in 5 mL of freshly distilled trifluoroacetic acid and heated at reflux for 5 min under nitrogen and allowed to cool to room temperature over the course of 10 min. The above heating and cooling sequence was repeated once more and the resulting dark oil was then cooled in an ice–salt bath. Freshly distilled triethyl orthoformate (5 mL) was then added dropwise with efficient stirring. After 10 min the solution was poured into 300 mL of ice water and let stand 30 min. The dark red precipitate was collected by filtration and washed well with water. Ethanol (ca. 50 mL) was then used to wash the precipitate from the filter funnel into 350 mL of 10% aqueous ammonia. The resulting yellow suspension was stirred well for an hour and then extracted with dichloromethane (5 × 150 mL). The dichloromethane extracts were washed with water, dried over $MgSO_4$, and evaporated to dryness on the rotorary evaporator to give **7** as an off-white mass. Two recrystallizations from chloroform–ethanol gave crystalline product (1.91 g, 68%) with mp 202–203 °C: ^{1}H NMR δ 1.00 (6 H, t, J = 8 Hz, CH_2CH_3), 1.07 (6 H, t, J = 7 Hz, CH_2CH_3), 2.18 (6 H, s, CH_3), 2.35–2.45 (8 H, m, CH_2CH_3), 3.80 (4 H, s, pyrrole$_2$-CH_2), 9.10 (1 H, s, NH), 9.15 (2 H, s, CHO), 9.95 (2 H, s, NH); IR (KBr) 1617 cm^{-1}; MS, m/e (relative intensity) 421 (31), 285 (19), 271 (51), 255 (71), 243 (42), 149 (100); high resolution MS, M^+ 421.27385 (calcd for $C_{26}H_{35}N_3O_2$ 421.27291).

4,5,9,24-Tetraethyl-10,23-dimethyl-13,20,25,26,27-pentaazapentacyclo[20.2.1.1^{3,6}.1^{8,11}.0^{14,19}]heptacosa-3,5,8,10,12,14(19),15,17,20,22,24-undecaene (1). A. Acid-Catalyzed Procedure. The diformyltripyrrane **7** (105 mg, 0.25 mmol) and *o*-phenylenediamine (27 mg, 0.25 mmol) were dissolved, with heating, in a degassed mixture of 300 mL of dry benzene and 50 mL of absolute methanol. Concentrated HCl (0.05 mL) was then added and the resulting gold solution heated at reflux for 24 h under nitrogen. After cooling, solid K_2CO_3 (20 mg) was added and the solution filtered through $MgSO_4$. The solvent was then removed on the rotorary evaporator and the resulting product dissolved in 50 mL of CH_2Cl_2 and refiltered (to remove unreacted **7**). Heptane (100 mL) was added to the filtrate and the volume reduced to 50 mL on the rotorary evaporator whereupon the flask was capped and placed in the freezer overnight. The resulting white powder was then collected by filtration, washed with hexane, and dried in vacuo to yield **1** (55 mg, 44%): mp 188–190 °C dec; ^{1}H NMR δ 1.08 (6 H, t, J = 7 Hz, CH_2CH_3), 1.14 (6 H, t, J = 7 Hz, CH_2CH_3), 2.20 (6 H, s, CH_3), 2.40 (4 H, q, CH_2CH_3), 2.52 (4 H, q, CH_2CH_3), 4.00 (4 H, d, pyrrole$_2$-CH_2), 7.18 (2 H, m, aromatic), 7.47 (2 H, m, aromatic), 8.10 (2 H, s, CHN), 11.12 (1 H, s, NH), 12.08 (2 H, s, NH); ^{13}C NMR δ 9.47, 15.45, 16.57, 17.24, 17.72, 22.32, 116.61, 120.26, 120.74, 125.28, 125.64, 126.80, 134.06, 137.97, 141.99, 142.01; IR 1625 (sh), 1607 cm^{-1}; UV–vis λ_{max} 365 nm; CI MS, $(M + H)^+$ 494; HRMS, M^+ 493.3220 (calcd for $C_{32}H_{39}N_5$ 493.3205).

