Pergamon

Tetrahedron Vol. 50, No. 45, pp. 12895-12902, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)00828-0

Stereoselective Synthesis of 2-(2'-Cycloalkenyl) Glycinates via [3,3] Sigmatropic Rearrangement of Chelated Ester-Enolates

Uli Kazmaier

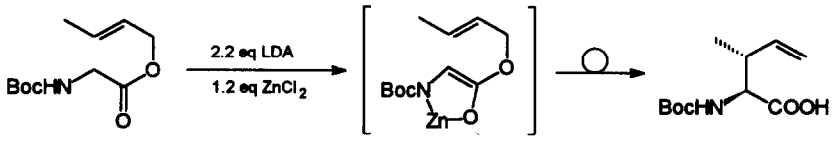
Organisch-Chemisches Institut der Universität, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany

Abstract: Ester-enolate Claisen rearrangement of chelated *N*-protected cycloalkenyl glycinates **1** results in the formation of cyclic γ,δ-unsaturated amino acids in good yields and in a highly diastereoselective fashion.

INTRODUCTION

γ,δ-Unsaturated amino acids are of great interest not only as naturally occurring non proteinogenic amino acids,[1] but also as intermediates for the synthesis of complex amino acids and peptides.[2] Like most of these atypical amino acids, cyclic derivatives show high activity as enzyme inhibitors.[3] Therefore, various approaches to the synthesis of this class of amino acids have been developed during the last few years. Besides the *N*-sulfonylimine ene reaction[4] and the nucleophilic allylation of glycine cation equivalents,[5] the Ireland-Claisen rearrangement is suitable for the diastereoselective construction of γ,δ-unsaturated amino acids. This methodology was investigated by Bartlett *et al.* in 1982.[6] They found a strong dependence of the diastereoselectivity on the ring size of the cycloalkenyl esters and the *N*-protecting group used. The best results with respect to yield and diastereoselectivity were obtained by the oxazole rearrangement developed by Steglich *et al.*[7]

In a previous communication we described a new variation of the ester-enolate Claisen rearrangement, one that is especially suitable for α-amino acid synthesis.[8] Deprotonation of *N*-protected glycine allylesters with LDA at -78 °C and subsequent addition of metal salts such as zinc chloride presumably results in the formation of a chelated zinc enolate which undergoes Claisen rearrangement upon warming to room temperature (Scheme 1).[9] Due to the fixed enolate geometry, as a result of chelate formation, the rearrangement proceeds with a high degree of diastereoselectivity, independent of the substitution pattern and the protecting groups used. In contrast to the corresponding lithium enolates, the chelated enolates are quite stable and can be warmed up to room temperature without decomposition.

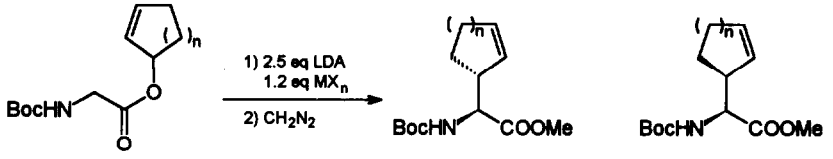


Scheme 1

Nevertheless, these chelated enolates show the high reactivity of metal enolates resulting in very mild rearrangement conditions. Therefore, in contrast to the rearrangement *via* silyl ketene acetals, the rearrangement of the chelated enolates proceeds at -20°C.

RESULTS AND DISCUSSION

Because of the good results obtained with acyclic substrates the chelate ester enolate rearrangement was also applied to the rearrangement of cycloalkenyl glycinates **1** (Scheme 2). The influence of the ring size as well as the metal salt used for chelation of the ester enolate was investigated. The results are listed in Table 1.



1 a-d (±)-**2 a-d** (±)-**3 a-d**

Scheme 2

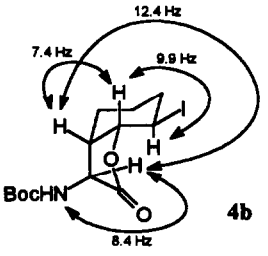
Table 1: Rearrangement of *N*-Boc protected cycloalkenyl glycinates **1 a-d**

