Studies on 2-Aziridinecarboxylic Acid. VII.[1] Formation of Dehydroamino Acid Peptides *via* Isomerization of Peptides Containing 2-Aziridinecarboxylic Acid by Tertiary Amines

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Peptides containing 1-(α-aminoacyl)-2-aziridinecarboxylic acid were isomerized into the corresponding dehydroamino acid peptides by treatment with the tertiary amines, triethylamine or 1,4-diazabicyclo[2.2.2]octane (Dabco). Dehydrohydantoin derivatives were also prepared by treatment of benzyloxycarbonyl-2-aziridinecarboxylic acid derivatives with tertiary amines.

Recently many biologically active peptides containing dehydroamino acid (DHA) have been isolated and much attention has been directed to their synthesis. Literature concerning the synthesis of DHA peptides has mainly dealt with β-elimination of the O-leaving group of β-hydroxy α-amino acid derivatives,[2] and a more recent paper has reported Hofmann degradation reaction of 2,3-diaminopropionic acid derivatives.[3]

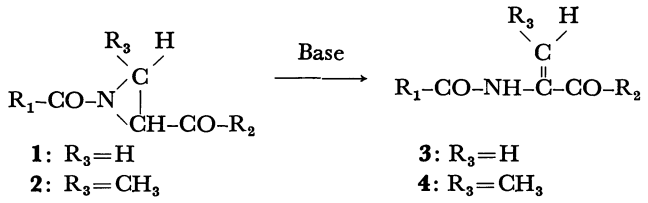
In the previous paper,[4] we reported the isomerization of peptides containing 2-aziridinecarboxylic acid (Azyline, Azy) and 3-methyl-2-aziridinecarboxylic acid (3-MeAzy) into the corresponding DHA peptides with NaI in an acetone solution. During our investigation on the reaction of Azy peptides with several amines, we found that they react with primary and secondary amines to form the corresponding amine adducts, α,β-diaminopropionic acid derivatives,[5] and the *trans*-acylation reaction occurs due to peptide bond cleavage.[5] Also, 1-acyl- and 1-(α-aminoacyl)-2-aziridinecarboxylic acid peptides are isomerized into the corresponding DHA peptides upon treatment with tertiary amines as in the reaction with NaI.

In the present study the reactions of Azy peptides with the tertiary amines, triethylamine and Dabco were observed in detail. The Azy and 3-MeAzy peptides used as the starting materials were synthesized by the mixed anhydride method from N-protected amino acid and Azy derivatives according to the procedure described

TABLE 1. YIELDS AND PROPERTIES OF AZY-PEPTIDES (**1**, **2**, **5**)

Azy peptide[a] ↓	Yield/%	Mp θ_m/°C	$[\alpha]_D^{23}$/°	Found (Calcd) (%) C	H	N
Z-Gly-Azy-$NHCH_3$ (**1a**)	70	193 (decomp)	−38.0 (*c* 0.8, MeOH)	57 84 (57.72	5 81 5.88	14.38 14 43)
Z-Gly-Azy-NHBzl (**1b**)	72	122.5—123.5	−90.0 (*c* 1.1, $CHCl_3$)	66.42 (66.48	5.53 5.58	11.11 11.08)
Z-Phe-Azy-$NHCH_3$ (**1c**)	56	170—171	−66.9 (*c* 1.1, $CHCl_3$)	66.08 (66.13	6.12 6.08	11.13 11.02)
Z-Ala-Azy-OBzl (**1d**)	83	58—61	−50.9 (*c* 1.0, DMSO)	65.91 (65.96	5.73 5.80	7.29 7.33)
Z-Phe-Azy-OBzl (**1e**)	72	68—69	−62.7 (*c* 1.0, DMSO)	70.69 (70.73	5.68 5.72	6.16 6.11)
Z-Gly-Azy-Gly-OBzl (**1f**)	92	118—119	−52.5 (*c* 1.0, MeOH)	62.23 (62.16	5.40 5.45	9.92 9.88)
Z-Phe-3-MeAzy-$NHCH_3$ (**2a**)	77	129—130	−25.3 (*c* 1.1,$CHCl_3$)	66.81 (66.82	6.27 6.37	10.69 10.63)
Z-Phe-3-MeAzy-NHBzl (**2b**)	62	157—157.5	−35.1 (*c* 0.23, $CHCl_3$)	71.28 (71.32	6.11 6.20	8.83 8.91)
Z-Phe-3-MeAzy-OBzl (**2c**)	80	95—97	−61.1 (*c* 1.0, MeOH)	71.26 (71.17	6.02 5.97	5.89 5.93)
Z-Gly-3-MeAzy-Gly-OBzl (**2d**)	90	123.5—124.5	−58.2 (*c* 1.0, AcOEt)	62.88 (62.86	5.70 5.73	9.68 9.56)
Z-Ala-3-MeAzy-Gly-OBzl (**2e**)	93	110—111	−59.7 (*c* 1.0, $CHCl_3$)	63.48 (63.50	5.98 6.00	9.30 9.27)
Z-Azy-Gly-OBzl (**5a**)	60	109—110	−50.6 (*c* 1.0, MeOH)	65.17 (65.21	5.50 5.47	7.71 7.60)
Boc-Azy-Gly-OBzl (**5b**)	61	71—71.5	−80.4 (*c* 1.0, MeOH)	61.22 (61.07	6.85 6.63	8.35 8.34)
Z-3-MeAzy-Gly-OBzl (**5c**)	73	62—64	−63.2 (*c* 1.0, MeOH)	65.95 (65.96	5.83 5.80	7.42 7.33)
Boc-3-MeAzy-Gly-OBzl (**5d**)	79	89.5—90	−70.0 (*c* 1.0, MeOH)	66.21 (66.06	7.24 7.34	8.01 8.04)

