**An Efficient Synthesis of 2,5-Dihydrofuran-fused Bicyclic Skeletons
via the Pd(II)-Catalyzed Tandem-Cyclization Reaction of
1, ω -Bisallenols**

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Supporting Information

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Synthesis of starting materials 1

The starting bis(2,3-allenol)s were prepared via the reaction of bis(propargylic bromide)s¹ and aldehydes in the presence of NaI and SnCl₂ in DMF according to the published procedure in the literature.² The optically active allenol-allenyl acetates (*S*)-**1n** and (*S*)-**1o** were prepared as follows.

1. Synthesis of 3-(1'-acetoxypropyl)-8-(1'-(*S*)-hydroxypropyl)-1,2,8,9-decatetraene (*S*)-**1n**

(1) The reaction of 1,10-dibromo-2,8-decadiyne **3n** with *n*-pentanal in the presence of NaI and SnCl₂ in DMF

To a solution of 1,10-dibromo-2,8-decadiyne **3n** (1.8063 g, 6.2 mmol) in 30 mL of DMF were added sequentially NaI (1.0290 g, 6.9 mmol) with five portions over 15 min and then SnCl₂ (1.3148 g, 6.9 mmol) with five portions over 15 min at rt. After the resulting slurry was stirred at rt for 2 h, a solution of *n*-pentanal (1.1082 g, 12.9 mmol) in 15 mL of DMF was then added dropwise at 0 °C. The reaction mixture was then stirred at 0 °C for additional 24 h. The reaction was quenched with 10 mL of water and extracted with diethyl ether (40 mL x 3). The combined organic layer was washed with brine and dried over *anhydrous* Na₂SO₄. Evaporation and column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, then 4:1) afforded **4n** (0.7442 g, X = Cl/Br/I = 31%/21%/48%, 39%) and **1i** (0.4776 g, 25%). **4n**: Liquid;

^1H NMR (300 MHz, CDCl_3) δ 4.92-4.81 (m, 2H), [4.14 (t, $J = 2.4$ Hz, (Cl, 0.62H)); 3.92 (t, $J = 2.4$ Hz, (Br, 0.41H)); 3.70 (t, $J = 2.4$ Hz, (I, 0.97H)), 2H], 4.08-3.96 (m, 1H), 2.30-2.15 (m, 2H), 2.09-1.90 (m, 2H), 1.70-1.45 (m, 7H), 1.44-1.20 (m, 4H), 0.90 (t, $J = 6.9$ Hz, 3H). This mixture of halides was submitted to the next step without further characterization. **1i**: solid, m.p. 55-56 $^\circ\text{C}$ (ethyl acetate/petroleum ether); ^1H NMR (300 MHz, CDCl_3) δ 4.88-4.78 (m, 4H), 4.08-3.95 (m, 2H), 2.10-1.88 (m, 4H), 1.78-1.44 (m, 10H), 1.43-1.20 (m, 8H), 0.90 (t, $J = 7.2$ Hz, 6H); IR (neat, cm^{-1}): 3329, 2955, 2932, 2859, 1955, 1459, 1030, 1008; MS (m/z): 245 ($\text{M}^+ - \text{H}_2\text{O} - \text{C}_3\text{H}_7$, 2.46), 231 ($\text{M}^+ - \text{H}_2\text{O} - \text{C}_4\text{H}_9$, 7.38), 41 (C_3H_5^+ , 100); Elemental analysis calcd for $\text{C}_{20}\text{H}_{34}\text{O}_2$: C, 78.38; H, 11.18; found: C, 78.39; H, 11.16.

(2) Synthesis of 3-(7'-iodo-5'-heptynyl)octa-1,2-dien-4-ol (**5n**)

To a solution of **4n** (0.7100 g, $\text{X} = \text{Cl}/\text{Br}/\text{I} = 31\%/21\%/48\%$, 2.3 mmol) in 23 mL of acetone was added NaI (1.0691 g, 7.1 mmol) at rt. After the reaction was refluxed for 5.5 hours, it was cooled to room temperature and quenched with 10 mL of water. The mixture was extracted with diethyl ether (30 mL x 3) and washed with brine. The organic layer was dried over *anhydrous* Na_2SO_4 . Evaporation and column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **5n** (0.6000 g, 75%): Liquid; ^1H NMR (300 MHz, CDCl_3) δ 4.92-4.82 (m, 2H), 4.08-3.96 (m, 1H), 3.70 (t, $J = 2.4$ Hz, 2H), 2.30-2.10 (m, 2H), 2.09-1.88 (m, 2H), 1.70-1.45 (m,

7H), 1.44-1.22 (m, 4H), 0.90 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.3, 107.2, 86.5, 78.8, 77.1, 72.0, 35.2, 28.0, 27.7, 27.2, 26.7, 22.6, 18.9, 14.1, -16.7; IR (neat, cm^{-1}): 3395, 2932, 2860, 2227, 1953, 1458, 1172, 1143, 1030; MS (m/z): 218 ($\text{M}^+ - \text{HI}$, 28.79), 161 ($\text{M}^+ - \text{HI} - \text{C}_4\text{H}_9$, 87.49), 91 (100); HRMS calcd for $\text{C}_{15}\text{H}_{23}\text{OI}$ (M^+): 346.0794; found: 346.0795.

(3) Synthesis of 3-(7'-iodo-5'-heptynyl)octa-1,2-dien-4-yl acetate (**6n**)

To a solution of **5n** (230.0 mg, 0.66 mmol) in 5 mL of diethyl ether were added sequentially a solution of Ac_2O (138.1 mg, 1.35 mmol) in 1 mL of diethyl ether and DMAP (9.6 mg) at rt. After the reaction was complete as monitored by TLC, it was quenched with 5 mL of water. The mixture was extracted with diethyl ether (3 x 20 mL) and washed with brine. The organic layer was dried over *anhydrous* Na_2SO_4 . Evaporation and column chromatography on silica gel (petroleum ether/diethyl ether = 25:1) afforded **6n** (209.7 mg, 81%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.18 (t, $J = 6.9$ Hz, 1H), 4.88-4.75 (m, 2H), 3.68 (t, $J = 2.4$ Hz, 2H), 2.24-2.12 (m, 2H), 2.04 (s, 3H), 2.00-1.86 (m, 2H), 1.64 (q, $J = 7.2$ Hz, 2H), 1.55-1.44 (m, 4H), 1.38-1.16 (m, 4H), 0.87 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 205.9, 170.5, 103.2, 86.4, 78.1, 77.1, 74.0, 32.5, 27.8, 27.6, 27.4, 26.5, 22.4, 21.2, 18.9, 14.0, -16.8; IR (neat, cm^{-1}): 2934, 2861, 2228, 1957, 1737, 1458, 1371, 1235, 1172, 1145, 1018; MS (m/z): 260 ($\text{M}^+ - \text{HI}$, 2.68), 43 (C_3H_7^+ , 100); HRMS calcd for $\text{C}_{17}\text{H}_{25}\text{O}_2\text{I}$ (M^+): 388.0899;

found: 388.0896.