	MX_n	$ZnCl_2$		$MgCl_2$		$Al(OiPr)_3$		$SnCl_2$	
1	n	Yield [%]	Ratio **2** : **3**	Yield [%]	Ratio **2** : **3**	Yield [%]	Ratio **2** : **3**	Yield [%]	Ratio **2** : **3**
a	1	79	80 : 20	57	79 : 21	47	75 : 25	76	67 : 33
b	2	83	90 : 10	94	92 : 8	91	90 : 10	88	71 : 21
c	3	73	92 : 8	79	92 : 8	69	89 : 11	71	63 : 37
d	4	57	86 : 14	78	91 : 9	42	79 : 21	74	41 : 59

The crude amino acids, obtained by the rearrangement process, are directly converted into the corresponding methyl esters **2** and **3** by the use of diazomethane. Best results concerning yield as well as stereoselectivity are obtained with cyclohexenyl glycinate **1b** (n = 2). In this case all metal salts gave the product in excellent yield. The same high degree of diastereoselectivity was obtained in the rearrangement of the homologous cycloheptenyl derivative **1c** (n = 3), while with the smaller ester **1a** (n = 1) and the larger and probably more flexible cyclooctenyl ester **1d** (n = 4) the selectivity decreases. The results with tin(II) chloride are in sharp contrast to the selectivities obtained in the presence of the other metal salts. Obviously tin(II) chloride is not able to form chelated enolates. Although the diastereomer **2** was formed preferentially in good yield, the diastereomeric ratio varied and was even inverted in the case of the cyclooctenyl ester **1d**. Even though this phenomenon is surprising it was also observed in the rearrangement of acyclic substrates.[8]

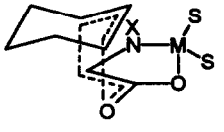
For determination of the diastereomeric ratio (**2** : **3**) the *N*-Boc-protected amino acid esters were converted into the corresponding *N*-trifluoroacetyl derivatives and the diastereomers were separated on a chiral GC column (Chira-Si-*L*-Val).

The configuration of the predominant isomer **2** was confirmed by two independent methods. Rearrangement of N-Boc glycine cyclohexenylester **1b** and subsequent iodocyclization gives iodo lactone **4b** as the sole product. The coupling constants as well as other spectroscopic data obtained are in good agreement with the data reported by Bartlett for this compound.[6] The diastereomeric mixture **2b/3b** was also converted into the corresponding *N*-acetyl derivatives **5b** and **6b**. Comparison of the spectroscopic data with the data and the X-ray structure published by Trowitzsch *et al.*[3d] clearly indicates, that the (±)-*R,S* diastereomer **2b** is formed preferentially.

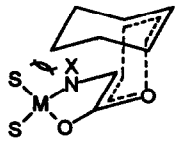


4b

The product formation as well as the high diastereoselectivity observed in the rearrangement of the six- and seven- membered allylic esters can be explained by rearrangement *via* a boat-like transition state which is discussed frequently for cyclic allylic substrates.[10] Steric interactions between the cycloalkenyl ring and the probably solvated chelating metal obviously disfavour the chair-like transition state.



boat



chair

X = Boc

S = Solvent

M = Zn, Mg, Al, Sn

CONCLUSION

The ester enolate Claisen rearrangement of chelated allylic ester enolates is not limited to acyclic substrates but can also be applied to cyclic substrates. Various metal salts can be used for chelation. The rearrangement occurs in a highly diastereoselective fashion *via* a boat-like transition state while the best results are obtained with six- and seven-membered cycloalkenyl esters.

EXPERIMENTAL SECTION

General Procedure. The allylic ester derivatives used as substrates were synthesized by coupling *N*-Boc-glycine and the corresponding allylic alcohol using dicyclohexylcarbodiimide and 4-(dimethylamino)pyridine.[11] All reactions were carried out in oven-dried glassware (100°C) under an atmosphere of argon. All solvents were dried before used. THF was distilled from sodium-benzophenone and diisopropylamine from calcium hydride. LDA solutions were prepared from freshly distilled diisopropylamine and commercially available butyllithium solution (15% in hexane) in THF at -20°C directly before use. The starting materials and the products were purified by flash chromatography on silica gel (32 - 63 μm). Mixtures of ethyl acetate and hexanes were used as eluants. TLC was performed on commercial precoated silica gel 60 F_{254} plates (Merck). Visualization was accomplished with iodine and potassium permanganate solution. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer. Chemical shifts were reported in δ relative to $CHCl_3$ as an internal reference. GC analyses were performed on a Hewlett-Packard 5890 Series II instrument equipped with a chiral fused silica coating Chirasi-L-Val column (25m × 0.25 mm, Chrompack). Diastereomeric ratios were also determined by NMR spectroscopy.