a) All Azy peptides were synthesized by the mixed anhydride method except **5a—d**. Arrow indicates final coupling position. Azy: (2*S*)-form, 3-MeAzy: (2*S*, 3*S*)-form.

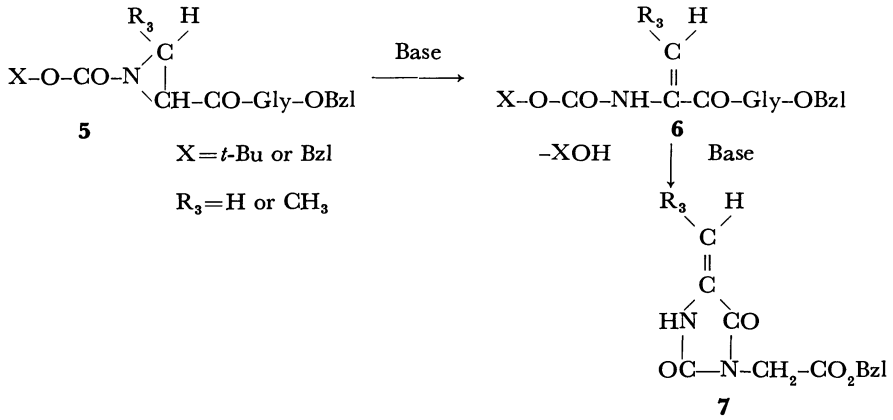


Scheme 1.

TABLE 2. YIELDS AND PROPERTIES OF DHA-PEPTIDES (**3**, **4**)

Product (**3**, **4**)	Yield/%	Mp θ_m/°C	Base[a]	Found (Calcd) (%) C	H	N	NH	NMR data of DHA δ, DMSO-d_6 =CH_2	CH_3
Z-Gly-⊿Ala-$NHCH_3$ (**3a**)	89	175 (decomp)	Et_3N(3)	57.84 57.72	5.81 5.88	14.38 14.43	9.01	5.58	6.20 —
Z-Gly-⊿Ala-NHBzl (**3b**)	84	117.5—118.5	Et_3N(3)	66.42 66.48	5.53 5.58	11.11 11.08	9.07	5.60	6.24 —
Z-Phe-⊿Ala-$NHCH_3$ (**3c**)	100	syrup	Et_3N(6)	66.08 66.13	6.12 6.08	11.13 11.02	8.58	6.30	6.60 —[b]
Z-Ala-⊿Ala-OBzl (**3d**)	100	syrup	Et_3N(3)	65.91 65.96	5.73 5.80	7.29 7.33	8.34	5.92	6.56 —[b]
Z-Phe-⊿Ala-OBzl (**3e**)	100	syrup	Et_3N(3)	70.69 70.73	5.68 5.72	6.16 6.11	8.12	5.92	6.60 —[b]
Z-Gly-⊿Ala-Gly-OBzl (**3f**)	100	133—136	Et_3N(6)	62.23 62.16	5.40 5.45	9.92 9.88	8.99	5.57	6.31 —
Z-Phe-⊿Aba-$NHCH_3$ (**4a**)	77	165—167	Dabco(24)	66.81 66.82	6.27 6.37	10.69 10.63	9.05	—	6.36q 1.40d
Z-Phe-⊿Aba-NHBzl (**4b**)	88	162.5—163.5	Dabco(24)	71.28 71.32	6.11 6.20	8.83 8.91	9.15	—	6.44q 1.40d
Z-Phe-⊿Aba-OBzl (**4c**)	90	151—152	Dabco(6)	71.26 71.17	6.02 5.97	5.89 5.93	9.20	—	6.67q 1.68d
Z-Gly-⊿Aba-Gly-OBzl (**4d**)	87	101—102	Dabco(24)	62.88 62.86	5.70 5.73	9.68 9.56	9.01	—	6.55q 1.66d
Z-Ala-⊿Aba-Gly-OBzl (**4e**)	87	139—140.5	Dabco(24)	63.48 63.50	5.98 6.00	9.30 9.27	9.02	—	6.52q 1.65d

