30 mL of CH₂Cl₂ was added dropwise over 20 min. The reaction mixture was stirred for 10 min at −78 °C, and Et₃N (52.0 mmol, 375 mmol) was added to the mixture at the temperature over 5 min. The reaction mixture was stirred at −78 °C for 5 min and at RT for 2 h. To the reaction mixture was added saturated aqueous NH₄Cl, and the aqueous layer was extracted three times with CH₂Cl₂. Combined organic layer was washed with saturated aqueous NaHCO₃, filtered through a paper filter, and concentrated under reduced pressure. The title compound was purified by silica gel column chromatography (hexane/AcOEt = 10/1 to 5/1 and hexane/Et₂O = 3/1 several times). The product was obtained in 28% yield (4.70 g, 21.3 mmol) including a small amount of an unidentified compound. This material was directly used for the next reaction without further purification because of its instability.

Rᶠ = 0.36 (hexane/Et₂O = 3/1); ¹H NMR (500 MHz, CDCl₃) δ 2.93 (s, 1H), 3.58 (d, J = 2.3 Hz, 2H), 7.21 (dd, J = 1.1, 7.4 Hz, 1H), 7.29 (dt, J = 7.5, 1.9 Hz, 2H), 7.32–7.42 (m, 4H), 7.60 (dd, J = 1.5, 7.8 Hz, 1H), 9.59 (t, J = 2.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 48.1, 80.8, 82.3, 121.7, 127.3, 127.6, 128.2, 128.9, 129.9, 130.2, 130.3, 130.6, 133.0, 141.1, 143.5, 199.8.

**Ethyl 4-[2-(2'-ethynylphenyl)phenyl]-3-oxobutanoate (8s)**

![8s](image)

To a suspension of SnCl₂ (398 mg, 2.10 mmol) and ethyl diazoacetate (2.86 mL, 23.1 mmol) in CH₂Cl₂ (40 mL) was added 2-[(2'-ethynylphenyl)phenyl]acetaldehyde (4.63 g, 21.0 mmol) in 30 mL of CH₂Cl₂, and the resulting reaction mixture was stirred for 23 h at RT. To the reaction mixture was added brine, and the aqueous layer was extracted three times with CH₂Cl₂. Combined organic layer was passed through a pad of silica gel and concentrated under reduced pressure. Purification was carried out by silica gel column chromatography (hexane/AcOEt = 9/1 to 2/1 and toluene/CH₂Cl₂ = 5/1 to CH₂Cl₂ only) to obtain 4.37g (14.3 mmol, 68% yield) of the title compound as a colorless oil (keto/enol = 97/3).

Rᶠ = 0.29 (hexane/AcOEt = 5/1); ¹H NMR (500 MHz, CDCl₃) δ 1.21 (t, J = 6.9 Hz, 3H), 2.93 (s, 1H), 3.21 (d, J = 16.1 Hz, 1H), 3.26 (d, J = 15.3 Hz, 1H), 3.72 (d, J = 16.9 Hz, 1H), 3.76 (d, J = 16.8 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 7.19 (dd, J = 1.6, 7.7 Hz, 1H),
7.21-7.42 (m, 6H), 7.60 (d, J = 7.7 Hz, 1H) (enol form: 1.25 (t, J = 6.9 Hz, 3H), 2.91 (s, 1H), 3.40 (d, J = 16.1 Hz, 1H), 3.46 (d, J = 16.1 Hz, 1H), 4.14 (q, J = 7.4 Hz, 2H), 4.67 (s, 1H), 12.0 (s, 1H)); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 14.0, 47.5, 48.5, 61.2, 80.7, 82.2, 121.6, 127.2, 127.5, 128.1, 128.8, 130.0, 130.2, 130.3, 131.8, 133.0, 140.7, 143.6, 167.0, 200.4; FTIR (neat) (cm$^{-1}$) 3281, 3061, 2944, 1741, 1718, 1648, 1475, 1440, 1409, 1366, 1309, 1254, 1231, 1193, 1154, 1027, 780; HRMS(APCI-) Calcd for C$_{20}$H$_{17}$O$_3$ [M-H]$^-$ 305.1183. Found: 305.1179; Anal. Calcd for C$_{20}$H$_{18}$O$_3$: C, 78.41; H, 5.92. Found: C, 78.21; H, 6.04.

**Scheme S5.** Synthesis of substrate 9s.

4-(2-Bromophenyl)-1-triisopropylsilylbut-1-yne

To a solution of 1-triisopropylsilyl-prop-1-yne (20.0 g, 84.5 mmol) in THF was added BuLi (53.5 mL of 1.58 M in hexane, 84.5 mmol) at $-78$ °C dropwise over 20 min and stirred at this temperature for 2.5 h. Then, 2-bromobenzyl bromide (20.3 g, 81.3 mmol) in 25 mL of THF was added to the solution over 30 min at $-78$ °C. The cooling bath was removed, and the reaction temperature was allowed to raise to RT. After stirring the reaction at RT for 13 h, the solvent was evaporated under reduced pressure. The crude mixture was passed through a pad of silica gel and distilled (127–128 °C, 0.12 Torr) to give 26.1 g (71.4 mmol, 88%) of the title compound as a
colorless oil. 
\(R_f = 0.53\) (hexane only); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 0.96–1.08 (m, 21H), 2.59 (t, \(J = 7.2\) Hz, 2H), 2.96 (t, \(J = 7.5\) Hz, 2H), 7.07 (dt, \(J = 1.7, 7.8\) Hz, 1H), 7.21 (dt, \(J = 1.2, 7.4\) Hz, 1H), 7.31 (dd, \(J = 1.7, 7.4\) Hz, 1H), 7.52 (dd, \(J = 1.1, 8.0\) Hz, 1H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 11.2, 18.6, 20.2, 35.4, 81.3, 107.5, 124.3, 127.3, 128.0, 131.0, 132.7, 139.6; FTIR (neat) (cm\(^{-1}\)) 2941, 2864, 2173, 1741, 1463, 1027, 996, 884, 749; Anal. Calcd for C\(_{19}\)H\(_{29}\)BrSi: C, 62.45; H, 8.00. Found: C, 62.49; H, 8.13.