General procedure for ester enolate Claisen rearrangement: 2.5 mmol of a freshly prepared LDA solution in 5 ml THF was added to a stirred mixture of 1 mmol allylic ester **1** and 1.1 mmol of the corresponding metal salt in dry THF at -78 °C. The mixture was allowed to warm up to room temperature overnight. The resulting clear solution was diluted with ether and hydrolyzed with 1 N hydrochloric acid. After separation of the aqueous layer the rearrangement product was extracted twice with 1 N sodium hydroxide solution. Acidification of the aqueous layer with $KHSO_4$ and re-extraction with ether gave the desired *N*-protected amino acids which was directly converted into the methyl ester **2** by addition of a solution of diazomethane in ether. After evaporation of the solvent the crude product was purified by flash chromatography (petroleum ether / ethyl acetate 75:25).

(2*SR*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclopent-2-enyl)glycine methyl ester (2a): ^{1}H NMR (300MHz, $CDCl_3$): δ 5.86 (m, 1H), 5.66 (m, 1H), 5.08 (d_{br}, J = 8.5Hz, 1H), 4.50 (dd, J = 8.1, 5.2Hz, 1H), 3.73 (s, 3H), 3.28 (m, 1H), 2.35 (m, 2H), 1.98 (m, 1H), 1.67 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$): δ 172.43, 155.32, 133.84, 130.14, 79.84, 56.52, 52.06, 48.51, 32.44, 28.31, 24.61.

(2*RS*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclopent-2-enyl)glycine methyl ester (3a): ^{1}H NMR (300MHz, $CDCl_3$) (selected signals): δ 5.96 (dd, J = 5.5, 2.2Hz, 1H), 5.54 (m, 1H), 4.45 (dd, J = 9.0, 4.0Hz, 1H), 3.37 (m, 1H), 2.11 (m, 1H). ^{13}C NMR (75MHz, $CDCl_3$) (selected signals): δ 172.68, 155.72, 135.96, 129.67, 56.72, 47.57, 32.08, 26.26.
Anal. Calcd for $C_{13}H_{21}NO_4$ (Mixture **2a/3a**): C, 61.16; H, 8.29; N, 5.49. Found: C, 61.30; H, 8.36; N, 5.46.

(2*SR*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclohex-2-enyl)glycine methyl ester (2b): ^{1}H NMR (300MHz, $CDCl_3$): δ 5.78 (ddd, J = 10.3, 7.3, 3.0Hz, 1H), 5.49 (d_{br}, J = 9.6Hz, 1H), 5.00 (d_{br}, J = 7.7Hz, 1H), 4.32 (dd, J = 8.3, 5.7Hz, 1H), 3.71 (s, 3H), 2.60 (m, 1H), 1.96 (m, 2H), 1.77 (m, 1H), 1.45 (m, 3H), 1.41 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$): δ 172.37, 155.49, 130.01, 126.74, 79.77, 56.98, 52.00, 38.73, 28.29, 24.79, 24.27, 21.34.
(2*RS*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclohex-2-enyl)glycine methyl ester (3b): ^{1}H NMR (300MHz, $CDCl_3$) (selected signals): δ 5.87 (ddd, J = 10.3, 7.0, 3.0Hz, 1H), 5.39 (d_{br}, J = 9.2Hz, 1H), 4.90 (d_{br}, J = 9.2Hz, 1H), 4.24 (dd, J = 9.5, 5.5Hz, 1H). ^{13}C NMR (75MHz, $CDCl_3$) (selected signals): δ 131.71, 125.02, 38.20, 26.20, 21.47.
Anal. Calcd for $C_{14}H_{23}NO_4$ (Mixture **2b/3b**): C, 62.43; H, 8.61; N, 5.20. Found: C, 62.40; H, 8.70; N, 5.12.

(2*SR*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclohept-2-enyl)glycine methyl ester (2c): ^{1}H NMR (300MHz, $CDCl_3$) δ 5.83 (m, 1H), 5.60 (dd, J = 11.3, 2.7Hz, 1H), 5.03 (d_{br}, J = 8.9Hz, 1H), 4.34 (dd, J = 8.9, 4.6Hz, 1H), 3.70 (s, 3H), 2.70 (m, 1H), 2.26 - 1.87 (m, 2H), 1.78 - 1.12 (m, 6H), 1.41 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$): δ 172.54, 155.43, 133.33, 132.27, 79.88, 57.88, 52.06, 42.55, 30.36, 29.05, 28.45, 28.27, 26.35.

