

and improves the quantum efficiency of the device. Figure 6 shows the L-I curves of the single and double layer EL devices.

Good processibility and pure red emission of the DAPPV-PTV, and the dramatic voltage dependent spectral change and the quantum efficiency improvement in the double layer device may make it a good candidate for application in polymer LEDs.

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Synthetic Studies on Carbapenam Skeletons (II)

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Syntheses of carbapenam skeletons were achieved from 3-benzyloxypropanal through 1,3-dipolar cycloaddition. 3-Benzyloxypropanal was reacted with *N*-hydroxyglycine ester to give *C*-(2-benzyloxyethyl)-*N*-alkoxycarbonylmethylnitron (6). 1,3-Dipolar cycloaddition of the nitron with ethyl crotonate gave 3-(2-benzyloxyethyl)isoxazolidine (7). Compound 7 was transformed to 4-(2-hydroxyethyl)-2-azetidinone (11). Compound 11 was converted to 4-(2-iodoethyl)-2-azetidinone (13) or 4-phenylthiocarbonylmethyl-2-azetidinone (16) which was cyclized to give 6-(1-hydroxyethyl)carbapenam-3-carboxylate (14, 17).

Introduction

Thienamycin (1) has a unique structure and shows broad and strong antimicrobial activity.^{1,2} Many synthetic studies, therefore, have been carried out to obtain thienamycin and its derivatives. One of the synthetic approach was through 1,3-dipolar cycloaddition of crotonates with nitrones to give isoxazolidine derivatives, which were transformed to carbapenems.³⁻⁵

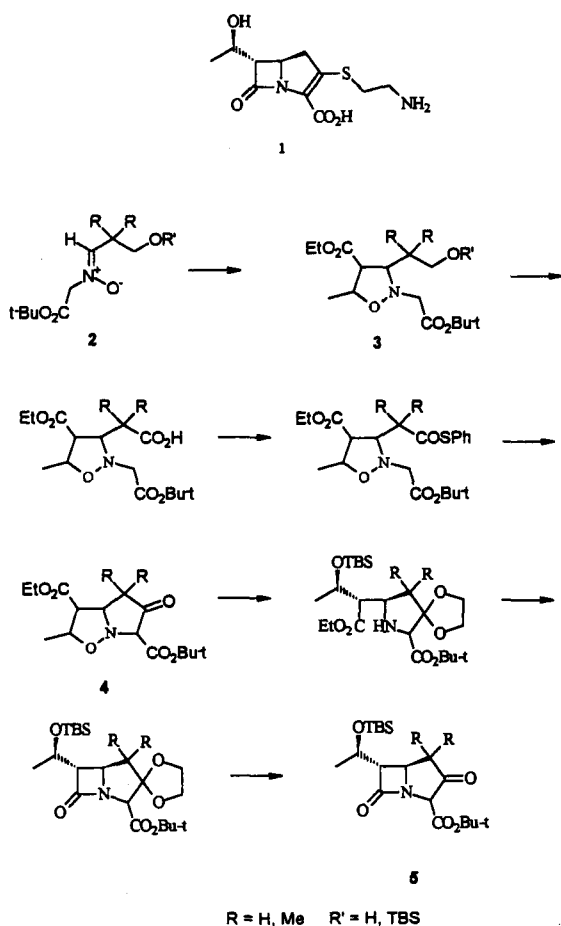
During the development of a new route for the synthesis of carbapenam analogs, the isoxazolidine derivatives (3) produced by 1,3-dipolar cycloaddition of *C*-(2-hydroxyethyl)-*N*-alkoxycarbonylmethylnitron (2) with crotonate were cyclized to give 3-methyl-7-oxo-2-azabicyclo[3.3.0]octane-4,8-dicarboxylate (4). The N-O bond of 4 was reduced to give β -amino esters, which could be cyclized by treatment with

a Grignard reagent to yield 6-(1-hydroxyethyl)-2-oxocarapenam-3-carboxylate (5). The results were published in the previous paper⁶ (Scheme 1).

As a part of the continued study, the present paper covers another conversion of isoxazolidine derivatives to carbapenam skeletons.

