Application of Intramolecular 1,3-Dipolar Cyclic Addition of Azide and Olefin; Construction of (Pyrrolidine-2-ylidene)glycinate and Glycinamides

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Oxopropyl *E*-(pyrrolidine-2-ylidene)glycinamide (5c) and allyl *E*-(pyrrolidine-2-ylidene)glycinate (5d) were effectively synthesized from 2,3,5-tri-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl(TBDMS)-D-arabinal (7) using intramolecular 1,3-dipolar cyclic reaction of azide and olefin as a key reaction. These results proved this cyclic reaction should be applicable for the synthesis of various (pyrrolidine-2-ylidene)glycinate and glycinamide. In addition, the development of a synthetic route for the precursor of an unsaturated cyclic dehydro amino acid involved in azinomycins (carzinophilin) using relating glycinate, methyl *E*-(pyrrolidine-2-ylidene)glycinate (5a) was described.

Key words cyclic addition; azide; olefin; (pyrrolidine-2-ylidene)glycinate; azinomycin

The 1-azabicyclo[3.1.0]-hex-2-ylidene)glycinate system like **3** is an important fragment involved in antitumor antibiotics, azinomycins[1,2] A (**1**), B (**2**) (carzinophilin[3,4]). We already reported[5] an efficient synthetic method for (pyrrolidin-2-ylidene)glycinates **5a** and **5b**, which are the basic skeleton of unique unsaturated cyclic dehydro amino acid **3**, by intramolecular-1,3-dipolar cyclic addition of azide and olefin as a key reaction using azide **4a** and **4b**. Recently, several synthetic studies[6,7] and investigation of biological properties of carzinophilin and its related synthetic products have been reported[8] and it is mentioned there that a five-membered unsaturated dehydro amino acid part like **3** has an important role in the biological activity of carzinophilin. Our work concerning the intramolecular 1,3-dipolar cyclic addition of azide and olefin would serve to construct (pyrrolidine-2-ylidene)glycinates, which are the key compounds for **3**.

In this paper, further application of this cyclic reaction was investigated to see if this method could be widely used to synthesize other (pyrrolidin-2-ylidene)glycinate and glycinamide. We chose newly an amide **4c** which has an azinomycin A related functional group ($R=NHCH_2COCH_3$) and another ester **4d** as substrates of azide. Intramolecular cyclic reaction of azide and olefin occurred in both cases of **4c** and **4d** and afforded cyclic dehydro amino acid **5c** and **5d** in high yield. Considering both the results obtained in a preliminary report[5] and that obtained in this paper, this reaction was revealed to be applicable for various esters **4a**, **4b**, **4d** ($R=OMe$, O^tBu, allyl) and also amide **4d** ($R=NHCOCH_3$). It is remarkable that the reaction occurred in the amide **4d**, which is presumed to have poor reactivity in this cyclic reaction considering the already described reaction mechanism,[5] because the amide group does not have enough electron-withdrawing force, hence it is difficult to construct the triazoline ring which is an important intermediate[5] for intramolecular 1,3-dipolar cyclic addition of azide and olefin.

In addition, the conversion of methyl (*E*)-(pyrrolidine-2-ylidene)glycinate **5a**, which was already synthesized by us,[5] to the key compound **6a** and **6b** for the precursor of aziridine construction for **3** was developed. These results will serve for the construction of **3**.

Results and Discussion

Our synthetic strategy for **5c** and **5d** is described below (Chart 1). Compound **8**, which was already synthesized *via* aldehyde **7** according to the procedure described in our previous paper,[5] would afford unsaturated carboxylic acid **9** by hydrolysis of the methyl ester **8**. Acid **9** would be converted to the amide **10**, which would give the alcohol **11**. Compound **11** would be converted to (pyrrolidine-2-ylidene)glycinamide **5c** conveniently *via* azide by intramolecular 1,3-dipolar cyclic addition of azide olefin in a similar manner as described in a preliminary report.[5] Acid **9** would also afford allyl ester **12**, which would give the alcohol **13**. Compound **13** would be cyclized to (pyrrolidine-2-ylidene)glycinate **5d** *via* azide in a similar way as described in Chart 1.

One important step in this strategy is removal of the *tert*-butyldimethylsilyl (TBS) group from **10** (*Z*) and **12** (*Z*), be-

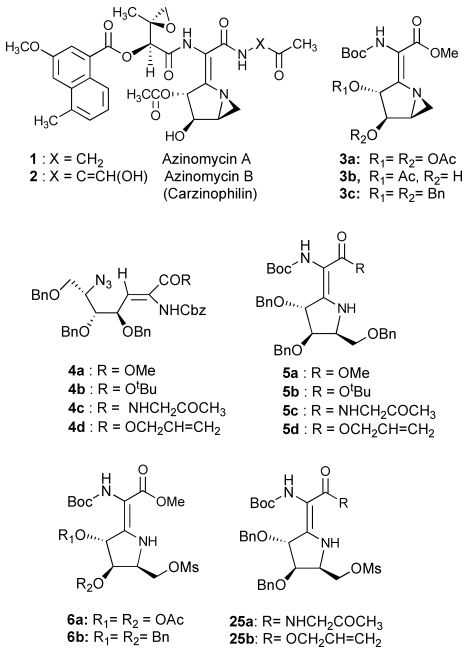

Fig. 1

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cause isomerization of the geometry resulting in unsaturated alcohol **11** and **13** would occur as already described in our previous paper.[5] Another is, if the amide **11** cyclizes by intramolecular 1,3-dipolar cyclic addition of azide olefin *via* azide **4c** to give **5c**, and optimization of its cyclic reaction should be required. The cyclic reaction of ester **13** is expected to give **5d** *via* azide **4d** similarly as methyl and *tert*-butyl ester (**4a**, **4b**) (Chart 1).

The synthesis of azide **4c** and its cyclic reaction for **5c** is initially described as follows (Chart 2). Horner–Emmons reaction of aldehyde **7**[5] with Horner reagent **14**[5,9] using DBU as a base in CH_2Cl_2 afforded the desired *Z*-olefine **8a** in 67% yield and the *E*-isomer **8b** in 10% yield. Stereo structures of **8a** and **8b** were determined by comparison with the NMR data obtained in our previous work.[5] Hydrolysis of **8a** by treatment with aqueous 1 N NaOH in dioxane afforded acid **9** quantitatively as a single product. Condensation of **9** and 1-amino-2-propanol using 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDCI·HCl) and 1-hydroxybenzotriazole (HOBt) as condensing reagents under *N*-ethyldiisopropylamine [EtN(*i*-Pr)$_2$] for neutralization of HCl in CH_2Cl_2 gave an amide alcohol **15** as a mixture of diastereomers in 85% yield. Oxidation of alcohol **15** with Dess–Martin reagent[10] afforded the desired ketone **10** in 95% yield. In the removal of the TBS group, pyridine was used as a mixed solvent to prevent *Z*-*E* isomerization by strong acid hydrogen fluoride (HF). The TBS group was removed by using HF-pyridine in a mixed solvent (tetrahydrofuran (THF): pyridine=1:1) to provide conformational isomers **11a** and **11b** in 89%, 9.0% yields, respectively (Chart 2).

A proof of the **11a** and **11b** as conformational isomers was given by NMR techniques of nOes and long-range selective proton decoupling experiments (LSPD) (Fig. 2). In both isomers, 5.8% and 2.7% nOes were observed at H-4 respectively, when 2-NH was irradiated. These results show **11a** and **11b** are both *Z*-form. C^{13}–H^1 coupling constants between H-3 and C-1 in **11a** and **11b** showed the values of 8.5, 7.5 Hz, respectively, by LSPD (Fig. 2). In the coupling constant of $^3J_{CH}$, an equation of $^3J_{CH}$ (*trans*)$>$$^3J_{CH}$ (*cis*) should be applied and the difference between $^3J_{CH}$ (*trans*) and $^3J_{CH}$ (*cis*) should be fairly large according to the literature.[5,11] The values of $^3J_{CH}$ in **11a** and $^3J_{CH}$ in **11b** are close to each other (8.5, 7.5 Hz), though the values are unexpectedly fairly large. These results indicate **11a** and **11b** are the conformational

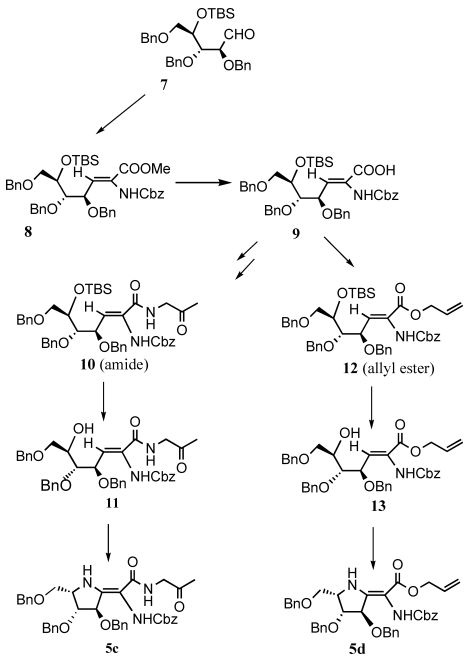

Chart 1. Strategy for **5c** and **5d**

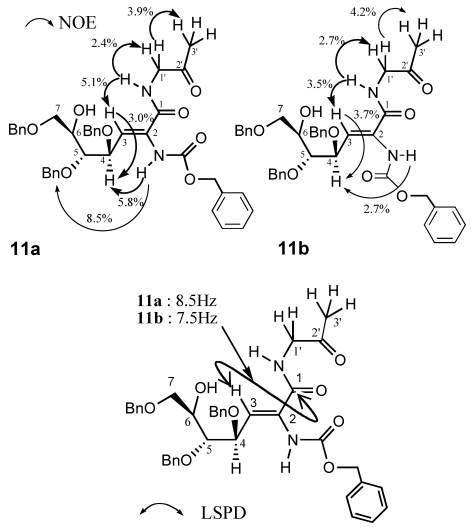

Fig. 2. NOE and LSPD Data of **11a** and **11b**

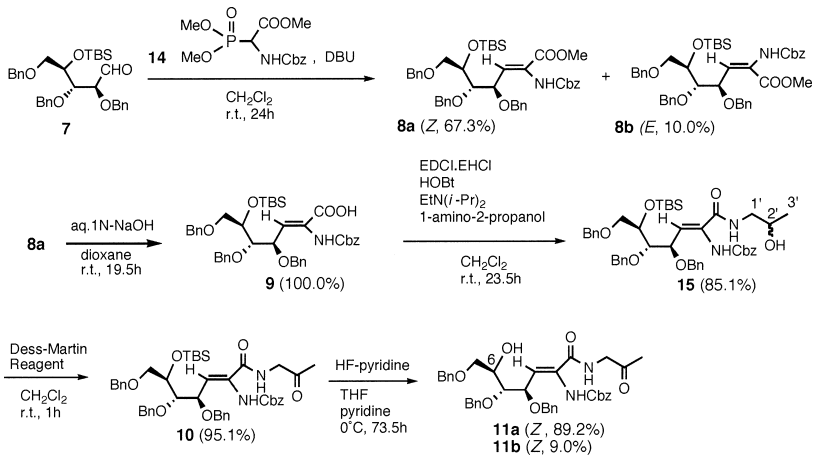

Chart 2

isomers and not the geometrical isomers around the olefinic structure and both should have *Z*-configuration (Fig. 2). It is assumed that **11a** and **11b** are rotational isomers to the axis of C2-NHCbz, because strong nOe between 2-NH and 5-benzyl-CH_2 (8.5%) was observed in **11a** and no nOe was detected in **11b**.