**4-[2'-{(2-Triisopropylsilyloxyethylphenyl)phenyl]-1-triisopropylsilylbut-1-yne**

![Chemical structure](image)

To a solution of 2-(2-triisopropylsilyloxyethyl)phenylboronic acid (25.2 g, 78.2 mmol), Pd(PPh\(_3\))\(_4\) (4.11 g, 3.56 mmol), and Ba(OH)\(_2\)\(\cdot\)8H\(_2\)O (56.1 g, 177.8 mmol) in DME 150 mL and H\(_2\)O 25 mL was added 4-(2-bromophenyl)-1-triisopropylsilylbut-1-yne (26.0 g, 71.0 mmol), and the resulting mixture was stirred at 80 °C for 21.5 h. After cooling the reaction mixture to 0 °C, 1N HCl was added to quench the reaction. The aqueous layer was extracted three times with AcOEt. Combined organic layer was washed brine, dried over MgSO\(_4\), and evaporated under reduced pressure. The product was purified by repeated silica gel column chromatography (hexane/Et\(_2\)O = 20 and hexane/AcOEt) to give 30.3 g of the title compound (53.9 mmol, 69%).

\(R_f = 0.25\) (hexane/Et\(_2\)O = 50/1); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 0.95 (br, 21H), 0.96–1.04 (m, 21H), 2.24–2.37 (m, 2H), 2.53–2.64 (m, 3H), 2.64–2.72 (m, 1H), 3.60–3.68 (m, 2H), 7.08–7.13 (m, 2H), 7.19–7.24 (m, 2H), 7.25–7.31 (m, 2H), 7.34–7.37 (m including d, \(J = 8.1\) Hz, 1H), 7.38–7.41 (m including d, \(J = 7.5\) Hz, 1H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 11.9, 17.9, 18.6, 20.8, 32.5, 36.9, 64.0, 80.9, 108.3, 125.9, 126.0, 127.27, 127.30, 129.4, 129.8 (2C), 130.1, 136.6, 138.1, 140.7, 141.0; FTIR (neat) (cm\(^{-1}\)) 2941, 2864, 2173, 1463, 1090, 1069, 884, 753; Anal. Calcd for C\(_{36}\)H\(_{58}\)OSi\(_2\): C, 76.80; H, 10.38. Found: C, 76.71; H, 10.35.
4-[2'-(2-Hydroxyethylphenyl)phenyl]but-1-yne

To a solution of 4-[2'-(2-triisopropylsilyloxyethyl)phenyl]-1-triisopropylsilylbut-1-yne (30.3 g, 53.9 mmol) in THF (100 mL) was added TBAF (129 mL of 1.0 M in THF, 129 mmol) at RT. After stirring at this temperature for 7.5 h, the reaction was quenched with saturated aqueous NH₄Cl. The aqueous layer was extracted three times with Et₂O. Combined organic layer was washed brine, dried over MgSO₄, and concentrated under reduced pressure. The titled compound was purified by silica gel column chromatography to give the title compound in 92% yield (12.4 g, 50.0 mmol). Since there were small amount of contamination in the product, which was difficult to remove, this material was used for the next reaction without further purification.

Rₛ = 0.15 (hexane/AcOEt = 5/1); ¹H NMR (500 MHz, CDCl₃) δ 1.40 (brs, 1H), 1.88 (t, J = 2.6 Hz, 1H), 2.27 (dt, J = 2.5, 7.7 Hz, 2H), 2.55–2.71 (m, 4H), 3.61 (ddd, J = 3.7, 7.2, 14.3 Hz, 2H), 7.09–7.16 (m, 2H), 7.22–7.29 (m, 2H), 7.29–7.36 (m, 4H); ¹³C NMR (125 MHz, CDCl₃) δ 19.4, 32.0, 36.4, 62.9, 68.8, 83.8, 126.15, 126.23, 127.5, 127.6, 129.0, 129.6, 129.9, 130.1, 136.0, 137.9, 140.6, 141.0.

4-[2'-(Formylmethylphenyl)phenyl]but-1-yne

To a solution of oxalyl chloride (4.61 mL, 54.5 mmol) in CH₂Cl₂ (200 mL) was added DMSO (7.73 mL, 109 mmol) in CH₂Cl₂ (10 mL) at –78 ºC over 15 min. Then, 4-[2'-(2-hydroxyethyl)phenyl]but-1-yne (12.4 g, 49.5 mmol) in 10 mL of CH₂Cl₂ was added to the reaction mixture dropwise over 20 min. The resulting mixture was stirred for 10 min at –78 ºC, and to the mixture was Et₃N (34.3 mmol, 248 mmol) at this temperature over 5 min. The reaction mixture was stirred at –78 ºC for 5 min and at RT for 2 h. To the reaction mixture was added saturated aqueous NH₄Cl, and the aqueous layer was extracted three times with CH₂Cl₂. Combined organic layer was washed with saturated aqueous NaHCO₃, filtered through a paper filter, and concentrated under...
reduced pressure. The residue was subjected to silica gel column chromatography (hexane/Et₂O = 10/1 to 5/1) to obtain the title product in 66% yield (8.16 g, 32.9 mmol) including small amount of unidentified compound, which was difficult to remove. This material was directly used for the next reaction without further purification.

Rf = 0.60 (hexane/AcOEt = 2/1); ¹H NMR (500 MHz, CDCl₃) δ 1.89 (t, J = 2.6 Hz, 1H), 2.27 (dt, J = 2.7, 7.5 Hz), 2.55 (ddd, J = 7.2, 7.2, 14.3 Hz, 1H), 2.64 (ddd, J = 7.3, 7.3, 14.6 Hz, 1H), 3.45 (dd, J = 2.0, 16.9 Hz, 1H), 3.50 (dd, J = 2.3, 16.6 Hz, 1H), 7.07 (dd, J = 1.2, 7.5 Hz, 1H), 7.22–7.30 (m, 3H), 7.32–7.41 (m, 4H), 9.56 (t, J = 2.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 19.5, 31.9, 48.2, 68.9, 83.6, 126.4, 127.4, 127.97, 128.00, 129.3, 130.0, 130.3, 130.4, 130.5, 137.9, 140.0, 141.5, 199.2.

