Conformationally Constrained Serine Analogues: Synthesis of New 2-Amino-3-hydroxynorbornanecarboxylic Acid Derivatives

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A synthesis of the new oxazolone **2**, functionalized with the ethoxycarbonyloxy group on methylenic carbon, is presented, starting from 4-hydroxymethylenoxazolone **1** and ethyl chlorocarbonate. Oxazolone **2** was reacted with cyclopentadiene in the presence of $EtAlCl_2$, giving the two diastereoisomeric cycloadducts *exo*-**3** and *endo*-**3** in a 70:30 ratio. Selective hydrolysis of the lactone ring (THF, HCl) gave the corresponding acids **5** and **6** which were transformed into hydroxyacid derivatives **7** and **8**, respectively, operating in an ethanolic solution of Me_2NH. The new 3-hydroxy-2-aminonorbornane-2-carboxylic acids **11** and **12**, in which the serine skeleton is included, were obtained by reduction of acids **5** and **6** to derivatives **9** and **10** and a subsequent hydrolysis with HCl.

Introduction

Carbocyclic constrained amino acids have useful biological properties owing to their structural features.[1] The synthesis of 2-aminonorbornane-2-carboxylic acids has attracted the attention of many researchers because they are characterized by different biological activities.[2] The general features of these amino acids are the bulkiness and apolarity of the ring and the maximal resistance to metabolic attack (e.g., the α-carbon should be *tertiary*). Furthermore, the conformational rigidity and the presence of a substituent on the ring allow for the formation of stereoisomeric derivatives which interest is related to attempts to clarify the conformational role of substituents in bioreceptorial interations.[2c]

The key reaction to obtain the norbornene skeleton is the Diels−Alder reaction starting from cyclopentadiene and dienophiles such as α-aminoacrylates,[3] α-cyanocinnamates,[4] 4-ylidene-5(4*H*)-oxazolones,[5] 4-methyleneoxazolidin-5-ones,[6] and methylenehydantoine derivatives.[7] These methods allow 2-aminonorbornene-2-carboxylic acid derivatives unsubstituted or substituted at C-3 with a group linked through a carbon atom to be obtained.

Only two examples of heterosubstituted amino acids are reported in which the heteroatom is linked to C-6. In both cases the starting materials for their preparation are the corresponding unsaturated amino acids.[8]

No examples of 3-heterosubstituted 2-aminonorbornane-2-carboxylic acid derivatives are known.

In continuing our research aimed at synthesizing new *β*-heterosubstituted α-amino acids,[9,10] we now report on the diastereoselective synthesis of 3-hydroxy-2-aminonorbornane-2-carboxylic acids in which the serine skeleton is included.

A valuable starting material for previous syntheses was the 4-chloromethylene-5(4*H*)-oxazolone which was used successfully for the preparation of α-amino-*β*-

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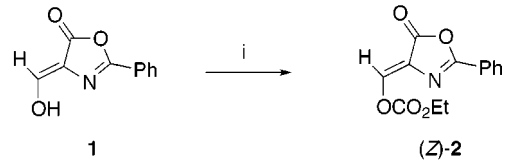
Scheme 1



hydroxycyclohexenecarboxylic acid.[10] Now a new oxazolone, **2**, functionalized with an ethoxycarbonyloxy group on a methylenic carbon, was prepared. The ethoxycarbonyloxy group has different advantages compared to chlorine atom; it allows for the direct introduction of the protected hydroxy group and increases the reactivity of the dienophile.

Results and Discussion

(*Z*)-Ethyl 2-phenyl-5-oxooxazol-4-methylenecarbonate (**2**) was obtained in good yield (90%) starting from 4-hydroxymethylene-5(4*H*)-oxazolone **1** and ethyl chlorocarbonate operating in dichloromethane and in the presence of triethylamine (Scheme 1).

The ^{1}H NMR signal of the methylenic proton at a very low field (8.07 δ) and the stretching of the lactone group at 1800 cm^{-1} in the IR spectrum, uncommon for unsaturated oxazolones, reveal the strong electron-withdrawing effect of the carbonate group. These spectroscopic data are agree with the good reactivity of the exocyclic double bond in respect to dienes.