B. Metal Template Procedure. The diformyltripyrrane tripyrrane **7** and *o*-phenylenediamine reactants were condensed together on a 0.25-mmol scale exactly as described above except that 1.0 equiv of either $Pb(SCN)_2$ (80 mg) or UO_2Cl_2 (85 mg) was added to the boiling solution at the outset of the reaction. Following workup as outlined above, 68 mg (69%) and 60 mg (61%) of **1** were obtained respectively for the Pb^{2+}- and UO_2^{2+}-catalyzed reactions. The products produced in this manner proved identical with that prepared by procedure A.

1·HSCN. The diformyltripyrrane **7** (84 mg, 0.20 mmol), $Pb(SCN)_2$ (64 mg, 0.20 mmol), and *o*-phenylenediamine (22 mg, 0.20 mmol) were dissolved in 300 mL of a boiling mixture of methanol and benzene (1:5 v/v), acidified with 1 drop of concentrated HCl, and heated at reflux for 12 h. The solutions were filtered while hot to remove ca. 50 mg of lead salts and taken to dryness on the rotorary evaporator. The residue was dissolved in 30 mL of CH_2Cl_2 and layered with hexanes. The large red needles which formed over the course of several days were filtered off and air dried (75 mg, 68%). A crystal of approximate dimensions 0.24 mm × 0.24 mm × 0.35 mm was used for the X-ray structure determination (see below). ^{1}H NMR δ 9.79 (1 H, s, NH), 11.52 (2 H, s, NH), all other features as per **1**. The CI MS and TLC chromatographic behavior of this product are identical with those of **1**.

Crystal data: $C_{32}H_{39}N_5$·HSCN, M_r = 552.78, trigonal, space group $R\bar{3}$, (No. 148), on hexagonal axes, a = 33.671 (18) Å, c = 14.934 (10) Å, V = 14663 (15) Å^3, Z = 18, D_m = 1.18 g cm^{-3}, D_x = 1.13 g cm^{-3}, (163 K), $F(000)$ = 5328, Mo Kα radiation, = 0.71069 Å, = 1.227 cm^{-1}. Data were collected on Syntex P2 diffractometer with LT-1 low-temperature attachment and the structure solved by direct methods[27] and refined anisotropically (except disordered methyl atoms C29A and C29B) by full-matrix least-squares procedures.[28] The position of H20 was located from the ΔF map, the other hydrogens were calculated and refined isotropically. R = 0.0794, wR = 0.0585 for 2447 unique reflections with 4° < 2θ < 55° with $F_o > 6(\sigma(F_o))$.

4,5,9,22-Tetraethyl-10,21-dimethyl-13,18,23,24,25-pentaazatetracyclo[18.2.1.1^{3,6}.1^{8,11}]pentacosa-3,5,8,10,12,18,20,22-octaene (2). This compound was prepared by using the same procedures used to prepare **1**. From 100 mg (0.24 mmol) of **7** and 25 L (0.25 mmol) of 1,4-diaminobutane was produced 35 mg (31%) of **2** in the absence of a metal template and 60 mg (53%) when 1 equiv of UO_2Cl_2 was used: mp 152–155 °C dec; ^{1}H NMR δ 1.04–1.11 (12 H, q, CH_2CH_3), 1.75 (4 H, br s, $CH_2CH_2CH_2CH_2$), 2.10 (6 H, s, CH_3), 2.38 (4 H, q, CH_2CH_3), 2.47 (4 H, q, CH_2CH_3), 3.50 (4 H, s, CH_2CHN), 3.86 (4 H, s, pyrrole$_2$-CH_2), 7.84 (2 H, s, CHN); ^{13}C NMR δ 5.77, 9.14, 15.41, 16.46, 17.25, 17.21, 22.34, 26.95, 120.13, 121.88, 122.78, 124.25, 147.80; IR 1640 cm^{-1}; UV–vis λ_{max} 349 nm; HRMS, M^+ 473.3513 (calcd for $C_{30}H_{43}N_5$ 473.3518).