**Ethyl 4-[[2'-{(but-3-ynyl)phenyl}phenyl]-3-oxobutanoate (9s)**

![Structure of 9s](image)

To a suspension of SnCl₂ (623 mg, 3.29 mmol) and ethyl diazoacetate (containing ~15% of CH₂Cl₂) (4.48 mL, 36.2 mmol) in CH₂Cl₂ (60 mL) was added 4-[2'-(formylmethylphenyl)phenyl]-but-1-yne (8.16 g, 32.9 mmol) in 20 mL of CH₂Cl₂, and the resulting mixture was stirred for 5 h at RT. To the reaction mixture was added brine, and the aqueous layer was extracted three times with CH₂Cl₂. Combined organic layer was passed through a pad of silica gel and concentrated under reduced pressure. Purification was carried out by repeated silica gel column chromatography (hexane/AcOEt and hexane/CH₂Cl₂) to obtain 3.72g (11.1 mmol, 34% yield) of the title compound as a pale yellow oil (keto/enol = 89/11).

Rf = 0.28 (hexane/AcOEt = 5/1); ¹H NMR (500 MHz, CDCl₃) δ 1.22 (t, J = 7.3 Hz, 3H), 1.90 (t, J = 2.7 Hz, 1H), 2.27 (dt, J = 3.1, 7.7 Hz, 2H), 2.53 (ddd, J = 7.3, 7.3, 14.5 Hz, 1H), 2.61 (ddd, J = 7.3, 7.3, 14.5 Hz, 1H), 3.16 (s, 2H), 3.55 (d, J= 16.8 Hz, 1H), 3.65 (d, J = 16.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 7.06 (dd, J = 1.6, 7.7 Hz, 1H), 7.16–7.21 (m, 1H), 7.22–7.28 (m, 2H), 7.30–7.39 (m, 4H) (enol form: 1.26 (t, J = 7.3 Hz, 3H), 3.23 (d, J = 15.3, 1H), 3.32 (d, J = 16.1 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 4.67 (s, 1H), 12.02 (s, 1H)); ¹³C NMR (125 MHz, CDCl₃) δ 14.0, 19.4, 31.7, 47.3, 48.9, 61.3, 68.9, 83.7, 126.4, 127.2, 127.8, 127.9, 129.2, 129.9, 129.99, 130.04, 130.6, 131.9, 138.0, 140.1, 141.0, 166.9, 200.2 (enol form: 19.4, 38.6, 60.0, 68.8, 90.4, 129.0, 130.0); FTIR
(neat) (cm\(^{-1}\)) 3289, 3061, 2984, 2937, 1745, 1718, 1652, 1478, 1444, 1409, 139, 1254, 1235, 1193, 1154, 1027, 757; Anal. Calcd for C\(_{22}\)H\(_{22}\)O\(_3\): C, 79.02; H, 6.63. Found: C, 78.86; H, 6.63.

**Scheme S5.** Synthesis of substrate 10s

![Scheme S5](image)

**4-Methyl-N-(prop-2-ynyl)benzenesulfonamide** (CAS: 55022-46-3)

To a solution of propargylamine (4.7 g, 85 mmol) in CH\(_2\)Cl\(_2\) was added 4-methyl-benzenesulfonyl chloride (20 g, 0.10 mol) and Et\(_3\)N (14 mL, 0.10 mol) at 0 °C. After the reaction mixture was stirred at RT for 18.5 h, water was added to the reaction mixture, and the aqueous layer was extracted three times with Et\(_2\)O. Combined organic layer was washed brine, dried over Na\(_2\)SO\(_4\), and concentrated in vacuo. Silica gel column chromatography of the crude compound gave the title compound (10 g, 48 mmol, 58%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 2.10 (t, \(J = 2.6\) Hz, 1H), 2.43 (s, 3H), 3.82 (dd, \(J = 2.6, 6.0\) Hz, 2H), 4.91 (brt, \(J = 5.7\) Hz, 1H), 7.31 (d, \(J = 8.0\) Hz, 2H), 7.78 (d, \(J = 8.0\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 21.5, 32.8, 72.9, 77.9, 127.4, 129.7, 136.5, 143.8.

**N-(3-Bromo-propyl)-4-methyl-N-(prop-2-ynyl)benzenesulfonamide**

To a solution of 4-methyl-N-(prop-2-ynyl)benzenesulfonamide (8.4 g, 40 mmol) and triphenylphosphine (14 g, 52 mmol) in THF (ca. 80 mL) was added
3-bromopropan-1-ol (3.6 mL, 40 mmol) and diethylazodicarboxylate (24 mL of 40% solution in toluene, 52 mmol) at 0 °C, and the resulting mixture was stirred at this temperature for 4 h. The solvent was evaporated in vacuo, and the residue was subjected to silica gel column chromatography (CH₂Cl₂/hexane = 2/1 to CH₂Cl₂ only) to obtain the title compound in 79% yield (10 g, 30 mmol) as a colorless oil. 

Rf = 0.53 (hexane/CH₂Cl₂ = 1/2); ¹H NMR (500 MHz, CDCl₃) δ 2.06 (t, J = 2.3 Hz, 1H), 2.17 (quint, J = 6.7 Hz, 2H), 2.43 (s, 3H), 3.33 (t, J = 6.6 Hz, 2H), 3.47 (t, J = 6.3 Hz, 2H), 4.13 (d, J = 2.9 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.6 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 21.5, 30.1, 31.1, 37.3, 45.4, 73.9, 76.5, 127.7, 129.6, 135.5, 143.7; FTIR (neat) (cm⁻¹) 3289, 3031, 2970, 2925, 2871, 2366, 2322, 1348, 1161, 1093, 660; Anal. Calcd for : C₁₃H₁₆BrNO₂S: C, 47.28; H, 4.88; N, 4.24. Found: C, 47.48; H, 4.84; N, 4.17.

Ethyl 3-oxo-7-[prop-2-ynyl-(toluene-4-sulfonyl)amino]heptanoate (10s)

The title compound was prepared by essentially the same method with that of ethyl 3-oxo-7-[2-(trimethylsilylethynyl)phenyl]heptanoate. The crude mixture was purified by silica gel column chromatography (hexane/ACOEt = 2 to 1 and CH₂Cl₂ only to CH₂Cl₂/MeOH = 50/1) to give the title compound in 12% yield (0.56 g, 1.5 mmol) (keto/enol = 94/6) as a pale yellow oil. 

