($CDCl_3$) δ 1.41 (d, J = 7.3 Hz, 3 H), 1.82–2.55 (m, 4 H), 2.57–2.80 (m, 1 H), 3.10–3.32 (m, 1 H), 4.57–4.84 (m, 1 H), 6.77–7.0 (m, 4 H).

Acknowledgment. This work has been funded by a grant of the National Science Foundation.

Registry No. (±)-*trans*-1, 61248-46-2; (1*S*,2*R*)-1, 74741-45-0; (1*R*,2*S*)-1, 74708-14-8; (±)-*cis*-2, 74708-15-9; (1*R*,2*R*)-2, 43119-27-3; (1*S*,2*S*)-2, 74708-16-0; (1*S*,2*R*)-3, 74708-17-1; (1*R*,2*S*)-3, 74708-18-2; (1*S*,2*S*)-3, 74708-19-3; (±)-*trans*-4, 74629-86-0; (1*S*,2*S*)-4, 74708-20-6; (1*R*,2*R*)-4, 74708-21-7; (±)-*cis*-5, 74629-87-1; (1*R*,2*S*)-5, 74708-22-8; (1*S*,2*R*)-5, 74708-23-9; (±)-*trans*-7, 74629-88-2; (1*S*,2*R*)-7, 74708-24-0; (1*R*,2*S*)-7, 74708-25-1; (±)-*trans*-8, 74629-89-3; (1*S*,2*R*)-8, 74708-26-2; (1*R*,2*S*)-8, 74708-27-3; (1*S**,2*S**,*S**)-(±)-12, 74629-90-6; (1*R**,2*S**,-*S**)-(±)-13, 74708-28-4; (1*R*,2*R*,*R*)-14a, 74629-91-7; (1*S*,2*R*,*R*)-14b, 74708-29-5; (*R*)-15, 42340-98-7; (1*R*,2*S*,*R*)-16a, 74629-92-8; (1*S*,2*R*,-*R*)-16b, 74708-30-8; 17a, 74708-31-9; (1*R*,2*R*,*R*)-18a, 74629-93-9; (1*S*,2*S*,*R*)-18b, 74708-32-0; (1*R*,2*S*,*R*)-19a, 74629-94-0; (1*S*,2*R*,*R*)-19b, 74629-95-1; (1*S*,2*S*,*R*)-20a, 74629-96-2; (1*R*,2*R*,*R*)-20b, 74629-97-3; (±)-2-(cyanomethyl)cyclohexanone, 74629-98-4; (*R*)-1-(1-naphthyl)-ethylamine, 3886-70-2; (±)-α-(cyanomethyl)-β-tetralone, 34087-39-3.

Enantiomerically Pure Lactones. 3. Synthesis of and Stereospecific Conjugate Additions to α,β-Unsaturated Lactones

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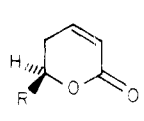
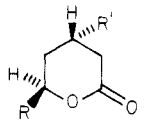
A general synthetic approach to both enantiomers of α,β-unsaturated lactones of general formula 1 has been devised, the first synthesis of the naturally occurring antipode of massoilactone (**1b**) exemplifying the approach. Interestingly, the specific rotation of massoilactone (and its enantiomer) is higher than that of the natural material isolated from formicine ants. A key step in the sequence involves chromatographic separation of rationally selected diastereomeric derivatives of racemic intermediates. Compounding the utility of an approach to optically active, type 1 lactones is the observation that conjugate additions of organometallic reagents to such lactones proceed with a high degree of stereospecificity, affording lactones of general formula 2. The conformational behavior of lactone **1a** is considered as is the solvation of δ-lactones by fluoroalcoholic chiral solvating agents such as 2,2,2-trifluoro-1-(9-anthryl)ethanol (8).

A general synthetic route to configurationally known enantiomerically pure unsaturated lactones of general formula 1 would be of value not only because these lactones are widely occurring natural products (fruits,[1] blossoms,[2] bark oil,[3,4] cane molasses,[5] insects,[4] butter[6]) but also because they are synthetically versatile precursors to other chiral molecules of considerable interest. For example, the naturally occurring enantiomer of parasorbic acid (**1a**) has



1a, R = CH_3
b, R = n-C_5H_{11}
c, R = n-$C_{13}H_{27}$



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served as a convenient starting material for the synthesis of a 4,6-dideoxy-L-ribose derivative,[7] of interest to those concerned with antibiotics. As is often the case with syntheses based upon chiral natural products, only one enantiomer of the product can be obtained for biological testing, owing to unavailability of the unnatural enantiomer of the starting material. Since racemic **1a** has been used to prepare DL-chalcose,[8] DL-desosamine,[8] and various DL-4,6-dideoxy sugars,[9] one presumes that access to either enantiomer of parasorbic acid would allow preparation of either product enantiomer.

Our past interest in the rational resolution of enantiomers by liquid chromatography has led to methodology for the preparation, in high enantiomeric purity, of both enantiomers of an assortment of ring-saturated lactonic pheromones.[10] Our interest in extending our approach to encompass type 1 lactones was additionally stimulated by the possibility that stereospecific 1,4 conjugate additions to these compounds might efficiently afford disubstituted ring-saturated lactones of general formula 2. Such a sequence would complement the asymmetric induction scheme recently described by Meyers and co-workers[11] for the preparation of simple, optically active, monosubstituted β-alkyl lactones.[12]

Since type 2 disubstituted lactones possess a chiral center relatively remote from the synthetically versatile lactone functionality, we deemed them synthetically useful precursors of yet more elaborate chiral molecules. Functionally remote chiral centers are common to many natural products (e.g., pheromones of the German cockroach and pine saw-fly) and often present difficult problems in stereochemical control and assay.

