4 H), 4.00 (d, 2 H), 2.43 (s, 3 H), 2.17 (m, 1 H), 1.90–1.03 (m, 8 H), 0.93 (s, 3 H), 0.80 (s, 3 H); ^{13}C NMR δ 144.3, 133.2, 128.6, 127.6, 69.8, 48.9, 48.7, 40.0, 37.0, 32.1, 24.3, 23.7, 21.6, 20.4, 20.2. A solution of the tosylate **2c** (29.0 g, 95 mmol) in DMF (200 mL) was reacted with LiCl (5.0 g, 120 mmol) as above to give **2d** (1.0 g), containing camphene (50%, GLC) as impurity, after distillation of the crude product.

(B) Run 13. The preparation of **2d** was carried out starting from **2b** (4.2 g, 27.2 mmol, endo:exo = 90:10) and PPh_3 (8.8 g, 33.2 mmol) in CCl_4 (25 mL) as above described for **1d**. After 120 h, fractional distillation of the crude product gave *endo*-**2d**: 1.82 g (39%); bp 90–96 °C (10 mm); $[\alpha]^{25}_D$ −4.23° (*c* 3.9, benzene), containing the exo isomer (20%); ^1H NMR δ 3.42 (d, 2 H), 2.42–1.15 (m, 9 H), 1.02 (s, exo, 0.6 H), 0.98 (s, endo, 2.4 H), 0.92 (s, exo, 0.6 H), 0.85 (s, endo, 2.4 H); MS, *m/z* 217 (M^+).

(1*R*,2*R*)-1,7,7-Trimethyl-2-(bromomethyl)bicyclo[2.2.1]heptane (*exo*-1e). Run 5. Hydroboration was carried out bubbling gaseous BH_3 (4 h) in a solution of **1a** (30.4 g, 200 mmol) in THF (100 mL) at −5 °C. Excess hydride was destroyed by the addition of dry methanol (30 mL). Bromine (10.6 mL, 32.0 g, 200 mmol) was placed in an addition funnel, and sodium methoxide [metallic Na (6.0 g, 260 mmol) in methanol (150 mL)] was placed in a second funnel. The bromine and base were added simultaneously at a rate such that the reaction mixture was always orange (1.5 h, 20–25 °C). The reaction mixture was hydrolyzed (saturated Na_2CO_3) and extracted with ether; the distillation of dry (Na_2SO_4) organic layer afforded **1e**: 7.0 g (15%); bp 90–98 °C (15 mm); (exo:endo = 60:40, GLC; ^1H NMR δ 3.70–3.07 (m, 2 H), 2.30–0.98 (m, 8 H), 0.95–0.71 (m, 9 H); MS, *m/z* 231 (M^+). The solid residue of distillation was then oxidized with NaOH (3 N) and H_2O_2 (36%), affording **1b**, 21.6 g (65%).

(1*R*,3*S*)-2,2-Dimethyl-3-(bromomethyl)bicyclo[2.2.1]heptane (*endo*-2e). (A) Run 6. The preparation of **2e** was carried out starting from **2a** (68.2 g, 500 mmol) and gaseous BH_3 in THF (200 mL) as described above. The bromination was performed with bromine (25.6 mL, 80.0 g, 500 mmol) and sodium methoxide [metallic Na (15g, 660 mmol) in dry methanol (250 mL)]. After the usual workup, the distillation of crude product gave *endo*-**2e**: 29.1 g (27%); bp 74 °C (0.25 mm); endo:exo = 75:25, GLC; MS, *m/z* 217 (M^+). The solid residue of distillation was oxidized with NaOH (3 N) and H_2O_2 (36%), affording **2b**, 46.2 g (60%).

(B) Run 15. A solution of PPh_3 (31.5 g, 120 mmol) in CH_2Cl_2 (80 mL) was added to a solution of **2b** (15.4 g, 100 mmol, endo:exo = 90:10) and CBr_4 (46.5 g, 140 mmol) in CH_2Cl_2 (100 mL). The mixture was stirred at room temperature for 20 h and then treated with pentane. Fraction distillation of crude product afforded **2e**: 9.8 g (45%); bp 48 °C (0.1 mm); endo:exo = 70:30, GlC; ^1H NMR δ 3.83–3.03 (m, 2 H, 2.50–0.87 (m, 15 H).

Acknowledgment. We thank the Ministero della Pubblica Istruzione (Rome, Italy) for partial support of this work.

(22) Meikle, P. I.; Whittaker, D. *J. Chem. Soc., Perkin Trans. 2*, **1974**, 322.

A General and Practical Synthesis of (*R*)-Phthalimido Aldehydes and D-α-Amino Acids from D-Mannitol

Johann Mulzer,* Alfred Angermann, Boris Schubert, and Carsten Seilz

Institut für Organische Chemie der Freien Universität Berlin, Takustrasse 3, 1000 Berlin 33, FRG

Received May 9, 1986

A short and practical synthesis of five D-α-amino acids is described from D-mannitol as the chiral educt. The key steps in the sequence are (a) the erythro-selective addition of organometals to (*R*)-2,3-*O*-isopropylideneglyceraldehyde, (b) the Mitsunobu inversion substituting *N*-phthalimide for hydroxyl, and (c) acetonide hydrolysis and glycol cleavage to give the *N*-phthaloyl-(*R*)-α-aminoaldehydes **7**. These are oxidized under Jones conditions to give the N-protected amino acids **8**. The examples investigated (alanine, aminobutyric acid, norvaline, and allyl- and vinylglycine) demonstrate the general applicability of the method.

The synthesis of enantiomerically pure D-α-amino acids has received much attention in recent years. These compounds are of considerable biological interest,[1] but, in general, they cannot be procured in sufficient quantities from natural sources. D-α-Amino acids have been prepared by resolution of racemic mixtures,[2] by asymmetrically induced $sp^2 \rightarrow sp^3$ transformations using a variety of chiral auxiliaries,[3] by diastereoselective 2,3-sigmatropic rearrangement of optically active allyl selenates,[4] by S_N2 N-O exchange of (*S*)-α-hydroxy acids,[5] or by "ex-chiral-pool" synthesis starting from L-serine.[6] These methods except the last mentioned one either need expensive resolving agents or chiral auxiliaries[3] or they lack generality[5] and

(1) See, for example: Monahan, M. W.; Amoss, M. S.; Anderson, H. A.; Vale, W. *Biochemistry* **1973**, *12*, 4616. Coy, D. H.; Vilchez-Martinez, J. A.; Coy, E. J.; Schallym, A. V. *J. Med. Chem.* **1976**, *19*, 423. Pert C. B.; Pert, A.; Chang, J. K.; Fong B. T. W. *Science (Washington, D.C.)* **1976**, *194*, 330. Thomas, G. A.; Scott, A. I.; Baxter, R. L. *J. Chem. Soc., Perkin Trans. 1* **1983**, 971. Kuzuhara, H.; Emoto, S. *Tetrahedron Lett.* **1975**, 1853. Konda, M.; Oh-ishi, T.; Yamada, S. *Chem. Pharm. Bull.* **1977**, *25*, 69.

(2) Wünsch, E.; Fürst, G. *Z. Physiol. Chem.* **1962**, *329*, 109 Friis, P.; Helboe, P.; Larsen, P. A. *Acta Chem. Scand. Ser. B* **1974**, *B28*, 317. Greenstein, J. P.; Winitz, M. *Chemistry of the Amino Acids*; Wiley: New York. 1961; Vol. 1, Chapter 9.

(3) Hydrogenation: Chaplar, V.; Comisso, G.; Sunic, V. *Synthesis* **1981**, 85. Poisel, H.; Schmidt, U. *Chem. Ber.* **1973**, *106*, 3408. Bycroft, B. W.; Lee, G. R. *J. Chem. Soc., Chem. Commun.* **1975**, 988. Corey, E. J.; McCaully, R. J.; Sachdev, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 2476. Corey, E. J.; Sachdev, H. S.; Gougoutas, J. Z.; Saenger, W. *J. Am. Chem. Soc.* **1970**, *92*, 2488. Alkylation: Yamada, S.; Oguri, T.; Shioiri, T. *J. Chem. Soc., Chem. Commun.* **1976**, 136. Schöllkopf, U. *Pure Appl. Chem.* **1983**, *55*, 1799; *Chem. Scr.* **1985**, *25*, 105. Bromination-amination: Oppolzer, W.; Pedrosa, R.; Moretti, R. *Tetrahedron Lett.* **1986**, *25*, 831.

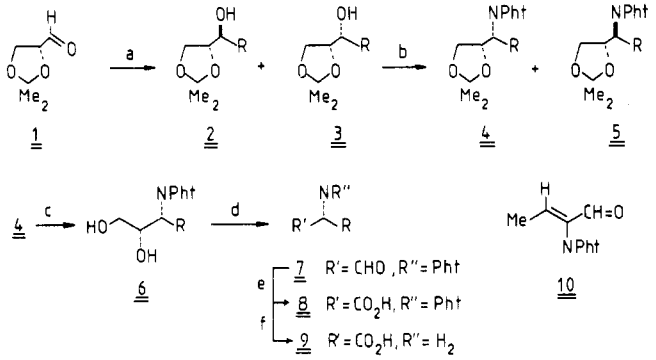
(4) Fitzner, J. N.; Shea, R. G.; Fankhauser, J. E.; Hopkins, P. B. *J. Org. Chem.* **1985**, *50*, 417.

(5) Effenberger, F.; Burhard, U.; Willfahrt, J. *Liebigs Ann. Chem.* **1986**, 314.

(6) Maurer, P. J.; Hiroki, T.; Rapoport, H. *J. Am. Chem. Soc.* **1984**, *106*, 1095.

