Synthesis of (*R*)-(−)-3-Methoxymethyl-3-propyl-3,4-dihydrocoumarin from a Chiral Michael Adduct: Absolute Configurations of the Allylated Products of Enantioselective Radical-Mediated Reactions

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(*R*)-3-Methoxymethyl-3-propyl-3,4-dihydrocoumarin was synthesized, starting from a chiral Michael adduct [(*S*)-methyl 2,3-dihydro-1-oxo-2-(3-oxobutyl)-1*H*-indene-2-carboxylate], in order to determine the absolute configurations of the products obtained by enantioselective radical-mediated allylation. Aldol cyclization of the Michael adduct proceeded smoothly with suppression of the retro Michael reaction to afford an optically active cyclized product. The Baeyer–Villiger reaction of (*R*)-2-methoxymethyl-2-propylindanone in the presence of $BF_3 \cdot Et_2O$ afforded the desired dihydrocoumarin.

Key words absolute configuration; 3-methoxymethyl-3-propyldihydrocoumarin; aldol reaction; Baeyer–Villiger reaction

In the field of asymmetric synthesis, construction of chiral quaternary carbon centers has received wide attention.[1,2] Asymmetric induction in radical-mediated reactions is also a current topic in synthetic organic chemistry.[2,3] We have reported the efficient creation of chiral quaternary carbon centers by enantioselective radical-mediated reactions catalyzed by a chiral Lewis acid. For example, the reactions of 3-alkyl-3-iododihydrocoumarins **1** with allyltributyltin in the presence of a chiral aluminum reagent proceeded enantioselectively to afford optically active 3-alkyl-3-allyldihydrocoumarins **2** as shown in Chart 1.[2] The absolute configurations of the allylated products **2** were determined by circular dichroism measurements of their derivatives.[2a] To confirm the result of such an empirical method for determining the absolute configurations of **2**, a direct chemical correlation of **2** with a configurationally defined compound seemed necessary. The present paper deals with the synthesis of (*R*)-3-methoxymethyl-3-propyldihydrocoumarin starting from a chiral Michael adduct, [(*S*)-methyl 2,3-dihydro-1-oxo-2-(3-oxobutyl)-1*H*-indene-2-carboxylate (**3**)], in order to determine the absolute configurations of **2** obtained by enantioselective radical-mediated allylation.

In our synthetic strategy, the methoxycarbonyl and 3-oxobutyl groups of a Michael adduct (*S*)-**3**, which is prepared by the asymmetric reaction reported by Wynberg and other workers,[4] are converted into methoxymethyl and propyl groups, respectively. In this study, the crucial steps are as follows: an aldol cyclization of (*S*)-**3** with suppression of the retro Michael reaction, and the Baeyer–Villiger reaction of an indanone, having a chiral quaternary carbon center, to afford an optically active dihydrocoumarin (Chart 2).

To protect the ketone moiety, conversion of (*S*)-**3** into enone **4** was considered. At first, aldol cyclization of a chiral Michael adduct (*S*)-**3** was carried out as described in the literature.[4b] Namely, treatment of (*S*)-**3** with NaOMe in MeOH provided enone **4**, the specific rotation of which, however, had a lower value {$[\alpha]_{577}$ +75.3° (c=2.58, benzene)} than that reported in the literature.[5] This result suggested that partial racemization, which is attributed to a retro Michael reaction and recombination of the side chain under basic conditions, occurred easily through the cyclization reaction. Indeed, cleavage of the side chain of the **3**, 3-oxobutyl group, took place quantitatively on treatment with *tert*-BuOK in *tert*-BuOH to give the carbomethoxyindanone. To improve the optical purity of the enone, we examined the cyclization under mild conditions. The aldol cyclization of (*S*)-**3** in benzene with pyrrolidine and acetic acid was found to give **4** in 61% isolated yield. The degree of specific rotation of this product was $[\alpha]_{577}$ +279.3° (c=2.44, benzene).

