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Supporting Information

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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 spectorometer 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®-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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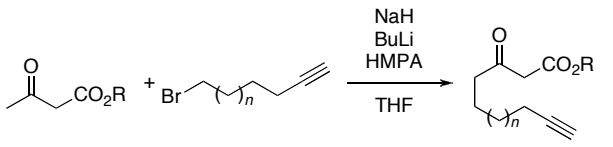
(1) W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43,* 2923–2925.
(2) A. B. Pangborn, M. A. Giardello, R. H. Grubbs, *Organometallics* **1996**, *15,* 1518–1520.

Preparation of Starting Materials

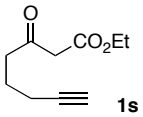
Compounds **1s–5s** were prepared by the reaction of dianion of β-dicarbonyl compounds with the corresponding alkyl halide according to the method reported by Malacria.[3]

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



1s *n* = 0, R = Et
2s *n* = 1, R = Me
3s *n* = 2, R = Me
4s *n* = 3, R = Et
5s *n* = 9, R = Me

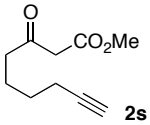
Ethyl 3-oxooct-7-ynoate (1s)



1s

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) 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)); ^{13}C NMR ($CDCl_3$, 125 MHz) 14.1, 17.6, 21.9, 41.3, 49.4, 61.4, 69.2, 83.3167.1, 202.1; FTIR (neat) (cm^{-1}) 3311, 2957, 1732, 1714, 1425, 1409, 1309, 1247, 1171, 1054, 1005, 882; Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found C, 65.64; H, 7.52.

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



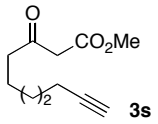
2s

A colorless oil; ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.2, 22.4, 27.6, 42.4, 49.0, 52.4, 68.6, 83.9, 167.6,

(3) P. Cruciani, R. Stammler, C. Aubert, M. Malacria, *J. Org. Chem.* **1998**, *63,* 9470–9475.

202.3; FTIR (cm^{-1}) 3294, 2957, 1746, 1716, 1436, 1409, 1320, 1252, 1171, 1054, 1005; Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found C, 65.82; H, 7.83.

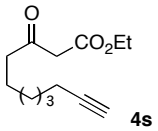
Methyl 3-oxodec-9-ynoate (3s)



3s

A colorless oil; ^1H NMR ($CDCl_3$) 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)); ^{13}C NMR ($CDCl_3$, 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 $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found C, 67.18; H, 8.43.

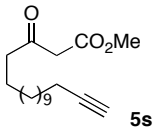
Ethyl 3-oxoundeca-10-ynoate (4s)



4s

A pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) 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* = 2.8 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)); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.70; H, 9.11.

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

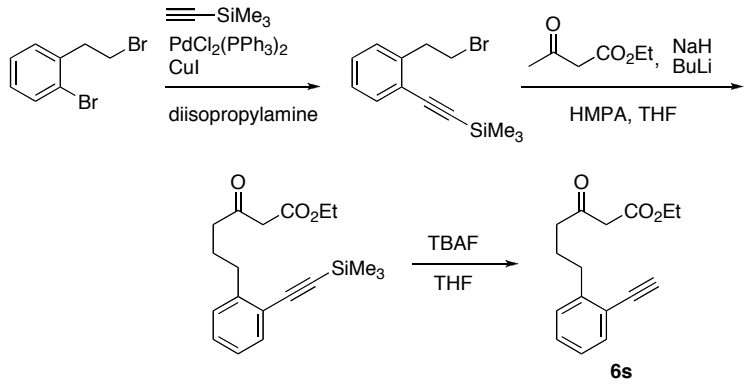


5s

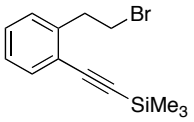
Colorless crystals; mp = 56.9–57.9 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23–1.33 (brs, 16H), 1.33–1.43 (m, 2H), 1.48–1.56 (m, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 2.18 (dt, *J* = 2.7,

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)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 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**.

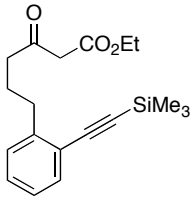


{[2-(2-Bromoethyl)phenyl]ethynyl}trimethylsilane



A mixture of 2-bromophenethyl bromide (12.5 g, 47 mmol), trimethylsilyl acetylene (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.