0022-3263/86/1951-5294$01.50/0

Scheme I[a]

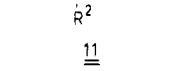


2–9	R
a	Me
b	Et
c	$CH_2CH{=}CH_2$
d	n-C_3H_7
e	$CH{=}CH_2$

[a] (a) See ref 7; (b) $(Ph)_3P$, $EtO_2CN{=}NCO_2Et$, phthalimide, THF, −10 to 22 °C, 16 h; (c) MeOH, 2 N H_2SO_4 or MeOH, CF_3CO_2H, 22 °C, 24 h; (d) $Pb(OAc)_4$, benzene, 22 °C, 15 min; (e) Jones' reagent, acetone, 0 °C; (f) N_2H_4, EtOH, reflux.

lead to optically impure products.[4] Our synthesis utilizes the observation[7] that (*R*)-2,3-isopropylideneglyceraldehyde (**1**), which is readily available from inexpensive D-mannitol in multigram quantities,[8] adds a variety of organometals to give the triol derivatives **2**/**3** in ratios varying from 2:1 to 9:1. Without separation these diastereomers are treated with diethyl azodicarboxylate, triphenylphosphine, and phthalimide[9] to give the 3-phthalimido diols **4**/**5**. From this mixture the syn isomer **4** is isolated by crystallization. This material is transformed via **5**, **6**, **7**, and **8** into the desired amino acids **9**, as exemplified in Scheme I for five different residues R_2.

The optical purity of the compounds thus obtained was checked by comparing the optical rotations of the amino acids **9** with literature data (see Experimental Section) which in view of the long-standing knowledge of amino acids in general may be safely assumed to correspond to optically pure material. On this basis, the following ee values were established: 99% for **9a–c**, 94% for **9d**, and 97% for **9e**, respectively. Furthermore, **8e** was hydrogenated to give **8b** and found to have an ee value of 96% by comparing its optical rotation with that of a sample obtained from **2b**. Additionally, **2a** and **2c**, both diastereomerically pure according to ^1H and ^{13}C NMR and HPLC analysis were treated with (*S*)-methoxy(trifluoromethyl)phenylacetic chloride (MTPA chloride[10]). The ^{13}C NMR spectra of the resulting MTPA esters were compared with those obtained from racemic **2a**/**c** and revealed a diastereomeric purity of 99% (corresponding to an ee value of 98%).[11] These findings clearly demonstrate that the optical integrity of the material has been maintained throughout the synthetic sequence and, hence, that the phthalimido aldehydes **7**, even the doubly activated derivative **7e**, are configurationally stable under the conditions applied.[12] Column chromatography, however, cleanly isomerizes **7e** into the conjugated derivative **10**. In addition to the amino acids **9** our procedure provides an easy access to other synthetically useful chiral amino derivatives. For instance, the N-protected amino diols **6** may be converted into amino epoxides under retention of configuration, or the amino aldehydes **7** may be transformed into allylamines by Wittig condensation, or into 1,2-amino alcohols by Grignard addition.[13] To enhance the synthetic potential of the approach, the reductive removal of the secondary hydroxy function in **6** was also envisaged. Gratifyingly, **11b**, readily obtained from **6c** via **11a**, on application of the modified Barton–McCombie protocol[14] cleanly furnished (*R*)-1-(benzoyloxy)-3-phthalimido-5-hexene (**11c**), which can be considered as a chiral equivalent to 3-amino-glutaric acid. Similar derivatives of this type have been used in the synthesis of β lactam or amino alcohol antibiotics by Ohno et al., who by contrast employed an enzymatic approach.[15] Interestingly, selective removal of either protecting group in the presence of the second one could be achieved by proper choice of the conditions to give phthalimido alcohol **11e** or the benzoyloxy amine **11d**, respectively. In conclusion, we have



11

11	R^1	R^2	R^3
a	PhCO	OH	Pht
b	PhCO	O(CS)Im	Pht
c	PhCO	H	Pht
d	PhCO	H	H_2
e	H	H	Pht

presented a short synthesis of D-α-amino acids (**9**) from **1** showing the following advantages: 1. It requires inexpensive starting materials and reagents and employs simple reaction conditions. Generally, diastereomer separation can be achieved by crystallization of **4** to **6**. If needs be, chromatographic separation of **4**/**5** is also easily possible. Overall yields of **9**, based on **2**/**3**, are between 20 (**9c**) and 50% (**9d**), and gram quantities of all compounds can be readily prepared. 2. Further synthetically useful intermediates like **6** and **7** are available en route. 3. The method is general within the limitations that R^2 must correspond to a stable organometallic derivative and permit Mitsunobu-type S_N2-displacement reactions at the neighboring carbon. A wide variety of additional functional groups may be introduced by means of R^2, as exemplified by the preparation of **9c** and **9e**. In this way further elaboration of **4**, **6**, or **7c**/**e** into more complicated structures should be possible. Applications of this concept to alkaloid synthesis are in progress.

Experimental Section

Melting points are uncorrected. Infrared spectra (IR) were obtained with a Perkin-Elmer IR 580 B spectrometer. Nuclear magnetic resonances spectra (NMR) were obtained with a Bruker WH 270 or AC 250 spectrometer in $CDCl_3$ unless noted otherwise

(7) Mulzer, J.; Angermann, A. *Tetrahedron Lett.* **1984**, *25*, 2843. Mead, K.; Macdonald, T. L. *J. Org. Chem.* **1985**, *50*, 422.
(8) Fischer, H. O. L.; Baer, E. *J. Biol. Chem.* **1939**, *128*, 463.
(9) Mitsunobu, O. *Synthesis* **1981**, 1.
(10) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2453.
(11) Mulzer, A.; Angermann, A.; Münch, W. *Liebigs Ann. Chem.* **1986**, 825. Mulzer, J.; Angermann, A.; Münch, W.; Hentzschel, A. *Liebigs Ann. Chem.*, in press.
(12) Regarding the configurational stability of N-protected α-amino aldehydes, see: Rittle, K. E.; Homnick, C. F.; Ponticello, G. S.; Evans, B. E. *J. Org. Chem.* **1982**, *47*, 3016.
(13) Hanson, G. J.; Lindberg, T. *J. Org. Chem.* **1985**, *50*, 5399.
(14) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. Rasmussen, J. R.; Slinger, C. J.; Kordish, R. J.; Newman-Evans, D. D. *J. Org. Chem.* **1981**, *46*, 4843.
(15) Okano, K.; Izawa, T.; Ohno, M. *Tetrahedron Lett.* **1983**, 24, 217. Okano, K.; Kyotani, Y.; Ishihama, H.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1983**, *105*, 7186. Wang, Y.-F.; Izawa, T.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1982**, *104*, 6465.

and are reported in ppm downfield of internal tetramethylsilane (δ units). Optical rotations were determined in $CHCl_3$ (unless stated otherwise) with a Perkin-Elmer 121 polarimeter. Mass spectra (MS) were recorded with a Varian MAT 711 spectrometer. HPLC separations were performed on a Knauer pump 64, with RI and UV detection. All reactions were performed in purified solvents and monitored by TLC plates (Merck 5554). Preparative column chromatography was performed by flash techniques[16] on silica gel (Merck 60) with ethyl acetate/hexane mixtures. (*R*)-2,3-*O*-Isopropylideneglyceraldehyde (1) was prepared according to the literature procedure.[8]

General Procedures. A. Conversion of Triols 2/3 into Phthalimido Diols 4/5. A mixture of **2/3** (1.0 molar equiv), triphenylphosphine (1.1 molar equiv), and phthalimide (1.1 molar equiv) in THF (20 mL/g **2/3**) was treated dropwise at −10 °C with diethyl azodicarboxylate (1.1 molar equiv) in THF (5 mL/g). After 3 h at −10 °C the mixture was stirred at 22 °C for another 15 h. Then the solvent was evaporated under reduced pressure and the product (**4/5**) was isolated by chromatography. Crystallization from ethanol furnished diastereomerically pure syn phthalimido diol **4**.

B. Hydrolysis of 4 to 6. **4** was dissolved in methanol (5 mL/g) and stirred with 10 vol % of 2 N sulfuric acid for 24 h at 22 °C. If necessary, the mixture was refluxed foor an additional 3 h. The solvent was removed under reduced pressure and the aqueous residue was extracted with methylene chloride, washed with water until neutral, dried over Na_2SO_4, and evaporated to give **6**, which was used for the next step without purification. Alternatively, the reaction was performed in methanol (5 mL/g) and trifluoroacetic acid (1 vol %) for 24 h at 22 °C. Workup was effected by evaporating the mixture to dryness.

C. Glycol Cleavage of 6 to 7. Crude diol **6** in benzene (10 mL/g) was treated with lead tetraacetate (1.1 molar equiv) in portions at 22 °C for 15 min. During the reaction the mixture turned yellow but decolorized within a few minutes. After 30 min the salt residue was removed by filtration and washed with several portions of benzene. The filtrate was shaken with water until colorless, dried ($MgSO_4$), and evaporated.

D. Oxidation of 7 to 8. Aldehyde **7** in acetone (20 mL/g) was treated with Jones' reagent at 0 °C until the orange color persisted for at least 5 min. Then a few drops of isopropyl alcohol were added and the mixture was evaporated under reduced pressure, redissolved in ether, and shaken with water and then with saturated aqueous bicarbonate. The bicarbonate extract was acidified with sulfuric acid and shaken with ether. The organic layer was separated, dried ($MgSO_4$), and evaporated.

E. Hydrazinolysis of 8 to 9. The phthalimido carboxylic acid **8** in ethanol (10 mL/g) was refluxed with an excess of hydrazine hydrate until a colorless precipitate of phthalazone was formed. Acetone (10 mL/g **8**) was added and refluxing was continued for another 30 min. Then the solvent was removed under reduced pressure and the residue was diluted with water (10 mL/g **8**), acidified with acetic acid to pH 4, and heated for another hour. The crystalline precipitate was removed by filtration and the filtrate was evaporated to dryness to give crude amino acid **9**.

