Monatshefte für Chemie 133, 1077–1084 (2002)

Monatshefte für Chemie
Chemical Monthly

A Novel Preparation of 2-Aminocyclopentanecarboxamides

Péter Csomós[1], **Gábor Bernáth**[1,2] and **Ferenc Fülöp**[1,*]

[1] Institute of Pharmaceutical Chemistry, University of Szeged, H-6720 Szeged, Hungary
[2] Research Group for Heterocyclic Chemistry of the Hungarian Academy of Sciences and the University of Szeged, H-6720 Szeged, Hungary

Summary. Different syntheses of *cis*- and *trans*-2-aminocyclopentanecarboxamides were studied. A convenient and effective method was devised for the preparation of *cis*-2-aminocyclopentanecarboxamide derivatives starting from the readily available 6-*tert*-butoxycarbonyl-6-azabicyclo[3.2.0]heptan-7-one.

Keywords. β-Amino acids; *cis-trans* Isomerization; β-Lactams; Small rings.

Introduction

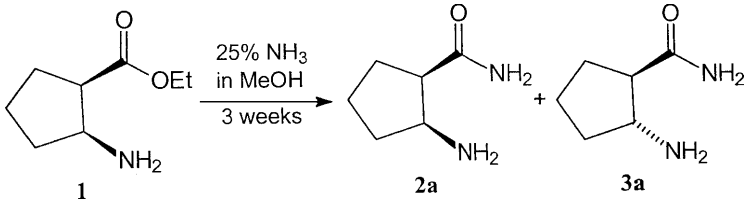
In recent years, a number of cyclic β-aminocarboxylic acid derivatives have been synthesized. Some of them have useful pharmacological effects, and they are widely used synthons for the preparation of saturated 1,3-heterocycles [1]. Various *cis*- and *trans*-2-aminocycloalkanecarboxamides have been produced in order to examine the relations between stereochemistry and pharmacological activity [2, 3] by the mixed anhydride method from N-protected 2-aminocycloalkanecarboxylic acids [3–8] or by amidation of alkyl 2-aminocycloalkanecarboxylates [9, 10].

The discovery of the antimycotic cispentacin, (-)-(1*R*,2*S*)-2-aminocyclopentanecarboxylic acid, among the natural amino acids aroused interest in investigations of cyclopentane derivatives [11], and the synthesis, transformations, and some of the biological features of 2-aminocyclopentanecarboxylic acids have been reviewed [12, 13]. During our investigations relating to cispentacin [13, 14], our aim was to prepare carboxamide derivatives of racemic *cis*- and *trans*-2-aminocyclopentanecarboxylic acids and to study the ring opening of the starting 6-azabicyclo[3.2.0]heptan-7-one and its N-*tert*-butoxycarbonyl derivative.

Results and Discussion

A simple and mild amidation procedure has been developed earlier in our laboratory for the preparation of 2-aminocyclohexanecarboxamides starting from the corresponding ethyl 2-aminocyclohexanecarboxylates [10]. Surprisingly, with

