Fluorinated Lactic Acids: Easily Accessible Reagents for the Analysis of Chiral Compounds by ^{19}F NMR Spectroscopy. ^{19}F NMR Separation of the Eight Isomers of Menthol

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The rapid development of asymmetric synthesis[1] necessitates the availability of efficient analytical methods and reagents. The increased use of the desired enantiomer in perfumes or medicaments[2] will lead to new analytical standards in patents and pharmacopoeias. Despite a number of methods, namely in chromatography[3] and NMR spectroscopy,[4] there is still a crucial need for new chiral reagents.[5] Among the different nuclei,[6,7] fluorine,[8] because it posses magnetic properties close to those of hydrogen, seems to be ideal, and fluorinated chiral NMR reagents have been developed.[9,10] α-Cyano-α-fluorophenylacetic acid (CFPA) is the most recent of these reagents with very large shift differences in the diastereoisomeric derivatives.[11]

We find that an entire class of fluorinated chiral compounds can be used in the analysis of chiral molecules by ^{19}F NMR. Our approach is based upon the easy and completely stereospecific arylation of the hydroxy group in (*S*)- or (*R*)-lactic acid.[12] These acids are readily accessible,[13] and the starting lactic esters[14] are extremely cheap. Furthermore, both enantiomers are available optically pure,[15] and a number of different chiral acids can be synthesized by simple and stereospecific phenol ether synthesis. The fluorinated acids **4**[16,17] were synthesized via Mitsunobu reaction,[18,19] which is known to proceed with inversion of configuration.[18,20] Thus after saponification of the aryloxy esters,[21] the chiral derivatizing agents (*R*)-**4a**, (*R*)-**4b**, (*R*)-**4c**, (*S*)-**4a**, and (*S*)-**4c** were obtained in good yield (Scheme I).

Though the Mitsunobu reaction usually proceeds with high steric integrity[18] little exact stereochemical support has been published. Determination of the optical purity of (*R*)- and (*S*)-**4c** methyl ester with $Eu(tfc)_3$ and $Pr(tfc)_3$ did not give any interpretable results. On the other hand, condensation of (*R*)- and (*S*)-**4c** with (−)-menthol or (*S*)-ethyl lactate via the acid chloride or 1,3-dicyclohexylcarbodiimide (DCC) method[22] led to (−)-menthtyl 2-(4-fluorophenoxy)propionates **5** and (*S*)-ethyl lactyl 2-(4-fluorophenoxy)propionates **6** with diastereomeric integrity close to 100%. These experimental results demonstrate the high optical purity of acids **4** and, at the same time,

(1) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, London, 1983–1985; Vols. 1–5.

(2) There exist numerous examples of contrasting physiological activities of the enantiomers, the most well-known for producing a negative effect being the soporitif thalidomide ((*R,S*)-3-phthalimidopiperidine-2,6-dione). Both enantiomers are narcotic; however, only the (*S*)-(−)-isomer shows teratogenic activities.

(3) (a) Allenmark, S. G. *Chromatographic Enantioseparation–Methods and Applications*; Ellis Horwood Ltd: Chichester, 1988. (b) König, W. A. *Nachr. Chem. Tech. Lab.* **1989**, *37*, 471.

(4) (a) Raban, M.; Mislow, K. In *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. A., Eds.; Interscience: New York, 1967; Vol. 2., p 199. (b) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates and Resolution*; Wiley: New York, 1981. (c) Reference 1, Vol. 1, Analytical Methods. (d) Parker, D. *Chem. Rev.* **1991**, *91*, 1441.

(5) Most of the chiral NMR reagents are not commercially available and, in many cases, not easily accessible.