1. (*R*)-Alanine (9a). 1.1. (2*R*,3*R*)-1,2-*O*-Isopropylidene-3-phthalimidobutane-1,2-diol (4a). A mixture of **2a/3a** (66:34 according to ^1H NMR analysis; 8.00g, 54.72 mmol) was treated with triphenylphosphine (14.50 g, 55.28 mmol), phthalimide (8.30 g, 56.41 mmol), and diethyl azodicarboxylate (9.60 g, 55.12 mmol) in THF (160 mL) according to procedure A to give after PCC (ethyl acetate/hexane, ea/h = 1/2) two fractions. The first fraction (7.89 g) consisted of crystalline **4a**, with a diastereomeric purity of 90:10 (according to ^1H NMR and HPLC analysis). The second fraction (2.02 g) contained **4a** and **5a** in a ratio of 65:35 and was oily. The first fraction was further purified by crystallization from ethanol at −25 °C to furnish 6.07 g (63% based on **2a**) of diastereomerically pure (>98% according to ^1H NMR analysis) **4a** of mp 117–118 °C as colorless needles: $[\alpha]^{20}_D$ −10.6° (*c* 1.0); ^1H NMR (270 MHz) δ 1.30, 1.38 (2 × s, 6 H, $C(CH_3)_2$), 1.42 (d, J = 6 Hz, CH_3), 3.87 (dd, $J_{11'}$ = 9 Hz, J_{12} = 5 Hz, 1 H, 1-H) 4.18 (dd, $J_{1'1}$ = 9 Hz, $J_{1'2}$ = 7 Hz, 1 H, 1'-H), 4.39 (dq, J_{34} = 6 Hz, J_{23} = 10.5 Hz, 1 H, 3-H), 4.78 (ddd, J_{21} = 5 Hz, $J_{21'}$ = 7 Hz, J_{23} = 10.5 Hz, 1 H, 2-H), 7.78 and 7.87 (mc, 2 × 2 H, Ar); IR (KBr) 3102 (w), 3070 (w), 3000 (m), 2950 (w), 2886 (w), 1718 (s, C=O), 1390 (s), 1280 (m), 1222 (m), 1173 (m), 1143 (m), 1068 (s), 1042 (m), 860 (m), 730 (m) cm^{-1}. Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.37; H, 6.47; N, 5.04. **5a** could be detected in the ^1H NMR spectrum by the following signals: δ 1.56 (d, J = 6 Hz, CH_3), 3.70 (dd, J = 6 and 8.5 Hz, 1 H, 1-H), 3.98 (dd, J = 6 and 8 Hz, 1'-H).

1.2. (2*R*,3*R*)-2-Phthalimidobutane-1,2-diol (6a). **4a** (6.00 g, 21.82 mmol) was treated with trifluoroacetic acid according to procedure B to give 5.09 g (99%) of **6a** as colorless needles which were recrystallized from $CHCl_3$/pentane: mp 94–95 °C; $[\alpha]^{20}_D$ −23.5° (*c* 1.0); ^1H NMR (270 MHz) δ 1.47 (d, J = 7.5 Hz, 1 H, CH_3), 2.92 (s, br, 1 H, OH), 3.57 (dd, $J_{11'}$ = 11 Hz, J_{12} = 6 Hz, 1 H, 1-H), 3.69 (dd, $J_{1'1}$ = 11 Hz, $J_{1'2}$ = 4 Hz, 1 H, 1'-H), 3.72 (s, br), 4.12 (m, 1 H, 2-H), 4.48 (quint, $J_{32} = J_{34}$ = 7.5 Hz, 1 H, 3-H), 7.73, 7.80 (mc, 2 × 2 H, Ar); IR (KBr) 3250 (s, OH), 3465 (s, OH), 3080 (w), 2998 (w), 2992 (w), 2958 (w), 2895 (w), (CH aliph), 1778 (m), 1698 (s, C=O), 1615 (w), 1469 (w), 1394 (s), 1141 (m), 1065 (m), 888 (m), 725 (m) cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.39; H, 5.49; N, 5.91.

1.3. (*R*)-2-Phthalimidopropanal (7a). Diol **6a** (4.50 g, 19.08 mmol) was treated with lead tetraacetate (8.91 g, 19.98 mmol) according to procedure C to give **7a** (2.84 g, 70%) which was recrystallized from ether/pentane: colorless platelets, mp 108–109 °C; $[\alpha]^{20}_D$ −4.0° (*c* 1.1); ^1H NMR (270 MHz) δ 1.63 (d, J = 7.5 Hz, 3 H, CH_3) 4.80 (q, J = 7.5 Hz, 1 H, 2-H), 7.83, 7.99 (mc, 2 × 2 H, Ar), 9.81 (s, 1 H, C*H*O); IR (KBr) 3075, 3040, 3000, 2960, 2920, and 2871 (all w, CH Ar and CH aliph), 1777 (s, C=O), 1731 (s, C=O), 1712 (s, C=O) 1611 (m), 1470 (w), 1391 (s), 1340 (m), 1176 (m), 1162 (m), 1120 (m), 1040 (s), 947 (m), 880 (m), 730 (s) cm^{-1}. Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.47; N, 6.89. Found: C, 65.30; H, 4.50; N, 6.91.

1.4. (*R*)-2-Phthalimidopropanoic Acid (8a). Application of procedure D to **7a** (2.10 g, 10.40 mmol) furnished 1.52 g (67%) of **8a** which gave colorless platelets of mp 142–142.5 °C after recrystallization from $CHCl_3$/pentane: $[\alpha]^{20}_D$ +19.9 (*c* 1.1), +24.2 (*c* 1.5, EtOH); ^1H NMR (270 MHz) δ 1.70 (d, J = 7 Hz, 3 H, CH_3), 4.99 (q, J = 7 Hz, 1 H, 2-H), 7.66, 7.76 (mc, 2 × 2 H, Ar), 11.04 (s br, COO*H*); IR (KBr) 3260 (s br, OH), 3078 (w), 3008 (w), 2980 (w), 2932 (w), 1780 (s, C=O), 1761 (s, C=O), 1705 (s, C=O), 1408 (s), 1349 (m), 1202 (m), 1080 (m), 1027 (m), 888 (m), 729 (m), 631 (m) cm^{-1}. Anal. Calcd for $C_{11}H_{19}NO_4$: C, 60.27; H, 4.14; N, 6.39. Found: C, 59.97; H, 4.20; N, 6.50.

For comparison, (*S*)-**8a** was prepared from (*S*)-alanine.[17] The sample thus obtained was identical in every respect with our material except for the optical rotation which was $[\alpha]^{20}_D$ −23.6° (*c* 1.5, EtOH).

1.5 (*R*)-Alanine (9a). **8a** (1.30 g, 5.97 mmol) was allowed to react with hydrazine hydrate according to procedure E to give 457 mg (86%) of **9a** which was recrystallized form acetone/water to furnish colorless needles of mp 305–306 °C dec; $[\alpha]^{20}_D$ −13.9° (*c* 1.9, 1 N HCl [lit.[18a] mp 291–293 °C $[\alpha]^{20}_D$ −14.2° (*c* 6, 1 N HCl).

2. (*R*)-Aminobutyric Acid (9b). 2.1. (2*R*,3*S*)-1,2-*O*-Isopropylidene-3-phthalimidopentane-1,2-diol (4b). The **2b/3b** mixture (20.00 g, 124.8 mmol) (diastereomeric ratio = 86:14) was converted into **4b/5b** according to procedure A. Column chromatography (ethyl acetate/hexane, 1/3) yielded 25.76 g (71%) of crystalline **4b** which was purified by recrystallization from ethanol to give colorless prisms of mp 107–108 °C: $[\alpha]^{20}_D$ +1.8° (*c* 2.1); ^1H NMR (270 MHz) δ 0.90 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 1.30 and 1.38 (2 × s, 2 × 3 H, CH_3), 1.55 and 2.16 (2 × mc, 2 × 1 H, CH_2CH_3), 3.87 (dd, $J_{11'}$ = 8 Hz, J_{12} = 5.5 Hz, 1 H, 1-H), 4.18 (dd, $J_{1'1}$ = 8 Hz, $J_{1'2}$ = 6 Hz, 1 H, 1'-H), 4.13–4.25 (m, 1 H, 3-H), 4.76 (dt, $J_{21} = J_{21'}$ = 5.5–6 Hz, 1 H, 2-H), 7.76, 7.87 (2 mc, 2 × 2 H, Ar); IR (KBr) 3068 (w), 3040 (w, CH arom.), 2995 (m), 2980 (m), 2940 (w), 2921 (w), 2885 (w, CH aliph.), 1773 (m), 1712 (s, C=O), 1470 (w), 1380 and 1370 (s, together CH), 1219 (w), 1068 (s), 849 (m), 712 (s) cm^{-1}. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.42; H, 6.62; N, 4.85. In the mother liquor **5b** could be detected by the following ^1H NMR signals: δ 0.86 (t, J = 7.5 Hz, CH_2CH_3), 1.29 (s, 3 H), 1.45 (s, 3 H), ca.

(16) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2933.

(17) Beckett, A. H.; Casy, A. F. *J. Chem. Soc.* **1955**, 900.

(18) (a) *Beilsteins Handbuch der organischen Chemie, Hauptwerk, 4. Aufl.*; Springer: Berlin, 1918; Vol. 4, p 385. (b) Reference 18a p 408.

1.39–1.51 (m), 1.97–2.13 (m), 3.72 (dd, J = 6 and 8 Hz), 3.99 (dd, J = 6 and 8 Hz). All other signals were superimposable with those of **4b**.

2.2. (2*R*,3*R*)-3-Phthalimidopentane-1,2-diol (6b). Diastereomerically pure **4b** (24.00 g, 82.80 mmol) was hydrolyzed with methanol–sulfuric acid according to procedure B to give **6b** (19.08 g, 92%) as a viscous oil, which was used for the next step without purification: ^{1}H NMR (270 MHz) δ 0.84 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 1.75 (mc, 1 H, CH_2CH_3), 2.04 (mc, 1 H, CH_2CH_3), 3.28 (s br,1 H, OH), 3.55 (dd, $J_{11'}$ = 11 Hz, J_{12} = 6 Hz, 1 H, 1-H), 3.70 (dd, $J_{1'1}$ = 11 Hz, $J_{1'2}$ = 4 Hz, 1 H, 1'-H), 3.99 (s br, 1 H, OH), 4.15 (mc, 1 H, 2-H)8 4.27 (ddd, J = 5 Hz, Hz, and 11 Hz, 1 H, 3-H, 7.78 and 7.85 (2 × mc, 2 × 2 H, Ar); IR (film) 3460 (s, OH)8 3063 (w), 3038 (w), 2978 (m), 2940 (m), 2882 (w), 1770 (m, C=O), 1708 (s, C=O), 1468 (m), 1392 (s), 1370 (s), 1338 (m), 1130 (m), 1055 (s), 900 (m), 723 (s) cm^{-1}.