With the optically active **4** available, we next focused our attention on the preparation of indanone **13**. Protection of the carbonyl group in the enone moiety in **4** provided ketal **5** in 53% yield. For conversion of the ester moiety, reduction of **5** with $LiAlH_4$ was carried out to give alcohol **6** in 92% yield, and methylation of this with MeI and NaH gave **7** in 93% yield. Deprotection of the ketal group in **7**, using SiO_2–10% aqueous oxalic acid, gave enone **8** in 97% yield.[6] Oxidative cleavage of the enone moiety in **8**, by ozone–H_2O_2, gave acid **9** to regenerate the indanone structure and remove one carbon atom. Selective reduction of the carboxyl group was carried out using borane–tetrahydrofuran complex ($BH_3 \cdot THF$) to give indanone **10** having an alcohol moiety, in 96% yield. Chlorination of alcohol **10** gave **11**, but reduction with tributyltin hydride did not produce a propyl group. Therefore, **11** was converted into iodide **12** in 88% yield. Reduction of **12** with tributyltin hydride successfully afforded (*R*)-2-methoxymethyl-2-propylindanone **13**.

Next, conversion of indanone **13** into dihydrocoumarin **14** by the Baeyer–Villiger oxidation was examined.[7,8] It is known that the reaction of indanone with CF_3CO_3H–CF_3CO_2H, perbenzoic acid or AcOH–H_2O_2, gives dihydrocoumarin.[7a—c] It is also reported that reaction of 2-methylindanones with CF_3CO_3H–Na_2HPO_4 gives the corresponding dihydrocoumarins.[7d] Recently, we reported that oxidation

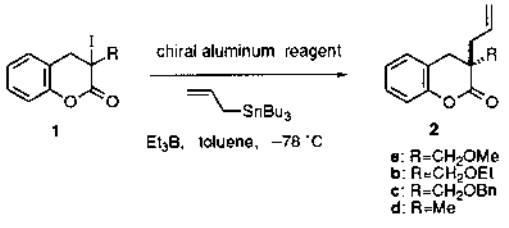

Chart 1

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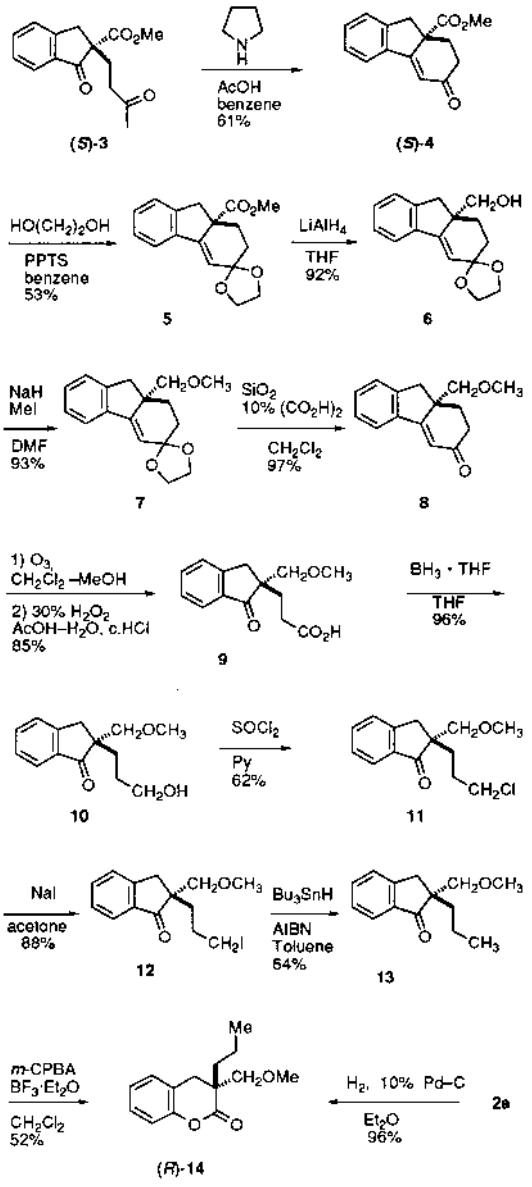

