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A Concise Synthesis of (–)- and (+)-*trans*-Whisky Lactones

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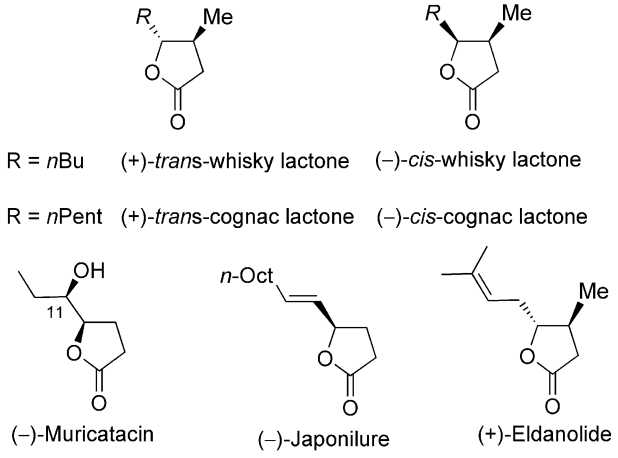
Concise enantioselective eleven-step syntheses leading to (–)- and (+)-*trans*-whisky lactones were developed. Propargyl alcohol was employed as starting material. The reaction sequences include highly diastereoselective electrophilic cyclization of γ-allenoic acids, dehydroiodination, and hydrogenation.

Introduction

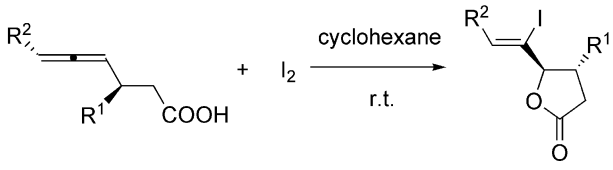
Chiral γ-butyrolactones are not only useful starting materials for various bioactive compounds,[1] but also act as core elements of many potentially useful natural products,[2] e.g. whisky lactones and cognac lactones in wine and other alcoholic beverages,[3] (–)-muricatacin isolated as the major component of a scalemic mixture from the seeds of annona muricata,[4] (–)-japonilure[5] and (+)-eldanolide[6] pheromones of the Japanese beetle and African sugarcane borer all have a γ-butyrolactone unit (Scheme 1).



Scheme 1.

There are many reports devoted to the synthesis of (–)- and (+)-*trans*-whisky lactones.[7–13] In most cases, the chiral centers in the targets were constructed by the reaction of an chiral reagent with a key intermediate to afford a pair of diastereoisomers, which were then separated by chromatography on silica gel followed by other transformations to prepare the target.[7] Studer et al. reported a six-step route from the stoichiometric enantioselective reaction of 2-pentynal with chiral TADDOL-derived 2,5-cyclohexadienyl Ti reagent.[8] Inomata et al.[9] and Momose et al.[10] reported two syntheses from the (+)-(2*S*,3*R*)-*cis*-*endo*-3-(hydroxymethyl) bicyclo[2.2.1]hept-5-ene-2-carboxylic acid lactone in five steps, and (*R*)-*N*-benzyl-3-hydroxy-*N*-methylpent-4-enamide in four steps, respectively. Fang et al. observed that chiral *trans*-whisky lactones could be prepared from the cyclization of (2*S*,3*R*)-1-(1,3-dithianylidene)-2-methyl-3-heptanol, which was prepared by enzymatic resolution of racemic 1-(1,3-dithianylidene)-2-methyl-3-heptyl acetate.[11] The most straightforward route is the sequential Baker's yeast reduction and lactonization of 3-methyl-4-oxooctanoic acid, which was prepared from the reaction of pentanal with ethyl but-2-enoate. However, for the synthesis of 5.6 g of (+)-*trans*-whisky lactone, 1.6 kg of baker's yeast and 1.3 kg of D-glucose are required.[12]

Recently, we have developed some methods for the synthesis of compounds with γ-lactone unit.[14] Of particular interest is the highly diastereoselective synthesis of *trans*-β,γ-disubstituted butyrolactones from the electrophilic iodolactonization of γ-allenoic acids via the 1,2-chiral induction[14a] [Equation (1)]. In this paper, We wish to report an efficient synthesis of (–)- and (+)-*trans*-whisky lactones in eleven steps from propargyl alcohol with this iodolactonization reaction as the key step.



(1)

Results and Discussion

As a start, we prepared the racemic 3-methylocta-4,5-dienoic acid (**4**). Thus, pent-1-yn-3-ol (**1**) was treated with ex-

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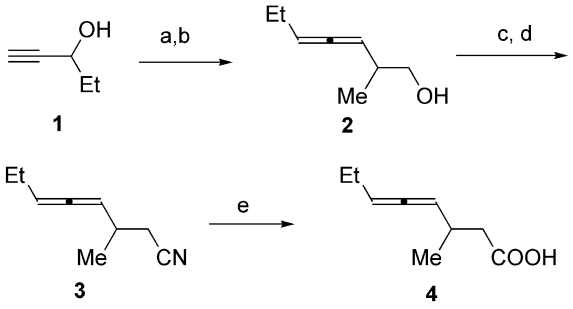
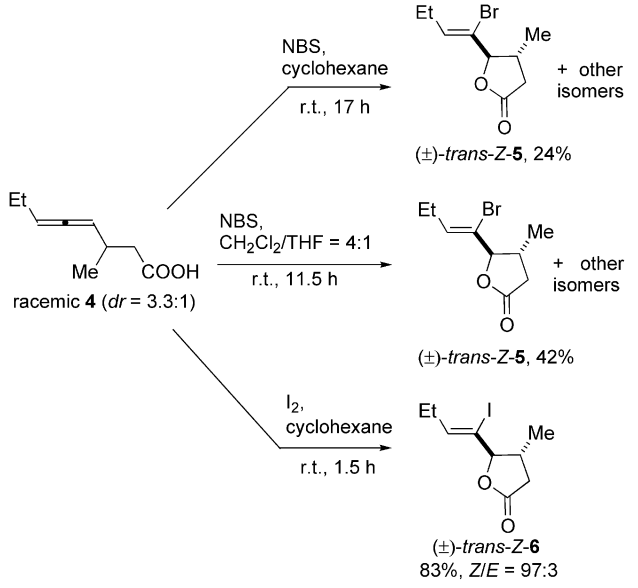
cess triethyl orthoacetate in the presence of a catalytic amount of propionic acid. The resulting ethyl 3,4-allenoate was then reduced with $LiAlH_4$ to form the related alcohol **2**, which was tosylated and subsequently converted into nitrile **3**. Finally, hydrolysis with NaOH in EtOH/H_2O afforded the 4,5-allenoic acid **4** (Scheme 2).



