dissolved in dichloromethane and passed through a silica gel plug. The nonpolar material was purified by LC on a Partisil column with hexane as the eluant to yield furodysinin (8; 4 mg, 0.6% dry weight) and a mixture of euryfuran (9; 1.5 mg, 0.2% dry weight) and pallescensin A (10; 1.2 mg, 0.2% dry weight). Furodysinin (8) and pallescensin A (10) were identified primarily by their ^{1}H NMR spectra and mass spectra.

Six specimens of *Hypselodoris porterae* were found on *Dysidea amblia* at Point Loma, San Diego, CA (-15 m), in June and Aug 1980. They were extracted in exactly the same manner as *H. californiensis*. The dichloromethane-soluble material was purified by LC on a Partisil column with hexane as the eluant to yield furodysinin (8; 3 mg, 4.9% dry weight) and euryfuran (9; 3 mg, 4.9% dry weight).

Euryspongia sp. was collected intertidally at Casa Cove, La Jolla, CA, on July 3, 1981. The sponge was steeped in methanol (2 L) at 5 °C for 2 days, the methanol was decanted, and the extraction was repeated for 2 days and finally for 2 weeks. The combined extracts were evaporated, and the aqueous residue (~200 mL) was extracted with dichloromethane (4 × 250 mL). The dichloromethane extracts were dried over sodium sulfate, and the solvent was evaporated to give an oil (1.54 g, 11.9% dry weight). The oil was chromatographed on silica gel, and the nonpolar fraction was purified by LC on a Partisil column with hexane as the eluant to yield euryfuran (9; 77 mg, 0.4% dry weight) and pallescensin A (10; 12 mg, 0.07% dry weight). Both materials are exceptionally volatile.

Agassizin (1): $[\alpha]_D$ -94° (*c* 1.2, MeOH); UV (MeOH) 225 nm (ϵ 9250) 266 (3470); ^{1}H NMR ($CDCl_3$) δ 0.87 (s, 3 H), 1.02 (d, 3 H, J = 7 Hz), 1.87 (m, 2 H), 2.4-2.7 (m, 3 H), 3.26 (d, 1 H, J = 15 Hz), 3.62 (d, 1 H, J = 15 Hz), 5.47 (d, 1 H, J = 9 Hz), 5.68 (d, 1 H, J = 5 Hz), 5.82 (m, 1 H), 6.19 (br s, 1 H), 7.16 (br s, 1 H); ^{1}H NMR (C_6D_6) δ 0.77 (s, 3 H), 0.82 (d, 3 H, J = 7 Hz), 1.63 (m, 2 H), 2.26 (m, 1 H), 2.45 (m, 1 H), 2.59 (m, 1 H, J = 7, 7, 7, 2.5 Hz), 3.27 (d, 1 H, J = 15 Hz), 3.47 (d, 1 H, J = 15 Hz), 5.40 (dd, 1 H, J = 9, 2.5 Hz), 5.51 (d, 1 H, J = 5 Hz), 5.74 (dd, 1 H, J = 9, 5 Hz), 5.99 (d, 1 H, J = 1.5 Hz), 7.06 (d, 1 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 149.3 (s), 142.5 (s), 139.4 (d), 132.1 (d), 123.1 (d), 120.4 (d), 117.6 (s), 112.2 (d), 38.5 (s), 34.3 (d), 34.2 (t), 32.7 (t), 19.7 (t), 17.1 (q), 14.1 (q); high-resolution mass measurement, obsd m/z 214.1356, $C_{15}H_{18}O$ requires 214.1358.