a) The reaction was carried out in a $CHCl_3$ solution at 35 °C and the base used was 2 equimolar against Azy peptide. The values in parenthesis are the reaction time/h. b) NMR spectrum in $CDCl_3$.



Scheme 2.

in our previous papers.[5-7] Their properties and yields are summarized in Table 1 and the reaction procedure of the Azy peptides with amines is shown in Scheme 1.

Azy and 3-MeAzy peptides (**1a**—**f** and **2a**—**e**) were treated with 2 equimolar amount of tertiary amine (Et_3N or Dabco) in $CHCl_3$ solution at 35 °C for 3—24 h, and then the corresponding dehydroamino acid (DHA, ⊿AA) derivatives were isolated by silica-gel column chromatography. The DHA produced was identified by NMR.

In the NMR data, characteristic signals of the DHA structure appeared at δ 5.5—5.9 for the vinyl proton of dehydroalanine (⊿Ala), and at δ 1.4—1.7 as a doublet for the methyl proton and at δ 6.3—6.8 as a quartet for the β-proton of dehydro-α-aminobutyric acid (⊿Aba). ⊿Aba was of the (Z)-configuration. The product (**3**, **4**)

TABLE 3. Boc- AND Z-⊿AA-GLY-OBZL (**6**) AND DEHYDROHYDANTOIN (**7**)

Azy peptide (**5**)	Base	React time/h	Product yields/% DHA (**6**)	Product yields/% Hydantoin (**7**)
Z-Azy-Gly-OBzl (**5a**)	Et_3N	12	—	75
	Dabco	6	—	80
Boc-Azy-Gly-OBzl (**5b**)	Et_3N	24	95	—
	Dabco	6	100	—
Z-3-MeAzy-Gly-OBzl (**5c**)	Et_3N	7[a)]	—	—
	Dabco	3[a)]	68	28
Boc-3-MeAzy-Gly-OBzl (**5d**)	Et_3N	7[a)]	—	—
	Dabco	4[a)]	85	—

a) Reaction time/d.

of the isomerization of the Azy peptides are summarized in Table 2.

The reaction results show that 1-acyl-2-aziridinecarboxylic acid peptides (**1a**—**f**) were easily isomerized into the corresponding ⊿Ala peptides (**3a**—**f**) by the treatment of triethylamine, but contrary to our expectation, 1-acyl-3-methyl-2-aziridinecarboxylic acid peptides (**2a**—**e**) were not isomerized into the ⊿Aba peptides (**4a**—**e**), even after 7 d of treatment. Use of the more basic Dabco as an isomerizing reagent was necessary to obtaine ⊿Aba peptides (**4a**—**e**).

This isomerization reaction seems to be induced by a direct withdrawing of the α-proton of Azy or 3-MeAzy with base. The α-proton of unsubstituted Azy (**1a**—**f**) could be easily withdrawn by Et_3N treatment, but not that of the substituted 3-MeAzy (**2a**—**e**) because of the methyl group on the aziridine ring. Thus, the more basic Dabco was needed to withdraw the α-proton of 3-MeAzy for its isomerization.