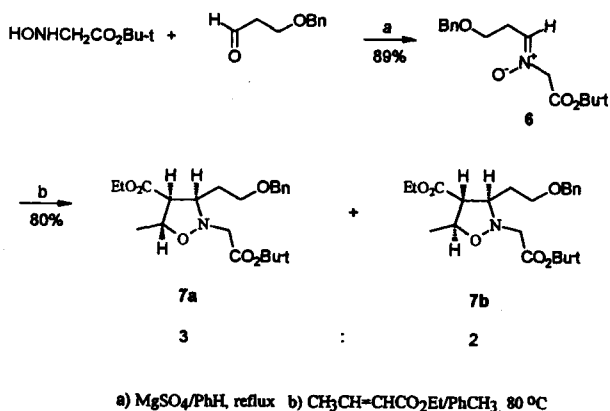
Results and Discussion

Synthesis of 1-(*t*-butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-hydroxyethyl)-2-azetidinone. Reflux of the benzene solution of *N*-hydroxyglycine *t*-butyl ester⁷ and 3-benzyloxypropanal⁸ for 30 min yielded *N*-(3-benzyloxypropylidene)glycine *N*-oxide *t*-butyl ester (6) in a good yield (89%). The product showed a triplet ($J=5.7$ Hz) at 6.82 ppm for N=CH, a singlet at 4.43

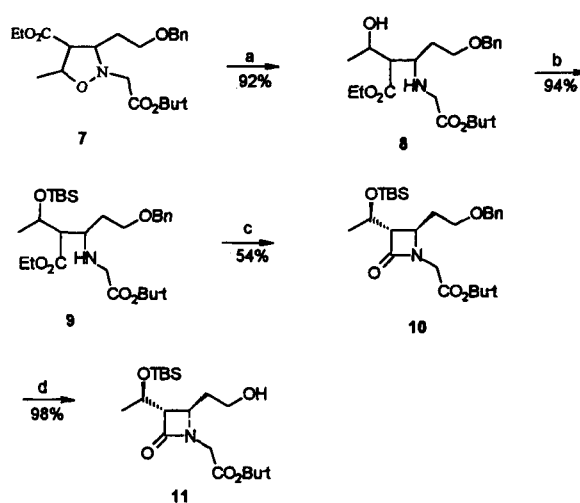


Scheme 1.

ppm for NCH_2CO_2 . The compound was unstable in the air and employed without purification in the next step. Compound **6** was reacted with crotonate in toluene at 80 °C for 48 h to yield two stereoisomers **7a** and **7b** of isoxazolidine-4-carboxylate in 80% yield. Isolation of the two isomers by silica gel column chromatography was unsuccessful. However, since only the *cis* isomer **7a** can be converted to a β -lactam,⁹ we employed the mixture directly for the next step. The signals in ^1H NMR spectrum of the mixture suggested that **7a** and **7b** existed in a 3 : 2 ratio. The proton signals of



Scheme 2.



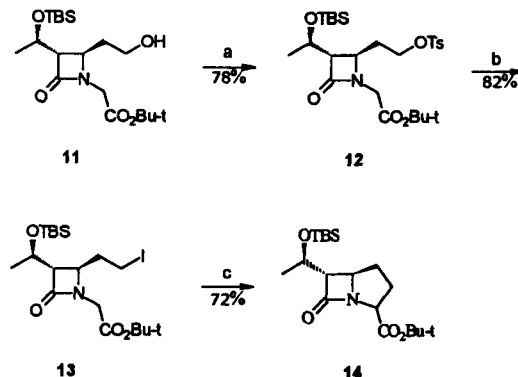
a) Zn/HOAc b) TBSCl , imidazole/ DMF c) MeMgBr/THF d) $\text{H}_2/\text{Pd-C}$

Scheme 3.

H-4 of **7a** were observed at 2.87 (dd, $J=9.0$ and 5.4 Hz) ppm, but those of **7b** at 3.00 (dd, $J=9.0$ and 8.9 Hz) ppm (Scheme 2).

The N-O bond of the isoxazolidine-4-carboxylate (**7**) was reduced with zinc powder in acetic acid-water to yield β -amino β -hydroxy ester (**8**) in 92% yield. Compound **8** showed a broad band around $3500\text{--}3200\text{ cm}^{-1}$ for NH and OH groups. The spot on the tlc (silica gel) plate gave a purple color on spraying of ninhydrin solution and heating. The hydroxy group of **8** was protected with *t*-butyldimethylsilyl group to give **9** in 96% yield. Compound **9** showed a band at 3350 cm^{-1} for the NH group and a band at 1255 cm^{-1} for the Si-C bond. Reaction of compound **9** in THF with methylmagnesium bromide at $-10\text{ }^\circ\text{C}$ for 4 h and at room temperature for 18 h yielded the β -lactam compound **10** in 54% yield. Compound **10** showed bands at 3320, 1750, and 1735 cm^{-1} for the NH, the β -lactam carbonyl, and the ester carbonyl groups, respectively. The coupling constant value 2.4 Hz between the protons on β -lactam ring (at C-3 and C-4) implied a *trans* relationship. Hydrogenation of **10** in ethyl acetate gave compound **11** in 98% yield (Scheme 3).