Investigation of optimal conditions for intramolecular 1,3-dipolar cyclic addition of azide olefin using **11a** was carried out (Chart 3). We initially adopted OTf as a leaving group. The desired alcohol **11a** was first converted to triflate **16** by treatment with triflic anhydride under 2,6-lutidine as a base in CH_2Cl_2, followed by conversion to its azide using NaN_3 under benzyltriethylanmmonium bromide in *N*,*N*-dimethylformamide (DMF) according to a similar way as described in our previous paper.[5] Formation of the triflate **16** could be detected; however, further conversion to azide did not occur.

Then, the investigation by using another leaving group for conversion of **11a** to azide was carried out. The alcohol **11a** was next transformed to methanesulfonyl (Ms) derivative **17** by treatment with mesylchloride in the presence of triethylamine in CH_2Cl_2 in 93% yield. But the conversion of **17** into azide **4c** did not occur by treatment with NaN_3 under either condition with $BnEt_3N^+Br^-$ as a phase catalyst in DMF or 15-crown-5 in HMPA.[12] Further examination using a monochloromethanesulfonyl (Mc) group, which is a much stronger leaving group than the mesyl group, was carried out. The alcohol **11a** was converted into Mc derivative[13] **18** in 85% yield by treatment with Mc-Cl in the presence of triethylamine in pyridine. Transformation of Mc derivative **18** into azide **4c** was carried out by treatment with NaN_3 in the presence of benzyltriethylammonium bromide in DMF. The reaction did not proceed under the conditions at room temperature. However, when the reaction temperature was raised to 50 °C, intramolecular 1,3-dipolar cyclic addition of azide olefin occurred successfully and **18** was directly transformed into (pyrrolidin-2-ylidene)glycinate **5c** in 71% yield from **18** presumably *via* azide **4c** though **4c** was not trapped as an intermediate. NOe experiment showed **5c** has the desired *E*-geometry because 2.3% nOe was observed at 3-H when α-NH was irradiated. The inversion of configuration at C-5 was confirmed because nOe was observed between 6-CH_2 and 3-H. This result shows **18** was once converted to azide **4c** by S_N2 reaction, then **4c** was cyclized immediately to afford pyrrolidine **5c** (Fig. 3). Total yield of **5c** from **9** is 43.4%.

Generally, intramolecular 1,3-dipolar cyclic addition of azide and olefin *via* triazoline occurs between azide dipole and electron-deficient dipolarphile such as olefin having an electron-withdrawing group (such as COOMe) to provide a heterocyclic compound successfully.[14,15] It has been scarcely reported that this cyclic reaction occurs between azide dipole and olefin dipolarphile having an amide group. In this meaning, our report should expand the application of azide olefin cyclic reaction to construct new heterocyclic compounds.

As described in the previous paper,[5] azide olefin cyclic reaction proceeded successfully, using Me ester **4a** and O*t*Bu ester **4b** as a substrate. In this paper, further examination was carried out using allyl ester **4d** as a substrate. Synthetic procedure for azide **4d** and its cyclic reaction for **5d** is described as follows (Chart 4).

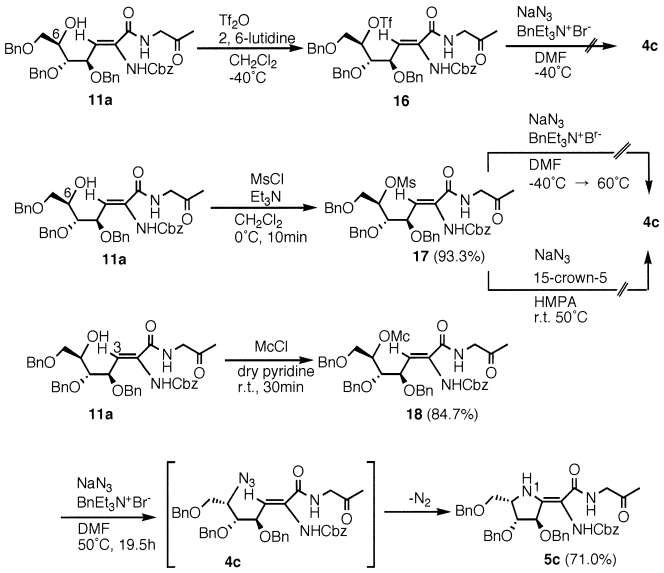

Chart 3

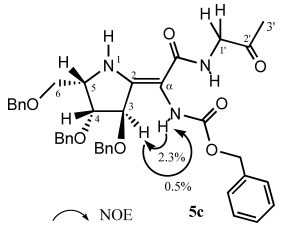

Fig. 3. NOE Data of **5c**

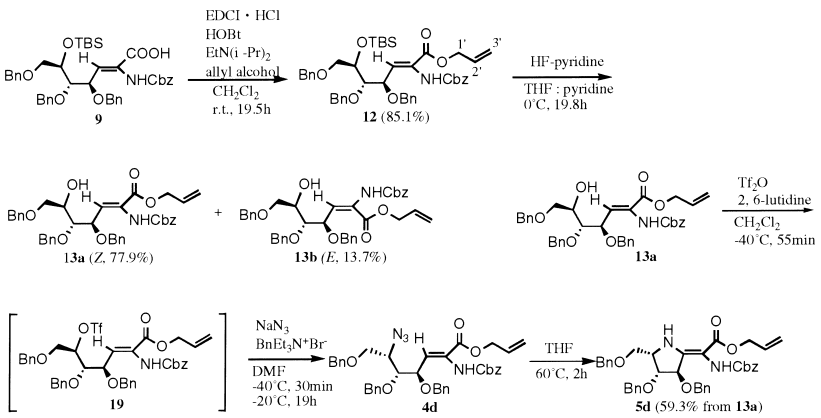

Chart 4

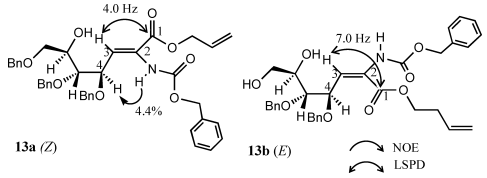

Fig. 4. NOE and LSPD Data of **13a** and **13b**

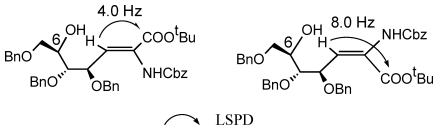

Fig. 5. LSPD Data of *t*-Butyl Ester[5)]

Condensation of acid **9** with allyl alcohol by using EDCI, HOBt, EtN(*i*-Pr)$_2$ in CH_2Cl_2 gave the allyl ester **12** in 85% yield in a similar way as the synthesis of amide **15**. Removal of the TBS group by HF-pyridine in THF-pyridine gave the *Z*-alcohol **13a** (78%) and *E*-alcohol **13b** (14%), respectively, as stereoisomers. The stereostructures were determined by the measurement of nOe and LSPD (Fig. 4).

In the isomer **13a**, 4.4% nOe was observed at 4-H when 2-NH was irradiated, hence **13a** has *Z*-configuration. In the isomer **13b**, the signal of 2-NH could not be observed due to overlapping with the signals of the phenyl group, so nOe measurement was impossible. Then, examination by LSPD was carried out (Fig. 4). The C^{13}–H^1 coupling constants between H-3 and C-1 in **13a** and **13b** showed the values of J=4.0, 7.0 Hz, respectively. According to the literature,[11)] it is said that the value of $^3J_{CH}$ (*trans*) is much larger than that of $^3J_{CH}$ (*cis*) and their reference are fairly large. In fact, *t*-butyl esters exhibited the values of $^3J_{CH}$ (*cis*)=4.0 Hz and $^3J_{CH}$ (*trans*)=8.0 Hz, respectively, as described in our previous report.[5)] (Fig. 5). This rule can be also applied to the isomers **13a** and **b**.

From these results, it is considered that **13a** and **13b** are the geometrical isomers and **13a** is the desired *Z*-olefin and **13b** is *E*-olefin. Treatment of the desired **13a** with triflic anhydride and 2,6-lutidine in CH_2Cl_2 at −40 °C provided triflate **19** which was immediately followed by transformation to the azide **4d** by adding DMF, NaN_3 and benzene-triethylammonium bromide directly in the reaction mixture of triflate at −40 °C for 30 min, followed at −20 °C for 19 h to afford the azide **4d**. Then, the azide **4d** was heated in THF at 60 °C for 2 h to provide (pyrrolidine-2-ylidene)glycinate **5d** in 59% yield from **13a**. The stereostructure of **5d** was determined by nOe measurement (Fig. 6). 1.8% nOe was observed at 3-H when α-NH was irradiated. This result shows **5d** has the desired *E* configuration. Total yield of **5d** from **9** was 40%.