(6) Some examples with ^1H NMR: Jacobus, J.; Raban, M. *J. Chem. Educ.* **1969**, *46*, 351. Parker, D. *J. Chem. Soc., Perkin Trans. 2*, **1983**, 83. Doolittle, R. E.; Heath, R. R. *J. Org. Chem.* **1984**, *49*, 5041. Kruizinga, W. H.; Bolster, J.; Kellogg, R. M.; Kamphuis, J.; Boesten, W. H. J.; Meijer, E. M.; Schoemaker, H. E. *J. Org. Chem.* **1988**, *53*, 1826. Bravo, P.; Piovosi, E.; Resnati, G.; Fronza, G. *J. Org. Chem.* **1989**, *54*, 5171. ^{13}C NMR: Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1988**, *29*, 6063. ^{31}P NMR: Anderson, R. C.; Shapiro, M. J. *J. Org. Chem.* **1984**, *49*, 1304. Alexakis, A.; Mutti, S.; Normant, J. F.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 437. Alexakis, A.; Mutti, S.; Mangeney, P. *J. Org. Chem.* **1992**, *57*, 1224. ^{195}Pt NMR: Salvadori, P.; Uccello-Barretta, G.; Bertozzi, S.; Settambolo, R.; Lazzaroni, R. *J. Org. Chem.* **1988**, *53*, 5768. Salvadori, P.; Uccello-Barretta, S.; Lazzaroni, R.; Caporusso, A. M. *J. Chem. Soc., Chem. Commun.* **1990**, 1121.

(7) It is possible to create a diastereomeric relationship with nonchiral reagents by self-discrimination. (a) Phosphorus: Feringa, B. L.; Smaardijk, A. A.; Wynberg, H. *J. Am. Chem. Soc.* **1985**, *107*, 4798. Feringa, B. L.; Stritveen, B.; Kellogg, R. M. *Tetrahedron Lett.* **1986**, *27*, 997. Feringa, B. L.; Strijtveen, B.; Kellogg, R. M. *J. Org. Chem.* **1986**, *51*, 5484. Strijtveen, B.; Feringa, B. L.; Kellogg, R. M. *Tetrahedron* **1987**, *43*, 123. Feringa, B. L. *J. Chem. Soc., Chem. Commun.* **1987**, 695. (b) Silicon: Chan, T. H.; Peng, Q. H.; Wang, D.; Guo, J. A. *J. Chem. Soc. Chem. Commun.* **1987**, 325. (c) Tin: Luchinat, C.; Roelens, S. *J. Am. Chem. Soc.* **1986**, *108*, 4873. (d) Praseodynium: Alvarez, C.; Barkaoui, L.; Goasdoue, N.; Daran, J. C.; Platzer, N.; Rudler, H.; Vaissermann, J. *J. Chem. Soc., Chem. Commun.* **1989**, 1507.

(8) Cavalli, L. Fluorine 19 NMR Spectroscopy. In *Annual Reports on NMR Spectroscopy*; Mooney, E. F., Ed.; Academic Press: New York, 1976; Vol. 6b.

(9) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1968**, *90*, 3732. Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. Sullivan, G. R.; Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 2143.

(10) Other fluorinated reagents: Houben-Weyl *Methoden der Organischen Chemie*; Thieme Verlag: Stuttgart, 1984; Vol. VI/1b, pp 6–9. Robert, D. U.; Costa, D. J.; Riess, J. G. *J. Chem. Soc., Chem. Commun.* **1975**, 29. Robert, D. U.; Costa, D. J.; Riess, J. G. *Org. Magn. Res.* **1975**, *7*, 291. Pirkle, W. H.; Simmons, K. A. *J. Org. Chem.* **1981**, *46*, 3239. Kawa, H.; Yamaguchi, F.; Ishikawa, N. *J. Fluorine Chem.* **1982**, *20*, 475. Hamman, S.; Berrelle, M.; Tetatz, F.; Beguin, C. G. *J. Fluorine Chem.* **1987**, *37*, 58. Takeuchi, Y.; Ogura, H.; Ishii, Y.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1*, **1989**, 1721.

(11) Takeuchi, Y.; Itoh, N.; Note, H.; Koizumi, T.; Yamaguchi, K. *J. Am. Chem. Soc.* **1991**, *113*, 6318.

(12) Holten, C. H.; Müller, A.; Rehbinder, D. *Lactic Acid*; Verlag Chemie: Weinheim, 1971.