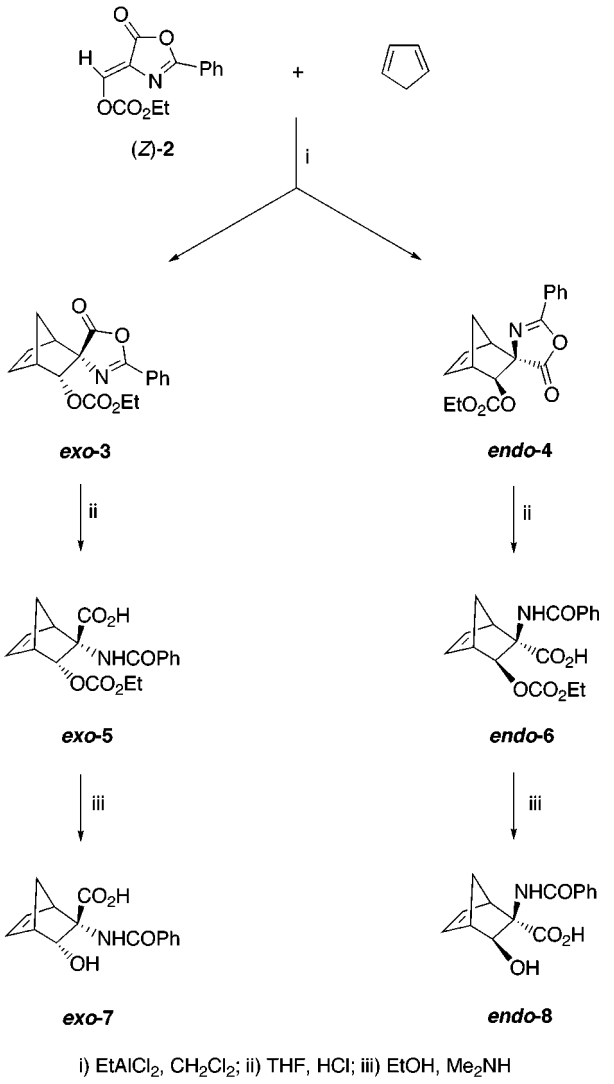
It should be noted that alkoxymethyleneoxazolones display a very weak reactivity in the cycloaddition reaction which is too low for practical use. In fact, by reaction of the above oxazolone with cyclopentadiene both in toluene at reflux and in dichloromethane in the presence of Lewis acid catalysts, only starting materials were recovered. Instead, compound **2** reacts with cyclopentadiene in a dichloromethane solution at 0 °C and in the presence of a catalytic amount of ethylaluminum dichloride. Two diastereoisomeric adducts in a 70:30 ratio were detected by ^{1}H NMR analysis of the crude reaction mixture. Workup of the reaction afforded a mixture of products in 75% total yield corresponding to cycloadducts *exo*-**3** and *endo*-**4** and a mixture of the corresponding *exo*-**5** and *endo*-**6** acids. These latter derived from moisture attack on the lactone group during the chromatographic process (Scheme 2).

To avoid the formation of such a mixture of oxazolone and acid derivatives, the crude reaction mixture was treated with THF in the presence of a catalytic amount of 37% HCl. The mixture of acids *exo*-**5** and *endo*-**6** was directly obtained.

Starting from pure **3** and **4** and operating under the same hydrolytic reaction conditions, the acids **5** and **6** were obtained in quantitative yield. As shown, these conditions prevent the hydrolysis of the carbonate group (Scheme 2).

To improve the formation of the *endo* adduct, the reaction was performed in dichloromethane using lithium perchlorate as the Lewis acid and operating both at room temperature and at 40 °C. In fact, it is known that this catalyst favors the formation of *endo* adduct.[5c,6] In our case no significant variation of the *endo*/*exo* ratio was observed, but an increase of total yield was experienced (86%).