Rf = 0.30 (hexane/ACOEt = 2/1); ¹H NMR (500 MHz, CDCl₃) δ 1.28 (t, J = 7.2 Hz, 3H), 1.55-1.69 (m, 4H), 2.01 (t, J = 2.6 Hz, 1H), 2.42 (s, 3H), 2.60 (t, J = 6.9 Hz, 2H), 3.19 (t, J = 6.9 Hz, 2H), 3.49 (s, 2H), 4.13 (d, J = 2.9 Hz, 2H), 4.20 (q, J = 7.3 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.6 Hz, 2H) (enol form: 4.98 (s, 1H), 12.10 (s, 1H)); ¹³C NMR (125 MHz, CDCl₃) δ 14.1, 20.1, 21.5, 26.5, 36.2, 42.0, 45.8, 49.3, 61.4, 73.8, 76.5, 127.7, 129.5, 135.8, 143.5, 167.2, 202.4; FTIR (neat) (cm⁻¹) 3273, 2981, 2939, 2872, 2372, 2322, 1743, 1717, 1340, 1161, 660; Anal. Calcd for : C₁₉H₂₆NO₅S: C, 60.14; H, 6.64; N, 3.69. Found: C, 59.98; H, 6.67; N, 3.67.
**In(NTf$_2$)$_3$-catalyzed cyclization reaction**

**Ethyl 5-methyl-2-oxocyclohexene-1-carboxylate (1pb)**

To a dried reaction vessel was introduced solution of In(NTf$_2$)$_3$ in MeCN (220 µL, 0.05 M, 11 µmol). The solvent was removed under vacuum (0.5 Torr) at 60 °C for 1 h. Toluene (11 mL) and substrate (198 mg, 1.1 mmol) were added into the vessel, and the mixture was stirred at 100 °C for 10 h. After cooled to RT, the resulting solution was filtered through a pad of silica gel with an elution of Et$_2$O. The filtrate was concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; hexane Et$_2$O/hexane = 40/60) to obtain the title compound 1pb in 90% yield.

White solid: mp 46–48 °C; $^1$H NMR (500 MHz, CDCl$_3$) δ 1.33 (t, $J = 7.4$ Hz, 3H) 1.99 (s, 3H), 2.04 (m, 2H), 2.39 (t, $J = 5.8$ Hz, 2H), 2.43 (t, $J = 5.8$ Hz, 2H), 4.32 (q, $J = 7.4$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 125 MHz) 14.2, 21.6, 22.1, 31.6, 36.8, 61.2, 133.3, 160.0, 166.7, 195.0; FTIR (neat) 2991, 2961, 1720, 1664, 1633, 1374, 1305, 1235, 1069, 1023, 876, 776: MS (EI) m/z 182 (M$^+$); Anal. Calcd for C$_{10}$H$_{14}$O$_3$: C, 65.91; H, 7.74. Found C, 65.71; H, 7.74.

(1Z,6Z)-Methyl 2-hydroxy-7-methylcyclohepta-1,6-dienecarboxylate (2pb) and (E)-Methyl 2-Methyl-7-oxocyclohept-1-ene carboxylate (2pc)

The reaction was carried out according to the standard procedure on the indium-catalyzed cyclization on a 0.3-mmol scale (1 mol% catalyst, 0.1 M in toluene, 100 °C, 2 h). The crude product was subjected to flash column chromatography (silica gel; hexane 100% to Et$_2$O/hexane = 30/70) to obtain the products 2pb and 2pc in 37% and 61% yields, respectively.

Pale yellow oil: $R_f = 0.12$ (ethyl acetate/ hexane = 20/80); $^1$H NMR (500 MHz, CDCl$_3$) δ 1.78–1.85 (m, 2H), 2.05 (s, 3H), 2.45 (t, $J = 6.3$ Hz, 2H), 2.62 (t, $J = 6.9$ Hz, 2H),
3.78 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 21.1, 23.6, 24.2, 34.4, 41.7, 52.0, 134.9, 156.9, 167.6, 202.0; FTIR (neat) (cm\(^{-1}\)) 2948, 2869, 1727, 1659, 1627, 1434, 1298, 1241, 1138, 1050, 737; GCMS (EI) \(m/z\) 182 (M\(^+\)); Anal. Calcd. for C\(_{10}\)H\(_{14}\)O\(_3\): C, 65.91; H, 7.74. Found C, 65.83; H, 7.91.

Pale yellow oil: \(R_f = 0.72\) (ethyl acetate/ hexane = 20/80); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 1.90 (s, 3H), 1.92–1.97 (m, 2H), 2.08–2.12 (m, 2H), 2.07 (t, \(J = 7.4\) Hz, 2H), 3.78 (s, 3H), 5.83 (t, \(J = 6.9\) Hz, 1H), 12.08 (s, 1H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 22.1, 24.5, 31.8, 33.4, 51.4, 101.9, 127.4, 134.0, 172.3, 178.9; FTIR (cm\(^{-1}\)) 2950, 2861, 1713, 1642, 1632, 1445, 1328, 1250, 1160, 1071, 882; GCMS (EI) \(m/z\) 182 (M\(^+\)); Anal. Calcd. for C\(_{10}\)H\(_{14}\)O\(_3\): C, 65.91; H, 7.74. Found C, 65.69; H, 7.74.

\((1Z, 8Z)\)-Methyl 2-hydroxy-8-methylcycloocta-1,7-diene-1-carboxylate (3pc)

The reaction was carried out according to the procedure for the synthesis of 1pb on 0.3-mmol scale in toluene (0.1 M) at 120 °C for 12 h with 1 mol% of the catalyst. Flash column chromatography on silica gel (eluent: hexane/ether = 95/5) gave the title compound (29 mg, 0.15 mmol, 51%).