(13) *O*-Aryl 2-hydroxypropionic acids are widely used as herbicides: *Herbicides*; Kearney, P. C.; Kaufman, D. D., Ed.; Marcel Dekker: New York and Basel, 1975; Vol. 1. Numerous patents exist, cf. Salz, U.; Rüchard, C. *Chem. Ber.* **1984**, *117*, 3457.

(14) Chiral α-hydroxy carboxylic acids can also be synthesized stereospecifically from the corresponding α-amino acids via deamination. For a recent example see: Kunz, H.; Lerchen, H.-G. *Tetrahedron Lett.* **1987**, *28*, 1873.

(15) (a) Optical purity of commercially available lactic esters, ee >97.6%: Hintzer, K.; Weber, R.; Schurig, V. *Tetrahedron Lett.* **1981**, *22*, 55. ee >99%: Massad, S. K.; Hawkins, L. D.; Baker, D. C. *J. Org. Chem.* **1983**, *48*, 5180. ee 99% Koppenhoefer, B.; Trettin, U.; Figura, R.; Lin, B. *Tetrahedron Lett.* **1989**, *30*, 5109. (b) For the purification of chiral 2-phenoxypropionic acids cf. Gabard, J.; Collet, A. *New J. Chem.* **1986**, *10*, 685.

(16) (a) The ethyl ester of acid **4c** has been synthesized via Mitsunobu reaction: Dirlam, N. L.; Moore, B. S.; Urban, F. J. *J. Org. Chem.* **1987**, *52*, 3587. (b) The fluorinated chiral acids with the opposite (S) configuration are accessible from commercially available (*R*)-(+)-isobutyl lactate.

(17) Only the para-fluorinated acid **4c** has been synthesized in optically active form: Sjöberg, B. *Arkiv Kemi* **1960**, *15*, 451. Racemic acids: Joshi, K. C.; Bahel, S. C. *J. Ind. Chem. Soc.* **1960**, *37*, 365 and 685.

(18) Mitsunobu, O. *Synthesis* **1981**, 1; Castro, B. R. *Org. React.* **1983**, *29*, 1. Synthesis of alkyl aryl ethers: Manhas, M. S.; Hoffman, W. H.; Lai, B.; Bose, A. K. *J. Chem. Soc., Perkin Trans. 1*, **1975**, 461.

(19) Tosylates are also suitable leaving groups for S_N2 reactions of lactic esters: Burkard, U.; Effenberger, F. *Chem. Ber.* **1986**, *119*, 1594. Effenberger, F.; Burkard, U.; Willfahrt, J. *Liebigs Ann. Chem.* **1986**, 314.

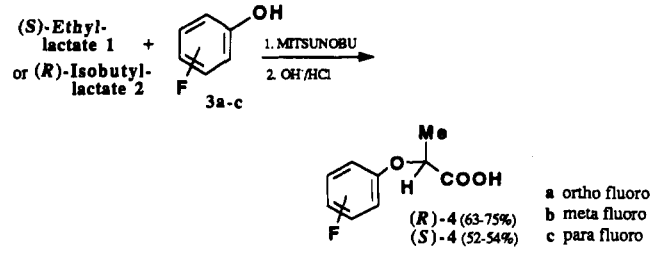
(20) In particular cases, retention of configuration has been observed, cf. Audia, J. E.; Colocci, N. *Tetrahedron Lett.* **1991**, *32*, 3779. Farina, V. *Tetrahedron Lett.* **1989**, *30*, 6645.

(21) Tottie, L.; Baeckström, P.; Moberg, C.; Tegenfeldt, J.; Heumann, A. *J. Org. Chem.* **1992**, *57*, 6579.

(22) Neises, B.; Steglich, W. *Agnew. Chem., Int. Ed. Engl.* **1978**, *17*, 522. Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, *19*, 4475. Neises, B.; Steglich, W. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VII, p 93.