Synthesis of Chiral α,β-Unsaturated Lactones. As a continuation of our studies directed toward the synthesis of enantiomerically pure lactones, we describe a general synthetic approach that affords both enantiomers of α,β-

(1) Kuhn, R.; Jerchel, D. *Chem. Ber.* **1943**, *76*, 413.
(2) Kaiser, R.; Lamparsky, D. *Tetrahedron Lett.* **1976**, 1659.
(3) Meijer, T. *Recl. Trav. Chim. Pays-Bas* **1940**, *59*, 191.
(4) Cavill, G. W. K.; Clark, D. V.; Whitfield, F. B. *Aust. J. Chem.* **1968**, *21*, 2819.
(5) Hashijume, T.; Kikuchi, N.; Sasaki, Y.; Sakata, I. *Agric. Biol. Chem.* **1968**, *32*, 1306.
(6) Nobuhara, A. *Agric. Biol. Chem.* **1968**, *32*, 1016.
(7) Jary, J.; Kefurt, K. *Collect. Czech. Chem. Commun.* **1966**, *31*, 1803.
(8) Torssell, K.; Tyagi, M. P. *Acta Chem. Scand., Ser. B* **1977**, *B31*, 7.
(9) Torssell, K.; Tyagi, M. P. *Acta Chem. Scand., Ser. B* **1977**, *B31*, 297, and references cited therein.
(10) Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1979**, *44*, 2169.
(11) Meyers, A. I.; Smith, R. K.; Whitten, C. E. *J. Org. Chem.* **1979**, *44*, 2250.
(12) Meyers' scheme is apparently unsuited for preparation of type 1 lactones and allows preparation of but a single lactone enantiomer, owing to the use of a naturally occurring chiral reagent only one enantiomer of which is available.

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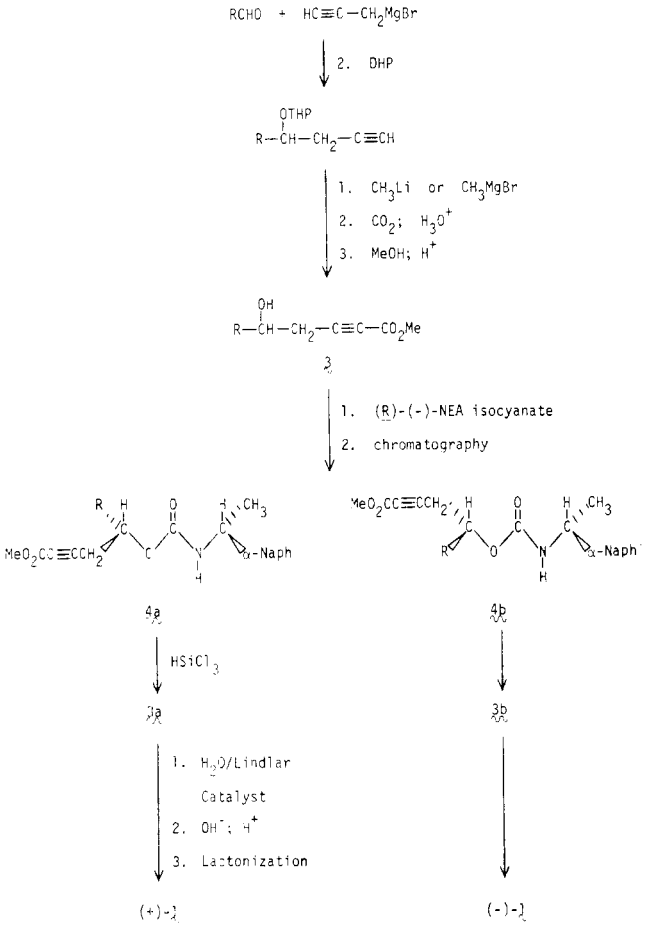
Scheme I



unsaturated lactones of general formula **1**. The present method is essentially a variation of the scheme we used to obtain chiral saturated γ-, δ-, and ε-lactones.[10] A key step in that sequence is the chromatographic resolution of diastereomeric derivatives of a lactone precursor.

Addition of propargylmagnesium bromide to aldehydes affords the corresponding acetylenic alcohols in moderate yields[13] (Scheme I). After protection as the THP ethers, carboxylation of the organometallic acetylides followed by esterification affords racemic hydroxy acetylenic esters of general formula **3**. Conversion of **3** to diastereomeric carbamates **4a,b** was achieved as previously described,[10] and the diastereomers were separated completely by automated multigram high-pressure LC.[14] Each resolved diastereomer was treated with trichlorosilane[15] to retrieve the corresponding enantiomerically pure hydroxy acetylenic ester. Standard Lindlar reduction of each ester, followed by hydrolysis and lactonization of the resulting hydroxy acid, affords each lactone enantiomer. Except for the first step, all conversions in this sequence occur in high yield.