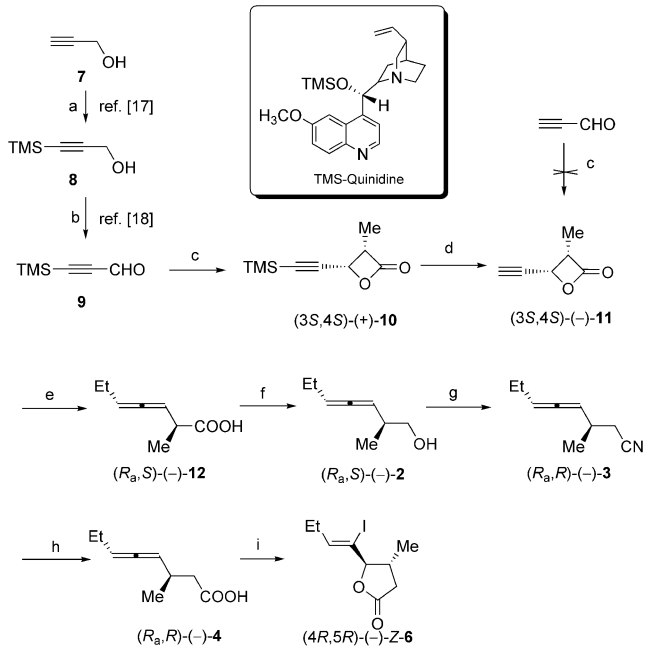
Scheme 2. Synthesis of racemic 3-methylocta-4,5-dienoic acid (**4**). (a) $EtC(OEt)_3$, $EtCO_2H$ (cat.), 140 °C; (b) $LiAlH_4$, THF, 0 °C; combined yield of two steps is 68%; (c) TsCl, pyridine; (d) NaCN, DMSO, room temp., 1.5 d, combined yield of two steps is 71%; (e) NaOH, EtOH/H_2O, 74%, *dr* = 3.3:1.

Then, we screened the conditions of the halolactonization of allenoic acid **4**. When it was submitted to the iodolactonization condition,[14a] the (±)-*trans*-*Z*-**6** was obtained in 83% yield. It should be noted that its reaction with NBS afforded the corresponding products in a much lower diastereoselectivity,[15] indicating the importance of the iodine atom in determining the diastereoselectivity of this electrophilic cyclization (Scheme 3).



Scheme 3. Halolactonization of racemic **4**.

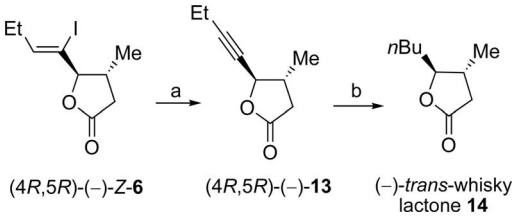
With this template reaction in hand, (4*R*,5*R*)-(–)-*Z*-**6** was prepared (Scheme 4). The direct synthesis of (3*S*,4*S*)-(–)-**11** from propynal using catalytic asymmetric acyl halide–aldehyde cyclocondensation reaction afforded a trace amount of product.[16] Thus, the total synthesis was commenced with the preparation of (trimethylsilyl)propynol (**8**),[17] which was then oxidized with PCC to afford 3-(trimethylsilyl)propynal (**9**) in 54% yield.[18] (3*S*,4*S*)-(+)-**10** was synthesized from **9** with propionyl chloride in 94% yield. The TMS group on the alkyne moiety was removed by TBAF (1 M, in THF) at –15 °C to afford β-lactone (3*S*,4*S*)-(–)-**11**, which was converted to chiral 3,4-allenoic acid (R_a,*S*)-(–)-**12** by S_N2'-type ring-opening reaction with EtMgBr catalyzed by $CuBr{\cdot}SMe_2$.[19] (R_a,*S*)-(–)-**12** was then reduced with $LiAlH_4$ to form the related alcohol (R_a,*S*)-(–)-**2**, which was tosylated, and subsequently converted to nitrile (R_a,*R*)-(–)-**3**. (R_a,*R*)-(–)-**3** was hydrolyzed with NaOH in EtOH/H_2O to afford the chiral γ-allenoic acid (R_a,*R*)-(–)-**4** (*dr* = 12.5:1), finally, the (4*R*,5*R*)-(–)-*Z*-**6** was obtained in 84% yield with 98.6% *ee* (Scheme 4).



Scheme 4. Preparation of (4*R*,5*R*)-(–)-*Z*-**6**. Conditions: (a) (i) EtMgBr, THF; (ii) TMSCl, 95%; (b) PCC, CH_2Cl_2, 54%; (c) EtCOCl, TMS-quinidine, $MgCl_2$, $EtN(iPr)_2$, Et_2O/CH_2Cl_2, –80 °C, 94%; (d) TBAF, THF, –15 °C, 64%; (e) EtMgBr, Me_2S, $CuBr{\cdot}Me_2S$, THF, –78 °C, 74%; (f) $LiAlH_4$, diethyl ether, 0–4 °C, 77%; (g) (i) TsCl, pyridine, 0–5 °C; (ii) NaCN, DMSO, 30 °C, combined yield of two steps is 77%; (h) (i) NaOH, H_2O/C_2H_5OH, 80 °C; (ii) H^+, 97%, (R_a,*R*)-**4**/(S_a,*R*)-**4** = 12.5:1, $[\alpha]_D^{20}$ = –67; (i) I_2, cyclohexane, 84%, *Z*/*E* = 97:3, 98.6% *ee*.

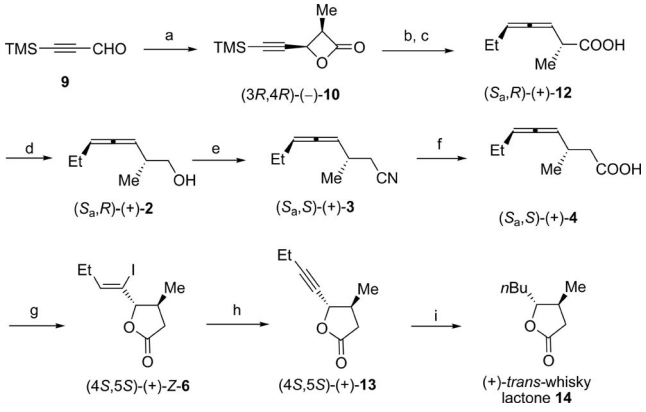
All attempts to deiodinate (±)-*trans*-*Z*-**6** were unsuccessful. Thus, none of the following reagents gave the desired *trans*-4-methyl-5-(1-butenyl)-γ-butyrolactone in an acceptable yield: Pd/C-H_2, *t*BuLi,[20] TTMSS,[21] and $Pd(PPh_3)_4$-HCO_2NH_4. Thus, we turned our attention to dehydroiodination.