0022-3263/93/1958-1276$04.00/0

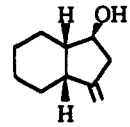
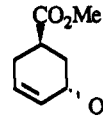
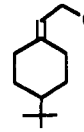
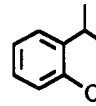
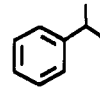
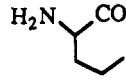
Scheme I



that no significant isomerization of the chiral acid (proton in α-position) had occurred during esterification. *O*-Aryllactic acids are good reagents for the obtention of chiral alcohols via kinetic resolution–esterification with DCC.[23] For enantiomeric excess determinations this is not wanted. Chiral acids **4** are reactive enough for esterification[24] (no kinetic resolution), when applied in slight excess, with common secondary alcohols. Kinetic resolution has been encountered with hindered alcohols such as *t*-BuCH(CH_3)OH and PhCH(CF_3)OH in reactions with MTPA.[9] With fluorophenoxy lactic acid **4c** esterification of these alcohols via the acid chloride proceeds without kinetic resolution. However condensation with DCC as reagent occurs without problems in the case of PhCH(CF_3)OH but leads to variable diastereomeric mixtures with *t*-BuCH(CH_3)OH. The esters of indanol **7** with fluorinated lactic acids **4** have been obtained via Pd-catalyzed cyclization of *cis*-1,2-divinylcyclohexane.[21] Appreciable shift differences (Δδ) of 0.02–0.127 ppm in the ^{19}F NMR spectra of the two diastereoisomic esters were found. Values of the same order of magnitude can be observed with various racemic alcohol, phenols, amines, and amino acids (Table I) after derivatization via DCC condensation (yields 65–86%). Signal separations of 0.007–0.336 ppm in the diastereoisomeric esters and amides are characteristic for **4**. These data are comparable to those usually observed with esters of MTPA.[9] The absolute value of the chemical shifts is concentration dependent (variation of the δ value: ±0.02 ppm); however, the shift differences between two diastereomeric isomers have been found to be more accurate than 0.001 ppm. Even in the case of the smallest difference, the derivative of (±)-2-ethylhexylamine **18**, the amino group being separated from the chiral tertiary carbon, there is still a well-defined splitting of 0.007 ppm thus showing the (NMR) nonequivalence of the three neighbouring methylene groups.

Several remarkable observations are worth mentioning. The chiral recognition is not limited to secondary substrates, and good separations are found with primary aliphatic and alicyclic alcohols or even phenols (**11**, **16**, and **17**). That means that the heteroatom does not necessarily have to be connected to a chiral carbon. The reagent is also able to recognize planar chirality[25] in alcohol **11** (Δδ 0.034 ppm). In all cases the fluorine atom is more than 8 atoms distant to the chiral center of the alcohol or amine, the longest distance being 10 atoms in derivatives of **16**.[26]

Table I. ^{19}F NMR Chemical Shifts of (*R*)-2-(4-Fluorophenoxy)propionic Acid Derivatives of Racemic Alcohols, Amines, and Amino Acids

	chemical shift[a] (ppm)		
	δ_1	δ_2	Δδ
 **7**	-123.074	-123.195	0.121
	-123.069	-123.196	0.127[b]
	-111.688	-111.708	0.02[c]
2-cyclohexenol **8**[d]	-123.199	-123.246	0.047
 **9**	-123.978	-123.987	0.009[e]
endo-norborneol **10**	-123.177	-123.234	0.057
 **11**	-123.108	-123.142	0.034
2-octanol **12**	-123.238	-123.353	0.115
1-hepten-3-ol **13**	-123.168	-123.310	0.142
sec-phenethyl alcohol **14**	-123.163	-123.197	0.034
α-tetralol **15**	-123.184	-123.241	0.057
 **16**	-122.603	-122.699	0.096
 **17**	-123.125	-123.21	0.085
2-ethylhexyl amine **18**	-122.354	-122.360	0.007[e]
sec-phenethyl amine **19**	-122.076	-122.213	0.137
phenylalanine methyl ester **20**	-121.872	-122.208	0.336
 **21**	-121.890	-122.059	0.169

[a] Bruker AM 200; ^{19}F NMR chemical shifts were recorded in $CDCl_3$ relative to $CFCl_3$ as external standard under proton decoupling conditions. [b] Ester with (*R*)-**1a**. [c] Ester with (*R*)-**1b**. [d] Ester with (*R*)-**1a**: δ_1 -123.715, δ_2 -123.769, Δδ 0.054 ppm. [e] No base-line separation.