Consideration on the Stereoselectivity in the Alcohols 11 and 13 by Heat of Formation (Hf) Using PM3 Calculated Method As described above, in the removal of the TBDMS group by HF-pyridine from amide **10** and allyl ester **12**, isomerization of geometry is expected, which is a similar case as shown in our previous paper.[5)] Amide **10** afforded both *Z*-alcohols **11a** (89%) and **11b** (9.0%) but did not provide *E*-form, while allyl ester **12** afforded **13a** (*Z*, 78%) and **13b** (*E*, 14%), respectively. We proposed the isomerization

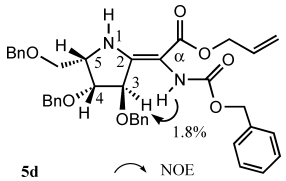

Fig. 6. NOE Data of **5d**

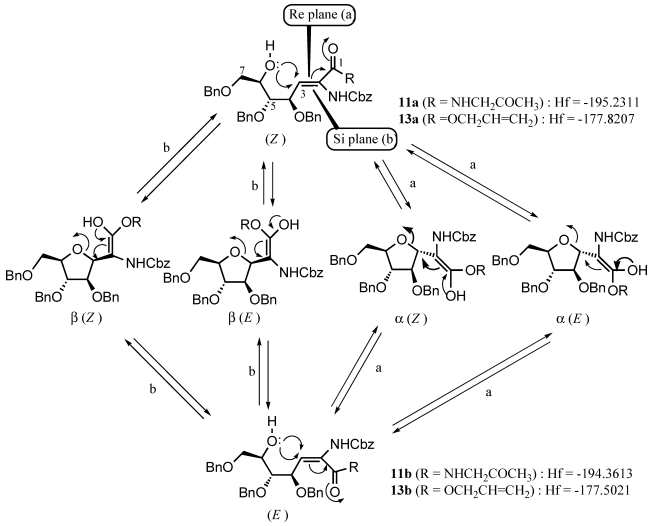

Fig. 7. Heat of Formation Values of **11a**, **11b** and **13a**, **13b** by PM3 Calculation

mechanism as shown in Fig. 7, which is the same as previously reported.[5)] After removal of the TBDMS group, Michael addition of the generated hydroxyl group at the β-position of the α,β-unsaturated ester would occur to afford a furan ring. In this addition, the hydroxyl group would attack from both sides of the *re* and *si* planes to afford β and α forms, and each form is accompanied with two isomers, *Z* and *E* forms, to give four stereoisomers of furans, β (*Z*), β (*E*), α (*Z*), α (*E*). And if the reaction proceeds under conditions of thermodynamic control, furan intermediates would accumulate to the more stable isomer having the smallest heat of formation (Hf) with the isomeric rearrangement; thus, they would return to **11a** and **13a** or isomerize to **11b** and **13b**.

The heats of formation were calculated by PM3 calculation with two pairs of isomers, **11a** and **11b**, **13a** and **13b**. Hf of **11a** and **11b** exhibited −195.2311, −194.3613 kcal/mol, respectively. These results explain **11a** (*Z*-form) is more stabilized than **11b** (*E*-form) with the difference of 0.87 kcal/mol; accordingly, thermodynamic equilibrium would proceed to produce the *Z*-form. These calculation data were coincident with our experimental data producing only *Z*-isomers **11a** and **11b**. The respective Hf of **13a** and **13b** exhibited −177.8207, −177.5021 kcal/mol, respectively, which explains **13a** is also more stabilized than **13b** and thermo-dynamic equilibrium would proceed to produce the *Z*-form. These results coincide with the experimental result, which showed the ratio of the *Z* and *E*-isomers (**13a** : **13b**=5.7 : 1).

Conversion of the (Pyrrolidin-2-ylidene)glycinate 5a to Precursors 6a and 6b toward 3 Initially, the conversion of **5a** to **6a** for the purpose of the synthesis of aziridine derivative **3a** was investigated (Chart 5). Considering the require-

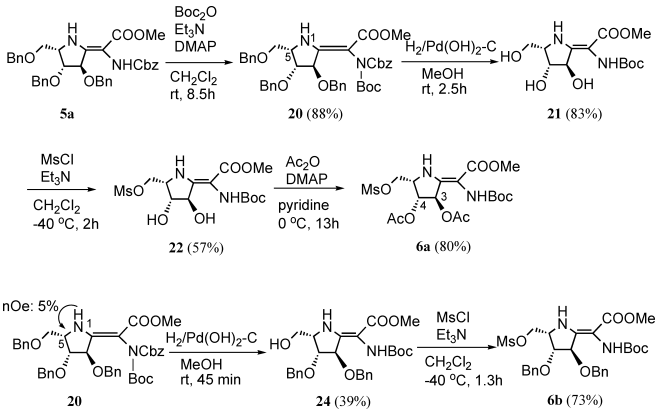

Chart 5

ment of the subsequent removal of the benzyl group, the Cbz group of **5a** should be interchanged to a Boc group. Thus, a Boc group was introduced to **5a** using Boc_2O in the presence of Et_3N, DMAP to provide **20** in 88% yield. It was determined that the Boc group was located in the same nitrogen having the Cbz group, because in nOe experiment by ^{1}H-NMR measurement, irradiation at 1-NH caused 5% nOe at 5-H. The removal of the benzyl group in **20** by Pd $(OH)_2$/C under hydrogen gave successively a triol **21** in 83% yield. Selective mesylation by treatment with mesyl chloride in the presence of Et_3N at $-40\,°C$ afforded **22** (57%). The location of the mesyl group was determined because the chemical shift value of 6-Ha in **22** exhibited more low field shift (δ 4.02→4.49) than 3-H and 4-H. Acetylation of **22** provided diacetate **6a**. The low field shift of the chemical shift values of 3-H (δ 4.93→6.03) and 4-H (δ 4.57→5.36) in **6a** by ^{1}H-NMR explained also the mesylation occurred at 6-OH in **21**. The construction of an aziridine ring using **6a** by tetrabutylammonium fluoride (TBAF) and potassium bis(trimethylsilyl) amide (KHMDS) was attempted. However, the desired **3a** was not obtained and also the starting material was not recovered. Only complicated by-products were obtained which is the same result as shown in the recent literature,[7] in which this result is explained by the base-induced elimination of the 3-OAc, producing imine, which decomposes or polymerizes.

Next, we changed the target of the precursor for **3** and planned the synthesis of the mesylbenzylether **6b**, because benzyl ethers should tolerate a strong anion such as F^- or a strong base such as KHMDS (Chart 5). Selective deprotection of tri-benzyl ether **20** was performed by catalytic reduction using $Pd(OH)_2$/C under hydrogen giving dibenzyl ether **24** in 39% yield. Mesylation by MsCl in the presence of Et_3N afforded mono mesyl derivative **6b** in 73% yield. The location of the mesyl group was determined by comparing the ^{1}H-NMR data of **24** and **6b**, which exhibited the low field shift of 6-Ha, 6-Hb in **6b** (6-Ha: 3.54→4.35; 6-Hb: 3.63→4.38). These results confirmed at the same time that the benzyl group at C-6 in **20** was selectively removed successively by reduction. Thus, a facile route to **6b** from **5a** was established.

Compounds **5c** and **5d** described previously should also afford their monomesyl esters **25a** and **25b** (Fig. 1) in a similar way as shown in Chart 5. We are now going to examine construction of an aziridine ring system using the precursor **6b** and also the conversion of **5c** and **5d** to their monomesyl ester.

In conclusion, pyrrolidine-2-ylidene glycin-amide (**5c**) and glycinate (**5d**) were effectively obtained from the alcohol **11** and **13** *via* azide **4c** and **4d**, respectively, by using intramolecular 1,3-dipolar cyclic reactions of azide and olefin. These results proved this cyclic reaction should be applicable for the synthesis of various pyrrolidine-2-ylidene glycinate and glycinamide.

Experimental

Melting points were taken on a Yanagimoto hot-stage and are uncorrected. Optical rotations were measured on a JASCO model DPI-1000 digital polarimeter. ^{1}H- and ^{13}C-NMR were recorded on a Varian VXR-300 (75 Hz), UNITY-400 (100.6 MHz) spectrometers. All the NMR spectra were taken using $CDCl_3$ as a solvent unless otherwise described. The signals were assigned by ^{1}H–^{1}H COSY, DEPT, HMQC, HMBC experiments. Mass spectra were obtained on a JEOL JMS-DX300 mass spectrometer (low-resolution mass spectrometry) and JEOL JMS-AX505 HA mass spectrometer (high-resolution mass spectrometry). *Rf* values and preparative TLC were done on Silica gel 60 PF254 (Merck). Flash column chromatography was done using Silica gel 60 (art. 1.09385, Merck).

The PM3 calculation was performed by the program CAChe WorkSystem (Ver. 4.9.3 for Machintosh) produced by Fujitsu using Machintosh G4 OS.9.2). Fifteen models were selected within conformers (625) by searching two points of dihedral angles, C-6,5,4,3 and C-5,4,3,2, which are concerned with cyclic reaction. After further optimerization of each structural parameter of fifteen models by MM2, the most stabilized structure was searched by PM3.