It is fortunate to note that the elimination of HI[21] from (4*R*,5*R*)-(–)-*trans*-*Z*-**6** afforded without racemization a 92% yield of *trans*-β-methyl-γ-(1-butynyl)butyrolactone (4*R*,5*R*)-(–)-**13**, which was then hydrogenated to afford the target (–)-*trans*-whisky lactone[9] in 86% yield and 98.5% *ee* (Scheme 5). Thus, the synthesis of (–)-*trans*-whisky lactone (**14**) was realized in eleven steps and 8% combined yield from propargyl alcohol.



Scheme 5. Transformation of (4*R*,5*R*)-(–)-*Z*-**6** to *trans*-whisky lactone (**14**). Conditions: (a) TBAF (3 equiv.), DMF, 25 °C, 5 h, 92%, 98.8% ee; (b) H_2 (25 atm),Pd/C (10 mol-%), ethyl acetate, room temp., 1 d, 86%, 98.5% *ee*, $[a]_D^{20}$ = –82.5 (*c* = 1.02, MeOH).

With this strategy in hand, its natural enantiomer[3a] could be prepared similarly (Scheme 6).



Scheme 6. Synthesis of (+)-*trans*-whisky lactone. Conditions: (a) EtCOCl, TMS-quinine, $MgCl_2$, $EtN(iPr)_2$, CH_2Cl_2/Et_2O, –80 °C, 88%; (b) TBAF, THF, –15 °C, (c) EtMgBr, CuBr·SMe_2, SMe_2, THF, –78 °C, combined yield of two steps is 57%; (d) $LiAlH_4$, diethyl ether, 0–4 °C, 74%; (e) (i) TsCl, pyridine, 0 °C; (ii) NaCN, DMSO, 30 °C, combined yield of two steps 73%; (f) NaOH, H_2O/C_2H_5OH, 80 °C then aq. HCl, 92%, *dr* = 12.5:1; (g) I_2, cyclohexane, room temp., 2 h, 86%, *Z*/*E* = 98:2; (h) TBAF, DMF, 25 °C, 5 h, 89%; (i) H_2 (25 atm), Pd/C (10 mol-%), room temp., 1 d, 90%, 98.5% *ee*, $[a]_D^{20}$ = +81.2 (*c* = 1.24, MeOH).

Conclusions

In conclusion, the iodolactonization of the chiral 4,5-allenoic acid was successfully applied to diastereoselective syntheses of (–)- and (+)-*trans*-whisky lactones. In contrast to earlier syntheses, the two required stereocenters were constructed via a catalytic asymmetric acyl halide–aldehyde cyclocondensation reaction[16] and a 1,2-chiral induction using a iodolactonization.[14a] The data of the prepared products are in consistent with the reported ones.[3a,9] This approach may be useful for the asymmetric synthesis of other potentially useful natural products. Further studies in this area are being pursued in this laboratory.

Experimental Section

Preparation of (±)-5-[(1*Z*)-1-Iodo-1-butenyl]-4-methyl-4,5-dihydro-2(3*H*)-furanone [(±)-*trans*-*Z*-6][15]

1. Preparation of 2-methylhepta-3,4-dien-1-ol (2): A mixture of pent-1-yn-3-ol (**1**) (2.0492 g, 0.024 mol), EtCOOH (0.7 mL, *d* = 0.99 g/mL, 0.693 g, 0.0094 mol), and $EtC(OEt)_3$ (12.6643 g, 0.072 mol) was heated at 140 °C for 3.5 h with a Dean–Stark apparatus to remove the in-situ formed EtOH and the excess $EtC(OEt)_3$. After removing most of the compounds with low boiling points, the mixture was cooled to room temp. and then purified by chromatography on silica gel to afford ethyl 2-methylhepta-3,4-dienoate. The product was used in the next step without further characterization. To an ice-cold suspension of $LiAlH_4$ (1.1154 g, 0.029 mol) in anhydrous THF (15 mL) under N_2 was added dropwise a solution of the above prepared ethyl 2-methylhepta-3,4-dienoate in THF (15 mL). After 2.3 h, the reaction was complete as monitored by TLC, diluted with 60 mL of Et_2O, quenched by slow addition of an aqueous NaOH solution (aq., 5 M, 6 mL, 0.030 mol), then filtered to remove the solid, evaporated, and purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1) to afford **2** (2.0799 g, combined yield of two steps is 68%) as colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.31–5.18 (m, 1 H, C*H*=), 5.15–5.04 (m, 1 H, C*H*=), 3.57–3.42 (m, 2 H, CH_2OH), 2.43–2.26 (m, 1 H, C*H*CH_2OH), 2.08–1.91 (m, 2 H, MeCH_2), 1.71 (br. s, 1 H, -O*H*), 1.08–0.93 (m, 6 H, 2 × Me) ppm. IR (neat): $\tilde{\nu}$ = 3335, 2965, 2932, 2872, 1961, 1458, 1376, 1325, 1269, 1035 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 126 (4.91) [M^+], 67 (100). HRMS: Calcd. for $C_8H_{14}O_2$ (M^+): 126.1045; found 126.1042.

2. Preparation of 3-Methylocta-4,5-dienenitrile (3): To an ice-cooled solution of **2** (4.2457 g, 0.034 mol) in dry pyridine (30 mL) was added *p*TsCl (19.5171 g, 0.102 mol) in several portions at 0–4 °C. After being stirred at 0–4 °C for an additional 6 h, the reaction was complete as monitored by TLC, and the mixture was poured into ice water and then extracted with diethyl ether (30 mL × 3). The combined organic layer was washed with water and brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. The product was then used in the next step without further purification. To a mixture of tosylate prepared above and anhydrous DMSO (30 mL) was added NaCN (1.7913 g, 0.037 mol) at room temperature. After 1.5 d, the reaction was complete as monitored by TLC, quenched with 30 mL of H_2O, and extracted with diethyl ether (30 mL × 3). The organic layer was washed with water and brine, dried with Na_2SO_4, filtered, evaporated, and purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 50:1) to afford **3** (3.2459 g, the combined yield from **2** to **3** is 71%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.39–5.29 (m, 1 H, C*H*=), 5.21–5.12 (m, 1 H, C*H*=), 2.61–2.48 (m, 1 H, C*H*CH_2CN), 2.46–2.26 (m, 2 H, CH_2CN), 2.09–1.96 (m, 2 H, MeCH_2), 1.21–1.13 (m, 3 H, Me), 1.01 (t, *J* = 7.4 Hz, 3 H, Me) ppm. IR (neat): $\tilde{\nu}$ = 2967, 2933, 2874, 2247, 1963, 1458, 1421, 1379, 1324, 1276, 1069 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 135 (7.22) [M^+], 120 (100). HRMS: Calcd. for $C_9H_{13}N$ (M^+): 135.1048; found 135.1045.

