1,2-Asymmetric Induction in the Zwitterionic Claisen Rearrangement of Allylamines

Udo Nubbemeyer

Institut für Organische Chemie, Freie Universität Berlin, Takustrasse 3, D-14195 Berlin, Germany

Received November 15, 1994[⊗]

A zwitterionic Claisen rearrangement has been developed for optically active *N*-allylpyrrolidines using a two-phase system. The inherent-1,2 asymmetric induction was investigated for the generation of a new C–C bond adjacent to a chiral C–O function. The reaction with acetyl chloride led to a small diastereomeric excess, whereas the rearrangement with propionyl chloride proceeded with a high simple and a high induced diastereoselection. The resulting γ,δ-unsaturated amides were cyclized to the corresponding optically active γ-butyrolactones, which are useful intermediates in natural product synthesis.

Introduction

The ketene Claisen rearrangement of allyl ethers and allyl thioethers was first described by Bellus in 1978.[1] Further investigations showed that this intermolecular variant of the [3.3]-sigmatropic reaction proceeds chemoselectively (allyl sulfide versus allyl ether) under mild conditions (20 °C up to 40 °C).[2] This reaction type is characterized by excellent chirality transfer from a C–S to a C–O bond[3] and by high 1,2-asymmetric induction.[4] The scope of the rearrangement is restricted to activated ketenes like chloro-, chloroalkyl-, and dichloroketene.

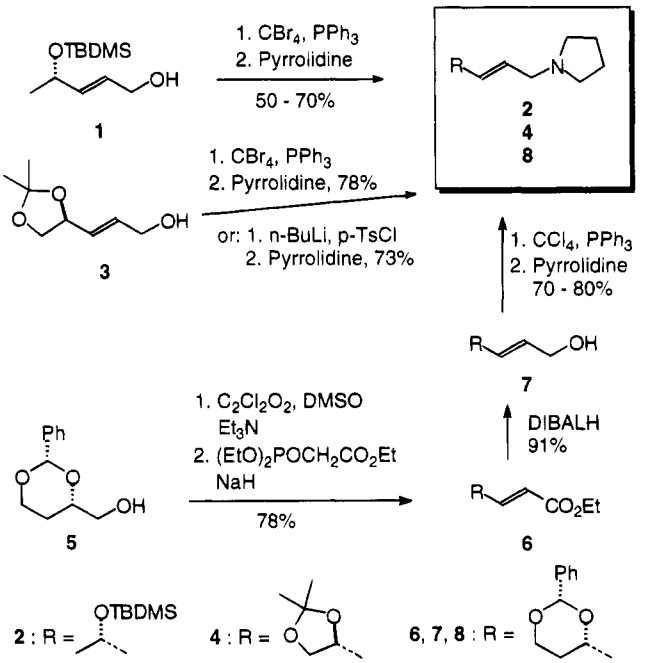
Most cases of amino ketene Claisen reaction have used dichloroketene and allylamines that either are incorporated in conformationally fixed bicyclic systems[5] or bear sterically unhindered monosubstituted double bonds.[6] Few additional examples [e.g., with stable ketenes (long reaction time, high temperatures)] have been reported.[7] All of these rearrangements are accompanied by varying amounts of tarry side products.

Results and Discussion

In this paper, the development and the 1,2-asymmetric induction of the ketene Claisen rearrangement of acyclic allylamines is reported. The optically active allylpyrrolidines **2**, **4**, and **8** were chosen for the initial investigation (Scheme 1).

Allylpyrrolidine **2** was generated from the known alcohol **1** (available in four steps from ethyl L-(−)-lactate)[8] in two steps: After bromination with CBr_4/PPh_3, the crude product was treated with pyrrolidine, producing **2** in 50–70% yields in two steps.[9] Allylamine **4** was synthesized from the known alcohol **3** (available in four steps from D-mannitol)[10] either analogously to amine **2** (78% yield) or in a one-pot procedure: **3** was first deprotonated with *n*-BuLi and then esterified with *p*-toluenesulfonyl chloride. The tosylate in situ was directly treated with pyrrolidine to give **4** in 73% yield.[11]

Scheme 1



The synthesis of allylpyrrolidine **8** began with the alcohol **5** (available in two steps from L-(−)-malic acid).[12] A one-pot Swern oxidation/Horner olefination led to the unsaturated ester **6** (78%).[13] After DIBALH reduction[14] to the allylic alcohol **7** (91%), the OH group was replaced by the pyrrolidinyl function as described for amine **2** (via chlorination with CCl_4/PPh_3), and allylamine **8**, with a conformationally fixed six-membered ring bearing an additional defined stereocenter in the protective group, was isolated in 70–80% yield.

[⊗] Abstract published in *Advance ACS Abstracts*, May 15, 1995.

(1) Malherbe, R.; Bellus, D. *Helv. Chim. Acta* **1978**, *61*, 3096.
(2) Malherbe, R.; Rist, G.; Bellus, D. *J. Org. Chem.* **1983**, *48*, 860.
(3) Öhrlein, R.; Jeschke, R.; Ernst, B.; Bellus, D. *Tetrahedron Lett.* **1989**, *30*, 3517.
(4) Nubbemeyer, U.; Öhrlein, R.; Gonda, J.; Ernst, B.; Bellus, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1465.
(5) Cid, M. M.; Eggnauer, U.; Weber, H. P.; Pombo-Villar, E. *Tetrahedron Lett.* **1991**, *32*, 7233. Cid, M. M.; Pombo-Villar, E. *Helv. Chim. Acta* **1993**, *76*, 1591.
(6) Edstrom, E. D. *J. Am. Chem. Soc.* **1991**, *113*, 6690.
(7) Ishida, M.; Muramaru, H.; Kato, S. *Synthesis* **1989**, 562. Roberts, S. M.; Smith, C.; Thomas, R. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1493.
(8) Hatakeyama, S.; Saijo, K.; Takano, S. *Tetrahedron Lett.* **1985**, *26*, 865.
(9) Axelrodt, E. H.; Milne, G. M.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139.
(10) Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109. Mulzer, J.; Kappert, M. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 63. Mulzer, J.; Kappert, M. *Tetrahedron Lett.* **1985**, *26*, 1631.
(11) Aneja, R.; Davies, A. P.; Knaggs, J. A. *Tetrahedron Lett.* **1974**, 67. Pieper, J. Diplomarbeit, Berlin, 1991.
(12) Herrandon, B. *Tetrahedron: Asymmetry* **1991**, *2*, 191.
(13) Nubbemeyer, U. *Synthesis* **1993**, 1120.
(14) Winterfeldt, E. *Synthesis* **1975**, 617.

0022-3263/95/1960-3773$09.00/0

Initial attempts to achieve the ketene Claisen rearrangement via standard methods failed. The in situ generation of several ketenes either via dehalogenation of α-halogen carboxylic acid chlorides with Zn/Cu alloy[2-4] or via dehydrohalogenation of carboxylic acid chlorides[5] in the presence of the allylamines under widely varied reaction conditions afforded only allyl chlorides **10** (via a von Braun type reaction[15]) and considerable amounts of tarry side products. Furthermore, the formation of ketenes according to Olah,[16] Brady,[17] Pericas,[18] Masamune,[19] or Clemens[20] gave no rearrangement product. A two-phase reaction was then successful. Treating the allylamines **2**, **4**, and **8** consecutively with acetyl chloride and trimethylaluminum in CH_2Cl_2 in the presence of K_2CO_3 at 0 °C generated the γ,δ-unsaturated amides in 60–90% isolated yields.[21] Small amounts (0–10%) of allyl chlorides **10** and *N*-acetylpyrrolidine **11** were found as side products. In view of these results, it seems reasonable that the first step of the reaction is the formation of the acylammonium salt **9**. Then, this intermediate is either attacked by the nucleophilic chloride ion, leading to the allyl chloride **10** (von Braun type reaction,[15] mostly suppressed under these reaction conditions), or deprotonated at the α-position of the activated CO group, generating the (hypothetical) zwitterionic intermediate **12**, which undergoes the [3.3]-sigmatropic rearrangement[22] to generate the desired γ,δ-unsaturated pyrrolidine amides **13**–**18** (Scheme 2).

As a result of the allylpyrrolidines being treated with acetyl chloride under the given conditions, pyrrolidine **2** gave the diastereomeric amides **13** and **14** (ratio, 2:1; 84% yield), **4** afforded **15** and **16** (ratio, 3:2; 82% yield), and **8** led to **17** and **18** (ratio, 7:4; 80% yield), respectively. The fixed conformation of the six-membered ring and the additional stereocenter in the protective group of **8** did not increase the diastereoselection of the rearrangement relative to the reaction of amine **4**. All diastereomeric amides were easily separated via preparative HPLC. The observed diastereomeric excesses of 20–33% are in the same range as those seen from other variants of the Claisen rearrangement.[8,23,24] According to the transition state models developed by Felkin,[25] Houk,[26] and Kahn,[27] the major diastereomers **13**, **15**, and **17** should have a *syn* configuration resulting from a rearrangement of the