Methyl (*Z* and *E*, 4*R*,5*S*,6*R*)-2-Benzyloxycarbonylamino-6-*tert*–butyldimethylsiloxy-4,5,7-tribenzyloxy-2-heptenoate (8a, 8b) To a solution of **14** (510 mg, 1.51 mmol) in CH_2Cl_2 (5 ml) was added DBU (226 μl, 1.51 mmol). After the solution was allowed to stir for 20 min, a solution of **7** (580 mg, 1.08 mmol) in CH_2Cl_2 (5 ml) was added and stirred for further 24 h. The reaction mixture was neutralized with aqueous 1 N-H_2SO_4 and diluted with AcOEt (100 ml), washed with saturated $NaHCO_3$ (4 ml×2), saturated NaCl (4 ml×2). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the resulting yellow oil (910 mg) by flash column chromatography (*n*-hexane/AcOEt=7:1) afforded **8a** (*Z*-form, 540 mg, 67.3%) and **8b** (*E*-form, 80.0 mg, 10.3%), respectively. **8a**: *Rf*=0.44 (*n*-hexane/AcOEt=5:1). $[\alpha]_D^{24}$ −11.60° (*c*=0.50, $CHCl_3$). ^{1}H-NMR (300 MHz) δ: −0.01, 0.05 (each 3H, s, $Si(CH_3)_2$), 0.83 (9H, s, $C(CH_3)_3$), 3.39 (1H, dd, *J*=9.0, 5.0 Hz, 7-Ha), 3.68 (1H, dd, *J*=9.0, 6.0 Hz, 7-Hb), 3.74 (1H, dd, *J*=7.0, 3.0 Hz, 5-H), 3.77 (3H, brs, $COOCH_3$), 3.91—3.98 (1H, m, 6-H), 4.36, 4.58 (each 1H, d, *J*=12.0 Hz, $OC\underline{H}_2Ph$), 4.43, 4.48 (each 1H, d, *J*=12.5 Hz, $OC\underline{H}_2Ph$), 4.43 (1H, dd, *J*=8.5, 7.0 Hz, 4-H), 4.67, 4.72 (each 1H, d, *J*=11.0 Hz, $OC\underline{H}_2Ph$), 5.03, 5.10 (each 1H, d, *J*=12.0 Hz, $COOC\underline{H}_2Ph$), 6.14 (1H, dd, *J*=8.5, 1.0 Hz, 3-H), 7.20—7.31 (20H, m, $OCH_2\underline{Ph}$×4), 7.53 (1H, brs, NHCO). HR-FAB-MS *m/z*: 762.3444 $[M+Na]^+$ Calcd for $C_{43}H_{53}O_8NSiNa$: 762.3438 [M+Na]. **8b**: *Rf*=0.51 (*n*-hexane/AcOEt=5:1). $[\alpha]_D^{24}$ +11.20° (*c*=0.50, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 0.07, 0.10 (each 3H, s, $Si(CH_3)_2$), 0.91 (9H, s, $C(CH_3)_3$), 3.65 (1H, dd, *J*=10.0, 5.5 Hz, 7-Ha), 3.65 (3H, brs, $COOCH_3$), 3.73 (1H, dd, *J*=5.0, 4.5 Hz, 5-H), 3.74 (1H, dd, *J*=10.0, 3.0 Hz, 7-Hb), 4.14 (1H, ddd, *J*=5.5, 5.0, 3.0 Hz, 6-H), 4.42, 4.62 (each 1H, d, *J*=12.0 Hz, $OC\underline{H}_2Ph$), 4.48, 4.51 (each 1H, d, *J*=12.0 Hz, $OC\underline{H}_2Ph$), 4.69, 4.72 (each 1H, d, *J*=12.3 Hz, $OC\underline{H}_2Ph$), 5.09 (1H, dd, *J*=9.5, 4.5 Hz, 4-H), 5.14, 5.19 (each 1H, d, *J*=12.5 Hz, $COOC\underline{H}_2Ph$), 6.82 (1H, brs, NHCO), 6.85 (1H, brd, *J*=9.5 Hz, 3-H), 7.22—7.41 (20H, m, $OCH_2\underline{Ph}$×4). HR-FAB-MS *m/z*: 762.3424 $[M+Na]^+$, Calcd for $C_{43}H_{53}O_8NSiNa$: 762.3438 [M+Na].

(*Z*,4*R*,5*S*,6*R*)-2-Benzyloxycarbonylamino-6-*tert*-butyldimethylsiloxy-4,5,7-tribenzyloxy-2-heptenoic Acid (9) To a solution of **8a** (482.4 mg, 0.653 mmol) in dioxane (3.6 ml) was added an aqueous solution of 1 N-NaOH (1.0 ml, 0.98 mmol). After the mixture was allowed to stir for 19.5 h, the reaction mixture was acidified with 10% HCl and extracted with $CHCl_3$ (100 ml×2). The combined organic layer was dried over Na_2SO_4, and concentrated *in vacuo* to afford **9** (474 mg, 100%) as colorless oil. Compound **9** was used for the next reaction without purification. *Rf*=0.40 ($CHCl_3$/MeOH=10:1). $[\alpha]_D^{24}$ +5.2° (*c*=1.08, $CHCl_3$). IR (KBr) cm^{-1}: 1720 (NHCOO), 1710 (COO), 1655 (C=C). ^{1}H-NMR (400 MHz) δ: 0.00 (6H, s, $Si(CH_3)_2$), 0.84 (9H, s, $C(CH_3)_3$), 3.41 (1H, dd *J*=9.5, 5.0 Hz, 7-Ha), 3.69 (1H, dd, *J*=9.5, 6.0 Hz, 7-Hb), 3.77 (1H, dd, *J*=6.5, 3.0 Hz, 5-H), 3.97 (1H, ddd, *J*=6.0, 5.0, 3.0 Hz, 6-H), 4.37, 4.58 (each 1H, d, *J*=12.0 Hz, $OC\underline{H}_2Ph$),

4.44, 4.49 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.46 (1H, dd, J=8.0, 6.5 Hz, 4-H), 4.67, 4.72 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 5.04, 5.10 (each 1H, d, J=12.0 Hz, COOC$\underline{H}_2$Ph), 6.38 (1H, d, J=8.5 Hz, 3-H), 7.20—7.32 (20H, m, OCH$_2\underline{Ph}$×4), 7.55 (1H, brs, NH). ^{13}C-NMR (100 MHz) δ: −4.99, −4.68 (q, Si(CH$_3$)$_2$), 18.04 (s, $\underline{C}$(CH$_3$)$_3$), 25.82 (q, C($\underline{C}$H$_3$)$_3$), 67.25 (t, COO$\underline{C}$H$_2$Ph), 70.60 (t, 7-C), 71.47 (t, O$\underline{C}$H$_2$Ph), 72.04 (d, 6-C), 73.29, 75.06 (each t, O$\underline{C}$H$_2$Ph×2), 75.40 (d, 4-C), 83.78 (d, 5-C), 127.58 (d, 3-C), 127.53, 127.66, 127.87, 127.94, 127.98, 128.09, 128.17, 128.22, 128.34, 128.45 (each d, OCH$_2\underline{Ph}$×4), 129.64 (s, 2-C), 135.84 (s, COOCH$_2\underline{Ph}$-1′-C),137.51, 137.79, 138.32 (each s, OCH$_2\underline{Ph}$-1′-C×3), 154.17 (s, NHCO), 167.02 (s, $\underline{C}$OOH). HR-FAB-MS m/z: 748.3281 [M+Na]$^+$. Calcd for $C_{42}H_{51}O_8NSiNa$: 748.3282 [M+Na].

(*Z*,4*R*,5*S*,6*R*)-*N*-2′-Hydroxypropyl-2-benzyloxycarbonylamino-6-*tert*-butyldimethyl-siloxy-4,5,7-tribenzyloxy-2-heptenamide (15) To a solution of **9** (652.5 mg, 0.90 mmol) in CH_2Cl_2 (9 ml) were added EDCI·HCl (346.2 mg, 1.80 mmol), HOBt (121.9 mg, 0.90 mmol), EtN(i-Pr)$_2$ (315 ml, 1.80 mmol), 1-amino-2-propanol (84 ml, 1.08 mmol) under argon and stirred for 23.5 h. The reaction mixture was diluted with $CHCl_3$ (100 ml), washed with H_2O (30 ml). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. Purification of the resulting yellow oil by flash column chromatography (n-hexane/AcOEt=3:2) afforded **15** (599 mg, 85.1%). Rf=0.49 ($CHCl_3$/MeOH=10:1). $[\alpha]_D^{23}$ −6.41° (c=1.28, $CHCl_3$). IR (KBr) cm^{-1}: 1720 (NHCOO), 1660 (CONH), 1640 (C=C), 1250 (OH), 1090 (OH). ^{1}H-NMR (400 MHz, DMSO-d_6) δ: −0.01, 0.00 (each 3H, s, Si(CH$_3$)$_2$), 0.81 (9H, s, C(CH$_3$)$_3$), 1.01 (3H, d, J=6 Hz, 3′-CH$_3$), 3.07 (2H, m, 1′-H$_2$), 3.47 (1H, dd, J=10.0, 6.5 Hz, 7-Ha), 3.62 (1H, dd, J=5.5, 2.5 Hz, 5-H), 3.65 (1H, m, 7-Hb), 3.68 (1H, m, 2′-H), 4.00, 4.15 (total 1H, each dt, J=6.0, 2.0 Hz; fifth, J=3.0 Hz, 6-H), 4.38, 4.39 (each 1H, d, J=13.0 Hz, OC$\underline{H}_2$Ph), 4.54, 4.58 (each 1H, d, J=12.5 Hz, OC$\underline{H}_2$Ph), 4.26, 4.49 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.44 (H, dd, J=9.0, 7.0 Hz, 4-H), 4.64, 4.65 (total 1H, each d, J=3.5 Hz, 2′-OH), 5.99, 6.24 (total 1H, J=9.0 Hz, 3-H), 7.87, 7.90 (total 1H, each t, J=6.0 Hz, CONH), 7.10—7.60 (20H, m, OCH$_2\underline{Ph}$×4), 8.45, 8.65 (total 1H, each br, NHCOO). HR-FAB-MS m/z: 805.3884 [M+Na]$^+$. Calcd for $C_{45}H_{58}O_8N_2SiNa$: 805.3860 [M+Na].

(*Z*,4*R*,5*S*,6*R*)-*N*-2′-Oxopropyl-2-benzyloxycarbonylamino-6-*tert*-butyldimethylsiloxy-4,5,7-tribenzyloxy-2-heptenamide (10) To a solution of **15** (9.3 mg, 0.012 mmol) in CH_2Cl_2 (1.0 ml) was added Dess–Martin reagent (26 mg, 0.06 mmol) under argon. After the reaction mixture was stirred for 40 min at room temperature, Dess–Martin reagent (5.1 mg, 0.012 mmol) was further added and stirred for 20 min. The reaction mixture was diluted with $CHCl_3$ (15 ml), washed with H_2O (5 ml). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by preparative TLC ($CHCl_3$/MeOH=30:1) afforded **10** (8.9 mg, 95.1%) as colorless oil. Rf=0.53 ($CHCl_3$/MeOH=20:1). $[\alpha]_D^{24}$ +30.27° (c=1.13, $CHCl_3$). IR (KBr) cm^{-1}: 1735 (NHCOO), 1725 (CO), 1660 (CONH), 1640 (C=C). ^{1}H-NMR (300 MHz) δ: −0.02, −0.01 (each 3H, s, Si(CH$_3$)$_2$), 0.82 (9H, s, C(CH$_3$)$_3$), 2.21 (3H, s, 3′-H$_3$), 3.37 (1H, dd, J=9.0, 4.0 Hz, 7-Ha), 3.69 (1H, dd, J=9.0, 7.0 Hz, 7-Hb), 3.71 (1H, dd, J=6.5, 2.5 Hz, 5-H), 3.92 (1H, ddd, J=7.0, 4.0, 2.5 Hz, 6-H), 4.17 (2H, brs, 1′-H$_2$), 4.38, 4.56 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.39 (1H, dd, J=8.5, 6.5 Hz, 4-H), 4.44, 4.48 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.70, 4.74 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 4.96, 5.06 (each 1H, d, J=12.0 Hz, COOC$\underline{H}_2$Ph), 5.92 (1H, d, J=8.5 Hz, 3-H), 6.63 (1H, brs, CONH), 7.10—7.60 (20H, m, OCH$_2\underline{Ph}$×4), 7.82 (1H, br s, NHCOO). ^{13}C-NMR (100 MHz) δ: −4.78, −4.63 (each q, Si(CH$_3$)$_2$), 18.09 (s, $\underline{C}$(CH$_3$)$_3$), 25.83 (q, C($\underline{C}$H$_3$)$_3$, 3′-CH$_3$), 67.20 (t, COO$\underline{C}$H$_2$Ph), 71.69 (t, 7-C), 71.80 (t, O$\underline{C}$H$_2$Ph), 72.22 (d, 6-C), 73.25 (t, O$\underline{C}$H$_2$Ph), 74.28 (d, 4-C), 74.42 (t, O$\underline{C}$H$_2$Ph), 83.67 (d, 5-C), 127.48 (d, 3-C), 127.59, 127.95, 128.04, 128.10, 128.19, 128.27, 128.30, 128.40, 128.43, 128.56 (each d, OCH$_2\underline{Ph}$×4), 133.55 (s, 2-C), 135.87 (s, COOCH$_2\underline{Ph}$), 137.35, 137.70, 138.00 (s, OCH$_2\underline{Ph}$×3), 153.90 (s, NHCOO), 164.06 (s, CONH), 202.43 (s, 2′-C). HR-FAB-MS m/z: 803.3705 [M+Na]$^+$, Calcd for $C_{45}H_{56}O_8N_2SiNa$: 803.3704 [M+Na].