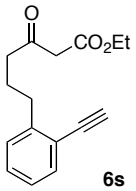
Ethyl 3-oxo-6-(2-trimethylsilylethynylphenyl)hexanoate



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 NH_4Cl and extracted with Et_2O (100 mL, 3 times). Combined organic layer was washed with water (50 mL) and brine (50 mL) successively and dried over Na_2SO_4. After filtration, the filtrate was concentrated in vacuo to afford a crude product. Flash column chromatography (silica gel, hexane/Et_2O = 85/15) of the crude product gave the title compound (1.20 g, 3.6 mmol, 9%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.28 (s, 9H), 1.26 (t, *J* = 6.9 Hz, 3H), 1.97 (m, 2H), 2.55 (t, *J* = 7.4 Hz, 2H), 2.80 (t, *J* = 6.3 Hz), 3.41 (s, 2H), 4.18 (q, *J* = 6.9 Hz, 2H), 7.12–7.17 (m, 2H), 7.24 (td, *J* = 7.4, 1.2 Hz, 1H), 7.42 (d, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.00, 14.1, 24.1, 28.5, 42.3, 49.3, 51.3, 98.1, 103.8, 122.6, 126.0, 128.7, 128.9, 132.6, 143.9, 167.2, 202.5; FTIR (KBr) (cm^{-1}) 2958, 2155, 1745, 1717, 1651, 1482, 1249, 1032, 867, 843, 759; Anal. Calcd for $C_{19}H_{26}O_3Si$: C, 69.05; H, 7.93. Found C, 68.89; H, 7.96.

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



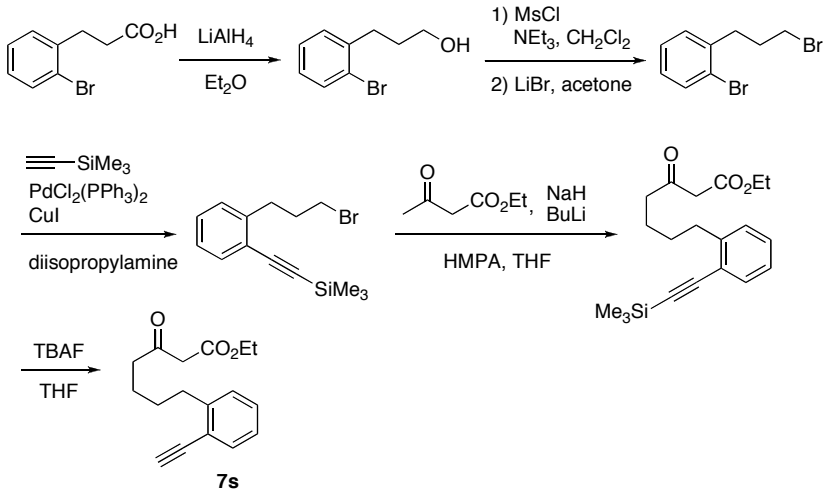
6s

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/Et_2O = 85/15) of the crude product gave the titled compound (0.50 g, 1.9 mmol, 54%).

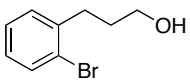
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, *J* = 7.2 Hz, 3H), 1,97 (m, 2H), 2.57 (t, *J* = 7.6 Hz, 2H), 2.82 (t, *J* = 7.6 Hz, 2H), 3.25 (s, 1H), 3.43 (s, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 7.14–7.19 (m, 2H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 24.1, 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 $C_{16}H_{19}O_3$: C, 74.39; H, 7.02. Found C, 74.18; H, 6.97.

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



7s

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

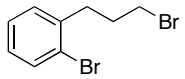


To a suspension of $LiAlH_4$ (6.2 g, 0.16 mol) in Et_2O (ca. 100 mL) was added a solution of 3-(2-bromophenyl)propionic acid (25 g, 0.11 mol) in THF (ca. 200 mL) dropwise via dropping funnel over 45 min. Then the reaction mixture was warmed to 75 °C and refluxed for 1 h. After cooling the solution to 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 Et_2O. Combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatographic separation of the crude mixture was carried out by silica gel (CH_2Cl_2 only to CH_2Cl_2/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.

^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.4, 32.7, 62.3, 124.4, 127.5, 127.6, 130.4, 132.8, 141.8.

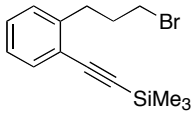
1-Bromo-3-(2-bromophenyl)propane (CAS: 1075-28-1)



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 CH_2Cl_2 was added MsCl (8.3 mL, 0.11 mol) and Et_3N (15 mL, 0.11 mol) at 0 °C and the reaction mixture was stirred for 1 h. To the reaction mixture was added H_2O and the crude compound was extracted three times with CH_2Cl_2 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 CH_2Cl_2, and the aqueous layer was extracted three times with CH_2Cl_2. 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.