In the proton spectra of diastereomeric esters and amides, two characteristic sets of signals of the lactic acid part at about 4.7 ppm (2 q, 1 H), and at 1.6 ppm (2 d, 3 H) permit an estimation of the chiral purity of the mixture. However, the determination of the exact value is only possible in rare cases (*sec*-phenethyl alcohol) **14** or ethyl lactate **1** for example). Of course, such an analysis is completely impossible for complex reaction mixtures such as the eight enantiomers of menthol (three chiral carbons). Hydrogenation of thymol leads to this mixture[27] whose most important isomer (1*R*,2*S*,5*R*)-(−)-menthol[28] is required in high optical purity. The ^{19}F NMR spectra (188.3 MHz) of the mixture of menthols, after derivatization with (*R*)-**4c** is shown in Figure 1. It is a remarkable feature of fluorinated lactic acids that all eight diastereomers of such

(23) Chinchilla, R.; Najera, C.; Yus, M.; Heumann, A. *Tetrahedron: Asymmetry* **1990**, *1*, 851.
(24) A practical DCC esterification protocol has been published after submission of this article: Paquette, L. A.; Maynard, G. D. *J. Am. Chem. Soc.* **1992**, *114*, 5018.
(25) Fiaud, J.-C.; Legros, J.-Y. *J. Org. Chem.* **1990**, *55*, 4840. We thank Drs. Fiaud and Legros for a sample of 11.
(26) For an interesting selone reagent for remote chiral centers, cf. Silks, L. A., Dunlap, R. B.; Odom, J. D. *J. Am. Chem. Soc.* **1990**, *112*, 4979.
(27) Bauer, K.; Garbe, D. *Common Fragrance and Flavor Materials*; VCH: Weinheim, 1985.
(28) Cf. Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *22*, 6901.