(4) Synthesis of 3-(1'-acetoxypropyl)-8-(1'-hydroxypropyl)-1,2,8,9-decatetraene

(1n)

To a solution of **6n** (535.0 mg, 1.38 mmol) in 10 mL of DMF was added SnCl_2 (320.1 mg, 1.69 mmol) at rt. After the resulting slurry was stirred at rt for 2 h, a solution of propionaldehyde (163.8 mg, 2.82 mmol) in 10 mL of DMF was then added dropwise at 0°C . The reaction mixture was stirred at 0°C for additional 22 hours. The reaction was then quenched with 10 mL of water and extracted with diethyl ether (30 mL x 3). The combined organic layer was washed with brine and dried over *anhydrous* Na_2SO_4 . Evaporation and column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **1n** (332.9 mg, 75%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.19 (t, $J = 6.9$ Hz, 1H), 4.87-4.76 (m, 4H), 4.00-3.90 (m, 1H), 2.04 (s, 3H), 2.03-1.86 (m, 4H), 1.74-1.52 (m, 5H), 1.51-1.42 (m, 4H), 1.38-1.20 (m, 4H), 0.91 (t, $J = 7.2$ Hz, 3H), 0.88 (t, $J = 6.6$ Hz, 3H); IR (neat, cm^{-1}): 3455, 2961, 2934, 2861, 1955, 1738, 1458, 1372, 1235, 1018; MS (m/z): 320 (M^+ , 1.04), 291 ($\text{M}^+ - \text{C}_2\text{H}_5$, 2.66), 260 ($\text{M}^+ - \text{HOAc}$, 15.87), 231 ($\text{M}^+ - \text{HOAc} - \text{C}_2\text{H}_5$, 35.73), 203 ($\text{M}^+ - \text{HOAc} - \text{C}_2\text{H}_5\text{CO}$, 48.50), 43 (C_3H_7^+ , 100); Elemental analysis calcd for $\text{C}_{20}\text{H}_{32}\text{O}_3$: C, 74.96; H, 10.06; found: C, 74.93; H, 10.06.

(5) Kinetic resolution of racemic **1n** for the synthesis of 3-(1'-acetoxypropyl)-

8-(1'-(*S*)-hydroxypropyl)-1,2,8,9-decatetraene (*S*)-1n³

Novozym-435 (248.1 mg) was added to a racemic mixture of **1n** (222.5 mg) and vinyl acetate (10 mL). After stirring at 60 °C for 69 h as monitored by TLC, the reaction mixture was worked up by filtration. After evaporation of the solvent, purification of the residue by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded (*R*)-**7n** (105.1 mg, 42%) and (*S*)-**1n** (91.6 mg, 41%). (*R*)-**7n**: liquid; $[\alpha]_D^{20} = +65.9^\circ$ ($c = 1.00$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 5.16 (t, $J = 6.6$ Hz, 1H), 5.10 (t, $J = 6.6$ Hz, 1H), 4.84-4.70 (m, 4H), 2.02 (s, 3H), 2.01 (s, 3H), 1.96-1.80 (m, 4H), 1.72-1.54 (m, 4H), 1.50-1.35 (m, 4H), 1.34-1.16 (m, 4H), 0.85 (t, $J = 7.2$ Hz, 6H); IR (neat, cm^{-1}): 2935, 2861, 1957, 1738, 1459, 1371, 1235, 1018; MS (m/z): 362 (M^+ , 0.56), 302 ($\text{M}^+ - \text{HOAc}$, 2.77), 273 ($\text{M}^+ - \text{HOAc} - \text{C}_2\text{H}_5$, 7.75), 260 ($\text{M}^+ - \text{C}_3\text{H}_7\text{OAc}$, 28.29), 43 (C_3H_7^+ , 100); HRMS calcd for $\text{C}_{22}\text{H}_{34}\text{O}_4$ (M^+): 362.2457; found: 362.2459. (*S*)-**1n**: Liquid; 99% *ee* (determined by the conversion to its 4-nitrobenzoyl ester (*S*)-**8n**); $[\alpha]_D^{20} = -1.2^\circ$ ($c = 1.20$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 5.19 (t, $J = 6.6$ Hz, 1H), 4.90-4.75 (m, 4H), 3.95 (t, $J = 6.0$ Hz, 1H), 2.04 (s, 3H), 2.03-1.88 (m, 4H), 1.75-1.40 (m, 9H), 1.39-1.18 (m, 4H), 0.91 (t, $J = 7.2$ Hz, 3H), 0.88 (t, $J = 6.6$ Hz, 3H); IR (neat, cm^{-1}): 3453, 2933, 2861, 1956, 1738, 1456, 1372, 1235, 1018; MS (m/z): 320 (M^+ , 1.91), 291 ($\text{M}^+ - \text{C}_2\text{H}_5$, 3.11), 273

($M^+ - C_2H_5 - H_2O$, 9.14), 260 ($M^+ - HOAc$, 42.58), 43 ($C_3H_7^+$, 100); HRMS calcd for $C_{20}H_{32}O_3$ (M^+): 320.2351; found: 320.2351.

Determination of the enantiopurity of (S)-1n:

(1) Synthesis of racemic 3-(1'-acetoxypentyl)-8-(1'-4-nitrobenzoylpropyl)-1,2,8,9-decatetraene (8n)

To a solution of **1n** (19.6 mg, 0.06 mmol) in 0.5 mL of CH_2Cl_2 were added 4-nitrobenzoyl chloride (46.0 mg, 0.25 mmol), DMAP (4.0 mg), and a solution of Et_3N (25.2 mg, 0.25 mmol) in 0.5 mL of CH_2Cl_2 at rt. After the reaction was complete as monitored by TLC, it was quenched with 5 mL of water. The mixture was extracted with diethyl ether (20 mL x 3) and washed with brine. The organic layer was dried over *anhydrous* Na_2SO_4 . Evaporation and column chromatography on silica gel (petroleum ether/diethyl ether = 10:1) afforded **8n** (23.3 mg, 81%): Liquid; 1H NMR (300 MHz, $CDCl_3$) δ 8.32-8.25 (m, 2H), 8.24-8.17 (m, 2H), 5.41 (t, J = 6.6 Hz, 1H), 5.17 (t, J = 6.9 Hz, 1H), 4.92-4.72 (m, 4H), 2.03 (s, 3H), 2.00-1.78 (m, 6H), 1.64 (q, J = 7.2 Hz, 2H), 1.55-1.40 (m, 4H), 1.38-1.16 (m, 4H), 0.96 (t, J = 7.2 Hz, 3H), 0.87 (t, J = 6.9 Hz, 3H); IR (neat, cm^{-1}): 2927, 2861, 1957, 1731, 1608, 1531, 1459, 1375, 1345, 1269, 1235, 1101, 1016; MS(ESI) (m/z): 492 [$M+Na^+$], 493 [$M+1+Na^+$], 508 [$M+K^+$]; HRMS calcd for $C_{27}H_{35}NO_6Na$ [$M+Na^+$]: 492.2357; found: 492.2371.

(2) Synthesis of 3-(1'-acetoxypentyl)-8-(1'-(S)-4''-nitrobenzoylpropyl)-1,2,8,9-decatetraene (S)-8n

Following the above procedure, the reaction of (S)-**1n** (19.0 mg, 0.06 mmol), 4-nitrobenzoyl chloride (46.7 mg, 0.25 mmol), DMAP (4.1 mg), and a solution of Et₃N (26.7 mg, 0.26 mmol) in 1 mL of CH₂Cl₂ afforded (S)-**8n** (24.8 mg, 88%): Liquid; 99% *ee* referred to the resolved chiral center, dr = 1:1 (HPLC condition: chiral AS-H column; rate, 0.4 mL/min, eluent: hexane/*i*-PrOH 99/1, λ = 254 nm); $[\alpha]_D^{20}$ = -12.8° (*c* = 0.84, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.32-8.26 (m, 2H), 8.24-8.18 (m, 2H), 5.41 (t, *J* = 6.6 Hz, 1H), 5.18 (t, *J* = 6.9 Hz, 1H), 4.94-4.72 (m, 4H), 2.04 (s, 3H), 2.00-1.80 (m, 6H), 1.70-1.56 (m, 2H), 1.55-1.40 (m, 4H), 1.36-1.17 (m, 4H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H); IR (neat, cm⁻¹): 2934, 2861, 1957, 1728, 1608, 1530, 1460, 1371, 1346, 1271, 1236, 1102, 1015; MS(ESI) (*m/z*): 492 [M+Na⁺], 493 [M+1+Na⁺], 508 [M+K⁺]; HRMS calcd for C₂₇H₃₅NO₆Na [M+Na⁺]: 492.2357; found: 492.2364.

