Articles

Synthesis of 3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone Derivatives

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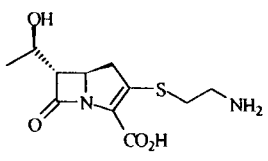
Isoxazolidine derivatives **7** and **8** were synthesized from *N*-benzyl-*C*-(2-benzyloxyethyl)nitrones by 1,3-dipolar cycloaddition with ethyl crotonate. The isoxazolidine derivatives were converted to β-amino acid esters **9a** and **9b** by reduction with zinc in acetic acid. The β-amino acid esters were reacted with methylmagnesium bromide to give the 2-azetidinones (**13a, 13b**). The benzyl group of 2-azetidinones were removed by Birch reduction. The products were oxidized with PDC to give 3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone derivatives (**2a, 2c**).

Introduction

Thienamycin (**1**)[1] shows strong antimicrobial activities and a lot of research has been carried out to synthesize it and its derivatives. 3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone derivatives (**2**), which are important intermediates for the synthesis of carbapenem antibiotics, are usually obtained from 3-[1-(*t*-butyldimethylsilyloxy)-ethyl]-4-acetoxy-2-azetidinone by substitution of its acetoxy group with enolates.[2] Compound **2** can be obtained by cyclization of β-amino acid esters which are synthesized from D-glucose.[3] L-Threonine and L-aspartic acid have been converted to 4-carboxy-2-azetidinone and then to compound **2**.[4] Isoxazolidines or isoxazolines which can be synthesized from nitrones or nitrile oxides by 1,3-dipolar cycloaddition with crotonate are reduced to give β-amino esters, whcih can be converted to compounds **2**.[5] The route for the synthesis of 3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone through isoxzolidines obtained by 1,3-dipolar cycloaddition of nitrones with crotonates is pretty simple and good to obtain 2-azetidinones having (*R*)-1-hydroxyethyl group at the C-3 position in the ring.

3-[1-(*t*-Butyldimethylsiloxy)ethyl]-4-carboxymethyl-2-azetidinone (**2a**) has been obtained from isoxazolidine derivative **4a** which is obtained from nitrone **3a**, that is the condensed product of *N*-benzylhydroxylamine with 3,3-dimethoxypropanal, by 1,3-dipolar cycloaddition reaction with benzyl crotonate.[6] Ito *et al.*[7] synthesized a chiral nitrone **3b** from (*S*)-(+)-3-(*t*-butyldimethylsilyloxy)-2-methylpropanal, which is obtained from methyl (*S*)-3-hydroxy-2-methylpropanoate, by reaction with *N*-benzylhydroxylamine. The nitrone **3b** has been reacted with benzyl crotonate to give a chiral 1,3-dipolar cycloadduct, (3*S*,4*S*)-3-[(1*R*)-1-(*t*-butyldimethylsilyloxy)ethyl]-4-[(1*R*)-1-carboxyethyl]-2-azetidinone (**2b**) which can be employed for the synthesis of a 1-β-methylcarbapenem (Scheme 1).

The isoxazolidines employed for the synthesis of carbapenems have been synthesized by 1,3-dipolar cycloaddition reaction of nitrones with benzyl crotonate. The benzyl group is removed after the reduction of the N-O bond to give β-amino acids, which are cyclized to β-lactam rings by treatment of dehydrating reagents (DCC or PySSPy-triphenylphosphine). However, removing of the benzyl group is not so easy and the yield is low. Thus, in the present report, we wish to report a new approach for the synthesis of 3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinones.



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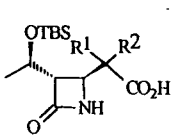
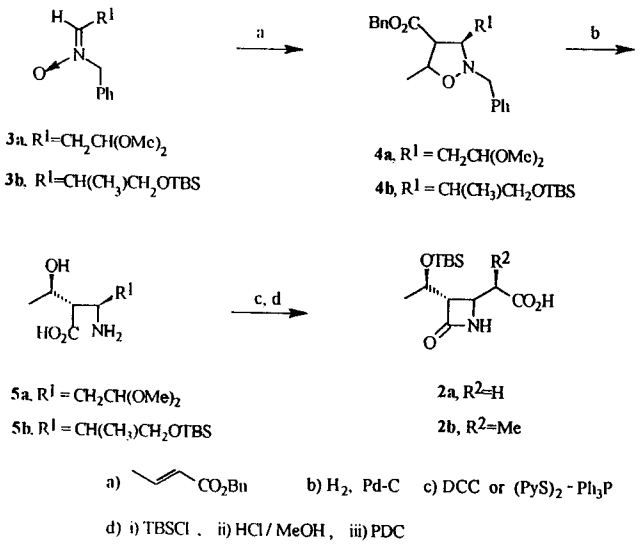
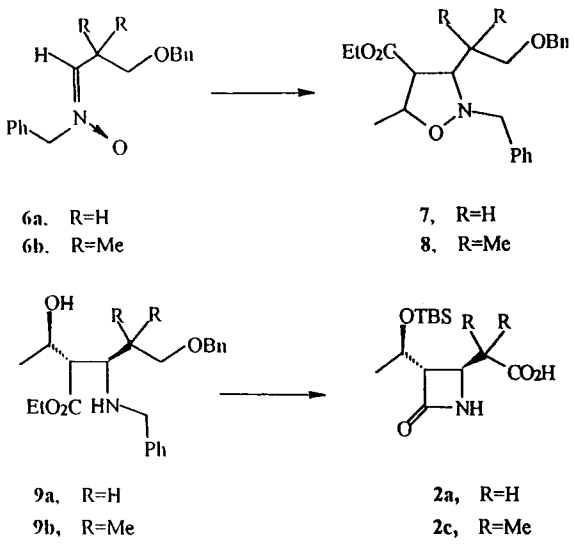


2a, R^1=R^2=H
2b, R^1=Me, R^2=H
2c, R^1=R^2=Me

Figure 1.



Scheme 1.

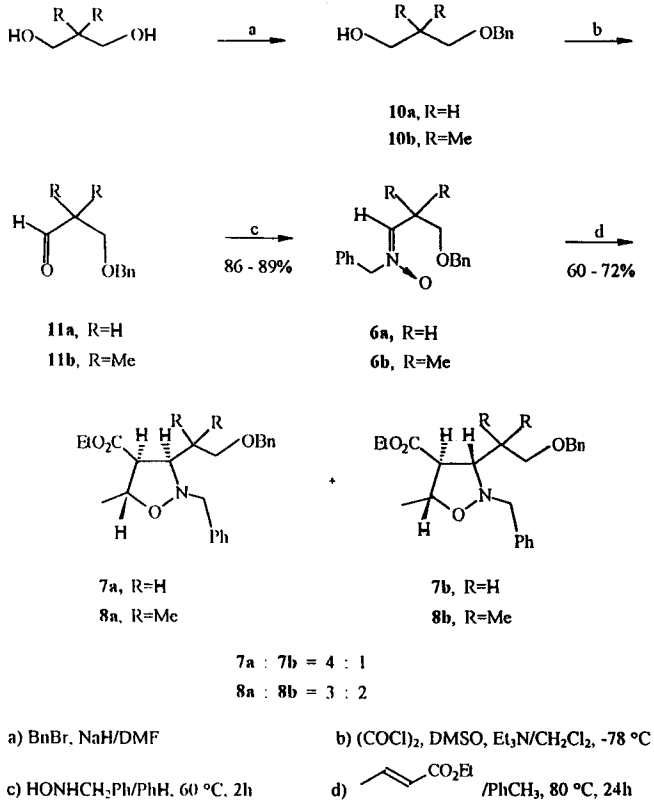


Scheme 2.