* Corresponding author. E-mail: fulop@pharma.szote.u-szeged.hu



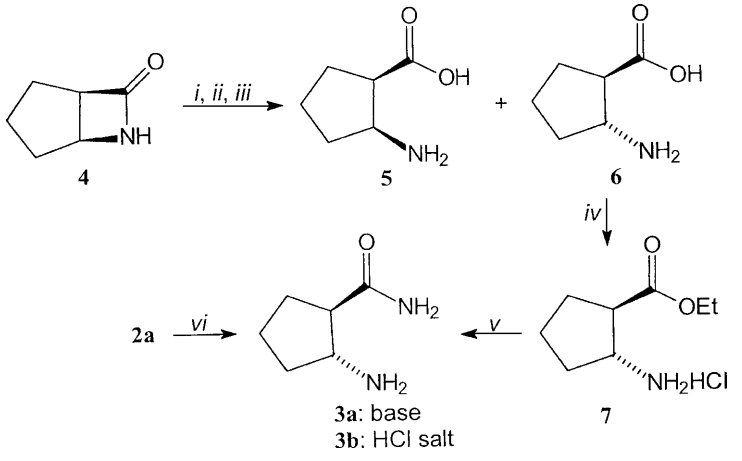
Scheme 1

the same method (25% methanolic ammonia at room temperature) the homologue ethyl *cis*-2-aminocyclopentanecarboxylate **1** resulted in a mixture of *cis*-2-aminocyclopentanecarboxamide (**2a**) and the corresponding *trans* isomer **3a** (Scheme 1). The ^{1}H NMR spectrum of the crude product revealed a 4:1 mixture of **2a** and **3a**.

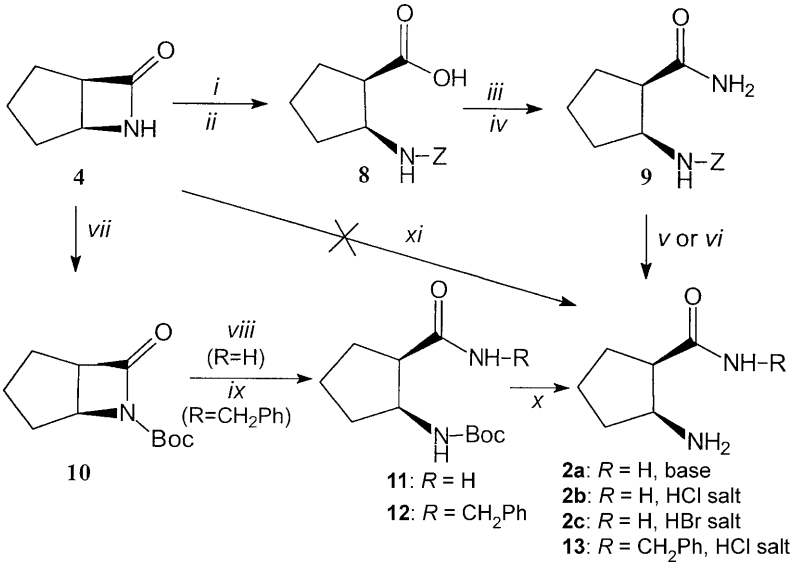
This fact led us to reinvestigate our earlier results; however, in accordance with those findings [10], no isomerization was observed in the amidation of ethyl *cis*- and *trans*-2-aminocyclohexanecarboxylates.

The isomerization of **2a** was also investigated. In the presence of 0.5 equivalents of sodium methoxide at 150°C, a mixture of **2a** and **3a** was obtained in a ratio of 1:9. From this mixture, the hydrochloride was prepared; it was recrystallized from ethanol/diethyl ether, furnishing **3b** (Scheme 2).

When 6-azabicyclo[3.2.0]heptan-7-one (**4**), readily available by cycloaddition of chlorosulfonyl isocyanate to cyclopentene [13, 16], was refluxed in dry ethanol with sodium ethoxide and the intermediate esters were hydrolyzed, *cis*- and *trans*-2-aminocyclopentanecarboxylic acids **5** and **6** were obtained in a ratio of 1:9. This mixture was recrystallized from ethanol and water, affording **6** in moderate overall yield. Esterification of *trans*-2-aminocyclopentanecarboxylic acid provided the hydrochloride of ethyl *trans*-2-aminocyclopentanecarboxylate (**7**). The amidation of **7** in 25% methanolic ammonia at room temperature gave *trans*-2-aminocyclopentanecarboxamide **3a** as a single product (Scheme 2).