Synthesis of 6-[1-(*t*-butyldimethylsilyloxy)ethyl]-carbapenam-3-carboxylates. The β -lactam compound



a) $\text{TsCl}/\text{Pyridine}$ b) $\text{NaI}/\text{Acetone}$ c) LiHMDS/THF , $-78\text{ }^\circ\text{C}$

Scheme 4.

11 was tosylated by *p*-treatment of toluenesulfonyl chloride in pyridine at 0–4 °C for a day yield to give **12** in 78% and the tosyloxy group of **12** was substituted with iodide by refluxing in acetone with sodium iodide for 6 h in 82% yield. Treatment of the iodo compound (**13**) in THF at –78 °C with lithium hexamethyldisilazide gave 6-[1-(*t*-butyldimethylsilyloxy)ethyl]carbapenam-3-carboxylate (**14**) in 72% yield. The IR spectrum of compound **14** showed bands at 1770 and 1730 cm⁻¹ for the β-lactam carbonyl and the ester carbonyl groups, respectively. Its ¹H NMR spectrum showed the signals of H-1 and H-2 around 2.04–2.58 ppm as a multiplet, and of H-6 at 2.78 ppm as a double doublet (*J*=7.0 and 2.1 Hz) (Scheme 4).

After the β-lactam compound **11** was oxidized for 12 h in DMF with PDC at room temperature to a carboxylic acid **15** in 87% yield, the product **15** was converted to an acid chloride by treatment of oxalyl chloride and pyridine in benzene at 0 °C for 1 h. After evaporation of benzene, thiophenol and 1 eq of pyridine was added to the reaction mixture to give a thioester **16** in 80% yield. Compound **16** was treated with lithium hexamethyldisilazide at –78 °C for 30 min to yield 2-oxocarbapenam-3-carboxylate (**17**) in 82% yield. The compound showed bands at 1785, 1770, and 1745 cm⁻¹ for the β-lactam carbonyl, the ketone carbonyl, and the ester carbonyl groups, respectively. In the ¹H NMR spectrum it showed two H-1 proton signals at 2.42 and 2.93 ppm as double doublets. The H-6 proton signal were observed at 3.18 ppm also as a double doublet.

Experimental

IR spectra were recorded with Perkin-Elmer 735-B IR or Jasco J-0068 FT IR spectrophotometer. ¹H NMR spectra were obtained with Varian EM-360, Bruker AC 80 or Varian VXR-200S NMR spectrometer with tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed as δ (ppm). Melting points were obtained with digital melting point measurement instrument made by Electrothermal Co. without correction. THF and ethyl ether were distilled in the presence of sodium and benzophenone. Benzene was washed with concentrated sulfuric acid and distilled over sodium. DMF was dried over KOH pellets before use. Other solvents are first grade and distilled before

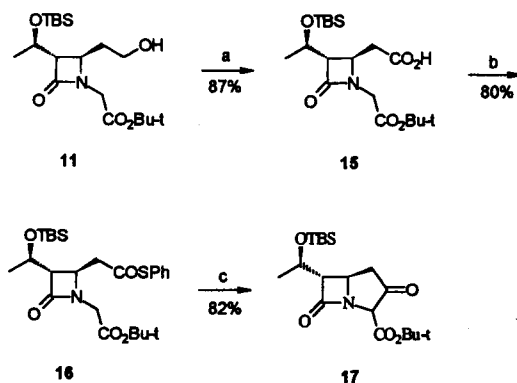
use. All the chemicals were purchased from Aldrich Chemical Co. or Merck Co.