2.3. (*R*)-2-Phthalimidobutanal (7b). From **6b** (19.00 g, 76.58 mmol), 12.86 g of **7b** (77%) were obtained according to procedure C: $[\alpha]^{20}_D$ +8.49° (c 1.5). The material was used for the next step without further purification. ^{1}H NMR (250 MHz): δ 0.96 (t, J = 7 Hz, 3 H, CH_2CH_3), 2.08 and 2.24 2 × mc, 2 × 1 H, CH_2CH_3), 4.64 (dd, J_{23} = 5 Hz, $J_{2'3}$ = 5 Hz, $J_{23'}$ = 10 Hz, 1 H, 2-H), 7.78 and 7.86 (2 × mc, 2 × 2 H, Ar), 9.70 (s, 1 H, CHO).

2.4. (*R*)-2-Phthalimidobutyric Acid (8b). **7b** (12.50 g, 57.39 mmol) was oxidized according to procedure D to furnish **8b** (10.22 g, 77%) which was recrystallized from ether/pentane: colorless needles, mp 79–81 °C; $[\alpha]^{20}_D$ −23.9° (c 2.1); ^{1}H NMR (270 MHz) δ 0.96 (t, J = 7.5 Hz, 3 H, CH_3), 2.30 (quint, J_{32} = J_{34} = 7.5 Hz, 2 H, CH_2CH_3), 4.87 (t, J_{23} = 7.5 Hz, 1 H, 2-H), 7.81 and 7.90 (2 × mc, 2.2 H, Ar), 10.61 (s br, COOH); IR (KBr) 3470 (s br, OH), 2993, 2978, 2940, 2918, 2880 (w, CH aliph.), 1771 (s) and 1718 (s, C=O), 1610 (m), 1468 (m), 1390 (s), 1292 (m), 1279 (m), 1154 (m), 1078 (m), 1040 (m), 900 (m), 800 (m), 751 (m), 720 (s), 641 (m), 531 (m) cm^{-1}; MS (70 °C, 80 eV), m/e (relative intensity) 233 (3.0 M$^+$), 189 (12.3, M$^+$ − CO_2), 188 (100, $C_{11}H_{10}NO_2$), 187 (2.1), 160 (15.4, $C_9H_6NO_2$), 148 (10.7, $C_8H_6NO_2$), 130 (32.7, C_8H_4NO); m/e for M$^+$ calcd 233.0690, found 233.0690.

2.5. (*R*)-Aminobutyric Acid (9b). Proceudre E converted **8b** (8.50 g, 36.0 mmol) into **9b** (3.11 g, 84%) which was recrystallized from water/acetone to give colorless platelets: mp >300 °C, $[\alpha]^{20}_D$ −7.8° (c 4.0, H_2O) [lit.[18b] $[\alpha]^{20}_D$ −7.9° (c, 4.0, H_2O)]; ^{1}H NMR (250 MHz) δ 0.99 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 1.91 (quint, J_{23} = J_{34} = 7 Hz, 2 H, CH_2CH_3), 3.72 (t, J_{23} = 7.5 Hz, 1 H, 2-H). Anal. Calcd for $C_4H_9NO_2$: C, 46.59; H, 8.80; N, 13.58. Found: C, 46.09; H, 8.73; N, 13.56.

3. (*R*)-Allylglycine (9c). 3.1. (2*R*,3*R*)-1,2-*O*-Isopropylidene-3-phthalimidohex-5-ene-1,2-diol (4c). The **2c/3c** mixture (61.00 g, 354.1 mmol) (diastereomeric ratio 85:15) was converted into **4c/5c** according to procedure A. Column chromatography (ethyl acetate/hexane, 1/2) yielded a polar fraction, which gave on crystallization from ethanol 50.30 g (43%, based on **2c**) of **4c**, diastereomerically pure according to ^{1}H NMR analysis, as colorless prisms: mp 87–87.5 °C; $[\alpha]^{20}_D$ +2.1° (c 1.0); ^{1}H NMR (270 MHz) δ 1.30, 1.38 (2 × s, 2 × 3 H, $C(CH_3)_2$), 2.33 (ddd, $J_{44'}$ = 16 Hz, J_{34} = 4 Hz, J_{45} = 5 Hz, 1 H, 4-H), 2.86 (ddd, $J_{44'}$ = 16 Hz, $J_{4'3}$ = 1 H, 4'-H), 3.88 (dd, $J_{11'}$ = 8.5 Hz, J_{12} = 5 Hz, 1 H, 1-H), 4.15 (dd, $J_{1'1}$ = 8.5 Hz, $J_{1'2}$ = 6 Hz, 1 H, 1'-H), 4.32 (ddd, J_{32} = 9 Hz, J_{34} = 4 Hz, $J_{34'}$ = 11 Hz, 1 H, 3-H), 4.74 (ddd, J_{23} = 9 Hz, J_{21} = 5 Hz, $J_{21'}$ = 6 Hz, 1 H, 2-H), 4.96 (d, J_{65} = 10 Hz, 1 H, cis-6-H), 5.10 (d, $J_{6'5}$ = 17 Hz, 1 H, trans-6-H), 5.67 (dddd, J_{56} = 10 Hz, $J_{56'}$ = 17 Hz, J_{54} = 5 Hz, $J_{54'}$ = 9 Hz, 1 H, 5-H), 7.70 and 7.80 (2 × dd, J = 3 Hz and 6 Hz, 2 × 2 H, Ar); IR (KBr) 3095, 3080 (w, C=C), 2998 (m), 2948 (m), 2892 (w, CH aliph), 1776 (m), 1720 (s, C=O), 1647 (w), 1618 (w), 1474 (w), 1448 (w), 1390 (s), 1216 (m), 1161 (m), 1102 (m), 1071 (m), 942 (m), 854 (m), 724 (s), 650 (w), 621 (w), 611 (w), 552 (w), 536 m, cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.35; N, 4.65. Found: C, 67.81; H, 6.23; N, 4.73. In the mother liquor **5c** was detectable by ^{1}H NMR signals at δ 3.68 (dd, J = 11 and 16 Hz, 1-H) and 3.96 (dd, J = 8.5 and 5 Hz, 1'-H). The unpolar fraction obtained from the chromatography consisted of 2.72 g (20%) of (*R*)-1,2-*O*-isopropylidene-3,5-hexadiene-1,2-diol formed from **2c/3c** by elimination in an E/Z ratio of 87:13: $[\alpha]^{20}_D$ +22.4° (c 22.4); ^{1}H NMR (270 MHz) of (*E*)-**6** δ 1.40, 1.44 (2 × s, 2 × 3 H, $C(CH_3)_2$), 3.58 (t, $J_{11'}$ = J_{12} = 8 Hz, 1 H, 1-H), 4.09 (dd, $J_{11'}$ = 8 Hz, $J_{1'2}$ = 6 Hz, 1 H, 1'-H), 4.52 (dt, J_{23} = J_{21} = 8 Hz, $J_{21'}$ = 6 Hz, 1 H, 2-H), 5.12 (d, J_{65} = 10 Hz, 1 H, cis-6-H), 5.23 (d, $J_{6'5}$ = 16 Hz, 1 H, 6'-H), 5.64 (dd, J_{32} = 8 Hz, J_{34} = 15 Hz, 1 H, 1 H, 3-H), 6.20–6.42 (m, 2 H, 4-H, 5-H); additional signals of (*Z*)-**6** δ 3.54 (t, J = 8 Hz, 1-H), 4.98 (dt, J = 6 Hz and 8 Hz, 2-H), 6.62 (dt, J = 11 Hz and 16 Hz, 1 H, 5-H); ^{13}C NMR ($CDCl_3$) δ 25.77 and 26.56 ($C(CH_3)_2$), 69.35 (trans-C-1), 72.09 (cis-C-1), 76.55 (C-2), 109.25 ($C(CH_3)_2$), 118.18 (trans-6-C), 119.76 (cis-6-C), 128.80 (cis), 130.74 (trans), 131.42 (cis), 132.76 (cis), 133.69 (trans), 135.90 (trans); MS (80 eV, 100 °C), m/e (relative intensity) 154 (M$^+$, 16.4), 140 (4.3), 139 (M$^+$ − CH_3, 46.3), 124 (M$^+$ − CHO, 15.2), 109 (13.6), 101 (1.8), 97 (8.0), 96 (15.2), 95 (13.9), 83 (3.2), 82 (1.8), 81 (14.9), 80 (5.6), 79 (43.1), 78 (6.0), 77 (11.3), 73 (3.9), 72 (7.8), 69 (3.8), 68 (12.4), 67 (3.8), 66 (18.6), 65 (9.8), 59 (10.7), 54 (24.8), 53 (9.2), 43 (100); m/e (M$^+$) for $C_9H_{14}O_2$ calcd 154.09938, found 154.0996; IR (neat) 3100 (w), 3055 (w, CH arom), 3000 (s), 2945 (m) and 2880 (m, CH aliph), 1610 (m), 1460 (w), 1383 (s) and 1375 (s) ($C(CH_3)_2$), 1250 (s), 1220 (s), 1160 (s), 1129 (w), 1065 (s, CO), 1030 (m), 1010 (s), 960 (w), 913 (m), 870 (s), 842 (w), 795 (w) cm^{-1}.