^{1}H NMR (500 MHz, $CDCl_3$) 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).

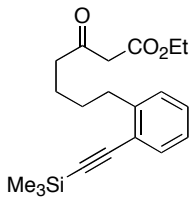
1-Bromo-3-[2-(trimethylsilylethynyl)phenyl]propane



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); ^{1}H NMR (500 MHz, $CDCl_3$) δ 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ –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

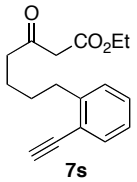


To a solution of NaH (1.4 g, 37 mmol, 63% in oil) in THF (ca. 40 mL) was added ethyl 3-oxo-butanoate dropwise via dropping funnel at 0 °C. During the addition, gas evolution was observed. After the reaction mixture was stirred for 20 min at this temperature, *n*-BuLi (24 mL of 1.55 M in hexane, 37 mmol) 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 NH_4Cl. The crude product was extracted three times with CH_2Cl_2 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.

R_f = 0.21 (hexane/AcOEt = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) 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), 7.42 (dd, *J* = 1.4, 7.6 Hz, 1H), (enol form: 4.97 (s, 1H), 12.10 (s, 1H)); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_3$: C, 69.72; H, 8.19. Found: C, 69.69; H, 8.27.

Ethyl 3-oxo-7-(2-ethynylphenyl)heptanoate (7s)

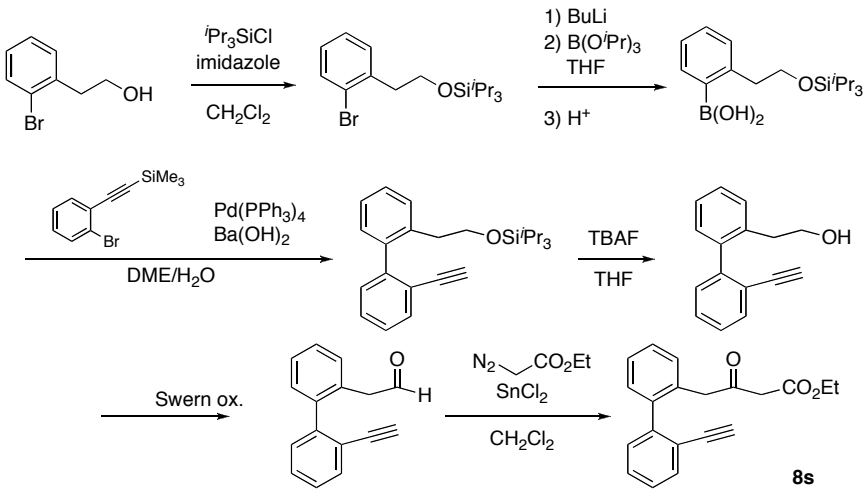


7s

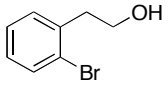
To a solution of ethyl 3-oxo-7-[2-(trimethylsilylethynyl)phenyl]heptanoate (7.6 g, 22 mmol) in THF was added TBAF (23 mL of 1.0 M in THF, 23 mmol) and stirred for 1 h at RT. Evaporation of THF and successive silica gel column chromatography (hexane/AcOEt = 5 to AcOEt only) gave the title compound (5.9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

R_f = 0.19 (hexane/AcOEt = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) 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)); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.14; H, 7.49.

***Scheme* S4**. Preparation of substrate **8s**



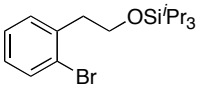
2-(2-Bromophenyl)ethane-1-ol (CAS: 1074-16-4)



To a suspension of $LiAlH_4$ (17.6 g, 464 mmol) in Et_2O (ca. 750 mL) was added a solution of 3-(2-bromophenyl)acetic acid (100 g, 464 mmol) in Et_2O (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 H_2O slowly. Then 18 mL of 15% aqueous NaOH and 54 mL of H_2O 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.

^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.3, 62.0, 124.7, 127.4, 128.2, 131.2, 132.9, 137.8.

2-(2-Bromophenyl)-1-triisopropylsilyloxyethane

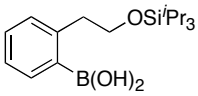


To a solution of the crude mixture of 2-(2-bromophenyl)ethan-1-ol (95.3 g, assumed as 464 mmol) in CH_2Cl_2 (ca. 500 mL) was added imidazole (34.8 g, 472

mmol) and chlorotriisopropylsilane (100 mL, 472 mmol) and stirred at RT for 1.5 h. To the reaction mixture was added H_2O and the aqueous layer was extracted three times with CH_2Cl_2. 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.