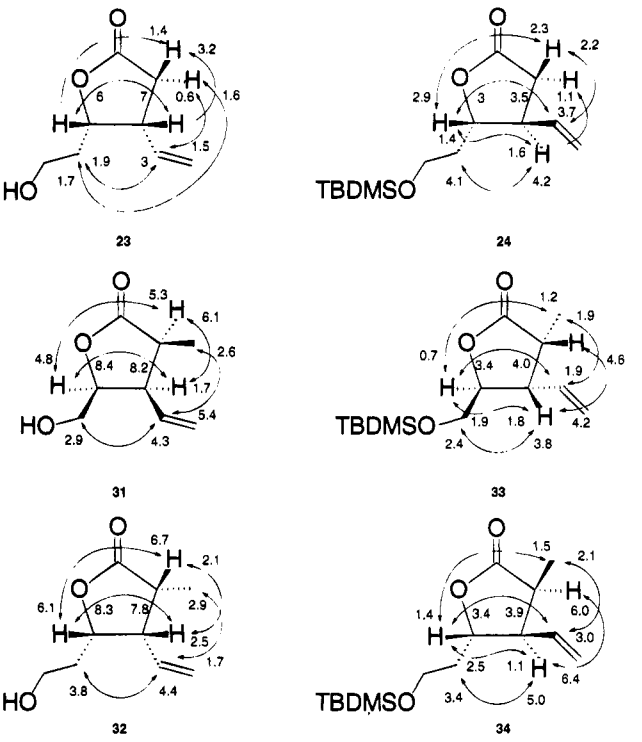
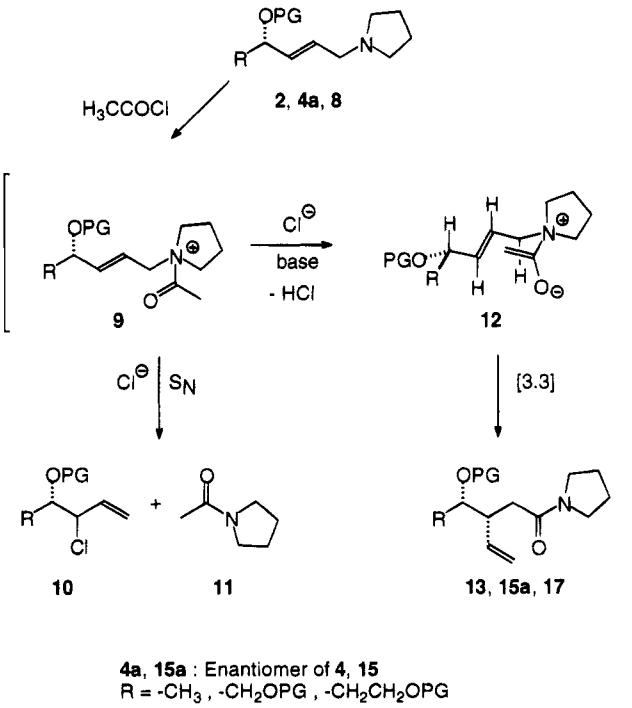


Figure 1. NOEDS data of the lactones **23**, **24**, and **31**–**34** (amplification in %).

Scheme 2



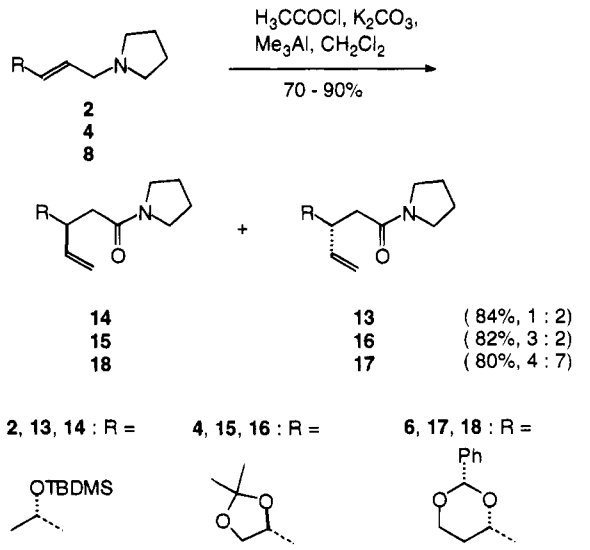
4a, **15a** : Enantiomer of **4**, **15**
R = -CH_3 , -CH_2OPG , -CH_2CH_2OPG

zwitterionic intermediate **12** (Figure 1) with minimal 1,3-diaxial interactions (Scheme 3).

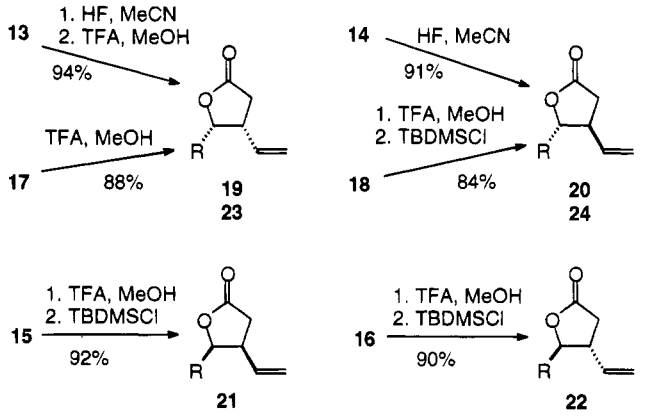
The relative stereochemistry of the γ,δ-unsaturated amides **13**–**18** could be confirmed after cyclization to the corresponding lactones **19**–**24**. Pyrrolidinamides **13** and **14** were desilylated with HF/acetonitrile,[28] the consecutive cyclization of amide **13** requiring a substantially longer reaction than that of **14**. The

(15) Hagemann, H. A. *Org. React. (N. Y.)* **1953**, *7*, 198.
(16) Olah, G. H.; Wu, A.-H.; Farooq, O. *Synthesis* **1989**, 568.
(17) Brady, W. T.; Vaughn, W. L.; Liddell, H. G. *J. Org. Chem.* **1966**, *31*, 626. Brady, W. T.; Owens, R. A. *Tetrahedron Lett.* **1976**, 1553.
(18) Valenti, E.; Pericas, M. A.; Serratosa, F.; Maha, D. *J. Chem. Res. Synop.* **1990**, 118.
(19) Brady, W. T.; Giang, Y.-F.; Marchand, A. P.; Wu, A.-H. *J. Org. Chem.* **1987**, *52*, 3457.
(20) Clemens, R. J.; Hyatt, J. A. *J. Org. Chem.* **1985**, *50*, 2431.
(21) In many experiments, the progress of the reaction stopped, leaving about 20–40% of the allylamine. In these cases, the reaction was worked up and the crude mixture was subjected to the reaction conditions again. The yield was determined after the workup of the second cycle.
(22) For a detailed discussion of the reaction mechanism, see ref 5b and the references cited therein.
(23) Cha, J. K.; Lewis, S. C. *Tetrahedron Lett.* **1984**, *25*, 5263.
(24) The direct comparison of these results with the high selections described by Bellus (ref 4) was impossible; the reaction of the allylamines with the bulky "dichloroketene" (dichloroacetyl chloride under the given conditions) afforded only the destruction of the material. Several disubstituted ketenes (e.g. dimethylketene and chloromethylketene) gave no reaction, whereas the thioallyl ethers did not react with the sterically nonhindered less activated ketene.
(25) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199.
(26) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. D.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880.
(27) Kahn, S. D.; Hehre, W. J. *J. Org. Chem.* **1988**, *53*, 301.
(28) Newton, R. F.; Reynolds, D. P.; Finch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, 3981.

Scheme 3

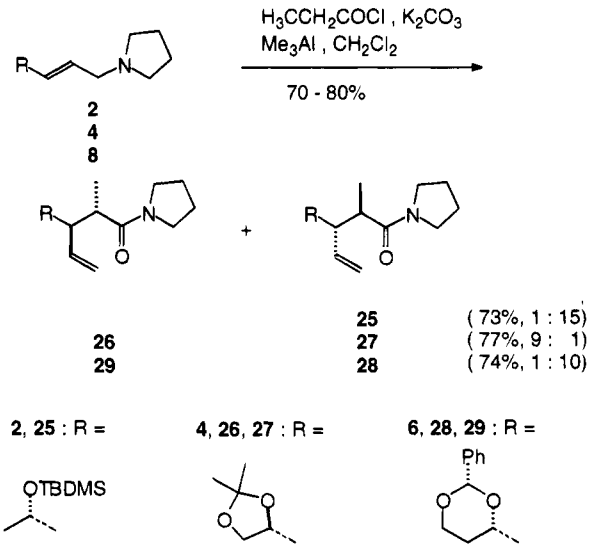


Scheme 4

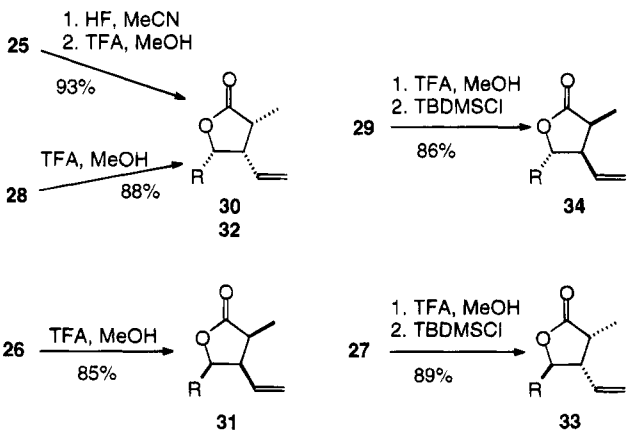


19 , **20** : R = H_3C- ; **21** , **22** : R = $TBDMSOCH_2$- ;
23 : R = $HOCH_2CH_2$- ; **24** : R = $TBDMSOCH_2CH_2$-

Scheme 5



Scheme 6



30 : R = H_3C- ; **31** : R = $HOCH_2$- ; **33** : R = $TBDMSOCH_2$- ;
33 : R = $HOCH_2CH_2$- ; **34** : R = $TBDMSOCH_2CH_2$- .

spectral data of the lactones **19** and **20** were identical to those published in the literature,[4,8] showing that the major rearrangement product **13** bears the expected *syn* stereochemistry.