N-(3-Benzyloxypropylidene)glycine N-oxide *t*-butyl ester (6). *N*-Hydroxyglycine *t*-butyl ester (2.94 g, 20 mmol) and 3-benzyloxypropnal (3.6 g, 22 mmol) were dissolved in benzene (50 mL) and the solution was refluxed for 30 min. After evaporation of the solvent, the liquid was chromatographed over silica gel with hexane-ethyl acetate (1 : 2) to give **6**. Yield, 5.25 g (89%); ¹H NMR (CDCl₃) δ 1.48 (s, 9H, C(CH₃)₃), 2.72 (dt, 2H, *J*=6.0, 5.7 Hz, CH₂), 3.80 (t, 2H, *J*=6.0 Hz, OCH₂), 4.36 (s, 2H, OCH₂Ph), 4.43 (s, 2H, NCH₂CO₂), 6.82 (t, 1H, *J*=5.7 Hz, N=CH), 7.32 (s, 5H, Ph); IR (neat) 3080–2845, 1740, 1595, 1365, 1150, 740, 700 cm⁻¹.

Ethyl 3-(2-benzyloxyethyl)-2-(*t*-butoxycarbonylmethyl)-5-methylisoxazolidine-4-carboxylate (7). Compound **6** (5.0 g, 17 mmol) and ethyl crotonate (5.71 g, 50 mmol) was dissolved in toluene and stirred at 80 °C for 48 h. After evaporation of the solvent, the oil was chromatographed over silica gel with hexane-ethyl acetate (8 : 1) to give **7**. Yield, 5.56 g (80%); ¹H NMR (CDCl₃) δ 1.2–1.9 (m, 8H, CH₂, OCH₂CH₃, 5-CH₃), 1.47 (s, 9H, C(CH₃)₃), 2.87 (dd, 0.6H, *J*=9.0, 5.4 Hz, H-4), 3.00 (dd, 0.4H, *J*=9.0, 8.9 Hz, H-4), 3.47–4.00 (m, 5H, H-3, OCH₂, NCH₂CO₂), 4.16 (q, 2H, *J*=7.0 Hz, OCH₂CH₃), 4.41 (m, 1H, H-5), 4.58 (s, 2H, OCH₂Ph), 7.42 (s, 5H, Ph); IR (neat) 3100–2860, 1740, 1360, 1150, 740, 700 cm⁻¹.

Ethyl 5-benzyloxy-3-(*t*-butoxycarbonylmethylamino)-2-(1-hydroxyethyl)pentanoate (8). Compound **7** (4.1g, 10 mmol) was dissolved in acetic acid (100 mL) and water (5 mL) was added. To the solution that was cooled in ice-water bath zinc powder (2.3 g, 30 mgatm) was added portion by portion. After the mixture was stirred at the same temperature for 2 h and at room temperature for 4 h. The reaction mixture was filtered and evaporated to give residue which was dissolved in ethyl acetate (100 mL). The solution was washed with 10% sodium bicarbonate solution and dried over magnesium sulfate. Evaporation of solvent gave a colorless oil which was chromatographed over silica gel with hexane-ethyl acetate (6 : 1) to give **8**. Yield, 3.78 g (92%); ¹H NMR (CDCl₃) δ 1.00–1.60 (m, 4H, CH₃, NH), 1.23 (t, 3H, *J*=7.0 Hz, OCH₂CH₃), 1.47 (s, 9H, C(CH₃)₃), 1.89–2.10 (m, 3H, CH₂, OH), 2.78 (dd, 1H, *J*=8.0, 3.0 Hz, H-2), 3.13–3.89 (m, 5H, NCH₂CO₂, NCH, CH₂O), 4.23 (q, 2H, *J*=7.0 Hz, OCH₂CH₃), 4.00–4.21 (m, 1H, CHOH), 4.53 (s, 2H, OCH₂Ph), 7.45 (s, 5H, Ph); IR (neat) 3600–2700, 3300, 3080–2860, 1725, 1720, 1100, 740, 700 cm⁻¹.

Ethyl 5-benzyloxy-3-(*t*-butoxycarbonylmethylamino)-2-[1-(*t*-butyldimethylsilyloxy)ethyl]pentanoate (9). Compound **8** (3.7 g, 9.0 mmol) and imidazole (0.68 g, 10 mmol) were dissolved in DMF (20 mL). *t*-Butyldimethylchlorosilane (1.38 g, 9.2 mmol) was added to the solution and stirred for 6 h at room temperature. The reaction was stopped by addition of diethyl ether (50 mL) and water (50 mL). The ethyl ether layer was separated and the water layer was extracted with ethyl ether (50 mL). The combined organic layer was washed with 1% HCl solution and water. After drying over magnesium sulfate, the solution was evaporated to give a colorless oil which was further purified by column chromatography over silica gel with hexane-ethyl acetate (8 : 1). Yield, 4.52 g (96%); ¹H NMR



a) PDC / DMF b) i. (COCl)₂, Pyridine ii. PhSH, Pyridine c) LiHMDS / THF, –78 °C

Scheme 5.

