+ 3 drops Me_2SO-d_6) 1.15 (t, 3 H), 2.92 (m, 2 H), 3,83 (t, 2 H), 4.06 (q, 2 H), 4.73 (q, 1 H), 6.88 (d, 2 H), 7.32 (d, 1 H), 7.46 (d, 2 H), 7.53 (m, 1 H), 7.98 (s, 1 H). Anal. Calcd for $C_{17}H_{17}IN_2O_4$: C, 41.60, H, 4.24, N, 6.93. Found: C, 41.40, H, 4.10, N, 6.61.

Registry No. 1, 768-32-1; 2, 591-50-4; 3, 3728-43-6; 4, 624-31-7; 5, 17964-29-3; 6, 35444-94-1; 7, 105089-60-9; 8, 105089-61-0; 9, 105120-26-1; 10, 105089-62-1; 11, 105089-63-2; $AgNO_3$, 7761-88-8; AgOBz, 532-31-0; $AgBF_4$, 14104-20-2; CF_3CO_2Ag, 2966-50-9.

Resolution and Assignment of Absolute Configuration to the Enantiomers of Anastrephin and Epianastrephin and Their Analogues

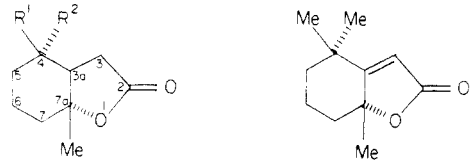
Lucjan Strekowski,[1] Melean Visnick, and Merle A. Battiste*

Department of Chemistry, The University of Florida, Gainesville, Florida 32611

Received August 13, 1984

A new chemical route for a facile resolution of racemates of trans-fused γ-lactones is presented. The method has been applied to the resolution of natural lactones anastrephin (**1a**) and epianastrephin (**1b**) and their three analogues **1c–e**. Racemic lactones **1** are reacted with (*R*)-(−)-α-phenylglycinol to give diastereomeric hydroxy amides **4**, which can easily be separated by using standard, low-pressure, silica gel chromatography. A mild base hydrolysis of **4** to produce hydroxy acids **5** is followed by regeneration of the lactone function. The lactones are assigned absolute configuration by application of NMR, optical, and chemical methods. The latter approach includes a stereospecific synthesis of (+)-*trans*-tetrahydroactinidiolide (**1d**) and (−)-dihydroactinidiolide (**1g**). A new stereoselective and efficient synthesis of (±)-**1d** is also presented.

Anastrephin (**1a**) and epianastrephin (**1b**) are major components of the male sex pheromone of both Caribbean, *Anastrepha suspensa* (Loew), and Mexican, *Anastrepha ludens* (Loew), fruit flies. The structures and relative configurations of these lactones have been established in this laboratory using chemical methods[2,3] and by others using an X-ray diffraction method.[4] We have shown that the natural lactones isolated from cultured *A. suspensa* males are not single enantiomers, although each is enantiomerically enriched. Application of the chiral NMR shift reagent has indicated enantiomeric excess in the range 55 ± 3 (−)/45 ± 3 (+) for both lactones **1a** and **1b** and suggested the 3a*S*,7a*S* configuration of the major (−) enantiomers.[2]