Chart 2

of 2-methoxymethylindanone using *m*-chloroperoxybenzoic acid (*m*-CPBA) afforded 3-methoxymethyldihydrocoumarin.[7e] However, indanone **13** under these conditions did not afford the desired product. Other agents, such as *m*-CPBA–CF_3CO_2H, *m*-CPBA–Na_2HPO_4, AcOOH, AcOOH–Na_2HPO_4, $K_2S_2O_8$–H_2SO_4, ceric ammonium nitrate or O_2–PhCHO–Fe_2O_3, were also found to be unsuitable for the oxidation of **13**.[8] These results are understandable because steric hindrance of the quaternary carbon adjacent to the carbonyl group, the reactivity of which is reduced due to conjugation to the benzene ring, influences the approach of the peracid.[9] Therefore, reaction in the presence of a Lewis acid, which would coordinate to the carbonyl group of **13** so that the energy of the transition state would be lower, was considered. As expected, the best result was obtained when the reaction was carried out in the presence of $BF_3 \cdot Et_2O$.[8a] Reaction of **13** with *m*-CPBA and $BF_3 \cdot Et_2O$ in CH_2Cl_2 at room temperature afforded (*R*)-**14** in 52% yield. The enantiomeric excess of (*R*)-**14** was determined by HPLC using a chiral column and found to be 92%, reflecting the enantiomeric purity of **4**.

On the other hand, hydrogenation of **2a** afforded **14**, the specific rotation of which was identical to that of (*R*)-**14** prepared from (*S*)-**3** (Chart 2). Thus, the absolute configuration of all the allylated products obtained by our enantioselective radical-mediated reactions was found to be *R*, because **2b**—**d** had already been correlated with **2a** by a chemical method.[2a]

In conclusion, the absolute configuration of **2a** was unequivocally established. The result is consistent with the previously assigned configuration using circular dichroism measurements. It was also demonstrated that a chiral Michael adduct was useful as a synthon for the synthesis of optically active indanones and dihydrocoumarins. These findings should provide an efficient approach to the syntheses of five- and six-membered optically active cyclic compounds bearing quaternary carbon centers.

Experimental

General All melting points were measured on a Yanagimoto (hot plate) melting point apparatus and are uncorrected. IR spectra were obtained with a Hitachi 260-10 or a Horiba FT-210 spectrophotometer. ^{1}H-NMR (270 MHz) and ^{13}C-NMR (67.5 MHz) spectra were recorded with a JEOL EX-270 spectrometer in $CDCl_3$ solution using tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi M-80, a JEOL JMS D-300 or a JEOL JMS-SX102A spectrometer. Specific rotations were measured on a JASCO DIP-360 digital polarimeter. The enantiomeric excess (ee) of **14** was determined by HPLC using chiral columns (DAICEL). Column chromatography was performed on silica gel.

A chiral Michael adduct (*S*)-**3** was prepared according to the method reported by Wynberg and his co-workers.[4a,b] After recrystallization from benzene–Et_2O, conversion of (*S*)-**3** was carried out.

Methyl (*S*)-1,2,9,9a-Tetrahydro-3-oxo-3*H*-fluorene-9a-carboxylate (4)[4b] To a solution of (*S*)-**3** {10.0 g, 38.5 mmol, $[\alpha]_{577}^{rt}$ −70.4° (*c*=2.16, benzene)} in benzene (175 ml) were added pyrrolidine (13 ml, 156 mmol) and AcOH (20 ml, 349 mmol). The mixture was stirred for 20 h at room temperature. After addition of water, the resulting mixture was extracted with benzene (50 ml×2). The extracts were washed successively with 10% aqueous HCl, saturated $NaHCO_3$ and saturated NaCl, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (Et_2O : hexane=1 : 1) followed by rinsing with Et_2O–hexane to afford (*S*)-**4** (5.7 g, 61%). mp 114—115 °C. $[\alpha]_{577}^{rt}$ +279.3° (*c*=2.44, benzene), $[\alpha]_{546}^{27}$ +354.0° (*c*=1.99, benzene). IR (Nujol) cm^{-1}: 2960, 2943, 2937, 2912, 2858, 1724, 1662, 1632, 1601, 1259, 1201, 1182. ^{1}H-NMR δ: 2.10—2.22 (1H, m), 2.51—2.56 (2H, m), 2.73—2.80 (1H, m), 3.05, 3.57 (each 1H, d, *J*=16.7 Hz), 3.63 (3H, s), 6.37 (1H, s), 7.29—7.63 (4H, m). ^{13}C-NMR δ: 32.9, 35.1, 43.0, 52.8, 54.4, 119.1 122.8, 125.3, 127.7, 131.9, 138.0, 145.6, 164.4, 173.8, 198.6.