(2*RS*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclohept-2-enyl)glycine methyl ester (3c): ^{1}H NMR (300MHz, $CDCl_3$) (selected signals): δ 5.47 (dd, J = 11.1, 3.0Hz, 1H). ^{13}C NMR (75MHz, $CDCl_3$) (selected signals): δ 134.12, 130.51, 42.75, 30.83, 29.83.
Anal. Calcd for $C_{15}H_{25}NO_4$ (Mixture **2c/3c**): C, 63.58; H, 8.89; N, 4.94. Found: C, 63.49; H, 8.80; N, 4.90.

(2*SR*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclooct-2-enyl)glycine methyl ester (2d): ^{1}H NMR (300MHz, $CDCl_3$) δ 5.75 (m, 1H), 5.40 (dd, J = 10.3, 9.2Hz, 1H), 5.04, (d_{br}, J = 8.4Hz, 1H), 4.29 (dd, J = 8.4, 6.3Hz, 1H), 3.73 (s, 3H), 2.92 (m, 1H), 2.19 (m, 1H), 2.07 (m, 1H), 1.74-1.18 (m, 8H), 1.44 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$): δ 172.71, 155.52, 131.88, 128.57, 79.87, 57.25, 51.94, 39.23, 31.71, 29.22, 28.31, 26.48, 26.41, 25.37.
(2*RS*,3*RS*)-N-t-Butyloxycarbonyl-2-(cyclooct-2-enyl)glycine methyl ester (3d): ^{1}H NMR (300MHz, $CDCl_3$) (selected signals): δ 5.28 (dd, J = 10.7, 9.2Hz, 1H), 1.43 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$) (selected signals): δ 132.24, 127.69, 128.13, 52.05, 39.35, 32.59, 29.67, 26.70, 26.62.
Anal. Calcd for $C_{16}H_{27}NO_4$ (Mixture **2d/3d**): C, 64.62; H, 9.15; N, 4.71. Found: C, 64.54; H, 9.22; N, 4.67.

(3*SR*, 3a*SR*, 7*RS*, 7a*RS*)-Hexahydro-7-iodo-3-((*t*-butyloxycarbonyl)amino)benzofuran-2(3H)-one (4b):[6b] 200 mg (0.78 mmol) (2*SR*,3*RS*)-*N*-*t*-Butyloxycarbonyl-2-(cyclohex-2-enyl)glycine was dissolved in 2 ml ether and was added to a solution of 200 mg (1.2 mmol) potassium iodide, 253 mg (1 mmol) iodine, 250 mg (1 mmol) $CuSO_4 \cdot 5H_2O$ and 70 mg (0.85 mmol) $NaHCO_3$ in 2 ml of water. The heterogeneous mixture was stirred vigorously overnight. The reaction mixture was diluted with water and ether. The organic layer was washed with 1N $KHSO_4$ and saturated $Na_2S_2O_3$ solution. Drying over Na_2SO_4 and evaporation of the solvent gave the crude iodo lactone. Purification by flash chromatography (petroleum ether / ethyl acetate 85 : 15) gave **4** (200 mg, 0.52 mmol, 67%) as a colorless foam. ^{1}H NMR (300MHz, $CDCl_3$) δ 5.07 (d, J = 8.4Hz, 1H), 4.76 (dd, J = 9.9, 7.4Hz, 1H), 4.52 (dd, J = 12.4, 8.4Hz, 1H), 3.94 (ddd, J = 12.4, 9.8, 4.0Hz, 1H), 2.53 (m, 1H), 2.41 (m, 1H), 1.46-2.08 (m, 5H), 1.42 (s, 9H). ^{13}C NMR (75MHz, $CDCl_3$): δ 174.01, 155.78, 83.35, 80.64, 50.41, 43.44, 36.63, 28.19, 26.97, 23.32, 22.44