3. Preparation of 3-Methylocta-4,5-dienoic Acid (4): To the round-bottom flask was added **3** (1.0716 g, 7.5 mmol), an aqueous NaOH solution (4.0802 g in 5 mL of H_2O, 100 mmol), and ethanol (15 mL) sequentially. Then the mixture was stirred at 80 °C for 10.5 h, the resulting mixture was concentrated in vacuo and the residue was quenched with water (10 mL). The aqueous solution was then extracted with diethyl ether to remove neutral impurities. The aqueous layer was then acidified with 5% HCl (aq.) to pH = 1 and extracted with diethyl ether (30 mL × 3). The ether extraction was washed with water and brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. Chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5:1) of the crude product afforded **4** (0.8990 g, 74%, *dr* = 3.3:1, *dr* value of **4** was determined by inverse gated decoupling ^{13}C NMR analysis[23]) as a colorless oil. ^1H NMR

(300 MHz, $CDCl_3$): δ = 11.9 (br. s, 1 H, COO*H*), 5.30–5.05 (m, 2 H, C*H*=C=C*H*), 2.73–2.56 (m, 1 H), 2.48–2.35 (m, 1 H), 2.34–2.23 (m, 1 H), 2.04–1.88 (m, 2 H, MeCH_2), 1.16–1.02 (m, 3 H, Me), 1.02–0.90 (m, 3 H, Me) ppm. IR (neat): $\tilde{\nu}$ = 2966, 2933, 1962, 1712, 1457, 1410, 1377, 1293, 1229, 1199 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 154 (19.88) [M^+], 97 (100). HRMS: Calcd. for $C_9H_{14}O_2$ (M^+): 154.0994; found 154.0997.

4. Preparation (±)-*trans*-*Z*-6: To a solution of **4** (46.7 mg, 0.3 mmol) in cyclohexane (4 mL) was added I_2 (0.1137 g, 0.45 mmol) with stirring at room temperature. After 1.5 h, the reaction was complete as monitored by TLC (eluent: petroleum ether/ethyl acetate = 5:1). It was quenched sequentially with H_2O (6 mL) and satd. aqueous solution of $Na_2S_2O_3$ (4 mL). The mixture was extracted with diethyl ether (30 mL × 3), washed with brine, and dried with Na_2SO_4. After filtration, evaporation of the solvent, and chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5:1) afforded (±)-*trans*-*Z*-**6** (0.0708 g, 83%, *Z*/*E* = 97:3) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.02 (t, *J* = 6.8 Hz, 1 H, EtC*H*=), 4.09 (d, *J* = 6.6 Hz, 1 H, =CI-C*H*), 2.81–2.70 (m, 1 H), 2.62–2.43 (m, 1 H), 2.27–2.12 (m, 3 H), 1.12 (d, *J* = 6.9 Hz, 3 H, Me), 1.00 (t, *J* = 7.7 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.4, 141.7, 105.5, 90.8, 36.2, 35.9, 29.1, 16.9, 12.3 ppm. IR (neat): $\tilde{\nu}$ = 2963, 2929, 2874, 1785, 1638, 1459, 1420, 1380, 1311, 1284, 1265, 1207, 1168, 1131, 1105, 1070, 1002 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 280 (100) [M^+]. HRMS: Calcd. for $C_9H_{13}IO_2$ (M^+): 279.9960; found 279.9969.

Synthesis of (–)-*trans*-Whisky Lactone [(–)-*trans*-14]

1. (3*S*,4*S*)-(+)-3-Methyl-4-(trimethylsilyl)ethynyloxetan-2-one [(3*S*,4*S*)-(+)-10]:[16] To a suspension of $MgCl_2$ (0.7536 g, 8 mmol) in 12 mL of anhydrous diethyl ether was added a solution of *N*,*N*-diisopropylethylamine (2.5826 g, 20 mmol) and *O*-(trimethylsilyl)-quinidine (0.3205 g, 0.8 mmol) in 25 mL of anhydrous CH_2Cl_2, under N_2 atmosphere. Then a solution of **9**[17,18] (0.9921 g, 8 mmol) in 5 mL of anhydrous CH_2Cl_2 was added at –80 °C. After being stirred at –80 °C for 20 min, a solution of propionyl chloride (1.4811 g, 16 mmol) in 10 mL of anhydrous CH_2Cl_2 was then added by a syringe pump (rate: 2 mL/h) at this temperature. The reaction mixture was stirred for 15 h at –80 °C and then quenched by adding a satd. aqueous NH_4Cl solution (50 mL). The resulting mixture was extracted with diethyl ether (50 mL × 3) and the combined organic extracts were washed successively with H_2O and brine, dried with Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel [eluent: petroleum ether (b.p. 30–60 °C)/ethyl acetate = 20:1] to afford (3*S*,4*S*)-(+)-**10** (1.3669 g, 94%) as a colorless oil. $[\alpha]_D^{20}$ = +10.7 (*c* = 2.72, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.12 (d, *J* = 6.3 Hz, 1 H, ≡CC*H*), 3.92–3.80 (m, 1 H, MeC*H*), 1.42 (d, *J* = 7.5 Hz, 3 H, Me), 0.21 (s, 9 H, $SiMe_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0, 98.3, 96.8, 64.5, 49.5, 10.2, –0.6 ppm. IR (neat): $\tilde{\nu}$ = 2962, 2179, 1839, 1458, 1381, 1339, 1252, 1138, 1083, 1053, 1018 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 182 (0.01) [M^+], 167 (1.65) [$M^+ - CH_3$], 123 (100). HRMS: Calcd. for $C_9H_{14}O_2Si$ (M^+): 182.0763; found 182.0765.

2. (3*S*,4*S*)-(–)-3-Methyl-4-ethynyloxetan-2-one[19] **[(3*S*,4*S*)-(–)-11]:** To a solution of (3*S*,4*S*)-(+)-**10** (0.7184 g, 4 mmol) in 4 mL of anhydrous THF was added a solution of TBAF in THF (4 mL, 1 M, 4 mmol) dropwise at –15 °C. After being stirred at this temperature for 15 min, the resulting mixture was filtered through a short column of silica gel eluting with CH_2Cl_2, and then concentrated in vacuo. The residue was purified by flash chromatography on silica gel [eluent: petroleum ether (b.p. 30–60 °C)/diethyl ether = 5:1] to afford (3*S*,4*S*)-(–)-**11** (0.2798 g, 64%) as a colorless oil. $[\alpha]_D^{20}$ = –5.5 (*c* = 1.14, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.11 (dd, J_1 = 6.5, J_2 = 2.3 Hz, 1 H, ≡CC*H*), 3.95–3.83 (m, 1 H, MeC*H*), 2.84 (d, *J* = 1.8 Hz, 1 H, *H*C≡), 1.40 (d, *J* = 7.5 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8, 80.4, 75.8, 64.0, 49.7, 10.2 ppm. IR (neat): $\tilde{\nu}$ = 3287, 2985, 2941, 2129, 1828, 1456, 1383, 1341, 1310, 1257, 1141, 1200, 1141, 1119, 1072, 1054, 1001 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 110 (0.07) [M^+], 66 (100). $C_6H_6O_2$ (110.11): calcd. C 65.45, H 5.49; found C 65.57, H 5.38.