(*S*)-3,3-Ethylenedioxy-9a-methoxycarbonyl-1,2,9,9a-tetrahydro-3*H*-fluorene (5) To a solution of (*S*)-**4** (10.0 g, 41.0 mmol) in benzene (150 ml) were added ethylene glycol (38 ml, 680.0 mmol) and pyridinium *p*-toluenesulfonate (PPTS) (2 g, 11.6 mmol). The resulting mixture was refluxed for 4 d in a flask equipped with a Dean–Stark trap. After addition of saturated $NaHCO_3$, the resulting mixture was extracted with benzene (50 ml×2). The extracts were washed successively with water and saturated NaCl, and dried over K_2CO_3. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (benzene : acetone= 8 : 1) followed by rinsing with Et_2O–hexane to afford (*S*)-**5** (6.23 g, 53%). mp 169—172 °C (iso-Pr_2O). $[\alpha]_{546}^{30}$ +178.0° (*c*=2.02, benzene). IR (Nujol) cm^{-1}: 2954, 2881, 1716, 1670, 1603, 1441, 1360, 1267, 1196, 1120, 1072. ^{1}H-NMR δ: 1.90—2.03 (3H, m), 2.45—2.57 (1H, m), 2.93, 3.38 (each 1H, d, *J*=15.8 Hz), 3.58 (3H, s), 3.63—3.97 (1H, m), 4.01—4.10 (3H, m), 5.90 (1H, d, *J*=1.0 Hz), 7.18—7.25 (3H, m), 7.33—7.49 (1H, m). ^{13}C-NMR δ: 32.1, 32.5, 43.1, 52.5, 54.4, 64.4, 65.0, 106.6, 118.2, 121.1, 124.8, 127.0, 128.9, 139.7, 142.8, 147.5, 175.6. MS *m/z*: 286 (M^+). HR-MS Calcd for $C_{17}H_{18}O_4$ 286.1203, Found 286.1200. *Anal.* Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.24; H, 6.30.

(*S*)-3,3-Ethylenedioxy-9a-hydroxymethyl-1,2,9,9a-tetrahydro-3*H*-fluorene (6) To a suspension of $LiAlH_4$ (1.2 g, 31.6 mmol) in tetrahydrofuran (THF) (100 ml) was added a solution of (*S*)-**5** (5.61 g, 19.6 mmol) in THF (80 ml) at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was quenched with water (1.2 ml), followed by 15% aqueous NaOH, and

then more water (3.6 ml) at 0 °C. The resulting mixture was dried over K_2CO_3. The solvent was removed under reduced pressure, and the crude product was purified by rinsing with Et_2O–hexane to afford (*S*)-**6** (4.74 g, 92%). mp 143—144 °C (iso-Pr_2O). $[\alpha]_{546}^{29}$ +136.1° (*c*=1.02, benzene). IR (Nujol) cm^{-1}: 3435, 1672, 1604, 1462, 1356, 1292, 1161, 1120, 1088. ^{1}H-NMR δ: 1.65 (1H, t, *J*=4.6 Hz), 1.76—2.00 (2H, m), 2.14—2.31 (2H, m), 2.62, 3.07 (each 1H, d, *J*=15.8 Hz), 3.30, 3.64 (each 1H, dd, *J*=4.6, 10.9 Hz), 3.89—4.10 (4H, m), 5.85 (1H, d, *J*=1.7 Hz), 7.15—7.41 (4H, m). ^{13}C-NMR δ: 28.7, 31.1, 41.1, 48.0, 64.4, 64.9, 65.6, 106.8, 118.0, 121.3, 125.6, 126.8, 129.0, 139.3, 144.2, 150.2. MS *m/z*: 258 (M^+). HR-MS Calcd for $C_{16}H_{18}O_3$ 258.1255, Found 258.1262. *Anal*. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.29; H, 7.01.