1a, R^1 = $CH{=}CH_2$, R^2 = CH_3

1b, R^1 = CH_3, R^2 = $CH{=}CH_2$

1c, R^1R^2 = CH_2CH_2

1d, $R^1{=}R^2$ = CH_3

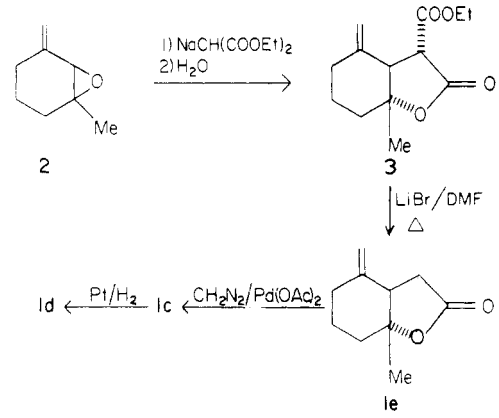
1e, R^1R^2 = CH_2

1f, R^1 = CH_3, R^2 = H

1g

In this paper we report a facile resolution of enantiomers of anastrephin and epianastrephin as well as confirmation of the previously suggested configurational assignments. In addition, we present the synthesis, resolution, and determination of the absolute stereochemistry of three analogues, **1c–e**, of these natural lactones, as well as the stereospecific transformation of optically active lactone **1e** into other lactones, namely, *trans*-tetrahydroactinidioilide[5] (**1d**), lactone **1f**, and dihydroactinidiolide[6-8] (**1g**). In spite of considerable interest in *trans*-tetrahydroactinidiolide, this compound has not been reported before in an optically active form.

Scheme I



Besides the intrinsic interest in development of a new methodology for a facile resolution of enantiomeric lactones, the optically active compounds, which are reported here, can serve as valuable probes in the investigation of the structure of the pheromone receptors in the species of *A. suspensa* and *A. ludens* flies. Bioassays of these

(1) Present address: Department of Chemistry, Georgia State University, Atlanta, GA 30303.

(2) Battiste, M. A.; Strekowski, L.; Vanderbilt, D. P.; Visnick, M.; King, R. W.; Nation, J. L. *Tetrahedron Lett.* **1983**, *24*, 2611.

(3) Visnick, M. Ph.D. Dissertation, University of Florida, 1983.

(4) Stokes, J. B.; Uebel, E. C.; Warthen, J. D.; Jacobson, M.; Flippen-Anderson, J. L.; Gilardi, R.; Spishakoff, L. M.; Wilzer, K. R. *J. Agric. Food Chem.* **1983**, *31*, 1162.

(5) For syntheses of (±)-*trans*-tetrahydroactinidiolide, see: (a) Hoye, T. R.; Caruso, A. J.; Kurth, M. J. *J. Org. Chem.* **1981**, *46*, 3550. (b) Hoye, T. R.; Kurth, M. J. *Ibid.* **1979**, *44*, 3461. (c) Hoye, T. R.; Kurth, M. J. *Ibid.* **1978**, *43*, 3693. (d) Saito, A.; Matsushita, H.; Tsuino, Y.; Kisaki, T.; Kato, K.; Noguchi, M. *Chem. Lett.* **1978**, 1065. (e) Matsumoto, T.; Sakata, G.; Tachibana, Y.; Fukui, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1147.

(6) For syntheses of the enantiomers of dihydroactinidiolide, see: (a) Mori, K.; Nakazono, Y. *Tetrahedron* **1986**, *42*, 283. (b) Isoe, S.; Hyeon, S. B.; Katsumura, S.; Sakan, T. *Tetrahedron Lett.* **1972**, 2517. (c) Kienzle, F.; Meyer, H.; Minder, R. E.; Thommen, H. *Helv. Chim. Acta* **1978**, *61*, 2616. (d) Eschenmoser, W.; Uebelhart, P.; Eugster, C. H. *Ibid.* **1982**, *65*, 353.

(7) For a review on the synthesis of (±)-dihydroactinidiolide, see ref 6a.

(8) For a review on the isolation of racemic or enantiomerically enriched dihydroactinidiolide from natural sources consult ref 6a.

0022-3263/86/1951-4836$01.50/0 © 1986 American Chemical Society

lactones of high optical purity will be reported elsewhere in due course.

With the recent improvement in the synthesis of (±)-anastrephin (**1a**) and (±)-epianastrephin (**1b**), these lactones are now readily available.[2,9] (±)-Lactone **1e** has also been prepared by us before.[10] In addition, we have synthesized this compound by an experimentally much simpler approach, which is presented in Scheme I. Thus the reaction of epoxide **2** with diethyl sodiomalonate furnished compound **3**, which was treated with LiBr in boiling dimethylformamide to give the methylene lactone **1e** in an excellent overall yield. Only one isomer of **3** was obtained, for which the trans configuration of the methyl and ethoxycarbonyl groups was assigned from the coupling constant (J = 11 Hz) for the protons 3-H and 3a-H. (±)-Lactone **1e** was further transformed into (±)-*trans*-tetrahydroactinidiolide (**1d**) by cyclopropanation of the methylene function to furnish spirolactone **1c**, followed by hydrogenation. Although many syntheses of compound (±)-**1d** have been reported,[5] the method presented by us deserves attention. It is 100% stereoselective, efficient, and simple.