3. (R_a,*S*)-(–)-2-Methylhepta-3,4-dienoic Acid[19] **[(R_a,*S*)-(–)-12]:** To a mixture of $CuBr{\cdot}SMe_2$ (22.8 mg, 0.11 mmol) and dimethyl sulfide (0.5 mL), was added a solution of (3*S*,4*S*)-(–)-**11** prepared above (120.5 mg, 11.3 mmol) in 10 mL of anhydrous THF under N_2 atmosphere. Then a solution of EtMgBr (3.3 mL, 1 M in THF, 3.3 mmol) was added dropwise to the mixture at –78 °C within 10 min. After being stirred at –78 °C for additional 25 min, the reaction was quenched with a satd. aqueous NH_4Cl solution (50 mL), and then acidified with 5% HCl (aq.) to pH = 1. The resulting mixture was extracted with diethyl ether (30 mL × 3), successively washed with H_2O and brine, dried with Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3:1) to afford (R_a,*S*)-(–)-**12** (113.5 mg, 74%) as colorless oil. $[\alpha]_D^{20}$ = –135.7 (*c* = 0.86, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 11.6 (br. s, 1 H, COO*H*), 5.39–5.24 (m, 2 H, C*H*=), 3.21–3.04 (m, 1 H, C*H*COO), 2.09–1.94 (m, 2 H, MeCH_2), 1.27 (d, *J* = 6.9 Hz, 3 H, Me), 0.99 (t, *J* = 7.2 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.4, 181.4, 95.6, 91.4, 39.2, 21.7, 16.1, 13.2 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2933, 1965, 1711, 1459, 1412, 1378, 1281, 1224 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 140 (7.77) [M^+], 125 (100). HRMS: Calcd. for $C_8H_{12}O_2$ (M^+): 140.0837; found 140.0843.

4. (R_a,*S*)-(–)-2-Methylhepta-3,4-dien-1-ol[15] **[(R_a,*S*)-(–)-2]:** To an ice-cold suspension of $LiAlH_4$ (0.2478 g, 6.5 mmol) in anhydrous diethyl ether (30 mL) under N_2 was added dropwise a solution of (R_a,*S*)-(–)-**12** (0.7273 g, 5.2 mmol) in anhydrous diethyl ether (10 mL). After 50 min, the reaction was complete as monitored by TLC, diluted with 60 mL of Et_2O, quenched by slow addition of an aqueous NaOH solution (aq., 5 M, 1.3 mL, 6.5 mmol), then filtered to remove the solid, evaporated, and purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1) to afford (R_a,*S*)-(–)-**2** (0.5024 g, 77%) as a colorless oil. $[\alpha]_D^{20}$ = –108.4 (*c* = 1.37, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.28–5.16 (m, 1 H, C*H*=), 5.12–5.02 (m, 1 H, C*H*=), 3.45 (d, *J* = 6.3 Hz, 2 H, CH_2OH), 2.40–2.20 (m, 2 H, C*H*CH_2O*H*), 2.05–1.90 (m, 2 H, MeCH_2), 1.05–0.90 (m, 6 H, 2×Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.9, 94.1, 94.0, 67.4, 36.1, 21.8, 16.5, 13.2 ppm. IR (neat): $\tilde{\nu}$ = 3356, 2964, 2930, 2872, 1959, 1459, 1377, 1325, 1263, 1034 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 126 (4.80) [M^+], 67 (100). HRMS: Calcd. for $C_8H_{14}O$ (M^+): 126.1045; found 126.1043.

5. (R_a,*R*)-(–)-3-Methylocta-4,5-dienenitrile[15] **[(R_a,*R*)-(–)-3]:** Following the procedure for the preparation of racemic **3**, the reaction of (R_a,*S*)-(–)-**2** (0.4209 g, 3.3 mmol) and *p*TsCl (1.9081 g, 10.0 mmol) in dry pyridine (10 mL) afforded tosylate, which was then used in the next step without further purification. The reaction of NaCN (0.1747 g, 3.6 mmol) and the product prepared above in anhydrous DMSO (5 mL) afforded (R_a,*R*)-(–)-**3** [0.3470 g, the combined yield from (R_a,*S*)-(–)-**2** to (R_a,*R*)-(–)-**3** is 77%] as a colorless oil. $[\alpha]_D^{20}$ = –50.9 (*c* = 1.08, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.39–5.29 (m, 1 H, C*H*=), 5.20–5.12 (m, 1 H, C*H*=), 2.60–2.44 (m, 1 H, C*H*CH_2CN), 2.44–2.23 (m, 2 H, CH_2CN), 2.09–1.92 (m, 2 H, MeCH_2), 1.13 (d, *J* = 6.6 Hz, 3 H, Me), 0.97 (t, *J* = 7.2 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.1, 118.4, 95.7, 94.6, 30.0, 24.0, 21.6, 19.6, 13.0 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2933, 2874, 2247, 1963, 1459, 1420, 1379, 1322, 1072 cm^{-1}.

MS (70 eV, EI): *m*/*z* (%) = 135 (6.97) [M^+], 120 (100). HRMS: Calcd. for $C_9H_{13}N$ (M^+): 135.1048; found 135.1046.

6. (R_a,*R*)-(–)-3-Methylocta-4,5-dienoic Acid[15] [(R_a,*R*)-(–)-4]: Following the procedure for the preparation of racemic **4**, the reaction of (R_a,*R*)-(–)-**3** (0.2883 g, 2.1 mmol), ethanol (5 mL), and NaOH solution (1.4630 g in 1.8 mL of H_2O, 36 mmol) afforded (R_a,*R*)-(–)-**4** [0.3182 g, 97%, (R_a,*R*)-**4**/(S_a,*R*)-**4** = 12.5:1, the *dr* value was determined by inverse gated decoupling ^{13}C NMR analysis[23]] as a yellow oil. $[\alpha]_D^{20}$ = –67.3 (*c* = 1.98, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 11.45 (br. s, 1 H, COO*H*), 5.30–5.08 (m, 2 H, C*H*=C=C*H*), 2.72–2.58 (m, 1 H, C*H*CH_2COO), 2.50–2.39 (m, 1 H), 2.35–2.23 (m, 1 H), 2.05–1.92 (m, 2 H, MeCH_2), 1.08 (d, *J* = 6.9 Hz, 3 H, Me), 0.99 (t, *J* = 7.4 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.1, 179.3, 96.2, 95.0, 41.1, 29.8, 21.9, 20.3, 13.2 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2932, 1962, 1709, 1457, 1411, 1377, 1294, 1231, 1199, 1070, 938, 876 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 154 (18.41) [M^+], 97 (100). HRMS: Calcd. for $C_9H_{14}O_2$ (M^+): 154.0994; found 154.0993.