We examined the 1,3-dipolar cycloaddition reaction of *N*-benzylnitrone with ethyl crotonate to give isoxazolidines, the cleavage of the N-O bond by reduction to give β-amino acid esters, and the cyclization of the β-amino acid esters by treatment of Grignard reagent to give *N*-benzyl-2-azetidinone derivatives. The *N*-benzyl group and the other protecting groups of the compounds are removed and the products are oxidized to give 3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone derivatives (Scheme 2).

Results and Discussion

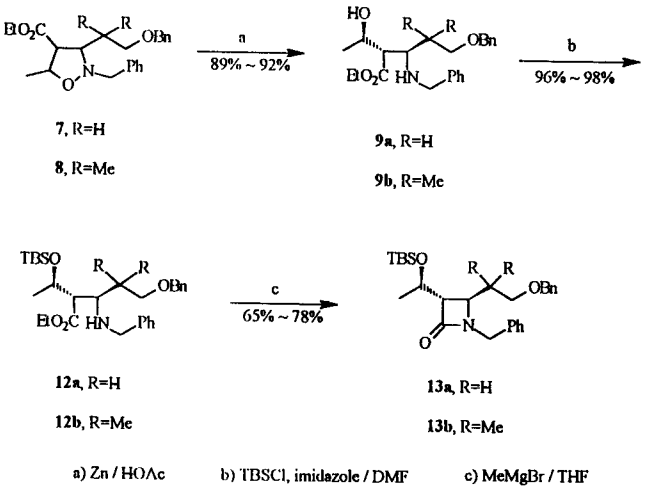
1,3-Dipolar Cycloaddition of *N*-Benzylnitrone to Ethyl Crotonate. The 3-benzyloxypropanals **11a** and **11b** are obtained by oxidation of 3-benzyloxy-1-propanols which are synthesized from 1,3-propandiols by benzylation. Excess of 1,3-propanediols (5 eq.) are treated with sodium hydride and reacted with 1 eq. of benzyl bromide to give 3-benzyloxy-1-propanols **10a** and **10b** in 96% and 92% yields, respectively. The 3-benzyloxy-1-propanols are oxidized by Swern oxidation to give 3-benzyloxypropanals **11a** and **11b** in 92% and 82% yields, respectively. Nitrones **6a** and **6b** are obtained in 86% and 89% yields by reaction of 3-benzyloxypropanals (**11**) with *N*-benzylhydroxylamine at 60 ℃ for 2 h in benzene. The nitrones show λ_{max} 236 nm. The protons of N=CH in nitrones **6a** and **6b** show a triplet (J=5.6 Hz) at 6.81 ppm and a singlet at 6.45 ppm, respectively. The nitrones (3 eq.) dissolved in toluene with ethyl crotonate are kept at 80 ℃ for 24 h to give isoxazolidines **7** and **8** in the yields of 72% and 60%, respectively (Scheme 3). From the analysis of ^{1}H NMR spectra compounds **7** and **8** are found to be mixtures of diastereomers **7a** and **7b**, and **8a** and **8b** in the ratios of 4 : 1 and 3 : 2, respectively. The diastereomers are attempted to be separated without success. The ^{1}H NMR spectra of **7a** and **7b** show the H-4 signals at 2.78 and 3.08 ppm, respectively, as double doublets. The diastereomers **7a** and **8a** are 1,3-dipolar cycloaddition products formed through an exo-transition state of the Z-nitrone with ethyl crotonate. The result is same with that reported by Tufariello *et al.*[9] and



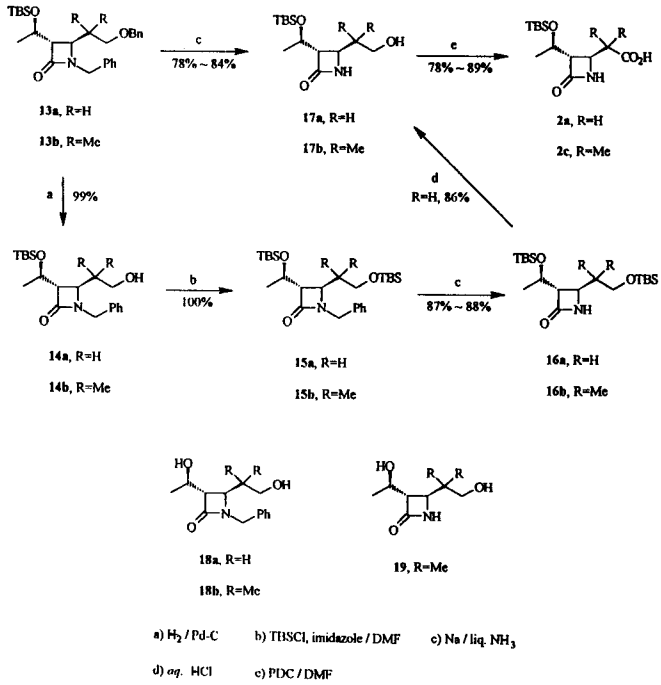
Scheme 3.

Kametani *et al.*[10]

Synthesis of β-Lactam Derivatives from Isoxazolidines. The isoxazolidines are converted to β-lactam compounds by employing the method reported by Tufariello *et al.*[11] Usually the reduction of the N-O bond in isoxazolidines are carried out through catalytic hydrogenation to give β-amino acid esters. But in this study we reduced the N-O bond of the isoxazolidines (**7, 8**) with zinc-acetic acid selectively to give β-amino acid esters (**9a, 9b**) in good yields. Catalytic reduction of the isoxazolidines would reduce not only the N-O bond but also the benzyloxy group. Compounds **9a** and **9b** show stretching bands of the OH and the NH at 3200-3500 and 3300 cm^{-1}, respectively. The hydroxy group of compounds **9a** and **9b** is protected with *t*-butyldimethylsilyl group by stirring the compounds in DMF with *t*-butyldimethylsilyl chloride and imidazole for 6 h at room temperature to give compounds **12a** and **12b**. The products show a stretching band of the N-H group at 3360 cm^{-1}. β-Amino acid esters **12a** and **12b** dissolved in THF are reacted with methylmagnesium bromide for 24 h at 0 ℃ to give β-lactam compounds **13a** and **13b** in 78% and 65% yields, respectively (Scheme 4). Compounds **13a** and **13b** show 2.15 Hz for the coupling constant between H-3 and H-4 protons in their ^{1}H NMR spectra. The coupling constant values imply that the two attached groups at C-3 and C-4 positions on the β-lactam rings in compounds **13a** and **13b** are *trans* each other. Compounds **13a** and **13b** show double doublets at 2.96 (J=2.15 and 5.33 Hz) and 2.94 (J=2.15 and 5.12 Hz), respectively in their ^{1}H NMR spectra. Both compounds show stretching bands at 1750 cm^{-1} for the β-lactam carbonyl groups in their ir spectra. The yield for the cyclization of **12b** to **13b** is



Scheme 4.