(*S*)-3,3-Ethylenedioxy-9a-methoxymethyl-1,2,9,9a-tetrahydro-3*H*-fuluorene (7) To a suspension of NaH (60% in oil, 1.45 g, 36.2 mmol) in dimethylformamide (DMF) (15 ml) was added MeI (5.8 ml, 91 mmol) at 0 °C. A solution of (*S*)-**6** (4.67 g, 18.1 mmol) in DMF (25 ml) was added at 0 °C, the mixture was stirred at room temperature for 3 h. After addition of water (100 ml) at 0 °C, the resulting mixture was diluted with benzene (60 ml) and AcOEt (120 ml). The organic layer was separated and washed with water, saturated NaCl, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (Et_2O : hexane=2 : 1) followed by distillation to afford (*S*)-**7** (4.6 g, 93%) as an oil. bp 225 °C (2 mmHg) (bulb-to-bulb distillation). $[\alpha]_{546}^{30}$ +126.0° (*c*=1.01, benzene). IR (NaCl) cm^{-1}: 2947, 2877, 1668, 1470, 1464, 1126, 1111, 1092. ^{1}H-NMR δ: 1.70—2.35 (4H, m), 2.60 (1H, d, *J*=15.8 Hz), 2.96 (1H, d, *J*=9.9 Hz), 3.18 (1H, d, *J*=15.8 Hz), 3.28 (3H, s), 3.43 (1H, d, *J*=9.9 Hz), 3.91—4.10 (4H, m), 5.82 (1H, d, *J*=1.3 Hz), 7.14—7.42 (4H, m). ^{13}C-NMR δ: 28.6, 30.9, 41.3, 47.2, 59.1, 64.4, 64.8, 74.6, 106.8, 117.6, 121.2, 125.6 126.6, 128.9, 139.4, 144.4, 150.6. MS *m/z*: 272 (M^+). HR-MS Calcd for $C_{17}H_{20}O_3$ 272.1411, Found 272.1415.

(*S*)-9a-Methoxymethyl-1,2,9,9a-tetrahydro-3-oxo-3*H*-fuluorene (8) To a suspension of silica gel (40 g; Silica gel 60 , Merck, 70—230 mesh) in CH_2Cl_2 (60 ml) was added a solution of 10% aqueous oxalic acid (4.1 g) at room temperature, and the mixture was stirred for 10 min. A solution of (*S*)-**7** (4.54 g, 16.7 mmol) in CH_2Cl_2 (20 ml) was added dropwise at room temperature, followed by stirring for 30 min. After addition of $NaHCO_3$ (powder, 1.4 g), the mixture was stirred for 5 min. The solid phase was separated by filtration and rinsed with CH_2Cl_2. Removal of the solvent under reduced pressure afforded (*S*)-**8** (3.7 g, 97%). mp 96—97 °C (Et_2O). $[\alpha]_{546}^{29}$ +329.5° (*c*=1.03, benzene). IR (Nujol) cm^{-1}: 2924, 2854, 1659, 1601, 1464, 1105. ^{1}H-NMR δ: 1.91—2.01 (1H, m), 2.44—2.72 (3H, m), 2.74 (1H, d, *J*=16.5 Hz), 3.13 (1H, d, *J*=9.2 Hz), 3.27 (1H, d, *J*=16.5 Hz), 3.32 (3H, s), 3.46 (1H, d, *J*=9.2 Hz), 6.32 (1H, s), 7.30—7.58 (4H, m). ^{13}C-NMR δ: 29.8, 34.1, 41.7, 48.2, 59.3, 75.7, 118.7, 123.0, 126.0, 127.3, 131.8, 137.8, 147.1, 168.4, 199.3. MS *m/z*: 228 (M^+). HR-MS Calcd for $C_{15}H_{16}O_2$ 228.1128, Found 228.1147. *Anal*. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.03; H, 7.05.