The diol-protecting groups of the amides **15**–**18** were removed by treatment with TFA in methanol. Compounds **16** and **18** cyclized spontaneously, while the lactonization of **15** and **17** required longer reaction times and increased temperatures, respectively. The spectral data of the lactones **21** and **22** (each after protection of the hydroxyl group as the TBDMS ether) were identical to those published previously.[13] The relative stereochemistry of **23** and **24** (after protection of the hydroxyl group of **24** as the TBDMS ether) was determined via NOEDS analysis. Thus, in analogy with the experiment with amine **2**, the rearrangement of **4** and **8** generated preferentially the *syn* products **15** and **17** (Scheme 4).

The treatment of the allylpyrrolidines **2**, **4**, and **8** with propionyl chloride proceeded with substantially higher diastereoselection. In contrast to the relatively unselective formation of all stereoisomers with acetyl chloride, only one diastereomer was preferentially generated (Scheme 5).

Allylpyrrolidine **2** rearranged to the γ,δ-unsaturated amide **25** and a second product (diastereomer?, not isolated) in a 15:1 ratio (73% yield), **4** gave **26** and the minor diastereomer **27** (ratio, 9:1; 77% yield), and **8** afforded **28** and the minor diastereomer **29** (ratio, 10:1; 74% yield). The relative stereochemistry of the optically active carbon atoms of the major diastereomers could be assigned as *syn* after cyclization to the corresponding γ-butyrolactones **30**–**32** as described above. The spectral data of **30** were identical with those of the compound described by Bellus.[4,29] The stereochemistry of **31**–**34** was unequivocally proven via NOEDS experiments. The new optically active carbon atoms of the minor diastereomers **33** and **34** were assigned to be *syn*, but they are in a position *anti* to the initial chiral C–O bond (Scheme 6).

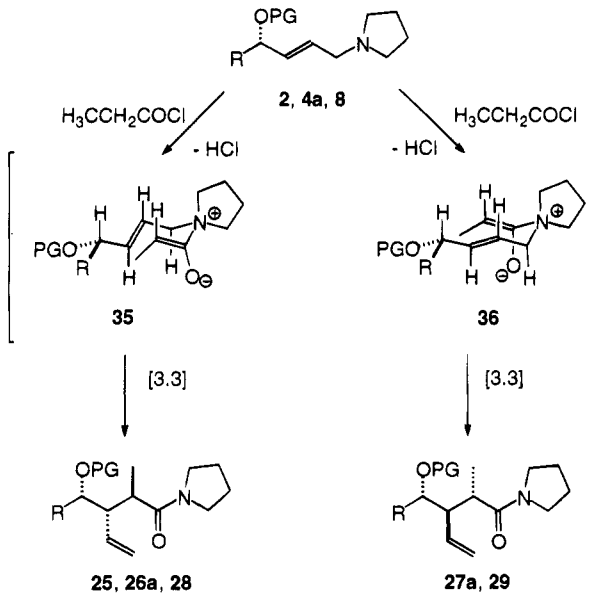
In view of these results and the observations made above for the rearrangement with acetyl chloride, the reaction with propionyl chloride should pass through the (hypothetical) intermediates **35** (major path) and **36** (minor path) characterized as follows.

(1) Minimal 1,3-diaxial interactions in a chairlike conformation.

(2) *Anti* arrangement of the ketene and the oxygen substituents leading to a high 1,2-asymmetric induction via **35**. In contrast to the acetyl chloride reaction, the

(29) Unpublished data of ref 4.

Scheme 7



4a, 26a, 27a : Enantiomer of **4, 26, 27**
R = -CH_3 , -CH_2OPG , -CH_2CH_2OPG

bulky methyl group of the propionyl chloride differentiates much more efficiently between the diastereotopic faces of the allylamine.[24,30] The corresponding *syn* arrangement via **36** is particularly less favored.

(3) Quasi equatorial position of the methyl group in **35** and **36** forming the (*Z*)-amide–enolate structure. Almost complete simple diastereoselection was observed even though the reaction was carried out at 0 °C (Scheme 7).

The zwitterionic Claisen rearrangement with allylamines is characterized by its mild reaction conditions. Neither the high reaction temperatures of the Johnson, Eschenmoser, and other amide enolate methods nor the superbases of the Ireland type process are necessary. Competing reactions such as the von Braun type substitution are largely suppressed, and excellent chemoselectivity was observed. In the experiments with acetyl chloride, only poor 1,2-asymmetric induction was operative, but the facile isolation and separation of the diastereomeric amides recommends this method for further synthetic investigation. The rearrangement with propionyl chloride allows for the generation of two new chiral centers in one step with high diastereomeric excess. All γ,δ-unsaturated amides were cyclized to the corresponding chiral γ-butyrolactones which represent key intermediates for numerous natural product syntheses.[8,13,31]

Experimental Section

For general experimental data, see ref 13. Coupling constants are given in hertz.

(30) Presumably, the bulkiness of the ketene substituent is the diastereoselection-determining factor; the reaction of thioallyl ethers and chloroketenes (ref 4) and the reaction of the allylamines with "methyl ketene" proceeded with high 1,2-asymmetric induction, whereas the rearrangement of the allylamines with "ketene" gave only poor diastereomeric excesses.

(31) Jefford, C. W.; Sledeski, A. W.; Boukouvalas, J. *Helv. Chim. Acta* **1989**, *72*, 1362. Koseki, K.; Ebata, T.; Kawakami, H.; Matsushita, H.; Naoi, Y.; Itoh, K. *Heterocycles* **1990**, *31*, 423.

(4*R*)-*N*-[4-[(*tert*-Butyldimethylsilyl)oxy]-2(*E*)-pentenyl]-pyrrolidine (2). Under argon, allylic alcohol **1** (7.5 g, 34.7 mmol) and PPh_3 (10.91 g, 41.6 mmol) were dissolved in dry acetonitrile (100 mL) and the solution was cooled to 0 °C. At this temperature, CBr_4 (13.8 g, 41.6 mmol) was added over a period of 15 min while the mixture was stirred. A pale yellow color occurred. After a further 40 min of stirring, the reaction was complete (TLC analysis). The solvent was evaporated, and most of the Ph_3PO was removed by filtration through a column of 10 cm of silica gel (EtOAc/hexane, 1:10).

Under argon, the crude allylic bromide was dissolved in dry Et_2O (90 mL) and the solution cooled to 0 °C. An excess of pyrrolidine (8.9 g, 10.4 mL, 125 mmol) was added while the mixture was stirred, and the mixture was allowed to warm to rt over 5 h. After completion of the reaction, 5% aqueous $NaHCO_3$ (80 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (5 × 30 mL), and the combined organic layers were dried ($MgSO_4$). After concentration, the residue was purified via Kugelrohr distillation (120 °C, 0.02 mm). Yield: 5.8 g (62%), light yellow liquid. $[\alpha]^{23}_D$: −6.3 (c = 1.9 in $CHCl_3$). IR (KBr, film): 1641, 1472, 1368, 1295 cm^{-1}. MS (EI, 70 eV, 40 °C): m/z 269 (M^+), 254 ($M^+ - CH_3$), 212, 198, 175, 147, 141, 138, 137, 110, 84, 75. HRMS (80 eV, 40 °C) (M^+) calcd 269.217 49, found 269.217 55. ^{1}H-NMR: δ 0.01 (2 s, 6 H), 0.84 (s, 9 H), 1.16 (d, J = 6.3, 3 H), 1.72 (m, br, 4 H), 2.44 (m, br, 4 H), 3.00 (t, br, J = 6, 2 H), 4.26 (m, br, 1 H), 5.6 (m, 2 H). ^{13}C-NMR: δ −4.9 (q), −4.7 (q), 18.1 (s), 23.3 (t), 24.4 (q), 25.8 (q), 53.8 (t), 57.8 (t), 68.8 (d), 126.1 (d), 137.1 (d).

(4*S*)-*N*-[4,5-(Isopropylidenedioxy)-2(*E*)-pentenyl]-pyrrolidine (4). Under argon, allylic alcohol **3** (10 g, 63.2 mmol) was dissolved in dry THF (100 mL) and the solution cooled to −70 °C. *n*-BuLi (25.3 mL, 63.2 mmol, 2.5 M in hexane) was added over a period of 30 min while the solution was stirred. After a further 60 min at −70 °C, a solution of *p*-toluenesulfonyl chloride (12.05 g, 63.2 mmol) in dry THF (50 mL) was added. The mixture was stored at about −22 °C overnight.

After completion of the tosylation and cooling to −70 °C, pyrrolidine (10.6 mL, 9 g, 0.13 mol) was added while the mixture was stirred. The temperature was allowed to rise to rt. After 3 d, the reaction was complete. Then, the reaction was quenched with H_2O (200 mL) and saturated aqueous $NaHCO_3$ (50 mL). The aqueous layer was extracted with ether (5 × 90 mL), and the combined organic layers were washed with brine (2 × 70 mL) and dried ($MgSO_4$). The solvent was removed, and the crude material was purified by distillation (0.01 mm, 78–82 °C). Yield: 9.7 g (73%). Alternatively, the reaction was carried out with the allylic alcohol **3** (21.7 g, 0.137 mol) in dry acetonitrile (400 mL) with the same conditions as described for allylic amine **2**. Yield: 22.6 g (78%). $[\alpha]^{23}_D$: 28.2 (c = 1.7 in $CHCl_3$). IR (KBr, film): 1459, 1379, 1369 cm^{-1}. MS (EI, 70 eV, 40 °C): m/z 211 (M^+), 196 ($M^+ - CH_3$), 153, 140, 136, 110, 84, 72. HRMS (80 eV, 40 °C) (M^+) calcd 211.157 23, found 211.157 15. ^{1}H-NMR: δ 1.40 (s, 3 H), 1.44 (s, 3 H), 1.84 (m, 4 H), 2.64 (m, 4 H), 3.22 (m, 2 H), 3.60 (t, J = 7.5, 2 H), 4.10 (dd, J = 6.3, J = 7.8, 1 H), 4.52 (q, br, J = 7.0, 1 H), 5.68 (dd, J = 7.5, J = 15, 1 H), 5.92 (td, J = 6.3, J = 15, 1 H). ^{13}C-NMR: δ 23.0 (t), 25.4 (q), 26.3 (q), 53.0 (t), 56.6 (t), 68.9 (t), 76.1 (d), 108.8 (s), 130.1 (d), 130.7 (d).