^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.0, 18.0, 39.7, 62.7, 124.6, 127.1, 127.9, 131.7, 132.6, 138.5.

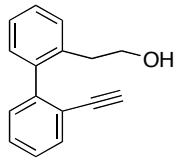
2-(2-Triisopropylsilyloxyethyl)phenylboronic acid



To a solution of the crude mixture of 2-(2-bromophenyl)-1-triisopropylsilyloxyethane (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 Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by recrystallization (hexane / Et_2O) to obtain 77.4 g (240 mmol, 52% yield) of the title compound as colorless crystals.

Mp = 76–77 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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.

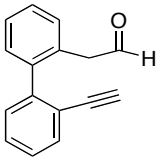
2-[(2'-Ethynylpheneyl)phenyl]ethanol



To a solution of 2-(2-triisopropylsilyloxyethyl)phenylboronic acid (40.0 g, 124 mmol), $Pd(PPh_3)_4$ (6.52 g, 5.64 mmol), and $Ba(OH)_2 \cdot 8H_2O$ (89.0 g, 282 mmol) in DME 200 mL and H_2O 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 Et_2O. Combined organic layer was washed brine, dried over Na_2SO_4, 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 NH_4Cl. The aqueous layer was extracted three times Et_2O. Combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The title compound was purified by silica gel column chromatography (hexane/AcOEt = 2/1 to 1 and CH_2Cl_2/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.

R_f = 0.28 (hexane/AcOEt = 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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

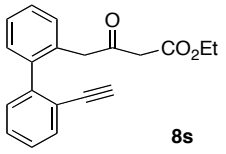


To a solution of oxalyl chloride (6.98 mL, 82.4 mmol) in CH_2Cl_2 (200 mL) was added DMSO (11.7 mL, 165 mmol), which was dissolved in CH_2Cl_2 (40 mL), at –78 °C over 15 min. Then, 2-[(2'-ethynylpheneyl)phenyl]ethanol (16.7 g, 75.0 mmol)

in 30 mL of CH_2Cl_2 was added dropwise over 20 min. The reaction mixture was stirred for 10 min at –78 °C, and Et_3N (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 NH_4Cl, and the aqueous layer was extracted three times with CH_2Cl_2. Combined organic layer was washed with saturated aqueous $NaHCO_3$, 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/Et_2O = 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.

R_f = 0.36 (hexane/Et_2O = 3/1); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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)



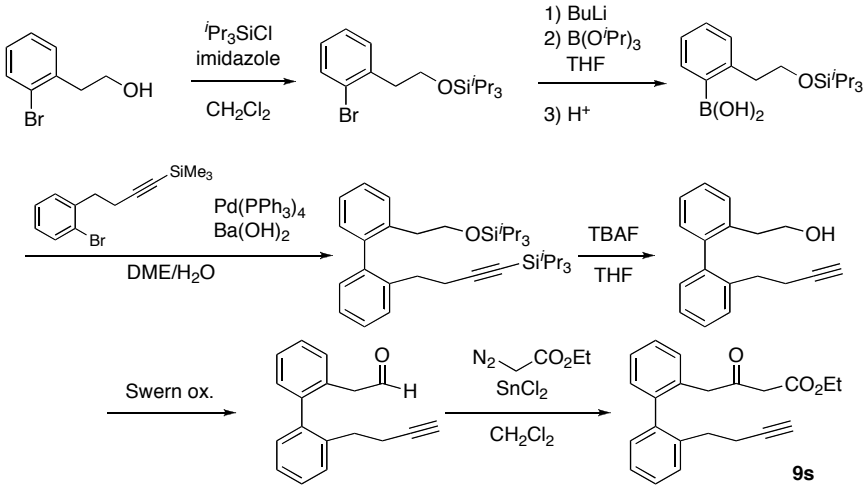
8s

To a suspension of $SnCl_2$ (398 mg, 2.10 mmol) and ethyl diazoacetate (2.86 mL, 23.1 mmol) in CH_2Cl_2 (40 mL) was added 2-[(2'-ethynylphenyl)phenyl]acetaldehyde (4.63 g, 21.0 mmol) in 30 mL of CH_2Cl_2, 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 CH_2Cl_2. 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/CH_2Cl_2 = 5/1 to CH_2Cl_2 only) to obtain 4.37g (14.3 mmol, 68% yield) of the title compound as a colorless oil (keto/enol = 97/3).