2. Synthesis of 3-(1'-acetoxypentyl)-7-(1'-(S)-hydroxypropyl)-1,2,7,8-nonatetraene (S)-1o

(1) The reaction of 1,9-dibromo-2,7-nonadiyne **3o with *n*-pentanal in the presence of NaI and SnCl₂ in DMF**

Following the procedure for the preparation of **4n**, the reaction of 1,9-dibromo-2,7-nonadiyne **3o** (4.4608 g, 16.0 mmol), NaI (2.6670 g, 17.8 mmol), SnCl₂ (3.3457 g, 17.6 mmol), and *n*-pentanal (2.8012 g, 32.6 mmol) in 120 mL of DMF afforded **4o** (1.6422 g, X = Cl/Br/I = 25%/23%/52%, 34%) and **1p** (1.2258 g, 26%). **4o**: liquid; ¹H NMR (300 MHz, CDCl₃) δ 4.94-4.80 (m, 2H), [4.14 (t, *J* = 2.4 Hz, (Cl, 0.50H)); 3.92 (t, *J* = 2.4 Hz, (Br, 0.45H)); 3.70 (t, *J* = 2.4 Hz, (I, 1.05H)), 2H], 4.08-3.97 (m, 1H), 2.35-2.20 (m, 2H), 2.16-1.98 (m, 2H), 1.75-1.46 (m, 5H), 1.45-1.20 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H). **1p**: Liquid; ¹H NMR (300 MHz, CDCl₃) δ 4.88-4.78 (m, 4H), 4.01 (t, *J* = 5.7 Hz, 2H), 2.18-1.90 (m, 6H), 1.70-1.42 (m, 6H), 1.41-1.20 (m, 8H), 0.89 (t, *J* = 6.9 Hz, 6H); IR (neat, cm⁻¹): 3355, 2955, 2932, 2860, 1955, 1724, 1459, 1270, 1015; MS (*m/z*): 292 (M⁺, 5.65), 235 (M⁺-C₄H₉, 8.37), 209 (M⁺-C₄H₉-C₂H₂, 56.21), 194 (M⁺-C₄H₉-C₂H₂-CH₃, 100); HRMS calcd for C₁₉H₃₂O₂ (M⁺): 292.2402; found: 292.2403.

(2) Synthesis of 3-(6'-iodo-4'-hexynyl)octa-1,2-dien-4-ol (**5o**)

Following the procedure for the preparation of **5n**, the reaction of **4o** (1.6422 g, X = Cl/Br/I = 25%/23%/52%, 5.5 mmol) and NaI (2.5012 g, 16.7 mmol) in 55 mL of acetone afforded **5o** (1.7551 g, 96%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 4.90-4.82

(m, 2H), 4.07-3.96 (m, 1H), 3.69 (t, $J = 2.4$ Hz, 2H), 2.30-2.18 (m, 2H), 2.15-1.96 (m, 2H), 1.74-1.46 (m, 5H), 1.45-1.20 (m, 4H), 0.90 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.2, 106.7, 86.2, 78.9, 77.4, 72.1, 35.2, 27.6, 26.6, 26.3, 22.6, 18.6, 14.1, -16.8; IR (neat, cm^{-1}): 3385, 2931, 2859, 2227, 1954, 1455, 1172, 1143, 1027; MS (m/z): 332 (M^+ , 4.69), 114 (100); HRMS calcd for $\text{C}_{14}\text{H}_{21}\text{OI}$ (M^+): 332.0637; found: 332.0638.

(3) Synthesis of 3-(6'-iodo-4'-hexynyl)octa-1,2-dien-4-yl acetate (**6o**)

Following the procedure for the preparation of **6n**, the reaction of **5o** (1.6650 g, 5.0 mmol), Ac_2O (1.0387 g, 10.2 mmol), and DMAP (69.1 mg) in 55 mL of diethyl ether afforded **6o** (1.4909 g, 79%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.18 (t, $J = 6.6$ Hz, 1H), 4.90-4.75 (m, 2H), 3.68 (t, $J = 2.4$ Hz, 2H), 2.28-2.18 (m, 2H), 2.05 (s, 3H), 2.04-1.95 (m, 2H), 1.72-1.55 (m, 4H), 1.40-1.16 (m, 4H), 0.88 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 205.8, 170.5, 102.8, 86.1, 78.3, 77.3, 74.1, 32.5, 27.6, 26.8, 26.1, 22.4, 21.2, 18.5, 14.0, -16.9; IR (neat, cm^{-1}): 2954, 2861, 2228, 1956, 1738, 1431, 1371, 1234, 1173, 1144, 1017, 957, 852; MS (m/z): 314 ($\text{M}^+ - \text{HOAc}$, 1.25), 185 (M^+ , 100); HRMS calcd for $\text{C}_{16}\text{H}_{23}\text{O}_2\text{I}$ (M^+): 374.0743; found: 374.0757.

(4) Synthesis of 3-(1'-acetoxypentyl)-7-(1'-hydroxypropyl)-1,2,7,8-nonatetraene (**1o**).

Following the procedure for the preparation of **1n**, the reaction of **6o** (1.4320 g, 3.83 mmol), SnCl₂ (0.8982 g, 4.73 mmol), and propionaldehyde (0.5018 g, 8.65 mmol) in 50 mL of DMF afforded **1o** (0.9842 g, 84%): liquid; ¹H NMR (300 MHz, CDCl₃) δ [5.18 (t, *J* = 6.6 Hz, 0.5H); 5.17 (t, *J* = 6.6 Hz, 0.5H), 1H], 4.87-4.75 (m, 4H), 4.00-3.90 (m, 1H), 2.04 (s, 3H), 2.03-1.90 (m, 4H), 1.78-1.45 (m, 7H), 1.39-1.17 (m, 4H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.88 (t, *J* = 6.6 Hz, 3H); IR (neat, cm⁻¹): 3448, 2959, 2934, 2873, 1956, 1737, 1458, 1372, 1235, 1018; MS (*m/z*): 306 (*M*⁺, 0.54), 246 (*M*⁺-HOAc, 6.82), 235 (*M*⁺-C₄H₉-C₂H₂, 15.05), 217 (*M*⁺-HOAc-C₂H₅, 33.72), 189 (*M*⁺-HOAc-C₂H₅CO, 53.58), 43 (C₃H₇⁺, 100); Elemental analysis calcd for C₁₉H₃₀O₃: C, 74.47; H, 9.87; found: C, 74.55; H, 9.81.

(5) Kinetic resolution of racemic 1o for the synthesis of 3-(1'-acetoxypentyl)-7-(1'-(*S*)-hydroxypropyl)-1,2,7,8-nonatetraene (*S*)-1o³

Following the procedure for the preparation of (*S*)-**1n**, the reaction of **1o** (197.0 mg) and novozym-435 (220.1 mg)⁴ in vinyl acetate (10 mL) afforded (*R*)-**7o** (109.2 mg, 49%) and (*S*)-**1o** (81.1 mg, 41%). (*R*)-**7o**: Liquid; [α]_D²⁰ = +46.1° (*c* = 1.28, CHCl₃);