(1′*S*,4*S*)-4,6-(Benzylidenedioxy)-2(*E*)-hexenoic Acid Ethyl Ester (6). Swern Oxidation. Under Ar, a solution of oxalyl chloride (7.8 mL, 11.35 g, 89.4 mmol) in dry THF (400 mL) was cooled to −60 °C. Dry DMSO (6.35 mL, 7.0 g, 89.4 mmol) in dry THF (120 mL) was slowly injected while the mixture was stirred. The reaction temperature was maintained at −60 °C for 1 h, and then **5** (11.6 g, 59.6 mmol) in dry THF (120 mL) was added. After the mixture was stirred for 1 h at -60 °C, dry Et_3N (31 mL, 22.6 g, 224 mmol) was injected slowly and a white precipitate of Et_3N/HCl formed. After being stirred for 1 h at −60 °C, the mixture was allowed to warm to rt. TLC monitoring indicated the completion of the oxidation after about 90 min. The mixture was then cooled to −70 °C.

Horner Reaction. Under Ar, to a slurry of NaH (7.2 g, 300 mmol) in dry THF (140 mL) was slowly added triethyl phosphonoacetate (60 mL, 67.2 g, 300 mmol) while the mixture

was stirred at 0 °C. The deprotonation was completed by stirring the mixture at rt for 2 h. The Horner reagent was then added to the aldehyde generated in situ at −70 °C while the mixture was stirred. The reaction mixture was allowed to warm to rt overnight. Cold H_2O (700 mL, 0 °C) was added after the mixture was cooled to 0 °C. The aqueous layer was extracted with Et_2O (5 × 150 mL). The combined organic layers were washed with brine (3 × 150 mL) and dried ($MgSO_4$). Evaporation of the solvent and chromatographic purification of the crude material on silica gel (EtOAc/hexane, 1:5, R_f = 0.2) gave 12.2 g (78%) of **6** (white needles), mp 67–68 °C. $[\alpha]^{23}_D$: −26.0 (c = 1.5 in $CHCl_3$). IR (KBr): 3034, 1722 (CO), 1688, 1469, 1451 cm^{-1}. MS (EI, 80 eV, 100 °C): m/z 262 (M^+), 218, 149, 140, 134, 125, 111. ^{1}H-NMR: δ 1.29 (t, J = 6.7, 3 H), 1.68 (d, br, J = 11.5, 1 H), 1.94 (dq, J = 5.0, J = 11.5, 1 H), 4.00 (dt, J = 2.0, J = 11.5, 1 H), 4.20 (q, J = 6.7, 2 H), 4.30 (dd, br, J = 5.0, J = 11.5, 1 H), 4.54 (d, br, J = 11.5, 1 H), 5.59 (s, 1 H), 6.14 (dd, J = 2, J = 15.7, 1 H), 6.94 (dd, J = 4.5, J = 15.7, 1 H), 7.37 (m, 3H), 7.52 (m, 2 H). ^{13}C-NMR: δ 14.0 (q), 30.5 (t), 60.3 (t), 66.6 (t), 75.1 (d), 100.9 (d), 120.5 (d), 125.9 (d), 128.0 (d), 128.7 (d), 138.1 (s), 145.8 (d), 166.2 (s). Anal. Calcd: C, 68.69; H, 6.92. Found: C, 68.65; H, 6.90.

(1′*S*,4*S*)-4,6-(Benzylidenedioxy)-2(*E*)-hexen-1-ol (7). Under Ar, the α,β-unsaturated ester **6** (10 g, 38.1 mmol) was dissolved in dry THF (150 mL) and the solution cooled to −70 °C. DIBALH (105 mL, 126 mmol, 1.2 M in toluene) was added while the mixture was stirred (KPG), and the temperature was maintained below −25 °C. After 6 h, the reaction was found to be complete. MeOH (8.4 mL) and 1 N aqueous NaOH (16.8 mL) were added consecutively while the mixture was cooled (ice bath) and vigorously stirred. When the exothermic sovolysis of the alumina compounds was finished, 30% aqueous potassium/sodium tatrate (39 mL) was added, and the resulting mixture was stirred until the Al_2O_3 precipitated. The organic layer was decanted, and the residue was extracted with ether (5 x 50 mL). The combined organic layers were washed with brine (2 × 50 mL) and dried ($MgSO_4$). The solvents were removed, and the crude material was purified via column chromatography (EtOAc/hexane, 1:1, R_f = 0.25). Yield: 7.7 g (91%). $[\alpha]^{23}_D$: 10.5 (c = 2.3 in $CHCl_3$). IR (KBr, film): 3418, br, (OH), 3034, 3010, 1496, 1454 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 220 (M^+), 219 (M^+ − H), 163, 149, 134, 105, 97. ^{1}H-NMR: δ 1.52 (d, br, J = 11.6, 1 H), 1.89 (dq, J = 5, J = 11.6, 1 H), 3.12 (s, br, 1 H, OH), 3.92 (dt, J = 2.5, J = 11.6, 1 H), 4.02 (m, br, 2 H), 4.24 (dd, br, J = 3.8, J = 11.6, 1 H), 4.33 (d, br, J = 11.6, 1 H), 5.52 (s, 1 H), 5.73 (dd, br, J = 5.0, J = 16.3, 1 H), 5.86 (td, J = 4.5, J = 16.3, 1 H), 7.35 (m, 3 H), 7.55 (m, 2 H). ^{13}C-NMR: δ 31.0 (t), 62.2 (t), 66.6 (t), 76.6 (d), 100.9 (d), 125.9 (d), 128.0 (d), 128.6 (d), 130.1 (d), 130.7 (d), 138.3 (s). Anal. Calcd: C, 70.89; H, 7.32. Found: C, 70.85; H, 7.29.

(1′*S*,4*S*)-*N*-[4,6-(Benzylidenedioxy)-2(*E*)-hexenyl]-pyrrolidine (8). Under argon, the allylic alcohol **7** (7 g, 31.8 mmol) and PPh_3 (9.2 g, 35 mmol) were dissolved in dry CCl_4 (180 mL), and the solution was heated to 80 °C. After about 10 h, the reaction was complete. The solvent was removed, and the residue was filtered through a column of 15 cm silica gel (elution with EtOAc/hexane, 1:5). The resulting colorless oil was dissolved in dry ether (200 mL) and treated with pyrrolidine (8 mL, 6.8 g, 95.3 mmol). After the mixture was stirred at rt for 3 d, the reaction was found to be complete. Aqueous $NaHCO_3$ (5%, 150 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (6 × 50 mL). The combined organic layers were dried ($MgSO_4$), and after evaporation of the solvent, the crude brown material was purified via chromatography on silica gel (EtOAc, R_f = 0.13). Yield: 6.9 g (79%). $[\alpha]^{23}_D$: 8.1 (c = 1.9 in $CHCl_3$). IR (KBr, film): 3065, 3034, 1643, 1454, 1399, 1373 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 273 (M^+), 202, 196, 166, 152, 139, 136, 123, 110, 105, 96, 84, 71. HRMS (80 eV, 100 °C) (M^+) calcd 273.172 88, found 273.172 93. ^{1}H-NMR: δ 1.56 (m, 1 H), 1.79 (m, 4 H), 1.92 (m, 1 H), 2.50 (m, 4 H), 3.11 (d, J = 6.3, 2 H), 3.96 (dt, J = 2.5, J = 12.3, 1 H), 4.24 (m, 1 H), 4.35 (m, 1 H), 5.56 (s, 1 H), 5.73 (dd, br, J = 5.5, J = 16.3, 1 H), 5.88 (dtd, J = 1, J = 6.2, J = 16.3, 1 H), 7.34 (m, 3 H), 7.52 (m, 2 H). ^{13}C-NMR: δ 23.1 (t), 31.1 (t), 53.7 (t), 57.5 (t), 66.5 (t), 76.7 (d), 100.8 (s), 125.8 (d), 127.8 (d), 128.4 (d), 129.1 (d), 131.7 (d), 138.4 (s).

Standard Procedure for the Zwitterionic Claisen Rearrangement. Under argon, dry K_2CO_3 (1.6 g, 11.6 mmol) was suspended in dry CH_2Cl_2 (35 mL) and the mixture cooled to 0 °C. *N*-Allylpyrrolidine (5 mmol) and acetyl chloride (0.43 mL, 471 mg, 6 mmol) were added subsequently by means of a syringe. After about 30 min of stirring at 0 °C, a solution of Me_3Al (0.25 mL, 0.51 mmol, 2 M in toluene) was added via syringe. The mixture was stirred at 0 °C. After 24 h, a second volume of Me_3Al was injected. After 2–3 d, the reaction was stopped by quenching it with saturated aqueous $NaHCO_3$ (50 mL) at 0 °C. The mixture was vigorously stirred until the layers separated clearly. Then, the aqueous layer was extracted with CH_2Cl_2 (5 × 20 mL), and the combined organic layers were dried ($MgSO_4$). The solvent was removed, and the crude mixture of diastereomeric amides was purified by column chromatography. The diastereomers were separated via HPLC or column chromatography on silica gel.