Ghiselinin (4): $[\alpha]_D$ +7.5° (*c* 0.27, MeOH); IR (CCl_4) 3010, 1545, 1245, 1200, 1100 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.69 (td, 1 H, J = 13, 13, 3 Hz), 0.86 (s, 3 H), 0.89 (s, 3 H), 0.92 (s, 3 H), 1.10 (m, 1 H), 1.11 (td, 1 H, J = 13, 13, 3 Hz), 1.38 (dt, 1 H, J = 13, 3, 3 Hz), 1.87 (br s, 3 H), 1.87 (m, 2 H), 2.55 (dd, 1 H, J = 14, 6 Hz), 2.86 (dd, 1 H, J = 14, 8 Hz), 3.86 (dd, 1 H, J = 8, 6 Hz), 5.50 (br s, 1 H), 6.24 (br s, 1 H), 7.23 (br s, 1 H), 7.31 (br s, 1 H); ^{13}C NMR (C_6D_6) 143.1, 140.4, 122.7, 111.7, 70.0, 58.4, 50.2, 42.4, 40.2, 38.1, 35.1, 33.5, 32.1, 25.2, 23.8, 22.4, 19.1, 14.6 (2 signals obscured by solvent); mass spectrum, m/z 300 (trace), 220 (M - C_5H_4O); high-resolution mass measurement, obsd m/z 300.2094, $C_{20}H_{28}O_2$ requires 300.2089.

Methoxy butenolide 5: $[\alpha]_D$ +38° (*c* 0.47, MeOH); IR (CCl_4) 1770 cm^{-1}; ^{1}H NMR ($CDCl_3$) see Table II; high-resolution mass measurement, obsd. m/z 262.1569, $C_{16}H_{22}O_3$ requires 262.1569.

Euryfuran (9): $[\alpha]_D$ -24° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 0.99 (s, 3 H), 1.20 (s, 3 H), 2.48 (m, 1 H, J = 16.5, 12, 7.5, 2.5 Hz), 2.76 (dd, 1 H, J = 16.5, 6.5 Hz), 7.04 (dd, 1 H, J = 2.5, 1.4 Hz), 7.07 (d, 1 H, J = 1.4 Hz); mass spectrum, m/z, 218, 203 (base peak); high-resolution mass measurement, obsd m/z 218.1686, $C_{15}H_{22}O$ requires 218.1671.

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Registry No. 1, 79827-32-0; 3, 76844-26-3; 4, 79827-31-9; 5, 79827-33-1; 6, 23262-34-2; 7, 76844-25-2; 8, 70546-63-3; 9, 79895-94-6; 10, 56881-68-6.

Asymmetric Synthesis of Five- and Six-Membered Lactones from Chiral Sulfoxides: Application to the Asymmetric Synthesis of Insect Pheromones, (*R*)-(+)-δ-*n*-Hexadecanolactone and (*R*)-(+)-γ-*n*-Dodecanolactone

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Two synthetic schemes, starting from the condensation of (*R*)-(+)-*tert*-butyl (*p*-tolylsulfinyl)acetate and dodecanal and pelargonaldehyde, were elaborated to prepare respectively (*R*)-(+)-δ-*n*-hexadecanolactone and (*R*)-(+)-γ-*n*-dodecanolactone. The observed enantiomeric excesses were higher than 80%. The absolute configuration of (+)-γ-*n*-dodecanolactone was assigned by circular dichroism.

Lactonic functionality is fairly common among natural products and in a variety of biologically active molecules. For this reason, the synthesis of chiral lactonic systems is still a challenging problem in a very active area of organic synthesis.

Until now the most general way to prepare optically active lactones has been the optical resolution of a chiral precursor as shown by Pirkle,[1] who proposed an elegant chromatographic resolution of hydroxy nitriles, or by Coke,[2] who used the classical crystallization process to resolve β-amino alcohols.

Chiral five-membered lactones were also prepared by microbial reduction of keto acids[15] and recently[3] from optically active α-acetylenic alcohols readily obtained by asymmetric reduction.