Scheme 2. *i*) 1.2 equiv. NaOEt, EtOH, reflux, 12 h; *ii*) 18% HCl, reflux, 24 h; *iii*) ion-exchange chromatography, recrystallization; *iv*) $SOCl_2$, EtOH, <-10°C, r.t., 3 h, reflux, 1 h; *v*) 25% NH_3/MeOH, 3 weeks; *vi*) 150°C, 0.5 equiv. NaOEt, 10 min, purification as HCl salt by recrystallization



Scheme 3. *i*) conc. HCl, r.t., 1 h; *ii*) *Z*–Cl, $NaOH/H_2O$; *iii*) ethyl chloroformate, Et_3N, toluene, $<-10°C$; *iv*) 25% NH_3/MeOH, $<-10°C$; *v*) HBr/AcOH, r.t., 1 h; *vi*) 10% Pd/C, H_2, MeOH, 1 atm, 40°C; *vii*) Boc_2O, *DMAP*, CH_2Cl_2, r.t., 17 h; *viii*) 25% NH_3/MeOH, 4°C, 12 h; *ix*) benzylamine, dry toluene, 24 h reflux; *x*) 3 *M* HCl/EtOH, r.t., 2 h; *xi*) 25% NH_3/MeOH, r.t., 3 weeks

For the preparation of amide **2a**, a 0.1 mol scale method was devised involving the mixed anhydride procedure (Scheme 3). Compound **2a** has also been prepared by this method earlier [6], but no experimental details and physical data were given. The *Z*-protected amino acid **8** reacted with ethyl chloroformate to give the anhydride which was allowed to react with 2 equivalents of ammonia in methanol. The protective *Z*-group was eliminated with 33% hydrobromic acid in glacial acetic acid or by hydrogenolysis with 10% palladium on activated charcoal.

No reaction was observed between β-lactam **4** and methanolic ammonia at room temperature. Although activated monocyclic derivatives can be opened with different amines [15], it was argued that by activating the lactam ring with the protecting group *Boc* the amidation reaction might be achieved under mild conditions. The reaction of the N-*Boc* derivative of the bicyclic β-lactam **10** with 25% methanolic ammonia was complete after 12 h at 4°C, resulting in the *cis*-carboxamide **11**. In this reaction no isomerization was observed. The *Boc* group was easily removed by 3 *M* hydrogen chloride in dry ethanol at room temperature, affording the hydrochloride **2b**.

When **10** was reacted with benzylamine at elevated temperature, benzamide **12** was formed in good yield. After removal of the *Boc* group, the benzamide **13** was obtained.

Experimental

Melting points were determined on a Kofler melting point apparatus and are uncorrected. 6-Azabicyclo[3.2.0]heptan-7-one (**4**) was prepared by 1,2-dipolar cycloaddition of chlorosulfonyl isocyanate to cyclopentene; from this, *cis*-2-aminocyclopentanecarboxylic acid hydrochloride was obtained by acidic hydrolysis [16].

The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or D_2O solution in 5 mm tubes at room temperature on a Bruker Avance DRX-400 spectrometer at 400.13 (^{1}H) and 100.61 (^{13}C) MHz, utilizing the deuterium signal of the solvent for the field-frequency lock and *TMS* as internal standard. Elemental analyses were found to agree satisfactorily with the calculated data.

trans-2-Aminocyclopentanecarboxylic acid (**6**; $C_6H_{12}NO_2$)

To a solution of 3.3 g **4** (30 mmol) in 50 cm^3 dry EtOH, 2.5 g EtONa (36 mmol) were added, and the mixture was refluxed for 12 h. The solvent was evaporated, and the residue was dissolved in 50 cm^3 18% HCl and refluxed for 24 h. After evaporation to dryness, the residue was dissolved in 30 cm^3 MeOH, and the inorganic salt was filtered off. The MeOH was evaporated, and the residue was purified on Varion KS ion-exchange resin. The ^{1}H NMR spectrum of the crude product revealed the presence of *cis*- and *trans*-2-aminocyclopentanecarboxylic acids **5** and **6** in a 1:9-ratio. This mixture was recrystallized, affording 3.04 g *trans*-2-aminocyclopentanecarboxylic acid **6** (78%).