If the crude product contained more than 10% allylic amine (occurred in the majority of the experiments), the mixture was subjected to these reaction conditions for a second cycle.

***N*-(3*R*,4*S*)-3-Ethenyl-4-[(*tert*-butyldimethylsilyl)oxy]-pentanoyl]pyrrolidine (13) and *N*-[(3*S*,4*S*)-3-Ethenyl-4-[(*tert*-butyldimethylsilyl)oxy]pentanoyl]pyrrolidine (14).** Reaction with allylamine **2** (750 mg, 2.8 mmol) following the standard procedure. Chromatography: EtOAc/hexane, 1:1, R_f = 0.27 (**13** and **14**). Yield: 733 mg (84%). Separation of the diastereomeric amides **13** and **14** (ratio, 2:1) via preparative HPLC: eluent, 2% 2-propanol in hexane. Major diastereomer amide **13**: retention time, 4.11 min; 495 mg (56.8%). $[\alpha]^{23}_D$: −9.7 (c = 1.7 in $CHCl_3$). IR (KBr, film): 3075, 1647 (CO), 1430 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 311 (M^+), 296 (M^+ − CH_3), 267, 254, 210, 159, 153, 113, 98, 73. HRMS (EI, 80 eV, 60 °C) calcd 311.228 06, found 311.228 13. ^{1}H-NMR: δ 0.02 (2 s, 6 H), 0.82 (s, 9 H), 1,00 (d, J = 5.8, 3 H), 1.79 (m, 4 H), 2,24 (dd, J = 8.3, J = 15, 1 H), 2.37 (dd, J = 6.3, J = 15, 1 H), 2.58 (m, 1 H), 3.35 (m, 4 H), 3.88 (dq, J = 2.5, J = 5.8, 1 H), 4.98 (d, br, J = 8.8, 1 H), 5.00 (d, br, J = 17.5, 1 H), 5.71 (td, J = 8.8, J = 17.5, 1 H). ^{13}C-NMR: δ −5.2 (q), −4.4 (q), 17.8 (s), 21.2 (q), 24.2 (t), 25.7 (q), 25.9 (t), 36.3 (t), 45.3 (t), 46.4 (t), 47.3 (d), 69.8 (d), 116.5 (t), 137.3 (d), 170.3 (s). Minor diastereomer amide **14**: retention time, 4.72 min; 237 mg (27.1%). $[\alpha]^{23}_D$: 10.0 (c = 1.3 in $CHCl_3$). IR (KBr, film): 3078, 1647 (CO), 1429 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 311 (M^+), 296 (M^+ − CH_3), 267, 254, 210, 159, 153, 113, 98, 75, 73. HRMS (EI, 80 eV, 60 °C) calcd 311.228 06, found 311.228 09. ^{1}H-NMR: δ 0.02 (s, 6 H), 0.86 (s, 9 H), 1.08 (d, J = 6.3, 3 H), 1.84 (m, 4 H), 2.23 (dd, J = 8.8, J = 15, 1 H), 2.50 (dd, J = 4.5, J = 15, 1 H), 2.60 (m, 1 H), 3.40 (m, 4 H), 3.77 (qi, br, J = 6.3, 1 H), 4.98 (d, br, J = 10.3, 1 H), 5.00 (d, br, J = 17.5, 1 H), 5.74 (ddd, J = 8.2, J = 10.3, J = 17.5, 1 H). ^{13}C-NMR: δ −4.9 (q), −4.4 (q), 17.9 (s), 21.3 (q), 24.3 (t), 25.8 (q), 26.0 (t), 34.8 (t), 45.4 (t), 46.6 (t), 47.8 (d), 70.5 (d), 115.8 (t), 139.1 (d), 170.7 (s).

***N*-[(3*S*,4*S*)-3-Ethenyl-4,5-(isopropylidenedioxy)-pentanoyl]pyrrolidine (15) and *N*-[(3*R*,4*S*)-3-Ethenyl-4,5-(isopropylidenedioxy)pentanoyl]pyrrolidine (16).** Reaction with allylamine **4** (5.0 g, 23.66 mmol) following the standard procedure. Chromatography: EtOAc, R_f = 0.17 (**15**) and R_f = 0.19 (**16**). Yield: 4.94 g (82.4%). Separation of the diastereomeric amides **15** and **16** (ratio, 3:2) via preparative HPLC: eluent, 20% 2-propanol in hexane. Major diastereomer amide **15**: retention time, 2.14 min; 3.0 g (50.0%). $[\alpha]^{23}_D$: 3.0 (c = 2.0 in $CHCl_3$). IR (KBr, film): 3076, 1639 (CO), 1437, 1379, 1369, 1342 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 253 (M^+), 238 (M^+ − CH_3), 195, 182, 160, 152, 113, 98, 70. HRMS (80 eV, 60 °C) (M^+) calcd 253.167 79, found 253.167 72. ^{1}H-NMR: δ 1.36 (s, 3 H), 1.46 (s, 3 H), 1.90 (m, 4 H), 2.40 (dd, J = 7.6, J = 15.1, 1 H), 2.52 (dd, J = 6.3, J = 15.1, 1 H), 2.88 (m, 1 H), 3.46 (m, 4 H), 3.68 (t, br, J = 6.8, 1 H), 4.00 (dd, J = 6.6, J = 7.0, 1 H), 4.23 (dt, J = 3.9, J = 6.6, 1 H), 5.16 (m, 2 H), 5.82 (ddd, J = 8.8, J = 9.7, J = 18.1, 1 H). ^{13}C-NMR: δ 24.0 (t), 24.8 (q), 25.7 (t), 25.9 (q), 36.3 (t), 42.1 (d), 45.3 (t), 46.4 (t), 66.6 (t), 76.9 (d), 108.5 (s), 117.2 (t), 136.0 (d), 169.5 (s). Minor diastereomer amide **16**: retention time, 1.81 min; 1.96 g (32.4%). $[\alpha]^{23}_D$: −4.6 (c = 1.8 in $CHCl_3$). IR (KBr, film): 3078, 1640 (CO), 1432 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 253 (M^+), 238 (M^+ − CH_3), 195, 182, 153, 113, 101, 98,

70. HRMS (80 eV, 60 °C) (M^+) calcd 253.167 79, found 253.167 96. ^{1}H-NMR: δ 1.36 (s, 3 H), 1.42 (s, 3 H), 1.90 (m, 4 H), 2.36 (dd, J = 9.1, J = 15.1, 1 H), 2.66 (dd, J = 4.2, J = 15.1, 1 H), 2.82 (m, 1 H), 3.44 (m, 4 H), 3.70 (dd, br, J = 6.5, J = 7.6, 1 H), 4.00 (q, J = 6.5, 1 H), 4.08 (dd, J = 6.5, J = 7.6, 1 H), 5.04 (d, J = 10.6, 1 H), 5.16 (d, J = 17.6, 1 H), 5.72 (ddd, J = 8.5, J = 10.6, J = 17.6, 1 H). ^{13}C-NMR: δ 24.3 (t), 25.4 (q), 26.0 (t), 26.6 (q), 36.2 (t), 44.1 (d), 45.5 (t), 46.6 (t), 68.0 (t), 77.6 (d), 109.1 (s), 117.1 (t), 137.4 (d), 170.0 (s).