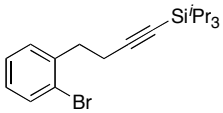
R_f = 0.29 (hexane/AcOEt = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, *J* = 6.9 Hz, 3H), 2.93 (s, 1H), 3.21 (d, *J* = 16.1 Hz, 1H), 3.26 (d, *J* = 15.3 Hz, 1H), 3.72 (d, *J* = 16.9 Hz, 1H), 3.76 (d, *J* = 16.8 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 7.19 (dd, *J* = 1.6, 7.7 Hz, 1H),

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, 2984, 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

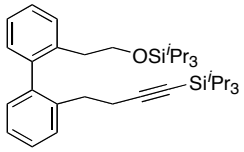


To a solution of 1-triisopropylsilylprop-1-yne (20.0 g, 84.5 mmol) in THF was added BuLi (53.5 mL of 1.58 M in hexane, 84.5 mmol) at –78 °C dropwise over 20 min and stirred at this temperature for 2.5 h. Then, 2-bromobenzyl bromide (20.3 g, 81.3 mmol) in 25 mL of THF was added to the solution over 30 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, $CDCl_3$) δ 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ 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.

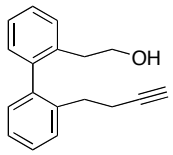
4-[2'-(2-Triisopropylsillyloxyethylphenyl)phenyl]-1-triisopropylsilylbut-1-yne



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 $Ba(OH)_2$•$8H_2O$ (56.1 g, 177.8 mmol) in DME 150 mL and H_2O 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_2O = 20 and hexane/AcOEt) to give 30.3 g of the title compound (53.9 mmol, 69%).

R_f = 0.25 (hexane/Et_2O = 50/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (brs, 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ 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.

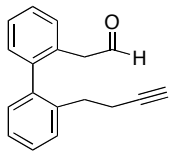
4-[2'-(2-Hydroxyethylphenyl)phenyl]but-1-yne



To a solution of 4-[2'-(2-triisopropylsillyloxyethyl)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 NH_4Cl. The aqueous layer was extracted three times with Et_2O. Combined organic layer was washed brine, dried over $MgSO_4$, 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.

R_f = 0.15 (hexane/AcOEt = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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

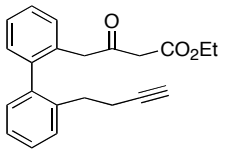


To a solution of oxalyl chloride (4.61 mL, 54.5 mmol) in CH_2Cl_2 (200 mL) was added DMSO (7.73 mL, 109 mmol) in CH_2Cl_2 (10 mL) at –78 °C over 15 min. Then, 4-[2'-(2-hydroxyethyl)phenyl]but-1-yne (12.4 g, 49.5 mmol) in 10 mL of CH_2Cl_2 was added to the reaction mixture dropwise over 20 min. The resulting mixture was stirred for 10 min at –78 °C, and to the mixture was Et_3N (34.3 mmol, 248 mmol) at this 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 NH_4Cl, and the aqueous layer was extracted three times with CH_2Cl_2. Combined organic layer was washed with saturated aqueous $NaHCO_3$, filtered through a paper filter, and concentrated under

reduced pressure. The residue was subjected to silica gel column chromatography (hexane/Et_2O = 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.

R_f = 0.60 (hexane/AcOEt = 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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-[2'-(but-3-ynyl)phenyl]phenyl}-3-oxobutanoate (9s)

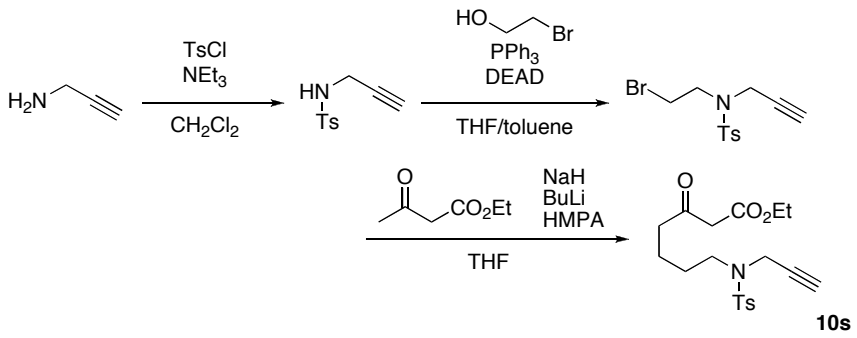


To a suspension of $SnCl_2$ (623 mg, 3.29 mmol) and ethyl diazoacetate (containing ~15% of CH_2Cl_2) (4.48 mL, 36.2 mmol) in CH_2Cl_2 (60 mL) was added 4-[2'-(formylmethylphenyl)phenyl]but-1-yne (8.16 g, 32.9 mmol) in 20 mL of CH_2Cl_2, and the resulting mixture was stirred for 5 h at RT. To the reaction mixture was added brine, and the aqueous layer was extracted three times with CH_2Cl_2. 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/CH_2Cl_2) to obtain 3.72g (11.1 mmol, 34% yield) of the title compound as a pale yellow oil (keto/enol = 89/11).