^1H NMR (300 MHz, CDCl_3) δ 5.14 (t, $J = 6.6$ Hz, 1H), 5.08 (t, $J = 6.6$ Hz, 1H), 4.84-4.70 (m, 4H), 2.01 (s, 3H), 2.00 (s, 3H), 1.98-1.85 (m, 4H), 1.70-1.46 (m, 6H), 1.35-1.14 (m, 4H), 0.84 (t, $J = 7.2$ Hz, 6H); IR (neat, cm^{-1}): 2936, 2862, 1957, 1739, 1456, 1372, 1236, 1018; MS (m/z): 348 (M^+ , 3.88), 288 ($\text{M}^+ - \text{HOAc}$, 2.60), 259 ($\text{M}^+ - \text{HOAc} - \text{C}_2\text{H}_5$, 9.38), 246 ($\text{M}^+ - \text{C}_3\text{H}_7\text{OAc}$, 28.77), 228 ($\text{M}^+ - 2\text{HOAc}$, 78.32), 43 (100); HRMS calcd for $\text{C}_{21}\text{H}_{32}\text{O}_4$ (M^+): 348.2301; found: 348.2297. (*S*)-**1o**: Liquid; 99% *ee* (determined by the conversion to its 4-nitrobenzoyl ester (*S*)-**8o**); $[\alpha]_{\text{D}}^{20} = -3.2^\circ$ ($c = 0.49$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 5.18 (t, $J = 6.0$ Hz, 1H), 4.90-4.76 (m, 4H), 3.96 (t, $J = 6.0$ Hz, 1H), 2.05 (s, 3H), 2.04-1.90 (m, 4H), 1.75-1.45 (m, 7H), 1.40-1.18 (m, 4H), 0.92 (t, $J = 7.5$ Hz, 3H), 0.89 (t, $J = 6.6$ Hz, 3H); IR (neat, cm^{-1}): 3458, 2959, 2934, 2873, 1955, 1738, 1456, 1372, 1235, 1101, 1018; MS (m/z): 306 (M^+ , 0.43), 246 ($\text{M}^+ - \text{HOAc}$, 4.36), 217 ($\text{M}^+ - \text{HOAc} - \text{C}_2\text{H}_5$, 17.38), 183 (M^+ , 100); HRMS calcd for $\text{C}_{19}\text{H}_{30}\text{O}_3$ (M^+): 306.2195; found: 306.2198.

Determination of the enantiopurity of (*S*)-**1o**:

(1) Synthesis of racemic 3-(1'-acetoxypentyl)-7-(1'-4''-nitrobenzoylpropyl)-1,2,7,8-nonatetraene (**8o**)

Following the procedure for the preparation of racemic **8n**, the reaction of **1o** (32.0 mg, 0.10 mmol), 4-nitrobenzoyl chloride (76.8 mg, 0.41 mmol), DMAP (4.5 mg), and

a solution of Et₃N (44.2 mg, 0.44 mmol) in 2 mL of CH₂Cl₂ afforded **8o** (38.7 mg, 81%): Liquid; ¹H NMR (300 MHz, CDCl₃) δ 8.32-8.26 (m, 2H), 8.24-8.17 (m, 2H), 5.41 (t, *J* = 6.6 Hz, 1H), 5.17 (t, *J* = 6.9 Hz, 1H), 4.94-4.70 (m, 4H), 2.03 (s, 3H), 2.10-1.92 (m, 4H), 1.91-1.78 (m, 2H), 1.70-1.52 (m, 4H), 1.36-1.18 (m, 4H), 0.96 (t, *J* = 7.5 Hz, 3H), 0.87 (t, *J* = 6.6 Hz, 3H); IR (neat, cm⁻¹): 2933, 2862, 1957, 1731, 1607, 1530, 1456, 1346, 1270, 1102, 1015; MS(ESI) (*m/z*): 478 [M+Na⁺], 479 [M+1+Na⁺], 494 [M+K⁺]; HRMS calcd for C₂₆H₃₃NO₆Na [M+Na⁺]: 478.2200; found: 478.2214.

(2) Synthesis of 3-(1'-acetoxypentyl)-7-(1'-(*S*)-4''-nitrobenzoylpropyl)-1,2,7,8-nonatetraene (*S*)-8o****

Following the procedure for the preparation of racemic **8n**, the reaction of (*S*)-**1o** (17.0 mg, 0.056 mmol), 4-nitrobenzoyl chloride (48.2 mg, 0.26 mmol), DMAP (3.1 mg), and a solution of Et₃N (28.2 mg, 0.28 mmol) in 1 mL of CH₂Cl₂ afforded (*S*)-**8o** (21.5 mg, 84%): Liquid; 99% *ee* (HPLC condition: chiral AS-H column; rate, 0.4 mL/min, eluent: hexane/*i*-PrOH 99/1, λ = 254 nm); [α]_D²⁰ = -13.1° (*c* = 0.93, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.32-8.25 (m, 2H), 8.24-8.17 (m, 2H), 5.41 (t, *J* = 6.6 Hz, 1H), 5.17 (t, *J* = 6.6 Hz, 1H), 4.94-4.70 (m, 4H), 2.04 (s, 3H), 2.00-1.92 (m, 4H), 1.91-1.78 (m, 2H), 1.70-1.55 (m, 4H), 1.35-1.16 (m, 4H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.87 (t, *J* = 6.6 Hz, 3H); IR (neat, cm⁻¹): 2932, 2861, 1957, 1728, 1608, 1530, 1460,

1371, 1346, 1270, 1236, 1102, 1015; MS(ESI) (m/z): 455 [M^+], 456 [M^++1], 478 [$M+Na^+$], 479 [$M+1+Na^+$]; HRMS calcd for $C_{26}H_{33}NO_6Na$ [$M+Na^+$]: 478.2200; found: 478.2199.

General procedure and analytical data for compounds 2

Cyclization of 1a and 1b under Conditions A:

(1) 3-Ethyl-8-methylene-7-(1'(Z)-propylidene)-5-(4'-toluenesulfonyl)-3,4,5,6,7,8-hexahydro-1H-furo[3,4-c]azepine (2a) (Conditions A)

A solution of **1a** (120.5 mg, 0.31 mmol) and PdCl_2 (2.9 mg, 5 mol%, 0.016 mmol) in 3 mL of DMF was stirred at 25 °C. After 4 h the reaction was complete as monitored by TLC, the resulting mixture was diluted with Et_2O (25 mL) and quenched with 6 mL of water, then extracted with Et_2O (25 mL x 2). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4 . Evaporation and column chromatography on silica gel (petroleum ether/diethyl ether = 3:1) afforded **2a** (71.2 mg, 62%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 5.79 (t, J = 7.5 Hz, 1H), 5.10 (s, 1H), 4.75-4.55 (m, 3H), 4.56 (s, 1H), 4.07 (d, J = 13.8 Hz, 1H), 3.97 (d, J = 13.8 Hz, 1H), 3.95 (d, J = 17.4 Hz, 1H), 3.83 (d, J = 17.4 Hz, 1H), 2.42 (s, 3H), 2.20-2.06 (m, 2H), 1.75-1.58 (m, 1H), 1.50-1.35 (m, 1H), 1.00 (t, J = 7.2 Hz, 3H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 143.4, 142.5, 135.7, 134.29, 134.27, 133.7, 132.7, 129.5, 127.1, 112.5,

89.3, 75.6, 46.5, 43.9, 27.0, 21.4, 21.2, 13.7, 8.6; IR (neat, cm^{-1}): 2964, 2931, 2873, 1597, 1456, 1338, 1161, 1031; MS (m/z): 374 [$M^+ + H$, 100], 396 [$M + Na^+$]; HRMS calcd for $C_{21}H_{27}NO_3S$ (M^+): 373.1712; found: 373.1715.

The following compound was prepared similarly.