7. (4*R*,5*R*)-(–)-5-[(1*Z*)-1-Iodo-1-butenyl]-4-methyl-4,5-dihydro-2(3*H*)-furanone[14a] [(4*R*,5*R*)-(–)-*Z*-6]: Following the procedure for the preparation of racemic *trans*-*Z*-**16**, the reaction of (R_a,*R*)-(–)-**4** (77.3 mg, 0.5 mmol) and I_2 (191.6 mg, 0.75 mmol) in cyclohexane (7.5 mL) afforded (4*R*,5*R*)-(–)-*Z*-**6** [0.1179 g, 84%, *Z*/*E* = 97:3, 98.6% *ee*, HPLC conditions: Chiralcel OJ-H column; rate, 0.8 mL/min; eluent, hexane/*i*PrOH = 90:10; λ = 254 nm; t_R 14.0 min (major), 20.7 min (minor)] as a colorless oil. $[\alpha]_D^{20}$ = –39.7 (*c* = 2.05, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.03 (t, *J* = 6.6 Hz, 1 H, EtC*H*=), 4.11 (d, *J* = 7.2 Hz, 1 H, =CI-C*H*), 2.83–2.71 (m, 1 H), 2.63–2.46 (m, 1 H), 2.29–2.14 (m, 3 H), 1.14 (d, *J* = 6.6 Hz, 3 H, Me), 1.02 (t, *J* = 7.5 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.4, 141.6, 105.5, 90.9, 36.3, 36.0, 29.1, 17.1, 12.4 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2932, 2875, 1789, 1637, 1459, 1420, 1381, 1311, 1284, 1265, 1208, 1169, 1131, 1002 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 280 (100) [M^+]. HRMS: Calcd. for $C_9H_{13}IO_2$ (M^+): 279.9960; found 279.9966.

8. (4*R*,5*R*)-(–)-5-(But-1-ynyl)-4-methyl-4,5-dihydro-2(3*H*)-furanone [(4*R*,5*R*)-(–)-13]:[22] To a solution of (4*R*,5*R*)-(–)-*Z*-**6** (0.1018 g, 0.36 mmol) in DMF (4 mL) was added TBAF (1.1 mL, 1 M in THF, 1.1 mmol), and the mixture was stirred at 25 °C for 5 h. After the reaction was complete as monitored by TLC (petroleum ether/ethyl acetate = 5:1), it was quenched with H_2O, acidified with 5% HCl (aq.) to pH = 1, and extracted with diethyl ether (30 mL × 3). The combined organic layer was washed with water and brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. Chromatography on silica gel [eluent: petroleum ether (b.p. 30–60 °C)/ethyl acetate = 5:1] of the crude product afforded (4*R*,5*R*)-(–)-**13** [0.0509 g, 92%, 98.8% *ee*, GC conditions: column: CP-Chirasil-DEX CB (25 m, 0.25 mm ID, 0.25 μm DF); carrier: N_2, 10.8 psi; injector: 250 °C; detector (FID, H_2, 0.11 MPa): 250 °C; oven temperature: 130 °C (60 min); t_R = 12.7 min (minor), 13.8 min (major)] as a colorless oil. $[\alpha]_D^{20}$ = –50.8 (*c* = 1.68, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 4.59 (dt, J_1 = 6.9, J_2 = 2.1 Hz, 1 H, ≡CC*H*), 2.80–2.68 (m, 1 H), 2.62–2.44 (m, 1 H), 2.30–2.09 (m, 3 H), 1.17 (d, *J* = 6.6 Hz, 3 H, Me), 1.12 (t, *J* = 7.5 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.5, 90.2, 75.9, 74.8, 38.5, 36.1, 17.0, 13.4, 12.3 ppm. IR (neat): $\tilde{\nu}$ = 2973, 2916, 2244, 1783, 1460, 1421, 1365, 1318, 1280, 1211, 1148, 1095, 993 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 152 (0.39) [M^+], 83 (100). HRMS: Calcd. for $C_9H_{12}O_2$ (M^+): 152.0837; found 152.0836.

9. (–)-*trans*-Whisky Lactone [(–)-*trans*-14]: To an autoclave was added (4*R*,5*R*)-(–)-**13** (46.1 mg, 0.30 mmol), ethyl acetate (6 mL), and Pd/C (dry, 10%, 33.1 mg, 0.03 mmol) sequentially. Then the mixture was stirred under H_2 (25 atm) at room temperature for 1 d, and the resulting mixture was filtered through a short column of silica gel eluted with diethyl ether. The filtrate was concentrated in vacuo. Chromatography on silica gel [eluent: petroleum ether (b.p. 30–60 °C)/ethyl acetate = 3:1] of the crude product to afford pure (–)-*trans*-whisky lactone [0.0405 g, 86%, 98.5% *ee*, GC conditions: column: CP-Chirasil-DEX CB (25 m, 0.25 mm ID, 0.25 μm DF); carrier: N_2, 10.8 psi; injector: 250 °C; detector(FID, H_2, 0.11 MPa): 250 °C; oven temperature: 130 °C (60 min); t_R = 12.3 min (minor), 12.6 min (major)] as a colorless oil. $[\alpha]_D^{20}$ = –82.5 (*c* = 1.02, MeOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 4.04–3.92 (m, 1 H, BuC*H*), 2.72–2.54 (m, 1 H), 2.28–2.08 (m, 2 H), 1.73–1.28 [m, 6 H, -(CH_2)$_3$-], 1.10 (d, *J* = 6.3 Hz, 3 H, Me), 0.88 (t, *J* = 7.1 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6, 87.3, 37.0, 36.0, 33.6, 27.7, 22.4, 17.3, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 2960, 2933, 2874, 1782, 1460, 1423, 1383, 1331, 1282, 1255, 1211, 1172, 1124, 1078, 986 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 156 (1.17) [M^+], 99 (100). HRMS: Calcd. for $C_9H_{16}O_2$ (M^+): 156.1150; found 156.1148.

Preparation of (+)-*trans*-Whisky Lactone (14)

1. (3*R*,4*R*)-(–)-3-Methyl-4-(trimethylsilyl)ethynyloxetan-2-one[16] [(3*R*,4*R*)-(–)-10]: Following the procedure for the preparation of (3*S*,4*S*)-(+)-**10**, the reaction of $MgCl_2$ (1.9010 g, 20 mmol), anhydrous diethyl ether (30 mL), *N*,*N*-diisopropylethylamine (6.4613 g, 50 mmol), *O*-trimethylsilylquinine (0.8006 g, 2.0 mmol), 60 mL of anhydrous CH_2Cl_2, **9**[17,18] (2.5013 g, 20 mmol)/anhydrous CH_2Cl_2 (10 mL), and propionyl chloride (3.7112 g, 40 mmol)/anhydrous CH_2Cl_2 (10 mL) afforded (3*R*,4*R*)-(–)-**10** (3.2181 g, 88%) as a colorless oil. $[\alpha]_D^{20}$ = –13.3 (*c* = 1.45, $CHCl_3$); lit. $[\alpha]_D$ = –11.9 (*c* = 2.6, $CHCl_3$);[14a] ^1H NMR (300 MHz, $CDCl_3$): δ = 5.11 (d, *J* = 6.6 Hz, 1 H, ≡CC*H*), 3.92–3.81 (m, 1 H, MeC*H*), 1.41 (d, *J* = 7.8 Hz, 3 H, Me), 0.20 (s, 9 H, $SiMe_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.1, 98.5, 96.8, 64.6, 49.6, 10.3, –0.5 ppm. IR (neat): $\tilde{\nu}$ = 2963, 2902, 2180, 1841, 1455, 1412, 1382, 1338, 1308, 1252, 1198, 1138, 1083, 1053, 1018, 844, 762 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 183 (0.36) [M^+ + 1], 182 (0.24) [M^+], 123 (100). HRMS: Calcd. for $C_9H_{14}O_2Si$ (M^+): 182.0763; found 182.0766.