During the last few years, we developed an asymmetic aldol-type condensation from (*R*)-(+)-*tert*-butyl (*p*-tolyl-

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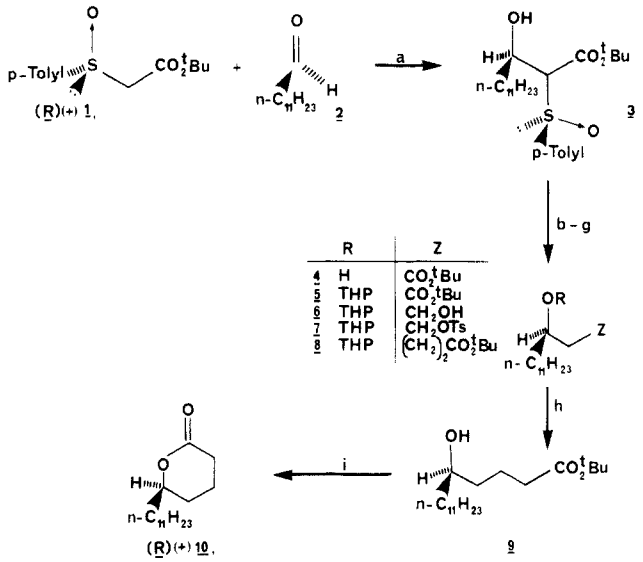
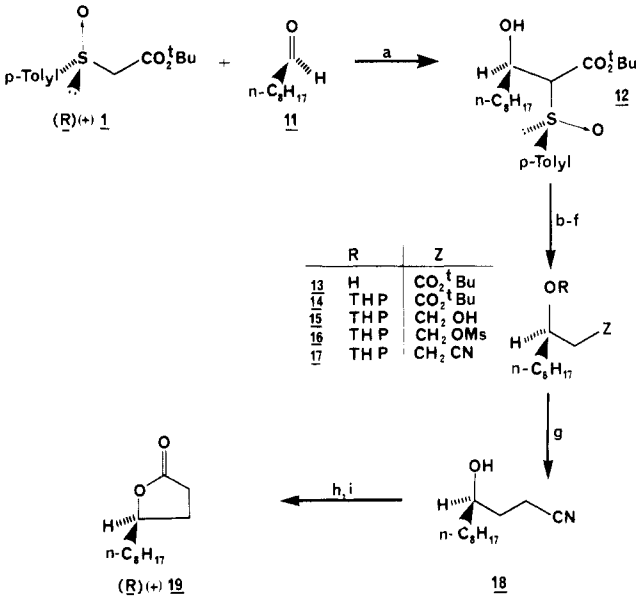
Scheme I[a]



[a] (a) *t*-BuMgBr, THF, −78 °C, 1 h; (b) Al/Hg, THF–10% H_2O, overnight; (c) DHP, CH_2Cl_2, PPTS; (d) $LiAlH_4$, Et_2O; (e) TsCl, pyridine; (f) MgI_2/Et_2O, reflux; (g) $LiCH_2CO_2$-*t*-Bu, THF–HMPT; (h) PPTS, EtOH, 55 °C, 4 h; (i) *p*-TsOH, benzene.

Scheme II[a]



[a] (a) *t*-BuMgBr, THF, −78 °C, 1 h; (b) Al/Hg, THF–10% H_2O, overnight; (c) DHP, CH_2Cl_2, PPTS; (d) $LiAlH_4$, Et_2O; (e) MsCl, THF, Et_3N; (f) KCN, THF–Me_2SO, 70 °C, overnight; (g) PPTS, EtOH, 55 °C, 4 h; (h) NaOH, H_2O–EtOH, reflux; (i) *p*-TsOH, benzene, reflux.

sulfinyl)acetate and reported very high stereoselectivity.[4-6] An application to the total synthesis of maytansine was recently published by Corey.[7]

We now report another application to the synthesis of chiral five- and six-membered lactones. Target molecules were chosen in the field of insect pheromones.

(*R*)-(+)-δ-*n*-Hexadecanolactone (10)

δ-*n*-Hexadecanolactone **10** is the pheromone responsible for some aspects of the social behavior of the Oriental hornet, *Vespa orientalis*.[8] This δ-lactone is also found in some fruits such as apricots and peaches.