3.2. (2*R*,3*R*)-3-Phthalimidohex-5-ene-1,2-diol (6c). **4c** (30.0 g, 98.75 mmol) was converted into **6c** (24.38 g, 94%) according to procedure B: viscous oil, $[\alpha]^{20}_D$ −8.2° (c 1.1); ^{1}H NMR (250 MHz) δ 2.52 (dt, $J_{44'}$ = 15 Hz, J_{43} = J_{45} = 5 Hz, 1 H, 4-H), 2.82 (dt, $J_{4'4}$ = 15 Hz, $J_{4'3}$ = $J_{4'5}$ = 10–11 Hz, 1 H, 4'-H), 3.04 (t, J = 5 Hz, 1 H, OH), 3.56 (ddd, $J_{11'}$ = 11 Hz, J_{12} = 6 Hz, J_1-OH = 7 Hz, 1 H, 1-H, 3.68 (ddd, $J_{1'1}$ = 11 Hz, $J_{1'2}$ = 4 Hz, $J_{1'}$-OH = 7 Hz, 1 H, 1'-H), 3.96 (d, J = 7 Hz, 1 H, OH), 4.14 (ddd, q with D_2O, J_{23} = 5 Hz, J_{21} = 6 Hz, $J_{21'}$ = 4 Hz, 1 H, 2-H), 4.49 (dt, J_{32} = J_{34} = 5 Hz, J_{34} = 11 Hz, 1 H, 3-H), 4.96 (d, J_{65} = 10 Hz, 1 H, cis-6-H), 5.04 (d, $J_{6'5}$ = 18 Hz, 1 H, trans-6-H), 5.70 (dddd, J_{54} = 5 Hz, $J_{54'}$ = 11 Hz, J_{56} = 10 Hz, $J_{56'}$ = 18 Hz, 1 H, 5-H), 7.76 and 7.84 (2 × mc, 2 × 2 H, Ar).

3.3. (2*R*)-2-Phthalimidopent-5-enal (7c). **6c** (24.00 g, 90.81 mmol) was converted into **7c** (15.83 g, 76%) which was obtained as a viscous oil: $[\alpha]^{20}_D$ +3.6° (c 1.4); ^{1}H NMR (270 MHz) δ 2.74–2.88 (m, 1 H, 3-H), 2.94–3.06 (m, 1 H, 3'-H, J_{23} = 10.5 Hz, $J_{23'}$ = 4.5 Hz, 1 H, 2-H), 5.03 (d, 1 H, J_{54} = 10 Hz, 1 H, cis-5-H, 5.08 (d, $J_{5'4}$ = 18 Hz, 1 H, trans-5-H), 5.70–5.88 (m, 1 H, 4-H), 7.80, 7.88 (2 × mc, 2 × 2 H, Ar), 9.74 (s, 1 H, CHO); MS (80 eV, 100 °C), m/e (relative intensity) 229 (M$^+$, 0.85), 203 (1.1), 202 (9.2, M$^+$ − C_2H_3), 201 (64.2, M$^+$ − C=O), 200 (100, M − CHO), 188 (3.5, M$^+$ − C_3H_5), 187 (1.0), 186 (7.5), 184 (1.2), 183 (7.4), 182 (31.0), 175 (4.0), 174 (1.6), 173 (6.4), 172 (3.1), 161 (5.2), 160 (40.0), 155 (2.2), 154 (4.6), 148 (4.7), 147 (5.1), 132 (4.9), 130 (19.2), 105 (7.9), 104 (14.4), 102 (6.3), 77 (9.9), 76 (17.6), 75 (6.1), 74 (4.8); m/e of M$^+$ calcd for $C_{13}H_{11}NO_3$ 229.073894, found 229.074336.

3.4. (*R*)-2-Phthalimidopent-4-enecarboxylic Acid (8c). **7c** (20.0 g, 86.87 mmol) was oxidized according to procedure D to give **8c** (17.40 g, 82%) as colorless crystals of mp 98–99 °C after recrystallization from ether/pentane: $[\alpha]^{20}_D$ +31.1 (c 1.2); ^{1}H NMR (270 MHz) δ 2.86–3.18 (m, 2 H, 3-H)8 5.03 (d, J_{54} = 11 Hz, 1 H, cis-5-H), 5.09 (d, $J_{5'4}$ = 17 Hz, 1 H, trans-5-H), 4.95–5.14 (m, 1 H, 2-H), 5.64–5.82 (m, 1 H, 4-H), 7.76 and 7.86 (2 × mc, 2 × 2 H, Ar), 10.74 (s br, 1 H, COOH). Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.62; H, 4.51; N, 5.70.

3.5. D-Allylglycine (9c). From **8c** (18.0 g, 72.00 mmol) was obtained **9c** (6.94 g, 82%) according to procedure E as colorless needles after recrystallization from ethanol/water: mp 250–257 °C dec; $[\alpha]^{20}_D$ +37.9° (c 1.3, H_2O) [lit.[19] mp 252–257 °C, $[\alpha]^{20}_D$ 37.8 (c 4.0, H_2O)]; ^{1}H NMR (270 MHz, D_2O) δ 2.55–2.78 (m, 2 H, 3-H and 3'-H), 3.84 (dd, j_{23} = 5.5 Hz, $J_{23'}$ = 6 Hz, 1 H, 2-H), 5.33 (d, J_{54} = 10 Hz, 1 H, cis-5-H), 5.35 (d, $J_{5'4}$ = 17 Hz, 1 H, trans-5-H), 5.73–5.92 (m, 1 H, 4-H); IR (KBr) 3410 (m, br), ca. 3300–2400, broad bands with maxima at 3091 (s), 2992 (s), 2941 (s) and 2621 (m) (NH and CH), 2310 (w, br), 1645 (s, shoulder), 1616 (s), 1599 (s), 1515 (s), 1442 (m), 1430 (m), 1410 (s), 1312 (w), 1351 (w), 1368 (w), 1295 (w), 1162 (w), 1001 (w), 926, 920 (w), 855 (w), 720 (w), 628 (w), 543 (m) cm^{-1}. Anal. Calcd for $C_5H_9NO_2$: C, 52.16; H, 7.88; N, 12.17. Found: C, 52.13; H, 7.83; N, 12.12.

4. (*R*)-Aminopentanoic Acid (D-Norvalin) (9d). 4.1. (2*R*,3*R*)-1,2-*O*-Isopropylidene-3-phthalimidohexane-1,2-diol (4d). The **2d/3d** mixture (40.00 g, 229.6 mmol; diastereomeric ratio 86:14) which was obtained from **2c/3c** by catalytic hydrogenation (CH_3OH, Pd/C, 95%) was converted according to

(19) Birnbaum, S. M.; Levintow, L.; Kingsley, R. B.; Greenstein, J. P. *J. Biol. Chem.* **1952**, *194*, 455, 486.

procedure A in **4d**. 51.63 g (76%) of Colorless crystals (51.63 g, 76%) were obtained after column chromatography (ethyl acetate/hexane, 1/3) and purification by crystallization from ethanol, mp 92–93 °C. The diastereomeric purity was >99% (HPLC, μ-Porasil 10, ea/h 8/92, flow 1.5 mL/min, 55 bar, retention time of **4b** 10.33 min, of **5b** 9.84 min): $[\alpha]^{20}_D$ +1.8 (*c* 1.0); ^{1}H NMR (270 MHz) δ 0.90 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 1.28 and 1.37 (2 × s, 2 × 3 H, $C(CH_3)_2$), 1.21–1.40 (m, superimposed by s, 2 H, 5-H, 4-H), 2.15 (mc, 1 H, 4′-H), 3.84 (dd, $J_{11'}$ = 8.5 Hz, J_{12} = 6 Hz, 1 H, 1-H), 4.15 (dd, $J_{1'1}$ = 8.5 Hz, $J_{1'2}$ = 6 Hz, 1 H, 1′-H), 4.24 (ddd, J_{34} = 3 Hz, $J_{34'}$ = 7 Hz, J_{32} = 10 Hz, 1 H, 3-H), 4.72 (dt, J_{21} = $J_{21'}$ = 6 Hz, J_{23} = 10 Hz, 1 H, 2-H), 7.80 and 7.91 (2 × mc, 2 × 2 H, Ar) [The assignment was secured by double resonance]; IR (KBr) 2960, 2930 and 2870 (all m, CH aliph), 1765 (m) and 1705 (s) (C=O), 1460 (w), 1384 (s, $C(CH_3)_2$), 1261 (w), 1238 (m), 1222 (m), 1153 (m), 1069 (m), 842 (m), 729 (s) cm^{-1}. Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.04; H, 7.30; N, 4.54. **5d** could be detected in the mother liquor by ^{1}H NMR signals at δ 3.72 (dd, *J* = 6 and 8 Hz) and 3.99 (dd, *J* = 6 and 8 Hz).

4.2. (2*R*,3*R*)-3-Phthalimidohexane-1,2-diol (6d). **4d** (40.00 g, 132.0 mmol) was hydrolyzed with methanol–sulfuric acid according to procedure B to give **6d** (31.0 g, 86%) which was used for the next step without purification: $[\alpha]^{20}_D$ −8.6 (*c* 1.0); ^{1}H NMR (270 MHz) δ 0.90 (t, *J* = 7 Hz, 3 H, CH_2CH_3), 1.28 (mc, 2 H, 5-H), 1.67 (mc, 1 H, 4-H), 2.07 (mc, 1 H, 4-H), 2.91 (t, *J* = 6 Hz, 1 H, OH), 3.58 (ddd, 1 H, $J_{11'}$ = 9 Hz, J_{12} = 5 Hz, $J_{1\text{-}OH}$ = 6 Hz, 1 H, 1-H), 3.66 (ddd, $J_{11'}$ = 9 Hz, $J_{1'2}$ = 4 Hz, $J_{1'\text{-}OH}$ = 6 Hz, 1 H, 1′-H), 3.85 (d, *J* = 8 Hz, 1 H, OH), 4.10 (mc, 1 H), 4.39 (ddd, *J* = 5 Hz, 6 Hz and 10 Hz, 1 H), 7.72 and 7.87 (2 × mc, 2 × 2 H, Ar).