Compound 3pc: white solid; mp 49–50 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 1.10 (dq, \(J = 4.6, 13.0\) Hz, 1H), 1.34–1.45 (m, 1H), 1.70–1.81 (m, 2H), 1.82–1.90 (br, 1H), 1.86 (s, 3H), 2.13–2.24 (m, 2H), 2.32 (dd, \(J = 8.4, 12.3\) Hz, 1H), 5.56 (t, \(J = 7.7\) Hz, 1H), 12.63 (d, \(J = 1.6\) Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 23.0, 24.1, 25.3, 27.8, 32.8, 51.6, 101.0, 129.7, 131.0, 173.1, 175.7; FTIR (neat) (cm\(^{-1}\)) 2933, 2854, 1664, 1634, 1602, 1447, 1322, 1233, 1073, 845; MS (EI) \(m/z\) 196 (M\(^+\)); Anal. Calcd for C\(_{11}\)H\(_{16}\)O\(_3\): C, 67.32; H, 8.22. Found: C, 67.18; H, 8.33. Recrystallization from hexane gave crystals suitable for X-ray diffraction study. ORTEP drawing showin in below (Figure S1).
(1Z, 8Z)-Ethyl 2-hydroxy-9-methylcyclonona-1,8-diene-1-carboxylate (4pc)

The reaction was carried out according to the procedure for the synthesis of 1pb on 0.3-mmol scale in toluene (0.04 M) at 150 °C for 8 h using 1 mol% of the catalyst. Compound 4pc were purified by silica gel column chromatography (eluent: EtOAc/hexane = 5/95).

Compound 4pc: 7%; $^1$H NMR (CDCl$_3$, 500 MHz) δ $^1$H NMR (CDCl$_3$, 500 MHz) δ 1.28 (t, J = 6.9 Hz, 3H), 1.27–1.38 (m, 1H), 1.50–1.64 (m, 4H), 1.65–1.75 (m, 1H), 1.82 (s, 3H), 1.88–1.96 (m, 1H), 2.02–2.10 (m, 1H), 2.15–2.33 (m, 2H), 4.11–4.17 (m, 1H), 4.27–4.33 (m, 1H), 5.54 (dd, J = 5.4, 10.0 Hz, 1H), 12.60 (d, J = 2.3 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 14.3, 23.6, 24.6, 27.4, 29.3, 29.4, 33.6, 60.2, 102.3, 131.2, 132.0, 172.2, 175.9; FTIR (neat) (cm$^{-1}$) 2927, 2854, 1748, 1710, 1641, 1453, 1395, 1372, 1324, 1253, 1226, 1156, 1100, 1054, 841; MS (APCI-) 223 ([M-H]); Anal. Calcd for C$_{13}$H$_{20}$O$_3$: C, 69.61; H, 8.99. Found: C, 69.46; H, 9.08.

Methyl 2-methyl-15-oxocyclopentadeca-1-ene-1-carboxylate (5pb)
The reaction was carried out according to the procedure for the synthesis of 1pc on 0.3-mmol scale in toluene (0.01 M) at 150 °C for 18 h using 2 mol% of the catalyst. Compound 5pb were purified by silica gel column chromatography (eluent: Et₂O/hexane = 10/90 to Et₂O/hexane = 30/70). Compound 5pb: 27%; ¹H NMR (400 MHz, CDCl₃) δ 1.20–1.74 (br, 20 H), 1.93 (s, 1H), 1.98 (m, 1H), 2.38 (m, 1H), 2.64 (m, 1H), 3.13 (m, 1H), 4.21 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 20.8, 25.0, 25.8, 26.4, 26.5, 26.62, 26.63, 26.7, 27.0, 27.5, 27.6, 34.8, 43.2, 51.7, 132.4, 157.5, 165.9, 204.8; FTIR (KBr) (cm⁻¹) 2925, 2853, 1725, 1641, 1435, 1224, 847, 789, 722; MS (APCI-) 293 ([M-H]⁻); Anal. Calcd for C₁₈H₃₀O₃; C, 73.43; H, 10.27. Found: C, 73.23; H, 10.35.

(E)-Ethyl 5-methyl-7-oxo-7,8,9,10-tetrahydrobenzo[8]annulene-6-carboxylate (6pa) and Ethyl 5-methylene-7-oxo-5,6,7,8,9,10-hexahydrobenzo[8]annulene-6-carboxylate (6pb)

The reaction was carried out according to the procedure for the synthesis of 1pb on 0.2-mmol scale in toluene (0.1 M) at 100 °C for 2 h using 1 mol% of the catalyst. Compound 6pa and 6pb were separated by silica gel column chromatography (eluent: Et₂O/hexane = 10/90 to Et₂O/hexane = 30/70). Compound 6pa: 17%; Rₜ = 0.36 (AcOEt/hexane = 20/80); yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 1.25 (t, J = 7.4 Hz, 3H), 1.68 (tdd, J = 12.0, 4.5, 4.0 Hz, 1H), 1.95 (tdd, J = 9.1, 4.6, 4.5 Hz) 1H), 2.28 (dt, J = 12.6, 4.6 Hz, 1H), 2.52 (td, J = 12.0, 4.6 Hz, 1H), 2.58 (td, J = 12.0, 4.0 Hz, 1H), 2.72 (dt, J = 13.8, 4.5 Hz, 1H), 4.18(q, J = 7.4 Hz, 2H), 4.36 (s, 1H), 5.17 (s, 1H) 5.51 (s, 1H), 7.11 (dd, J = 8.6, 1.7 Hz, 1H), 7.24 (td, J = 7.4, 1.0 Hz, 1H), 7.25–7.28 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.1, 27.0, 31.6, 38.1,
61.5, 122.1, 126.1, 128.5, 128.7, 130.1, 138.4, 139.7, 140.9, 168.0, 206.0; FTIR (neat) (cm$^{-1}$) 2937, 1739, 1715, 1436, 360, 1204, 1146, 989; MS (EI) m/z 258 (M+); Anal. Calcd for C$_{16}$H$_{18}$O$_3$: C, 74.39; H, 7.02. Found C, 74.12; H, 7.06.