(2) 7-(1'(Z)-Hexylidene)-8-methylene-3-pentyl-5-(toluene-4-sulfonyl)-3,4,5,6,7,8-hexahydro-1H-furo[3,4-c]azepine (2b)

The reaction of PdCl_2 (1.9 mg, 5 mol%, 0.011 mmol) and **1b** (94.8 mg, 0.20 mmol) in DMF (2 mL) afforded **2b** (71.1 mg, 78%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.68 (d, $J = 8.1$ Hz, 2H), 7.29 (d, $J = 8.1$ Hz, 2H), 5.79 (t, $J = 7.5$ Hz, 1H), 5.08 (s, 1H), 4.73-4.50 (m, 3H), 4.54 (s, 1H), 4.09 (d, $J = 13.5$ Hz, 1H), 3.96 (d, $J = 13.5$ Hz, 1H), 3.95 (d, $J = 16.8$ Hz, 1H), 3.84 (d, $J = 16.8$ Hz, 1H), 2.42 (s, 3H), 2.10 (q, $J = 7.5$ Hz, 2H), 1.65-1.47 (m, 1H), 1.45-1.16 (m, 13H), 0.95-0.80 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 143.3, 142.7, 135.9, 134.7, 133.6, 133.3, 133.1, 129.5, 127.2, 112.4, 88.5, 75.3, 46.5, 43.6, 34.2, 31.8, 31.4, 28.9, 27.7, 24.5, 22.6, 22.4, 21.5, 14.0; IR (neat, cm^{-1}): 2955, 2928, 2856, 1597, 1466, 1342, 1161, 1112; MS (m/z): 457 (M^+ , 57.71), 386 ($M^+ - \text{C}_5\text{H}_{11}$, 30.24), 91 ($\text{CH}_3\text{C}_6\text{H}_4^+$, 100); Elemental analysis calcd for $\text{C}_{27}\text{H}_{39}\text{NO}_3\text{S}$: C, 70.86; H, 8.59; N, 3.06; found: C, 70.95; H, 8.54; N, 2.83.

Cyclization of 1c – 1j under Conditions B:

(1) 1-Ethyl-4-methylene-5-(1'(E)-propylidene)-3,4,5,6,7,8-hexahydro-1H-cyclo-

hepta[c]furan (**2c**) (Conditions B)

To a mixture of PdCl₂ (1.8 mg, 5 mol%, 0.010 mmol) and NaI (15.6 mg, 0.10 mmol) were added **1c** (48.8 mg, 0.21 mmol) and DMF (2 mL). After being stirred at 80 °C for 1 h the reaction was complete as monitored by TLC, the resulting mixture was cooled to room temperature and diluted with Et₂O (25 mL), then quenched with 5 mL of water. The mixture was extracted with Et₂O (25 mL x 2). The combined organic layer was washed with saturated aqueous solution of Na₂S₂O₃ and brine and dried over anhydrous Na₂SO₄. Evaporation and column chromatography on silica gel (petroleum ether/diethyl ether = 25:1) afforded **2c** (26.1 mg, 58%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 5.57 (t, *J* = 7.2 Hz, 1H), 5.02 (d, *J* = 1.8 Hz, 1H), 4.80-4.68 (m, 3H), 4.50 (d, *J* = 1.8 Hz, 1H), 2.46-2.34 (m, 1H), 2.33-2.22 (m, 1H), 2.20-2.01 (m, 4H), 1.87-1.64 (m, 3H), 1.57-1.42 (m, 1H), 1.01 (t, *J* = 7.5 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 146.6, 140.7, 137.9, 130.8, 128.9, 109.7, 90.9, 76.1, 28.1, 26.9, 26.2, 24.8, 21.0, 14.2, 8.7; IR (neat, cm⁻¹): 2962, 2931, 2871, 1647, 1586, 1455, 1355, 1160, 1119, 1026; MS (*m/z*): 218 (M⁺, 19.48), 189 (M⁺-C₂H₅, 81.32), 57 (C₂H₅CO⁺, 100); HRMS calcd for C₁₅H₂₂O (M⁺): 218.1671; found: 218.1670.

The following compounds were prepared according to this procedure.

(2) 1-(4'-Chlorophenyl)-4-methylene-5-(1'(E)-4''-chlorobenzylidene)-3,4,5,6,7,8-

hexahydro-1*H*-cyclohepta[*c*]furan (**2d**)

The reaction of PdCl₂ (1.2 mg, 5 mol%, 0.0068 mmol), NaI (7.8 mg, 0.052 mmol), and **1d** (46.0 mg, 0.11 mmol) in DMF (1 mL) afforded **2d** (22.4 mg, 51%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.27 (m, 4H), 7.26-7.17 (m, 4H), 6.62 (s, 1H), 5.60 (t, *J* = 3.9 Hz, 1H), 5.33 (s, 1H), 5.10-5.01 (m, 1H), 4.98-4.88 (m, 1H), 4.80 (s, 1H), 2.62-2.40 (m, 2H), 2.24-2.05 (m, 1H), 1.94-1.77 (m, 2H), 1.75-1.60 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 146.1, 144.3, 140.1, 138.5, 136.1, 133.9, 132.4, 131.0, 130.0, 128.7, 128.6, 128.4, 125.7, 112.5, 92.3, 77.0, 29.1, 26.5, 25.4; IR (neat, cm⁻¹): 2932, 2858, 1900, 1651, 1592, 1488, 1450, 1408, 1089, 1064, 1014; MS (*m/z*): 386 (M⁺ (2 x ³⁷Cl), 2.42), 384 (M⁺(³⁷Cl, ³⁵Cl), 12.00), 382 (M⁺(2 x ³⁵Cl), 18.05), 245 (M⁺-ClC₆H₄CO(³⁷Cl), 20.25), 243 (M⁺-ClC₆H₄CO(³⁵Cl), 61.20), 139 (³⁵ClC₆H₄CO⁺, 100); HRMS calcd for C₂₃H₂₀OC₂Cl₂ (M⁺(2 x ³⁵Cl)): 382.0891; found: 382.0902.

(3) 3-Ethyl-8-methylene-7-(1'(*Z*)-propylidene)-4,6,7,8-tetrahydro-1*H*,3*H*-

furo[3,4-*c*]oxepin (**2e**)

The reaction of PdCl₂ (3.4 mg, 5 mol%, 0.019 mmol), NaI (30.3 mg, 0.20 mmol),

and **1e** (95.0 mg, 0.40 mmol) in DMF (4 mL) afforded **2e** (49.8 mg, 57%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.81 (t, $J = 7.5$ Hz, 1H), 5.23 (s, 1H), 4.85-4.70 (m, 3H), 4.66 (s, 1H), 4.36 (d, $J = 13.2$ Hz, 1H), 4.28 (d, $J = 17.1$ Hz, 1H), 4.22 (d, $J = 13.2$ Hz, 1H), 4.18 (d, $J = 17.1$ Hz, 1H), 2.22-2.08 (m, 2H), 1.74-1.58 (m, 1H), 1.54-1.36 (m, 1H), 1.02 (t, $J = 7.5$ Hz, 3H), 0.91 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 142.6, 137.8, 136.3, 131.9, 131.4, 111.7, 88.7, 76.1, 67.7, 67.4, 27.4, 20.9, 14.1, 8.5; IR (neat, cm^{-1}): 2964, 2932, 2873, 2841, 1585, 1455, 1366, 1248, 1202, 1172, 1121, 1073, 1035; MS (m/z): 220 (M^+ , 0.57), 191 ($\text{M}^+ - \text{C}_2\text{H}_5$, 3.32), 84 ($\text{C}_5\text{H}_8\text{O}^+$, 100); HRMS calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$ (M^+): 220.1463; found: 220.1472.

(4) 7-(1'(Z)-Isobutylidene)-3-isopropyl-8-methylene-4,6,7,8-tetrahydro-1H,3H-furo[3,4-c]oxepin (2f)

The reaction of PdCl_2 (2.9 mg, 5 mol%, 0.016 mmol), NaI (22.5 mg, 0.15 mmol), and **1f** (79.2 mg, 0.30 mmol) in DMF (3 mL) afforded **2f** (49.7 mg, 67%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.65 (d, $J = 9.9$ Hz, 1H), 5.23 (s, 1H), 4.80-4.74 (m, 2H), 4.72-4.67 (m, 1H), 4.66 (s, 1H), 4.43 (d, $J = 12.9$ Hz, 1H), 4.29 (d, $J = 16.8$ Hz, 1H), 4.20 (d, $J = 12.9$ Hz, 1H), 4.16 (d, $J = 16.8$ Hz, 1H), 2.73-2.55 (m, 1H), 1.80-1.62 (m, 1H), 1.05-0.98 (m, 9H), 0.81 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 142.7, 137.7, 136.2, 135.9, 132.1, 111.6, 92.7, 76.8, 67.6, 67.5, 32.1, 27.0, 23.1, 19.5, 14.8; IR (neat, cm^{-1}): 2960, 2929, 2870, 2841, 1654, 1585, 1465, 1384, 1364, 1296, 1280,

1251, 1182, 1127, 1080, 1038; MS (m/z): 248 (M^+ , 5.80), 205 ($M^+ - C_3H_7$, 83.60), 81 (100); Elemental analysis calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74; found: C, 77.34; H, 9.79.