(*Z*,4*R*,5*S*,6*R*)-*N*-2′-Oxopropyl-2-benzyloxycarbonylamino-6-hydroxy-4,5,7-tribenzyloxy-2-heptenamide (11a, 11b) To a mixture of **10** (99.9 mg, 0.128 mmol) in THF (0.7 ml) and dry pyridine (0.7 ml) was added HF-pyridine (820 μl) dropwise during 7 min under argon at 0 °C and stirred for 73.5 h. The reaction mixture was adjusted to pH 7—8 with saturated $NaHCO_3$ solution, then extracted with $CHCl_3$ (100 ml×3). The combined organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by preparative TLC (n-hexane/AcOEt=1:2) afforded **11a** (76.0 mg, 89.2%) and **11b** (7.7 mg, 9.0%), respectively, as a yellow oil. **11a**: Rf=0.16 (n-hexane/AcOEt=1:2). $[\alpha]_D^{24}$ +2.15° (c=1.21, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 2.21 (3H, s, 3′-CH$_3$), 2.62 (1H, brs, 6-OH), 3.55 (1H, dd, J=9.5, 5.0 Hz, 7-Ha), 3.59 (1H, dd, J=9.5, 4.0 Hz, 7-Hb), 3.70 (1H, dd, J=7.0, 4.0 Hz, 5-H), 3.93 (1H, m, 6-H), 4.17 (2H, brs, 1′-CH$_2$), 4.33, 4.54 (each 1H, d, J=11.5 Hz, OC$\underline{H}_2$Ph), 4.41 (1H, dd, J=7.0, 4.0 Hz, 4-H), 4.48, 4.52 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.52, 4.58 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 5.01, 5.06 (each 1H, d, J=12.0 Hz, COOC$\underline{H}_2$Ph), 6.00 (1H, d, J=7.0 Hz, 3-H), 6.62 (1H, brs, CONH), 7.19—7.34 (20H, m, OCH$_2\underline{Ph}$×4), 7.44 (1H, br s, NHCOO). ^{13}C-NMR (100 MHz) δ: 27.32 (q, 3′-C), 50.04 (t, 1′-C), 67.36 (t, COO$\underline{C}$H$_2$Ph), 70.29 (d, 6-C), 70.49 (t, 7-C), 71.63, 73.45, 74.60 (each t, O$\underline{C}$H$_2$Ph×3), 75.56 (d, 4-C), 80.80 (d, 5-C), 122.97 (d, 3-C), 127.85, 127.88, 128.0, 128.13, 128.21, 128.39, 128.42, 128.44, 128.47 (each d, OCH$_2\underline{Ph}$×4), 133.53 (s, 2-C), 135.71 (s, COOCH$_2\underline{Ph}$), 137.29, 137.31, 137.61 (each s, OCH$_2\underline{Ph}$×3), 153.96 (s, NHCOO), 164.16 (s, CONH), 202.39 (s, 2′-C). HR-FAB-MS m/z: 689.2829 [M+Na]$^+$, Calcd for $C_{39}H_{42}O_8N_2Na$: 689.2839 [M+Na]. **11b**: Rf=0.24 (n-hexane/AcOEt=1:2). $[\alpha]_D^{24}$ +93.44° (c=0.63, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 2.19 (3H, s, 3′-CH$_3$), 2.82 (1H, brs, 6-OH), 3.46 (1H, dd, J=9.5, 5.5 Hz, 7-Ha), 3.55 (1H, dd, J=9.5, 3.0 Hz, 7-Hb), 3.56 (1H, brs, 6-H), 3.84 (1H, dd, J=8.5, 3.2 Hz, 5-H), 4.17 (2H, brs, 1′-CH$_2$), 4.38, 4.63 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.41, 4.48 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 4.52 (1H, dd, J=9.0, 3.2 Hz, 4-H), 4.53, 4.86 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 5.06, 5.12 (each 1H, d, J=12.0 Hz, COOC$\underline{H}_2$Ph), 6.12 (1H, d, J=9.0 Hz, 3-H), 6.64 (1H, brs, CONH), 7.20—7.35 (20H, m, OCH$_2\underline{Ph}$×4), 7.59 (1H, brs, NHCOO). ^{13}C-NMR (100 MHz) δ: 27.33 (q, 3′-C), 50.05 (t, 1′-C), 67.35 (t, COO$\underline{C}$H$_2$Ph), 70.23 (t, 7-C), 70.74 (d, 6-C), 71.39, 73.34, 74.81 (each t, O$\underline{C}$H$_2$Ph×3), 75.92 (d, 4-C), 80.34 (d, 5-C), 123.71 (d, 3-C), 134.13 (s, 2-C), 135.84, 137.49, 137.93 (each s, OCH$_2\underline{Ph}$×4), 154.07 (s, NHCOO), 164.04 (s, CONH), 202.44 (s, 2′-C). HR-FAB-MS m/z: 689.2860 [M+Na]$^+$, Calcd for $C_{39}H_{42}O_8N_2Na$: 689.2839 [M+Na].

(*Z*,4*R*,5*S*,6*R*)-*N*-2′-Oxopropyl-2-benzyloxycarbonylamino-6-methanesulfonyl-4,5,7-tribenzyloxy-2-heptenamide (17) To a solution of **11a** (23.8 mg, 0.036 mmol) in CH_2Cl_2 (1.0 ml) were added triethylamine (15.0 ml) and MsCl (3.0 μl, 0.0396 mmol) at 0 °C under argon. After the reaction mixture was stirred for 10 min at 0 °C, it was diluted with H_2O (10 ml) and extracted by $CHCl_3$ (50 ml×2). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the resulting oil (31.5 mg) by preparative TLC (silica gel, n-hexane/AcOEt=1:2) afforded **17** (25.0 mg, 93.3%) as a colorless oil. Rf=0.40 (n-hexane/AcOEt=1:2). ^{1}H-NMR (400 MHz) δ: 2.20 (3H, s, 3′-CH$_3$), 2.92 (3H, s, SO$_2$CH$_3$), 3.75 (1H, dd, J=11.0, 7.0 Hz, 7-Ha), 3.83 (1H, dd, J=11.0, 3.5 Hz, 7-Hb), 3.90 (1H, t, J=4.0 Hz, 5-H), 4.16 (2H, brs, 1′-CH$_2$), 4.36 (1H, dd, J=7.0, 4.0 Hz, 4-H), 4.38, 4.51 (each 1H, d, J=11.5 Hz, OC$\underline{H}_2$Ph), 4.50 (2H, s, OC$\underline{H}_2$Ph), 4.62, 4.68 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 4.80, 5.05 (each 1H, d, J=12.0 Hz, OC$\underline{H}_2$Ph), 5.51 (1H, m, 6-H), 5.92 (1H, d, J=7.0 Hz, 3-H), 6.65 (1H, brt, J=4.0 Hz, 1-NH), 7.20—7.40 (20H, m, OCH$_2\underline{Ph}$×4). HR-FAB-MS m/z: 767.2594 [M]$^+$, Calcd for $C_{40}H_{44}O_{10}N_2SNa$: 767.2594 [M]. m/z: 767.2594 [M]$^+$, Calcd for $C_{40}H_{44}O_{10}N_2SNa$: 767.2614 [M].

(*Z*,4*R*,5*S*,6*R*)-*N*-2′-Oxopropyl-2-benzyloxycarbonylamino-6-monochloromethane sulfonyl-4,5,7-tribenzyloxy-2-heptenamide (18) To a solution of **11a** (134.2 mg, 0.202 mmol) in pyridine (2 ml), was added MeCl (90 μl, 1.01 mmol) at 0 °C under argon and stirred for 30 min at room temperature. The reaction mixture was diluted with H_2O (10 ml), extracted by $CHCl_3$ (20 ml×3). The combined $CHCl_3$ layer was dried over Na_2SO_4, and concentrated *in vacuo* to afford a yellow oil (223.8 mg). Purification of the residue by flash column chromatography (n-hexane/AcOEt=1:2) provided the desired product **18** (133.1 mg, 87.4%) as a colorless oil. Rf=0.36 (n-hexane/AcOEt=1:2). $[\alpha]_D^{24}$ +5.08° (c=1.30, $CHCl_3$). IR (KBr) cm^{-1}: 1725 (CO, NHCOO), 1650 (CONH), 1640 (C=C), 1370 (OSO$_2$). ^{1}H-NMR (400 MHz) δ: 2.21 (3H, s, 3′-CH$_3$), 3.75 (1H, dd, J=11.5, 7.0 Hz, 7-Ha), 3.86 (1H, dd, J=11.5, 3.0 Hz, 7-Hb), 3.99 (1H, t, J=4.0 Hz, 5-H), 4.16 (2H, brs, 1′-CH$_2$), 4.37 (1H, dd, J=7.5, 4.0 Hz, 4-H), 4.38, 4.51 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 4.50, 4.62 (each 1H, d, J=12.5 Hz, OC$\underline{H}_2$Ph), 4.50 (2H, s, SO$_2$CH$_2$Cl), 4.60, 4.67 (each 1H, d, J=11.0 Hz, OC$\underline{H}_2$Ph), 4.98, 5.06 (each 1H, d, J=12.0 Hz, COOC$\underline{H}_2$Ph), 5.12 (1H, ddd, J=7.0, 4.0, 3.0 Hz, 6-H), 5.90 (1H, d, J=7.5 Hz, 3-H), 6.62 (1H, brt, J=4.0 Hz, CONH), 7.20—7.40 (20H, m, OCH$_2\underline{Ph}$×4). ^{13}C-NMR (100 MHz) δ: 27.30 (q, 3′-C), 50.02 (t, 1′-C), 54.15 (t, SO$_2\underline{C}$H$_2$Cl), 67.50 (t, COO$\underline{C}$H$_2$Ph), 68.68 (d, 6-C), 71.79 (t, 7-C), 73.61, 75.07, 75.12 (each t, O$\underline{C}$H$_2$Ph×3), 80.29 (d, 4-C), 83.18 (d, 5-C), 121.44 (d, 3-C), 127.50—129.40 (each d, OCH$_2\underline{Ph}$×4), 133.93 (s, 2-C), 135.63 (s, COOCH$_2\underline{Ph}$), 136.62, 136.98, 137.12 (each s, OCH$_2\underline{Ph}$×3), 153.73 (s, NHCOO), 164.08 (s, CONH), 202.32 (s, 2′-C). HR-FAB-MS m/z: 801.2255 [M+Na]$^+$, Calcd for $C_{40}H_{43}O_{10}N_2ClSNa$: 801.2225 [M+Na].