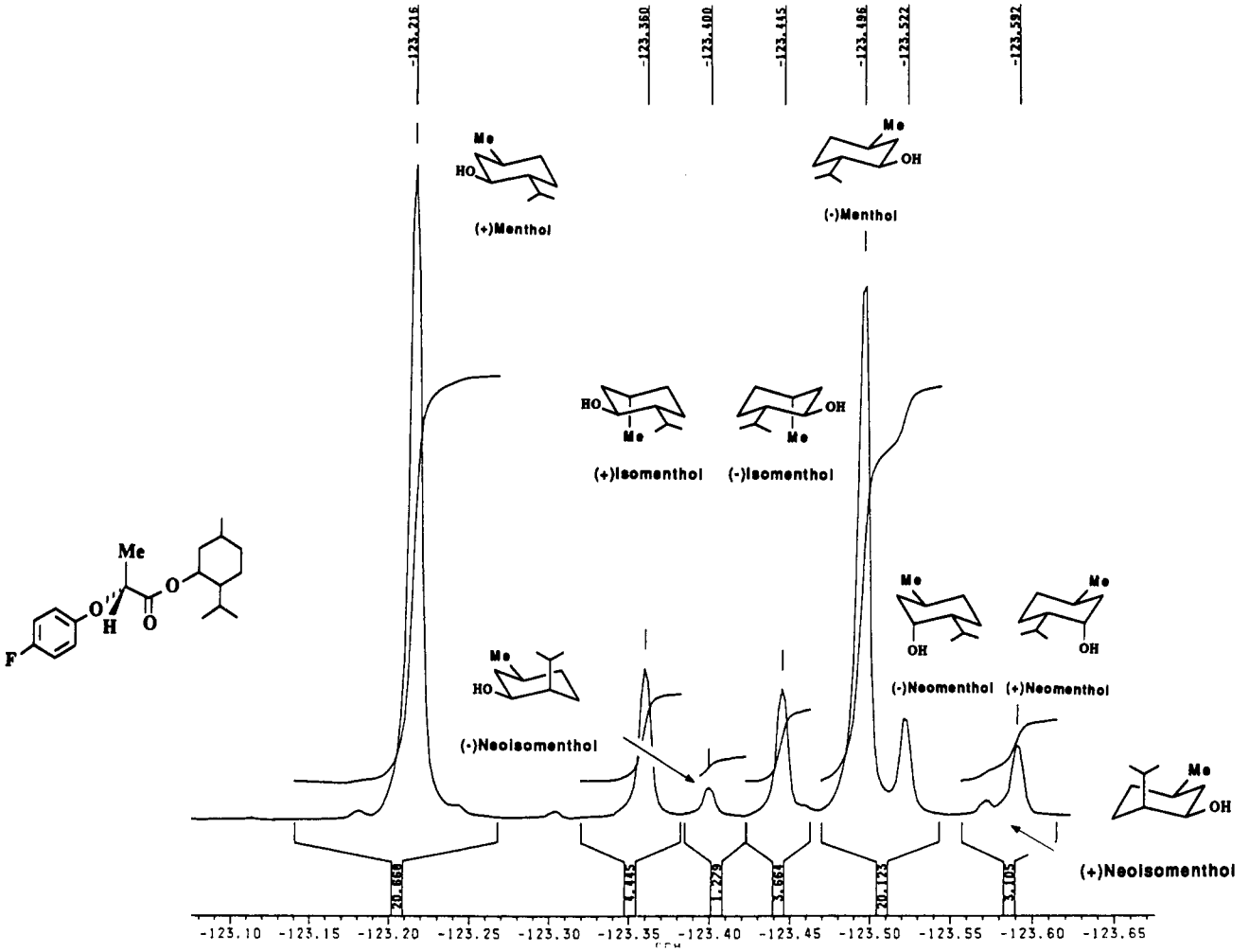


Figure 1. ^{19}F NMR spectra of (*R*)-2-(4-fluorophenoxy)propionic esters of the four stereoisomers of industrial menthol (188.3 MHz).

closely related structures can be attributed unambiguously on the same NMR spectrum of the corresponding esters. The same experiment with MTPA esters[9] only shows three broad peaks which do not allow any analysis of the mixture.[29]

The rationalization of the phenomena of chiral discrimination either in terms of reactivity or spectroscopy is still a different task. Nevertheless, it is fundamentally a spacial and topological problem. Phenyl-substituted α-alkoxy carboxylic esters (e.g., MTPA- or *O*-methoxy mandelic esters) are known[30] to adopt distinct preferred conformations in solution, a behavior that is being used for determination of absolute configurations by proton NMR[31] as well as for efficiently controlling asymmetric Diels–Alder reactions.[32] Methyl groups in the ortho position seem to amplify this effect and literally freeze the aromatic group of the mandelate into the perpendicular conformation. Comparable to the diastereofacial discrimination in highly efficient asymmetric reactions,[32] (conformationally) well-defined orientations of the phenyl group in derivatives of **4** create the different spatial interactions with the racemic alcohol or amine parts. That these chiral acids are particularly well situated to transmit conformational and configurational changes via the ^{19}F NMR resonances is demonstrated in the menthol series.[33]

Experimental Section

NMR Methods. The ^{19}F NMR spectra have been recorded on Bruker AM 200 and AC 100 instruments at 188.3 and 94.1 MHz, respectively. Chemical shifts were recorded in $CDCl_3$ solutions relative to $CFCl_3$ as external standard (SR 595).

Synthesis of (*R*)-*O*-(Fluoroaryl)lactic Acids (*R*)-4.[21] A solution of DEAD (diethyl azodicarboxylate) or DIAD (diisopropyl azodicarboxylate) (0.1 mol) in THF (75 mL) was added dropwise to a mixture of (*S*)-ethyl lactate (0.1 mol) (Merck or Fluka), the fluorophenol (0.1 mol), and triphenylphosphine (0.1 mol) in THF (150 mL). The mixture was stirred overnight at room temperature. After evaporation of the THF, a mixture of hexane and diethyl ether (1:1, 250 mL) was added to the viscous residue and stirring continued until a crystalline precipitate had separated (1 h). The crystalline precipitate was filtered off, and the filtrate was washed successively with 1 N NaOH (2 × 100 mL), brine, and water. After the solvent was evaporated the crude product was directly hydrolyzed (2 h, room temperature or 30 min at 60 °C) in menthol (400 mL) with 2 N NaOH (100 mL). The methanol was evaporated with minimum heat, and water (100 mL) was added. Extraction with diethyl ether (3 × 100 mL) eliminated most of the impurities. After being cooled