(5) 3-Butyl-8-methylene-7-(1'(Z)-pentylidene)-4,6,7,8-tetrahydro-1*H*,3*H*-furo[3,4-*c*]oxepin (2g)

The reaction of $PdCl_2$ (2.8 mg, 5 mol%, 0.016 mmol), NaI (22.7 mg, 0.15 mmol), and **1g** (88.6 mg, 0.30 mmol) in DMF (3 mL) afforded **2g** (53.7 mg, 65%): liquid; 1H NMR (300 MHz, $CDCl_3$) δ 5.83 (t, $J = 7.5$ Hz, 1H), 5.23 (s, 1H), 4.85-4.70 (m, 3H), 4.66 (s, 1H), 4.36 (d, $J = 13.2$ Hz, 1H), 4.29 (d, $J = 17.1$ Hz, 1H), 4.24 (d, $J = 13.2$ Hz, 1H), 4.20 (d, $J = 17.1$ Hz, 1H), 2.14 (q, $J = 7.2$ Hz, 2H), 1.66-1.51 (m, 1H), 1.50-1.20 (m, 9H), 0.95-0.80 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 138.2, 136.7, 131.2, 130.6, 111.7, 87.9, 76.0, 67.7, 67.5, 34.4, 31.7, 27.3, 26.7, 22.7, 22.4, 14.0, 13.9; IR (neat, cm^{-1}): 2956, 2928, 2858, 1654, 1585, 1466, 1377, 1251, 1195, 1123, 1097, 1036; MS (m/z): 276 (M^+ , 36.42), 219 ($M^+ - C_4H_9$, 100); Elemental analysis calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21; found: C, 78.24; H, 10.21.

A solution of PdI₂ (5.3 mg, 5 mol%, 0.015 mmol) and **1g** (86.7 mg, 0.29 mmol) in 3 mL of DMF was stirred at 25 °C. After 4 h the reaction was complete as monitored by TLC. After the workup as above, the reaction afforded **2g** (56.5 mg, 69%).

(6) 3-Ethyl-8-methylene-7-(1'(Z)-propylidene)-4,6,7,8-tetrahydro-1H,3H-thiepine[3,4-c]furan-5,5-dioxide (2h)

The reaction of PdCl₂ (1.9 mg, 5 mol%, 0.011 mmol), NaI (14.0 mg, 0.09 mmol), and **1h** (54.2 mg, 0.19 mmol) in DMF (1.9 mL) afforded **2h** (41.2 mg, 81%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 6.01 (t, *J* = 7.5 Hz, 1H), 5.32 (s, 1H), 4.90-4.70 (m, 3H), 4.84 (s, 1H), 3.99 (s, 2H), 3.81 (s, 2H), 2.40-2.24 (m, 2H), 1.88-1.68 (m, 1H), 1.62-1.44 (m, 1H), 1.08 (t, *J* = 7.5 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 141.9, 139.3, 137.1, 127.8, 126.8, 115.5, 89.9, 75.5, 55.7, 48.7, 26.6, 22.2, 13.3, 8.9; IR (neat, cm⁻¹): 2967, 2934, 2875, 2847, 1642, 1589, 1459, 1412, 1319, 1237, 1146, 1120, 1029; MS (*m/z*): 268 (*M*⁺, 0.50), 239 (*M*⁺-C₂H₅, 32.51), 203 (100); HRMS calcd for C₁₄H₂₀O₃S (*M*⁺): 268.1133; found: 268.1135.

(7) 1-Butyl-4-methylene-5-(1'(E)-pentylidene)-1,3,4,5,6,7,8,9-octahydro-cycloocta[c]furan (2i)

The reaction of PdCl₂ (1.9 mg, 5 mol%, 0.011 mmol), NaI (15.2 mg, 0.10 mmol), and **1i** (64.8 mg, 0.21 mmol) in DMF (2 mL) afforded **2i** (41.7 mg, 68%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 5.27 (t, *J* = 7.5 Hz, 1H), 4.84 (d, *J* = 2.1 Hz, 1H), 4.82-4.67 (m, 3H), 4.60 (d, *J* = 2.1 Hz, 1H), 2.41-2.14 (m, 4H), 2.10 (q, *J* = 6.9 Hz, 2H), 1.70-1.58 (m, 3H), 1.57-1.46 (m, 2H), 1.45-1.25 (m, 9H), 0.96-0.82 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 146.1, 142.8, 137.3, 131.7, 127.9, 112.8, 90.0, 75.7, 34.0, 31.6, 29.8, 27.6, 27.4, 26.4, 24.0, 22.8, 22.5, 22.2, 14.1, 14.0; IR (neat, cm⁻¹): 2956, 2929, 2858, 1642, 1585, 1454, 1374, 1092, 1036; MS (*m/z*): 288 (M⁺, 22.77), 231 (M⁺-C₄H₉, 100); Elemental analysis calcd for C₂₀H₃₂O: C, 83.27; H, 11.18; found: C, 83.28; H, 11.17.

(8) 5-(1'(*E*)-4''-Chlorobenzylidene)-1-(4'-chlorophenyl)-4-methylene-1,3,4,5,6,7,8,9-octahydrocycloocta[*c*]furan (2j)

The reaction of PdCl₂ (0.9 mg, 5 mol%, 0.005 mmol), NaI (7.6 mg, 0.05 mmol), and **1j** (42.0 mg, 0.10 mmol) in DMF (1 mL) afforded **2j** (30.0 mg, 75%): liquid; ¹H

The reaction of PdCl₂ (1.0 mg, 5 mol%, 0.005 mmol), NaI (7.6 mg, 0.05 mmol), and **11** (43.2 mg, 0.11 mmol) in DMF (1 mL) afforded **21** (28.3 mg, 77%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.28 (m, 2H), 7.25-7.19 (m, 2H), 6.25 (s, 1H), 4.98 (d, *J* = 1.5 Hz, 1H), 4.87 (dd, *J*₁ = 10.8 Hz, *J*₂ = 5.1 Hz, 1H), 4.83-4.72 (m, 3H), 2.65-2.45 (m, 2H), 2.42-2.28 (m, 1H), 2.27-2.14 (m, 1H), 1.74-1.60 (m, 3H), 1.56-1.22 (m, 7H), 0.91 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 146.8, 145.5, 137.5, 136.2, 132.1, 132.0, 130.4, 128.3, 125.6, 113.9, 89.9, 75.5, 34.0, 31.0, 27.4, 26.1, 22.8, 22.1, 14.1; IR (neat, cm⁻¹): 2930, 2857, 1642, 1587, 1489, 1454, 1092, 1034, 1014; MS (*m/z*): 344 (M⁺(³⁷Cl), 3.37), 342 (M⁺(³⁵Cl), 8.15), 285 (M⁺(³⁵Cl)-C₄H₉, 100); HRMS calcd for C₂₂H₂₇ClO (M⁺, ³⁵Cl): 342.1745; found: 342.1761.