2. (S_a,*R*)-(+)-2-Methylhepta-3,4-dienoic Acid[19] [(S_a,*R*)-(+)-12]: Following the procedure for the preparation of (3*S*,4*S*)-(–)-**11**, the reaction of (3*R*,4*R*)-(–)-**10** (2.7344 g, 15 mmol) and tetrabutylammonium fluoride (15 mL, 1 M in THF, 15 mmol) in 15 mL of THF afforded (3*R*,4*R*)-(+)-**11** as a colorless oil. It was used in the next step without any purification. Following the procedure for the preparation of (R_a,*S*)-(–)-**12**, the mixture of (3*R*,4*R*)-(+)-**11** prepared above, CuBr·SMe_2 (234.1 mg, 1.13 mmol), dimethylsulfide (7.5 mL), and anhydrous THF (128 mL) was treated with EtMgBr (34 mL, 1 M in THF, 34 mmol) at –78 °C for 2.2 h to afford (S_a,*R*)-(+)-**12** (1.1887 g, combined yield of two steps is 57%) as colorless oil. $[\alpha]_D^{20}$ = +129.5 (*c* = 0.91, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 11.5 (br. s, 1 H, COO*H*), 5.40–5.24 (m, 2 H, C*H*=C=C*H*), 3.21–3.04 (m, 1 H, C*H*COO), 2.09–1.94 (m, 2 H, MeCH_2), 1.27 (d, *J* = 6.4 Hz, 3 H, Me), 1.00 (t, *J* = 7.6 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.4, 181.4, 95.6, 91.4, 39.2, 21.7, 16.1, 13.2 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2936, 1964, 1711, 1459, 1413, 1378, 1329, 1261, 1225, 1078, 1029, 905, 876 cm^{-1}. MS (70 eV, EI): *m*/*z* (%) = 140 (10.92) [M^+], 125 (100). HRMS: Calcd. for $C_8H_{12}O_2$ (M^+): 140.0837; found 140.0840.

3. (S_a,*R*)-(+)-2-Methylhepta-3,4-dien-1-ol[15] [(S_a,*R*)-(+)-2]: Following the procedure for the preparation of **2**, the suspension of $LiAlH_4$ (0.5382 g, 14.2 mmol) in anhydrous diethyl ether (60 mL) under N_2 was treated with a solution of (S_a,*R*)-(+)-**12** (1.6390 g, 11.7 mmol) in anhydrous diethyl ether (10 mL) to afford (S_a,*R*)-(+)-**2** (1.0931 g, 74%) as a colorless oil. $[\alpha]_D^{20}$ = +93.1 (*c* = 1.39,

$CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.28–5.16 (m, 1 H, C*H*=), 5.12–5.02 (m, 1 H, C*H*=), 3.46 (t, J = 5.6 Hz, 2 H, CH_2O), 2.40–2.25 (m, 1 H), 2.10 (br. s, 1 H, -O*H*), 2.05–1.90 (m, 2 H, MeCH_2), 1.05–0.90 (m, 6 H, 2 × Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.8, 94.0, 93.9, 67.3, 35.9, 21.7, 16.3, 13.1 ppm. IR (neat): $\tilde{\nu}$ = 3331, 2965, 2932, 2872, 1960, 1457, 1376, 1325, 1035, 876 cm^{-1}. MS (70 eV, EI): m/z (%) = 126 (4.46) [M^+], 67 (100). HRMS: Calcd. for $C_8H_{14}O$ (M^+): 126.1045; found 126.1047.

4. (*S*$_a$,*S*)-(+)-3-Methylocta-4,5-dienenitrile[15] [(*S*$_a$,*S*)-(+)-3]: Following the procedure for the preparation of racemic **3**, the reaction of (*S*$_a$,*R*)-(+)-**2** (0.8450 g, 6.7 mmol) and *p*TsCl (3.9297 g, 20.6 mmol) in dry pyridine (10 mL) afforded tosylate, which was then used in the next step without further purification. The reaction of NaCN (0.3528 g, 7.2 mmol) and the product prepared above in anhydrous DMSO (10 mL) afforded (*S*$_a$,*S*)-(+)-**3** [0.6637 g, the combined yield from (*S*$_a$,*R*)-(+)-**2** to (*S*$_a$,*S*)-(+)-**3** is 73%] as a colorless oil. $[\alpha]_D^{20}$ = +43.6 (c = 0.83, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.39–5.29 (m, 1 H, C*H*=), 5.21–5.12 (m, 1 H, C*H*=), 2.62–2.47 (m, 1 H, C*H*CH$_2$CN), 2.46–2.26 (m, 2 H, CH_2CN), 2.09–1.95 (m, 2 H, MeCH_2), 1.18 (d, J = 6.6 Hz, 3 H, Me), 1.01 (t, J = 7.4 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.2, 118.6, 95.9, 94.7, 30.1, 24.1, 21.7, 19.8, 13.1 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2933, 2873, 2247, 1962, 1459, 1421, 1379, 1321, 1273 cm^{-1}. MS (70 eV, EI): m/z (%) = 135 (7.01) [M^+], 120 (100). HRMS: Calcd. for $C_9H_{13}N$ (M^+): 135.1048; found 135.1045.