Table I summarizes the lactones obtained by using the present approach. Entry **1b** (massoilactone) is of interest since the *R* enantiomer has been identified as the defense allomone of the formicine ant.[4] This lactone has also been isolated from cane molasses,[5] bark oil, and jasmine blossoms.[2] Mori[16] has reported a synthesis of the unnaturally occurring *S* enantiomer from (*R*)-glyceraldehyde acetonide.

Table I. Chiral α,β-Unsaturated Lactones of General Formula 1

entry	chromatographic α of carbamates	$[\alpha]_D$, deg	
		S	*R*
1a	1.95		
1b	1.80	109.0	−110.5
1c	1.20	32.8	−31.3

It is interesting to note that although Mori started with enantiomerically pure material, the optical purity of his final product was approximately 75%,[17] presumably owing to one or more synthetic conversions having proceeded with partial racemization. Mori's synthesis illustrates the difficulties sometimes encountered in a protracted synthetic sequence originating from a chiral natural product. Not only might one encounter unanticipated and possibly undetected partial racemization but also one may be able to obtain but a single enantiomer of the target compound and that may be the undesired one. Contrast this approach with one in which the efficient and largely predictable resolution of a racemate is delayed until a late stage of the synthesis.

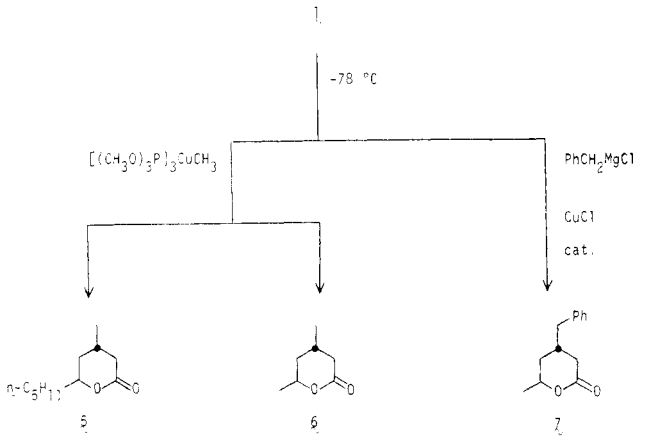
Although a large assortment of type 1 lactones has not been prepared by the present scheme, our experience with the chemistry and chromatographic separations thus far encountered suggests that this sequence will be of considerable generality. A great many aldehydes (starting materials of Scheme I) are readily available for synthesis of a variety of type 1 lactones. Since the ability to separate the carbamate diastereomers is essential to the resolution of the lactones, we investigated the chromatographic separability of type 4 carbamates with R = CH_3, n-C_5H_{11}, and n-$C_{13}H_{27}$. The observed α values, a measure of chromatographic separability, have a nearly linear inverse relationship with the number of carbons in the linear alkyl substituent. The inference is clear that linear alkyl substituents smaller than ca. C_{15} will give rise to easily separable carbamate diastereomers.

Absolute configurations of these lactones are readily assignable from the elution orders of the corresponding carbamates,[10,18] as well as NMR spectral differences noted between a pair of diastereomers.[18,19] The assertion that the lactone enantiomers are obtained in very high enantiomeric purity[20] is based upon the observed total chromatographic separation of the diastereomeric carbamates and upon the similarity of the present subsequent conversions to previously reported nonracemizing procedures.[10]

Conjugate Additions of Organometallic Reagents. Several highly stereospecific reactions of parasorbic acid (**1a**) have been reported to date. Both epoxidation[7,8] and the Michael addition[9] of either methanol or aziridine have been reported to give only trans products. We now report that the hitherto undescribed 1,4 conjugate addition of organometallic reagents to type 1 lactones has a similar stereochemical outcome.

(13) (a) Crombie, L. *J. Chem. Soc.* **1955**, 995. (b) Bernady, K. F.; Floyd, M. B.; Poletto, J. F.; Weiss, M. J. *J. Org. Chem.* **1979**, *44*, 1438 and references cited therein.
(14) Pirkle, W. H.; Anderson, R. W. *J. Org. Chem.* **1974**, *39*, 3901.
(15) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 2781.
(16) Mori, K. *Agric. Biol. Chem.* **1976**, *40*, 1617.
(17) By comparison with the specific rotation reported by Mori[16] and that in Table I.
(18) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 1839.
(19) Pirkle, W. H.; Boeder, C. W.; Simmons, K. *J. Org. Chem.* **1979**, *44*, 4891.
(20) (a) However, the enantiomeric purity of the final product will reflect that of the resolving agent, unless solid intermediates result which are subject to recrystallization. We have determined the enantiomeric purity of the (*R*)-α-NEA used in this study to be in the range of 96–98%.[20b] (b) Pirkle, W. H.; House, D. W. *J. Org. Chem.* **1979**, *44*, 1957.