Colourless crystals; m.p.: 262°C (90% EtOH; Ref. [17]: m.p.: 239–240°C); ^{1}H NMR (D_2O): $\delta = 1.65$–2.20 (m, $3 \times CH_2$), 2.68 (m, H-1), 3.77 (m, H-2) ppm; ^{13}C NMR (D_2O): $\delta = 23.0$ (C4), 29.7 (C5), 30.6 (C3), 51.9 (C1), 55.3 (C2), 181.7 (COOH) ppm.

Ethyl trans-2-aminocyclopentanecarboxylate hydrochloride (**7**; $C_8H_{16}ClNO_2$)

Thionyl chloride (0.56 cm^3, 7.6 mmol) was added dropwise under stirring to 7 cm^3 dry EtOH below −10°C, followed by 0.9 g (7 mmol) **6** in one portion, and the mixture was stirred for 30 min at 0°C. After stirring for additional 3 h at room temperature, the mixture was refluxed for 1 h and evaporated. To the brown oily residue, diethyl ether was added, and upon standing at −18°C 1.06 g of a white crystalline powder was obtained (78%).

M.p.: 67–72°C (EtOAc); ^{1}H NMR (D_2O): $\delta = 1.26$ (t, $J = 7.2$, CH_2CH_3), 1.62–2.32 (m, $3 \times CH_2$), 2.96 (m, H-1), 3.90 (m, H-2), 4.20 (q, $J = 7.2$, CH_2CH_3) ppm; ^{13}C NMR (D_2O): $\delta = 13.7$ (CH_3), 23.1 (C4), 29.0 (C5), 30.9 (C3), 48.8 (C1), 54.3 (C2), 62.8 (CH_2CH_3), 175.7 (COO) ppm.

trans-2-Aminocyclopentanecarboxamide (**3a**; $C_6H_{12}N_2O$)

Ethyl *trans*-2-aminocyclopentanecarboxylate (**7**; 0.46 g, 2.93 mmol) was dissolved in 10 cm^3 of 25% ammonia in dry MeOH. The solution was kept at room temperature for 3 weeks. The solvent was then evaporated, and the white crystalline powder was recrystallized resulting in 0.28 g **3a** (74%).

Colourless crystals; m.p.: 123–124°C (EtOAc); ^{1}H NMR ($CDCl_3$): $\delta = 1.32$–2.22 ($3 \times CH_2$), 1.59 (bs, $CHNH_2$), 2.25 (m, H-1), 3.24 (m, H-2), 5.50 (bs, $CONH_2$), 7.05 (bs, $CONH_2$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 22.4$ (C4), 27.2 (C5), 37.9 (C3), 53.3 (C1), 58.0 (C2), 178.0 ($CONH_2$) ppm.

cis-2-Benzyloxycarbonylaminocyclopentanecarboxylic acid (**8**; $C_{14}H_{17}NO_4$)

cis-2-Aminocyclopentanecarboxylic acid hydrochloride (49.7 g, 0.3 mol) was dissolved under stirring in 120 cm^3 10% NaOH, and a few crystals of phenolphthalein were added. The solution was cooled with ice-H_2O, and 61.4 g benzyl chloroformate (0.36 mol) and 10% NaOH were then added in parallel dropwise during 1 h; care was taken that the reaction mixture always remained slightly alkaline. Stirring was continued at 0°C for 1 h and for further 4 h at room temperature. The excess benzyl chloroformate was next removed from the mixture by extraction with 100 cm^3 diethyl ether. The aqueous phase was cooled in ice and acidified to *pH* 2 with 18% HCl. The oil that separated was extracted with 3×200 cm^3 $CHCl_3$. The organic phase was dried (Na_2SO_4), filtered, and evaporated. Trituration of the oily residue with *n*-hexane gave 55.3 g **8** as a white crystalline powder (70%). After filtration, the powder was used for the next step. A small sample was purified by recrystallization from diisopropyl ether.