Scheme 2



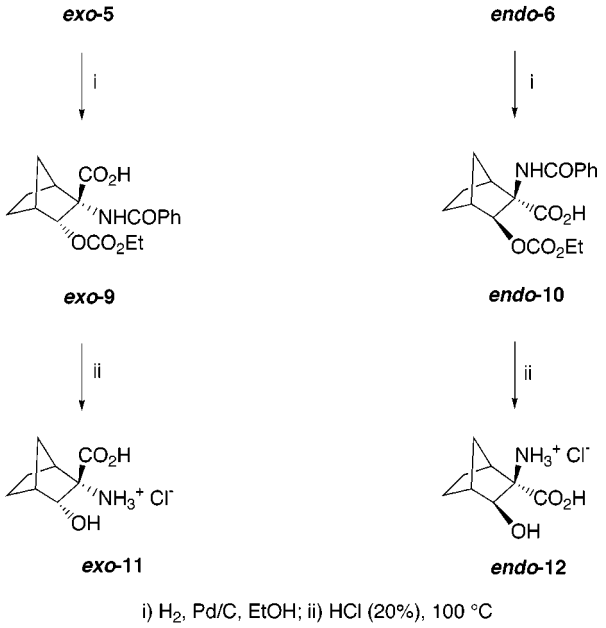
The cycloaddition reaction is characterized by high diastereoselectivity, and the final configuration is the same as in the starting dienophile in both diastereoisomers. Furthermore, the reaction proceeded with good *exo*-diastereofacial selectivity. It was reported that when starting from an achiral oxazolone the *endo*/*exo* ratio was about 0.82.[5g] In our case this value was 0.43. The increase of the amount of the *exo*-adduct could be ascribed to a positive interaction between the diene system and the carbonate group.

The cycloaddition reaction was also performed using a chiral catalyst, i.e., (*R*)-1,1′-binaftalen-2,2′-dioltitanodibromide. The chiral HPLC analysis evidenced that neither changes of diastereofacial selectivity nor enantioselection occurred. The chiral catalyst's failure in the stereochemistry induction in cycloadditions reaction involving ylideneoxazolones is also reported by other authors.[5]

The hydroxy group was selectively deprotected by reaction in an ethanolic solution of dimethylamine at reflux. The hydroxy acid derivatives *exo*-**7** and *endo*-**8** were respectively obtained in satisfactory yield (75%) starting from acids **5** and **6** (Scheme 2).

The acids *exo*-**5** and *endo*-**6** were reduced with hydrogen in EtOH at room temperature. The corresponding

Scheme 3



norbornane derivatives *exo*-**9** and *endo*-**10** were obtained in quantitative yield (Scheme 3).

Finally, the acids *exo*-**9** and *endo*-**10** were hydrolyzed in more drastic hydrolytic conditions (HCl 20%, at reflux), giving the corresponding 3-hydroxyamino acids *exo*-**11** and *endo*-**12**, respectively, in good yield (Scheme 3).

The structure of compounds **3**−**12** was confirmed by spectroscopic data which agree with those reported in the literature[5] for *exo* and *endo* 3-substituted compounds. Characteristic doublets associated with H-3 of cycloadduct and acid, respectively, at δ 5.20 and 6.02 in the *exo* series and at δ 4.49 and 5.43 in the *endo* series are present in the ^{1}H NMR spectra. A further confirmation of the steric relationship between H-3 and H-4 protons is given by *J* values which are more than 3 Hz in the *exo* series and about 2 Hz in the *endo* series. The NOE experiment on *exo*-acid **5** showed evidence of the spatial proximity between H-7s and H-3. In the case of *endo*-acid **6**, a strong NOESY effect occurs between H-3 and H-4 but not with H-7s. In both cases a positive Overhauser effect was observed between the phenyl protons and the OCH_2 protons, confirming the *cis* relationship between the nitrogen and oxygen atoms. These data confirm indirectly the (*Z*) configuration of the starting oxazolone considering that, in the reaction conditions adopted for Diels Alder reactions, the isomerization of the double bond of alkylideneoxazolones does not occur significatively.[5,10]

Analogous spectra were observed for hydroxy acids **7** and **8** in which the signal of the H-3 proton is at high field (δ 4.99, 4.35, respectively).

The ^{1}H NMR spectra of amino acidic compounds *exo*-**11** and *endo*-**12** show respectively a doublet at δ 4.31(J = 4.0) and 4.20 (J = 1.5) associated with H-3, signals associated with H-4 at δ 2.52 and 2.16, and at δ 2.31 and 2.38 associated with H-1. A doublet at δ 1.80 (J = 11.0) and 1.83 (J = 11.4) associated with H-7s in the *exo* and *endo* compounds, respectively, and a multiplet in the δ 1.63−1.15 and δ 1.58−1.10 region confirm the structure of the norbornane skeleton.