(*R*)-3-(2-Methoxymethyl-1-oxoindan-2-yl)propanoic Acid (9) A solution of (*S*)-**8** (1.85 g, 8.1 mmol) in MeOH (90 ml)–CH_2Cl_2 (90 ml) was cooled to −78 °C. Ozone was introduced at −78 °C over a period of 5 h in order to keep the color of the solution blue. The solution was then purged with argon, allowed to warm to room temperature. To the resulting solution were added AcOH (3 ml), water (3 ml), 36% aqueous HCl (1 ml) and 30% aqueous H_2O_2 (12 ml), in that order. After being stirred for 20 h at room temperature, 10% Pd–C (1 g) was added, and the mixture was stirred for 17 h. After filtration, the solution was concentrated to a volume of *ca*. 5 ml. The resulting mixture was diluted with Et_2O, and then treated with saturated aqueous Na_2SO_3 to make the aqueous phase basic. The aqueous layer was separated, and then acidified with 10% aqueous HCl. The mixture was extracted with Et_2O (100 ml×2) and the extracts were washed with saturated NaCl and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by rinsing with Et_2O–hexane to afford (*R*)-**9** (1.71 g, 85%). mp 149—150 °C (benzene). $[\alpha]_{546}^{28}$ −3.7° (*c*=1.06, $CHCl_3$). IR (KBr) cm^{-1}: 3053, 2926, 1713, 1687, 1606, 1435, 1107. ^{1}H-NMR δ: 1.87—2.06 (2H, m), 2.16—2.37 (2H, m), 2.93 (1H, d, *J*=17.5 Hz), 3.26 (3H, s), 3.37 (1H, d, *J*=17.5 Hz), 3.45, 3.57 (each 1H, d, *J*=8.9 Hz), 7.33—7.75 (4H, m). ^{13}C-NMR δ: 28.8, 29.2, 35.9, 52.9, 59.3, 77.0, 124.1, 126.5, 127.5, 135.2, 136.5, 153.2, 178.7, 208.3. MS *m/z*: 248 (M^+). HR-MS Calcd for $C_{14}H_{16}O_4$ 248.1046, Found 248.1044. *Anal*. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.82; H, 6.50.

(*R*)-2-(3-Hydroxypropyl)-2-methoxymethyl-1-indanone (10) To a solution of (*R*)-**9** (1.65 g, 6.7 mmol) in THF (30 ml) was added a 0.98 M solution of BH_3·THF complex (6.7 ml, 6.6 mmol) over a period of 30 min at −14 °C, and the mixture was stirred for 1 h. The mixture was warmed to 0 °C and then stirred for 1 h. Additional BH_3·THF complex (1 ml, 0.98 mmol) was added, and the mixture was stirred for 5 h at 0 °C. After addition of water at 0 °C, the resulting mixture was extracted with Et_2O (100 ml×2). The extracts were washed with water, saturated NaCl, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by distillation to afford (*R*)-**10** (1.52 g, 96%) as an oil. bp 200 °C (2 mmHg) (bulb-to-bulb distillation). $[\alpha]_{546}^{30}$ −16.1° (*c*=0.75, $CHCl_3$). IR (NaCl) cm^{-1}: 3406, 2927, 2877, 1709, 1608, 1466, 1109. ^{1}H-NMR δ: 1.25—1.76 (4H, m), 2.99 (1H, d, *J*=17.3 Hz), 3.24 (3H, s), 3.33 (1H, d, *J*=17.3 Hz), 3.43 (1H, d, *J*=8.6 Hz), 3.51 (1H, t, *J*=6.4 Hz), 3.60 (1H, d, *J*=8.6 Hz), 7.31—7.73 (4H, m). ^{13}C-NMR δ: 27.1, 30.8, 35.6, 53.4, 59.3, 62.7, 77.1, 123.8, 126.4, 127.2, 134.9, 136.8, 153.7, 209.5. MS *m/z*: 234 (M^+). HR-MS Calcd for $C_{14}H_{18}O_3$ 234.1254, Found 234.1246.