Scheme II



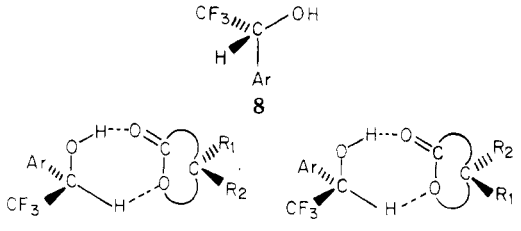
Each enantiomer of 2-decen-5-olide (**1b**) was allowed to react with a trimethyl phosphite–attenuated methylcopper reagent[21] to afford the corresponding enantiomers of trans lactone **5** (Scheme II). This reaction was also performed on racemic parasorbic acid (**1a**) to afford *trans*-**6**, a compound of relatively simple structure and deemed more suitable for NMR determination of reaction stereospecificity. Noting that Carroll et al.[22] have reported that, in the presence of $Eu(fod)_3$, the cis and trans isomers of **6** are perceptibly anisochronous, we conducted similar experiments at 220 MHz and found that the amount of cis isomer in our crude reaction product was too small to detect. Stereohomogeneity of lactones **5** and **6** was also indicated by ^{13}C NMR. In an experiment suggested by the report of Carroll et al.,[22] *trans*-**6** was epimerized by treatment with 6 M hydrochloric acid to give a GLC-separable mixture of cis and trans isomers. Having authentic *cis*-**6** allowed us to estimate by GLC that the maximum amount of *cis*-**6** produced in the aforementioned conjugate addition was less than 2%.

We have observed these conjugate additions to be rapid and to proceed in high yield. However, we did have difficulty in removing trimethyl phosphite (or its aqueous hydrolysis product) from lactone **6** by preparative GLC. This prompted us to attempt lactone purification by liquid chromatography upon silica. Owing to the quantity of phosphite present, this material tailed into the lactone band. While a second pass through silica should suffice to remove the last traces of phosphite, lactone **6** was ultimately purified by preparative GLC at lower temperature (100 °C). Alternatively, the use of phosphite can be avoided. For example, addition of benzylmagnesium chloride to **1a** (catalyzed by cupric chloride) afforded benzyl-substituted lactone **7** in high yield. The purification of **7** by chromatography upon silica gel was quite routine. As in the case of the previously mentioned organocopper conjugate additions, none of the corresponding cis lactone could be detected in the reaction product either by ^{13}C or ^1H NMR spectroscopy.

Discussion

In view of the obvious steric aspects, attempts to account for the strong preference shown by various reagents for trans addition to δ-substituted, α,β-unsaturated δ-lactones might seem superfluous. Strictly speaking, this preference arises from the energy difference between the product-determining transition states—conformational behavior of the lactones being relevant only insofar as the transition states are "early", resembling starting materials. One can see from Dreiding models that α,β-unsaturated lactones are conformationally simple, carbon 6 being puckered out of the plane occupied by the remaining ring members. Conformational change involves flipping carbon 6 from one ring face to the other, the 6-substituent being either pseudoaxial or pseudoequatorial. In the pseudoequatorial position, the 6-substituent has no obvious bearing upon cis vs. trans addition.[23a] In the pseudoaxial position, the 6-substituent clearly hinders cis but not trans addition. Although it has been suggested that the 6-substituent preferentially occupies the pseudoequatorial position,[23b] it is not evident from models that this is necessarily so, owing to the absence of 1,3-diaxial interactions. In fact, indirect NMR evidence suggests that the 6-substituent spends a significant fraction of the time in a pseudoaxial position.

We have previously shown[24] that chiral γ-lactones form diastereomeric solvates of the general formula **9a,b** in the presence of chiral solvating agent **8**. The γ-lactones are



Ar = 9-anthryl

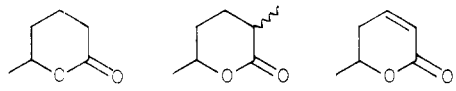
viewed as being roughly planar and, on a time-averaged basis, as being coplanar with the approximately planar chelate ring. Thus, the relative dispositions of R_1 and R_2 (between diastereomeric solvates **9a,b**) with respect to the chemical shift perturbing (shielding) 9-anthryl group accounts for the origin of the enantiotopic chemical shift differences observed at these sites.[24] For γ-lactones, this nonequivalence is usually of sufficient magnitude to allow ready NMR determination of enantiomeric purity and absolute configuration provided the R_1 and R_2 signals can be discerned.

Since δ-lactones are much less planar than γ-lactones, we suggested earlier[24b] that one would probably have to

(21) House, H. O.; Fischer, W. F. *J. Org. Chem.* **1968**, *33*, 949.
(22) Carroll, F. I.; Mitchell, G. N.; Blackwell, J. T.; Sobti, A.; Meck, R. *J. Org. Chem.* **1974**, *39*, 3890.