Colourless crystals; m.p.: 92–94°C; ^{1}H NMR ($CDCl_3$): $\delta = 1.48$–2.12 ($3 \times CH_2$), 3.03 (m, H-1), 4.26 (m, H-2), 5.11 (m, NCH_2Ph), 7.20–7.48 (m, $5 \times CH$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 22.6$, 23.3 (C4), 28.1, 28.5 (C5), 32.2, 32.6 (C3), 47.1 (C1), 54.9, 55.9 (C2), 67.5, 68.3 (OCH_2Ph), 128.8, 129.2 (Ph, C2′–C6′), 137.1 (Ph, C1′), 156.7, 158.8 (NHCOO), 179.0, 179.9 (COOH) ppm.

cis-2-Benzyloxycarbonylaminocyclopentanecarboxamide (**9**; $C_{14}H_{18}N_2O_3$)

To a salt-ice cooled, intensively stirred solution of 31.6 g **8** (0.12 mol) and 12.1 g triethylamine (0.12 mol) in 400 cm^3 dry toluene, 13.0 g ethyl chloroformate (0.12 mol) was added dropwise below −10°C. After 15 min at −10°C, 16.3 g 25% ammonia in dry MeOH (0.24 mol NH_3) was added in a steady stream (during the addition, the reaction temperature rose to −5°C). The reaction mixture was stirred at −10°C for 3 h and then allowed to stand at room temperature overnight. The crystals that precipitated were filtered off and washed 4 times with 100 cm^3 of dist. H_2O and 2 times with 100 cm^3 toluene. The obtained 21.4 g of white crystalline powder (68%) were used for the next step. A small sample was further purified by recrystallization.

Colourless crystals; m.p.: 166–168°C (MeOH); ^{1}H NMR ($CDCl_3$): $\delta = 1.45$–2.15 (m, $3 \times CH_2$), 2.89 (m, H-1), 4.19 (m, H-2), 5.07 (AB, $J = 12$ Hz, OCH_2Ph), 5.32 (bs, $CONH_2$), 5.45 (bs, CHN*H*CO), 5.60 (bs, $CONH_2$), 7.27–7.43 (m, $5 \times CH$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 23.3$ (C4), 28.71 (C5), 33.10 (C3), 47.68 (C1), 55.22 (C2), 67.32 (OCH_2Ph), 128.75, 129.15 (Ph, C2′–C6′), 137.23 (Ph, C1′), 157.08 (NHCOO), 176.73 ($CONH_2$) ppm.

cis-2-Aminocyclopentanecarboxamide (**2a**; $C_6H_{12}N_2O$)

cis-2-Benzyloxycarbonylaminocyclopentanecarboxamide (**9**; 20 g, 0.076 mol) were dissolved in 600 cm^3 MeOH and hydrogenated in the presence of 2 g 10% Pd/C at atmospheric pressure at 40°C until the indicated amount of hydrogen was absorbed (8 h). The catalyst was removed by filtration. After evaporation, **2a** was obtained as a white crystalline powder (7.6 g, 78%) which was purified by recrystallization.

Colourless crystals; m.p.: 135–137°C (EtOAc); ^{1}H NMR ($CDCl_3$): $\delta = 1.51$–2.08 (6H, $3 \times CH_2$), 1.56 (2H, bs, $CHNH_2$), 2.62 (1H, m, H-1), 3.56 (1H, m, H-2), 5.73 (1H, bs, $CONH_2$), 6.74 (1H, bs, $CONH_2$) ppm, ^{13}C NMR ($CDCl_3$): $\delta = 22.4$ (C4), 26.1 (C5), 34.1 (C3), 50.3 (C1), 54.6 (C2), 179.8 ($CONH_2$) ppm.

trans-2-Aminocyclopentanecarboxamide hydrochloride (**3b**; $C_6H_{13}ClN_2O$)

cis-2-Aminocyclopentanecarboxamide (**2a**; 1.1 g, 8.6 mmol) was thoroughly mixed with sodium methoxide (0.23 g, 4.3 mmol), and the mixture was maintained at 150°C for 10 min. After cooling to room temperature, the reaction mixture was washed with 3×25 cm^3 hot ethyl acetate and filtered. After evaporation of the solvent, the ^{1}H NMR spectrum of the crude product revealed **3a** and **2a** in a ratio of 9:1. The hydrochloride of this mixture was prepared. Upon trituration of the residue with ethyl acetate and EtOH, 0.45 g of a white crystalline powder were obtained. The hydrochloride **3b** was obtained by recrystallization (yield 32%).