4.3. (2*R*)-Phthalimidopentanal (7d). From **6d** (30.00 g, 113.8 mmol), 23.48 g (89%) of **7d** were obtained (procedure C) as a viscous oil: $[\alpha]^{20}_D$ −18.0° (*c* 1.0); ^{1}H NMR (270 Mz) δ 0.98 (t, *J* = 7 Hz, 3 H, CH_2CH_3), 1.40 (sext., *J* = 7 Hz, 2 H, CH_2CH_3), 2.15 (mc, 2-H, 3-H), 4.73 (dd, J_{23} = 6 Hz, $J_{23'}$ = 9 Hz, 1 H, 2-H), 7.85 and 7.95 (2 × mc, 2 × 2 H, Ar), 9.71 (s, 1 H, CHO); IR (neat) 3050 and 3031 (w, CH Ar), 2960, 2938 and 2872 (m, CH aliph), 1772 (s, C=O), 1710 (ss, C=O), 1610 (w), 1468 (m), 1382 (ss), 1338 (s, shoulder), 1192 (w), 1174 (w), 1150 (m), 1053 (s), 879 (m), 797 (w), 722 (s) cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found C, 65.89; H, 5.89; N, 5.68.

4.4. (*R*)-2-Phthalimidopentanoic Acid (8d). From 21.40 g (93.0 mmol) of **7d**, 18.00 g (79%) **8d** were obtained (procedure D) as colorless prisms of mp 71–72 °C (ethanol): $[\alpha]^{20}_D$ +15.8° (*c* 1.0); ^{1}H NMR (270 MHz) δ 0.95 (t, *J* = 7 Hz, 3 H, CH_2CH_3), 1.36 (sext., J_{34} = J_{45} = 7 Hz, 2 H, CH_2CH_3), 2.16 and 2.32 (2 × mc, 2 × 1 H, 3-H, 3′-H) 4.94 (dd, J_{23} = 5 Hz, $J_{23'}$ = 11 Hz, 1 H, 2-H), 7.79 and 7.95 (2 × mc, 2 × 2 H, Ar), ca. 6.60–8.40 (br, 1 H, COOH); IR (KBr) 3440 (s, br, OH), 3062 and 3030 (w, CH Ar), 2965 and 2870 (w, CH aliph), 1773 (m, C=O), 1705 (ss, C=O), 1610 (w), 1465 (w), 1383 (s), 1278 (s), 1152, 1082, 1049, 928 (all w), 718 (m) cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 62.86; H, 5.40; N, 5.60.

4.6. D-Norvaline (9d). Procedure E converted 16.00 g (60.0 mmol) of **8d** into 6.70 g (94%) of **9d**: mp >300 °C; $[\alpha]^{20}_D$ −23.6° (*c* 2.0, 2 N HCl) [lit.[20] $[\alpha]^{20}_D$ −25.0° (*c* 2.0, 2 N HCl)]; ^{1}H NMR (250 MHz, D_2O) δ 0.93 (t, *J* = 7 Hz, 3 H, CH_3), 1.39 (sext., J_{34} = J_{45} = 7 Hz, 2 H, 4-H), 1.82 (mc, 2 H, 3-H), 3.74 (t, J_{23} = 6 Hz, 1 H, 2-H). Anal. Calcd for $C_5H_{11}NO_2$: C, 51.26; H, 9.47; N, 11.96. Found: C, 51.23; H, 9.51; N, 11.98.

5. (*R*)-2-Amino-2-butenoic Acid (D-Vinylglycine) (9e). 5.1. (2*R*,3*R*)- and (2*R*,3*S*)-1,2-*O*-Isopropylidene-3-phthalimidopent-4-ene-1,2-diol (4e and 5e). The **2e/3e** mixture (40.00 g, 252.83 mmol, diastereomeric ratio 60:40) was converted into **4e/5e** according to procedure A. After PCC (ea/h 1/2), 35.45 g (49%) of a crystalline **4e/5e** mixture (diastereomeric ratio 59.4:40.6 as determined by HPLC, μPorasil 10, 1.5 mL/min, 59 bar, retention time of **4e** 4.52 min, of **5e**, 4.84 min) were obtained. Recrystallization from ethanol gave diastereomerically pure (HPLC analysis) **4e** (17.70 g, 41% based on **2e**): colorless prisms, mp 106.5–107 °C; $[\alpha]^{20}_D$ +42.9° (*c* 1.6); ^{1}H NMR (270 MHz) δ 1.28 and 1.39 (2 × s, 2 × 3 H, acetonide-CH_3) 3.88 (dd, $J_{11'}$ = 9 Hz, J_{12} = 4.5 Hz, 1 H, 1-H), 4.06 (dd, $J_{1'1}$ = 9 Hz, $J_{1'2}$ = 6 Hz, 1 H, 1′-H), 4.69 (t, J_{23} = J_{34} = 9 Hz, 1 H, 3-H), 4.81 (ddd, J_{12} = 4.5 Hz, $J_{1'2}$ = 6 Hz, J_{34} = 8 Hz, 1 H, 2-H), 5.26 (d, J_{54} = 10 Hz, 1 H, cis-5-H), 5.35 (d, $J_{5'4}$ = 17 Hz, 1 H, trans-5-H), 6.14 (ddd, J_{45} = 10 Hz, $J_{45'}$ = 17 Hz, J_{43} = 8 Hz, 1 H, 4-H), 7.65 and 7.77 (2 × mc, 2 × 2 H, Ar); IR (KBr) 3080 (m), 3048 (m) 3010 (m), 2998 (m), 2940 (s), 2870 (m), 1738 and 1712 (s, C=O), 1608 (w), 1591 (w), 1502 (m), 1460 (m), 1419 (m), 1400 (m), 1388 (m), 1339 (m), 1300 (s), 1254 (s), 1240 (s), 1189 (s), 1100 (m), 1069 (m), 1022 (m), 951 (m), 862 (w), 790 (m), 780 (m), 736 (s), 708 (s) cm^{-1}. Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.87; H, 5.96; N, 4.88. Found: C, 66.61; H, 5.92; N, 4.89. **5e** was detectable by the following signals in the mother liquor: δ 1.38 and 1.46 (2 × s, 2 × 3 H, acetonide-CH_3), 3.76 (dd, $J_{11'}$ = 9 Hz, J_{12} = 4.5 Hz, 1 H), 4.00 (dd, $J_{11'}$ = 9 Hz, $J_{1'2}$ = 5.5 Hz, 1 H, 1′-H), 4.74 (t, J_{32} = J_{34} = 8 Hz, 1 H, 3-H), 4.83 (mc, 1 H, 2-H), 5.25–5.42 (2 × dd, cis- and trans-5-H), 6.32 (ddd, J_{45} = 10 Hz, $J_{45'}$ = 17 Hz, J_{43} = 7 Hz, 1 H, 4-H).

5.2. (2*R*,3*R*)-3-Phthalimidopent-4-ene-1,2-diol (6e). The crystalline **4e/5e** mixture (30.00 g, 104.45 mmol) was hydrolyzed with CH_3OH–H_2SO_4 (procedure B) to give 23.45 g (91%) oily diastereomeric mixture which was crystallized from benzene (100 mL) to yield after 2 days at 5 °C 11.02 g (71% based on **4e**) of crystalline **6e**, diastereomerically pure according to ^{1}H NMR and HPLC (μPorasil 10, *i*-PrOH/hexane 5/95, 2 mL/min, 65 bar, retention time of **6e** 17.30 min, of erythro-diast. 18.29 min): mp 114–115 °C; $[\alpha]^{20}_D$ +49.5° (*c* 1.0); ^{1}H NMR (270 MHz) δ 3.30 (t, *J* = 7.5 Hz, 1 H, OH), 3.56 (ddd, $J_{11'}$ = 1.5 Hz, J_{12} = 6 Hz, $J_{1\text{-}OH}$ = 7.5 Hz, 1 H, 1-H), 3.70 (ddd, $J_{1'1}$ = 11.5 Hz, $J_{1'2}$ = 4 Hz, $J_{1'\text{-}OH}$ = 7.5 Hz, 1 H, 1′-H), 4.10 (s, br, 1 H, OH), 4.29 (ddd, J_{23} = 9 Hz, J_{21} = 6 Hz, $J_{21'}$ = 4 Hz, 1 H, 2-H), 4.82 (t, J_{34} = J_{32} = 9 Hz, 1 H, 3-H), 5.23 (d, 1 H, J_{54} = 10 Hz, 1 H, cis-5-H), 5.30 (d, $J_{5'4}$ = 17 Hz, 1 H, trans-5-H), 6.16 (ddd, J_{45} = 10 Hz, $J_{45'}$ = 17 Hz, J_{43} = 9 Hz, 1 H, 4-H), 7.65 and 7.72 (2 × mc, 2 × 2 H, Ar); IR (KBr) 3480 (s, br, OH), 3305 (s, br, OH), 3086 (w), 2980, 2965, 2940 and 2905 (all w, CH aliph), 1775 (w, C=O), 1745 (ss, C=O), 1653 (w), 1620 (w), 1475 (m), 1390 (s), 1365 (s, shoulder), 1339 (m), 1292 (m), 1220 (m), 1120 (s), 1082 (m), 1048 (m), 1010 (m), 980 (w), 955 (m), 914 (m), 890 (m), 808 (w), 770 (m), 725 (s), 696 (m), 652 (m), 540 (w) cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.0; N, 5.67. Found: C, 62.89; H, 5.35; N, 5.52. Alternatively, the hydrolysis was performed with diastereomerically pure **4e** (15.00 g, 52.25 mmol) to furnish pure **6e** (12.50 g, 97%) immediately.