(23) (a) **Note added in proof**: In a recent discussion of the stereoselectivity of conjugate additions to these lactones, Professor J. Seyden-Penne made the suggestion "the high stereoselectivity observed could be interpreted similarly to the situation described for stereoelectronic control of conjugate additions to 5-alkyl-2-cyclohexenones [E. Toromanoff, *Tetrahedron*, **34**, 2105 (1978)]: axial entry of the cuprate methyl group should lead to an axially substituted 4-CH_3, which would thus be in a trans relationship to R_6, provided that the reaction takes place on the lactone conformer bearing a pseudo equatorial R_6 substituent." We are grateful to Professor Seyden-Penne for permission to quote her suggestion. (b) This suggestion (Elvidge, J. A.; Ralph, P. D. *J. Chem. Soc. B* **1966**, 243) was made partly on the basis of the observed vicinal coupling (10.3 and 5.4 Hz) between the proton on C-6 and those on C-5. The inferred dihedral angles, 160° and 40°, appear to have been derived from Figure 14 in: Conroy, H. *Adv. Org. Chem.* **1960**, *2*, 265. This Karplus curve does not consider the effects of electronegative substituents which are now known to perturb the relationship between dihedral angles and coupling constants. In conjunction with the Karplus argument, Elvidge and Ralph note that treatment of **1a** with methoxide leads to *cis*-α,β-*trans*-γ,δ-hexadienoic acid and infer that it arose from the pseudoequatorial conformation of **1a**. This view may be correct, but it is conceivable that the cis–cis isomer, formation of which would have been adjudged indicative of ring opening from the pseudoaxial conformation, might not be stable under the reaction conditions. Reversible Michael reactions (reclosure, methoxide addition) could provide avenues for the formation of the ultimately isolated product from an initial undetected product.
(24) (a) Pirkle, W. H.; Sikkenga, D. L. *J. Org. Chem.* **1977**, *42*, 1370. (b) Pirkle, W. H.; Sikkenga, D. L.; Pavlin, M. S. *Ibid.* **1977**, *42*, 384.

take lactone conformation into account if the preceding solvation model were to be extended to δ- (and larger) lactones. We can now report that lactone conformation is indeed relevant to the magnitude and sense of enantiomeric NMR nonequivalence induced by fluoro alcohol 8. In particular, we find for δ-lactones that only those substituents which occupy an axial position show appreciable enantiomeric nonequivalence in the presence of alcohol 8. For example, addition of a considerable excess of (−)-8 to racemic lactones[10] **10** or *trans*-**11** produces no



10 **11** **1a**

detectable nonequivalence (90 MHz) for any of the enantiotopic methyls. However, *cis*-**11** shows 5-Hz nonequivalence for the δ-methyl but none for the α-methyl. The explanation for this seems straightforward. The stable conformations of **10** and *trans*-**11** place the methyls in equatorial positions,[25] positions which place them very near the plane of the chelate ring during solvation by alcohol 8. Substituents lying in this plane will not experience differential shielding (**9a** vs. **9b**) by the anthryl group. In the case of *cis*-**11**, the α-methyl is preferentially placed in an equatorial position,[25] the δ-methyl then being axial. In the axial position, the δ-methyl lies well away from the plane of the chelate ring, thus experiencing differential shielding (by anthryl) in diastereomers **9a,b**.

Against this background, the observation of 3-Hz (90 MHz) nonequivalence for the enantiotopic methyls of racemic **1a** (in the presence of excess (−)-**8**) is clearly suggestive that these methyls do not always lie near the plane of the chelate ring during solvation by **8**. Examination of models shows that this condition is fulfilled when the 6-methyl is in the pseudoaxial (but not the pseudoequatorial) position. Hence, we infer the substantial population of the pseudoaxial conformation. Implicit in the foregoing discussion is that solvation by alcohol **8** has no great influence upon lactone conformation. Although this contention cannot be presently substantiated, it seems reasonable and is consistent with all data at hand.

Conclusion

A general synthetic sequence for the resolution of δ-substituted, α,β-unsaturated lactones has been devised. The conjugate addition of organometallic reagents to these lactones proceeds with a very high degree of stereospecificity, affording products capable of further structural elaboration. NMR determination of the enantiomeric purity or absolute configuration of δ-lactones with chiral solvating agents such as **8** will be most feasible for those lactones having substituents in an axial conformation.

Experimental Section

General Methods. ^{1}H NMR spectra were recorded by using Varian-EM 390 or HR 220 spectrometers. ^{13}C NMR were obtained by using a JEOLCO JNM FX 60 instrument. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. IR spectra were recorded on a Perkin-Elmer 237B spectrometer. Optical rotations were obtained by using a Zeiss visual polarimeter with a 1.0-dm tube. A Varian Aerograph Series 1800 gas chromatograph was used for some purifications. Carbowax refers to 15% Carbowax 20-M on Chromosorb W (0.25 in. × 10 ft). SE-30 refers to 15% SE-30 on Chromosorb W (0.25 in. × 6 ft). All solvents were reagent grade except for hexane. Microanalyses were performed by J. Nemeth and Associates, University of Illinois. Acetylenes were purchased from Farchan Chemical Co. and were used without further purification. All solutions were dried over anhydrous magnesium sulfate. The liquid chromatographic separations of the diastereomeric carbamates were performed with an automated preparative system.[14] Chromatographic implements (columns, adsorbent, TLC plates, etc.) and sources are identical with those previously described.[10]

1-[3-(Carbomethoxy)-2-propynyl]heptyl *N*-[1-(1-Naphthyl)ethyl]carbamates (13a,b). These carbamates were synthesized from (±)-methyl 5-hydroxy-2-hexynoate[13a] (**12**) and (*R*)-1-(1-naphthyl)ethyl isocyanate (**14**)[26] by the method previously described[10] for similar compounds, and the diastereomers were completely separated by chromatography (silica gel, 10:1 PhH–ether, $\alpha = 1.80$). The yield of the diastereomeric carbamates may be increased by allowing the diastereomeric mixture to stand at room temperature for several days as a neat oil prior to chromatography.