The asymmetric synthesis of (*R*)-(+)-δ-*n*-hexadecanolactone (**10**) started from the condensation of (*R*)-(+)-*tert*-butyl (*p*-tolylsulfinyl)acetate[5,9] and dodecanal (**2**, Scheme I). The crude adduct **3**, obtained in quantitative yield with respect to the chiral reagent (+)-**1**, was desulfurized with aluminum amalgam. After protection of the hydroxyl group with dihydropyran and reduction of the ester function, the primary alcohol **6** was first converted to the tosylate and then the corresponding iodide was allowed to react with the lithium enolate of *tert*-butyl acetate. Finally, after hydrolysis of the tetrahydropyran protecting group, *tert*-butyl δ-hydroxyhexadecanoate **9** was cyclized in the presence of *p*-toluenesulfonic acid to (*R*)-(+)-*n*-hexadecanolactone **10**, the absolute configuration being known from the work of Coke.[2]

The optical rotation of lactone **10** obtained in this asymmetric synthesis ($[\alpha]^{23}_D$ +27.6°) was higher than the value reported by Pirkle[1] ($[\alpha]^{23}_D$ +24.2°) after optical resolution through chromatographic separation of diastereoisomers. By ^1H NMR in the presence of a chiral europium complex tris[((trifluoromethyl)hydroxymethylene)-*d*-3-camphorato]europium(III), it was shown that the enantiomeric excess of *tert*-butyl β-hydroxymyristate **4** could be estimated to be higher than 80% from the nonequivalent *tert*-butyl signals ($\Delta\delta$ = 0.2 ppm) and from the hydrogen attached to the asymmetric carbon atom signals ($\Delta\delta$ = 1.3 ppm). This value is therefore the lower limit for the optical purity of lactone **10**.

(*R*)-(+)-γ-*n*-Dodecanolactone (19)

Pyrigidial glands of *Bledius mandibularis* from the Atlantic coasts of the United States and *Bledius spectabilis* from the French Atlantic coasts (Roscoff) were shown to contain respectively 70% and 77% of γ-*n*-dodecanolactone.[11] The pyrigidial secretion of these insects is believed to serve as a defensive function. It is also feasible that one or more components regulate the growth of algae which fluorish within the burrows of *Bledius* and upon which the insects feed.

The asymmetric synthesis of (*R*)-(+)-γ-*n*-dodecanolactone, **19**, started from the condensation of (*R*)-(+)-*tert*-butyl (*p*-tolylsulfinyl)acetate (**1**) and pelargonaldehyde (**11**, Scheme II). The crude adduct **12** was desulfurized with aluminum amalgam. After protection of the hydroxyl group with dihydropyran and reduction of the ester function, the primary alcohol **15** was first converted to the mesylate and then the mesylate group was displaced with potassium cyanide. Finally after removal of the protecting group, the nitrile was hydrolyzed to a carboxyl group and the product was cyclized to (+)-γ-*n*-dodecanolactone.

According to the highest maximum value of the optical rotation of this lactone,[15] the enantiomeric excess was 80%,

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(14) Circular dichroism measurements were performed in the laboratory of Professor Daune, who is gratefully acknowledged.

a value consistent with the enantiomeric excess of *tert*-butyl β-hydroxyundecanoate **14** determined by ^{1}H NMR in the presence of tris[(heptafluoropropyl)hydroxymethylene)-*d*-3-camphorato]europium(III): 83% from the *tert*-butyl signals ($\Delta\delta$ = 0.33 ppm) and the hydrogen, α to the hydroxyl group, signals ($\Delta\delta$ = 3.8 ppm).

The absolute configuration of (+)-**19** was determined by circular dichroism, a negative Cotton effect at 215 nm being characteristic of the *R* configuration and a negative Cotton effect at 245 nm followed by a positive one at 212 nm being characteristic of the *R* configuration of (+)-**10**.[12,14] This result rules out the relationship proposed by Pirkle[1] to correlate the absolute configuration and the chromatographic mobility of diastereoisomeric carbamate which led to assignment of the *S* configuration to (+)-dodecanolactone.

In conclusion, these results showed that the asymmetric addition of (*R*)-(+)-*tert*-butyl (*p*-tolylsulfinyl)acetate to prochiral carbonyl groups leading to large enantiomeric excess of highly functionalized molecules, α-sulfinyl β-hydroxy esters, can be of wide use in organic synthesis as exemplified by the preparation of five- and six-membered lactones of high optical purity.