We also examined the reaction of 1-benzyloxycarbonyl- and 1-*t*-butoxycarbonyl-2-aziridinecarboxylic acid peptides (**5a**—**d**) with amines. As shown in Scheme 2 and Table 3, the reaction of the Azy peptides blocked by urethane-type groups with tertiary amines afforeded not only the corresponding DHA peptides, but also dehydrohydantoin derivatives (**7a**, **7b**). Again, the 3-MeAzy peptides (**5c**, **5d**) were not isomerized with Et_3N and the benzyloxycarbonyl derivatives were more easily isomerized into the corresponding DHA peptides than the *t*-butoxycarbonyl peptides. The results of the dehydrohydantoin (**7**) formation reaction, which occurred *via* reaction of the DHA peptides produced by the reaction with tertiary amines, agreed very well with the results of the β-elimination reaction of O-activated Z-Ser- or Z-Thr- derivatives found by Campbell and Behr,[8)] us,[9)] and, Shin *et al.*[10)] Thus the benzyloxycarbonyl group of the aziridine is more labile than the *t*-butoxycarbonyl group in the basic conditions, that is, Z-Azy-Gly-OBzl (**5a**) and Z-3-MeAzy-Gly-OBzl (**5c**) isomerized more easily than Boc-Azy-Gly-OBzl (**5b**) and Boc-3-MeAzy-Gly-OBzl (**5d**) as shown in Table 3. The benzyloxycarbonyl group attached to the unsubstituted aziridinecarboxylic acid (**5a**) seemed to be very labile and Z-⊿Ala-Gly-OBzl could not be isolated after the reaction of **5a** with tertiary amine, even in Et_3N.

From the isomerization reaction of Azy and 3-MeAzy described above, it is concluded that Azy and 3-MeAzy has a distinctly different reactivity against tertiary amines and the isomerization by the tertiary amines, which can be used to the selective synthesis of DHA peptides, differs from that by NaI or the synthesis of DHA peptides *via* β-elimination of β-hydroxy α-amino acid.

Experimental

Uncorrected melting points are reported. The homogeneity of the products was checked by thin-layer chromatography on silica-gel plates. The optical rotations were determined at the D line on a Perkin-Elmer 141 polarimeter. The NMR spectra were obtained with a Hitachi R20B high-resolution NMR spectrometer, the chemical shifts being obtained using TMS as the internal reference. All the *N*-aminoacyl Azy and 3-MeAzy peptides used in this study were synthesized by the method described in literature,[6,7)] and their properties and yield are summarized in Table 1.

(2S)-Z-Azy-Gly-OBzl (5a). To a solution of (2*S*)-H-Azy-Gly-OBzl[11)] (1.63 g, 6.96 mmol) and Et_3N (0.97 ml, 6.96 mmol) in $CHCl_3$ (15 ml), was added Z-ON[1)] (1.95 g, 6.96 mmol) with stirring at 0 °C. After being stirred overnight at 25 °C, the solvent was removed *in vacuo* and the residue was dissolved in ethyl acetate. The ethyl acetate solution was washed with 10% citric acid, 1 M $NaHCO_3$ and water, and dried over Na_2SO_4, concentrated *in vacuo*. The residue was crystallized from ethyl acetate–hexane, 1.53 g (60%) of **5a** was obtained, mp 109—110 °C, $[\alpha]_D^{23}$ −50.6° (*c* 1.0, MeOH). NMR ($CDCl_3$) δ: 2.38 (1H q, J_{gem}=0.8 Hz, J_{trans}=3.5 Hz, Azy β-proton), 2.53 (1H q, J_{gem}=0.8 Hz, J_{cis}=6.3 Hz, Azy β-proton), 3.07 (1H q, J_{trans}=3.5 Hz, J_{cis}=6.3 Hz, Azy α-proton). Z-ON can be replaced with Z-Cl.[1)]

Found: C, 65.17; H, 5.50; N, 7.71%. Calcd for $C_{20}H_{20}O_5N_2$: C, 65.21; H, 5.47; N, 7.60%.

(2S)-Boc-Azy-Gly-OBzl (5b). To a solution of (2*S*)-H-Azy-Gly-OBzl[11)] (4.0 g, 17.1 mmol) and Et_3N (2.38 ml, 17.1 mmol) in $CHCl_3$ (50 ml), was added Boc-ON[1)] (4.63 g, 18.8 mmol) with stirring at 0 °C. After the reaction mixture had been worked up as described above, the product was crystallized from ethyl acetate–hexane, 3.51 g (61.3%) of **5b** was obtained. mp 71.0—72.5 °C, $[\alpha]_D^{23}$ −80.4° (*c* 1.0, MeOH). NMR ($CDCl_3$) δ: 2.30 (1H q, J_{gem}=0.8 Hz, J_{trans}=3.8 Hz, Azy β-proton), 2.49 (1H q, J_{gem}=0.8 Hz, J_{cis}=6.6 Hz, Azy β-proton), 3.03 (1H q, J_{trans}=3.8 Hz, J_{cis}=6.6 Hz, Azy α-proton).