A total of 2.68 g (84.5%) of the high-R_f (*S,R*-**13a**) diastereomer was isolated as a colorless viscous oil: IR 3335, 2245, 1748–1680 (br), 1613 cm^{-1}; NMR ($CDCl_3$) δ 0.85 (br t, 3 H), 1.07–1.46 (m, 8 H), 1.62 (d, $J = 7.0$ Hz, 3 H), 2.42–2.74 (br d, 2 H), 3.71 (s, 3 H), 4.70–5.01 (m, 1 H), 5.13 (d, $J = 7.5$ Hz, 1 H), 5.40–5.82 (m, 1 H), 7.33–8.19 (m, 7 H); $[\alpha]^{22.4}_D$ +34.8° (*c* 13.1, $CHCl_3$).

Anal. Calcd for $C_{24}H_{29}NO_4$: C, 72.91; H, 7.34; N, 3.54. Found: C, 72.70; H, 7.37; N, 3.66.

A total of 2.8 g (88.3%) of the low-R_f (*R,R*-**13b**) diastereomer was isolated as a white solid: mp 55–56 °C; IR (Nujol) 3335, 2240, 1745–1670 (br), 1610 cm^{-1}; NMR ($CDCl_3$) δ 0.85 (br t, 3 H), 1.01–1.43 (m, 8 H), 1.60 (d, $J = 7.0$ Hz, 3 H), 2.57 (d, $J = 5.5$ Hz, 2 H), 3.67 (s, 3 H), 4.58–4.92 (m, 1 H), 5.03–5.32 (br d, 1 H), 5.38–5.76 (m, 1 H), 7.28–8.17 (m, 7 H); $[\alpha]^{23.8}_D$ −41.6° (*c* 8.8, $CHCl_3$).

Anal. Calcd for $C_{24}H_{29}NO_4$: C, 72.91; H, 7.34; N, 3.54. Found: C, 73.10; H, 7.60; N, 3.71.

(*S*)-(−)-Methyl 5-Hydroxy-2-decynoate (12). Procedure A. To a stirred solution of 2.3 g (5.81 mmol) of **13a** and 651 mg (6.45 mmol) of Et_3N in 40 mL of dry PhH under N_2 was added 874 mg (6.45 mmol) of $HSiCl_3$ in 10 mL of PhH over a 10-min period. The mixture was stirred at 25 °C for 20 h and poured with stirring into 50 mL of saturated aqueous NH_4Cl. The organic layer was collected and the aqueous layer further extracted with ether (3 × 30 mL). The combined organic layers were dried and concentrated in vacuo at less than 30 °C. The residue was chromatographed immediately on silica gel (4:1 hexane–EtOAc). (*R*)-(−)-**14** is first to elute,[27] usually followed by a trace of unreacted carbamate. The desired hydroxy ester eluted immediately after the unreacted carbamate. A 1.02-g (88.6%) amount of pure (*S*)-(−)-**12** was collected: IR 3400, 2240, 1720 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (br t, 3 H), 1.12–1.77 (m, 8 H), 2.50 (d, $J = 5.8$ Hz, 2 H), 3.33 (br s, 1 H, exchanges with D_2O), 3.60–3.96 (m, 1 H), 3.70 (s overlapping m, 3 H); $[\alpha]^{24.2}_D$ −12.5° (*c* 3.0, EtOH).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.09. Found: C, 66.21; H, 8.94.

(*R*)-(+)-12. In a similar manner **13b** was converted to (+)-**12**, which possesses spectral and physical properties identical with those of the (−) enantiomer; $[\alpha]^{24.2}_D$ +11.8° (*c* 1.7, EtOH).

(*S*)-(+)-2-Decen-5-olide (1b). Procedure B. A mixture of 950 mg (4.79 mmol) of (−)-**12**, 150 mg of quinoline, 150 mg of 5% Pd on $BaSO_4$, and 25 mL of EtOAc was hydrogenated until 1 equiv of hydrogen had been absorbed. The catalyst was filtered and the solvent concentrated to afford the crude hydroxy olefinic ester, which was stirred 1 h at reflux in 25 mL of 2:1 EtOH–H_2O containing 1.0 g of NaOH. After being cooled, the solution was acidified with dilute hydrochloric acid and extracted with ether (3 × 20 mL). The combined organic layers were dried and concentrated to afford the crude hydroxy olefinic acid, which was lactonized in 30 mL of PhH at reflux for 1.5 h (azeotropic removal of H_2O). The solution was concentrated, and the residue was molecularly distilled at 0.2 torr to afford 690 mg (85.8%) of pure (+)-**1b**. An analytical sample was collected by preparative GLC (20% SE-30 on Chromosorb W, 170 °C): IR 1730, 1630, 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (br t, 3 H), 1.07–1.92 (m, 8 H), 2.16–2.45 (m, 2 H), 4.12–4.53 (m, 1 H), 5.77–6.03 (m, 1 H), 6.67–6.92 (m,

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(27) In this manner the resolving agent is recovered as the isocyanate.

1 H); ^{13}C NMR ($CDCl_3$) δ 164.6, 145.0, 121.5, 78.0, 34.9, 31.6, 29.4, 24.5, 22.5, 14.0; $[\alpha]^{22.6}_D$ +109.6° (c 2.0, $CHCl_3$) [lit.[16] $[\alpha]^{22}_D$ +82.5°].

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.43; H, 9.52. Found: C, 71.01; H, 9.60.