Experimental Section

***tert*-Butyl α-(*p*-Tolylsulfinyl)-β-hydroxymyristate (3).** To a solution of 1.50 g (6 mmol) of (+)-(*R*)-*tert*-butyl (*p*-tolylsulfinyl)acetate[5] in 400 mL of THF, cooled at −78 °C, was added 40 mL (16 mmol) of *tert*-butylmagnesium bromide (prepared from 3 g of magnesium, 16 mL of *tert*-butyl bromide, and 50 mL of Et_2O) dropwise over a period of 1 h. The mixture was then stirred for 30 min at −78 °C, and 1.6 g (12 mmol) of dodecanal in 15 mL of THF was added dropwise. After 1 h at −78 °C, the reaction mixture was hydrolyzed with 50 mL of a saturated solution of ammonium chloride and then with 150 mL of water and extracted with chloroform (2 × 100 mL). The extract was dried with sodium sulfate and concentrated. Thin-layer chromatography of the crude product showed the absence of *tert*-butyl (*p*-tolylsulfinyl)acetate and therefore a quantitative yield with respect to the chiral reagent.

This crude product was then rapidly purified by column chromatography on silica gel with 30/70 ether/hexane as eluant to remove the excess of dodecanal: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.7–1.7 (m, 32 aliphatic H), 2.40 (s, benzylic CH_3), 3.2–4.0 (m, 3 H, CHOH, CHS(O)) 7.2–7.8 (m, 4 aromatic H).

(*R*)-(+)-*tert*-Butyl β-Hydroxymyristate (4). A total of 15 g of aluminum amalgam (5 × 3 g) was added to 2 g (6.4 mmol) of ester **3** diluted with 400 mL of THF and 40 mL of water, maintaining the temperature between 20 and 23 °C. The reaction mixture was then left overnight under vigorous stirring. After filtration and washing with 50 mL of chloroform, the product was dried over sodium sulfate and the solvent evaporated. The residue was purified by column chromatography on silica gel (eluant, 50/50 hexane/ether) to yield 80% of a liquid: IR (CCl_4) ν_{OH} 3200–3700 cm^{-1}, $\nu_{C=O}$ 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.8–1.5 (m, 32 aliphatic H with the *tert*-Bu singlet at 1.40), 2.10–2.70 (ABX system, 2 H, CH_2 α to the carboxylic group), 2.9–3.1 (br d, 1 H exchanged with D_2O, OH), 3.8–4.10 (m, 1 H, CHOH); $[\alpha]^{23}_D$ +0.47° (*c* 2.78, EtOH), $[\alpha]^{23}_D$ −12.66° (*c* 3.3, $CHCl_3$).

(*R*)-*tert*-Butyl (*O*-Tetrahydropyranyl)-β-hydroxymyristate (5). To a solution of 2.73 (9 mmol) of hydroxy ester **4** in 50 mL of methylene chloride were added 225 mg (0.9 mmol) of pyridinium *p*-toluenesulfonate (PPTS) and 1.58 mL of dihydropyran (DHP) at room temperature. A complete disappearance of the starting material was observed by TLC after 3 h of stirring. The reaction mixture was diluted with 30 mL of methylene chloride and washed with 50 mL of a half-saturated sodium chloride solution. The organic layer was dried over sodium carbonate and the solvent evaporated. The residue was then quickly filtered over silica gel and eluted with ether/hexane (5/95) to give a quantitative yield: IR (CCl_4) $\nu_{C=O}$ 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.80–2.0 (m, 30 aliphatic H), 3.20–4.0 (m, 6 H, 1 exchanged with D_2O), 4.4–4.6 (m, 2 H).

(*R*)-*tert*-Butyl δ-Hydroxyhexadecanoate (9). 1. To a solution of 2.4 g (7.6 mmol) of alcohol **6** in 30 mL of pyridine was added 1.6 g (1.1 equiv) of tosyl chloride in four batches at 0 °C, and the mixture was left overnight at the same temperature (complete disappearance of the starting material by TLC). The reaction mixture was then poured into ice and water and extracted with ether (2 × 100 mL); the organic layer was washed twice with 50 mL of 10% hydrochloric acid solution and then with water (2 × 50 mL) and dried over sodium carbonate. The solvent was evaporated and the residue, tosylate **7**, was used directly in the next step.