5. (*S*$_a$,*S*)-(+)-3-Methylocta-4,5-dienoic[15] [(*S*$_a$,*S*)-(+)-4]: Following the procedure for the preparation of **4**, the reaction of (*S*$_a$,*S*)-(+)-**3** (0.6011 g, 4.5 mmol), ethanol (11 mL), and NaOH solution (3.0831 g in 4 mL of H_2O, 77 mmol) afforded (*S*$_a$,*S*)-(+)-**4** [0.6282 g, 92%, (*S*$_a$,*S*)-**4**/(*R*$_a$,*S*)-**4** = 12.5:1, the *dr* value was determined by inverse gated decoupling ^{13}C NMR analysis[23]] as a yellow oil. $[\alpha]_D^{20}$ = +69.1 (c = 1.71, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 12.00 (br. s, 1 H, COO*H*), 5.30–5.08 (m, 2 H, C*H*=C=C*H*), 2.74–2.57 (m, 1 H, C*H*CH$_2$COO), 2.50–2.38 (m, 1 H), 2.35–2.23 (m, 1 H), 2.05–1.92 (m, 2 H, MeCH_2), 1.08 (d, J = 6.6 Hz, 3 H, Me), 0.98 (t, J = 7.4 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.1, 179.6, 96.2, 95.0, 41.2, 29.8, 21.9, 20.3, 13.2 ppm. IR (neat): $\tilde{\nu}$ = 2966, 2932, 1962, 1710, 1457, 1411, 1376, 1294, 1230, 1199, 1070 cm^{-1}. MS (70 eV, EI): m/z (%) = 154 (22.55) [M^+], 97 (100). HRMS: Calcd. for $C_9H_{14}O_2$ (M^+): 154.0994; found 154.0993.

6. (4*S*,5*S*)-(+)-5-[1′-Iodo-1′(*Z*)-butenyl]-4-methyl-4,5-dihydro-2(3*H*)-furanone[14a] [(4*S*,5*S*)-(+)-*Z*-6]: Following the procedure for the preparation of *trans*-*Z*-**6**, the reaction of (*S*$_a$,*S*)-(+)-**4** (243.4 mg, 1.6 mmol) and I_2 (0.6061 g, 2.4 mmol) in cyclohexane (24 mL) afforded (4*S*,5*S*)-(+)-*Z*-**6** [0.3810 g, 86%, *Z*/*E* = 98:2, 99.3% *ee*, HPLC conditions: Chiralcel OJ-H column; rate, 0.8 mL/min; eluent, hexane/*i*PrOH = 90:10; λ = 254 nm; t_R = 14.2 min (minor), 19.8 min (major)] as a colorless oil. $[\alpha]_D^{20}$ = +37.2 (c = 2.45, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.03 (td, J_1 = 6.8, J_2 = 0.6 Hz, 1 H, EtC*H*=), 4.10 (d, J = 6.9 Hz, 1 H, =CI-C*H*), 2.82–2.70 (m, 1 H), 2.61–2.43 (m, 1 H), 2.27–2.14 (m, 3 H), 1.13 (d, J = 6.6 Hz, 3 H, Me), 1.01 (t, J = 7.5 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.4, 141.7, 105.5, 90.9, 36.3, 35.9, 29.1, 17.0, 12.4 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2932, 2875, 1785, 1637, 1458, 1419, 1381, 1284, 1265, 1209, 1169, 1132, 1002, 940, 914 cm^{-1}. MS (70 eV, EI): m/z (%) = 280 (56.05) [M^+], 83 (100). HRMS: Calcd. for $C_9H_{13}IO_2$ (M^+): 279.9960; found 279.9957.

7. (4*S*,5*S*)-(+)-5-(But-1-ynyl)-4-methyl-4,5-dihydro-2(3*H*)-furanone[22] [(4*S*,5*S*)-(+)-13]: Following the procedure for the preparation of (4*R*,5*R*)-(–)-**13**, the reaction of (4*S*,5*S*)-(+)-*Z*-**6** (0.2768 g, 0.99 mmol) and TBAF (3 mL, 1 M in THF, 3 mmol) in DMF (11 mL) afforded (4*S*,5*S*)-(+)-**13** [0.1361 g, 89%, 98.9% *ee*, GC conditions: CP-Chirasil-DEX CB (25 m, 0.25 mm ID, 0.25 μm DF); carrier: N_2, 10.8 psi; injector: 250 °C; detector (FID, H_2, 0.11 MPa): 250 °C; oven temperature: 130 °C (60 min); t_R = 12.7 min (major), 13.9 min (minor)] as a colorless oil. $[\alpha]_D^{20}$ = +51.0 (c = 0.86, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 4.59 (dt, J_1 = 6.6, J_2 = 1.8 Hz, 1 H, ≡CC*H*), 2.80–2.68 (m, 1 H), 2.62–2.44 (m, 1 H), 2.30–2.09 (m, 3 H), 1.18 (d, J = 6.6 Hz, 3 H, Me), 1.13 (t, J = 7.5 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.5, 90.3, 75.9, 74.9, 38.6, 36.1, 17.0, 13.4, 12.3 ppm. IR (neat): $\tilde{\nu}$ = 2977, 2939, 2880, 2244, 1785, 1458, 1420, 1365, 1319, 1280, 1211, 1148, 1095 cm^{-1}. MS (70 eV, EI): m/z (%) = (%)153 (26.26) [M^+ + 1], 152 (3.75) [M^+], 83 (100). HRMS: Calcd. for $C_9H_{12}O_2$ (M^+): 152.0837; found 152.0832.

8. (+)-*trans*-Whisky Lactone [(+)-*trans*-14]: Following the procedure for the preparation of (–)-*trans*-whisky lactone, the mixture of (4*S*,5*S*)-(+)-**13** (117.9 mg, 0.78 mmol), ethyl acetate (16 mL), and Pd/C (dry, 10%, 84.1 mg, 0.078 mmol) was stirred under H_2 atmosphere (25 atm) at room temperature for 1 d to afford pure (+)-*trans*-whisky lactone[10] [0.1090 g, 90%, 98.5% *ee*, GC conditions: CP-Chirasil-DEX CB (25 m, 0.25 mm ID, 0.25 μm DF); carrier: N_2, 10.8 psi; injector: 250 °C; detector (FID, H_2, 0.11 MPa): 250 °C; oven temperature: 120 °C (60 min); t_R = 18.3 min (major), 20.5 min (minor)] as a colorless oil. $[\alpha]_D^{20}$ = +81.2 (c = 1.24, MeOH), lit. $[\alpha]_D^{15}$ = +79 (c = 1.04, MeOH);[3a] ^1H NMR (300 MHz, $CDCl_3$): δ = 4.02–3.92 (m, 1 H, BuC*H*), 2.73–2.54 (m, 1 H), 2.28–2.08 (m, 2 H), 1.73–1.25 [m, 6 H, -(CH_2)$_3$-], 1.11 (d, J = 6.6 Hz, 3 H, Me), 0.89 (t, J = 7.2 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6, 87.4, 37.0, 36.0, 33.6, 27.8, 22.4, 17.4, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 2960, 2934, 2874, 1782, 1461, 1424, 1382, 1331, 1283, 1255, 1212, 1172, 1125, 1078 cm^{-1}. MS (70 eV, EI): m/z (%) = 157 (100) [M^+ + 1], 156 (6.15) [M^+]. HRMS: Calcd. for $C_9H_{16}O_2$ (M^+): 156.1150; found 156.1148.

The **Supporting Information** (see also the footnote on the first page of this article): ^1H NMR, ^{13}C NMR, and HPLC spectra of all compounds. Table S1 shows details for the deiodination of (±)-*trans*-*Z*-**6**.

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