(CDCl₃) δ 0.02 (s, 6H, 2 SiCH₃), 0.87 (s, 9H, SiC(CH₃)₃), 1.07-1.45 (m, 7H, OCH₂CH₃, CH₃, NH), 1.47 (s, 9H, C(CH₃)₃), 1.87-2.18 (m, 2H, CH₂), 2.80 (m, 1H, H-2), 3.03-3.45 (m, 1H, NCH), 3.47-3.97 (m, 5H, NCH₂CO₂, CH₂O, CHOSi), 4.23 (q, 2H, $J=7.0$ Hz, OCH₂CH₃), 4.58 (s, 2H, OCH₂Ph), 7.50 (s, 5H, Ph); IR (neat) 3350, 3080-2860, 1730, 1725, 1450, 1255, 1095, 835, 780, 740, 700 cm⁻¹.

4-(2-Benzoyloxyethyl)-1-(*t*-butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (10). Compound 9 (4.2 g, 8.0 mmol) was dissolved in THF (150 mL) and the solution was cooled to -10 °C in ice-water bath. Under nitrogen gas methylmagnesium bromide in ether (3 M, 4.0 mL, 12 mmol) was added to the solution with stirring. The mixture was stirred at the same temperature for 4 h and at room temperature for 18 h. The reaction was stopped by adding saturated ammonium sulfate solution (50 mL). The reaction products were extracted with ethyl acetate. The extract was washed with water and dried over magnesium sulfate. The solvent was evaporated and the residue was chromatographed over silica gel with hexane-ethyl acetate (2:1). Yield, 2.06 g (54%); ¹H NMR (CDCl₃) δ 0.08 (s, 6H, 2 SiCH₃), 0.89 (s, 9H, SiC(CH₃)₃), 1.32 (d, 3H, $J=6.4$ Hz, CH₃), 1.47 (s, 9H, OC(CH₃)₃), 1.96 (m, 2H, CH₂), 3.00 (dd, 1H, $J=8.8, 2.4$ Hz, H-3), 3.51 (t, 2H, $J=7.0$ Hz, CH₂O), 3.66 (d, 1H, $J=17.8$ Hz, NCHCO₂), 3.78 (m, 1H, H-4), 4.06 (d, 1H, $J=17.8$ Hz, NCHCO₂), 4.17 (m, 1H, CHOSi), 4.36 (s, 2H, OCH₂Ph), 7.33 (s, 5H, Ph); IR (neat) 3080-2840, 1750, 1735, 1255, 835, 780, 740, 700 cm⁻¹.

1-(*t*-Butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-hydroxyethyl)-2-azetidinone (11). Compound 10 (1.92 g, 4.0 mmol) in ethyl acetate (40 mL) was hydrogenated with hydrogen gas at 40 psi in the presence of Pd-C (10%, 0.8 g) for 4 h. After filtration, the solution was evaporated to give the product, an oily residue. Yield, 1.52 g (98%); ¹H NMR (CDCl₃-D₂O) δ 0.012 (s, 6H, 2 SiCH₃), 0.90 (s, 9H, SiC(CH₃)₃), 1.33 (d, 3H, $J=6.4$ Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 1.96 (m, 2H, CH₂), 3.03 (dd, 1H, $J=8.8, 2.4$ Hz, H-3), 3.66 (d, 1H, $J=17.8$ Hz, NCHCO₂), 3.73 (m, 3H, H-4, CH₂O), 4.06 (d, 1H, $J=17.8$ Hz, NCHCO₂), 4.17 (m, 1H, CH-O); IR (neat) 3430, 2930, 1750, 1735, 1255, 1155, 835, 780 cm⁻¹.