Compound 6pb: 58%; $R_f = 0.21$ (AcOEt/hexane = 20/80); yellow oil; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 1.36 (t, $J = 7.4$ Hz, 3H), 1.70 (ddt, $J = 2.9$, 5.2, 13.2 Hz, 1H), 2.13–2.20 (m, 1H), 2.27 (dt, $J = 4.6$, 11.5Hz, 1H), 2.78 (ddd, $J = 2.9$, 5.2, 13.2 Hz, 1H), 2.90 (dt, $J = 5.2$, 13.2 Hz, 1H), 4.35 (dq, $J = 4.6$, 7.2 Hz, 2H), 7.20–7.22 (m, 1H), 7.30–7.36 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 14.2, 25.3, 30.0, 31.1, 38.6, 61.2, 126.6, 127.8, 129.1, 129.4, 137.7, 138.5, 139.5, 148.8, 167.4, 200.8; FTIR (neat) (cm$^{-1}$) 2941, 1729, 1648, 1447, 1320, 1239, 1139, 1058, 764; MS (EI) m/z 258 (M+); Anal. Calcd for C$_{16}$H$_{18}$O$_3$: C, 74.39; H, 7.02. Found C, 74.13; H, 7.14.

$^{(E)}$-Ethyl 5H-11-methyl-9-oxo-6,7,8,9-tetrahydrobenzo[9]annulene-10-carboxylate (7pa) and

$^{(Z)}$-Ethyl 5H-7-hydroxy-5-methylene-8,9,10,11-tetrahydrobenzo[9]annulene-6-carboxylate (7pb)

The reaction was carried out according to the procedure for the synthesis of 1pb on 0.3-mmol scale in toluene (0.05 M) at 120 °C for 12 h using 1 mol% of the catalyst. Compound 7pa and 7pb were separated by silica gel column chromatography (eluent: CH$_2$Cl$_2$/hexane = 60/40).

Compound 7pa: 11%; $R_f = 0.78$ (AcOEt/hexane = 20/80); yellow oil; keto/enol = 11/89; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 1.18 (t, $J = 7.2$ Hz, 3H), 1.70 (br, 4H), 2.75 (br 4H), 4.10 (q, $J = 7.2$ Hz, 2H), 5.33 (d, $J = 1.9$ Hz, 1H), 5.37 (d, $J = 1.9$ Hz, 1H), 7.02–7.06 (m,
1H), 7.14–7.17 (m, 2H), 7.36–7.40 (m, 1H), 13.00 (s, 1H), keto form 1.26 (t, J = 7.2 Hz, 3H), 1.54–1.84 (m, 4H), 4.18 (q, J = 7.2 Hz, 2H), 4.58 (s, 1H), 5.26 (s, 1H), 5.87 (s, 1H); 13C NMR (125 MHz, CDCl3) δ 14.0, 25.3, 28.5, 31.2, 31.6, 60.5, 105.1, 121.9, 125.5, 127.1, 129.5, 131.0, 140.9, 142.2, 144.4, 172.0, 176.0; FTIR (neat) (cm⁻¹) 2937, 1752, 1637, 1606, 1316, 1227, 1158, 1038, 860, 760; MS (EI) m/z 272 (M⁺); Anal. Calcd for C17H20O3: C, 74.97; H, 7.40. Found C, 74.81; H, 7.53.

Compound 7pb: 60%; Rf = 0.44 (AcOEt/hexane = 20/80); yellow oil; 1H NMR (500 MHz, CDCl3) δ 1.30 (t, J = 7.4 Hz, 3H), 1.50–1.59 (m, 1H), 1.76–1.99 (m, 3H), 2.45 (s, 3H), 2.59 (dd, J = 9.7, 14.4 Hz, 1H), 2.68–2.82 (dd, J = 8.9, 14.4 Hz, 2H), 4.23 (qd, J = 7.2, 11.5 Hz, 1H), 4.30 (qd, J = 7.2, 11.5 Hz, 1H), 7.06–7.08 (m, 1H), 7.18–7.25 (aromatic, 3H); 13C NMR (125 MHz, CDCl3) δ 14.1, 22.6, 24.3, 26.2, 29.2, 135.2, 136.8, 141.5, 154.0, 163.9, 207.8; FTIR (neat) (cm⁻¹) 2934, 1727, 1695, 1444, 1235, 1197, 1058, 764; MS (EI) m/z 272 (M⁺); Anal. Calcd for C17H20O3: C, 74.97; H, 7.40. Found C, 74.88; H, 7.58.

Ethyl 5,6,7,8-tetrahydro-5-methylene-7-oxo-dibenzo[a,c:8]annulene-6-carboxylate (8pa)