(*R*)-(−)-1b. In an analogous manner (+)-**12** was converted to (−)-**1b** and found to possess spectral and physical properties identical with those of the (+) enantiomer; $[\alpha]^{21.4}_D$ −110.5° (c 2.5, $CHCl_3$) [lit.[4] $[\alpha]^{25}_D$ −97°].

1-[3-(Carbomethoxy)-2-propynyl]tetradecyl *N*-[1-(1-Naphthyl)ethyl]carbamates (15a,b). These carbamates were prepared from (±)-methyl 5-hydroxy-2-octadecynoate[28] (**16**) by a procedure similar to that used for **13a,b**. The diastereomers were separated by chromatography (silica gel, 3:1 PhH–hexane, α = 1.20).

A total of 8.12 g (81.2%) of the high-R_f ((*S,R*)-**15a**) diastereomer was isolated as a white solid and was recrystallized from MeOH: mp 60–61.5 °C; IR (Nujol) 3460, 2320, 1755–1680 (br), 1602 cm^{-1}; NMR ($CDCl_3$) δ 0.84 (br t, 3 H), 1.06–1.37 (m, 24 H), 1.57 (d, *J* = 6.5 Hz, 3 H), 2.40–2.60 (br d, 2 H), 3.57 (s, 3 H), 4.50–4.93 (m, 2 H), 5.20–5.53 (m, 1 H), 7.06–7.84 (m, 7 H); $[\alpha]^{23}_D$ +29.0° (c 2.5, $CHCl_3$).

Anal. Calcd for $C_{32}H_{45}NO_4$: C, 75.74; H, 8.87; N, 2.76. Found: C, 75.61; H, 9.03; N, 2.91.

A total of 8.42 g (84.2%) of the corresponding low-R_f ((*R,R*)-**15b**) diastereomer was isolated as a white solid and recrystallized from MeOH: mp 54.5–55.5 °C; IR (Nujol) 3450, 2310, 1750–1675, 1605 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (br t, 3 H), 1.10–1.38 (m, 24 H), 1.63 (d, *J* = 6.4 Hz, 3 H), 2.62 (d, *J* = 6.0 Hz, 2 H), 3.72 (s, 3 H), 4.72–5.08 (m, 1 H), 5.20–5.57 (m, 1 H), 5.56–5.97 (m, 1 H), 7.31–8.15 (m, 7 H); $[\alpha]^{23}_D$ −33.9° (c 5.2, $CHCl_3$).

Anal. Calcd for $C_{32}H_{45}NO_4$: C, 75.74; H, 8.87; N, 2.76. Found: C, 75.76; H, 8.76; N, 2.90.

(*S*)-(−)-Methyl 5-Hydroxy-2-octadecynoate (16). Procedure A was used to convert **15a** to a 4.1-g (91.4%) amount of (−)-**16**: IR (Nujol) 3430 (br), 2252, 1716 cm^{-1}; NMR ($CDCl_3$) δ 0.84 (br t, 3 H), 1.0–1.58 (m, 25 H), 2.41 (d, *J* = 6.0 Hz, 2 H), 3.48–3.79 (m, 1 H), 3.60 (s overlapping m, 3 H); $[\alpha]^{23}_D$ −2.54° (c 6.6, $CHCl_3$).

Anal. Calcd for $C_{19}H_{34}O_3$: C, 73.54; H, 10.97. Found: C, 73.14; H, 10.64.

(*R*)-(+)-16. In a similar manner **15b** was converted to (+)-**16**, which possesses spectral and physical properties identical with those of the (−) enantiomer: $[\alpha]^{22.9}_D$ +2.37° (c 7.4, $CHCl_3$).

(*S*)-(+)-2-Octadecen-5-olide (1c). Procedure B was used to convert (−)-**16** to 3.8 g (82.6%) of (+)-**1c**. An analytical sample was purified by preparative GLC (SE-30, 235 °C): IR (Nujol) 1725, 1647 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (br t, 3 H), 1.10–1.78 (m, 24 H), 2.20–2.41 (m, 2 H), 4.26–4.62 (m, 1 H), 6.03–6.24 (m, 1 H), 6.89–7.14 (m, 1 H); $[\alpha]^{24.2}_D$ +32.8° (c 1.3, $CHCl_3$).

Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.14; H, 11.43. Found: C, 77.04; H, 11.81.

(*R*)-(−)-1c. In an analogous manner (+)-**16** was converted to (−)-**1c** and found to possess spectral and physical properties identical with those of the (+) enantiomer: $[\alpha]^{22}_D$ −31.3° (c 1.4, $CHCl_3$).