Colourless crystals; m.p.: 198–201°C (90% EtOH); ^{1}H NMR (D_2O): $\delta = 1.62$–2.38 ($3 \times CH_2$), 2.88 (m, H-1), 3.86 (m, H-2) ppm; ^{13}C NMR (D_2O): $\delta = 23.5$ (C4), 30.6 (C5), 30.9 (C3), 49.4 (C1), 54.3 (C2), 178.5 ($CONH_2$) ppm.

cis-2-Aminocyclopentanecarboxamide hydrobromide (**2c**; $C_6H_{13}BrN_2O$)

cis-2-Benzyloxycarbonylaminocyclopentanecarboxamide (**9**; 2.62 g, 10 mmol) was added to 8.8 cm^3 33% HBr in glacial acetic acid. The solution was stirred for 1 h, during which time a precipitate was

formed. To the suspension, 20 cm^3 diethyl ether were added, and 1.80 g of white crystalline powder were filtered off (86%), washed with diethyl ether, and purified by recrystallization.

Colourless crystals; m.p.: 338–233°C ($EtOH/Et_2O$); ^1H NMR (D_2O): $\delta = 1.70–2.22$ ($3 \times CH_2$), 3.04 (m, H-1), 3.87 (m, H-2) ppm; ^{13}C NMR (D_2O): $\delta = 21.9$ (C4), 28.5 (C5), 30.6 (C3), 45.7 (C1), 53.8 (C2), 177.9 ($CONH_2$) ppm.

6-tert-Butoxycarbonyl-6-azabicyclo[3.2.0]heptan-7-one (**10**; $C_{11}H_{17}NO_3$)

6-Azabicyclo[3.2.0]heptan-7-one (**4**; 3.3 g, 30 mmol) was dissolved in 20 cm^3 dry CH_2Cl_2. The solution was stirred, and 0.37 g 4-dimethylaminopyridine was added, followed by 7.2 g Boc_2O (33 mmol). After stirring at room temperature for 5 h, the reaction mixture was left overnight. The brownish reaction mixture was then extracted with brine and dried (Na_2SO_4). Evaporation left a pale-yellow oil which was passed over a short column, with toluene:ethyl acetate = 4:1 as eluent. After evaporation, 5.26 g of **10** were obtained as a white crystalline powder upon trituration with *n*-hexane (83%).

Colourless crystals; m.p.: 47–50°C (i-Pr_2O); ^1H NMR ($CDCl_3$): $\delta = 1.36–2.25$ ($3 \times CH_2$), 1.52 (s, $3 \times CH_3$), 3.47 (m, H-1), 4.33 (m, H-2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.1$ (C3), 25.9 (C2), 28.6 ($3 \times CH_3$), 29.4 (C4), 54.7 (C1), 58.0 (C5), 83.31 ($OC(CH_3)_3$), 148.0 (NCOO), 168.2 (CON) ppm.

cis-2-tert-Butoxycarbonylaminocyclopentanecarboxamide (**11**; $C_{11}H_{20}N_2O_3$)

6-*tert*-Butoxycarbonyl-6-azabicyclo[3.2.0]heptan-7-one (**10**; 3 g, 14.2 mmol) was dissolved in 30 cm^3 25% solution of NH_3 in dry MeOH. The reaction mixture was allowed to stand at 4°C for 12 h and was then evaporated, first at room temperature and then on a 60°C water bath. The white crystalline powder obtained was purified by recrystallization (2.50 g, yield 77%).