N-[(1′S,3R,4S)-4,6-(Benzylidenedioxy)-3-ethenylhexanoyl]pyrrolidine (17) and N-[(1′S,3S,4S)-4,6-(Benzylidenedioxy)-3-ethenylhexanoyl]pyrrolidine (18). Reaction with allylamine **8** (2.0 g, 7.32 mmol) following the standard procedure. Chromatography: EtOAc, R_f = 0.22 (**17**) and R_f = 0.24 (**18**). Yield: 1.84 g (79.7%). Separation of the diastereomeric amides **17** and **18** (ratio, 7:4) via preparative HPLC: eluent, 10% 2-propanol in hexane. Major diastereomer amide **17**: retention time, 3.15 min; 1.17 g (50.7%). $[\alpha]^{23}_D$: 1.9 (c = 1.6 in $CHCl_3$). IR (KBr, film): 3070, 3034, 1637 (CO), 1451, 1432, 1396, 1361 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 315 (M^+), 314, 268, 238, 209, 180, 163, 152, 139, 113, 107, 105, 98, 91, 79, 70. ^{1}H-NMR: δ 1.32 (d, br, J = 12.5, 1 H), 1.78 (m, 4 H), 1.89 (m, 1 H), 2.28 (dd, J = 6.2, J = 15, 1 H), 2.61 (dd, J = 7.5, J = 15, 1 H), 2.84 (m, 1 H), 3.35 (m, 4 H), 3.87 (dt, J = 2.5, J = 11.2, 1 H), 3.94 (td, J = 2.0, J = 11.2, 1 H), 4.16 (dd, br, J = 5.0, J = 11.2, 1 H), 5.05 (d, br, J = 10.0, 1 H), 5.09 (d, br, J = 17.0, 1 H), 5.40 (s, 1 H), 5.85 (ddd, J = 8.7, J = 10.0, J = 17.0, 1 H), 7.28 (m, 3 H), 7.40 (m, 2 H). ^{13}C-NMR: δ 24.1 (t), 25.8 (t), 28.3 (t), 35.7 (t), 44.8 (t), 45.3 (d), 46.4 (t), 66.7 (t), 77.8 (d), 100.9 (s), 117.0 (t), 125.8 (d), 127.9 (d), 128.4 (d), 137.0 (d), 138.8 (s), 170.0 (s). Anal. Calcd: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.40; H, 8.02; N, 4.50. Minor diastereomer **18**: retention time, 2.96 min; 669 mg (29.0%). $[\alpha]^{23}_D$: 22.8 (c = 1.5 in $CHCl_3$). IR (KBr, film): 3070, 3034, 2971, 2928, 2871, 1636 (CO), 1451, 1433, 1364, 1241, 1128, 1102, 1026, 995, 915, 755, 700 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 315 (M^+), 314, 254, 209, 180, 163, 152, 138, 113, 107, 105, 98, 91, 79, 70. ^{1}H-NMR: δ 1.54 (d, br, J = 13.7, 1 H), 1.74 (m, 5 H), 2.33 (dd, J = 8.0, J = 15.0, 1 H), 2.62 (dd, J = 5.0, J = 15.0, 1 H), 2.82 (m, 1 H), 3.33 (m, 4 H), 3.79 (m, 1 H), 3.88 (dt, J = 2.5, J = 11.3, 1 H), 4.20 (dd, br, J = 4.5, J = 11.3, 1 H), 5.07 (d, br, J = 10.0, 1 H), 5.14 (d, br, J = 17.5, 1 H), 5.44 (s, 1 H), 5.78 (ddd, J = 8.8, J = 10.0, J = 17.5, 1 H), 7.31 (m, 3 H), 7.42 (m, 2 H). ^{13}C-NMR: δ 24.1 (t), 25.8 (t), 29.3 (t), 35.2 (t), 45.3 (t), 45.6 (d), 46.5 (t), 66.9 (t), 78.5 (d), 101.1 (s), 116.9 (t), 125.9 (d), 127.9 (d), 128.5 (d), 137.5 (d), 138.7 (s), 170.2 (s). Anal. Calcd: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.43; H, 8.04; N, 4.51.

(4R,5S)-4-Ethenyl-5-methyl-2(3H)-furanone (19). The pyrrolidine amide **13** (500 mg, 1.6 mmol) was dissolved in acetonitrile (45 mL) and 48% aqueous HF (3 mL). The mixture was stirred at rt until the deprotection of the hydroxyl goup is found to be complete (about 8 h). Then, the mixture was treated with ice and neutralized with solid $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (5 × 10 mL), the combined organic layers were dried ($MgSO_4$), and the solvent was removed. The residue (slight yellow liquid) was taken up in MeOH (5 mL) and treated with TFA (2 mL). After the mixture was refluxed for 2 d, the reaction was found to be complete. The solvent was evaporated, and the crude material was purified by chromatography on silica gel (EtOAc/hexane, 1:5, R_f = 0.17). Yield: 190 mg (94.1%). The spectral data are listed because they are not yet completely published.[4,8] $[\alpha]^{23}_D$: −51.4 (c = 1.6 in $CHCl_3$) (lit.[4,8] −54.3, $CHCl_3$). IR (KBr, film): 3083, 1777 (CO), 1643 cm^{-1}. MS (EI, 70 eV, 30 °C): m/z 126 (M^+), 111 ($M^+ - CH_3$), 98, 82, 67, 54. HRMS (EI, 80 eV, 30 °C) calcd 126.068 08, found 126.068 12. ^{1}H-NMR: δ 1.21 (d, J = 6.5, 3 H), 2.42 (dd, J = 6.3, J = 17.5, 1 H), 2.62 (dd, J = 8.0, J = 17.5, 1 H), 3.15 (qi, br, J = 7.5, 1 H), 4.67 (qi, J = 6.5, 1 H), 5.12 (dd, J = 1.2, J = 17.0, 1 H), 5.17 (dd, J = 1.2, J = 10.4, 1 H), 5.72 (ddd, J = 8.2, J = 10.4, J = 17.0, 1 H). ^{13}C-NMR: δ 16.1 (q), 33.7 (t), 43.1 (d), 78.9 (d), 118.0 (t), 133.8 (d), 176.0 (s).

(4S,5S)-4-Ethenyl-5-methyl-2(3H)-furanone (20). The pyrrolidine amide **14** (300 mg, 0.96 mmol) was dissolved in acetonitrile (27 mL) and 48% aqueous HF (1.8 mL). The mixture was stirred at rt until the deprotection of the hydroxyl goup and the consecutive cyclization are found to be complete (about 16 h). Then, the mixture was treated with ice and neutralized with solid $NaHCO_3$. After dilution with H_2O (20 mL), the aqueous layer was extracted with CH_2Cl_2 (5 × 15 mL), the combined organic layers were dried ($MgSO_4$), and the solvent was removed. The residue was purified via chromatography on silica gel (EtOAc/hexane, 1:5, R_f = 0.22). Yield: 111 mg (91.6%). The spectral data are listed because they are not yet completely published.[8] $[\alpha]^{23}_D$: −73.2 (c = 1.4 in $CHCl_3$) (lit.[8] −75.9, $CHCl_3$). IR (KBr, film): 3084, 1786 (CO), 1645, 1446 cm^{-1}. MS (EI, 70 eV, 30 °C): m/z 126 (M^+), 111 ($M^+ - CH_3$), 98, 82, 67, 54. HRMS (EI, 80 eV, 30 °C) calcd 126.068 08, found 126.068 01. ^{1}H-NMR: δ 1.35 (d, J = 6.5, 3 H), 2.43 (dd, J = 6.5, J = 12.5, 1 H), 2.61 (dd, J = 7.5, J = 12.5, 1 H), 2.66 (qi, br, J = 7.0, 1 H), 4.20 (dq, J = 6.5, J = 7.0, 1 H), 5.10 (d, J = 10.0, 1 H), 5.14 (d, J = 17.5, 1 H), 5.67 (ddd, J = 7.5, J = 10.0, J = 17.5, 1 H). ^{13}C-NMR: δ 18.4 (q), 35.3 (t), 48.0 (d), 80.6 (d), 117.9 (t), 135.0 (d), 175.4 (s).

(4S,5S)-5-[[(tert-Butyldimethylsilyl)oxy]methyl]-4-ethenyl-2(3H)-furanone (21). The amide **15** (150 mg, 0.59 mmol) was dissolved in methanol (5 mL). TFA (1 mL) was added. The mixture was stirred at 60 °C (about 16 h) until the reaction was found to be complete. Then, the solvent was removed, and the crude material was vacuum-dried. The hydroxyl actone was dissolved in dry CH_2Cl_2 (8 mL) and the solution subsequently treated with imidazole (121 mg, 1.78 mmol) and TBDMSCl (187 mg, 1.24 mmol). After the mixture was stirred for 6 h at rt, the reaction was completed. The reaction was quenched with H_2O (25 mL), and the aqueous layer was extracted with CH_2Cl_2 (5 × 10 mL). The combined organic layers were dried ($MgSO_4$). After concentration, the residue was purified via chromatography on silica gel (EtOAc/hexane, 1:10, R_f = 0.14). Yield: 140 mg (92.5%). For detailed spectral data, see ref 13.

(4R,5S)-5-[[(tert-Butyldimethylsilyl)oxy]methyl]-4-ethenyl-2(3H)-furanone (22). Reaction with amide **16** (160 mg, 0.63 mmol) using conditions as described for lactone **21**; stirring at rt! Chromatography: EtOAc/hexane, 1:10, R_f = 0.18. Yield: 146 mg (89.8%). For detailed spectral data, see ref 13.

(4S,5S)-4-Ethenyl-5-(2-hydroxyethyl)-2(3H)-furanone (23). The amide **17** (180 mg, 0.57 mmol) was dissolved in methanol (5 mL). TFA (1.5 mL) was added. The mixture was stirred at 60 °C (about 36 h) until the reaction was found to be complete. Then, the solvent was removed, and the crude material was vacuum-dried. The residue was purified via chromatography on silica gel (EtOAc/hexane, 1:1, R_f = 0.11). Yield: 79 mg (88.6%). $[\alpha]^{23}_D$: −77.5 (c = 1.1 in $CHCl_3$). IR (KBr, film): 3420 (OH), 3083, 1776 (CO), 1641, 1420 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 156 (M^+), 138, 127, 111, 100, 82, 73, 54. HRMS (EI, 80 eV, 100 °C) calcd 156.078 65, found 156.078 75. ^{1}H-NMR: δ 1.74 (q, br, J = 6.5, 2 H), 2.39 (dd, J = 5.5, J = 17, 1 H), 2.70 (dd, J = 8.0, J = 17, 1 H), 2.70 (s, br, 1 H, OH), 3.16 (m, 1 H), 3.72 (t, br, J = 6.5, 2 H), 4.72 (q, br, J = 6.5, 1 H), 5.11 (d, br, J = 17, 1 H), 5.15 (d, br, J = 10.5, 1 H), 5.71 (ddd, J = 8.5, J = 10.5, J = 17, 1 H). ^{13}C-NMR: δ 33.5 (t), 34.3 (t), 42.7 (d), 58.9 (t), 80.2 (d), 118.2 (t), 133.7 (d), 176.3 (s).