(2*SR*,3*RS*)-*N*-Acetyl-2-(cyclohex-2-enyl)glycine methyl ester (5b): 5 ml of a saturated solution of HCl in dioxane was added to 135 mg (0.5 mmol) of *N*-*t*-Butyloxycarbonyl-2-(cyclohex-2-enyl)glycine methyl ester (**2b/3b**) in 1 ml ether at 0°C. The mixture was stirred for 1h at room temperature, before the solvent was removed *in vacuo*. The residue was dissolved in 5 ml methylene chloride and 0.5 ml pyridine. 0.1 ml Acetic anhydride was added slowly at 0°C and the mixture was allowed to warm up to room temperature overnight. The solution was diluted with methylene chloride and was washed with water, sat. $NaHCO_3$ solution as well as 1N $KHSO_4$ solution. After drying over Na_2SO_4 the solvent was removed *in vacuo*. The residue was crystallized from methylene chloride / petroleum ether giving 76 mg (0.36 mmol, 72%) colorless needles, mp 106 - 107 °C. ^{1}H NMR (300MHz, $CDCl_3$) δ 6.03 (d_{br}, J = 7.3Hz, 1H), 5.79 (ddd, J = 9.9, 6.1, 2.9Hz, 1H), 5.49 (ddd, J = 9.9, 1.8, 1.1Hz, 1H), 4.68 (dd, J = 8.5, 5.5Hz, 1H), 3.72 (s, 3H), 2.64 (m, 1H), 2.00 (s, 3H), 1.97 (m, 2H), 1.76 (m, 1H), 1.60 (m, 1H), 1.52 (m, 1H), 1.36 (m, 1H). ^{13}C NMR (75MHz, $CDCl_3$): δ 172.19, 169.86, 130.15, 126.58, 55.43, 52.12, 38.70, 24.78, 24.40, 23.15, 21.33. Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.33. Found: C, 62.62; H, 8.04; N, 6.39.

(2*RS*,3*RS*)-*N*-Acetyl-2-(cyclohex-2-enyl)glycine methyl ester (6b): ^{1}H NMR (300MHz, $CDCl_3$) (selected signals): δ 5.87 (ddd, J = 10.3, 6.3, 3.0Hz, 1H), 5.42 (dd, J = 10.3, 1.6Hz, 1H), 4.59 (dd, J = 8.8, 4.4Hz, 1H), 3.71 (s, 3H), 2.69 (m, 1H), 2.01 (s, 3H). ^{13}C NMR (75MHz, $CDCl_3$) (selected signals): δ 172.32, 131.81, 125.01, 55.52, 38.18, 26.18, 21.44.

(2*SR*,3*RS*)-*N*-Acetyl-2-(cyclohex-2-enyl)glycine (7b):[3d] To a solution of 53 mg (0.25 mmol) *N*-Acetyl-2-(cyclohex-2-enyl)glycine methyl ester (**5b/6b**) in 3 ml 50% methanol was added dropwise 0.3 ml of a 1N NaOH solution. The mixture was stirred overnight and the solvent was removed *in vacuo*. The residue was dissolved in water and the resulting clear solution was washed twice with ether. Acidification of the aqueous layer with $KHSO_4$ and extraction with ethyl acetate gave 41 mg (0.21 mmol, 83%) of the amino acid. ^{1}H NMR (300MHz, CD_3OD) δ 5.79 (ddd, J = 10.3, 6.6, 2.5, 1H), 5.54 (dd, J = 10.3, 2.0Hz, 1H), 4.90 (s_{br}, 2H), 4.48 (d, J = 6.3Hz, 1H), 3.30 (m, 1H), 2.68 (m, 2H), 1.98 (s, 3H), 1.85-1.40 (m, 4H). ^{13}C NMR (75MHz, CD_3OD): δ 174.51, 173.43, 130.75, 128.27, 57.31, 39.31, 25.88, 25.43, 22.52, 22.35.

(2*RS*,3*RS*)-*N*-Acetyl-2-(cyclohex-2-enyl)glycine (8b): ^{1}H NMR (300MHz, CD_3OD) (selected signals): δ 5.83 (m, 1H), 4.38 (d, J = 5.9Hz, 1H), 2.00 (s, 3H).). ^{13}C NMR (75MHz, CD_3OD) (selected signals): δ 131.43, 127.08, 57.66, 39.06, 27.34, 25.94, 22.65.

Acknowledgment. I thank Prof. Dr. G. Helmchen for his generous promotion of this work. Financial support by the Deutsche Forschungsgemeinschaft as well as the Fonds der Chemischen Industrie is gratefully acknowledged.