Experimental Section

General. Melting points are uncorrected. IR spectra using the Nujol method were measured using NaCl plates. ^{1}H and ^{13}C NMR were recorded in $CDCl_3$ at 200, 300 and 50, 75 MHz, respectively, with $CHCl_3$ as internal standard. *J* values are given in hertz. Ethanol-free CH_2Cl_2 was used in all experiments. Oxazolone **1**[11] is a known compound. Freshly distilled cyclopentadiene was used.

(*Z*)-Ethyl 2-Phenyl-5-oxooxazol-4-methylenecarbonate 2. To a stirred suspension of anhydrous oxazolone **1** (1.89 g, 10 mmol) in anhydrous CH_2Cl_2 (35 mL) under a nitrogen atmosphere at −5 °C was added ethyl chlorocarbonate (1.05 mL, 11 mmol). Triethylamine (1.55 mL, 11 mmol) was dropped at this temperature in 20 min, and stirring was continued for 2 h. The organic solution was washed with a 10% solution of HCl (15 mL) and H_2O (15 mL) and then dried over Na_2SO_4. After solvent evaporation, the crude reaction mixture was recrystallized from CH_2Cl_2/*i*-Pr_2O, giving pure oxazolone **2** (2.35 g, 90%): mp 138 °C; IR ν_{max} 1800, 1770, 1680 cm^{-1}; ^{1}H NMR δ 1.42 (t, J = 7.1, 3 H), 4.43 (q, J = 7.1, 2 H), 7.47−8.14 (m, 5 H), 8.07 (s, 1 H); ^{13}C NMR δ 14.5, 67.0, 123.4, 125.6, 128.9, 129.4, 133.9, 139.9, 151.6, 163.1, 167.3. Anal. Calcd: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.93; H, 4.26; N, 5.39.

General Procedure for the Diels−Alder Reaction. (a) To a stirred solution of oxazolone (*Z*)-**2** (522 mg, 2 mmol) and freshly distilled cyclopentadiene (528 mg, 8 mmol) in anhydrous CH_2Cl_2 (10 mL) under nitrogen at 0 °C was added $EtAlCl_2$ (450 μL, 0.25 equiv, 1.8 M in toluene). After 2 h the solvent was evaporated and the crude reaction mixture was chromatographed [2 cm width plate; silica gel Kieselgel 60 (Merck); 230−400-mesh ASTM; *n*-pentane/AcOEt (20:1) eluant; 7 mL/min] to give two fractions, the first containing pure cycloadduct *exo*-**3** (262 mg, 40%) and the second pure cycloadduct *endo*-**4** (125 mg, 19%). Elution with AcOEt/MeOH gave a third fraction containing a mixture of acids *exo*-**5** and *endo*-**6** (111 mg, 16%). (b) The cycloaddition reaction was performed as described in part a. The solvent was evaporated, and the crude reaction mixture was taken up with THF (10 mL) and stirred in the presence of a catalytic amount of HCl (36%). After 2 h, THF was eliminated by vacuum and the solid dissolved in AcOEt (10 mL) and extracted with a solution of $NaHCO_3$ (5 × 3 mL). The aqueous solution was acidified with HCl (10%, Congo red) and extracted with CH_2Cl_2 (3 × 10 mL). After drying over Na_2SO_4, a mixture of pure acids *exo*-**5** and *endo*-**6** was obtained. Chromatography of the acid mixture with AcOEt/MeOH gave a first fraction containing the acid *exo*-**5** (345 mg, 40%), a mixture of acids *exo*-**5** and *endo*-**6** (142 mg, 20%), and the acid *endo*-**6** (109 mg, 16%). (c) $LiClO_4$ (532 mg, 5 mmol) was added to a stirred solution of oxazolone (*Z*)-**2** (261 mg, 1 mmol) and freshly distilled cyclopentadiene (264 mg, 4 mmol) in anhydrous CH_2Cl_2 (5 mL) under nitrogen at 25 °C. After 24 h the solvent was evaporated and the crude reaction mixture was taken up with THF (5 mL) and stirred in the presence of a catalytic amount of HCl (36%) for 2 h. The reaction mixture was then worked up as described in part b. A mixture of pure acids *exo*-**5** and *endo*-**6** (280 mg, 86%) was isolated.