Note Added in Proof: The didehydroconjugated analogue of **1** has now been prepared; by treating **1** with $CdCl_2$ and O_2, the aromatic cadmium complex is obtained.

Acknowledgment. We thank Murat Argun for the synthesis of pyrrole **4** and Don Fletcher for help with the NMR analyses. We are grateful to the Research Corporation, The Camille and Henry Dreyfus Foundation (Distinguished New Faculty Award 1984), The National Science Foundation (Presidential Young Investigator Award 1986), and the Procter and Gamble Co. for financial support.

Registry No. **1**, 109930-00-9; **1**·HSCN, 109930-01-0; **2**, 109930-02-1; **3**, 16200-52-5; **4**, 3750-36-5; **5**, 109929-97-7; **6**, 109929-98-8; **7**, 109929-99-9; *o*-phenylenediamine, 95-54-5; 1,4-diaminobutane, 110-60-1; porphyrinogen, 4396-11-6.

Supplementary Material Available: Tables of atomic thermal factors, atomic positional parameters, and bond distances and angles (12 pages). Ordering information is given on any current masthead page.

(27) MULTAN78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data; Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J.-P.; Woolfson, M. M.; Univs. of York, England and Louvain, Belgium: 1978.

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Menthyl 2-Bromocrotonate and Menthyl 4-Bromocrotonate: Reagents for Chiral Vinylogous Darzen and Reformatsky Reactions

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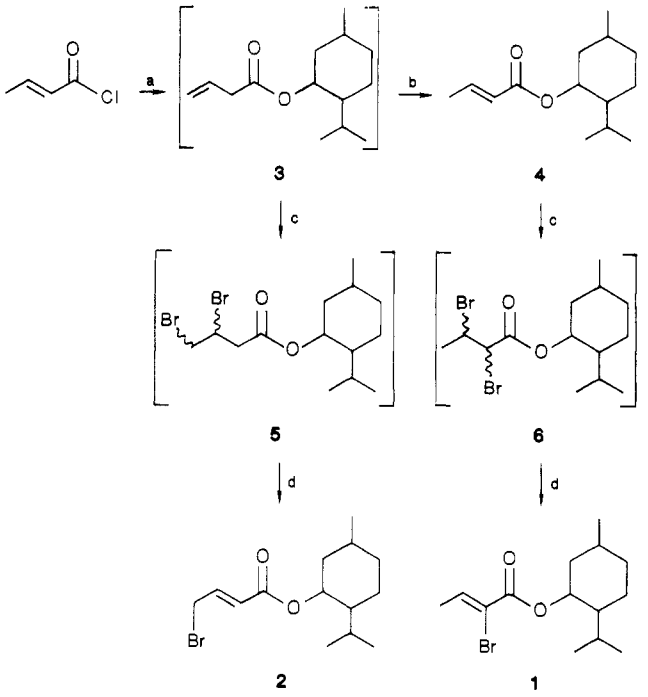
In connection with the development of new methods of asymmetric carbon–carbon bond formation, we required esters **1** and **2** in relatively large amounts and in both optical series. The ethyl analogues of both **1** and **2** have been successfully used in a new vinylcyclopropanation sequence[2] and in the synthesis of functionalized dienes via

(1) Fellow of the Alfred P. Sloan Foundation, 1981–5; recipient of the NIH Research Career Development Award, 1984–9.

(2) Hudlicky, T.; Radesca, L.; Luna, H.; Anderson, F. E. *J. Org. Chem.* **1986**, *51*, 4746.