Racemic lactones **1a–e** are poor candidates for successful, direct resolution of the enantiomers using chiral liquid chromatography columns.[11] Therefore, our resolution plan called for reaction of the racemic lactones with an enantiomerically pure amine to give diastereoisomeric hydroxy amides,[12] which could be separated chromatographically on a standard adsorbent, followed by hydrolysis to hydroxy carboxylic acids and then regeneration of the lactone function.

Although virtually any primary amine can be reacted with lactones to produce hydroxy amides, hydrolysis of the latter compounds is often a difficult task. For example, attempted hydrolysis of the hydroxy amides derived from lactones **1a** or **1e** and α-methylbenzylamine, either through nitrosamide rearrangement[13] or on treatment with acid[12c] or sodium peroxide,[14] did not produce the desired hydroxy acids. In addition, apparently for steric reasons, the trans-hydroxyl group in these compounds did not catalyze the base hydrolysis of the amide function.[15] We reasoned that the latter difficulty could be overcome by preparation of amides from these trans-fused bicyclic lactones and a conformationally flexible amino alcohol. (*R*)-(−)-α-Phenylglycinol was a suitable reagent here, since it is commercially available and UV-active, thus permitting ready monitoring of chromatographic separations. We have found that the diastereoisomeric hydroxy amides **4a–e**, obtained from trans-fused lactones **1a–e** and the phenylglycinol, are easily separable on a standard, low-pressure silica gel column.[16] Pure diastereomers were

Scheme II

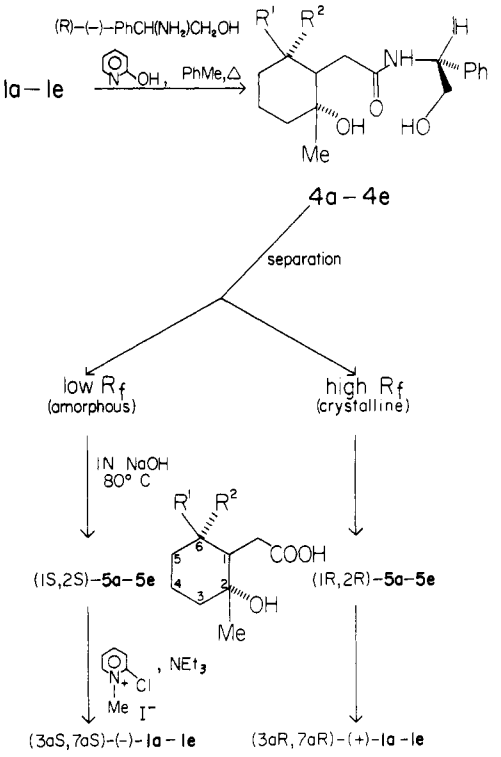


Table I. Specific Optical Rotations $[\alpha]^{25}_{\lambda}$ (Hexanes, c 0.04 g/mL) for 3a*R*,7a*R* Lactones[a] 1 Prepared from the High-R_f Diastereoisomeric Amides 4

3a*R*,7a*R* lactone	λ, nm			
	589	546	436	365
1a	+48.8	+61.4	+114.1	+206.6
1b	+74.7	+90.3	+161.9	+281.1
1c	+30.1	+38.7	+74.6	+131.5
1d	+71.0	+86.1	+153.6	+260.5
1e	−40.1	−46.4	−69.3	−96.1
1f	+51.1	+61.2	+116.0	+204.8