(29) Supplementary material.
(30) Indirect experimental evidences, supported by recent ab initio calculations, cf. Tucker, J. A.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1990**, *112*, 5465.
(31) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092. Lemiére, G. L.; Willaert, J. J.; Dommisse, R. A.; Lepoivre, J. A.; Alderweireldt, F. C. *Chirality* **1990**, *2*, 175.
(32) Tripathy, R.; Carroll, P. J.; Thornton, E. R. *J. Am. Chem. Soc.* **1990**, *112*, 6743.
(33) Synthesis of (+)-neoisomenthol: Lombardo, L. *Org. Synth.* **1987**, *65*, 81. Wilhelm, D.; Bäckvall, J. E.; Nordberg, R. E.; Norin, T. *Organometallics* **1985**, *4*, 1296.

on an ice bath the aqueous phase was neutralized with concd HCl (20–25 mL). The free acid was extracted with diethyl ether (3 × 100 mL). After drying ($MgSO_4$) and evaporation the residue was distilled in a Kugelrohr apparatus or recrystallized from hexane. Small enantiomeric impurities were removed via Collet's *n*-propylamine purification procedure.[15b] The chiral acid (35 mmol) was dissolved in EtOAc (14 mL), and *n*-propylamine (2.1 mL) was added. After the warm solution was cooled the salt crystallized within some hours. The white precipitate was filtered and washed with a small amount of ethyl acetate. The free acid was liberated with 1 N HCl in the usual way.

Synthesis of (*S*)-*O*-(Fluoroaryl)lactic Acids (*S*)-4. These acids were obtained from (*R*)-(+)-isobutyl lactae (Aldrich, >97%).

Esterification with DCC-DMAP.[22] 1,3-Dicyclohexylcarbodiimide (DCC, 0.55 mmol), chiral acid **4** (0.55 mmol), and the alcohol (0.5 mmol) were dissolved in anhydrous THF or ethanol-free CH_2Cl_2 (5 mL), and some crystals of 4-(dimethylamino)-pyridine or 4-pyrrolidinopyridine were added. The clear solution became rapidly cloudy on stirring. Reaction time: 12–24 h at room temperature. The solution was filtered and the solvent evaporated without heating. The solid or semisolid residue was transferred to a silica gel column (2 g) and the product(s) eluted with 10-mL fractions of hexane and 1, 2, 5, 10, and 20% ether/hexane mixtures. All fractions containing the diastereomeric esters, frequently fractions 3 and 4 (2 and 5% ether) were combined and the solvent evaporated (TLC: 20% EtOAc/hexane), yields 65–86%.

Esterification via Acid Chloride/Pyridine. The solution of acid **4** (1.1 mmol) and freshly distilled thionyl chloride (0.25 mL) in benzene (2.5 mL) was refluxed for 2 h. Benzene and the remaining thionyl chloride were evaporated (water aspiration and high vacuum pump), and the alcohol (1 mmol) was dissolved in benzene (3 mL) added together with pyridine (0.6 mL). After the mixture was allowed to stand for 3 h, ether/hexane (3/7, 30 mL) was added and the organic phase washed successively with water (2×), dilute HCl (1×), and water (1×). After drying ($MgSO_4$) and evaporation the residue was analyzed directly by NMR, yields 75–96%.

Supplementary Material Available: Experimental data of (*R*)- and (*S*)-2-(2-, 3-, and 4-fluorophenoxy)propionic acids **4** and esters **5**, **6**, **22**, and **23**, ^1H and/or ^{19}F NMR spectra of (*R*)-2-(3-fluorophenoxy)propionic acid (*R*)-**4b**, (*R*)-MTPA esters of the four stereoisomeric menthols, and the esters of (−)-menthol, (*S*)-ethyl lactate, (*R*,*S*)-2,2-dimethyl-3-butanol, and (*R*,*S*)-α-(trifluoromethyl)benzyl alcohol with (*R*)- and (*S*)-**4c** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.