0022-3263/87/1952-4397$01.50/0

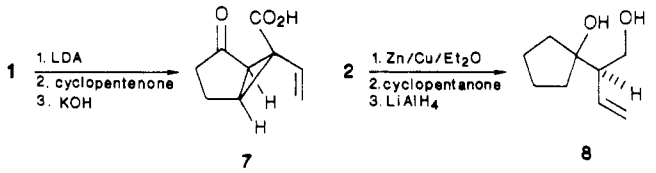
Scheme I[a]



[a] Reagents: (a) menthol (both *d* and *l* isomers), Et_3N; (b) DBU, THF; (c) Br_2, CCl_4; (d) DBU, DME.

the regioselective vinylogous Reformatsky reaction,[3] respectively. The use of menthyl esters **1** and **2** in identical sequences was shown to have a good chiral auxiliary effect and the above reactions produced chiral vinylcyclopropanes[4] or chiral 1,3-diols,[5] respectively. The preparation of both halo esters in the *l* series commenced with the condensation of crotonyl chloride with *l*-menthol to provide quantitatively ester **3** via an intermediate ketene–allene. For the preparation of **1** the reconjugation was accomplished in situ by treatment of **3** with DBU in DME or THF in excellent yield. On a large scale, DBU was added directly to the crude reaction mixture and *l*-menthyl crotonate (**4**), not requiring purification, was isolated in an overall yield of 90%, Scheme I. The deconjugated ester **3** was brominated to provide the dibromide **5** which was immediately treated with DBU to give *l*-menthyl 4-bromocrotonate (**2**) in quantitative yield. This compound could not, in our hands, be prepared by the usual NBS bromination of **4**. Treatment of crotonate **4** with Br_2 followed by DBU elimination furnished excellent yield of *l*-menthyl 2-bromocrotonate (**1**) as a mixture of *E*/*Z* isomers (1:1). The preparation of both compounds was found amenable to large-scale reactions and could be carried through without purification to yield crystalline **2** in 90% overall yield and **1** as an oil in 88% overall yield. The identical sequence of operations was used to prepare the corresponding *d*-menthyl esters in comparable yields.

For example, esters **1** and **2** were used to prepare chiral compounds of type **7** and **8** with good asymmetric induction.[4,5] Details of these endeavors will be disclosed in due course.



Experimental Section

All nonhydrolytic reactions were carried out in a nitrogen or argon atmosphere, using standard techniques for the exclusion of air and moisture. Glassware used for moisture-sensitive reactions was flame-dried with an internal inert gas sweep. All solvents were distilled prior to use from appropriate drying agents.

Infrared spectra were recorded on neat samples, unless otherwise specified, on a Perkin-Elmer 257 spectrometer; ν_{max} is expressed in cm^{-1}. ^1H NMR spectra were obtained on Varian EM390, JEOL-FX-200, or IBM-200, or WP-270 instruments, using $CDCl_3$ as solvent and TMS as internal reference. Chemical shifts are expressed in δ units and the coupling constants indicated in parentheses and expressed in hertz; multiplicities of the signals are indicated as follows: d for doublet, t for triplet, q for quartet, m for multiplet, and any combinations as appropriate. Unspecified signals are singlets. The abbreviation br next to signal multiplicity connotes broad. ^{13}C NMR spectra were recorded on FX-200, IBM-200, or NR-80 instruments using $CDCl_3$ as solvent and TMS as internal reference. Chemical shifts are in δ units and multiplicites are as specified.

Flash chromatography was performed by the procedure of Still and co-workers,[6] using Kiesel gel 60 (230–400 mesh) by EM reagents. Mass spectra were recorded on a Dupont 20-491 or a Varian MAT-112 instrument (low resolution) or on a double focusing Dupont 21-110C or VG instruments (exact mass).