2. A solution of the crude tosylate **7** in 30 mL of ether was added dropwise to a solution of magnesium iodide in ether, prepared[10] from 3.85 g (30 mmol) of I_2 and 2 g (80 mmol) of magnesium in 25 mL of ether. The reaction mixture was then heated 5 h under reflux and hydrolyzed with 40 mL of cold water. The organic layer was washed with a 5% sodium thiosulfate solution and water and dried over sodium carbonate. The solvent was evaporated and the residue, the corresponding iodide, was used directly in the next step.

3. To a solution of 1.2 mL (7 mmol) of *N*-isopropylcyclohexylamine in 50 mL of THF was added 30 mL (5.7 mmol) of *n*-butyllithium in hexane at −78 °C. After the mixture was stirred for 1 h at this temperature, 1 mL (7 mmol) of *tert*-butyl acetate was added and the mixture was left for 1 h at −78 °C. Then the crude iodide, prepared in the preceding step, dissolved in 10 mL of THF and 2 mL of hexamethylphosphoric triamide (HMPT), was added dropwise. The reaction mixture was left overnight at −35 °C and then poured into a mixture of ice and water, acidified with a 10% hydrochloric acid solution, and finally extracted with ether. The organic layer was dried over sodium sulfate and the solvent was evaporated. A rapid chromatography on silica gel (eluant, 50/50 ether/hexane) was used to purify the product, which was a mixture of esters **8** and **9**, the *O*-tetrahydropyranyl group being partly hydrolyzed during workup.

4. This mixture of esters **8** and **9** was diluted with 50 mL of ethanol and heated under reflux for 3 h in the presence of a catalytic amount (70 mg) of pyridinium *p*-toluenesulfonate. The solvent was evaporated and the residue was dissolved in ether and washed with a half-saturated sodium chloride solution. The ether layer was then dried over sodium sulfate and the solvent was evaporated. The crude ester **9** was used directly in the next step.

(*R*)-(+)-δ-*n*-Hexadecanolactone (10). The crude ester **9**, diluted with 50 mL of benzene, was heated under reflux for 3 h in the presence of a catalytic amount of *p*-toluenesulfonic acid to hydrolyze the ester function. Then the reflux was continued for 1 h with azeotropic distillation of water in a Dean–Stark apparatus. Solvent was then evaporated and the residue was purified by column chromatography on silica gel (eluant, 25/75 ether/hexane) to yield 770 mg of lactone **10**: 40% yield from alcohol **6**; mp 30–31 °C (lit.[1] mp 31–32 °C); IR (CCl_4) $\nu_{C=O}$ 1750 cm^{-1}; NMR ($CDCl_3$, 60 MHz δ 1.0–1.37 (m, 20 aliphatic H), 1.40–2.0 (m, 4 H), 2–2.6 (m, 2 H), 4.0–4.4 (m, 1 H); $[\alpha]^{23}_D$ +27.6° (*c* 3.8, THF) (lit.[1] $[\alpha]^{24.6}_D$ +24.2 (*c* 3.6, THF); circular dichroism, γ 245 nm ($\Delta\epsilon$ = −0.05), λ 212 nm ($\Delta\epsilon$ = +0.07) (*c* 0.3, EtOH). Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.59; H, 11.81. Found: C, 75.49; H, 11.78.

***tert*-Butyl α-(*p*-Tolylsulfinyl)-β-hydroxyundecanoate (12).** This was prepared by procedure used for **3** from 1.5 g (6 mmol) of (*R*)-(+)-*tert*-butyl (*p*-tolylsulfinyl)acetate and 1.6 g (12 mmol) of pelargonaldehyde. A quantitative yield with respect to the chiral reagent was obtained and purified as already described for ester **3**: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.7–1.7 (m, 26 aliphatic H), 2.40 (s, benzylic CH_3), 3.2–4.0 (m, 3 H, CHOH, CH(SO)), 7.2–7.8 (m, 4 aromatic H).