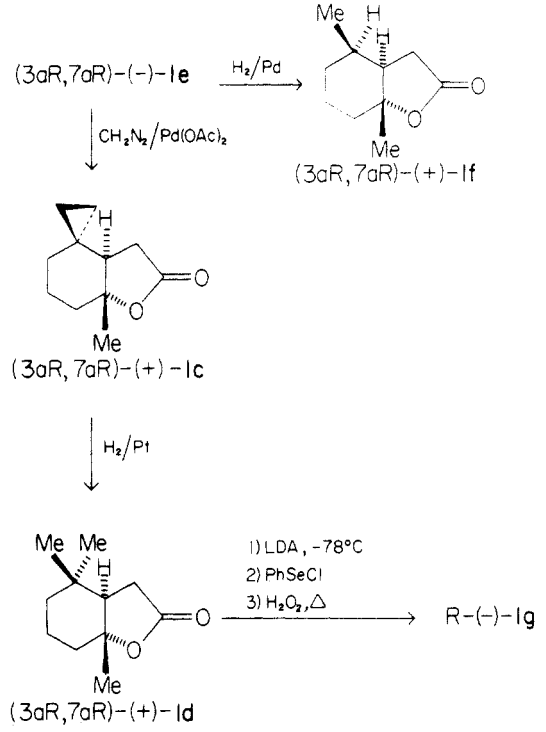
[a] The optical purity of all the enantiomeric lactones **1a–f** is higher than 99%.

hydrolyzed in 1 N NaOH to give the respective enantiomeric hydroxy acids **5a–e** in essentially quantitative yield (Scheme II). The rate of this hydrolysis is comparable to that for alkyl esters of acids **5a–e**, thus reflecting the unusual mildness of this method. The value of this saponification method is further stressed by noting that the reported facile acid hydrolysis[12c] of amides derived from phenylglycinol is not applicable to amides **4a–e** which contain acid-sensitive tertiary hydroxyl functions.

The acids **5a-e** were lactonized in an essentially quantitative yield using the 2-chloro-1-methylpyridinium iodide/triethylamine method, reported by us recently.[10] The enantiomeric lactones thus obtained were assigned absolute configurations by using several independent methods. The (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol-induced magnetic nonequivalence[15b,17] of the 7a-methyl group in the lactones allowed the establishment of the absolute configuration as well as enantiomeric purity.[18] All lactones **1a-e**, derived from the high-R_f crystalline diastereomers and from the low-R_f amorphous diastereomers, were found

(9) Saito, A.; Matsushita, H.; Kaneko, H. *Chem. Lett.* **1984**, 729.
(10) Strekowski, L.; Visnick, M.; Battiste, M. A. *Synthesis* **1983**, 493.
(11) As defined by Pirkle, in terms of affinity, chiral recognition requires a minimum of three simultaneous interactions between the chiral stationary phase (CSP) and at least one enantiomer. At least one of these interactions must be stereochemically dependent: (a) Pirkle, W. H.; House, D. W. *J. Am. Chem. Soc.* **1981**, *103*, 3964. (b) Pirkle, W. H.; Finn, J. M. *J. Org. Chem.* **1982**, *47*, 4037 and references cited therein. Although a weak, three-point, differential binding can be predicted for interactions of unsaturated lactones **1a**, **1b**, and **1e** with chiral CSP's, a much weaker (if any) differential binding can be expected for saturated lactones **1c** and **1d**.
(12) (a) Openshaw, H. C.; Whittaker, N. *J. Chem. Soc. C* **1969**, 89. (b) Helmchen, G.; Nill, G.; Flockerzi, D.; Schuhle, W.; Youssef, M. S. K. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 62. (c) Helmchen, G.; Nill, G.; Flockerzi, D.; Youssef, M. S. K. *Ibid.* **1979**, *18*, 63.
(13) White, E. M. *J. Am. Chem. Soc.* **1955**, *77*, 6011.
(14) Vaughn, H. L.; Robbins, M. D. *J. Org. Chem.* **1975**, *40*, 1187.
(15) (a) Morris, J. J.; Page, M. I. *J. Chem. Soc., Chem. Commun.* **1978**, 591. (b) Pirkle, W. H.; Sikkenga, D. L. *J. Org. Chem.* **1977**, *42*, 1370. (c) Pirkle, W. H.; Adams, P. E. *Ibid.* **1980**, *45*, 4111.
(16) Diastereomers of hydroxy amides **4a–e** showed the separability factor α of 1.20 ± 0.05.
(17) (a) Pirkle, W. H.; Sikkenga, D. L.; Pavlin, M. S. *J. Org. Chem.* **1977**, *42*, 384. (b) Pirkle, W. H.; Dennis, J. *Top. Stereochem.* **1982**, *13*, 263.
(18) See Experimental Section (General Methods) for the conditions.