1-(*t*-Butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-tosyloxyethyl)-2-azetidinone (12). Compound 11 (0.58 g, 1.5 mmol) in pyridine (5.0 mL) was cooled to 0 °C and *p*-toluenesulfonyl chloride (0.86 g, 4.5 mmol) was added under nitrogen gas. The solution was stirred at the same temperature for 2 h and kept in the refrigerator for 24 h. The reaction mixture was poured into crushed ice (20 g) and extracted with ethyl acetate (20 mL \times 2). The extract was washed with 1% hydrochloric acid solution, water, and sodium bicarbonate solution (5%), and then with water. After drying over magnesium sulfate, the solution was evaporated to give solid which was purified by chromatography over silica gel with hexane-ethyl acetate (4:1). Yield, 0.63 g (78%); ¹H NMR (CDCl₃) δ 0.02 (s, 6H, 2 SiCH₃), 0.89 (s, 9H, SiC(CH₃)₃), 1.33 (d, 3H, $J=6.4$ Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 1.97 (m, 2H, CH₂), 2.51 (s, 3H, CH₃), 3.08 (dd, 1H, $J=8.7, 2.4$ Hz, H-3), 3.60-4.10 (m, 5H, CH₂O, NCH₂CO₂, H-4), 4.20 (m, 1H, CHOSi), 7.33 (dd, 2H, Ar), 7.70 (dd, 2H, Ar); IR (neat) 3100-2800, 1750-1720,

1350, 1255, 1175, 835, 780 cm⁻¹.

1-(*t*-Butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-iodoethyl)-2-azetidinone (13).

Compound 12 (0.54 g, 1.0 mmol) and sodium iodide (0.45 g, 3.0 mmol) in acetone (5.0 mL) was refluxed for 6 h. After filtration, the solution was evaporated to give a brown oily residue. The residue was dissolved in ether (10 mL) with water (10 mL). The ether layer was separated and washed with 5% sodium thiosulfate solution and 5% sodium chloride solution, and dried over sodium sulfate. Evaporation of the solution gave a colorless oil which was chromatographed over silica gel with hexane-ethyl acetate (4:1) to give compound 13. Yield, 0.41 g (82%); ¹H NMR (CDCl₃) δ 0.083 (s, 6H, 2 SiCH₃), 0.88 (s, 9H, SiC(CH₃)₃), 1.26 (d, 3H, $J=6.2$ Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 2.26 (m, 2H, CH₂), 2.86 (dd, 1H, $J=6.2, 2.3$ Hz, H-3), 3.13 (m, 2H, CH₂I), 3.79 (m, 1H, H-4), 3.85 (s, 2H, NCH₂CO₂), 4.18 (m, 1H, CHOSi); IR (neat) 2920, 1760, 1740, 1250, 1155, 835, 775 cm⁻¹.

***t*-Butyl 6-[1-(*t*-butyldimethylsilyloxy)ethyl]carbamate-3-carboxylate (14).** Compound 13 (0.37 g, 0.74 mmol) in THF (5.0 mL) under nitrogen gas was cooled in dry ice-acetone bath. To this solution with stirring was injected the THF solution of LiHMDS (1 M, 0.9 mL, 0.9 mmol). The solution was stirred at the same temperature for 30 min and warmed up to room temperature slowly during 1 h. The reaction was stopped by adding saturated ammonium chloride and the mixture was extracted with ethyl acetate (5.0 mL). The extract was washed with water and dried over magnesium sulfate. Evaporation of the solvent gave the product which was purified by chromatography over silica gel with hexane-ethyl acetate (4:1). Yield, 0.20 g (72%); ¹H NMR (CDCl₃) δ 0.02 (s, 6H, 2 SiCH₃), 0.87 (s, 9H, SiC(CH₃)₃), 1.23 (d, 3H, $J=6.2$ Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 2.04-2.58 (m, 4H, H-1, H-2), 2.78 (dd, 1H, $J=7.0, 2.1$ Hz, H-6), 3.84-3.91 (m, 1H, H-5), 4.12 (m, 1H, H-8), 4.30 (t, 1H, $J=8.0$ Hz, H-3); IR (neat) 2980, 1770, 1730, 1255, 1100, 835, 775 cm⁻¹.