Found: C, 61.22; H, 6.85; N, 8.35%. Calcd for $C_{17}H_{22}O_5N_2$: C, 61.07; H, 6.63; N, 8.34%.

(2S, 3S)-Z-3-MeAzy-Gly-OBzl (5c). To a solution of (2*S*, 3*S*)-H-3-MeAzy-Gly-OBzl[7)] (1.87 g, 7.54 mmol) and Et_3N (1.05 ml, 7.54 mmol) in $CHCl_3$ (15 ml), was added

Z–ON[1] (1.95 g, 7.54 mmol) with stirring at 0 °C. The reaction mixture was stirred overnight and worked up as described above. The product was crystallized from ethyl acetate–hexane, 2.10 g (72.8%) of **5c** was obtained, mp 62—64 °C, $[\alpha]_D^{23}$ −63.2° (*c* 1.0, MeOH). NMR ($CDCl_3$) δ: 1.28 (3H d, J=5.5 Hz, CH_3), 2.79 (1H m, 3-MeAzy, β-proton), 3.14 (1H d, J=7.0 Hz, 3-MeAzy, α-proton). Z–ON can be replaced with Z–Cl.

Found: C, 65.96; H, 5.83; N, 7.42%. Calcd for $C_{21}H_{22}O_5N_2$: C, 65.96; H, 5.80; N, 7.33%.

(2S, 3S)-Boc-3-MeAzy-Gly-OBzl (5d). To a solution of (2*S*, 3*S*)-H-3-MeAzy-Gly-OBzl[7] (1.25 g, 5.06 mmol) and Et_3N (0.70 ml, 5.06 mmol) in $CHCl_3$ (15 ml), was added Boc–ON[1] (1.40 g, 6.07 mmol) with stirring at 0 °C. The reaction mixture was stirred overnight and worked up as described above. The product was crystallized from ethyl acetate–hexane, 1.38 g (78.5%) of **5d** was obtained, mp 89.5—90.0 °C, $[\alpha]_D^{23}$ −70.0° (*c* 1.0, MeOH). NMR ($CDCl_3$) δ: 1.27 (3H d, J=5.5 Hz, CH_3), 2.74 (1H m, 3-MeAzy β-proton), 3.09 (1H d, J=6.4 Hz, 3-MeAzy α-proton).

Found: C, 62.21; H, 6.88; N, 8.01%. Calcd for $C_{18}H_{24}O_5N_2$: C, 62.06; H, 6.94; N, 8.04%.

Z–Gly–ΔAla–NHBzl (3b). General Isomerization Procedure of Azy with Et_3N: A solution of **1b** (100 mg, 0.27 mmol) and Et_3N (0.08 ml, 0.54 mmol) in $CHCl_3$ (5 ml) was stirred at 35 °C for 3 h. After the solvent had been removed *in vacuo*, the residue was dissolved in ethyl acetate. The ethyl acetate solution was washed with 10% citric acid and water, and then dried over Na_2SO_4, concentrated *in vacuo*. After the obtained residue was purified by the silica-gel column chromatography, the product was crystallized from $CHCl_3$–ether–hexane, 84.3 mg (84.3%) of **3b** was obtained, mp 117.5—118.5 °C.

Z–Gly–ΔAba–Gly–OBzl (4d). General Isomerization Procedure of 3-MeAzy with Dabco: A solution of **2d** (200 mg, 0.45 mmol) and Dabco (102 mg, 0.91 mmol) in $CHCl_3$ (5 ml) was stirred at 35 °C for 24 h. After the reaction mixture had been worked up as described above, the residue was crystallized from ethyl acetate–hexane, 174 mg (87%) of **4d** was obtained, mp 101—102 °C [lit, mp 102—104 °C[4]].

Benzyl 5-Methylenehydantoin-3-acetate (7a). Using Et_3N: A solution of **5a** (200 mg, 0.54 mmol) snd Et_3N (0.15 ml, 1.09 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 12 h. After the reaction mixture had been worked up as described above, the residue was purified with silica-gel column chromatography and was crystallized from ethyl acetate–ether–hexane, 105 mg (75%) of **7a** was obtained, mp 171—172 °C. NMR ($CDCl_3$) δ: 4.32 (2H s), 4.92, (1H d, J=1.8 Hz), 5.15, 5.17 (4H 2s), 5.42 (1H d, J=1.8 Hz), 7.32 (5H s), 8.35 (1H bs).