(4R,5S)-5-[2-[(tert-Butyldimethylsilyl)oxy]ethyl]-4-ethenyl-2(3H)-furanone (24). Reaction with amide **18** (120 mg, 0.38 mmol) using conditions as described for lactone **21**; stirring at rt! Chromatography: EtOAc/hexane, 1:10, R_f = 0.17. Yield: 86 mg (83.7%). $[\alpha]^{23}_D$: −56.5 (c = 1.3 in $CHCl_3$). IR (KBr, film): 3084, 1784 (CO), 1644 cm^{-1}. MS (EI, 80 eV, 70 °C): m/z 270 (M^+), 255 ($M^+ - CH_3$), 225, 213, 183, 171, 139, 131, 101, 75. HRMS (EI, 80 eV, 70 °C) calcd 270.165 12, found 270.165 23. ^{1}H-NMR: δ 0.03 (s, 6 H), 0.87 (s, 9 H), 1.76 (m, 1 H), 1.89 (m, 1 H), 2.42 (dd, J = 10.5, J = 17.0, 1 H), 2.65 (dd, J = 8.3, J = 17.0, 1 H), 2.81 (m, 1 H), 3.72 (m, 2 H), 4.31 (dt, J = 3.0, J = 8.7, 1 H), 5.12 (d, J = 10.0, 1 H), 5.16 (d, J = 17.5, 1 H), 5.70 (ddd, J = 7.8, J = 10.0, J = 17.5, 1 H). ^{13}C-NMR: δ −5.5 (q), 18.1 (s), 25.8 (q), 35.3 (t), 36.7 (t), 46.1 (d), 59.1 (t), 81.3 (d), 117.9 (t), 135.4 (d), 175.6 (s).

N-[(2R,3S,4S)-4-[(tert-Butyldimethylsilyl)oxy]-3-ethenyl-2-methylpentanoyl]pyrrolidine (25). Reaction

with allylamine **2** (1.0 g, 3.71 mmol) and propionyl chloride (0.42 mL, 445 mg, 4.81 mmol) following the standard procedure. Chromatography: EtOAc/hexane 1:1, R_f = 0.25. Yield: 883 mg (73.1%). $[\alpha]^{23}_D$: −46.6 (c = 1.7 in $CHCl_3$). IR (KBr, film): 3075, 1645 (CO), 1459 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 325 (M^+), 310 ($M^+ - CH_3$), 268, 224, 199, 166, 159, 127, 115, 98, 73. HRMS (EI, 80 eV, 60 °C) (M^+) calcd 325.243 71, found 325.243 70. ^{1}H-NMR: δ 0.01 (s, 6 H), 0.82 (s, 9 H), 1,00 (d, J = 5.5, 3 H), 1.08 (d, J = 6.3, 3 H), 1.77 (m, 4 H), 2.08 (dt, J = 2.7, J = 9.3, 1 H), 2.76 (qd, J = 6.3, J = 9.3, 1 H), 3.33 (m, 4 H), 4.02 (dq, J = 2.0, J = 5.5, 1 H), 4.94 (d, J = 9.3, 1 H), 4.96 (d, J = 17.5, 1 H), 5.68 (td, J = 9.3, J = 17.5, 1 H). ^{13}C-NMR: δ −5.2 (q), −3.8 (q), 14.7 (q), 17.9 (s), 22.2 (q), 24.2 (t), 25.7 (q), 25.8 (t), 38.9 (d), 45.4 (t), 46.6 (t), 54.4 (d), 66.2 (d), 118.0 (t), 135.2 (d), 175.0 (s).

***N*-[(2*S*,3*R*,4*S*)-3-Ethenyl-4,5-(isopropylidenedioxy)-2-methylpentanoyl]pyrrolidine (26) and *N*-[(2*R*,3*S*,4*S*)-3-Ethenyl-4,5-(isopropylidenedioxy)-2-methylpentanoyl]-pyrrolidine (27).** Reaction with allylamine **2** (3.45 g, 16.33 mmol) and propionyl chloride (1.71 mL, 1.81 g, 19.59 mmol) following the standard procedure. Chromatography: EtOAc, R_f = 0.25 (**26**) and R_f = 0.39 (**27**). Yield: 3.37 g (77.3%). Major diastereomer **26**. Yield: 3.03 g (69.4%). $[\alpha]^{23}_D$: 54.3 (c = 2.1 in $CHCl_3$). IR (KBr, film): 3076, 1640 (CO), 1456, 1434 cm^{-1}. MS (EI, 80 eV, 60 °C): m/z 267 (M^+), 252 ($M^+ - CH_3$), 209, 194, 166, 152, 127, 98, 70. HRMS (70 eV, 60 °C) (M^+) calcd 267.183 44, found 267.183 39. ^{1}H-NMR: δ 1.09 (d, J = 6.3, 3 H), 1.23 (s, 3 H), 1.28 (s, 3 H), 1.76 (m, 4 H), 2.30 (dt, br, J = 2.0, J = 8.8, 1 H), 2.70 (qd, br, J = 6.3, J = 10.0, 1 H), 3.31 (m, 4 H), 3.52 (t, J = 7.5, 1 H), 3.84 (dd, J = 7.0, J = 7.5, 1 H), 4.17 (dt, br, J = 7.0, J = 7.5, 1 H), 4.98 (d, J = 16.5, 1 H), 5.00 (d, J = 10.0, 1 H), 5.66 (td, J = 10.0, J = 16.5, 1 H). ^{13}C-NMR: δ 14.7 (q), 24.1 (t), 24.9 (q), 25.8 (t), 25.9 (q), 39.6 (d), 45.3 (t), 46.4 (t), 48.3 (d), 66.8 (t), 73.6 (d), 108.4 (s), 118.5 (t), 134.5 (d), 173.8 (s). Minor diastereomer **27**. Yield: 337 mg (7.7%). $[\alpha]^{23}_D$: −27.1 (c = 1.5 in $CHCl_3$). IR (KBr, film): 3073, 1640 (CO), 1461, 1431 cm^{-1}. MS (EI, 70 eV, 50 °C): m/z 267 (M^+), 252 ($M^+ - CH_3$), 209, 192, 166, 152, 127, 101, 98, 70. HRMS (EI, 80 eV, 50 °C) (M^+) calcd 267.183 44, found 267.183 65. ^{1}H-NMR: δ 0.98 (d, J = 7.5, 3 H), 1.18 (s, 3 H), 1.27 (s, 3 H), 1.78 (m, 4 H), 2.09 (dt, J = 5.0, J = 10.0, 1 H), 2.94 (dq, J = 5.5, J = 7.5, 1 H), 3.34 (m, 4 H), 3.42 (t, J = 7.5, 1 H), 3.67 (m, 1 H), 3.76 (m, 1 H), 3.84 (m, 1 H), 4.92 (dd, J = 2, J = 17.0, 1 H), 4.96 (dd, J = 2.0, J = 10.0, 1 H), 5.88 (td, J = 10.0, J = 17.0, 1 H). ^{13}C-NMR: δ 15.9 (q), 24.2 (t), 25.5 (q), 25.9 (t), 26.7 (q), 37.6 (d), 45.3 (t), 46.4 (t), 52.8 (d), 68.5 (t), 76.0 (d), 108.7 (s), 112.8 (t), 135.0 (d), 173.4 (s).

(1′*S*,2*R*,3*S*,4*S*)-4,6-(Benzylidenedioxy)-3-ethenyl-2-methylhexanoyl]pyrrolidine (28) and *N*-[(1′*S*,2*S*,3*R*,4*S*)-4,6-(Benzylidenedioxy)-3-ethenyl-2-methylhexanoyl]-pyrrolidine (29). Reaction with allylamine **3** (2.0 g, 7.32 mmol) and propionyl chloride (0.83 mL, 880 mg, 9.51 mmol) following the standard procedure. Chromatography: EtOAc, R_f = 0.28 (**28**) and R_f = 0.45 (**29**). Yield: 1.79 g (74.2%). Major diastereomer **28**. Yield: 1.63 g (67.6%). $[\alpha]^{23}_D$: −57.4 (c = 1.6 in $CHCl_3$). IR (KBr, film): 3071, 3034, 1636 (CO), 1455, 1434 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 329 (M^+), 252, 223, 194, 166, 152, 127, 107, 105, 98, 70. HRMS (EI, 80 eV, 100 °C) (M^+) calcd 329.199 09, found 329.199 36. ^{1}H-NMR: δ 1.20 (d, J = 6.3, 3 H), 1.26 (m, 1 H), 1.82 (m, 4 H), 2.04 (m, 1 H), 2.47 (dt, J = 2.0, J = 9.0, 1 H), 2.94 (qd, J = 6.3, J = 9.0, 1 H), 3.42 (m, 4 H), 3.98 (dt, J = 2.0, J = 11.5, 1 H), 4.12 (m, 1 H), 4.26 (dd, br, J = 5.0, J = 11.5, 1 H), 5.10 (m, 2 H), 5.5 (s, 1 H), 5.91 (ddd, J = 9.0, J = 13.7, J = 18.7, 1 H), 7.38 (m, 3 H), 7.50 (m, 2 H). ^{13}C-NMR: δ 14.8 (q), 24.1 (t), 25.7 (t), 28.7 (t), 39.0 (d), 45.4 (t), 46.5 (t), 51.4 (d), 66.9 (t), 75.1 (d), 101.0 (d), 118.2 (t), 125.8 (d), 127.9 (d), 128.4 (d), 135.6 (d), 138.8 (s), 174.2 (s). Minor diastereomer **29**. Yield: 163 mg (6.8%). $[\alpha]^{23}_D$: 28.8 (c = 1.3 in $CHCl_3$). IR (KBr, film): 3070, 3034, 1632 (CO), 1460, 1436 cm^{-1}. MS (EI, 70 eV, 100 °C): m/z 329 (M^+), 252, 223, 208, 194, 166, 152, 127, 98, 70. HRMS (EI, 80 eV, 100 °C) (M^+) calcd 329.199 09, found 329.199 04. ^{1}H-NMR: δ 0.97 (d, J = 7.0, 3 H), 1.60 (m, 6 H), 2.20 (dt, br, J = 5.0, J = 10.5, 1 H), 3.02 (dq, J = 5.0, J = 7.0, 1 H), 3.16 (m, 2 H), 3.35 (m, 2 H), 3.80 (m, 2 H), 4.15 (m, 1 H), 4.96 (dd, J = 1.5, J = 17.0, 1 H), 5.08 (dd, J = 2.0, J = 10.5, 1 H), 5.51 (s, 1 H), 6.14 (td, J = 10.5, J = 17.0, 1 H), 7.25 (m, 3 H), 7.35 (m, 2 H). ^{13}C-NMR: δ 15.8 (q), 24.1 (t), 25.6 (t), 30.3 (t), 35.6 (d), 45.2 (t), 46.2 (t), 54.7 (d), 67.0 (t), 77.1 (d), 101.5 (d), 118.3 (t), 125.9 (d), 127.9 (d), 128.6 (d), 135.5 (d), 138.5 (s), 174.1 (s).