(1*R,2*S**,3*R**,4*S**)-3-Ethoxycarbonyloxybicyclo[2.2.1]-hept-5-ene-2-spiro-4′[2′-phenyl-5′(4′*H*)-oxazolone] 3:** mp 116 °C (CH_2Cl_2/*i*-Pr_2O); IR ν_{max} 1790, 1715, 1630 cm^{-1}; ^{1}H NMR δ 7.99−7.39 (m, 5 H), 6.58−6.48 (m, 2 H), 5.20 (d, J = 3.7, 1 H), 3.92−3.86 (m, 2 H), 3.33 (bs, 1 H), 3.09 (bs, 1 H), 2.31 (d, J = 10.0, 1 H), 1.67 (dt, J = 1.8, 10.0, 1 H), 1.04 (t, J = 7.2, 3 H); ^{13}C NMR δ 14.0, 42.3, 45.7, 53.6, 64.5, 75.2, 84.3, 125.9, 128.2, 128.7, 132.8, 135.3, 137.1, 155.0, 162.6, 180.4. Anal. Calcd: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.83; H, 5.41; N 4.14.

(1*R,2*R**,3*S**,4*S**)-3-Ethoxycarbonyloxybicyclo[2.2.1]-hept-5-ene-2-spiro-4′[2′-phenyl-5′(4′*H*)-oxazolone] 4:** mp 136 °C (CH_2Cl_2/*i*-Pr_2O); IR ν_{max} 1795, 1705, 1630 cm^{-1}; ^{1}H NMR

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δ 8.03−7.40 (m, 5 H), 6.46−6.34 (m, 2 H), 4.49 (d, J = 2.0, 1 H), 3.92 (q, J = 7.1, 2 H), 3.22 (bs, 1 H), 2.89 (bs, 1 H), 2.68 (d, J = 9.2, 1 H), 1.92 (dq, J = 1.8, 3.5, 9.2, 1 H), 1.05 (t, J = 7.1, 3 H); ^{13}C NMR δ 14.1, 47.6, 47.7, 53.6, 64.5, 73.1, 83.9, 126.1, 128.0, 128.7, 132.8, 135.0, 136.3, 154.9, 161.9, 178.9. Anal. Calcd: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.91; H, 5.30; N 4.19.

(1*R,2*S**,3*R**,4*S**)-2-Benzoylamino-3-ethoxycarbonyloxybicyclo [2.2.1]hept-5-ene-2-carboxylic acid 5**: mp 152 °C (CH_2Cl_2/*i*-Pr_2O); IR ν_{max} 3350, 1740, 1720, 1620 cm^{-1}; ^{1}H NMR δ 9.50−8.00 (bs, 1 H, exch.), 7.78−7.44 (m, 5 H), 6.99 (s, 1 H, exch.), 6.35−6.31, 6.18−6.14 (two m, 2 H), 6.02 (d, J = 3.7, 1 H), 4.26 (q, J = 7.1, 2 H), 3.93 (bs, 1 H), 3.39 (bs, 1 H), 1.84 (d, J = 10.3, 1 H), 1.66 (dt, J = 1.8, 10.3, 1 H), 1.33 (t, J = 7.1, 3 H); ^{13}C NMR δ 14.3, 42.7, 45.9, 49.8, 64.9, 66.8, 79.6, 127.4, 129.0, 132.1, 133.0, 135.4, 136.4, 153.2, 170.3, 171.9. Anal. Calcd: C, 62.60; H, 5.55; N, 4.06. Found: C, 62.33; H, 5.49; N 3.84.