The reaction was carried out according to the procedure for the synthesis of 1pb on 0.5-mmol scale in toluene (0.05 M) at 100 °C for 1 h using 1 mol% of the catalyst. Compound 8pa was purified by silica gel column chromatography (hexane/EtO = 10/1 to 3/1). This compound was obtained as a mixture of keto and enol forms in a ratio of 47/53 and each form was composed of two diastereomers: keto form: major/minor = 90/10; enol form: major/minor = 94/6.
Compound 8pa: R_f = 0.6 (hexane/Et_2O = 2/1); colorless viscous oil; ^1^H NMR (CDCl_3, 500 MHz) 1.26 (t, J = 7.3 Hz, 3H (keto/major)), 1.32 (t, J = 7.3 Hz, 3H (enol/major)), 3.29 (brd, J = 16.1 Hz, 1H (enol/major)), 3.39 (brd, J = 15.3 Hz, 1H (enol/major)), 3.45 (d, J = 11.5 Hz, 1H (keto/major)), 3.47 (d, J = 13.8 Hz, 1H (keto/minor)), 3.61 (d, J = 13.8 Hz, 1H (keto/minor)), 4.03 (d, J = 11.5 Hz, 1H (keto/major)), 4.11–4.33 (m, 2H of all the isomers) including s, 1H (keto/major)), 4.41 (s, 1H (keto/minor)), 4.67 (d, J = 1.6 Hz, 1H (enol/minor)), 4.70 (d, J = 1.6 Hz, 1H (enol/major)), 4.79 (s, 1H (keto/major)), 4.90 (s, 1H (keto/minor)), 4.99 (d, J = 1.6 Hz, 1H (enol/minor)), 5.02 (d, J = 1.5 Hz, 1H (enol/major)), 5.20 (s, 1H (keto/major)), 5.59 (s, 1H (keto/minor)), 7.17–7.46 (m, 8H of all the isomers), 13.47 (s, 1H (enol/major)); ^1^C NMR (125 MHz, CDCl_3) δ 14.0 (keto/major), 14.2 (enol/major), 40.3 (enol/major), 47.6 (keto/major), 48.4 (keto/minor), 60.9 (major), 61.3 (keto/minor), 61.7 (major), 63.9 (keto/minor), 66.3 (keto/major), 103.7 (enol/major), 120.6 (keto/minor), 122.0 (enol/major), 123.1 (keto/major), 126.8 (major), 127.0 (major), 127.4 (major), 127.48 (major), 127.50 (major), 127.62 (major), 127.64 (major), 127.7 (minor), 127.8 (major), 128.1 (minor), 128.2 (minor), 128.3 (minor), 128.4 (major), 129.1 (major), 129.3 (major), 129.6 (major), 129.7 (major), 129.9 (major), 130.3 (minor), 132.2 (major), 132.46 (major), 132.52 (minor), 138.6 (major), 138.7 (minor), 139.5 (major), 140.06 (major), 140.10 (major), 140.4 (major), 141.7 (major), 141.8 (minor), 142.3 (major), 142.6 (minor), 142.9 (major), 167.4 (keto/minor), 168.1 (major), 172.6 (major), 175.5 (major), 200.7 (keto/minor), 201.4 (keto/major); FTIR (neat) (cm^-1) 3061, 2984, 1733, 1714, 1637, 1590, 1478, 1444, 1397, 1374, 1274, 1231, 1177, 1027, 919, 745; HRMS (APCI-) Calcd for C_{20}H_{17}O_3 [M-H]^− 305.1177. Found: 305.1186.

**Ethyl 9,10,11,12,13,14-hexahydro-12-methylene-10-hydroxy-10-ene-dibenzo[a,c:10]annulene-11-carboxylate (9pa)**

The reaction was carried out according to the procedure for the synthesis of 1pb on 0.5-mmol scale in toluene (0.05 M) at 100 °C for 8 h using 1 mol% of the catalyst. Compound 9pa was purified by silica gel column chromatography (hexane/Et_2O = 20/1 to Et_2O only) and subsequent recrystallization (hexane and Et_2O) to obtain crystals suitable for X-ray diffraction study. ORTEP drawing shown in below (Figure S2).
Colorless crystals; mp = 113–115 °C; Rf = 0.69 (hexane/Et₂O = 3/1, broad); ¹H NMR (CDCl₃, 500 MHz) 1.26 (t, J = 6.9 Hz, 3H), 2.38–2.46 (m, 1H), 2.50–2.59 (m, 2H), 2.69–2.78 (m, 1H), 3.01 (d, J = 13.0 Hz, 1H), 3.72 (dd, J = 2.3, 13.0, 1H), 4.13 (dq, J = 10.7, 7.1 Hz, 1H), 4.25 (dq, J = 10.7, 7.2 Hz, 1H), 4.65 (d, J = 2.3 Hz, 1H), 4.79 (d, J = 2.3 Hz, 1H), 7.00–7.07 (m, 2H), 7.19 (brt, J = 7.7 Hz, 1H), 7.24 (brt, J = 7.3 Hz, 1H), 7.33 (dt, J = 1.6, 7.7 Hz, 1H), 7.34–7.42 (m, 2H), 7.85 (d, J = 7.7 Hz, 1H), 12.99 (d, J = 2.3 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 14.2, 29.1, 34.5, 37.4, 60.6, 103.3, 119.6, 125.4, 126.6, 127.3, 127.5, 127.8, 129.7, 130.1, 130.2, 134.2, 139.1, 141.4, 141.7, 141.8, 172.3, 173.3; FTIR (neat) (cm⁻¹) 3022, 2957, 2907, 1637, 1328, 1216, 1162, 1034, 842, 772, 753; HRMS(APCI-) Calcd for C₂₂H₂₁O₃[M-H] - 333.1491. Found: 333.1502; Anal. Calcd for C₂₂H₂₂O₃: C, 79.02; H, 6.63. Found: C, 79.15; H, 6.88.

**Figure S2.** ORTEP drawing of 9pa (50% thermal ellipsoids).

**Ethyl 3-methylene-5-oxo-N-(toluene-4-sulfonyl)-azonane-4-carboxylate (10pa) and Ethyl 2-methyl-4-oxo-N-(toluene-4-sulfonyl)-1,4,5,6,7,8-hexahydro-1H-azonine-4-carboxylate (10pb)**

The reaction was carried out according to the procedure for the synthesis of
**1pb** on 0.3-mmol scale in toluene (0.04 M, 10 mol% catalyst) at 150 °C for 1.5 h. Compound **10pa** and **10pb** were separated by silica gel column chromatography (eluent: hexane/Et₂O = 2/1 to 1/10). Compounds **10pa** was obtained as a mixture of keto and enol form (keto/enol = 34/66). **¹H** NMR spectrum of the compound was broad at RT probably because of slow ring inversion. Measurement at 100 °C sharpened the peaks.