***l*-Menthyl 3-Butenoate (3).** *l*-Menthol (25 g, 0.16 mol) was dissolved in 45 mL of freshly distilled Et_3N and mechanically stirred. Crotonyl chloride (25.1 g, 0.24 mol) was added dropwise at 0 °C. A very thick white paste was formed. The reaction was quenched with 3 N HCl (until acidic) and diluted with 100 mL of ethyl ether. The organic layer was washed with 20 mL of 3 N HCl, and the combined aqueous layers were extracted with ethyl ether (2 × 100 mL). The organic layer was washed with 10% KOH, 3 N HCl, and brine and dried with Na_2SO_4, and the solvent was evaporated to give 36 g (100%) of crude ester **3** which was used in the next step without further purification: R_f 0.60 (hex:Et_2O = 90:10); bp (Kugelrohr temp) 150 °C at 10^{-3} mm; $[\alpha]_D$ −76.2° (*c* 6.76, EtOH); IR (neat, NaCl) 3100, 2970, 2880, 1740, 1650 cm^{-1}; ^1H NMR ($CDCl_3$, TMS) δ 0.75 (d, 3 H, J = 8 Hz), 0.80–1.15 (m, 9 H), 1.30–1.60 (m, 2 H), 1.60–1.7 (br d, 2 H), 1.75–1.9 (m, 1 H), 1.9–2.05 (br d, 1 H), 3.05 (dd, 2 H, J = 7, 2 Hz), 4.7 (dt, 1 H), 5.15 (br d, 1 H), 5.20 (br d, 1 H), 5.9 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 171.00 (C), 130.54 (CH), 118.18 (CH_2), 74.42 (CH), 47.04 (CH), 40.90 (CH_2), 39.50 (CH_2), 34.27 (CH_2), 31.37 (CH), 26.30 (CH), 23.55 (CH_2), 21.98 (CH_3), 20.68 (CH_3), 16.37 (CH_3); mass spectrum (70 eV), *m*/*e* (relative intensity) $(M)^+$ 224 (18), 138 (80), 123 (35), 95 (70), 83 (100), 69 (94).

***d*-Menthyl 3-butenoate:** $[\alpha]_D$ +74.9° (*c* 1.17, EtOH).

***l*-Menthyl 3,4-Dibromocrotonate (5).** *l*-Menthyl 3-butenoate (**3**) (30 g, 0.134 mol) was dissolved in 50 mL of CCl_4 at 0 °C and mechanically stirred. Bromine (34 g, 0.214 mol) was added dropwise at 0 °C. After the addition was complete the solvent was evaporated and the dibromide **5** used without further purification: R_f 0.60 (hex:Et_2O = 90:10); bp (Kugelrohr temp) 200 °C at 10^{-3} mm; $[\alpha]_D$ −35.3° (*c* 5.61, EtOH); IR (neat, NaCl) 2960, 2880, 1730 cm^{-1}; ^1H NMR ($CDCl_3$, TMS) δ 0.75 (dd, 3 H, J = 7, 2 Hz), 0.8–1.15 (m, 9 H), 1.3–1.6 (m, 2 H), 1.6–1.75 (br d, 2 H), 1.85–2.1 (m, 2 H), 2.8 (m, 1 H), 3.3 (m, 1 H), 3.7 (m, 1 H), 3.9 (dd, 1 H, J = 7.3 Hz), 4.5 (m, 1 H), 4.75 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.14 (C), 75.25 (CH), 46.88 (CH), 45.11 (CH), 41.95 (CH_2), 40.70 (CH_2), 35.44 (CH_2), 34.12 (CH_2), 31.31 (CH), 26.16 (CH) 23.35 (CH_2) 21.92 (CH_3), 20.66 (CH_3), 16.25 (CH_3); mass spectrum,

(3) For recent examples of diene synthesis via the vinylogous Reformatsky reaction, see the following publications: (a) Hudlicky, T.; Kwart, L. D.; Tiedje, M. H.; Ranu, B. C.; Short, R. P.; Frazier, J. O.; Rigby, H. L. *Synthesis* **1986**, 716. (b) Hudlicky, T.; Frazier, J. O.; Seoane, G.; Tiedje, M.; Seoane, A.; Kwart, L. D.; Beal, C. *J. Am. Chem. Soc.* **1986**, *108*, 3755. (c) Short, R. P.; Ranu, B. C.; Revol. J. M.; Hudlicky, T. *J. Org. Chem.* **1983**, *48*, 4453.