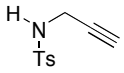
R_f = 0.28 (hexane/AcOEt = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.3 Hz, 3H), 1.90 (t, *J* = 2.7 Hz, 1H), 2.27 (dt, *J* = 3.1, 7.7 Hz, 2H), 2.53 (ddd, *J* = 7.3, 7.3, 14.5 Hz, 1H), 2.61 (ddd, *J* = 7.3, 7.3, 14.5 Hz, 1H), 3.16 (s, 2H), 3.55 (d, *J*= 16.8 Hz, 1H), 3.65 (d, *J* = 16.1 Hz, 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)); ^{13}C NMR (125 MHz, $CDCl_3$) 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**



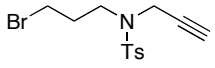
4-Methyl-*N*-(prop-2-ynyl)benzenesulfonamide (CAS: 55022-46-3)



To a solution of propargylamine (4.7 g, 85 mmol) in CH_2Cl_2 was added 4-methyl-benzenesulfonyl chloride (20 g, 0.10 mol) and Et_3N (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_2O. Combined organic layer was washed brine, dried over Na_2SO_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, $CDCl_3$) δ 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, $CDCl_3$) δ 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**

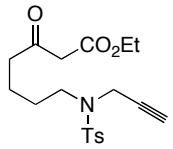


To a solution of 4-methyl-*N*-(prop-2-ynyl)benzenesulfonamide (8.4 g, 40 mmol) and triphenylphosphine (14 g, 52 mmol) in THF (ca. 80 mL) was added

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 (CH_2Cl_2/hexane = 2/1 to CH_2Cl_2 only) to obtain the title compound in 79% yield (10 g, 30 mmol) as a colorless oil.

R_f = 0.53 (hexane/CH_2Cl_2 = 1/2); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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 : $C_{13}H_{16}BrNO_2S$: 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)



10s

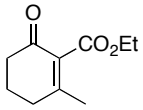
The title compound was prepared by essentially the same method with that of ethyl 3-oxo-7-[2-(trimethylsilylethynyl)phenyl]heptanoate. The crude mixture was purified by silica gel column chromatography (hexane/AcOEt = 2 to 1 and CH_2Cl_2 only to CH_2Cl_2/MeOH = 50/1) to give the title compound in 12% yield (0.56 g, 1.5 mmol) (keto/enol = 94/6) as a pale yellow oil.

R_f = 0.30 (hexane/AcOEt = 2/1); ^{1}H NMR (500 MHz, $CDCl_3$) 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)); ^{13}C NMR (125 MHz, $CDCl_3$) 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 : $C_{19}H_{25}NO_5S$: 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)

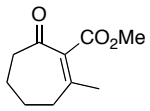
To a dried reaction vessel was introduced solution of $In(NTf_2)_3$ in MeCN (220 μL, 0.05 M, 11 μmol). The solvent was removed under vacuum (0.5 Torr) at 60 °C for 1 h. Toluene (11 mL) and substrate (198 mg, 1.1 mmol) were added into the vessel, and the mixture was stirred at 100 °C for 10 h. After cooled to RT, the resulting solution was filtered through a pad of silica gel with an elution of Et_2O. The filtrate was concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; hexane Et_2O/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.

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

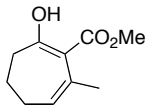
The reaction was carried out according to the standard procedure on the indium-catalyzed cyclization on a 0.3-mmol scale (1 mol% catalyst, 0.1 M in toluene, 100 °C, 2 h). The crude product was subjected to flash column chromatography (silica gel; hexane 100% to Et_2O/hexane = 30/70) to obtain the products **2pb** and **2pc** in 37% and 61% yields, respectively.



2pb

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, $CDCl_3$) δ 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.

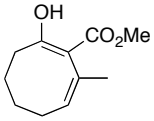


2pc

Pale yellow oil: R_f = 0.72 (ethyl acetate/ hexane = 20/80); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90 (s, 3H), 1.92–1.97 (m, 2H), 2.08–2.12 (m, 2H), 2.27 (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, $CDCl_3$) δ 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.

(1*Z*, 8*Z*)-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%).



3pc

Compound **3pc**: white solid; mp 49–50 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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).