(2) 1-(4-Chlorophenyl)-4-methylene-5-(1'(*E*)-pentylidene)-1,3,4,5,6,7,8,9-octahydrocycloocta[*c*]furan (2m)

The reaction of PdCl₂ (0.8 mg, 5 mol%, 0.005 mmol), NaI (7.9 mg, 0.053 mmol), and **1m** (43.6 mg, 0.11 mmol) in DMF (1 mL) afforded **2m** (34.9 mg, 94%): liquid;

^1H NMR (300 MHz, CDCl_3) δ 7.33-7.27 (m, 2H), 7.25-7.18 (m, 2H), 5.59-5.52 (m, 1H), 5.31 (t, $J = 7.2$ Hz, 1H), 5.10 (dd, $J_1 = 11.1$ Hz, $J_2 = 5.4$ Hz, 1H), 4.95 (d, $J = 1.8$ Hz, 1H), 4.91 (dd, $J_1 = 11.1$ Hz, $J_2 = 3.3$ Hz, 1H), 4.74 (d, $J = 1.8$ Hz, 1H), 2.36-2.15 (m, 3H), 2.14-1.97 (m, 3H), 1.60-1.48 (m, 2H), 1.42-1.25 (m, 5H), 0.98-0.82 (m, 1H), 0.90 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 145.9, 142.4, 140.4, 136.9, 133.6, 132.2, 128.50, 128.48, 128.3, 113.9, 92.0, 76.9, 31.6, 29.7, 27.6, 26.0, 24.0, 22.5, 22.2, 14.0; IR (neat, cm^{-1}): 2927, 2855, 1582, 1489, 1452, 1405, 1089, 1036, 1014; MS (m/z): 344 (M^+ (^{37}Cl), 5.04), 342 (M^+ (^{35}Cl), 18.20), 139 ($^{35}\text{ClC}_6\text{H}_4\text{CO}^+$, 100); HRMS calcd for $\text{C}_{22}\text{H}_{27}\text{ClO}$ (M^+ , ^{35}Cl): 342.1745; found: 342.1757.

(3) 1-Ethyl-4-methylene-5-(1'(*E*)-propylidene)-1,3,4,5,6,7,8,9-octahydro-cycloocta[*c*]furan (2n)

The reaction of PdCl_2 (0.9 mg, 5 mol%, 0.005 mmol), NaI (7.8 mg, 0.052 mmol), and **1n** (32.8 mg, 0.10 mmol) in DMF (1 mL) afforded **2n** (21.3 mg, 80%): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.28 (t, $J = 7.2$ Hz, 1H), 4.85 (d, $J = 2.1$ Hz, 1H), 4.84-4.66 (m, 3H), 4.60 (d, $J = 2.1$ Hz, 1H), 2.41-2.15 (m, 4H), 2.10 (q, $J = 7.2$ Hz, 2H), 1.81-1.26 (m, 10H), 0.95-0.84 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 146.1, 142.8, 136.9, 132.0, 127.9, 112.9, 90.9, 75.9, 31.6, 29.8, 27.6, 27.0, 26.3, 24.0, 22.5, 22.1, 14.0, 9.2; IR (neat, cm^{-1}): 2956, 2928, 2856, 1646, 1585, 1454, 1378, 1354, 1119, 1098, 1034; MS (m/z): 260 (M^+ , 53.64), 231 ($\text{M}^+ - \text{C}_2\text{H}_5$, 100); HRMS calcd for

C₁₈H₂₈O (M⁺): 260.2140; found: 260.2147.

(4) (S)-1-Ethyl-4-methylene-5-(1'(*E*)-propylidene)-1,3,4,5,6,7,8,9-octahydro-cycloocta[*c*]furan (S-2n).

The reaction of PdCl₂ (1.1 mg, 5 mol%, 0.006 mmol), NaI (7.9 mg, 0.053 mmol), and (S)-1n (35.0 mg, 0.11 mmol, 99% *ee*) in DMF (1 mL) afforded (S)-2n (22.8 mg, 80%, 99% *ee*), HPLC condition: ReGIS (S,S)-whelk-01 column; rate, 0.6 mL/min, eluent: hexane/*i*-PrOH 100/0.1, $\lambda = 214$ nm. $[\alpha]_D^{20} = +3.6^\circ$ ($c = 0.96$, CHCl₃): liquid; ¹H NMR (300 MHz, CDCl₃) δ 5.28 (t, $J = 7.2$ Hz, 1H), 4.85 (d, $J = 2.1$ Hz, 1H), 4.84-4.66 (m, 3H), 4.60 (d, $J = 2.1$ Hz, 1H), 2.41-2.15 (m, 4H), 2.10 (q, $J = 7.2$ Hz, 2H), 1.81-1.26 (m, 10H), 0.96-0.80 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 146.1, 142.8, 137.0, 132.0, 127.9, 112.9, 90.9, 75.9, 31.6, 29.8, 27.6, 27.0, 26.3, 24.0, 22.5, 22.2, 14.0, 9.2; IR (neat, cm⁻¹): 2928, 2855, 1646, 1585, 1454, 1378, 1354, 1034; MS (m/z): 260 (M⁺, 53.64), 231 (M⁺-C₂H₅, 100); HRMS calcd for C₁₈H₂₈O (M⁺): 260.2140; found: 260.2140.

(5) 1-Ethyl-4-methylene-5-(1'(*E*)-pentylidene)-3,4,5,6,7,8-hexahydro-1H-cyclohepta[*c*]furan (2o).

The reaction of PdCl₂ (1.9 mg, 5 mol%, 0.011 mmol), NaI (15.6 mg, 0.10 mmol), and **1o** (63.0 mg, 0.21 mmol) in DMF (2 mL) afforded **2o** (43.8 mg, 74%): liquid; ¹H NMR (300 MHz, CDCl₃) δ 5.57 (t, *J* = 7.2 Hz, 1H), 5.02 (d, *J* = 1.2 Hz, 1H), 4.80-4.66 (m, 3H), 4.50 (d, *J* = 1.2 Hz, 1H), 2.46-2.22 (m, 2H), 2.21-2.00 (m, 4H), 1.87-1.74 (m, 2H), 1.73-1.64 (m, 1H), 1.55-1.42 (m, 1H), 1.42-1.28 (m, 4H), 0.95-0.84 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 146.6, 141.1, 137.9, 130.8, 127.5, 109.7, 90.9, 76.1, 31.8, 28.1, 27.5, 26.9, 26.1, 24.7, 22.5, 14.0, 8.7; IR (neat, cm⁻¹): 2958, 2927, 2858, 1645, 1582, 1456, 1374, 1350, 1119, 1045, 1023; MS (*m/z*): 246 (*M*⁺, 28.97), 217 (*M*⁺-C₂H₅, 100); HRMS calcd for C₁₇H₂₆O (*M*⁺): 246.1984; found: 246.1978.

(6) (*S*)-1-Ethyl-4-methylene-5-(1'(*E*)-pentylidene)-3,4,5,6,7,8-hexahydro-1*H*-cyclohepta[*c*]furan (*S*-2o**).**

The reaction of PdCl₂ (1.0 mg, 5 mol%, 0.006 mmol), NaI (7.9 mg, 0.05 mmol), and (*S*)-**1o** (32.4 mg, 0.11 mmol, 99% *ee*) in DMF (1 mL) afforded (*S*)-**2o** (19.9 mg, 76%, 99% *ee*), HPLC condition: ReGIS (S,S)-whelk-01 column; rate, 0.6 mL/min,

eluent: hexane/*i*-PrOH 100/0.1, $\lambda = 214$ nm. $[\alpha]_{\text{D}}^{20} = -28.3^\circ$ ($c = 0.71$, CHCl_3): liquid; ^1H NMR (300 MHz, CDCl_3) δ 5.58 (t, $J = 7.2$ Hz, 1H), 5.02 (d, $J = 1.2$ Hz, 1H), 4.80-4.68 (m, 3H), 4.50 (d, $J = 1.2$ Hz, 1H), 2.46-2.22 (m, 2H), 2.21-2.00 (m, 4H), 1.87-1.74 (m, 2H), 1.73-1.64 (m, 1H), 1.55-1.42 (m, 1H), 1.42-1.28 (m, 4H), 0.96-0.80 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 146.7, 141.1, 137.9, 130.9, 127.5, 109.7, 90.9, 76.1, 31.9, 28.2, 27.5, 26.9, 26.2, 24.7, 22.5, 14.0, 8.7; IR (neat, cm^{-1}): 2958, 2928, 2858, 1648, 1587, 1455, 1356, 1160, 1119, 1045, 1023; MS (m/z): 246 (M^+ , 28.97), 217 ($\text{M}^+ - \text{C}_2\text{H}_5$, 100); HRMS calcd for $\text{C}_{17}\text{H}_{26}\text{O}$ (M^+): 246.1984; found: 246.1980.