(*R*)-(+)-*tert*-Butyl β-Hydroxyundecanoate (13). This was obtained by desulfuration with aluminum amalgam by the same procedure used for **4**. The product was purified by chromatography on silica gel (eluant, 20/80 ether/hexane) to yield 80% of **13**: IR (CCl_4) ν_{OH} 3200–3700 cm^{-1}, ν_{CO} 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.9 (br t, 3 H, CH_3), 1–1.40 (m, 14 aliphatic H), 1.45 (s, 9 H, *t*-Bu), 2.2–2.6 (ABX system, 2 H, CH_2 α to the carboxylic group), 2.9–3.1 (br d, 1 H, OH), 3.6–4.2 (m, 1 H, CHOH); $[\alpha]^{23}_D$

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+0.95° (c 1.04, EtOH), $[\alpha]^{23}_D$ -10.67° (c 5.24, $CHCl_3$).

(R)-tert-Butyl (O-Tetrahydropyranyl)-γ-hydroxyundecanoate (14). This was prepared as **5** from 1.5 g (5.8 mmol) of hydroxy ester **13** in a quantitative yield, following the procedure used for compound **5**: IR (CCl_4) $\nu_{C=O}$ 1725 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.7–1.7 (m, 30 aliphatic H), 2.10–2.8 (m, 2 H), 3.2–4.1 (m, 3 H), 4.60 (br s, 1 H).

(R)-3-(O-Tetrahydropyranyl)-1,3-undecanediol (15). This was prepared from 2 g (5.8 mmol) of ester **14** by the procedure used for **6**. The yield of crude product was 95%: IR (CCl_4) ν_{OH} 3500, 3620 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.8–2.0 (m, 23 aliphatic H), 3.2–4.10 (m, 6 H, 1 H exchanged with D_2O), 4.4–4.8 (m, 2 H).

(R)-γ-Hydroxydodecanonitrile (18). 1. To a solution of 1.2 g (4.2 mmol) of alcohol **15** in 25 mL of THF were added 0.9 mL (6.3 mmol) of triethylamine at 0 °C and 0.4 mL (4.2 mmol) of mesyl chloride over a period of 15 min. After complete disappearance of the starting material by TLC (15 min), the reaction mixture was diluted with 25 mL of ether and washed with cold water (2 × 50 mL). The organic layer was then washed twice with a saturated sodium bicarbonated solution 2 × 50 mL) and water and dried over sodium carbonate. The solvent was evaporated and the residue, the corresponding mesylate **16**, was used directly in the next step.

2. To a solution of the crude mesylate in 20 mL of THF and 15 mL of Me_2SO (freshly distilled over $CaCl_2$) was added 2 equiv (5.4 g, 8.2 mmol) of potassium cyanide and the mixture was heated at 70 °C for 4 h. Then 2 equiv of potassium cyanide was again added and the mixture was left overnight at 70 °C and then, after cooling, poured on a mixture of ice and water. The solution was finally extracted with methylene chloride. The organic layer was washed twice with a 20% hydrochloric acid solution and twice with water and then dried over sodium carbonate, and the solvent was evaporated. A rapid chromatography on silica gel (eluant, 50/50 ether/hexane) was used to purify the product, which was a mixture of nitriles **17** and **18**, the *O*-tetrahydropyranyl group being partly hydrolyzed during the workup.

3. This mixture of nitriles **17** and **18** was diluted with 50 mL of ethanol and heated under reflux for 3 h in the presence of a catalytic amount (70 mg) of pyridinium *p*-toluenesulfonate. The solution was then filtered over silica gel and the solvent was evaporated. The crude nitrile **18** was used directly in the next step: IR ($CHCl_3$) ν_{OH} 3200–3500, 3620 cm^{-1}, ν_{CN} 2230 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.9 (br t, 3 H), 1.0–2.2 (m, 17 H), 2.45 (t, 2 H, J = 7.8 Hz), 3.40–3.9 (m, 1 H).