1-(*t*-Butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone (15). Compound 11 (0.58 g, 1.5 mmol) in DMF (2.0 mL) was added to the solution of PDC (2.0 g, 5.3 mmol) in DMF (3.0 mL) and the mixture was stirred at room temperature for 12 h. The reaction mixture was poured to water (30 mL) and the product was extracted with ethyl acetate (10 mL \times 2). After washing with water and saturated sodium chloride solution, the extract was dried over magnesium sulfate. Evaporation of the solvent gave the product as a colorless solid which was purified by recrystallization in ethyl acetate-diethyl ether. Yield, 0.52 g (87%); ¹H NMR (CDCl₃) δ 0.02 (s, 6H, 2 SiCH₃), 0.87 (s, 9H, SiC(CH₃)₃), 1.22 (d, 3H, $J=6.2$ Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 2.58 (dd, 1H, $J=16.0, 9.5$ Hz, CHCO₂), 2.78 (dd, 1H, $J=16.0, 4.0$ Hz, CHCO₂), 2.87 (dd, 1H, $J=6.2, 2.2$ Hz, H-3), 3.66 (d, 1H, $J=17.8$ Hz, NCHCO₂), 3.98 (m, 1H, H-4), 4.06 (d, 1H, $J=17.8$ Hz, NCHCO₂), 4.20 (m, 1H, CHOSi), 10.62 (br s, 1H, COOH); IR (neat) 3500-2500, 1760, 1730, 1250, 1155, 835, 775 cm⁻¹.

1-(*t*-Butoxycarbonylmethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-phenylthiocarbonylmethyl-2-azetidinone (16). Pyridine (0.11 mL, 1.30 mmol) and

oxalyl chloride (0.12 mL, 1.4 mmol) were added to the benzene (5.0 mL) solution of compound **15** (0.50 g, 1.25 mmol) which was cooled in ice-water bath (0 °C) and stirred for 1 h at the same temperature. After evaporation of benzene, pyridine (5.0 mL) and thiophenol (1.14 g, 1.30 mmol) were added and the mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with diethyl ether (10 mL) and water (10 mL). The ether layer was separated, washed with 1% hydrochloric acid solution and water, and dried over magnesium sulfate. Evaporation of the solvent gave the product as an oily residue. Yield, 0.48 g (80%); ¹H NMR (CDCl₃) δ 0.02 (s, 6H, 2 SiCH₃), 0.87 (s, 9H, SiC(CH₃)₃), 1.22 (d, 3H, *J*=6.2 Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 2.58 (dd, 1H, *J*=16.0, 9.5 Hz, CHCOS), 2.78 (dd, 1H, *J*=16.0, 4.0 Hz, CHCOS), 2.87 (dd, 1H, *J*=6.2, 2.2 Hz, H-3), 3.66 (d, 1H, *J*=17.8 Hz, NCHCO₂), 3.98 (m, 1H, H-4), 4.06 (d, 1H, *J*=17.8 Hz, NCHCO₂), 4.20 (m, 1H, CHOSi), 7.42 (s, 5H, Ph); IR (neat) 3080-2920, 1760, 1725, 1250, 1155, 835, 775, 700 cm⁻¹.

***t*-Butyl 6-[1-(*t*-butyldimethylsilyloxy)ethyl]-2-oxocarbapenam-3-carboxylate (17)**. The THF solution of LiHMDS (1.0 M, 2.1 mL, 2.1 mmol) was added to the solution of compound **16** (0.34 g, 0.71 mmol) in THF (5.0 mL) which was cooled in dry ice-acetone bath (-78 °C). The mixture was stirred at the same temperature for 30 min and warmed up to 0 °C. The reaction was stopped by adding saturated ammonium chloride solution (5.0 mL) and the reaction mixture was extracted with ethyl acetate (10 mL). The extract was washed with water and dried over magnesium sulfate to give an oily residue product. The product was purified by column chromatography over silica gel with hexane-ethyl acetate (4:1). Yield, 0.22 g (82%); ¹H NMR (CDCl₃) δ 0.02 (s, 6H, 2 SiCH₃), 0.87 (s, 9H, SiC(CH₃)₃), 1.35 (d, 3H, *J*=6.5 Hz, CH₃), 1.47 (s, 9H, C(CH₃)₃), 2.42 (dd, 1H, *J*=19.0, 8.0 Hz, H-1), 2.93 (dd, 1H, *J*=19.0, 6.4 Hz, H-1), 3.18 (dd, 1H, *J*=6.8, 2.1 Hz, H-6), 3.84-3.91

(m, 1H, H-5), 4.12 (m, 1H, H-8), 4.67 (s, 1H, H-3); IR (neat) 2980, 1785, 1770, 1745, 1255, 1100, 835, 775 cm⁻¹.

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