References:

1. (a) Gleiter, R.; Ritter, J.; Irngartinger, H.; Lichtenthäler, J. *Tetrahedron Lett.* **1991**, 32, 2883. (b) Gleiter, R.; Rittinger, S.; Langer, H. *Chem. Ber.* **1991**, 124, 357.
2. Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 621.
3. (a) Xu, D.; Li, Z.; Ma, S. *Chem. Eur. J.* **2002**, 8, 5012. (b) Xu, D.; Li, Z.; Ma, S. *Tetrahedron: Asymmetry* **2003**, 14, 3657.
4. With a less amount of Novozym 435, the reaction requires much longer time to afford (*S*)-**10** in acceptable *ee*.

dyq-10-172-1h

Data File D:\HPCHEM\1\DATA\DYQ\DYQ00040.D

Sample Name: dyq-10-143

chiral AS-H; n-Hexane:i-PrOH=99/1; 254 nm; 0.4 ml/min

Injection Date : 9/20/2008 6:30:09 PM
 Sample Name : dyq-10-143
 Acq. Operator : dyq
 Acq. Method : D:\HPCHEM\1\METHODS\ERIC.M
 Last changed : 9/20/2008 6:27:55 PM by dyq
 (modified after loading)
 Analysis Method : D:\HPCHEM\1\METHODS\ERIC.M
 Last changed : 9/20/2008 8:02:14 PM by dyq

Location

Area Percent Report

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Sample Amount : 1.00000 [ng/ul] (not used in calc.)
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	23.432	VV	0.5932	6675.38721	175.12875	24.7315
2	24.730	VB	0.6728	6928.22559	158.55818	25.6682
3	28.172	BV	0.8942	6711.57129	115.85690	24.8655
4	30.300	VB	1.1085	6676.29590	91.70620	24.7348

Totals : 2.69915e4 541.25004

Results obtained with enhanced integrator!

Data File D:\HPCHEM\1\DATA\DYQ\DYQ00056.D

Sample Name: dyq-10-173

chiral AS-H; n-Hexane:i-PrOH=99/1; 254 nm; 0.4 ml/min

=====
Injection Date : 10/9/2008 5:46:50 PM
Sample Name : dyq-10-173
Acq. Operator : dyq
Acq. Method : D:\HPCHEM\1\METHODS\ERIC.M
Last changed : 10/9/2008 5:44:37 PM by dyq
(modified after loading)
Analysis Method : D:\HPCHEM\1\METHODS\ERIC.M
Last changed : 10/17/2008 1:04:33 PM by fz

Location : -

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	23.119	VB	0.7349	1.21705e4	252.16943	48.2135
2	28.223	BB	1.1589	1.30724e4	170.06721	51.7865

Totals : 2.52429e4 422.23665

Results obtained with enhanced integrator!

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*** End of Report ***

dyq-10-140-1h

Data File D:\HPCHEM\1\DATA\DYQ\DYQ00051.D

Sample Name: dyq-10-166

chiral As-H; n-Hexane:i-PrOH=99/1; 254 nm; 0.4 ml/min

Injection Date : 10/4/2008 3:53:54 PM
Sample Name : dyq-10-166
Acq. Operator : dyq
Method : D:\HPCHEM\1\METHODS\ERIC.M
Last changed : 10/4/2008 3:35:38 PM by dyq
(modified after loading)

Location : -

racemic 80

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	21.912	PV	0.4681	3.49256e4	1188.24597	25.8430
2	22.728	VP	0.5401	3.59576e4	1040.47437	26.6066
3	24.973	BV	0.6357	3.27352e4	818.08453	24.2222
4	26.611	VB	0.7756	3.15269e4	646.58649	23.3281

Totals : 1.35145e5 3693.39136

Results obtained with enhanced integrator!

*** End of Report ***

Sample Name: dyq-10-167

```

=====
Injection Date   : 10/4/2008 4:27:33 PM
Sample Name     : dyq-10-167
Acq. Operator   : dyq
Acq. Method     : D:\HPCHEM\1\METHODS\ERIC.M
Last changed    : 10/4/2008 3:35:38 PM by dyq
                  (modified after loading)
Analysis Method : D:\HPCHEM\1\METHODS\ERIC.M
Last changed    : 10/4/2008 5:37:57 PM by dyq
                  (modified after loading)
=====

```

Location :

Area Percent Report

```
Sorted By      :      Signal
Multiplier    :      1.0000
Dilution      :      1.0000
Sample Amount  :      1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	22.395	BB	0.5500	4.52008e4	1303.86548	51.4154
2	24.603	BB	0.6836	4.27121e4	979.31104	48.5846

Totals : 8.79128e4 2283.17651

Results obtained with enhanced integrator!

*** End of Report ***

Instrument 1 10/4/2008 5:38:18 PM dyg
PDF "pdfFactory Pro" "www.fineprint.com.cn"

Page 1 of 1

dyq-7-16h

dyq-8-26h

dyq-8-26c

142.584
 137.832
 136.309
 131.933
 131.446

111.667

88.668

77.425
 77.000
 76.575
 76.148
 67.715
 67.388

27.401

20.886

14.138

8.540

dyq-8-26

dyq-8-191h

HPLC REPORT

Sample Name:dyq-10-141...che

Date:2008-10-10

Time:14:09

Method:

Column:

Flow Rate:

Wave Length:

Mobile Phase:

No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	6.968	116892.6	1135460.8	49.9622
2	2	Unknown	7.810	103406.7	1137179.4	50.0378
Total				220299.3	2272640.2	100.0000

HPLC REPORT

Sample Name:dyq-10-174...che

Time:14:20

Column:

Wave Length:

Date:2008-10-10

Method:

Flow Rate:

Mobile Phase:

No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	6.977	398898.8	4818352.5	99.3073
2	2	Unknown	7.808	2354.7	33607.7	0.6927
Total				401253.4	4851960.2	100.0000

7.260

5.596
5.572
5.548

5.019
5.014
4.498
4.733
4.494

2.401
2.360
2.298
2.275
2.150
2.125
2.059
2.034
1.852
1.830
1.787
1.765
1.744
1.400
1.380
1.374
1.324
0.930
0.922
0.914
0.887
0.883
0.873
-0.009

dyq-9-42h

146.631
141.052
137.871
130.810
127.456

109.691

90.857

77.422
77.000
76.575
76.084

31.837
28.105
27.459
26.900
26.128
24.674
22.461
14.025
8.685

HPLC REPORT

Sample Name:DYQ-10-170. che

Time:08:21

Column:

Wave Length:

Date:2008-10-07

Method:

Flow Rate:

Mobile Phase:

No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	10.132	146869.1	2049709.7	49.1286
2	2	Unknown	11.452	122816.7	2122421.3	50.8714
Total				269685.8	4172131.0	100.0000

HPLC REPORT

Sample Name: DYQ-10-171..che

Date: 2008-10-07

Time: 09:25

Method:

Column:

Flow Rate:

Wave Length:

Mobile Phase:

No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	10.433	253625.8	4387211.4	99.6070
2	2	Unknown	11.907	941.0	17307.9	0.3930
Total				254566.8	4404519.3	100.0000