(1*R,2*R**,3*S**,4*S**)-2-Benzoylamino-3-ethoxycarbonyloxybicyclo [2.2.1]hept-5-ene-2-carboxylic acid 6**: mp 183 °C (CH_2Cl_2/*i*-Pr_2O); IR ν_{max} 3350, 1740, 1720, 1620 cm^{-1}; ^{1}H NMR δ 9.50−8.00 (bs, 1 H, exch.), 7.88−7.51 (m, 5 H), 7.00 (s, 1 H, exch.), 6.37−6.33, 6.24−6.20 (two m, 2 H), 5.46 (d, J = 1.8, 1 H), 4.28 (q, J = 7.1, 2 H), 3.88 (bs, 1 H), 3.08 (bs, 1 H), 2.00 (d, J = 9.9, 1 H), 1.85 (dq, J = 1.8, 3.5, 9.9, 1 H), 1.34 (t, J = 7.1, 3 H); ^{13}C NMR δ 14.3, 45.6, 47.5, 47.7, 65.0, 66.1, 78.8, 127.4, 129.0, 132.7, 132.9, 135.6, 136.5, 153.2, 169.7, 170.7. Anal. Calcd: C, 62.60; H, 5.55; N; 4.06. Found: C, 62.48; H, 5.54; N 3.87.

General Procedure for Hydrolysis of Spirooxazolone. Cycloadduct **3** or **4** (327 mg, 1 mmol) was dissolved in THF (5 mL) in the presence of a catalytic amount of HCl (37%). The solution was stirred at room temperature for 0.30 h. The solvent was evaporated, and the solid was taken up with in CH_2Cl_2 (10 mL) and dried over Na_2SO_4. After solvent evaporation, pure acid **5** or **6** was obtained in quantitative yield (345 mg).

General Procedure for Hydrolysis of Carbonate. The acid **5** or **6** (345 mg, 1 mmol) was suspended in an ethanolic solution of dimethylamine (5 mL, 33%) and the solution was refluxed for 2 h. After solvent evaporation, the residue was taken up with a solution of HCl (10 mL, 10%) and extracted with AcOEt (3 × 15 mL). The organic layers were dried over Na_2SO_4. After recrystallization, pure compound **7** or **8** was obtained.

(1*R,2*S**,3*R**,4*S**)-2-Benzoylamino-3-hydroxybiciclo-[2.2.1]hept-5-ene-2-carboxylic acid 7**: yield 166 mg, 61%; mp 164 °C (dec) (CH_2Cl_2); IR ν_{max} 3400−3200, 1695, 1620 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 12.4 (bs, 1 H, exch.), 7.85−7.37 (m, 5 H), 7.35 (s, 1 H, exch.), 6.25 (d, J = 15.5, 1 H, exch.), 6.17−6.13, 6.06−6.02 (two m, 2 H), 4.35 (bs, 1 H), 3.79 (bs, 1 H), 3.05 (bs, 1 H), 1.70 (d, J = 9.7, 1 H), 1.55 (d, J = 9.7, 1 H); Anal. Calcd: C, 65.92; H, 5.53; N; 5.13. Found: C, 65.78; H, 5.60; N 5.05.

(1*R,2*R**,3*S**,4*S**)-2-Benzoylamino-3-hydroxybycyclo-[2.2.1]hept-5-ene-2-carboxylic acid 8**: yield 161 mg, 59%; mp 140 °C (dec) (CH_2Cl_2); IR ν_{max} 3400−3200, 1695, 1620 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 8.15 (s, 1 H, exch.), 7.81−7.39 (m, 5 H), 6.14 (bs, 2 H), 6.00−5.60 (bm, 2 H, exch.), 4.35 (bs, 1 H), 3.58 (bs, 1 H), 2.71 (bs, 1 H), 1.89 (d, J = 9.2, 1 H), 1.64 (d, J = 9.2, 1 H); ^{13}C NMR δ 45.8, 47.3, 49.3, 64.8, 74.1, 127.3, 128.8, 132.3, 133.4, 135.5, 136.3, 168.8, 172.3. Anal. Calcd: C, 65.92; H, 5.53; N; 5.13. Found: C, 65.83; H, 5.61; N 5.00.

General Procedure for the Hydrogenation Reaction. The acid **5** or **6** (294 mg, 0.85 mmol) was suspended in EtOH (50 mL) and reduced at room temperature and atmospheric pressure with hydrogen over 10% Pd/C (91 mg, 0.85 mmol). After 2 h the catalyst was filtered off and washed with EtOH (10 mL). The solvent was eliminated and the solid crystallized, giving pure compound **9** or **10**.