Scheme 5.

relatively low, probably because of the steric hindrance between the two methyl groups at the β-position from the amino group and *t*-butyldimethylsilyloxy group attached to the α-position from the ethoxycarbonyl group, and partly because the ratio of *cis*- to *trans*-isomers in the isoxazolidine compound (**8**) is low due to the steric hindrance of the two methyl groups attached to the α-position of nitrone during its 1,3-dipolar cycloaddition reaction.

From these syntheses we are able to prepare 2-azetidinone derivatives with *trans* substituents at 3- and 4-positions, and that have a stereochemically controlled 1-hydroxyethyl group at 3-position. Cyclization of β-amino acid esters, the isomers of which are not separated, with Grignard reagents looks very good to give 2-azetidinone derivatives with *trans*-configuration for the substituents at 3- and 4-positions.

Synthesis of 4-Carboxymethyl-2-azetidinone Derivatives. We synthesized 3-carboxymethyl-2-azetidinone derivatives from β-lactam compounds **13a** and **13b** (Scheme 5). Compound **13a** or **13b** is dissolved in acetic acid and hydrogenated in the presence of 10% Pd-C under pressure (60 psi) of hydrogen gas to remove the benzyl group. But the *N*-benzyl group is not removed, instead *t*-butyldimethylsilyl group and the *O*-benzyl group are hydrogenolyzed to give diols **18a** or **18b** quantitatively. The diols **18a** and **18b** are converted quantitatively to compounds **15a** and **15b**, respectively, by reaction with *t*-butyldimethylsilyl chloride in DMF in the presence of imidazole. Hydrogenation of compounds **13a** and **13b** in ethyl acetate with 10% Pd-C under 30 psi of hydrogen gas removes the *O*-benzyl group only to give compounds **14a** and **14b**, the hydroxy group of which are protected with *t*-butyldimethylsilyl chloride to give compounds **15a** and **15b** quantitatively. To remove the *N*-benzyl group in compounds **15a** and **15b**, they are oxidized with CAN only to give compounds **18** which are produced by deprotecting of the silyl group of compounds **15**. But Birch reduction of compounds **15a** and **15b** give the desired products **16a** and **16b** in 88% and 87% yields, respectively. Birch reductions were carried out with compound **15a** or **15b** dissolved in liquid ammonia at −78 ℃. A small amount of ethanol is added as the source of proton to the liquid ammonia solution and sodium is added portion by portion until the solution become deep blue color. But the yield of the reaction was low due to the low solubility of compounds **15a** and **15b**. Thus, the compound **15a** or **15b** is dissolved in liquid-ammonia-THF (2 : 1) mixture and we carried out the same reaction to give compound **16a** or **16b** in good yields (87-88%).

We next tried to remove the protecting group at the primary hydroxy group of compounds **16a** and **16b** selectively by dissolving them in methanol with 1 eq. HCl in aqueous solution. Compound **16a** gave the desired product **17a** in 86% yield, but compound **16b** gave a product in which both protecting groups of primary and secondary hydroxy groups were removed. Loss of selectivity in deprotection in compound **16b** is probably due to the two methyl groups at the β-position from the primary hydroxy group, which might impose almost the same degree of steric hindrance around the primary hydroxy group as the secondary hydroxy group. Thus, we attempted to reduce both *N*-benzyl and *O*-benzyl groups of compound **13** to give compound **17**. Compound **13a** or **13b** dissolved in liquid ammonia-THF with a small amount of ethanol was treated with 12 eq. of sodium to give compound **17a** (84% yield) or **17b** (78% yield), in which both *N*-benzyl and *O*-benzyl groups of compounds **13a** or **13b** are removed. Compounds **17a** and **17b** are oxidized by PDC method reported by Corey[12] to give carboxylic acids (**2a** and **2c**). To the DMF solution of 2.5 eq. of PDC 1 eq. of compound **17a** or **17b** is added and the mixture was stirred at room temperature for 12 h to give **2a** or **2c** in 78-89% yields.

From the results obtained in this study we conclude that the best method for transformations of compounds **13a** and **13b** to 4-carboxymethyl-2-azetidinone derivatives (**2a** and **2c**) is reducing the compounds by Birch method with excess of sodium to remove both benzyl groups at the amino and the hydroxy group to give **17a** and **17b**, and oxidizing their

hydroxymethyl groups with PDC. Thus, we could obtain **2a** and **2c**, which are important intermediates for the construction of carbapenem analogs, from **13a** and **13b** in two steps in overall yields 76% and 61%, respectively.

Experimental Section

General. IR spectra were recorded with Perkin-Elmer 735-B IR or Jasco J-0068 FT IR spectrophotometer. ^{1}H NMR spectra were obtained with Varian EM-360 (60 MHz), Bruker AC 80 (80 MHz) or Varian VXR-200S (200 MHz) NMR spectrometer with tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed as δ (ppm). Microanalyses were carried out with Carlo-Erba 1108 elemental analyzer. 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 1st grade and distilled before use. All the chemicals were purchased from Aldrich Chemical Co. or Merck Co.

3-Benzyloxy-1-propanol (10a). After addition of 60% sodium hydride (1.6 g, 40 mmol) to DMF (50 mL) the mixture was stirred vigorously at 0 ℃. To this solution 1,3-propanediol (3.04 g, 40 mmol) was added portion by portion. The mixture was stirred for 30 min at the same temperature, then at room temperature for 1 h. The temperature of the solution was lowered to 0 ℃ and benzyl bromide (1.2 mL, 10 mmol) dissolved in DMF (10 mL) was added slowly. The mixture was stirred for 1 h at the same temperature, then for 4 h at room temperature. The reaction mixture was poured into the well crushed ice (100 g)-water (100 g) and the product was extracted with ethyl ether (50 mL×2). The ether solution was washed with water (50 mL) and saturated sodium chloride solution (50 mL) and dried over anhydrous magnesium sulfate. Evaporation of the ether gave **10a** (1.59 g) as a colorless liquid. Yield 1.59 g (96%); ^{1}H NMR ($CDCl_3$) δ 1.67-2.13 (m, 2H, CH_2), 2.70 (br s, 1H, OH), 3.39-3.50 (m, 4H, 2 OCH_2), 4.22 (s, 2H, OCH_2Ph), 7.30 (s, 5H, Ph); IR (neat) 3400, 3020, 2930, 2860, 1095, 740, 700 cm^{-1}.

3-Benzyloxy-2,2-dimethyl-1-propanol (10b). Neopentyl glycol (4.16 g, 10 mmol) was reacted with benzyl bromide (1.2 mL, 10 mmol) and the product was isolated as described for the preparation of **10a**. Yield, 1.78 g (92%); ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 6H, 2 CH_3), 2.65 (br s, 1H, OH), 3.38 (s, 2H, $HOCH_2$), 3.76 (s, 2H, OCH_2), 4.20 (s, 2H, OCH_2-Ph), 7.28 (s, 5H, Ph); IR (neat) 3400, 2930, 2870, 1100, 740, 700 cm^{-1}.