Found: C, 60.05; H, 4.72; N, 10.72%. Calcd for $C_{13}H_{12}O_4N_2$: C, 59.99; H, 4.65; N, 10.77%.

Z–ΔAla–Gly–OBzl (6a) could not be prepared by this procedure.

Using Dabco: A solution of **5a** (200 mg, 0.54 mmol) and Dabco (121 mg, 1.08 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 6 h. After the reaction mixture had been worked up as described above, 112 mg (80%) of **7a** was obtained. **6a** could not be prepared.

Boc–ΔAla–Gly–OBzl (6b). Using Et_3N: A solution of **5b** (100 mg, 0.29 mmol) and Et_3N (0.08 ml, 0.58 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 24 h. After the reaction mixture had been worked up as described above, 95 mg (95%) of **6b** was obtained as an oily material. NMR ($CDCl_3$) δ: 1.48 (9H s), 4.12 (2H d, J=5.0 Hz) 5.15 (1H m) 5.18 (2H s), 6.00 (1H d, J=1.8 Hz), 6.78 (1H bt), 7.25 (1H bs), 7.32 (5H s).

Found: C, 61.15; H, 6.72; N, 8.28%. Calcd for $C_{17}H_{22}O_5N_2$: C, 61.07; H, 6.63; N, 8.34%. **7b** could not be prepared.

Using Dabco: A solution of **5b** (300 mg, 0.86 mmol) and Dabco (194 mg, 1.73 mmol) in $CHCl_3$ (5 ml) was stirred at 35 °C for 6 h. After the reaction mixture had been worked up as described above, 300 mg (100%) of **6b** was obtained as an oily material. **7b** could not be prepared.

Z–ΔAba–Gly–OBzl (6c) and Benzyl 5-Ethylidenehydantoin-3-acetate (7c). Using Dabco: A solution of **5c** (200 mg, 0.5 mmol) and Dabco (112 mg, 1 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 3 d. After the reaction mixture had been worked up as described above, the crude product of two components was subjected to silica-gel column chromatography developed by $CHCl_3$, yielding 136 mg (68%) of **6c**, mp 99—100 °C, and 38 mg (28%) of **7c**, mp 186—186.5 °C. **6c**: NMR ($CDCl_3$) δ: 1.70 (3H d, J=7.0 Hz), 4.16 (2H d, J=5.5 Hz), 5.12 (2H s), 5.20 (2H s), 6.52 (1H q, J=7.0 Hz), 6.76 (1H bs), 7.30 (10H s), 7.00 (1H bs), 7.15 (1H bs). **7c**: NMR ($CDCl_3$) δ: 1.83 (3H d, J=7.5 Hz), 4.35 (2H s), 5.19 (2H s), 5.98 (1H q, J=7.5 Hz), 7.32 (5H s), 9.05 (1H bs).

6c; Found: C, 66.02; H, 5.86; N, 7.23%. Calcd for $C_{21}H_{22}O_5N_2$: C, 65.96; H, 5.80; N, 7.33%.

7c; Found: C, 61.28; H, 5.20; N, 10.32%. Calcd for $C_{14}H_{14}O_4N_2$: C, 61.31; H, 5.15; N, 10.21%.

Using Et_3N: A solution of **5c** (200 mg, 0.5 mmol) and Et_3N (0.14 ml, 1 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 7 d. No reaction occurred and only **5c** was recovered.

Boc–ΔAba–Gly–OBzl (6d). Using Dabco: A solution of **5d** (200 mg, 0.57 mmol) and Dabco (128 mg, 1.14 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 4 d. After the reaction mixture had been worked up as described above, 170 mg (85%) of **6d** was obtained, mp 119.5—120.5 °C. NMR ($CDCl_3$) δ: 1.45 (9H s), 1.75 (3H d, J=7.0 Hz), 4.14 (2H d, J=5.5 Hz), 5.20 (2H s), 6.49 (1H q, J=7.0 Hz), 6.69 (1H bs), 7.34 (5H s), 7.28 (1H bs).

Found: C, 62.18; H, 6.81; N, 8.12%. Calcd for $C_{18}H_{24}O_5N_2$: C, 62.06; H, 6.94; N, 8.04%.

7d could not be prepared.

Using Et_3N: A solution of **5d** (100 mg, 0.29 mmol) and Et_3N (0.08 ml, 0.58 mmol) in $CHCl_3$ (3 ml) was stirred at 35 °C for 7 d. No reaction occurred and only **5d** was recovered.

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