(1*R,2*S**,3*R**,4*S**)-2-Benzoylamino-3-ethoxycarbonyloxybicyclo [2.2.1]heptane-2-carboxylic acid 9**: 296 mg, 100%; mp 143 °C (CH_2Cl_2/*i*-Pr_2O); IR ν_{max} 3350, 1695, 1630 cm^{-1}; ^{1}H NMR 7.87−7.46 (m, 5 H), 7.26 (s, 1 H, exch.), 5.71 (d, J = 4.0, 1 H), 4.28 (q, J = 7.2, 2 H), 3.32 (bs, 1 H), 2.81 (bs, 1 H), 1.74 (d, J = 11.0, 1 H), 1.80−1.40 (m, 5 H), 1.37 (t, J = 7.2, 3 H). Anal. Calcd: C, 62.24; H, 6.09; N, 4.03. Found: C, 62.18; H, 6.15; N 4.00.

(1*R,2*R**,3*S**,4*S**)-2-Benzoylamino-3-ethoxycarbonyloxybicyclo [2.2.1]heptane-2-carboxylic acid 10**: 296 mg, 100%; mp 189 °C (CH_2Cl_2/*i*-Pr_2O); IR ν_{max} 3300, 1705, 1690, 1620 cm^{-1}; ^{1}H NMR 7.86−7.50 (m, 5 H), 7.56 (s, 1 H, exch.), 5.57 (d, J = 1.5, 1 H), 4.27 (q, J = 7.1, 2 H), 3.29 (bs, 1 H), 2.50 (bs, 1 H), 1.94 (d, J = 10.2, 1 H), 1.80−1.40 (m, 5 H), 1.35 (t, J = 7.1, 3 H). Anal. Calcd: C, 62.24; H, 6.09; N; 4.03. Found: C, 62.10; H, 6.15; N 3.98.

General Procedure for the Preparation of Amino Acids 11 and 12. Compound **9** or **10** (174 mg, 0.50 mmol) was suspended in HCl (5 mL, 20%) in a sealed tube and placed in an oven at 100 °C for 15 h. After cooling, the benzoic acid that had separated was filtered. The aqueous layer was washed with Et_2O (5 mL) and then was evaporated to dryness under reduced pressure, affording pure amino acid **11** or **12**. Amino acid derivative was drided with P_2O_5 *in a vacuum*.

(1*R,2*S**,3*R**,4*S**)-2-Amino-3-hydroxybicyclo[2.2.1]-heptane-2-carboxylic acid hydrochloride 11:** yield 90 mg, 93%; mp 225 °C (dec); IR ν_{max} 1710 cm^{-1}; ^{1}H NMR (D_2O/CF_3CO_2D) 4.31 (d, J = 4.0, 1 H), 2.52 (bs, 1 H), 2.31 (bs, 1 H), 1.80 (d, J = 11.0, 1 H), 1.63−1.15 (m, 5 H); ^{13}C NMR (D_2O) δ 16.9, 22.5, 33.2, 40.6, 44.4, 63.2, 71.5, 173.5. Anal. Calcd: C, 46.27; H, 6.80; N, 6.75. Found: C, 46.00; H, 7.01; N 6.50.

(1*R,2*R**,3*S**,4*S**)-2-Amino-3-hydroxybicyclo[2.2.1]-heptane-2-carboxylic acid hydrochloride 12:** yield 92 mg, 95%; mp 215 °C (dec); IR ν_{max} 1700 cm^{-1}; ^{1}H NMR (D_2O/CF_3CO_2D) 4.20 (d, J = 1.5, 1 H), 2.38 (bs, 1 H), 2.16 (bs, 1 H), 1.83 (d, J = 11.4, 1 H), 1.58−1.10 (m, 5 H); ^{13}C NMR (D_2O) δ 22.8, 23.5, 34.5, 44.5, 45.3, 68.8, 75.5, 172.6. Anal. Calcd: C, 65.92; H, 5.53; N; 5.13. Anal. Calcd: C, 46.27; H, 6.80; N, 6.75. Found: C, 45.93; H, 7.10; N 6.48.

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