REFERENCES AND NOTES

1. a) Katagiri, K.; Tori, K.; Kimura, Y.; Yoshida, T.; Nagasaki, T.; Minato, H. J. *Med. Chem.* **1967**, *10*, 1149. b) Cramer, U.; Rehfeldt, A. G.; Spener, F. *Biochemistry* **1980**, *19*, 3074. c) Tsubotani, S.; Funabashi, Y.; Takamoto, M.; Hakoda, S.; Harada, S. *Tetrahedron* **1991**, *47*, 8079.
2. a) Bartlett, P. A.; Tanzella, D. J.; Barstow, J. F. *Tetrahedron Lett.* **1982**, *23*, 619. b) Ohfune, Y.; Kurokawa, N. *Tetrahedron Lett.* **1985**, *26*, 5307. c) Kurokawa, N.; Ohfune, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6041. d) Baumann, H.; Duthaler, R. O. *Helv. Chim. Acta* **1988**, *71*, 1025. e) Broxterman, Q. B.; Kaptein, B.; Kamphuis, J.; Schoemaker, H. E. *J. Org. Chem.* **1992**, *57*, 6286.
3. a) Dennis, R. L.; Plant, W. J.; Skinner, C. G.; Sutherland, G. L. *J. Am. Chem. Soc.* **1955**, *77*, 2362. b) Edelson, J.; Fissekis, J. D.; Skinner, C. G.; Shive, W. *J. Am. Chem. Soc.* **1958**, *80*, 2698. c) Shannon, P.; Marcotte, P.; Coppersmith, S.; Walsh, C. *Biochemistry* **1979**, *18*, 3917. d)) Santoso, S.; Kemmer, T.; Trowitzsch, W. *Liebigs Ann. Chem.* **1981**, 642. e) Santoso, S.; Kemmer, T.; Trowitzsch, W. *Liebigs Ann. Chem.* **1981**, 658.
4. a) Achmatowicz, O., Jr.; Pietraszkiewicz, M. *J. Chem. Soc. Perkin Trans. 1*, **1981**, 2680. b) Tschaen, D. M.; Weinreb, S. M. *Tetrahedron Lett.* **1982**, *23*, 3015. c) Tschaen, D. M.; Turos, E.; Weinreb, S. M. *J. Org. Chem.* **1984**, *49*, 5058.
5. a) Williams, R. M.; Sinclair, P. J.; Zhai, D.; Chen, D. *J. Am. Chem. Soc.* **1988**, *110*, 1547. b) Easton, C. J. Easton, Scharfbilling, I. M. *J. Org. Chem.* **1990**, *55*, 384. c) Roos, E. C.; Mooiweer, H. H.; Hiemstra, H.; Speckamp, W. C.; Kaptein, B.; Boesten, W. H. J.; Kamphuis, J. *J. Org. Chem.* **1992**, *57*, 6769. d) Roos, E. C.; Lopez, M. C.; Brook, M. A.; Hiemstra, H.; Speckamp, W. C.; Kaptein, B.; Kamphuis, J.; Schoemaker, H. E. J. *Org. Chem.* **1993**, *58*, 3259.
6. a) Bartlett, P. A.; Barstow, J. F. *Tetrahedron Lett.* **1982**, *23*, 623. b) Bartlett, P.A.; Barstow, J. F. *J. Org. Chem.* **1982**, *47*, 3933.
7. a) Kübel, B.; Höfle, G.; Steglich, W. *Angew. Chem.* **1975**, *87*, 64; *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 58. b) Engel, N.; Kübel, B.; Steglich, W. *Angew. Chem.* **1977**, *89*, 408; *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 394.
8. Kazmaier,U. *Angew. Chem.* **1994**,*106*, 1046; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 998.

9. This is in contrast to the observation made in Aza-Claisen rearrangements of *N*-acyl-glycine amides. See: Tsunoda, T.; Tatsuki, S.; Shiraishi, Y.; Akasaka, M.; Ito, S. *Tetrahedron Lett.* **1993**, *34*, 3297.
10. Wipf, P. *"Comprehensive Organic Synthesis"* Vol. 5, ed. by Trost, B. M.; Fleming, I. A.; Pergamon Press, Oxford, **1991**, p. 827.
11. Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, 4475

(*Received in Germany* 12 *August* 1994; *accepted* 21 *September* 1994)