5.3. (*R*)-2-Phthalimido-3-butenal (7e). Pure **6e** (10.00 g, 40.50 mmol) was transformed into **7e** according to procedure C. Crude aldehyde (6.55 g, 75%) was obtained and, due to its instability, immediately transferred to the next step: ^{1}H NMR (270 MHz) δ 5.25 (d, J_{23} = 8 Hz, 1 H, 2-H), 5.36 (d, J_{43} = 17 Hz, 1 H, trans-4-H), 5.43 (d, $J_{4'3}$ = 11 Hz, 1 H, 4′-H), 6.00–6.70 (m, 1 H, 3-H), 7.77 (mc, 4 H, Ar), 9.66 (s, 1 H, CHO). PCC (ea/h 1/2) led to double-bond migration under formation of the conjugated aldehyde **10**: ^{1}H NMR (270 MHz) δ 2.01 (d, *J* = 7 Hz, 3 H, CH_3), 7.22 (q, *J* = 7 Hz, 1 H, =CH), 7.72 and 7.84 (2 × mc, 2 × 2 H, Ar), 9.45 (s, 1 H, CHO); IR (neat) 3080 (w), 2885 (w), 2822 (w), 1792 (s), 1772 (s), 1725 (s), 1698 (s), 1660 (s), 1615 (m), 1471 (m), 1414 (s), 1378 (s), 1312 (s), 1226 (m), 1178 (w), 1120 (m), 1090 (m), 893 (s), 735 (s), 707 (w), 682 (w), 539 (w), 518 (w) cm^{-1}. Anal. Calcd for $C_{12}H_9NO_3$: C, 66.97; H, 4.21; N, 6.51. Found: C, 66.07; H, 4.26; N, 6.26.

5.4. (*R*)-2-Phthalimido-4-butenoic Acid (8e). Crude aldehyde **7e** (6.00 g, 27.90 mmol) was converted into **8e** (4.88 g, 76%) according to procedure D: viscous oil, $[\alpha]^{20}_D$ +54.1° (*c* 1.1); ^{1}H NMR (270 MHz) δ 5.30 (d, J_{43} = 17 Hz, 1 H, trans-4-H), 5.34 (s, $J_{4'3}$ = 10 Hz, 1 H, cis-4-H), 5.43 (d, J_{23} = 6.5 Hz, 1 H, 2-H), 6.36 (ddd, J_{34} = 17 Hz, $J_{34'}$ = 10 Hz, J_{32} = 6.5 Hz, 1 H, 3-H), 7.68 and 7.82 (2 × mc, 2 × 2 H, Ar), 9.20 (s, br, 1 H, COOH); IR (neat) 3300–2700 (s, br, with superimposed bands, OH), maxima at 3101 (s), 3033 (s) and 2942 (m), 1770 (s), 1745 (s), 1720 (s), 1688 (s, C=O, i.e., C=C), 1612 (m), 1465 (m), 1396 (s), 1205 (s), 1115 (w), 1089 (w), 1000 (m), 949 (w), 907 (w), 725 (s) cm^{-1}. Anal. Calcd for $C_{12}H_9NO_4$: C, 62.34; H, 3.92; N, 6.05. Found: C, 62.21; H, 3.83; N, 5.92. For further characterization, **8e** was converted into the methyl ester with diazomethane in ether: yield 93%, colorless needles, mp 76–77 °C (pentane); $[\alpha]^{20}_D$ +64.5° (*c* 1.1); ^{1}H NMR (270 MHz) δ 3.76 (s, 3 H, CH_3), 5.30 (d, J_{43} = 17 Hz, 1 H, trans-4-H), 5.32 (d, $J_{4'3}$ = 10 Hz, 1 H, cis-4-H), 5.39 (d, J_{23} = 6.5 Hz, 1 H, 2-H), 6.36 (ddd, J_{43} = 17 Hz, $J_{4'3}$ = 10 Hz, J_{32} = 6.5 Hz, 1 H, 3-H), 7.72 and 7.84 (2 × mc, 2 × 2 H, Ar); IR (KBr) 3025

(20) Black, S.; Wright, N. G. *J. Biol. Chem.* **1954**, *212*, 39.

(w), 2962 (w), 2930 (w) and 2857 (w) (CH), 1775 (m), 1749 (s), 1718 (s), 1645 (w), 1610 (w), 1441 (w), 1390 (s), 1335 (w), 1280 (m), 1239 (m), 1106 (w), 1028 (w), 940 (w), 908 (w), 750 (w), 723 (m), 680 (w) cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.47; H, 4.63; N, 5.71. To secure the optical of purity of the material, **8e** (460 mg, 2.00 mmol) was hydrogenated in methanol (30 mL) over Pd/C (10 mg) at 25 °C, 1 bar, to give 431 mg (93%) of **8b** with $[\alpha]^{20}_D$ +22.9° (*c* 2.0) (ee >95%).

5.5. (*R*)-2-Amino-3-butenoic Acid (D-Vinylglycine) (9e). **8e** (3.00 g, 13.01 mmol) was transformed into **9e** (794 mg, 87%) according to procedure E. The crude product was heated in 2 N HCl (30 mL) and crystallized from acetone. Further recrystallization from ethanol/acetone gave **9e**·HCl (510 mg, 45% based on **8e**) as colorless needles: mp 172–174 °C; $[\alpha]^{20}_D$ −76.1° (*c* 1.3, H_2O), 93.4 (*c* 1.0, 2 N, HCl) [lit.[21] mp 175–177 °C dec; $[\alpha]^{20}_D$ +78.5° (*c* 1.9, H_2O), 96 (*c* 1, 2 N HCl) for (*S*)-**9e**·HCl]; ^1H NMR (270 MHz, D_2O) δ 4.78 (d, J_{23} = 7 Hz, 1 H, 2-H), 5.72 (d, 1 H, J_{43} = 17 Hz, 1 H, trans-4-H), 5.74 (d, 1 H, $J_{4'3}$ = 10 Hz, cis-4′-H), 6.15 (ddd, J_{34} = 17 Hz, $J_{4'3}$ = 10 Hz, J_{32} = 7 Hz, 1 H, 3-H); IR (KBr) 3400–2300 (ss, br) maxima at 3000, 2627, 2535 and 2428, 1969 (m), 1747 (ss), 1600 (m), 1499 (s), 1417 (m), 1361 (w), 1224 (s), 1159 (m), 1132 (m), 990 (w), 961 (m), 818 (m), 750 (w), 635 (w) cm^{-1}. Anal. Calcd for C, 34.92; H, 5.86; N, 10.18. Found: C, 34.18; H, 6.22; N, 10.72.

6. Chiral Derivatives of 3-Aminoglutaric Acid. 6.1. (2*R*,3*R*)-1-(Benzoyloxy)-3-phthalimido-5-hexen-2-ol (11a). Diol **6c** (18.50 g, 70.80 mmol) in pyridine (100 mL) was treated dropwise with benzoyl chloride (10.70 g, 76.10 mmol) in pyridine (30 mL) at −10 °C. The mixture was stirred at 22 °C for 16 h, diluted with water and extracted with $CHCl_3$. The organic phase was washed with 2 N sulfuric acid and bicarbonate, dried ($MgSO_4$), and evaporated to give after column chromatography (ethyl acetate/hexane, 1/2) oily **11a** (18.16 g, 70%) (R_f 0.29) and crystalline dibenzoate (4.00 g, 12%) (R_f 0.40) with mp 88–90 °C.

11a: $[\alpha]^{20}_D$ −7.4 (*c* 3.1); ^1H NMR (250 MHz) δ 2.62 (mc, 1 H, 4-H), 2.84 (mc, 1 H, 4-H), 4.12–4.50 (m, 4 H), 4.43 (dt, *J* = 5 Hz, *J* = 6 Hz, 1 H), 4.94 (d, J_{65} = 10 Hz, 1 H, cis-6-H), 5.03 (d, $J_{6'5}$ = 17 Hz, 1 H, trans-6-H), 5.65–5.86 (m, 1 H, 5-H), 7.36 (t, *J* = 7 Hz, 2 H, benzoyl-H), 7.48 (t, *J* = 7 Hz, 1 H, benzoyl-H), 7.64 and 7.76 (2 × mc, 2 × 2 H, phthalimide), 7.98 (d, *J* = 7 Hz, 2 H, benzoyl-H); IR (neat) 3460 (s, br, OH), 3062, 3035, 3006 (all w), 2980, 2958, and 2924 (w, CH aliph), 1770 (s, C=O), 1705 (ss, C=O), 1640 (w), 1611 and 1600 (w), 1468 (w), 1450 (m), 1390 and 1369 (ss), 1270 (ss), 1177 (m), 1112 (ss), 1070 (s), 1026 (m), 995 (m), 922 (m), 874 (m), 795 (w), 712 (s), 688 (w), 531 (m) cm^{-1}; MS (80 eV, 60 °C), *m/e* (relative intensity) 365 (M^+, 2), 324 ($M^+ - C_3H_5$, 15), 243 ($M^+ - C_6H_5CO$, 7), 231 (5), 230 (28), 201 (38), 200 (100), 187 (10), 182 (16), 165 (16), 160 (36), 149 (14), 130 (15), 105 (81, $C_6H_5CO^+$), 77 ($C_6H_5^+$, 24), 53 (22); M^+ *m/e* calcd for $C_{21}H_{19}NO_5$ 365.12631, found 365.12646. Anal. Calcd: C, 69.03; H, 5.24; N, 3.83. Found: C, 69.07; H, 5.38; N, 3.68.

Dibenzoate: ^1H NMR (270 MHz) δ 2.67 (mc, 1 H, 4-H), 3.13 (mc, 1 H, 4′-H), 4.57 (dd, $J_{11'}$ = 12 Hz, J_{12} = 5 Hz, 1 H, 1-H), 4.79 (dd, $J_{1'1}$ = 12 Hz, $J_{1'2}$ = 4 Hz, 1 H, 1′-H), 4.90 (m, 1 H, 3-H), 4.99 (d, J_{65} = 10 Hz, 1 H, cis-6-H), 5.12 (d, $J_{6'5}$ = 17 Hz, 1 H, trans-6-H), 5.70 (mc, 1 H, 5-H), 6.03 (ddd, J_{21} = 5 Hz, $J_{21'}$ = 4 Hz, J_{23} = 7 Hz, 1 H, 2-H), 7.36 and 7.43 (2 × t, *J* = 7 Hz, 2 × 2 H, benzoyl-H), 7.49 and 7.54 (2 × t, *J* = 7 Hz, 2 × 1 H, benzoyl-H), 7.64 and 7.79 (2 × mc, 2 × 2 H, phthalimide H), 7.94 and 8.01 (2 × d, *J* = 7 Hz, 2 × 2 H, benzoyl-H).