Scheme III



to have the 3a*R*,7a*R* and 3a*S*,7a*S* configurations, respectively. For lactones **1a-d** these assignments were further confirmed by correlation of the sign of the Cotton effect with the respective molecular models[19] (Table I). However, for enantiomeric lactones **1e** the sector lactone rule gave different absolute configuration assignments than those predicted from the NMR studies. Apparently, application of the optical method resulted in an erroneous assignment which may be due to a strong influence of the olefinic chromophore in the molecule on the observed long-wavelength optical rotation. In fact, the configurations of the enantiomeric lactones **1e**, derived from the NMR studies, were in agreement with those predicted using the alkene octant rule.[20]

A further proof for our absolute configurational assignments is presented in Scheme III. Thus, hydrogenation of the olefinic chromophore in compound (-)-**1e** gave lactone (+)-**1f**, which was assigned the 3a*R*,7a*R* configuration by both the NMR method and the sector lactone rule.[21] Furthermore, the (-)-methylene lactone **1e** was transformed into the (+)-cyclopropane lactone **1c** and then by hydrogenation of the latter compound into (+)-*trans*-tetrahydroactinidiolide (**1d**). Transformation of this lactone as shown into (-)-dihydroactinidiolide (**1g**), the *R* configuration of which having been previously[6] established, thus provides an independent proof for the absolute configurations of the lactones under discussion.

Experimental Section

General Methods. (±)-Anastrephin (**1a**) and (±)-epianastrephin (**1b**) were prepared by the method reported by us recently.[2] Melting points were determined on a Thomas-Hoover Unimelt capillary melting point apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA. Specific rotations were obtained on a Perkin-Elmer 141 polarimeter. Mass spectra were obtained with 70-eV ionizing energy. ^{1}H NMR spectra were recorded on a Varian EM360 spectrometer with $CDCl_3$ as solvent and Me_4Si as an internal standard.

For nonequivalence measurements the ^{1}H NMR spectra were recorded at 25 °C on a Nicolet NT-300 spectrometer, operating at a field of 7 T (300 MHz). The spectra were determined by using solutions of 70 mg of (*R*)-(-)-2,2,2-trifluoro-1-(9-anthryl)ethanol, 10 mg of 3a*S*,7a*S* lactone, and 5 mg of 3a*R*,7a*R* lactone in 0.5 mL of $CDCl_3$. Typically a 20 ± 1 Hz low-field position was obtained for the signal of the 7a-methyl group of the major enantiomer relative to that of the methyl group of the minor enantiomer.[22]

(±)-3-(Ethoxycarbonyl)-7a-methyl-4-methylene-*trans*-hexahydrobenzofuran-2(3*H*)-one (3). A solution of diethyl sodiomalonate, prepared from 15 mL of ethanol, 0.35 g (15.2 mmol) of sodium, and 2.42 g (15.1 mmol) of diethyl malonate, was treated with 1.86 g (15 mmol) of 1-methylene-2,3-epoxy-3-methylcyclohexane[23] (**2**), and the resultant solution was stirred and heated to 90 °C. After 15 min of heating a white precipitate, presumably a sodium salt of **3**, was formed. After 1 h the mixture was cooled to 0 °C, treated with 10 g of crushed ice and then with 15 mL of 1 N HCl, and shaken until all precipitate disappeared. The solution was extracted with two 50-mL portions of dichloromethane. The extract was washed with an aqueous solution of NaCl and dried over Na_2SO_4. The extract was washed with an aqueous solution of NaCl and dried over Na_2SO_4. Evaporation of the solvent on a rotary evaporator was followed by a fractional distillation of the residue to give a crystalline product **3**; bp 115 °C (0.25 torr). Crystallization from hexane afforded 2.5 g (70%) of **3**: mp 74.5–75 °C; ^{1}H NMR δ 1.19 (s, 3 H), 1.30 (t, 3 H, *J* = 7 Hz), 1.5–2.7 (m, 6 H), 3.17 (br d, 1 H, *J* = 11 Hz), 3.70 (d, 1 H, *J* = 11 Hz), 4.27 (q, 2 H, *J* = 7 Hz), 4.69 (br s, 1 H), 4.93 (br s, 1 H). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.59; H, 7.64.