**Compound 10pa**: 52%; R<sub>f</sub> = 0.31 (hexane/Et₂O = 1/1); viscous oil (solidify when rubbed with spoon); **¹H** NMR (500 MHz, toluene-<sup>d<sub>8</sub></sup>, 100 °C) δ 1.03 (t, J = 7.2 Hz, 3H (keto)), 1.09 (t, J = 6.9 Hz, 3H (enol)), 1.40–1.49 (m, 1H (keto)), 1.49–1.74 (m, 2H (keto) and 4H (enol)), 1.74–1.85 (m, 1H (keto)), 2.03 (s, 3H (keto) and 3H (enol)), 2.33 (brs, 2H (enol)), 2.48–2.56 (m, 2H (keto)), 2.68 (ddd, J = 3.9, 8.6, 13.8 Hz, 1H (keto)), 2.86 (brs, 2H (enol)), 3.13 (ddd, J = 4.5, 8.6, 13.4 Hz, 1H (keto)), 3.28 (d, J = 14.5 Hz, 1H (keto)), 3.74 (brs, 2H (enol)), 3.50–4.79 (m including q (4.04 ppm), J = 7.1 Hz, 3H (keto) and 2H (enol)), 4.67 (s, 1H (keto)), 4.92 (s, 1H (enol)), 5.05 (s, 1H (keto)), 5.20 (s, 1H (keto)), 5.38 (s, 1H (keto)), 6.89 (d, J = 7.6 Hz, 2H (keto) and 2H (enol)), 7.52 (d, J = 7.6 Hz, 2H (keto)), 7.60 (d, J = 8.3 Hz, 2H (enol)), 13.07 (s, 1H (enol)); **¹³C** NMR (125 MHz, toluene-<sup>d<sub>8</sub></sup>, 100 °C) δ 13.9, 14.1, 20.9, 23.0, 24.1, 27.4, 27.8, 30.4, 41.4, 47.3, 49.8, 56.0, 56.8, 60.5, 61.0, 62.8, 102.5, 120.2, 121.4, 129.5, 136.4, 139.5, 141.4, 142.6, 143.0, 167.9, 171.9, 177.6, 203.3 (several peaks were overlapped with the peaks of toluene-<sup>d<sub>8</sub></sup>); FTIR (KBr) (cm⁻¹) 2994, 2963, 2940, 2898, 2869, 2361, 2344, 1646, 1600, 1376, 1334, 1299, 1242, 1161, 1094, 666; Anal. Calcd for C<sub>18</sub>H<sub>23</sub>NO<sub>4</sub>S: C, 60.14; H, 6.64; N, 3.69. Found: C, 60.14; H, 6.77; N, 3.53.

**Compound 10pb**: 9%; R<sub>f</sub> = 0.1 (hexane/Et₂O = 1/1); viscous oil; **¹H** NMR (500 MHz, CDCl<sub>3</sub>) δ 1.27 (t, J = 6.9 Hz, 3H), 1.84–1.92 (m, 4H), 2.12 (s, 3H), 2.45 (s, 3H),
2.74–2.79 (m, 2H), 2.81–2.86 (m, 2H), 3.67 (s, 2H), 4.21 (q, \(J = 7.1\) Hz, 2H), 7.35 (d, \(J = 8.3\) Hz, 2H), 7.68 (d, \(J = 8.2\) Hz, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 14.0, 20.4, 21.5, 23.0, 28.7, 43.0, 51.4, 56.2, 60.9, 128.2, 129.7, 132.6, 133.4, 144.2, 150.1, 163.7, 205.0; FTIR (KBr) (cm\(^{-1}\)) 2981, 2970, 2939, 2912, 2864, 2847, 2361, 2344, 1704, 1689, 1635, 1358, 1239, 1187, 1170, 1089, 1076, 728, 656; HRMS (APCI-) Calcd for C\(_{19}\)H\(_{24}\)NO\(_5\)S\(^{-}\) ([M-H]) 378.1375. Found: 378.1377.

**Synthesis of Muscone**

**Methyl 2-oxo-14-methylcyclopentadecane-1-carboxylate**

A vigorously stirred mixture of the 15-membered ring product 5pb (12 mg, 0.05 mmol) and Pd/C (6 mg) in 0.5 mL of EtOH was exposed to a hydrogen atmosphere and stirred for 3.5 h. The mixture was filtered through the pad of silica gel. The solvent was removed in vacuo to obtain a crude product of methyl 2-oxo-14-methylcyclopentadecane-1-carboxylate (12 mg). The product was obtained as a mixture of two diastereomers (57/43) via epimerization of the \(\alpha\)-carbon center of carbonyl groups. This material was used in the next step without further purification.

\(^1\)H NMR (500 MHz, CDCl\(_3\)), major diastereomer: \(\delta\) 0.92 (d, \(J = 6.9\) Hz, 3H), 1.20–1.33 (m, 20H), 1.52–1.63 (m, 2H), 2.30–2.38 (m, 1H), 2.40–2.62 (m, 2H), 3.34 (d, \(J = 10.3\) Hz, 1H), 3.70 (s, 3H); minor diastereomer: \(\delta\) 1.06 (d, \(J = 6.9\) Hz, 3H), 1.20–1.33 (m, 20H), 1.66–1.76 (m, 2H), 2.15–2.19 (m, 1H), 2.40–2.62 (m, 2H), 3.59 (d, \(J = 3.4\) Hz, 1H), 3.71 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 17.6, 17.8, 21.9, 22.0, 24.5, 25.7, 25.9, 26.0, 26.1, 26.17, 26.20, 26.29, 26.35, 26.42, 26.45, 26.49, 27.1, 27.11, 27.30, 27.33, 29.6, 31.9, 32.7, 33.38, 33.44, 34.53, 41.3, 42.2, 51.8, 52.16, 62.0, 65.9, 169.6, 170.3, 205.9, 206.5; GCMS (EI) \(m/z\) 296 (M+).

**(±)-Muscone**

Methyl 2-oxo-14-methylcyclopentadecane-1-carboxylate (12 mg) was dissolved in 2 mL of aqueous DMF, and sodium chloride (8 mg, 0.13 mmol) was added. The mixture was refluxed at 150 °C for 36 h. After cooled to RT, 1 mL of water was added. Aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3 mL, 5 times). Combined organic phase was dried over MgSO\(_4\). Solvent was removed in vacuo to afford a crude product. The crude product was purification by flash column chromatography (hexane/ether = 95/5) to obtain (±)-muscone (7 mg, 58% from 5pb). \(^1\)H and \(^{13}\)C NMR spectra were in
agreement with the literature data.\(^4\)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 0.93 (d, \(J = 6.9\) Hz, 3H), 1.21–1.39 (m, 22H), 1.54–1.62 (m, 1H), 1.65–1.70 (m, 1H), 2.03–2.07 (m, 1H), 2.18 (dd, \(J = 5.2, 15.5\) Hz, 1H), 2.41 (t, \(J = 6.9\) Hz, 2H and peaks of 1H is overlapped.); \(^1\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 21.1, 23.0, 25.0, 26.1, 26.2, 26.49, 26.53, 26.58, 26.7, 27.1, 27.5, 29.0, 35.5, 42.1, 50.4, 212.2.