(*R*)-2-(3-Chloropropyl)-2-methoxymethyl-1-indanone (11) A mixture of (*R*)-**10** (1.46 g, 6.23 mmol) and $SOCl_2$ (10 ml) was stirred for 4 h at room temperature. To this solution was added pyridine (1 ml) and the resulting mixture was stirred for 2 h at room temperature, then refluxed for 6 h. The mixture was poured into ice-water, and then extracted with Et_2O (50 ml×2). The extracts were washed successively with 10% aqueous HCl, saturated $NaHCO_3$ and saturated NaCl, and dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded (*R*)-**11** (970 mg, 62%) as an oil. bp 200—210 °C (3 mmHg) (bulb-to-bulb distillation). $[\alpha]_{546}^{25}$ −0.7° (*c*=1.08, benzene). IR (NaCl) cm^{-1}: 2926, 1709, 1608, 1463, 1275, 1105, 744. ^{1}H-NMR δ: 1.54—1.79 (4H, m), 2.97 (1H, d, *J*=17.5 Hz), 3.26 (3H, s), 3.37 (1H, d, *J*=17.5 Hz), 3.41—3.46 (2H, m,), 3.44, 3.59 (each 1H, d, *J*=8.7 Hz), 7.32—7.75 (4H, m). ^{13}C-NMR δ: 27.2, 32.0, 35.7, 45.0, 53.2, 59.3, 77.0, 123.9, 126.4, 127.3, 135.0, 136.7, 153.4, 208.8. MS *m/z*: 252, 254 (M^+). HR-MS Calcd for $C_{14}H_{17}{}^{35}ClO_2$ 252.0915, Found 252.0909, Calcd for $C_{14}H_{17}{}^{37}ClO_2$ 254.0887, Found 254.0904.

(*R*)-2-(3-Iodopropyl)-2-methoxymethyl-1-indanone (12) To a solution of (*R*)-**11** (866.3 mg, 3.43 mmol) in acetone (10 ml) was added NaI (5.14 g, 3.43 mmol). After being refluxed for 7 h, the solvent was removed under reduced pressure. After addition of water, the resulting mixture was extracted with $CHCl_3$ (50 ml×2) and the extracts were washed with 10% $Na_2S_2O_3$ and saturated NaCl, and dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded (*R*)-**12** (1.04 g, 88%) as an oil. bp 200—210 °C (2 mmHg) (bulb-to-bulb distillation). $[\alpha]_{546}^{25}$ −0.6° (*c*=1.00, benzene). IR (NaCl) cm^{-1}: 2926, 2848, 1709, 1608, 1464, 1296, 1277, 1200, 1111, 741. ^{1}H-NMR δ: 1.58—1.76 (4H, m), 2.96 (1H, d, *J*=17.5 Hz), 3.05—3.11 (2H, m), 3.26 (3H, s), 3.35 (1H, d, *J*=17.5 Hz), 3.42, 3.58 (each 1H, d, *J*=8.6 Hz), 7.33—7.76 (4H, m). ^{13}C-NMR δ: 6.4, 28.1, 35.6, 35.8, 53.5, 59.4, 77.0, 124.0, 126.5, 127.4, 135.1, 136.7, 153.5, 208.8. MS *m/z*: 344 (M^+). HR-MS Calcd for $C_{14}H_{17}IO_2$ 344.0273, Found 344.0268.