(±)-7a-Methyl-4-methylene-*trans*-hexahydrobenzofuran-2(3*H*)-one (1e). A solution of 6.0 g (25.2 mmol) of compound **3** and 12 g (138 mmol) of LiBr in 150 mL of dimethylformamide[24] was refluxed under an argon atmosphere for 8 h. Concentration to 100 mL on a rotary evaporator was followed by addition of 100 g of crushed ice and extraction with five 100-mL portions of pentane. The pentane extract was washed with an aqueous solution of NaCl, dried over $MgSO_4$, and concentrated to 30 mL. Flash chromatography, using 50 g of silica gel in pentane and ethyl ether–pentane (1:9) as an eluent, furnished 3.75 g (90%) of crystalline lactone **1e**; mp 35–37 °C. This product gave a virtually identical ^{1}H NMR spectrum with that for **1e** obtained by our previously published procedure.[10]

(±)-7a-Methyl-2-oxo-*trans*-octahydrobenzofuran-4-spirocyclopropane (1c). Cyclopropanation of (±)-methylene lactone **1e** by diazomethane in the presence of palladium diacetate, using a general method for cyclopropanation of terminal olefins,[25] furnished spiro lactone **1c**. The crude product **1c** was purified by flash chromatography on 30 g of silica gel in ethyl ether–pentane (5:95), using ethyl ether–pentane (20:80) as an eluent, and then distilled on Kugelrohr at 110 °C (0.5 torr) to give 1.04 g (96%) of a crystalline material: mp 48–50 °C; ^{1}H NMR δ 0.2–0.8 (m, 4 H), 1.0–2.8 (m, 12 H; including s, 3 H, at δ 1.35); MS, *m/e* (relative intensity) 180.1146 (calcd 180.1150), 180 (2), 122 (52), 94 (40), 79 (83), 43 (100). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.36; H, 8.95.

(±)-Tetrahydroactinidiolide (1d). To a solution prepared from 3.1 g of compound **1c**, 5 mL of ethyl acetate, and 10 mL of acetic acid was added 0.5 g of Adams catalyst, and the resultant mixture was stirred for 9 h at 50 °C under a pressure of 5 atm

(19) Beecham, A. F. *Tetrahedron Lett.* **1968**, 3591.

(20) Legrand, M.; Rougier, M. J. In *Stereochemistry, Fundamentals and Methods*; Kagan, H. B., Ed.; George Thieme: Stuttgart, 1977; p 55.

(21) The cis configuration of the two methyl groups in compound **1f** was tentatively assigned on the basis of the steric approach control for catalytic reduction. The absolute stereochemistry at carbon atom C-4 does not affect the assignments of the absolute configuration at the carbon atoms C-3a and C-7a, both by application of the sector lactone rule and the NMR method.

(22) (3a*S*,7a*S*)-(-)-Anastrephin (**1a**) gave 12- and 5-Hz low-field positions for the signals of $CH{=}CH_2$ and $CH{=}CH_2$, respectively, in addition to a 3-Hz high-field position for 4-CH_3, relative to those of the respective groups of (3a*R*,7a*R*)-(+)-anastrephin, in full agreement with the reported structure (cf. ref 2). As expected, the methyl and vinyl sense of nonequivalence was reversed for epianastrephin (**1b**).

(23) Marino, J. R.; Abe, H. *Synthesis* **1980**, 872.

(24) Reagent grade DMF can be used. Water content up to 1% does not affect the yield of **1e**.