(*E*,3*R*,4*R*,5*S*)-*N*-Benzyloxycarbonyl-*N*′-2′-oxopropyl-α-(5-benzyloxymethyl-3,4-dibenzyl-oxypyrrolidine-2-ylidene)glycinamide (5c) To a solution of **18** (133.1 mg, 0.17 mmol) in DMF (1.7 ml) were added $BnEt_3N^+Br^-$ (23.3 mg, 0.09 mmol), NaN_3 (119.9 mg, 1.71 mmol) under

argon. After the solution was stirred for 19.5 h at 50 °C, it was diluted with H_2O (7 ml) and extracted with a mixture of solvents (*n*-hexane/AcOEt=1:1) (15 ml×3). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the resulting yellow oil (135.6 mg) by flash column chromatography (*n*-hexane/AcOEt=1:2) afforded **5c** (80.5 mg, 71.0%) as a yellow oil. *Rf*=0.40 (*n*-hexane/AcOEt=1:2). $[\alpha]_D^{24}$ +20.98° (*c*=1.02, $CHCl_3$). IR (KBr) cm^{-1}: 1720 (NHCO), 1710 (CO), 1655 (CONH), 1645 (C=C). ^{1}H-NMR (400 MHz) δ: 2.15 (3H, s, 3′-CH_3), 3.54 (1H, dd, *J*=9.5, 6.5 Hz, 6-Ha), 3.63 (1H, dd, *J*=9.5, 4.0 Hz, 6-Hb), 4.04, 4.45 (each 1H, m, 1′-CH_2), 4.10 (1H, br, 5-H), 4.11 (1H, brs, 4-H), 4.44, 4.54 (each 1H, d, *J*=12.0 Hz, OC$\underline{H}_2$Ph), 4.46, 4.49 (each 1H, d, *J*=11.0 Hz, OC$\underline{H}_2$Ph), 4.48, 4.51 (each 1H, d, *J*=11.5 Hz, OC$\underline{H}_2$Ph), 4.58 (1H, brs, 3-H), 5.05 (1H, d, *J*=12.0 Hz, $COOCH_2$Ph-Ha), 5.15 (1H, brs, $COOCH_2$Ph-Hb), 5.86 (1H, brs, NHCOO), 6.39 (1H, brs, CONH), 7.15—7.40 (20H, m, $OCH_2\underline{Ph}$×4), 8.34 (1H, brs, 1-H). ^{13}C-NMR (100 MHz) δ: 27.18 (q, 3′-C), 49.58 (t, 1′-C), 59.57 (d, 5-C), 67.15 (t, COOC$\underline{H}_2$Ph), 69.15 (t, 6-C), 72.31, 73.46 (each t, OC$\underline{H}_2$Ph×3), 80.43, (d, 4-C) 83.29 (d, 3-C), 94.22 (s, α-C), 127.0—129.5 (each d, $OCH_2\underline{Ph}$×4), 136.33 (s, $COOCH_2\underline{Ph}$), 137.20, 137.32, 137.93 (s, $OCH_2\underline{Ph}$×3), 156.429 (s, 2-C), 156.76 (s, NHCOO), 168.48 (s, CONH), 203.89 (s, 2′-C). HR-FAB-MS *m/z*: 664.3025 $[M+Na]^+$, Calcd for $C_{39}H_{42}O_7N_3$: 664.3023 [M+Na].

Allyl (*Z*,4*R*,5*S*,6*R*)-2-Benzyloxycarbonyamino-6-*tert*-butyldimethyl-siloxy-4,5,7-tribenzyloxy-2-heptenoate (12) To a solution of **9** (511.4 mg, 0.71 mmol) in CH_2Cl_2 (7 ml) were added EDCI·HCl (406.0 mg, 2.12 mmol), HOBt (145.7 mg, 1.06 mmol), EtN (*i*-Pr)$_2$ (370 μl, 2.12 mmol), allyl alcohol (96 μl, 1.41 mmol) under argon. After the solution was stirred for 19.5 h at room temperature, it was partitioned between H_2O (80 ml) and $CHCl_3$ (120 ml) and the aqueous layer was further extracted with $CHCl_3$ (120 ml×2). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The resulting yellow oil (615.5 mg) was purified by flash column chromatography (*n*-hexane/AcOEt=12:1) to provide **12** (458.7 mg, 85.1%) as a yellow oil. *Rf*=0.30 (*n*-hexane/AcOEt=5:1). $[\alpha]_D^{24}$ −3.33° (*c*=0.40, $CHCl_3$). IR (KBr) cm^{-1}: 1735 (COO), 1725 (NHCO), 1655 (CH=CH_2), 1635 (C=C). ^{1}H-NMR (300 MHz) δ: −0.01 (6H, s, $Si(CH_3)_2$), 0.83 (9H, s, $C(CH_3)_3$), 3.39 (1H, dd, *J*=9.0, 4.5 Hz, 7-Ha), 3.69 (1H, dd, *J*=9.0, 6.5 Hz, 7-Hb), 3.74 (1H, dd, *J*=6.5, 3.0 Hz, 5-H), 3.94 (1H, ddd, *J*=6.5, 4.5, 3.0 Hz, 6-H), 4.38, 4.59 (each 1H, d, *J*=11.5 Hz, OC$\underline{H}_2$Ph), 4.44, 4.48 (each 1H, d, *J*=11.5 Hz, OC$\underline{H}_2$Ph), 4.45 (1H, dd, *J*=8.5, 6.5 Hz, 4-H), 4.68 (2H, m, 1′-H_2), 4.68, 4.72 (each 1H, d, *J*=11.0 Hz, OC$\underline{H}_2$Ph), 5.03, 5.09 (each 1H, d, *J*=12.0 Hz, $COOC\underline{H}_2$Ph), 5.24 (1H, dd, *J*=10.0, 1.0 Hz, 3′-*cis*-H), 5.34 (1H, dd, *J*=17.0, 1.0 Hz, 3′-*trans*-H), 5.91 (1H, ddt, *J*=17.0, 10.0, 5.5 Hz, 2′-H), 6.18 (1H, d, *J*=8.5 Hz, 3-H), 7.16—7.35 (20H, m, $OCH_2\underline{Ph}$×4), 7.54 (1H, brs, NH). ^{13}C-NMR (75.0 MHz) δ: −4.97, −4.65 (q, $Si(CH_3)_2$), 18.20 (s, $\underline{C}(CH_3)_3$)25.78 (q, $C(\underline{C}H_3)_3$), 66.06 (t, 1′-C), 67.22 (t, $COO\underline{C}H_2$Ph), 70.49 (t, 7-C), 71.34 (t, O$\underline{C}H_2$Ph), 71.91 (d, 6-C), 73.24, 75.04 (each t, O$\underline{C}H_2$Ph×2), 75.30 (d, 4-C), 83.88 (d, 5-C), 118.41 (t, 3′-C), 127—129 (each d, $OCH_2\underline{Ph}$×4), 130.41 (d, 3-C), 130.86 (s, 2-C), 131.80 (d, 2′-C), 135.91 (s, $COOCH_2\underline{Ph}$), 137.48, 137.87, 138.38 (each s, $OCH_2\underline{Ph}$×3), 153.73 (s, NHCO), 163.57 (s, $\underline{C}$OOallyl). HR-FAB-MS *m/z*: 788.3602 $[M+Na]^+$, Calcd for $C_{45}H_{55}O_8NSiNa$: 788.3595 [M+Na].