(*R*)-2-Methoxymethyl-2-propyl-1-indanone (13) Under an argon atmosphere, to a solution of (*R*)-**12** (944.9 mg, 2.75 mmol) in toluene (10 ml) were added Bu_3SnH (0.62 ml, 3.0 mmol) and 2,2′-azobisisobutyronitrile (AIBN) (10 mg, 0.04 mmol). After being refluxed for 5 h, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (Et_2O : acetone=10 : 1) to afford (*R*)-**13** (385.1 mg, 64%) as an oil. bp 150 °C (2 mmHg) (bulb-to-bulb distillation). $[\alpha]_{546}^{26}$ +6.6° (*c*=1.07, benzene). IR (NaCl) cm^{-1}: 2958, 2929, 2873, 1713, 1610, 1466, 1113. ^{1}H-NMR δ: 0.83 (3H, t, *J*=7.1 Hz), 0.98—1.29 (2H, m), 1.47—1.67 (2H, m), 2.98 (1H, d, *J*=17.2 Hz), 3.24 (3H, s), 3.32 (1H, d, *J*=17.2 Hz), 3.42, 3.61 (each 1H, d, *J*=8.7 Hz), 7.30—7.99 (4H, m). ^{13}C-NMR δ: 14.5, 17.2, 35.6, 37.1, 54.0, 54.0, 59.3, 77.2, 123.8, 126.3, 127.1, 134.7, 137.0, 153.7, 209.5. MS *m/z*: 218 (M^+). HR-MS Calcd for $C_{14}H_{18}O_2$ 218.1306, Found 218.1307.

(*R*)-3-Methoxymethyl-3-propyl-3,4-dihydrocoumarin (14) Conversion of **2a** to **14**: A solution of **2a** (74% ee, 300.1 mg, 1.29 mmol), which was prepared by an enantioselective radical reaction according to Chart 1,[2a] in Et_2O (10 ml) was hydrogenated over 10% Pd–C (30 mg) under H_2 at room temperature for 6 h. After filtration, the solvent was removed under reduced pressure, and the crude product was purified by distillation to afford (*R*)-**14** (290.9 mg, 96%) as an oil. bp 130—140 °C (1 mmHg) (bulb-to-bulb distillation). $[\alpha]_D^{27}$ −12.0° (*c*=1.01, acetone). IR (NaCl) cm^{-1}: 2960, 2931, 2873, 1767, 1591, 1167, 1109. ^{1}H-NMR δ: 0.83 (3H, t, *J*=7.3 Hz), 1.16—1.45 (2H, m), 1.48—1.56 (2H, m), 2.80, 3.22 (each 1H, d, *J*=16.3 Hz), 3.38 (3H, s), 3.51 (1H, d, *J*=9.2 Hz), 3.68 (1H, d, *J*=9.2 Hz), 6.98—7.26 (4H, m). ^{13}C-NMR δ: 14.3, 17.3, 32.2, 35.0, 45.4, 59.5, 74.6, 116.0, 121.8, 124.4, 127.9, 128.6, 150.9, 170.6. MS *m/z*: 234 (M^+). HR-MS Calcd for $C_{14}H_{18}O_3$ 234.1254, Found 234.1252.

Conversion of **13** to **14**: To a solution of (*R*)-**13** (150 mg, 0.69 mmol) in CH_2Cl_2 (18 ml) were added 70% *m*-CPBA (1.83 g, 7.42 mmol) and BF_3·Et_2O (1.5 ml, 11.8 mmol), and the resulting mixture was stirred for 42 h at

room temperature. After addition of hexane, the mixture was filtered. The filtrate was washed with saturated $NaHCO_3$, saturated NaCl, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (benzene) followed by distillation to afford (*R*)-**14** (83.9 mg, 52%) as an oil. bp 130—140 °C (1 mmHg) (bulb-to-bulb distillation). 92% ee; HPLC [chiralcel OD; hexane : 2-propanol = 50 : 1; flow rate 0.5 ml/min]. $[\alpha]_D^{27}$ −16.5° (*c* = 1.13, acetone). ^{1}H-NMR and mass spectra were identical to those for the product obtained from **2a**.

References and Notes

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