(25) Suda, M. *Synthesis* **1981**, 714.

of hydrogen. A filtered solution was concentrated on a rotary evaporator and treated with 200 mL of pentane. The pentane solution was washed with an aqueous solution of $NaHCO_3$ and with an aqueous solution of NaCl, dried over Na_2SO_4, and concentrated to 10 mL. Flash chromatography on 50 g of silica gel packed in ethyl ether–pentane (5:95), using ethyl ether–pentane (1:9) as an eluent, furnished an oily material, which solidified on standing. Kugelrohr distillation gave 2.9 g (93%) of crystalline lactone **1d**; mp 72–74 °C (reported[5e] mp 71–74.5 °C). This product gave a virtually identical ^1H NMR spectrum with that reported.[5c-e]

Preparation of the Diastereoisomeric Amides 4a–e. A solution prepared from 1 mmol of the respective (±)-lactone **1**, 411 mg (3 mmol) of (*R*)-(−)-α-phenylglycinol, 95 mg (1 mmol) of 2-hydroxypyridine, and 1 mL of toluene was heated at 123 °C for 45 h under an argon atmosphere. Flash chromatography on 30 g of silica gel packed in dichloromethane and using a mixture of methanol–dichloromethane (3:97) as an eluent furnished two diastereomers, each 90% pure. The high-R_f compound was crystallized from chloroform–hexane, and the low-R_f diastereomer was purified by flash chromatography again. Typical yields of 80–85% for each diastereomer were obtained. Melting points (°C) for the high-R_f diastereomers were as follows: **4a**, 169–170; **4b**, 155.5–156; **4c**, 142–143; **4d**, 153–154; **4e**, 168–169. The low-R_f compounds **4a–e** are amorphous solids. All individual diastereomers **4a–e** gave microanalysis data that compared well with the respective calculated values: C, ±0.13; H, ±0.08; N, ±0.07.

Hydrolysis of the Amides 4a–e. A mixture of 1 mmol of amide **4**, 400 mg (10 mmol) of sodium hydroxide, 6 mL of water, and 4 mL of ethanol was heated at 80 °C for 3 h. Phenylglycinol was extracted from the mixture with four 30-mL portions of ethyl ether. The solution was acidified with 6 N hydrochloric acid to pH 3 at 0 °C and extracted with five 20-mL portions of ethyl ether again. Crude hydroxy acid, obtained by evaporation of ether, was crystallized from chloroform–hexane. Typically a yield of 97–98% was obtained. The high-R_f amides and low-R_f amides gave (+)- and (−)-acids, respectively. Acid, mp (°C), $[\alpha]^{25}_D$ (ethanol, *c* 0.05 g/mL): (+)-**5a**, 108–109, +23.1°; (−)-**5a**, 108–109, −23.1°; (+)-**5b**, 95–96, +35.4°; (−)-**5b**, 95–96, −35.5°; (+)-**5c**, 71–72, +13.5°; (−)-**5c**, 70–72, −13.4°; (+)-**5d**, 108–109, +5.3°; (−)-**5d**, 108–109, −5.3°; (+)-**5e**, 127–128, +49.8°; (−)-**5e**, 127–129, −50.0°. All individual enantiomers of **5a-c** gave microanalysis data that compared well with the respective calculated values: C, ±0.14; H, ±0.05. The enantiomers of **5d** and **5e** gave virtually identical ^1H NMR spectra with those for the corresponding racemic hydroxy acids.[5e,10,26]

Lactonization of Trans Hydroxy Acids 5a–e. A general procedure, published by us recently,[10] was followed without modifications. Crude optically active lactones **1a–e**, prepared by this method, were purified by flash chromatography on silica gel packed in ethyl ether–pentane (5:95) and using ethyl ether–pentane (1:9) as an eluent. The ^1H NMR nonequivalence measurements showed an optical purity better than 99% for all these lactones. For specific rotations see Table I. As a general rule, the melting points of all these optically active lactones were higher than those of the respective racemic mixtures. Enantiomeric lactones showed the same melting points. Optically active lactone, mp (°C): **1a**, 94–95; **1b**, 48–50; **1c**, 53–54; **1d**, 76–77; **1e**, 43.5–44.5.