6.2. (2*R*,3*S*)-1-(Benzoyloxy)-3-phthalimido-2-*O*-(imidazolylthiocarbonyl)-5-hexen-2-ol (11b). **11a** (14.10 g, 36.6 mmol) was refluxed with *N,N*-thiocarbonyldiimidazole (14.50 g) in THF (250 mL) for 4 h. The solvent was evaporated and the sirupy residue was dissolved in CH_2Cl_2 and washed with 1 N HCl, bicarbonate, and water, dried ($MgSO_4$), and purified by column chromatography (ethyl acetate/hexane, 1/1) to give **11b** (15.93 g, 92%) as a yellow oil: $[\alpha]^{20}_D$ −49.9° (*c* 1.8); ^1H NMR (270 MHz) δ 2.71 (mc, 1 H, 4-H), 3.15 (mc, 1 H, 4′-H, 4.61 (dd, $J_{11'}$ = 13 Hz, J_{12} = 4 Hz, 1 H, 1-H), 4.92 (dd, $J_{1'1}$ = 13 Hz, $J_{1'2}$ = 3 Hz, 1 H, 1′-H), 4.94–5.06 (m, 1 H, 3-H), 5.03 (d, J_{65} = 10 Hz, 1 H, cis-6-H), 5.12 (d, $J_{6,5}$ = 17 Hz, 1 H, trans-6-H), 5.63–5.81 (m, 1 H, 5-H), 6.48 (ddd, J_{21} = 4 Hz, $J_{21'}$ = 3 Hz, J_{23} = 7 Hz, 1 H, 2-H), 6.97 (s, 1 H, 4-H or 5-H of imidazole), 7.41 (t, *J* = 7 Hz, 2 H, benzoyl-H), 7.57 (t, *J* = 7 Hz, 1 H, benzoyl-H), 7.63 (s, 1 H, 4-H or 5-H of imidazole), 7.72 and 7.82 (2 × mc, 2 × 2 H, phthalimide H), 7.97 (d, *J* = 7 Hz, 2 H, benzoyl-H), 8.34 (s, 1 H, 2-H of imidazole); IR (neat) 3158 (w), 3160 (m), 3065 (m), 3030 (w), 3008 (w), 2980 (m), 2959 (m), 2927 (w), 1770 (s, C=O), 1705 (ss, C=O), 1640 (m), 1599 (m), 1580 (m), 1465 (s), 1458 (m), 1385 (ss), 1320 (ss), 1282 (ss), 1222 (ss), 1172 (m), 1105 (ss), 1068 (s) 1021 (s), 998 (s), 959 (s), 922 (s), 870 (m), 833 (m), 750 (ss), 710 (ss), 651 (s), 530 (s) cm^{-1}, MS (80 eV, 120 °C), *m/e* (relative intensity) 475 (M^+, 7), 348 ($M^+ - C_4H_3N_2OS$, 11), 347 (7), 306 (8), 242 (7), 226 (13), 225 (57), 200 (10), 160 (8), 148 (9), 130 (8), 105 ($C_6H_5CO^+$, 100), 79 (10), 78 ($C_6H_6^+$, 9), 77 ($C_6H_5^+$, 16), 60 (COS^+, 12); M^+ *m/e* calcd for $C_{25}H_{21}N_3OS_5$ 475.12018, found 475.12059.

6.3. (*R*)-1-(Benzoyloxy)-3-phthalimido-5-hexene (11c). **11b** (15.30 g, 32.2 mmol) in toluene (250 mL) was added dropwise to a boiling solution of tributyltin hydride (15.3 g, 51.0 mmol) in toluene (1500 mL). After the mixture was refluxed for 16 h, the solvent was evaporated under reduced pressure and the residue was partitioned between hexane (200 mL) and acetonitrile (200 mL). The acetonitrile phase was evaporated and the residue was purified by column chromatography (ethyl acetate/hexane, 1/2) to give **11c** (9.19 g, 82%) as a colorless syrup: $[\alpha]^{20}_D$ −79.08° (*c* 2.1); ^1H NMR (270 MHz) δ 2.15–2.31 (m, 1 H), 2.50–2.74 (m, 2 H) and 2.77–2.95 (m, 1 H), (2-H, 2′-H, 4-H, 4′-H), 4.28 (ddd, $J_{11'}$ = 12 Hz, J_{12} = 4 Hz, $J_{12'}$ = 8 Hz, 1 H, 1-H), 4.42 (dt, $J_{11'}$ = 12 Hz, $J_{12'} = J_{6'5'}$ = 5.5 Hz, 1 H, 1′-H), 4.58 (mc, 1 H, 3-H), 4.99 (d, J_{56} = 10 Hz, 1 H, cis-6H), 5.07 (d, $J_{56'}$ = 17 Hz, 1 H, trans-6-H), 5.74 (mc, 1 H, 5-H), 7.34 (t, *J* = 7.5 Hz, 2 H, benzoyl-H), 7.49 (t, *J* = 7.5 Hz, 1 H, benzoyl-H), 7.66 and 7.78 (2 ′ mc, 2 × 2 H, phthalimide-H), 7.93 (d, *J* = 7.5 Hz, 2 H, benzoyl-H); IR (neat) 3070 (w), 3041 (w), 2965 and 2935 (w, CH-aliph.), 1770 (s, C=O), 1710 (ss, C=O), 1642 (w), 1602 (w), 1583 (w), 1469 (m), 1451 (m), 1393 (s)8 1371 (s), 1337 (m), 1317 (m), 1275 (ss), 1278 (m), 1113 (s), 1071 (m), 1029 (m), 998 (w), 922 (m), 875 (w), 715 (ss), 535 (w) cm^{-1}; MS (80 eV, 60 °C), *m/e* (relative intensity) 349 (M^+, 3), 308 ($M^+ - C_3H_5$, 7), 200 (11), 187 (12), 186 (100), 130 (5), 105 ($C_6H_5CO^+$, 17), 77 ($C_6H_5^+$, 10), 76 (9); M^+ *m/e* calcd for $C_{21}H_{19}NO_4$ 349.1314, found 349.1316. Anal. Calcd C, 72.19; H, 5.48; N, 4.01. Found: C, 71.61; H, 5.31; N, 4.03.

6.4. (*R*)-3-Amino-1-(benzoyloxy)-5-hexene (11d). **11c** (1.60 g, 4.60 mmol) was refluxed with hydrazine hydrate (280 mg, 5.60 mmol) in ethanol (10 mL) for 4 h. Then the mixture was diluted with ether (100 mL), filtrated, and concentrated under reduced pressure. The residue was dissolved in ether, washed with 1 N NaOH and water, dried (Na_2SO_4), and evaporated to furnish 910 mg (90%) of **11d** as colorless needles: mp 98–99 °C ($CHCl_3$/hexane); ^1H NMR (270 MHz) δ 1.49 (mc, 1 H), 1.97 (mc, 1 H) and 2.43 (mc, 1 H) (3-H, 3′-H, 2-H, 2′-H), 3.66 (mc, 2 H, 4-H, 4′-H), 4.40 (mc, 1 H, 3-H), 5.16 (d, J_{56} = 10 Hz, 1 H, 6-H), 5.18 (d, $J_{56'}$ = 17 Hz, 1 H, 6′-H), 5.84 (mc, 1 H, 5-H), 6.19 (s, br, 2 H, NH_2), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.48 (t, *J* = 7.5 Hz, 1 H), 7.73 (d, 2 H, *J* = 7.5 Hz, 2 H, benzoyl-H); IR (KBr) 3415 (m) and 3302 (s) (NH), 3080 (w), 3020 (w), 2957 (m), 2936 (w), 2906 (w), 2865 (w) (CH aliph), 1630 (ss, C=O), 1603 (w), 1570 (w), 1535 (s), 1450 (m), 1321 (w), 1309 (w), 1290 (w), 1058 (m), 1032 (m), 1000 (m), 928 (m), 803 (w), 702 (s) cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 69.80; H, 7.85; N, 6.04.

6.5 (*R*)-3-Phthalimido-5-hexen-1-ol (11e). **11d** (1.00 g, 2.90 mmol) was stirred with 50 mL of MeOH containing 10% potassium carbonate for 48 h at 22 °C. Then the solution was neutralized with 2 N H_2SO_4, concentrated under reduced pressure, and extracted with methylene chloride. The organic phase was washed with water, dried ($MgSO_4$), and evaporated to give **11e** (560 mg, 80%) as a colorless oil: $[\alpha]^{20}_D$ −5.7° (*c* 2.1); ^1H NMR (270 MHz) δ 2.00 (mc, 1 H, 4-H), 2.30 (mc, 1 H, 4′-H), 2.53 (mc, 1 H, 2-H), 2.67 (s, 1 H, OH), 2.86 (mc, 1 H, 2′-H), 3.51 (mc, 2 H, 1- and 1′-H), 4.51 (mc, 1 H, 3-H), 4.93 (d, *J* = 11 Hz, 1 H, cis-6-H), 5.02 (d, *J* = 17 Hz, 1 H, trans-6-H), 5.61–5.79 (m, 1 H, 5-H), 7.65 and 7.76 (mc, 2 × 2 H, phthalimide H).

Acknowledgment. This work was financially supported by the Deutsche Forschungsgemeinschaft (DFG) and the Fonds der Chemischen Industrie. We also thank the Schering AG, Berlin–Bergkamen, and the BASF AG, Ludwigshafen for fine chemicals and solvents.

(21) Afzali-Arkadani, A.; Rapoport, H. *J. Org. Chem.* **1980**, *45*, 4817.