3-Benzyloxypropanal (11a). Oxalyl chloride (0.88 mL, 10 mmol) was dissolved in dichloromethane (20 mL) at −78 ℃ under nitrogen gas. After addition of DMSO (1.472 mL, 19 mmol) dissolved in dichloromethane (2 mL) the mixture was stirred for 2 min at the same temperature. Then 3-benzyloxy-1-propanol (1.49 g, 9.0 mmol) dissolved in dichloromethane (8.0 mL) was added slowly over 5 min and the mixture was stirred for 15 min at the same temperature. Then triethylamine (6.06 mL, 43.3 mmol) was added and the mixture was stirred for 10 min. After stirring for 1 h more at room temperature water (40 mL) was added to the mixture. The dichloromethane layer was separated and the water layer was further extracted with dichloromethane (20 mL). The combined dichloromethane solution was washed with 1% HCl solution (50 mL), water, 5% sodium bicarbonate solution, and water in sequence. The dichloromethane solution was dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a yellow colored liquid. The liquid was chromatographed over a silica gel column with hexane-ethyl acetate (10 : 1) to give a colorless liquid. Yield, 1.36 g (92%); ^{1}H NMR ($CDCl_3$) δ 2.67 (dt, 2H, J=6.0 and 2.0 Hz, CH_2), 3.82 (t, 2H, J=6.0 Hz, OCH_2), 4.53 (s, 2H, OCH_2Ph), 7.32 (s, 5H, Ph), 9.87 (t, 1H, J=2.0 Hz, CHO); IR (neat) 2860, 1720, 1100, 740, 700 cm^{-1}.

3-Benzyloxy-2,2-dimethylpropanal (11b). 3-Benzyloxy-2,2-dimethyl-1-propanol (1.68 g, 8.66 mmol) was converted to 3-benzyloxy-2,2-dimethylpropanal by employing the same method as described for the synthesis of **11a**. Yield, 1.43 g (86%); ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 6H, 2 CH_3), 3.80 (s, 2H, OCH_2), 4.52 (s, 2H, OCH_2Ph), 7.30 (s, 5H, Ph), 9.80 (s, 1H, CHO); IR (neat) 2870, 1715, 1090, 740, 700 cm^{-1}.

***N*-(3-Benzyloxypropylidene)benzylamine *N*-oxide (6a).** 3-Benzyloxypropanal (3.61 g, 22 mmol) in benzene (5 mL) was added slowly to *N*-benzylhydroxylamine (2.46 g, 20 mmol) in benzene (50 mL) under nitrogen gas with stirring. The mixture was stirred for 1 h at room temperature and further for 2 h at 60 ℃. Evaporation of the reaction mixture gave a colorless liquid. Yield, 4.2 g (78%); ^{1}H NMR ($CDCl_3$) δ 2.72 (dt, 2H, J=6.4and5.6Hz,CH_2),3.80(t,2HJ=6.4 Hz, OCH_2), 4.36 (s, 2H, OCH_2Ph), 4.81 (s, 2H, NCH_2-Ph), 6.81 (t, 1H, J=5.6 Hz, N=CH), 7.36 (m, 10H, 2 Ph); IR (neat) 3080-2840, 1590, 1150, 1100, 740, 700 cm^{-1}.

***N*-(3-Benzyloxy-2,2-dimethylpropylidene)benzylamine *N*-oxide (6b).** 3-Benzyloxy-2,2-dimethylpropanal (4.22 g, 22 mmol) was condensed with *N*-benzylhydroxylamine (2.46 g, 20 mmol) to give **6b** as the same method used for the synthesis of **6a**. The product was crystallized from ethyl ether-petroleum ether (2 : 1) to give white plates. Yield, 4.88 g (82%); mp 96.5 ℃; ^{1}H NMR ($CDCl_3$) δ 1.13 (s, 6H, 2 CH_3), 3.53 (s, 2H, OCH_2), 4.36 (s, 2H, OCH_2Ph), 4.80 (s, 2H, NCH_2Ph), 6.45 (s, 1H, N=CH), 7.36 (m, 10H, 2 Ph); IR (KBr) 3100-2860, 1595, 1150, 1100, 740, 700 cm^{-1}; UV (95% EtOH) λ_{max}=236 nm.

Ethyl 2-benzyl-3-(2-benzyloxyethyl)-5-methylisoxazolidine-4-carboxylate (7). The toluene solution (50 mL) of *N*-(3-benzyloxypropylidene)benzylamine *N*-oxide (4.0 g, 14.9 mmol) and ethyl crotonate (5.08 g, 44.6 mmol) was refluxed under nitrogen gas for 48 h. Evaporation of the reaction mixture gave a light red colored liquid, which was chromatographed over a silica gel column with hexane-ethyl acetate (4 : 1) to give a colorless liquid. Yield, 4.1 g (72%); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 3H, J=7.0 Hz, $OCH_2\underline{CH_3}$), 1.37 (d, 3H, J= 7.0 Hz, CH_3), 1.78-2.10 (m, 2H, CH_2), 2.78 (dd, 0.8H, J=8.9 and 5.7 Hz, H-4), 3.03 (dd, 0.2H, J=9.0 and 8.9 Hz, H-4), 3.20-4.00 (m, 3H, CH_2O, H-3), 4.05-4.48 (m, 3H, $O\underline{CH_2}CH_3$, H-5), 4.46 (s, 2H, NCH_2Ph), 4.62 (s, 2H, OCH_2Ph), 7.47 (s, 5H, Ph), 7.50 (s, 5H, Ph); IR (neat), 3100-2860, 1725, 1600, 1450, 1370, 1185, 1090, 745, 700 cm^{-1}.

Ethyl 2-benzyl-3-(2-benzyloxy-1,1-dimethylethyl)-5-methylisoxazolidine-4-carboxylate (8). *N*-(3-Benzyloxy-2,2-dimethylpropylidene)benzylamine *N*-oxide (4.6 g, 15.5 mmol) was condensed with ethyl crotonate (5.3 g, 46.5

mmol) by the same method described for the synthesis of **7** to give **8**. Yield, 3.82 g (60%); ^{1}H NMR ($CDCl_3$) δ 0.87-1.23 (m, 9H, 2 CH_3, $OCH_2C\underline{H}_3$), 1.38 (d, 3H, J=7.0 Hz, CH_3), 2.70 (dd, 0.6H, J=8.9 and 6.0 Hz, H-4), 2.93-3.40 (m, 1.4H, H-3, H-4), 3.53 (s, 2H, OCH_2), 4.00-4.48 (m, 3H, $OC\underline{H}_2CH_3$, H-5), 4.45 (s, 2H, NCH_2Ph), 4.62 (s, 2H, OCH_2Ph), 7.47 (s, 5H, Ph), 7.50 (s, 5H, Ph); IR (neat), 3080-2870, 1725, 1600, 1450, 1370, 1185, 1100, 1030, 745 cm^{-1}.