Allyl (*Z* and *E*,4*R*,5*S*,6*R*)-2-Benzyloxycarbonylamino-6-hydroxy-4,5,7-tribenzyloxy-2-heptenoate (13a, 13b) To a solution of **12** (636.9 mg, 0.83 mmol) in the solvent of THF–pyridine (1:1) (8 ml) was added HF–pyridine (5.6 μl) during 30 min at 0 °C under argon. After the solution was allowed to stir for 19.8 h at 0 °C, it was adjusted to pH 8—9 with saturated $NaHCO_3$ dropwise and extracted with $CHCl_3$ (150 ml×3). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The resulting yellow oil (634 mg) was purified by flash column chromatography (*n*-hexane/AcOEt=3:1) to give **13a** (*Z*-form, 422.7 mg, 77.9%) and **13b** (*E*-form, 74.2 mg, 13.7%) as a colorless oil, respectively. **13a** *Rf*=0.27 (*n*-hexane/AcOEt=2:1). $[\alpha]_D^{24}$ 0.00° (*c*=0.50, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 2.82 (1H, d, *J*=5.5 Hz, 6-OH), 3.61 (1H, dd, *J*=5.0, 10.0 Hz, 7-CHa), 3.65 (1H, dd, *J*=3.5, 10.0 Hz, 7-CHb), 3.81 (1H, dd, *J*=3.2, 7.0 Hz, 5-OH), 4.00 (1H, m, 6-H), 4.39 (1H, d, *J*=10.5 Hz, benzyl-CHa), 4.53—4.65 (5H, m, benzyl-CHb), 4.54 (1H, m, 4-H), 4.72 (2H, d, *J*=5.3 Hz, Allyl-OCH_2), 5.09, 5.13 (each 1H, d, *J*=12.0 Hz, benzyl-CH_2), 5.29 (1H, dq, *J*=10.5, 1.0 Hz, Allyl=CH_2-*cis*), 5.38 (1H, dq, *J*=16.0, 1.0 Hz, Allyl=CH_2-*trans*), 5.95 (1H, m, Allyl-CH=), 6.43 (1H, d, *J*=8.0 Hz, 3-H), 7.22—7.45 (20H, m, $OCH_2\underline{Ph}$). HR-FAB-MS *m/z*: 674.2730 $[M+Na]^+$, Calcd for $C_{39}H_{41}O_8NNa$: 674.2730. **13b** *Rf*=(hexane:AcOEt=2:1). $[\alpha]_D^{24}$ +127.99° (*c*=0.50, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.46 (1H, dd, *J*=10.0, 5.5 Hz, 7-Ha). 3.56 (1H, dd, *J*=10.0, 3.0 Hz, 7-Hb), 3.59 (1H, ddd, *J*=8.5, 5.5, 3.0 Hz, 6-H), 3.85 (1H, dd, *J*=8.5, 3.0 Hz, 5-H), 4.37, 4.66 (each 1H, brd, *J*=12.0 Hz, benzyl-CH_2), 4.42, 4.48 (each 1H, d, *J*=11.5 Hz, benzyl-CH_2), 4.54, 4.86 (each 1H, d, *J*=11.0 Hz, benzyl-CH_2), 4.58 (1H, dd, *J*=9.0, 3.0 Hz, 4-H), 4.66 (2H, br, OCH_2), 5.10, 5.14 (each 1H, d, *J*=12.0 Hz, COOBn-CH_2), 5.23 (1H, brd, *J*=10.0 Hz, Allyl=CH_2-*cis*), 5.33 (1H, brd, *J*=17.0 Hz, Allyl=CH_2-*trans*), 5.91 (1H, m, Allyl-CH=), 6.37 (1H, d, *J*=9.0 Hz, 3-H), 7.20—7.37 (20H, m, $OCH_2\underline{Ph}$). HR-FAB-MS *m/z*: 674.2730 $[M+Na]^+$, Calcd for $C_{39}H_{41}O_8NNa$: 674.2730.

Allyl (*Z*,4*R*,5*R*,6)-6-Azido-2-benzyloxycarbonylamino-4,5,7-tribenzyloxy-2-heptenoate (4d) To a solution of **13a** (1.238 g, 1.90 mmol) in CH_2Cl_2 (19 ml) were added 2,6-lutidine (1.1 ml, 9.50 mmol), Tf_2O (1.6 ml, 9.50 mmol) at −40 °C under argon. After the mixture was allowed to stir for 55 min, $BnEt_3N^+Br^-$ (262.7 mg, 0.96 mmol), NaN_3 (1.24 g, 19.10 mmol) were added and stirred for 30 min at −40 °C after which it was allowed to warm to −20 °C, stirred for 19 h. The resulting mixture was diluted with H_2O (100 ml) and extracted with *n*-hexane/AcOEt (1:1) (250 ml×3). The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo* to provide light brown oil **4d** (2.16 g) as a crude substance, which was used directly in the next reaction because of its instability. *Rf*=0.58 (toluene/acetone=10:1). IR (KBr) cm^{-1}: 3400 (NH), 2100 (N_3), 1730 (COO, NHCOO), 1675 (CH=CH_2), 1620 (C=C).

Allyl (*E*,3*R*,4*R*,5*S*)-*N*-Benzyloxycarbonyl-*N*-*tert*-butoxycarbonyl-α-(5-benzyloxymethyl-3,4-dibenzyloxypyrrolidin-2-ylidene)glycinate (5d) Compound **4d** was dissolved in THF (38 ml) and stirred for 2 h at 60 °C under argon. After that, the solvent was removed and the resulting residue was purified by flash column chromatography (silica gel, toluene/acetone=50:1) to afford **5d** (729.9 mg, 59.3% from **13a** as a light yellow oil. *Rf*=0.43 (toluene/acetone=10:1). $[\alpha]_D^{25}$ +10.3° (*c*=1.05, $CHCl_3$). IR (KBr) cm^{-1}: 1735 (COO), 1720 (NHCO), 1680 (CH=CH_2), 1610 (C=C). ^{1}H-NMR (400 MHz) δ: 3.59 (1H, dd, *J*=9.5, 8.0 Hz, 6-Ha), 3.66 (1H, *J*=9.5, 4.0 Hz, 6-Hb), 4.06 (1H, brs, 4-H), 4.18 (1H, m, 5-H), 4.40, 4.52 (each 1H, d, *J*=12.0 Hz, 4-OC$\underline{H}_2$Ph), 4.45, 4.49 (each 1H, d, *J*=11.0 Hz, 3-OC$\underline{H}_2$Ph), 4.50, 4.57 (each 1H, d, *J*=11.5 Hz, 6-OC$\underline{H}_2$Ph), 4.61 (2H, brd, *J*=5.0 Hz, 1′-H_2), 4.67 (1H, brs, 3-H), 5.12, 5.15 (each 1H, d, *J*=12.0 Hz, $COOC\underline{H}_2$Ph), 5.16 (1H, brd, *J*=11.0 Hz, 3′-*cis*-H), 5.28 (1H, brd, *J*=17.0 Hz, 3′-*trans*-H), 5.68 (1H, brs, NHCO), 5.89 (1H, ddd, *J*=17.0, 11.0, 5.0 Hz, 2′-H), 7.18—7.45 (20H, m, $OCH_2\underline{Ph}$×4), 7.90 (1H, brs, 1-H). ^{13}C-NMR (100 MHz) δ: 60.48 (d, 5-C), 64.25 (t, 1′-C), 66.78 (t, COOC$\underline{H}_2$Ph), 68.99 (t, 6-C), 72.05 (t, 4-O$\underline{C}H_2$Ph), 72.68 (3-O$\underline{C}H_2$Ph), 73.47 (t, 6-O$\underline{C}H_2$Ph), 79.94 (d, 4-C), 82.54 (d, 3-C), 92.37 (s, α-C), 117.10 (t, 3′-C), 127.69, 127.82, 127.98, 128.17, 128.30, 128.40, 128.47 (each d, $OCH_2\underline{Ph}$×4), 132.92 (d, 2′-C), 136.75 (s, $COOCH_2\underline{Ph}$), 137.34, 137.83 (s, $OCH_2\underline{Ph}$×3), 156.28 (s, NHCO), 159.83 (s, 2-C), 167.47 (s, $\underline{C}$OOAllyl). HR-FAB-MS *m/z*: 671.2754 $[M+Na]^+$, Calcd for $C_{39}H_{40}O_7N_2Na$: 671.2733 [M+Na].

Methyl (*E*,3*R*,4*R*,5*S*)-*N*-Benzyloxycarbonyl-*N*-*tert*-butoxycarbonyl-α-(3,4-dibenzyloxy-5-benzyloxymethylpyrrolidin-2-ylidene)glycinate (20) To a solution of **5a** (37.0 mg, 0.06 mmol) in CH_2Cl_2 (0.8 ml) were added DMAP (3.7 mg, 0.03 mmol), Et_3N (4 μl, 0.03 mmol), Boc_2O (1.4 μl, 0.06 mmol). After the solution was stirred for 1 h at 0 °C under argon, further reagents, DMAP (3.7 mg), Et_3N (4 μl), Boc_2O (1.4 μl) were added and stirred for additional 4 h, then the solvent was removed *in vacuo*. Resulted yellow oil (63.5 mg) was purified by preparative TLC (silica gel, *n*-hexane/AcOEt=1:1) to give **20** (37.6 mg, 88%) as a light yellow oil. *Rf*=0.32 (*n*-hexane/AcOEt=2:1). $[\alpha]_D^{24}$ +5.40° (*c*=1.00, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 1.38 (9H, s, $C(CH_3)_3$), 3.55 (1H, dd, *J*=9.6, 7.8 Hz, 6-Ha), 3.58 (3H, s, $COOCH_3$), 3.67 (1H, dd, *J*=9.6, 5.0 Hz, 6-Hb), 4.06 (1H, dd, *J*=5.0, 2.7 Hz, 4-H), 4.18 (1H, dt, *J*=7.8, 5.0 Hz, 5-H), 4.37, 4.47 (each 1H, d, *J*=11.4 Hz, OCH_2Ph), 4.45, 4.50 (each 1H, d, *J*=12.0 Hz, OC$\underline{H}_2$Ph), 4.50, 4.56 (each 1H, d, *J*=12.0 Hz, O$\underline{C}H_2$Ph), 4.54 (1H, d, *J*=2.7 Hz, 3-H), 4.72, 5.07 (each 1H, d, *J*=12.5 Hz, $COOCH_2$Ph), 7.12—7.40 (20H, m, $OCH_2\underline{Ph}$×4), 7.98 (1H, brs, 1-H). ^{13}C-NMR δ: 27.89 (q, $C(\underline{C}H_3)_3$), 50.80 (q, $COO\underline{C}H_3$), 60.38 (d, 5-C), 67.57 (t, COO$\underline{C}H_2$Ph), 69.15 (t, 6-C), 72.24, 72.85, 73.53 (each t, O$\underline{C}H_2$Ph×3), 79.89 (d, 4-C), 82.95 (s, $\underline{C}(CH_3)_3$), 83.00 (d, 3-C), 96.20 (s, α-C), 127.62, 127.65, 127.67, 127.70, 127.74, 127.82, 127.91, 127.95, 128.17, 128.01, 128.26, 128.30, 128.33, 128.35, 128.40, 128.46 (each d, $OCH_2\underline{Ph}$×4), 136.00 (s, $COOCH_2\underline{Ph}$-1′-C), 137.15, 137.26, 137.81 (each s, $OCH_2\underline{Ph}$-1′-C×3), 152.09 (s, NHCO), 153.82 (s, $\underline{C}OOCH_2$Ph), 158.40 (s, 2-C), 167.70 (s, $\underline{C}OOCH_3$). HR-FAB-MS *m/z*: $[M-H]^+$ 721.3127, Calcd for $C_{42}H_{45}O_9N_2Na$: 721.3125.