(3*S*,5*S*)-*trans*-(−)-β-Methyl-δ-*n*-pentylvalerolactone (5). Procedure C. The procedure used is essentially that of House and Fischer.[21] To a stirred 0 °C suspension of 403 mg (2.1 mmol) of CuI and 2 mL of ether under N_2 was added 516 mg (4.16 mmol) of trimethyl phosphite. A 1.4-mL sample of 1.5 M CH_3Li (2.08 mmol in ether) was added followed by an additional 258-mg amount of trimethyl phosphite. This solution was cooled to −78 °C while a solution of 350 mg (2.08 mmol) of (+)-**1b** in 3 mL of ether was added over a 5-min period. After warming to 0 °C, the mixture was poured into 30 mL of saturated aqueous NH_4Cl and extracted with ether (3 × 25 mL). The combined organic layers were dried and concentrated to afford the crude lactone contaminated with much trimethyl phosphite. GLC (20% SE-30 on Chromosorb W, 160 °C) of the product mixture and (+)-**1b** revealed that all of the starting material had been consumed. A pure sample of (−)-**5** was collected by preparative GLC employing the preceding conditions: IR 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (br t, 3 H), 1.13 (d, *J* = 6.3 Hz, 3 H), 1.20–2.73 (m, 13 H), 4.14–4.60 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 172.5, 77.1, 37.5, 35.6, 35.0, 31.6, 24.9, 23.8, 22.5, 21.4, 13.9; $[\alpha]^{23.8}_D$ −65.2° (c 2.1, $CHCl_3$).

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.74; H, 10.87. Found: C, 71.31; H, 10.74.

(3*R*,5*R*)-*trans*-(+)-5. In an identical manner (−)-**1b** was converted to (+)-**5** and found to possess spectral and physical properties identical with those of the (−) enantiomer; $[\alpha]^{20}_D$ +62.8° (c 2.0, $CHCl_3$).

(±)-2-Hexen-5-olide (1a). A procedure similar to that used for the preparation of (±)-**12** was used to convert 4-pentyn-2-ol[29] to methyl 5-hydroxy-2-hexynoate (37% overall).[30] Procedure B was used to convert this hydroxy acetylenic ester to the known racemic **1a**:[1] IR 1725, 1645 cm^{-1}; NMR ($CDCl_3$) δ 1.46 (d, *J* = 6.0 Hz, 3 H), 2.18–2.46 (m, 2 H), 4.28–4.75 (m, 1 H), 5.87–6.06 (m, 1 H), 6.69–6.93 (m, 1 H).

***trans*-(±)-β-Methyl-δ-methylvalerolactone (6).** In a manner analogous to the preparation of the enantiomers of **5** (procedure C), (±)-**1a** was converted to *trans*-**6**. GLC analysis of the product mixture and **1a** confirmed that all the starting material had reacted. A pure sample of *trans*-**6** was collected by preparative GLC (15% Apiezon N on Chromosorb P, 100 °C): IR 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.09 (d, *J* = 6.2 Hz, 3 H), 1.36 (d, *J* = 6.3 Hz, 3 H), 1.24–2.67 (m, 5 H), 4.22–4.67 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 171.8, 73.3, 37.3, 36.7, 23.7, 21.3 (C-3 and C-5 methyl overlap).

Anal. Calcd for $C_7H_{12}O_2$: C, 65.62; H, 9.37. Found: C, 65.42; H, 9.27.

***trans*-(±)-β-Benzyl-δ-methylvalerolactone (7).** To a stirred solution of 4.46 mmol of benzylmagnesium chloride (from 108 mg of Mg, 564 mg of benzyl chloride, and 300 mg of CuCl) in 20 mL of ether at −78 °C was added a solution of 500 mg (4.46 mmol) of **1a** in 10 mL of ether over a 10-min period. The mixture was slowly warmed to 25 °C and poured into 40 mL of saturated aqueous NH_4Cl. The aqueous layer was further extracted with ether (3 × 25 mL), and the combined organic layers were dried and concentrated to afford crude **7**. A 623-mg amount (68.5%) of pure **7** was isolated by column chromatography on silica gel (254-nm UV detection): IR 1750, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 (d, *J* = 7.0 Hz, 3 H), 1.56–1.80 (m, 2 H), 1.92–2.75 (m, 5 H), 4.31–4.68 (m, 1 H), 6.89–7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 172.1, 138.6, 128.9, 128.6, 126.6, 73.6, 41.9, 35.3, 34.4, 30.6, 21.3.

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.39; H, 7.98.

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Registry No. (±)-**1a**, 10385-75-8; (*R*)-**1b**, 51154-96-2; (*S*)-**1b**, 61248-45-1; (*R*)-**1c**, 74591-83-6; (*S*)-**1c**, 74591-84-7; (3*S*,5*S*)-**5**, 74591-85-8; (3*R*,5*R*)-**5**, 74591-86-9; *trans*-(±)-**6**, 52950-00-2; *trans*-(±)-**7**, 74591-87-0; (±)-**12**, 67093-59-8; (*S*)-**12**, 74643-91-7; (*R*)-**12**, 74643-92-8; **13a**, 74591-88-1; **13b**, 74591-89-2; (*R*)-**14**, 42340-98-7; **15a**, 74591-90-5; **15b**, 74591-91-6; (±)-**16**, 74591-92-7; (*S*)-**16**, 74643-93-9; (*R*)-**16**, 74643-94-0; benzyl chloride, 100-44-7.

(28) Prepared by a route analogous to that used for (±)-**12** with one modification. The THP ether acetylene was converted to the lithium acetylide with methyllithium prior to carboxylation.

(29) This hydroxyacetylene was purchased from Farchan Chemical Co.

(30) The (*R*)-α-NEA carbamates of methyl 5-hydroxy-2-hexynoate were chromatographically separated on silica gel with 7:1 PhH–ether (α = 1.95). No attempt was made to convert these carbamates to the corresponding enantiomers of **1a** (parasorbic acid).