Ethyl 3-benzylamino-5-benzyloxy-2-(1-hydroxyethyl)-pentanoate (9a). Zinc powder (purity 85%, 1.6 g, 20.8 mmol) was added portion by portion to the acetic acid (50 mL) solution of ethyl 2-benzyl-3-(2-benzyloxyethyl)-5-methylisoxazolidine-4-carboxylate (4.0 g, 10.4 mmol). The mixture was stirred for 12 h at room temperature. The reaction mixture was filtered to remove insoluble material and the solvent was evaporated to give a colorless liquid. The liquid was dissolved in ethyl acetate (100 mL) and the solution was washed with 10% aqueous sodium bicarbonate solution (100 mL). The ethyl acetate solution was dried over sodium sulfate and it was evaporated to give a colorless oil, which was chromatographed over a silica gel column with hexane-ethyl acetate (4 : 1) to give the desired product. Yield, 3.58 g (89%); ^{1}H NMR ($CDCl_3$) δ 1.07-1.60 (m, 5H, CH_3, NH, OH), 1.25 (t, 3H, J=7.0 Hz, CH_3), 2.08 (m, 2H, CH_2), 2.77 (dd, 1H, J=8.0 and 3.0 Hz, H-2), 3.13-3.80 (m, 4H, OCH_2, NCH, OCH), 3.89 (s, 2H, NCH_2), 4.23 (q, 2H, J=7.0 Hz, OCH_2), 4.53 (s, 2H, OCH_2Ph), 7.42 (s, 5H, Ph), 7.45 (s, 5H, Ph); IR (neat) 3600-2700 (O-H), 3300 (N-H), 3080-2860, 1725 (C=O), 1100, 740, 700 cm^{-1}.

Ethyl 3-benzylamino-5-benzyloxy-2-(1-hydroxyethyl)-4,4-dimethylpentanoate (9b). Ethyl 2-benzyl-3-(2-benzyloxy-1,1-dimethylethyl)-5-methylisoxazolidine-4-carboxylate (3.8 g, 9.24 mmol) was reduced with 85% zinc powder (1.42 g, 18.5 mmol) by the same method employed for the preparation of **9a**. The reacton product was isolated by silica gel column chromatography with hexane-ethyl acetate (5 : 1). Yield, 3.51 g (92%); ^{1}H NMR ($CDCl_3$) δ 0.92 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.07-1.43 (m, 8H, 2 CH_3, NH, OH), 2.62 (dd, 1H, J=8.0 and 4.0 Hz, H-2), 3.17-3.50 (m, 4H, NCH_2, NCH, OCH), 4.02 (s, 2H, OCH_2), 4.20 (q, 2H, J=7.0 Hz, OCH_2), 4.53 (s, 2H, OCH_2Ph), 7.43 (s, 10H, 2 Ph); IR (neat) 3600-2750 (O-H), 3320 (N-H), 3100-2760, 1450, 1365, 1095, 740, 700 cm^{-1}.

Ethyl 3-benzylamino-5-benzyloxy-2-[1-(*t*-butyldimethylsilyloxy)ethyl]pentanoate (12a). *t*-Butyldimethylsilyl chloride (1.38 g, 9.16 mmol) was added to the solution of ethyl 3-benzylamino-5-benzyloxy-2-(1-hydroxyethyl)pentanoate (3.52 g, 9.14 mmol) and imidazole (0.64 g, 9.5 mmol) in DMF (20 mL) and the mixture was stirred at room temperature for 12 h under nitrogen gas. The reaction mixture was diluted with diethyl ether (100 mL) and to this mixture water (100 mL) was added. The diethyl ether layer was separated and the aqueous layer was extracted with diethyl ether (50 mL). The combined diethyl ether solution was washed with water (3×100 mL), 2% HCl solution (50 mL), and saturated sodium chloride solution (100 mL). The ether solution was dried over sodium sulfate and the solvent was evaporated to give a colorless liquid which was chromatographed over a silica gel column with hexane-ethyl acetate (8 : 1) to give a colorless liquid. Yield, 4.47 g (98%); ^{1}H NMR ($CDCl_3$) δ 0.023 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$), 0.92 (s, 9H, $C(CH_3)_3$), 1.07-1.47 (m, 6H, 2 CH_3), 1.67-2.17 (m, 3H, CH_2, NH), 2.80 (m, 1H, H-2), 3.03-3.45 (m, 1H, NCH), 3.47-3.97 (m, 5H, NCH_2, OCH_2, OCH), 4.23 (q, 2H, J=7.0 Hz, OCH_2), 4.58 (s, 2H, OCH_2Ph), 7.47 (s, 5H, Ph), 7.50 (s, 5H, Ph); IR (neat) 3330 (N-H), 3080-2850, 1725, 1450, 1375, 1255, 1095, 835, 780, 740, 700 cm^{-1}.

Ethyl 3-benzylamino-5-benzyloxy-2-[1-(*t*-butyldimethylsilyloxy)ethyl]-4,4-dimethylpentanoate (12b). Ethyl 3-benzylamino-5-benzyloxy-2-(1-hydroxyethyl)-4,4-dimethylpentanoate (3.48 g, 8.43 mmol) was reacted with *t*-butyldimethylsilyl chloride (1.27 g, 8.44 mmol) by following the same method as used in the preparation of **12a**. Yield, 4.26 g (96%), ^{1}H NMR 0.023 (s, 3H, $SiCH_3$), 0.079 (s, 3H, $SiCH_3$), 0.83 (s, 9H, $C(CH_3)_3$), 0.89 (s, 3H, CH_3), 1.02 (s, 1H, NH), 1.05 (s, 3H, CH_3), 1.12-1.40 (m, 6H, 2 CH_3), 2.75 (m 1H, H-2), 3.00-3.83 (m, 4H, NCH_2, NCH, OCH), 3.98 (s, 2H, OCH_2), 4.20 (q, 2H, J=7.0 Hz, OCH_2), 4.55 (s, 2H, OCH_2Ph), 7.45 (s, 10H, 2 Ph); IR (neat) 3360 (N-H), 3080-2850, 1725, 1255, 1100, 835, 775, 735, 700 cm^{-1}.

1-Benzyl-4-(2-benzyloxyethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (13a). Methylmagnesium bromide (diethyl ether, 3 M, 4.46 mL, 13.4 mmol) was added slowly to the THF solution (50 mL) of ethyl 3-benzylamino-5-benzyloxy-2-[1-(*t*-butyldimethylsilyloxy)ethyl]pentanoate (4.45 g, 8.92 mmol) at 0 ℃ under nitrogen gas. The mixture was stirred at the same temperature for 1 h and at room temperature for 18 h. The reaction mixture was diluted with diethyl ether (100 mL) and poured into saturated ammonium chloride solution (100 mL). The diethyl ether layer was separated. The water layer was extracted with diethyl ether (50 mL). The combined diethyl ether solution was washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of the diethyl ether gave a colorless liquid, which was chromatographed over a silica gel column with hexane-ethyl acetate (4 : 1) to give **13a**. Yield, 3.15 g (78%); ^{1}H NMR δ 0.04 (s, 6H, 2 $SiCH_3$), 0.87 (s, 9H, $C(CH_3)_3$), 1.22 (d, 3H, J=6.4 Hz, CH_3), 1.90 (m, 2H, CH_2), 2.95 (dd, 1H, J=5.6 and 2.4 Hz, H-3), 3.50 (t, 2H, J=7.0 Hz, OCH_2), 3.83 (m, 1H, H-4), 4.13-4.80 (m, 3H, OCH, NCH_2), 4.52 (s, 2H, OCH_2Ph), 7.42 (s, 5H, Ph), 7.45 (s, 5H, Ph); IR (neat) 3080-2850, 1750, 1600, 1255, 835, 775, 735, 700 cm^{-1}.