Methyl (*E*,3*R*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-α-(3,4-dihydroxy-5-hydroxymethyl-pyrrolidine-2-ylidene)glycinate (21) To a solution of **20** (472 mg, 0.654 mmol) in MeOH (20 ml) was added $Pd(OH)_2$/C (377.8 mg) in MeOH (11 ml). After the mixture was stirred under hydrogen gas for 2.5 h at room temperature, the reaction mixture was evaporated *in vacuo*. Resulting yellow oil (222.5 mg) was purified by flash column chromatography (silica gel, *n*-hexane/AcOEt=2:1) to provide **21** (172.3 mg, 83%) as a light yellow

oil. *Rf*=0.11 (*n*-hexane/AcOEt=1:5), IR (KBr) cm^{-1}: 3400 (OH, NH), 1670 (COO, NHCOO), 1590 (C=C), 1480, 1430 (Ph). $[\alpha]_D^{24}$ −47.8° (*c*=1.00, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 1.48 (9H, s, $C(CH_3)_3$), 3.71 (3H, s, $COOCH_3$), 3.97 (1H, dd, *J*=12.0, 5.0 Hz, 6-Ha), 4.02 (1H, dd, *J*=12.0, 4.0 Hz, 6-Hb), 4.17 (1H, dt, *J*=5.0, 4.0 Hz, 5-H), 4.32 (1H, dd, *J*=4.0 Hz, 4-H), 4.66 (1H, br, 3-H), 5.63 (1H, brs, NHCO), 7.69 (1H, brs, 1-H). ^{13}C-NMR δ: 28.27 (q, $C(\underline{C}H_3)_3$), 51.22 (q, $COO\underline{C}H_3$), 60.77 (d, 6-C), 62.63 (d, 5-C), 74.87 (d, 4-C), 78.63 (s, 3-C), 91.24 (s, $\underline{C}(CH_3)_3$), 99.23 (s, α-C), 158.73 (s, 2-C), 158.75 (s, $\underline{C}OOC(CH_3)_3$), 162.99 (s, NHCO), 168.63 (s, $\underline{C}OOCH_3$). HR-FAB-MS *m/z*: 318.1431 $[M]^+$, Calcd for $C_{13}H_{22}O_7N_2$: 318.1427.

Methyl (*E*,3*R*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-α-(3,4-dihydroxy-5-methanesulfonyloxymethyl-pyrrolidine-2-ylidene)glycinate (22) To a solution of **21** (24.5 mg, 0.08 mmol) in CH_2Cl_2 (60 ml) were added Et_3N (44 μl, 0.32 mmol), MsCl (9 μl, 0.08 mmol). After the solution was stirred for 16 h under argon at −40 °C, Et_3N (66 μl, 0.48 mmol), MsCl (9 μl, 0.12 mmol) were further additioned and stirred for 4 h. The reaction mixture was diluted with $CHCl_3$ (20 ml), washed with saturated $NaHCO_3$ (1 ml×2), saturated NaCl (1 ml), dried over Na_2SO_4, evaporated *in vacuo*. The residue (51.8 mg) was purified by preparative TLC (silica gel, *n*-hexane/AcOEt=1:10) to afford **22** (17.5 mg, 57%) as a light yellow oil. *Rf*=0.44 (*n*-hexane/AcOEt=1:10). $[\alpha]_D^{24}$ −49.20° (*c*=1.00, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 1.48 (9H, s, $C(CH_3)_3$), 3.09 (3H, s, SO_2CH_3), 3.72 (3H, s, $COOCH_3$), 4.28 (1H, dd, *J*=10.5, 7.5 Hz, 6-Ha), 4.38 (1H, m, 5-H), 4.49 (1H, dd, *J*=10.5, 3.2 Hz, 6-Hb), 4.57 (1H, dd, *J*=8.5, 3.0 Hz, 4-H), 4.93 (1H, brd, *J*=3.0 Hz, 3-H), 5.64 (1H, s, NHCO), 7.84 (1H, brs, 1-H). HR-FAB-MS *m/z*: 419.1119 $[M+Na]^+$, Calcd for $C_{14}H_{24}O_9N_2SNa$: 419.1120.

Methyl (*E*,3*R*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-α-(3,4-diacetoxy-5-methanesulfonyloxymethyl-pyrrolidine-2-ylidene)glycinate (6a) To a solution of **22** (24.1 mg, 0.06 mmol) in dry pyridine (0.7 mg) were added dimethylaminopyridine (DMAP) (2.4 mg, 0.06 mmol), Ac_2O (14 μl, 0.15 mmol). After the mixture was stirred for 13 h at 0 °C, EtOH was added to quench Ac_2O and stirred for 5 min. The solvent was removed *in vacuo* to give a yellow oil (37.2 mg), which was purified by preparative TLC (silica gel, *n*-hexane/AcOEt=1:3) to give **6a** (23.5 mg, 80%) as a light yellow oil. *Rf*=0.50 (*n*-hexane/AcOEt=1:3). $[\alpha]_D^{24}$ −14.60° (*c*=1.00, $CHCl_3$). ^{1}H-NMR (400 MHz) δ: 1.42 (9H, s, $C(CH_3)_3$), 2.08, 2.12 (each 3H, s, $OCOCH_3$×2), 3.11 (3H, s, OSO_2CH_3), 3.70 (3H, s, $COOCH_3$), 4.20 (1H, dd, *J*=10.0, 6.0 Hz, 6-Ha), 4.37 (1H, dd, *J*=10.0, 5.0 Hz, 6-Hb), 4.38 (1H, m, 5-H), 5.30 (1H, s, NHCO), 5.36 (1H, dd, *J*=5.0, 3.5 Hz, 4-H), 6.03 (1H, d, *J*=3.5 Hz, 3-H), 7.98 (1H, brs, 1-H). HR-FAB-MS *m/z*: 480.1415 $[M]^+$, Calcd for $C_{18}H_{28}O_{11}N_2S$: 480.1413.

Methyl (*E*,3*R*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-α-(3,4-dibenzyloxy-5-hydoxymethylpyrrolidin-2-ylidene)glycinate (24) To a solution of **20** (93.5 mg, 0.129 mol) in MeOH (20 ml) was added $Pd(OH)_2$/C (37.4 mg) in MeOH (1 ml). The mixture was stirred for 45 min under hydrogen gas at room temperature, after that it was filtered off, evaporated *in vacuo*. Resulted oil (69.9 mg) was purified by preparative TLC (silica gel, *n*-hexane/AcOEt=1:3) to obtain **24** (25.3 mg, 39%) as a light yellow oil. *Rf*=0.38 (*n*-hexane/AcOEt=1:4). $[\alpha]_D^{24}$ −47.60° (*c*=1.00, $CHCl_3$). ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.34 (9H, s, $C(CH_3)_3$), 3.55 (3H, s, $COOCH_3$), 3.54 (1H, td, *J*=11.0, 6.5 Hz, 6-Ha), 3.63 (1H, td, *J*=11.0, 5.0 Hz, 6-Hb), 3.99 (1H, m, 5-H), 3.99 (1H, dd, *J*=4.5, 1.0 Hz, 4-H), 4.36, 4.46 (each 1H, d, *J*=11.5 Hz, $OC\underline{H}_2Ph$), 4.52, 4.58 (each 1H, d, *J*=12.0 Hz, $OC\underline{H}_2Ph$), 4.61 (1H, brd, *J*=1.0 Hz, 3-H), 4.91 (1H, dd, 6-OH), 7.23—7.37 (10H, m, $OCH_2\underline{Ph}$), 7.52 (1H, brs, NHCO), 7.83 (1H, brs, 1-H). ^{13}C-NMR δ: 28.16 (q, $C(\underline{C}H_3)_3$), 50.36 (q, $COO\underline{C}H_3$), 59.76 (d, 6-C), 63.31 (t, 5-C), 70.74, 71.14 (each t, $O\underline{C}H_2Ph$×2), 77.61 (s, $\underline{C}(CH_3)_3$), 79.15 (d, 4-C), 80.83 (d, 3-C), 92.30 (s, α-C), 127.52, 127.63, 127.68 127.79 127.97, 128.14 (each d, $OCH_2\underline{Ph}$×2), 137.87 (each, s, $OCH_2\underline{Ph}$-1′-C×2), 155.67 (s, NHCO), 159.49 (s, 2-C), 168.05 (s, $\underline{C}OOCH_3$). HR-FAB-MS *m/z*: 498.2367 $[M]^+$, Calcd for $C_{27}H_{34}O_7N_2$: 498.2366.

Methyl (*E*,3*R*,4*R*,5*S*)-*N*-*tert*-Butoxycarbonyl-α-(3,4-dibenzyloxy-methanesulfonyloxymethyl-pyrrolidine-2-ylidene)glycinate (6b) To a solution of **24** (94.6 mg, 0.19 mol) in CH_2Cl_2 (60 ml) were added Et_3N (80 μl, 0.51 mmol), MsCl (22 μl, 0.28 mmol). After the solution was stirred for 1.2 h under argon at −78 °C, the reaction mixture was diluted with $CHCl_3$ (60 ml), washed with saturated $NaHCO_3$ (2 ml), saturated NaCl (2 ml), dried over Na_2SO_4, concentrated *in vacuo*. Resulting yellow oil (174 mg) was purified by preparative TLC (silica gel, *n*-hexane/AcOEt=1:2) to provide **6b** (79.7 mg, 73%) as a light yellow oil. *Rf*=0.35 (*n*-hexane/AcOEt=1:1). $[\alpha]_D^{26}$ −13.60° (*c*=1.00, $CHCl_3$). ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 1.34 (9H, s, $C(CH_3)$), 3.17 (3H, s, SO_2Me), 3.56 (3H, s, $COOCH_3$), 4.12 (1H, d, *J*=5.0, 1.5 Hz, 4-H), 4.20 (1H, td, *J*=5.5, 5.0, 5-H), 4.35, 4.38 (each 1H, dd, *J*=12.5, 5.5, 6-H_2), 4.45, 5.51 (each 1H, d, *J*=11.4 Hz, $OC\underline{H}_2Ph$), 4.53, 4.58 (each 1H, d, *J*=11.5 Hz, $OC\underline{H}_2Ph$), 4.66 (1H, d, *J*=1.5 Hz, 3-H), 7.20—7.42 (10H, m, $OCH_2\underline{Ph}$×2), 7.56 (1H, brs, NHCO), 7.85 (1H, brs, 1-H). HR-FAB-MS *m/z*: 576.2156 $[M]^+$, Calcd for $C_{28}H_{36}O_9N_2S$: 576.2141.

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