(4) Hudlicky, T.; Radesca, L. 38th Southeast Regional Meeting of the American Chemical Society, Louisville, KY, Nov 1986; Abstract #208.

(5) Hudlicky, T.; Allison, S.; Rigby, H. L. 38th Southeast Regional Meeting of the American Chemical Society, Louisville, KY, Nov 1986; Abstract #214.

(6) Still, C. W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

chemical ionization m/e (relative intensity) $(M + 1)^+$ 385 (6), 289 (3), 247 (10), 225 (10), 139 (100).

***d*-Menthyl 3,4-dibromocrotonate**: $[\alpha]_D$ +32.9° (*c* 1.32, EtOH).

***l*-Menthyl 4-Bromocrotonate (2).** Dibromide **5** was used without further purification. The crude product was dissolved in 50 mL of DME freshly distilled, and 30.5 g (0.20 mol) of DBU was added dropwise at 0 °C. When the addition was finished, the reaction was quenched with 3 N HCl (until acidic) and 70 mL of ethyl ether. The organic layer was washed with 20 mL of 3 N HCl. The combined aqueous layers were extracted with ethyl ether (3 × 80 mL). The combined organic layers were then washed with brine and dried with Na_2SO_4 and the solvent was evaporated. Ester **2** (36.5 g, 90% from menthyl 3-butenoate) was obtained after filtration through silica gel: R_f 0.4 (hex:Et_2O = 90:10); mp 35–36 °C; bp (Kugelrohr temp) 200 °C at 10^{-3} mm; $[\alpha]_D$ −60.2° (*c* 3.32, EtOH); IR (neat, NaCl) 2980, 2880, 1730, 1655 cm^{-1}; ^1H NMR ($CDCl_3$, TMS) δ 0.75 (d, 3 H, *J* = 7 Hz), 0.85–1.15 (m, 9 H), 1.35–1.6 (m, 2 H), 1.6–1.75 (br d, 2 H), 1.8–1.9 (m, 1 H), 1.95–2.1 (br d, 1 H), 4.0 (dd, 2 H, *J* = 8, 2 Hz), 4.75 (dt, 1 H), 6.05 (br d, 1 H, *J* = 16), 7.0 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 164.96 (C), 141.30 (CH), 125.05 (CH), 74.58 (CH), 47.00 (CH), 40.81 (CH_2), 34.18 (CH_2), 31.30 (CH), 29.07 (CH_2), 26.28 (CH), 23.48 (CH_2), 21.91 (CH_3), 20.62 (CH_3), 16.36 (CH_3). Anal. Calcd for $C_{14}H_{23}BrO_2$: C, 55.46; H, 7.59; Br, 26.37. Found: C, 55.00; H, 7.59; Br, 26.64.