(R)-(+)-γ-n-Dodecanolactone (19). The crude nitrile **18** (410 mg, 2 mmol) and 1.2 g of sodium hydroxide were dissolved in 50 mL of a 3:1 mixture of ethanol and water, and the mixture was heated overnight under reflux. After cooling, the solution was neutralized with a 10% hydrochloric acid solution and the ethanol was evaporated. The residue was extracted with ether (2 × 100 mL) and then with 100 mL of chloroform. The organic layer was dried over sodium sulfate and the solvent was evaporated. The residue, dissolved in 25 mL of benzene, was heated for 1 h in the presence of a catalytic amount of *p*-toluenesulfonic acid with azeotropic distillation of water in a Dean–Stark trap. The solvent was then evaporated and the residue was purified by column chromatography on silica gel (eluant, 25/75 ether/hexane) to yield 95% of **19**: IR (CCl_4) ν_{CO} 1775 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.9 (br t, 3 H), 1–2 (m, 16 H), 2.1–2.70 (m, 2 H), 4.10–4.70 (m, 1 H); $[\alpha]^{23}D$ +32.70° (c 0.71, CH_3OH) (lit.[1] $[\alpha]_D$ +33.3° (0.73, MeOH), lit.[3] $[\alpha]_D$ +37.7° (1, MeOH), lit.[15] $[\alpha]^{20}_D$ +41.1 (5, MeOH); circular dichroism, λ 215 nm ($\Delta\epsilon$ = −0.08) (0.3, EtOH). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.73; H, 11.11. Found: C, 72.93; H, 11.03.

Registry No. (*R*)-(+)-**1**, 58059-08-8; **2**, 112-54-9; **3**, 79816-64-1; (*R*)-(+)-**4**, 79816-65-2; (*R*)-**5**, 79827-26-2; (*R*)-**6**, 79816-66-3; (*R*)-**7**, 79816-67-4; (*R*)-**8**, 79816-68-5; (*R*)-**9**, 79816-69-6; (*R*)-(+)-**10**, 59812-96-3; **11**, 124-19-6; **12**, 79816-70-9; (*R*)-(+)-**13**, 79816-71-0; (*R*)-**14**, 79816-72-1; (*R*)-**15**, 79816-73-2; (*R*)-**16**, 79816-74-3; (*R*)-**17**, 79816-75-4; (*R*)-**18**, 69830-97-3; (*R*)-(+)-**19**, 69830-91-7; *tert*-butyl acetate, 540-88-5; (*R*)-1-iodo-(*O*-tetrahydropyranyl)-3-tetradecanol, 79816-76-5.

Useful Synthesis of α,β-Dehydrotryptophan Derivatives[1]

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N-Acyl-α,β-dehydrotryptophan (ΔTrp) esters **4a–h** were directly synthesized by the reaction of 3-[(1-pyrrolidinyl)methylene]-3*H*-indole (**2**) with *N*-acylglycinates **3a–h** in reasonable yields. Of these, *N*-formyl-substituted ΔTrp methyl ester (**4a**) was easily converted into ΔTrp methyl ester (**7**) in a high yield by acidolysis with dry methanol–hydrogen chloride. Furthermore, **7** was successfully used for the preparation of a dipeptide, *N*-alanyl-substituted ΔTrp methyl ester (**10**).

The synthesis of biologically active amino acids and peptides is of continuing interest in amino acid and peptide chemistry. In particular, the syntheses of α,β-dehydroamino acids have recently received increased attention in the preparation of biologically active compounds.[2] From this point of view, the synthesis of α,β-dehydrotryptophan (ΔTrp) which is a constituent of telomycine,[3] antibiotic A-128-OP,[4] etc. is also currently desired. Besides this, ΔTrp derivatives are useful starting materials for asymmetric syntheses of optically active tryptophan and its analogues. For example, Knowles et al. reported[5] an enantioselective synthesis of (*S*)-tryptophan in 93% ee using N,N'-Ac_2ΔTrp. In subsequent work, Hengartner et al.

(1) Synthesis of Amino Acids and Related Compounds. 24. For part 23 see ref 14.

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