1-Benzyl-4-(2-benzyloxy-1,1-dimethylethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (13b). Ethyl 3-benzylamino-5-benzyloxy-2-[1-(*t*-butyldimethylsilyloxy)ethyl]-4,4-dimethylpentanoate (4.2 g, 7.97 mmol) was reacted with methylmagnesium bromide (diethyl ether, 3 M, 4.0 mL, 12.0 mmol) by the same method as described for the synthesis of **13a**. Yield, 2.49 g (65%); ^{1}H NMR ($CDCl_3$) δ 0.023 (s, 3H, $SiCH_3$), 0.079 (s, 3H, $SiCH_3$), 0.86 (s, 3H, CH_3), 0.87 (s, 9H, $C(CH_3)_3$), 0.93 (s, 3H, CH_3), 1.26 (d, 3H, J=6.2 Hz, CH_3), 3.00 (dd, 1H, J=6.4 and 2.16 Hz, H-3), 3.10 (s, 2H, CH_2O), 3.70 (d, 1H, J=2.16 Hz, H-4), 4.12 (m, 2H, OCH, NCHPh), 4.36 (s, 2H, OCH_2Ph), 4.60 (d, 1H, J=16.0 Hz, NCHPh), 7.27 (m, 10H, 2 Ph); IR (neat), 2950, 2920, 2850, 1750, 1255, 1100, 835, 700 cm^{-1}.

1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-hydroxyethyl)-2-azetidinone (14a). 1-Benzyl-4-(2-benzyloxyethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (1.2 g, 2.65 mmol) was dissolved in ethyl acetate (20 mL) and 10% Pd-C (1.0 g) was added to the solution. The mixture was stirred at room temperature for 4h under 30 psi of hyd-

rogen gas. The reaction mixture was filtered and the filtrate was evaporated to give a colorless liquid. Yield, 0.94 g (98%); ^{1}H NMR ($CDCl_3$) δ 0.015 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$), 0.87 (s, 9H, $C(CH_3)_3$), 1.37 (d, 3H, J=6.0 Hz, CH_3), 1.75-2.10 (m, 3H, OH, CH_2), 2.95 (dd, 1H, J=5.6 and 2.1 Hz, H-3), 3.10-3.50 (m, 3H, OCH_2, H-4), 3.98-4.28 (m, 2H, OCH, NCHPh), 4.84 (d, 1H, J=15.0 Hz, NCHPh), 7.30 (m, 5H, Ph); IR (neat), 3450, 2960, 2920, 1730, 1255, 1090, 835, 775, 700 cm^{-1}.

1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-hydroxy-1,1-dimethylethyl)-2-azetidinone (14b). 1-Benzyl-4-(2-benzyloxy-1,1-dimethylethyl)-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (1.0 g, 2.08 mmol) was dissolved in ethyl acetate (20 mL) and 10% Pd-C (0.82 g) was added to the solution. The mixture was hydrogenated for 4 h under 30 psi of hydrogen gas to give white crystals. Yield, 0.778 g (96%); mp 65 ℃; ^{1}H NMR ($CDCl_3$) δ 0.014 (s, 3H, $SiCH_3$), 0.087 (s, 3H, $SiCH_3$), 0.82 (s, 3H, CH_3), 0.87 (s, 9H, $C(CH_3)_3$), 0.94 (s, 3H, CH_3), 1.37 (d, 3H, J=6.0 Hz, CH_3), 1.56 (s, 1H, OH), 2.91 (dd, 1H, J=5.2 and 2.16 Hz, H-3), 3.11-3.30 (m, 3H, OCH_2, H-4), 3.98 (m, 1H, OCH), 4.06 (d, 1H, J=15.0 Hz, NCHPh), 4.86 (d, 1H, J=15.0 Hz, NCHPh), 7.29 (m, 5H, Ph); IR (neat), 3450, 2950, 2920, 1730, 1255, 1100, 835, 775, 700 cm^{-1}.

1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (15a). 1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-(2-hydroxyethyl)-2-azetidinone (0.84 g, 2.32 mmol), imidzole (0.163 g, 2.40 mmol) and *t*-butyldimethylsilyl chloride (0.361 g, 2.4 mmol) were dissolved in DMF (5.0 mL) and stirred at room temperature under nitrogen gas for 12 h. The reaction mixture was diluted with diethyl ether (10 mL), mixed with water (20 mL), and stirred for 30 min. The ether layer was separated and the aqueous layer was extracted with diethyl ether (10 mL). The combined ether solution was washed with water (10 mL×2) and saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. Evaporation of the ether gave a colorless liquid, which was chromatographed over a silica gel column with hexane-ethyl acetate (6 : 1) to give **15a**. Yield, 1.02 g (92%); ^{1}H NMR ($CDCl_3$) δ 0.027-0.057 (m, 12H, 4 $SiCH_3$), 0.85 (s, 18H, 2 $C(CH_3)_3$), 1.21 (d, 3H, J=6.2 Hz, CH_3), 1.71 (m, 2H, CH_2), 2.86 (dd, 1H, J=5.1 and 2.15 Hz, H-3), 3.56 (t, 2H, J=6.2 Hz, OCH_2), 3.72 (m, 1H, H-4), 4.18 (m, 1H, OCH), 4.20 (d, 1H, J=15.7 Hz, NCHPh), 4.52 (d, 1H, J=15.7 Hz, NCHPh), 7.28 (m, 5H, Ph); IR (neat), 2920, 2860, 1750, 1255, 1100, 835, 775 cm^{-1}.

1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)-1,1-dimethylethyl]-2-azetidinone (15b). 1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-[2-hydroxy-1,1-dimethylethyl]-2-azetidinone (0.64 g, 1.64 mmol) was reacted with *t*-butyldimethylsilyl chloride (0.249 g, 1.65 mmol) in the presence of imidazole (0.114 g, 1.65 mmol) in DMF (5 mL) by the same method as described for the synthesis of **15a**. Yield, 0.778 g (94%); ^{1}H NMR ($CDCl_3$) δ 0.020-0.090 (m, 12H, 4 $SiCH_3$), 0.76 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 0.87 (s, 9H, $C(CH_3)_3$), 0.91 (s, 9H, $C(CH_3)_3$), 1.24 (d, 3H, J=6.2 Hz, CH_3), 2.94 (dd, 1H, J=5.2 and 2.15 Hz, H-3), 3.20 (s, 2H, OCH_2), 3.71 (d, 1H, J=2.15 Hz, H-4), 4.10 (m, 1H, OCH), 4.27 (d, 1H, J=16.5 Hz, NCHPh), 4.53 (d, 1H, J=16.5 Hz, NCHPh), 7.28 (m, 5H, Ph); IR (neat) 2950, 2930, 1750, 1255, 1100, 835, 775, 700 cm^{-1}.