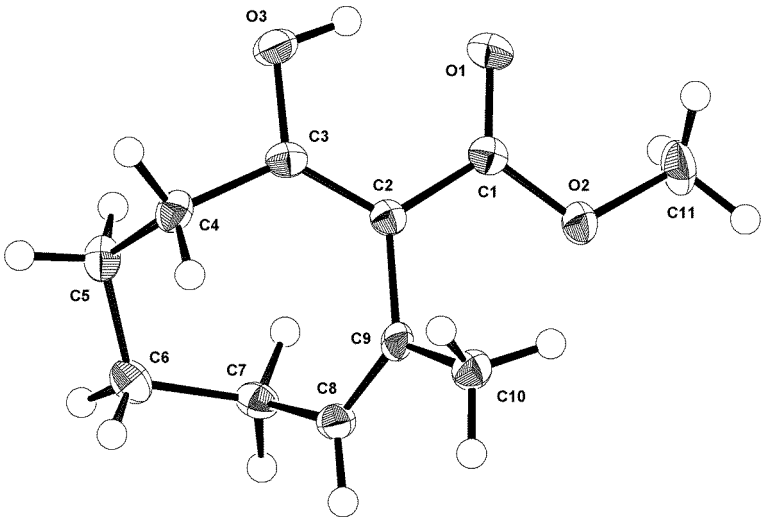
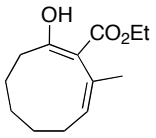


Figure S1. ORTEP drawing of **3pc** (50% thermal ellipsoids).

(1*Z*, 8*Z*)-Ethyl 2-hydroxy-9-methylcyclonona-1,8-diene-1-carboxylate (4pc)

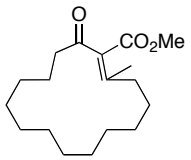
The reaction was carried out according to the procedure for the synthesis of **1pb** on 0.3-mmol scale in toluene (0.04 M) at 150 °C for 8 h using 1 mol% of the catalyst. Compound **4pc** were purified by silica gel column chromatography (eluent: EtOAc/hexane = 5/95).



4pc

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), 1.83 (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, 1607, 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)



5pb

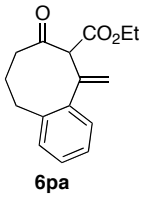
The reaction was carried out according to the procedure for the synthesis of **1pc** on 0.3-mmol scale in toluene (0.01 M) at 150 °C for 18 h using 2 mol% of the catalyst. Compound **5pb** were purified by silica gel column chromatography (eluent: Et_2O/hexane = 10/90 to Et_2O/hexane = 30/70).

Compound **5pb**: 27%; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{18}H_{30}O_3$; 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)

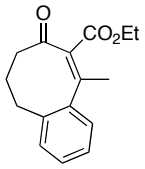
The reaction was carried out according to the procedure for the synthesis of **1pb** on 0.2-mmol scale in toluene (0.1 M) at 100 °C for 2 h using 1 mol% of the catalyst. Compound **6pa** and **6pb** were separated by silica gel column chromatography (eluent: Et_2O/hexane = 10/90 to Et_2O/hexane = 30/70).



6pa

Compound **6pa**: 17%; R_f = 0.36 (AcOEt/hexane = 20/80); yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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.



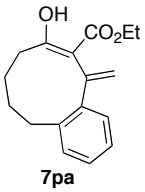
6pb

Compound **6pb**: 58%; R_f = 0.21 (AcOEt/hexane = 20/80); yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 5*H*-11-methyl-9-oxo-6,7,8,9-tetrahydrobenzo[9]annulene-10-carboxylate (7pa) and

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

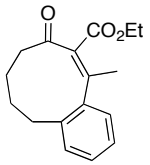
The reaction was carried out according to the procedure for the synthesis of **1pb** on 0.3-mmol scale in toluene (0.05 M) at 120 °C for 12 h using 1 mol% of the catalyst. Compound **7pa** and **7pb** were separated by silica gel column chromatography (eluent: CH_2Cl_2/hexane = 60/40).



7pa

Compound **7pa**: 11%; R_f = 0.78 (AcOEt/hexane = 20/80); yellow oil; keto/enol = 11/89; ^{1}H NMR (500 MHz, $CDCl_3$) δ 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), 2.57–2.62 (m. 4H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.58 (s, 1H), 5.26 (s, 1H), 5.87 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found C, 74.81; H, 7.53.