***d*-Menthyl 4-bromocrotonate**: $[\alpha]_D$ +57.0° (*c* 0.50, EtOH).

***l*-Menthyl 2-Butenoate (4).** *l*-Menthol (25 g, 0.16 mol) was dissolved in 45 mL of freshly distilled Et_3N, and the mixture was mechanically stirred. Crotonly chloride (25.1 g, 0.24 mol) was added dropwise at 0 °C. A very thick white paste was formed. Freshly distilled THF (50 mL) was added to wash the walls of the flask, and then 30.5 g (0.20 mol) of DBU was added dropwise, at 0 °C. Workup of the reaction mixture prior to the addition of DBU resulted in quantitative isolation of deconjugated ester **3**. The mixture was allowed to warm up to room temperature and stirred for 3 h. The reaction mixture was diluted with ethyl ether and washed with 10% HCl (until acidic), and the combined aqueous layers were extracted with ethyl ether (3 × 80 mL). The combined organic layer was washed with 10% KOH, 10% HCl, and brine. It was then filtered through a plug of silica gel and dried with Na_2SO_4, and the solvent was evaporated to yield 35.1 g (98%) of crude ester **4** as a mixture of *E*:*Z* isomers (5:1): *E* R_f 0.54 (hex:Et_2O = 90:10), *Z* R_f in 0.67 (hex:EtO_2 = 90:10); bp (Kugelrohr temp) 150 °C at 10^{-3} mm; $[\alpha]_D$ −85.3° (*c* 1.73, EtOH) (of the 5:1 mixture); IR (neat, NaCl) 2930, 2880, 1710, 1660 cm^{-1}; *E* isomer ^1H NMR ($CDCl_3$, TMS) δ 0.75 (d, 3 H, *J* = 8 Hz), 0.9 (m, 6 H), 0.95–1.20 (m, 4 H), 1.35–1.60 (m, 2 H), 1.60–1.75 (br d, 2 H), 1.85 (dd, 3 H, *J* = 7, 2 Hz), 1.95–2.1 (br d, 1 H), 4.75 (dt, 1 H, *J* = 6 Hz, 12 Hz), 6.80 (dd, 1 H *J* = 2 Hz, 15 Hz), 6.95 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 165.87 (C), 143.74 (CH), 123.18 (CH_2), 73.60 (CH), 47.07 (CH), 40.91 (CH_2), 34.21 (CH_2), 31.29 (CH), 26.23 (CH), 23.50 (CH_2), 21.87 (CH_3), 20.59 (CH_3), 17.69 (CH_3) 16.30 (CH_3); mass spectrum, chemical ionization m/e (relative intensity) $(M + 1)^+$ 225 (3.7), 139 (100).

***d*-Menthyl 2-butenoate**: $[\alpha]_D$ +79.4° (*c* 0.77, EtOH).

***l*-Menthyl 2,3-Dibromocrotonate (6).** *l*-Menthyl 2-butenoate (**4**) (34.5g, 0.15 mol) was dissolved in 50 mL of CCl_4 and mechanically stirred. Bromine (39 g, 0.25 mol) was added dropwise at 0 °C. After the addition was complete the solvent was evaporated to afford ester **6**, which was used immediately without further purification: R_f 0.67 (hex:Et_2O = 90:10); bp (Kugelrohr temp) 200 °C at 10^{-3} mm; $[\alpha]_D$ −32.1° (*c* 6.73, EtOH); IR (neat, NaCl) 2960, 2880, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, TMS) δ 0.75 (dd, 3 H, *J* = 8, 2.5 Hz), 0.90–1.00 (m, 7 H), 1.00–1.15 (m, 2 H), 1.4–1.6 (m, 2 H), 1.6–1.8 (br d, 2 H) 1.9 (d, 3 H, *J* = 6 Hz), 2.0–2.1 (m, 2 H), 4.3–4.6 (m, 2 H), 4.7–4.8 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 167.18 (C), 76.40 (CH), 50.03 (CH), 46.92 (CH), 45.59 (CH), 39.81 (CH_2), 34.11 (CH_2), 31.29 (CH), 25.96 (CH), 23.83 (CH_3) 23.24 (CH_2) 21.91 (CH_3), 20.64 (CH_3), 16.05 (CH_3); mass spectrum, chemical ionization m/e (relative intensity) $(M + 1)^+$ 385 (5.7), 225 (12), 139 (100).