3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (16a). To liquid ammonia (40 mL) obtained by condensing ammonia gas by cooling in dry ice-acetone bath 1-benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (0.98 g, 2.05 mmol) solution in THF (20 mL)-absolute ethanol (0.72 mL) was dropped slowly. Then, pieces of sodium metal (0.283 g, 12.3 mmol) was added. When the color of the reaction mixture was deep blue and sustained more than 30 min. the addition of sodium was stopped. The reaction mixture was removed from the dry ice-acetone bath and nitrogen gas was passed to remove ammonia. To the reaction mixture was added ethyl acetate (25 mL)-saturated ammonium chloride solution (25 mL). The ethyl acetate layer was separated and the aqueous layer was extracted with ethyl acetate (10 mL). The combined ethyl acetate solution was washed with 5% sodium chloride solution (20 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent gave a residue which was chromatographed over a silica gel column with hexane-ethyl acetate (2 : 1) to give **16a**. Yield, 0.698 g (88%); ^{1}H NMR ($CDCl_3$) δ 0.028 (s, 6H, 2 $SiCH_3$), 0.047 (s, 6H, 2 $SiCH_3$), 0.85 (s, 9H, $C(CH_3)_3$), 0.87 (s, 9H, $C(CH_3)_3$), 1.20 (d, 3H, J=6.2 Hz, CH_3), 1.84 (m, 2H, CH_2), 2.76 (ddd, 1H, J=5.2, 2.3, and 1.2 Hz, H-3), 3.69 (t, 2H, J=5.6 Hz, OCH_2), 3.62-3.77 (m, 1H, H-4), 4.14 (m, 1H, OCH), 6.07 (s, 1H, NH); IR (neat), 3200, 2960, 2840, 1745, 1255, 1095, 835, 775 cm^{-1}.

3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)-1,1-dimethylethyl]-2-azetidinone (16b). 1-Benzyl-3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)-1,1-dimethylethyl]-2-azetidinone (0.75 g, 1.48 mmol) was dissolved in THF (10 mL)-absolute ethanol (0.52 mL) was reduced with sodium (0.204 g, 8.88 mmol)-liquid ammonia (20 mL) and isolated by the same method as described for the synthesis of **16a** to give **16b**. Yield, 0.534 g (87%), ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 6H, 2 $SiCH_3$), 0.07 (s, 6H, 2 $SiCH_3$), 0.84 (s, 3H, CH_3), 0.88 (s, 12H, $C(CH_3)_3$, CH_3), 0.89 (s, 9H, $C(CH_3)_3$), 1.22 (d, 3H, J=6.2 Hz, CH_3), 2.86 (m, 1H, H-3), 3.35 (s, 2H, OCH_2), 3.60 (d, 1H, J=2.15 Hz, H-4), 4.18 (m, 1H, OCH), 5.76 (s, 1H, NH); IR (KBr), 3150, 2950, 2920, 1755, 1255, 1090, 835, 775 cm^{-1}.

3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-(2-hydroxyethyl)-2-azetidinone (17a). 〈Method A〉. 1 N HCl solution (1.67 mL) was added to 3-[1-(*t*-butyldimethylsilyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)ethyl]-2-azetidinone (0.65 g, 1.68 mmol) dissolved in methanol (50 mL)-water (10 mL) and the solution was cooled to 0 ℃. The mixture was stirred for 24 h at the same temperature. Then, sodium bicarbonate powder was added until the pH of the reaction mixture arrived to neutral. The reaction mixture was saturated with sodium chloride and extracted with ethyl acetate (50 mL×2). The ethyl acetate solution was washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a colorless liquid which was chromatographed over a silica gel column with hexane-ethyl acetate (1 : 1) to give **17a**. Yield, 0.458 g (86%); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 6H, 2 $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.21 (d, 3H, J=6.2 Hz, CH_3), 1.76-2.20 (m, 3H, CH_2, OH), 2.78 (ddd, 1H, J=5.2, 2.3, and 1.2 Hz, H-3), 3.69 (t, 2H, J=5.6 Hz, OCH_2), 3.62-3.78 (m, 1H, H-4), 4.14 (m, 1H, OCH), 6.13 (br s, 1H, NH); IR (neat), 3500-3200, 2960, 2840, 1750, 1255,

1100, 835, 775 cm^{-1}.

〈**Method B**〉 3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-(2-benzyloxyethyl)-2-azetidinone (0.64 g, 1.41 mmol) dissolved in THF (10 mL)-absolute ethanol (0.50 mL) was dropped to the liquid ammonia (20 mL) condensed in a flask cooled in dry ice-acetone bath. Then, pieces of sodium (0.194 g, 8.46 mmol) were added portion by portion and addition of sodium was stopped when the color of the reaction solution became deep blue and the color was sustained more than 30 min. Ammonia was removed from the reaction mixture by passing nitrogen gas. The residue was diluted with ethyl acetate (20 mL) and washed with saturated ammonium chloride solution (20 mL). The aqueous layer was extracted with ethyl acetate (20 mL). The combined ethyl acetate solution was washed with 5% sodium chloride solution (40 mL) and dried over magnesium sulfate. Evaporation of the solvent gave a white solid which was chromatographed over a silica gel column with hexane-ethyl acetate (2 : 1) to give **17a**. Yield, 0.323 g (84%).

3-[1-Hydroxyethyl)-4-(2-hydroxy-1,1-dimethylethyl)-2-azetidinone (19). 3-[1-(*t*-Butyldimethyl-silyloxy)ethyl]-4-[2-(*t*-butyldimethylsilyloxy)-1,1-dimethylethyl]-2-azetidinone (0.50 g, 1.20 mmol) in methanol (20 mL)-water (5 mL) was cooled to 0 ℃. To this solution was added 1 N HCl solution, and the mixture was stirred for 24 h at the same temperature. After the pH of the solution was adjusted to neutral by addition of sodium bicarbonate powder, the reaction mixture was saturated with sodium chloride and extracted with ethyl acetate (20 mL×2). The ethyl acetate solution was washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a colorless liquid, which was chromatographed over a silica gel column with hexane-ethyl acetate (3 : 1). Yield, 0.184 g (82%); ^1H NMR ($CDCl_3$) δ 0.84 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 1.23 (d, 3H, J=6.2, Hz, CH_3), 2.12 (br s, 2H, 2 OH), 2.87 (m, 1H, H-3), 3.35 (s, 2H, OCH_2), 3.62 (d, 1H, J=2.1 Hz, H-4), 4.08 (m, 1H, OCH), 6.02 (s, 1H, NH); IR (neat), 3500-3200, 2960, 2840, 1740, 1100 cm^{-1}.

3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-(2-hydroxy-1,1-dimethylethyl)-2-azetidinone (17b). 1-Benzyl-4-(2-benzyloxy-1,1-dimethylethyl)-3-[1-(*t*-butyldimethylsilyloxy) ethyl]-2-azetidinone (1.00 g, 2.08 mmol) was reduced with sodium (0.287 g, 12.48 mgatm) by the same method as described for the synthesis of **17a** (Method B). The product was isolated by a silica gel column chromatography with hexane-ethyl acetate (3 : 1). Yield, 0.488 g (78%); ^1H NMR ($CDCl_3$) δ 0.02 (s, 6H, 2 $SiCH_3$), 0.84 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.89 (s, 9H, $SiC(CH_3)_3$), 1.22 (d, 3H, J=6.2 Hz, CH_3), 2.21 (br s, 1H, OH), 2.86 (m, 1H, H-3), 3.35 (s, 2H, OCH_2), 3.60 (d, 1H, J=2.15 Hz, H-4), 4.18 (m, 1H, OCH), 5.76 (s, 1H, NH); IR (KBr), 3500-3200, 2960, 2860. 1750, 1255, 1090, 835, 775 cm^{-1}.