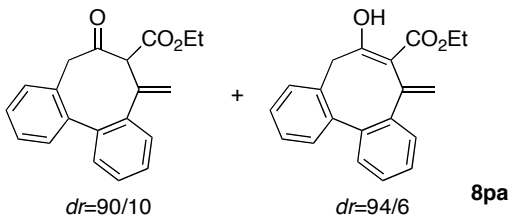


7pb

Compound **7pb**: 60%; R_f = 0.44 (AcOEt/hexane = 20/80); yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.6, 24.3, 30.1, 30.5, 41.8, 60.8, 126.2, 127.1, 128.2, 129.2, 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 $C_{17}H_{20}O_3$: 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/Et_2O = 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.

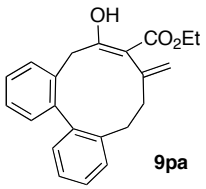


dr=90/10 *dr*=94/6 **8pa**

Compound **8pa**: R_f = 0.6 (hexane/Et_2O = 2/1); colorless viscous oil; ^1H 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)); ^{13}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 showin in below (Figure S2). .



9pa

Colorless crystals; mp = 113–115 °C; R_f = 0.69 (hexane/Et_2O = 3/1, broad); ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{22}H_{21}O_3$ $[M-H]^-$ 333.1491. Found: 333.1502; Anal. Calcd for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63. Found: C, 79.15; H, 6.88.

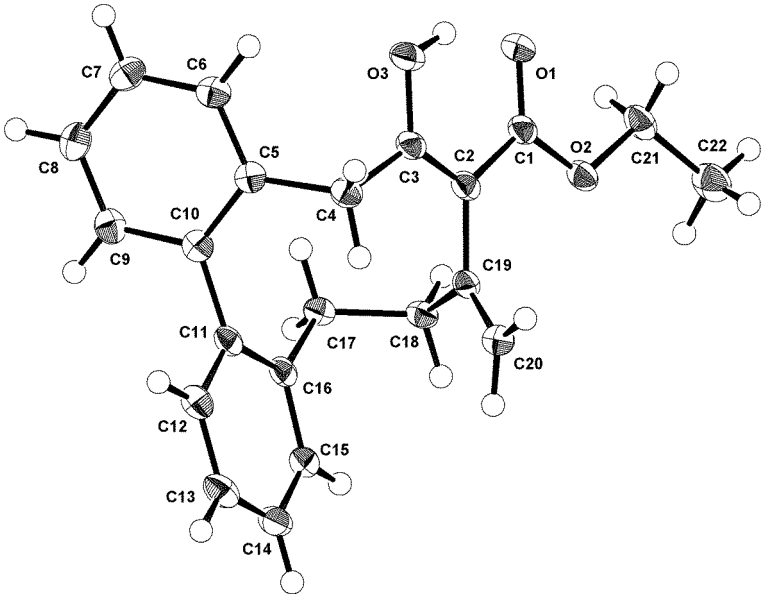
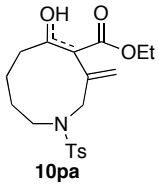


Figure S2. ORTEP drawing of **9pa** (50% thermal ellipsoids).

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-1*H*-azonine-4-carboxylate (10pb)

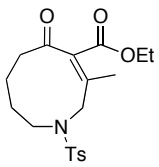
The reaction was carried out according to the procedure for the synthesis of

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/Et_2O = 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.



10pa

Compound **10pa**: 52%; R_f = 0.31 (hexane/Et_2O = 1/1); viscous oil (solidify when rubbed with spoon); ^1H NMR (500 MHz, toluene-d_8, 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 (enol)), 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)); ^{13}C NMR (125 MHz, toluene-d_8, 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-d_8); FTIR (KBr) (cm^{-1}) 2994, 2963, 2940, 2898, 2869, 2361, 2344, 1646, 1600, 1376, 1334, 1299, 1242, 1161, 1094, 666; Anal. Calcd for $C_{18}H_{23}NO_4S$: C, 60.14; H, 6.64; N, 3.69. Found: C, 60.14; H, 6.77; N, 3.53.



10pb

Compound **10pb**: 9%; R_f = 0.1 (hexane/Et_2O = 1/1); viscous oil; ^1H NMR (500 MHz, $CDCl_3$) 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, $CDCl_3$) δ 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 $C_{19}H_{24}NO_5S^-$ ($[M-H]^-$) 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 α-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: δ 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: δ 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, $CDCl_3$) δ 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_2Cl_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, $CDCl_3$) δ 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.); ^{13}C NMR (125 MHz, $CDCl_3$) δ 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.

(4) (a) Q. Branca, A. Fischli, *Helv. Chim. Acta* **1977**, *60*, 925–944. (b) M. Yamaguchi, T. Shiraishi, M. Hirama, *J. Org. Chem.* **1996**, *61*, 3520–3530.