(3a*R*,4*R*,7a*R*)-(+)-4,7a-Dimethyl-*trans*-hexahydrobenzofuran-2(3*H*)-one (1f). Hydrogenation of 0.166 g (1 mmol) of lactone (−)-**1e** dissolved in 10 mL of ethyl acetate, in the presence of 0.05 g of a catalyst consisting of 5% palladium deposited on carbon and under a pressure of 5 atm of hydrogen furnished compound (+)-**1f**. Flash chromatography purification, using 10 g of silica gel in ethyl ether–pentane (5:95) and a mixture of ethyl ether–pentane (1:9) as an eluent, gave 0.16 g (95%) of a crystalline material; mp 51–52 °C. For specific rotations, see Table I. The ^1H NMR spectrum and the ^1H NMR nonequivalence measurements indicated one single compound, for which cis configuration of the two methyl groups was tentatively assigned: ^1H NMR δ 1.02 (d, 3 H, *J* = 7 Hz), 1.36 (s, 3 H), 1.5–2.7 (m, 10 H); MS, *m/e* (relative intensity) 168.1123 (calcd 168.1150), 168 (3), 153 (49), 125 (35), 109 (29), 82 (94), 81 (27), 68 (54), 67 (53), 55 (51), 43 (100).

(3a*R*,7a*R*)-(+)-Tetrahydroactinidiolide (1d). (+)-Spiro lactone **1c** was hydrogenated as described above for hydrogenation of (±)-**1c**, to give (+)-**1d**; $[\alpha]^{25}_D$ +71° (hexane, c 0.05 g/mL); mp 75–76 °C.

(7a*R*)-(−)-Dihydroactinidiolide (1g). Compound (+)-**1d** was transformed into (−)-**1g** by using a modification of the selenylation–oxidation–elimination route reported by Hoye[5c] for the preparation of racemic **1g**. Thus, substitution of phenylselenyl chloride for diphenyl diselenide in the original procedure resulted in a slightly improved yield (50%) of (−)-**1g**; $[\alpha]^{25}_D$ −111° (hexanes, *c* 0.04 g/mL) [reported[6a] $[\alpha]^{24}_D$ −121° ($CHCl_3$)]. This product gave virtually identical IR and ^1H NMR spectra with those reported for dihydroactinidiolide which was obtained from natural sources.[8]

Acknowledgment. Financial support by the Florida Citrus Commission, Department of Citrus, State of Florida, and, in part, the Institute of Food and Agricultural Sciences, University of Florida, is gratefully acknowledged. We also thank the Instrument Program, Chemistry Division, National Science Foundation for financial assistance toward the purchase of the 300-MHz spectrometer.

Registry No. ±)-**1a**, 86003-24-9; (+)-**1a**, 86852-66-6; (−)-**1a**, 77670-94-1; (±)-**1b**, 87248-73-5; (+)-**1b**, 86852-65-5; (−)-**1b**, 77670-93-0; (±)-**1c**, 104575-77-1; (+)-**1c**, 104640-82-6; (−)-**1c**, 104640-85-9; (±)-**1d**, 71075-17-7; (+)-**1d**, 104640-83-7; (−)-**1d**, 104641-34-1; (±)-**1e**, 104575-76-0; (+)-**1e**, 104640-84-8; (−)-**1e**, 104640-86-0; (+)-**1f**, 104575-83-9; (−)-**1g**, 17092-92-1; (±)-**2**, 104575-74-8; (±)-**3**, 104575-75-9; **4a** (isomer 1), 104575-78-2; **4a** (isomer 2), 104640-68-8; **4b** (isomer 1), 104640-67-7; **4b** (isomer 2), 104640-69-9; **4c** (isomer 1), 104575-79-3; **4c** (isomer 2), 104640-70-2; **4d** (isomer 1), 104575-80-6; **4d** (isomer 2), 104640-71-3; **4e** (isomer 1), 104575-81-7; **4e** (isomer 2), 104640-72-4; (+)-**5a**, 104640-73-5; (−)-**5a**, 104640-77-9; (+)-**5b**, 104640-74-6; (−)-**5b**, 104640-78-0; (+)-**5c**, 104575-82-8; (−)-**5c**, 104640-79-1; (+)-**5d**, 104640-75-7; (−)-**5d**, 104640-80-4; (+)-**5e**, 104640-76-8; (−)-**5e**, 104640-81-5; diethyl sodiomalonate, 996-82-7; (*R*)-(−)-PhCH(NH_2)CH_2OH, 56613-80-0.

(26) Ohloff, G.; Schade, G. *Chem. Ber.* **1958**, *91*, 2017.