(3*R*,4*S*,5*S*)-3,5-Dimethyl-4-ethenyl-2(3*H*)-furanone (30). Reaction with pyrrolidinamide **25** (430 mg, 1.32 mmol) using conditions as described for lactone **19**. Chromatography: EtOAc/hexane, 1:5, R_f = 0.22. Yield: 173 mg (93.0%). The spectral data are listed because they are not yet completely published.[4] $[\alpha]^{23}_D$: −43.5 (c = 1.5 in $CHCl_3$) (lit.[4] −43.9, $CHCl_3$). IR (KBr, film): 3082, 3020, 1773 (CO), 1642, 1455 cm^{-1}. MS (EI, 70 eV, 30 °C): m/z 140 (M^+), 125 ($M^+ - CH_3$), 112, 81, 68, 53. HRMS (EI, 80 eV, 40 °C) (M^+) calcd 140.083 73, found 140.083 72. ^{1}H-NMR: δ 1.03 (d, J = 7.3, 3 H), 1.21 (d, J = 6.5, 3 H), 2.79 (qi, J = 7.3, 1 H), 2.90 (ddd, J = 4.8, J = 7.3, J = 10.4, 1 H), 4.52 (dq, J = 4.8, J = 6.5, 1 H), 5.11 (dd, J = 1.8, J = 16.8, 1 H), 5.20 (dd, J = 1.8, J = 10.0, 1 H), 5.46 (td, J = 10.0, J = 16.8, 1 H). ^{13}C-NMR: δ 10.5 (q), 16.2 (q), 39.9 (d), 50.2 (d), 77.2 (d), 120.0 (t), 131.1 (d), 178.8 (s).

(3*S*,4*R*,5*S*)-4-Ethenyl-5-(hydroxymethyl)-3-methyl-2(3H)-furanone (31). Reaction with amide **26** (1.60 g, 5.98 mmol) using conditions as described for lactone **21** without the silylation step. Chromatography: EtOAc/hexane, 1:1, R_f = 0.17. Yield: 790 mg (84.6%). $[\alpha]^{23}_D$: 57.9 (c = 1.8 in $CHCl_3$). IR (KBr, film): 3425 (br, OH), 3089, 1771 (CO), 1644, 1454, 1382, 1358 cm^{-1}. MS (EI, 70 eV, 70 °C): m/z 156 (M^+), 125, 97, 79, 68, 53. HRMS (EI, 80 eV, 70 °C) (M^+) calcd 156.078 65, found 156.078 67. ^{1}H-NMR: δ 1.11 (d, J = 7.2, 3 H), 2.92 (qi, J = 7.2, 1 H), 3.16 (ddd, J = 5.0, J = 7.2, J = 10.5, 1 H), 3.56 (s, br, 1 H, OH), 3.65 (dd, J = 4.3, J = 12.5, 1 H), 3.76 (dd, J = 7.5, J = 12.5, 1 H), 4.60 (ddd, J = 4.3, J = 5.0, J = 7.5, 1 H), 5.24 (dd, J = 1.6, J = 16.3, 1 H), 5.28 (dd, J = 1.6, J = 10.5, 1 H), 5.58 (td, J = 10.5, J = 16.3, 1 H). ^{13}C-NMR: δ 10.3 (q), 39.3 (d), 47.3 (d), 62.1 (t), 81.7 (d), 120.2 (t), 130.5 (d), 178.9 (s).

(3*R*,4*S*,5*S*)-4-Ethenyl-5-(2-hydroxyethyl)-3-methyl-2(3*H*)-furanone (32). Reaction with amide **28** (750 mg, 2.28 mmol) using conditions as described for lactone **21** without the silylation step. Chromatography: EtOAc/hexane, 1:1, R_f = 0.18. Yield: 340 mg (87.7%). $[\alpha]^{23}_D$: −62.5 (c = 1.3 in $CHCl_3$). IR (KBr, film): 3436 (br, OH), 3081, 1769 (CO), 1642, 1454, 1428, 1381, 1355 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 170 (M^+), 142, 124, 114, 105, 96, 68. HRMS (EI, 80 eV, 60 °C) (M^+) calcd 170.094 30, found 170.094 22. ^{1}H-NMR: δ 1.00 (d, J = 7.0, 3 H), 1.68 (m, 2 H), 2.78 (qi, J = 7.0, 1 H), 2.93 (ddd, J = 4.5, J = 7.0, J = 11.0, 1 H), 3.40 (s, br, 1 H, OH), 3.63 (t, J = 6.3, 2 H), 4.54 (td, J = 4.5, J = 8.8, 1 H), 5.08 (dd, J = 1.3, J = 16.3, 1 H), 5.17 (dd, J = 1.3, J = 11.0, 1 H), 5.42 (td, J = 11.0, J = 16.3, 1 H). ^{13}C-NMR: δ 10.3 (q), 33.6 (t), 39.7 (d), 49.3 (d), 58.6 (t), 78.4 (d), 120.2 (t), 131.0 (d), 179.0 (s).

(3*R*,4*S*,5*S*)-5-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4-ethenyl-3-methyl-2(3*H*)-furanone (33). Reaction with amide **27** (200 mg, 0.75 mmol) using conditions as described for lactone **21**. Chromatography: EtOAc/hexane, 1:10, R_f = 0.25. Yield: 180 mg (89.0%). $[\alpha]^{23}_D$: 60.6 (c = 1.7 in $CHCl_3$). IR (KBr, film): 3083, 1780 (CO), 1642, 1461 cm^{-1}. MS (EI, 70 eV, 60 °C): m/z 270 (M^+), 255, 213, 185, 169, 155, 141, 127, 117, 101, 89, 75. HRMS (EI, 80 eV, 70 °C) (M^+) calcd 270.165 12, found 270.165 18. ^{1}H-NMR: δ 0.01 (2 s, 6 H), 0.85 (s, 9 H), 1.11 (d, J = 7.5, 3 H), 2.87 (qi, J = 7.5, 1 H), 3.08 (dt, J = 4.8, J = 9.5, 1 H), 3.68 (dd, J = 2.8, J = 11.3, 1 H), 3.85 (dd, J = 2.5, J = 11.3, 1 H), 4.22 (m, 1 H), 5.11 (d, J = 17.0, 1 H), 5.15 (dd, J = 1.0, J = 9.5, 1 H), 5.70 (td, J = 9.5, J = 17.0, 1 H). ^{13}C-NMR: δ −5.7 (q), −5.6 (q), 11.4 (q), 18.1 (s), 25.7 (q), 38.1 (d), 45.0 (d), 63.3 (t), 82.6 (d), 118.4 (t), 134.2 (d), 179.4 (s).

(3*S*,4*R*,5*S*)-5-[2-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4-ethenyl-3-methyl-2(3*H*)-furanone (34). Reaction with amide **29** (95 mg, 0.29 mmol) using conditions as described for lactone **21**. Chromatography: EtOAc/hexane, 1:10, R_f = 0.21. Yield: 71 mg (86.3%). $[\alpha]^{23}_D$: −60.5 (c = 1.3 in $CHCl_3$). IR (KBr, film): 3083, 1779 (CO), 1643, 1472, 1463 cm^{-1}. MS (EI, 70 eV, 50 °C): m/z 284 (M^+), 283, 269, 254, 239, 227, 213, 197, 183, 171, 153, 131, 101, 89, 75. HRMS (EI, 80 eV, 60 °C) (M^+) calcd 287.180 77, found 287.180 69. ^{1}H-NMR: δ 0.06 (s, 6 H),

0.87 (s, 9 H), 1.16 (d, J = 7.5, 3 H), 1.82 (m, 2 H), 2.78 (qi, J = 7.5, 1 H), 2.84 (m, 1 H), 3.76 (dd, J = 5.0, J = 6.3, 2 H), 4.46 (m, 1 H), 5.16 (d, J = 16.3, 1 H), 5.20 (dd, J = 1.0, J = 10.5, 1 H), 5.69 (ddd, J = 8.0, J = 10.5, J = 16.3, 1 H). ^{13}C-NMR: δ −5.5 (q), 11.3 (q), 18.2 (s), 25.8 (q), 36.7 (t), 38.6 (d), 49.3 (d), 59.2 (t), 79.3 (d), 119.0 (t), 133.4 (d), 179.2 (s).

Acknowledgment. I thank the DFG and the Fonds der Chemischen Industrie for support of this research.

Supplementary Material Available: NOEDS data for compounds **23**, **24**, and **31**−**34**, and ^{1}H and ^{13}C NMR spectra for all new and incompletely described compounds (50 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.

JO941932M