Colourless crystals; m.p.: 163–166°C (EtOAc); ^1H NMR ($CDCl_3$): $\delta = 1.32–2.15$ ($3 \times CH_2$), 1.42 (s, $3 \times CH_3$), 2.92 (m, H-1), 4.14 (m, H-2) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 23.3$ (C4), 28.5 (C5), 29.0 ($3 \times CH_3$), 33.2 (C4), 47.9 (C1), 54.8 (C2), 80.1 ($OC(CH_3)_3$), 156.7 (NHCOO), 176.9 ($CONH_2$) ppm.

cis-2-Aminocyclopentanecarboxamide hydrochloride (**2b**; $C_6H_{13}ClN_2O$)

cis-2-*tert*-Butoxycarbonylaminocyclopentanecarboxamide (**11**; 1.8 g, 7.9 mmol) was dissolved in 20 cm^3 3 *M* HCl solution in EtOH. The reaction mixture was left to stand at room temperature for 2 h and then evaporated at room temperature. After evaporation, 1.10 g **2b** were obtained as a white crystalline powder (85%) which was purified by recrystallization.

Colourless crystals; m.p.: 243°C ($EtOH/Et_2O$); ^1H NMR (D_2O): $\delta = 1.70–2.22$ ($3 \times CH_2$), 3.04 (m, H-1), 3.87 (m, H-2) ppm; ^{13}C NMR (D_2O): $\delta = 21.9$ (C4), 28.4 (C5), 30.6 (C3), 45.7 (C1), 53.8 (C2), 177.9 ($CONH_2$) ppm.

cis-N-Benzyl-2-tert-butoxycarbonylaminocyclopentanecarboxamide (**12**; $C_{18}H_{26}N_2O_3$)

6-*tert*-Butoxycarbonyl-6-azabicyclo[3.2.0]heptan-7-one (**10**; 1.59 g, 7.5 mmol) was dissolved in 50 cm^3 dry toluene, and 0.81 g benzylamine (7.5 mmol) and a catalytic amount of *p*-toluenesulfonic acid were added. The mixture was refluxed for 24 h, extracted with 5% $NaHCO_3$ solution, dried (Na_2SO_4), and evaporated. The 2.20 g resulting white crystalline powder (92%) were purified by recrystallization.

Colourless crystals; m.p.: 146–148°C (EtOAc); ^{1}H NMR ($CDCl_3$): $\delta = 1.40$ (s, $3 \times CH_3$), 1.48–2.14 ($3 \times CH_2$), 2.82 (m, H-1), 4.11 (qui, $J = 7.8$, H-2), 4.41 (AB system, $J = 8$ Hz, coup. with NH, NHCH_2Ph), 5.10 (b, CONHCH$_2$), 6.05 (bs, NHCOO), 7.20–7.38 (m, $5 \times$ CH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 23.3$ (C4), 28.8 (C5), 29.1 ($3 \times CH_3$), 33.3 (C3), 44.3 (NCH_2Ph), 48.7 (C1), 54.9 (C2), 79.9 (OC(CH$_3$)$_3$), 128.1 (Ph, C4′), 128.4 (Ph, C3′, C5′), 129.4 (Ph, C2′, C6′) 138.9 (Ph, C1′), 156.6 (NHCOO), 174.3 (CHCON) ppm.

cis-N-Benzyl-2-aminocyclopentanecarboxamide (**13**; $C_{13}H_{19}ClN_2O$)

cis-N-Benzyl-2-*tert*-butoxycarbonylaminocyclopentanecarboxamide (**12**; 0.7 g, 2.2 mmol) was dissolved in a 3 *M* HCl solution in 20 cm^3 dry EtOH. The reaction mixture was left to stand at room temperature for 2 h and evaporated at room temperature. The 0.44 g obtained white crystalline powder (78%) were purified by recrystallization.