***d*-Menthyl 2,3-dibromocrotonate**: $[\alpha]_D$ +32.0° (*c* 0.59, EtOH).

***l*-Menthyl 2-Bromocrotonate (1).** Dibromide **6**, which was used immediately without further purification was dissolved in 100 mL of DME and 30.5 g (0.20 mol) of DBU was added dropwise at 0 °C with mechanical stirring. After addition was completed, the reaction was quenched with 3 N HCl (until acidic) and 100 mL of ethyl ether. The organic layer was washed with 20 mL of 3 N HCl. The combined aqueous layers were extracted with ethyl ether (2 × 80 mL). The combined organic layers were washed with brine and dried with Na_2SO_4 and the solvent was evaporated. After filtration through a bed of silica gel, 41.0 g (88% from menthyl 2-butenoate) of ester **1** was obtained as a 50:50 *Z*:*E* mixture: *E* R_f 0.43 (hex:Et_2O = 95:5), *Z* R_f 0.34 (hex:Et_2O = 95:5); bp (of the 1:1 mixture) (Kugelrohr temp) 200 °C at 10^{-3} mm; $[\alpha]_D$ −74.3° (*c* 5.57, EtOH); IR (neat, NaCl) 2900, 2850, 1710, 1630 cm^{-1}; *E* isomer ^1H NMR ($CDCl_3$, TMS) δ 0.75 (d, 3 H, *J* = 7 Hz), 0.85–1.0 (m, 7 H), 1.0–1.2 (m, 2 H) 1.4–1.6 (m, 2 H), 1.65–1.75 (br d, 2 H), 205 (d, 3 H, 8 Hz), 2.0 (m, 2 H) 4.75 (dt, 1 H), 6.7 (q, 1 H, *J* = 8 Hz); ^{13}C NMR ($CDCl_3$) 162.40 (C), 140.46 (CH), 112.33 (C), 76.23 (CH), 46.95 (CH) 40.63 (CH_2), 34.11 (CH_2), 31.35 (CH), 26.14 (CH), 23.35 (CH_2), 21.89 (CH_3), 20.65 (CH_3), 17.69 (CH_3), 16.15 (CH_3); *Z* isomer ^1H NMR ($CDCl_3$, TMS) δ 0.75 (d, 3 H, *J* = 7 Hz), 0.85–1.0 (m, 7 H), 1.0–1.2 (m, 2 H), 1.4–1.6 (m, 2 H), 1.95 (d, 3 H, *J* = 6 Hz), 2.0 (m, 2 H), 4.75 (dt, 1 H), 7.35 (q, 1 H, *J* = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 161.72 (C), 142.17 (CH), 118.26 (C), 76.39 (CH), 46.95 (CH), 40.63 (CH_2), 34.11 (CH_2), 31.35 (CH), 26.29 (CH), 23.45 (CH_2), 21.89 (CH_3), 20.65 (CH_3), 17.21 (CH_3), 16.35 (CH_3).

***d*-Menthyl 2-bromocrotonate**: 60:40 *Z*/*E* mixture $[\alpha]_D$ +72.9° (*c* 1.23, EtOH).

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An Effective Process for the Isolation of Docosahexaenoic Acid in Quantity from Cod Liver Oil

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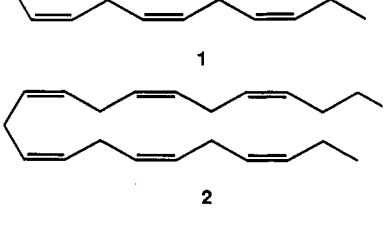
The marine-derived polyunsaturated fatty acids eicosapentaenoic acid (**1**) (EPA) and docosahexaenoic acid (**2**) (DHA) are currently of unusual interest because of several lines of evidence that point to beneficial effects of dietary fish lipid on cardiovascular health.[1-3] The mechanisms by which these cardioprotective effects arise are obscure and are likely to remain so until careful biochemical and biological studies on the role of the *individual* acids **1** and



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