3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-carboxymethyl-2-azetidinone (2a). 3-[1-(*t*-Butyldimethylsilyloxy)-ethyl]-4-(2-hydroxyethyl)-2-azetidinone (0.273 g, 1.00 mmol) dissolved in DMF (2.0 mL) was added to PDC (0.94 g, 2.50 mmol) dissolved in DMF (5.0 mL) and the mixture was stirred for 6 h at room temperature. The reaction mixture was poured to the water (10 mL) and extracted with ethyl acetate (10 mL×2). The ethyl acetate solution was washed with water (20 mL×2) and saturated sodium chloride solution (20 mL), and dried over anhydrous magnesium sulfate. The solvent was evaporated to give a yellow solid, which was crystallized in diethyl ether-ethyl acetate (1 : 1) to give **2a**. Yield, 0.255 g (89%); mp 160 ℃ (reported value 162 ℃); ^1H NMR ($CDCl_3$) δ 0.07 (s, 6H, 2 $SiCH_3$), 0.87 (s, 9H, $SiC(CH_3)_3$), 1.22 (d, 3H, J=6.0 Hz, CH_3), 2.58 (dd, 1H, J=16.0 and 9.5 Hz, $CHCO_2$), 2.78 (dd, J=16.0 and 4.0 Hz, $CHCO_2$), 2.87 (dd, 1H, J=7.0 and 2.1 Hz, H-3), 3.96 (m, 1H, H-4), 4.21 (m, 1H, OCH), 6.37 (br s, 1H, NH), 11.2 (br s, 1H, COOH); IR (neat), 3600-2560, 2980, 1740, 1255, 1100, 835, 775 cm^{-1}; Anal. Calcd for $C_{13}H_{25}NO_4Si$: C, 54.32; H, 8.77; N, 4.87. Found: C, 54.38; H, 8.72; N, 4.85.

3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-(1-carboxy-1-methylethyl)-2-azetidinone (2c). 3-[1-(*t*-Butyldimethylsilyloxy)ethyl]-4-(2-hydroxy-1,1-dimethylethyl)-2-azetidinone (0.301 g, 1.00 mmol) was oxidized with PDC (0.94 g, 2.50 mmol) in DMF (5.0 mL) by stirring for 12 h by following the method described for the synthesis of **2a** to give **2c**. The product was crystallized from diethyl ether-ethyl acetate (1 : 1). Yield, 0.246 g (78%); mp 178 ℃; ^1H NMR ($CDCl_3$) δ 0.02 (s, 6H, 2 $SiCH_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 1.18 (s, 3H, CH_3), 1.23 (d, 3H, J=6.0 Hz, CH_3), 1.26 (s, 3H, CH_3), 3.06 (dd, 1H, J=5.2 and 2.15 Hz, H-3), 3.98 (d, 1H, J=2.15 Hz, H-4), 4.24 (m, 1H, OCH), 6.08 (br s, 1H, NH), 10.86 (br s, 1H, COOH); IR (KBr), 3600-3300, 2960, 1745, 1255, 1090, 835, 775 cm^{-1}; Anal. Calcd for $C_{15}H_{29}NO_4Si$: C, 57.11; H, 9.27; N, 4.44. Found: C, 57.04; H, 9.32; N, 4.45.

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Characteristics of K_2NiF_4-Type Oxides $(Sr,Sm)_2FeO_{\sim 4}$

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$Sr_{1+x}Sm_{1-x}FeO_{4-y}$ solid solutions with a composition range $0.00 \leq x \leq 1.00$ have been prepared at 1200 ℃ in air under normal atmospheric pressure. All the solutions exhibit the K_2NiF_4-type structure of tetragonal system. Mohr salt analysis shows that the mole ratio of Fe^{4+} ion to Fe^{3+} ion or the τ value increases with the x value. Nonstoichiometric chemical formulas have been formulated from the x, τ, and y values. Electrical conductivity was measured in the temperature range of 173-373 K under atmospheric air pressure. The conductivities of each sample are varied within the semiconductivity range. The conductivity at constant temperature increases steadily with x value and activation energies are varied from 0.14 to 0.32 eV. The conduction mechanism of the ferrite system may be proposed as a hopping model of conduction electrons between the mixed valence states. The Mössbauer spectrum for the composition of $x=0.00$ shows a six line pattern by which the existence of Fe^{3+} (I.S.=0.32 mm/sec) can only be identified. The spectra for the compositions of $x=0.50$ and 1.00 presents broad single line patterns showing a mixed valence state.

Introduction

Up to date various oxides and halogenides showing the K_2NiF_4-type structure[1~7] have been investigated by many researchers. Those compounds are distinctive in chemical and physical properties because they show mixed valency of the transition metal ion, and consequently a considerable amount of oxygen deficiency. The K_2NiF_4-type structure can be described as a sequence of layers of tetragonally distorted octahedra with the K^+ ions alternating in 9-coordinated sites between the layers. As a result of relatively weak interplanar interactions between magnetic ions, K_2NiF_4-type compounds generally show the so-called 2-dimensional (2D) behaviour.[8~10] According to the results of many researches, 3d cations in octahedral sites can have two or more oxidation states. The perovskite type oxides[11~13] show considerable changes in their physical properties by partial replacement of the Fe(III) by the Fe(IV) ions. Especially, the electrical and magnetic properties are sensitive to the mixed valency state of the transition metal in the oxide system. In the present study solid solutions of the $(Sr,Sm)_2FeO_{\sim 4}$ system have been prepared and the cell parameters and crystal system were determined by X-ray powder diffraction method. The mixed valency state between Fe^{3+} and Fe^{4+} ions in the system was analysed by Mohr salt titration method and then identified by Mössbauer spectroscopy. The electrical conductivities and the activation energies measured in the temperature range of 173-373 K are discussed with taking the changes in the x and τ values into account.

Experimental

The starting materials such as Sm_2O_3 (99.99%), $SrCO_3$ (99.99%), and Fe_2O_3 (99.9%) were weighed in appropriate mole ratio to obtain five different samples with various x values. After mixing and grinding, the mixtures were heated at 1200 ℃ in air for 24hr and then quenched. The weighing, grinding, and heating process were repeated several times under the same conditions to obtain homogeneous solid solutions. After the heat treatment, the samples were analysed by the X-ray diffraction method to make sure the homogeneous phase of the solid solution. Each powder sample was pressed into a pellet under a pressure of 2 ton/cm^2 for 2 minutes and then all the pellets were sintered also under the same conditions as described above. The pellets were used for the study of the electrical conductivity. X-ray diffraction patterns of all compositions were obtained using X-ray diffraction powder method with monochromatized CuKα radiation. Comparing the observed d value with the theoretical d value calculated from the least-square method, we confirmed reasonable Miller indices of each line and then determined the crystal system, the lattice parameters, and the lattice volume of the unit cell.

The residual amount of Fe^{2+} ion of the Mohr salt which