Colourless crystals; m.p.: 150–153°C (*i*-Pr_2O); ^{1}H NMR ($CDCl_3$): $\delta = 1.70$–2.28 ($3 \times CH_2$), 3.04 (m, H-1), 3.87 (m, H-2), 4.41 (AB, $J = 15.3$, NHCH_2Ph), 5.10 (b, CONHCH$_2$), 7.34–7.45 (m, $5 \times$ CH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 21.9$ (C4), 28.7 (C5), 30.6 (C3), 43.3 (NCH_2Ph), 46.1 (C1), 53.9 (C2), 127.6 (Ph, C3′, C5′), 127.9 (Ph, C4′), 129.3 (Ph, C2′, C6′), 138.3 (Ph, C1′), 175.0 ($CONH_2$) ppm.

Acknowledgements

We express thanks to the Hungarian Scientific Research Foundation for grants OTKA F032355 and T030452.

References

[1] Fülöp F, Bernáth G, Pihlaja K (1998) Adv Heterocycl Chem **69**: 349
[2] Bernáth G, Gera L, Göndös G, Pánovics I, Ecsery Z (1976) Acta Chim Acad Sci Hung **89**: 61
[3] Gera L, Göndös G, Bernáth G (1979) Acta Chim Acad Sci Hung **99**: 175; Bernáth G, Gera L, Göndös G, Kovács K, Jánváry I, Sebestyén L, Ecsery Z, Hermann J (1977) Ger Offen 2,624,290; Chem Abstr (1977) **87**: 102009
[4] Göndös G, Gera L, Wittmann G, Baláspiri L, Kovács K (1987) Acta Chim Acad Sci Hung **124**: 187
[5] Göndös G, Szécsényi I, Dombi G (1991) Liebigs Ann Chem 591
[6] Ohki H, Inamoto Y, Kawabwta K, Kamimura T, Sakane K (1991) J Antibiotics **44**: 546
[7] Yamazaki T, Zhu Y-F, Probstl A, Chadha RK, Goodman M (1991) J Org Chem **56**: 6644
[8] Szakonyi Z, Fülöp F, Bernáth G, Török G, Péter A (1998) Tetrahedron Asymm **9**: 993
[9] Armarego WLF, Kobayashi T (1969) J Chem Soc (C) 1635
[10] Pihlaja K, Fülöp F, Mattinen J, Bernáth G (1987) Acta Chem Scand **B41**: 228
[11] Konishi M, Nishio M, Saitoh K, Miyaki T, Oki T, Kawaguchi H (1989) J Antibiotics **42**: 1749; Iwamoto T, Tsujii E, Ezaki M, Fujie A, Hashimoto S, Okuhara M, Kohsaka M, Imanaka H, Kawabata K, Inamoto Y, Sakane K (1990) J Antibiotics **43**: 1
[12] Fülöp F (2000) Studies in Natural Products Chemistry. In: Atta-ur-Rahman (ed) The Chemistry of 2-Aminocyclopentanecarboxylic Acid. Elsevier, New York, pp 273–306; Fülöp F (2000) Farmaco **55**: 181
[13] Fülöp F (2001) Chem Rev **101**: 2181
[14] Kanerva LT, Csomós P, Sundholm O, Bernáth G, Fülöp F (1996) Tetrahedron Asymm **7**: 1705; Csomós P, Kanerva LT, Bernáth G, Fülöp F (1996) Tetrahedron Asymm **7**: 1789

[15] Ojima I, Delaloge F (1997) Chem Soc Rev **26**: 377; Palomo C, Aizpurua JM, Ganboa I (1997) In: Juaristi E (ed) Enantioselective Synthesis of β-Amino Acids. Wiley-VHC, New York, pp 279–357; Palomo C, Oiarbide M, Bindi S (1998) J Org Chem **63**: 2469; Jin Z, Kim DH (1998) Bioorg Med Chem Lett **8**: 3515; Cundy DJ, Donohue AC, McCarthy TD (1999) J Chem Soc Perkin Trans 1, 559; Khim S-K, Nuss J (1999) M Tetrahedron Lett **40**: 1827
[16] Nativ E, Rona P (1972) Isr J Chem **10**: 55
[17] Bernáth G, Göndös G, Márai P, Gera L (1972) Acta Chim Acad Sci Hung **74**: 479

Received November 11, 2001. Accepted (revised) November 26, 2001