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Synthetic Studies on Penems and Carbapenems(IV). Practical Preparation of (3*R*, 4*R*)-4-Acetoxy-3-[(1*R*)-1-hydroxyethyl]azetid-2-one Derivatives from 6-Aminopenicillanic Acid

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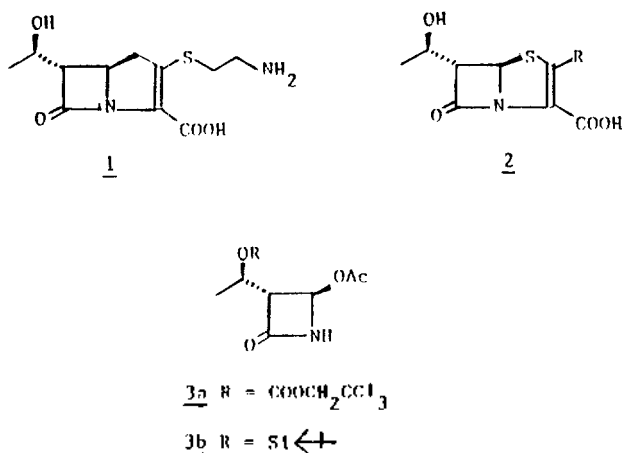
Preparation of optically pure (3*R*, 4*R*)-4-acetoxy-3-[(1*R*)-1-hydroxyethyl]azetid-2-one derivatives, which can be employed as starting materials for synthesis of carbapenem and penem antibiotics, was established in high efficiency from 6-aminopenicillanic acid (6-APA). 6-APA was diazotized and brominated to give 6,6-dibromopenicillanic acid and its methyl ester was metalated with methylmagnesium bromide and condensed with acetaldehyde. The product, methyl 6-bromo-6-(1-hydroxyethyl)penicillanate was reduced with Zn-NH₄Cl-NH₄OH-acetone efficiently to give methyl 6-(1-hydroxyethyl)penicillanate, which was protected either with β,β,β-trichloroethoxycarbonyl group or with *t*-butyldimethylsilyl group. The thiazolidine rings of these compounds were cleaved by treatment of mercury(II) acetate in acetic acid and permanganate in acetone in sequence to afford the desired optically pure final products.

Introduction

After discovery of a carbapenem antibiotic, thienamycin (1)¹ and Woodward's report² on penems (2), much efforts have been focused on the synthesis of new nonclassical β-lactam antibiotics and on the establishment of their structure-antimicrobial activity relationships³. Our current interest in synthesis of new penem and carbapenem antibiotics demands us to develop a practical method for preparation of the stereochemically pure (3*R*, 4*R*)-4-acetoxy-3-[(1*R*)-1-hydroxyethyl]azetid-2-one derivatives (3a and 3b). For the construction of penem or carbapenem structures, these azetid-2-one derivatives are good starting materials on many respects, since many well established methods for the

functionalization⁴ at the C-4 position of the azetid-2-one ring have been developed and the formation⁵ of fused azetidione bicyclic systems from these azetid-2-ones can be easily achieved.

There have been several reports on the construction of derivatives of 3-(1-hydroxyethyl)azetid-2-one. McCombie reported on the preparation of 3-(1-hydroxyethyl)-4-ethylthioazetid-2-one⁶ from 4-acetoxyazetid-2-one and also from 6-APA(4). The azetid-2-one derivative was used for the construction of a penem antibiotic, Sch 29482. Chemists at Merck & Co. described the preparation of 4-acetoxy-3-(1-hydroxyethyl)azetid-2-one from aspartic acid⁷ and 4-acetoxy-3-[1-(*p*-nitrobenzyloxycarbonyloxy)ethyl]azetid-2-one from 6-APA in a patent⁸. However, it

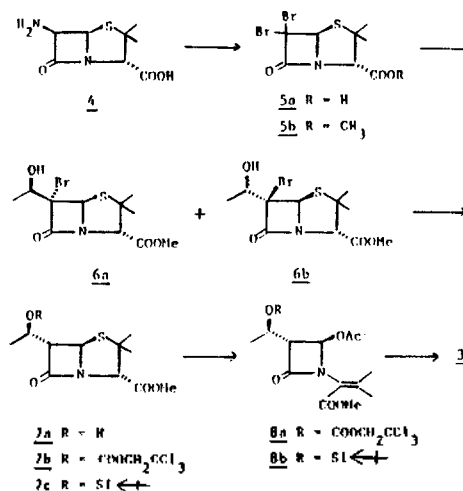


was necessary to reinvestigate the latter process to develop practical methods for preparation of stereochemically pure 4-acetoxy-3-(1-hydroxyethyl)azetidin-2-one derivatives with appreciable yield. We approached the synthesis of compound **3** from 6-APA (**4**) by application of various reported methods. A very good reduction method for the intermediate, methyl 6-bromo-6-(1-hydroxyethyl)penicillanate was developed. In this report, a reliable method for preparation of the optically pure (3*R*, 4*R*)-4-acetoxy-3-[(1*R*)-1-hydroxyethyl]azetidin-2-one derivatives is described.

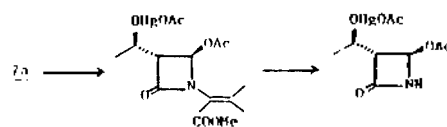
Results and Discussion

For the preparation of the desired azetidin-2-one derivatives(**3**) from the relatively inexpensive and readily available 6-APA, the amino group of 6-APA was converted stereospecifically to an 1-hydroxyethyl group to afford 6-(1-hydroxyethyl)penicillanate derivatives. 6-APA was diazotized and brominated by a reported procedure⁹ to give 6,6-dibromopenicillanic acid(**5a**) in 84% yield, in which 6-APA was added portion by portion to a methylene chloride-sulfuric acid-bromine biphasic solution that had been treated with sodium nitrite and maintained at 0° - 5°C. The compound **5a** was recrystallized from benzene and esterified with diazomethane in 93% yield. Preparation of methyl 6,6-dibromopenicillanate (**5b**) from methyl 6-aminopenicillanate was first reported by Clayton¹⁰ with 34% yield and later its benzyl ester analog from benzyl 6-aminopenicillanate by chemists at Merck & Co.¹¹ with 44% yield. Introduction of an 1-hydroxyethyl group at the C-6 position of compound **5b** was achieved by a reported procedure¹¹. Methylmagnesium bromide was prepared by adding slowly the ethereal solution of methyl bromide to the ether suspended with magnesium. The ethereal methylmagnesium bromide solution was titrated and used for the condensation of acetaldehyde with **5b** to give methyl 6-bromo-6-(1-hydroxyethyl)penicillanate (**6**) in 90% yield. Chemists at Merck & Co. reported that this condensation reaction produced predominantly the (6*S*) isomer, **6a**[**6a**:other isomers(**6b**) = 3:1]. This reaction was also markedly influenced by the nature of the solvent and the type of the metal cation present in the solution as well as the halide atom of the molecule involved¹². Recently methyl 6,6-diiodopenicillanate was reported to produce a better isomeric ratio when the reaction was carried out by a similar method with methylmagnesium iodide as the metalation reagent¹³. The mixture of methyl 6-bromo-6-(1-

hydroxyethyl)penicillanate was reduced to give the desired (6*S*) isomer as the dominant major product in a mixture of four possible isomers. Reduction of bromine atom in methyl or benzyl 6-bromo-6-(1-hydroxyethyl)penicillanate can be achieved by several methods: hydrogenation on 10% Pd-CaCO₃-charcoal^{14,15}, Zn(Ag)-MeOH (or with AcOH)¹¹, Zn-AcOH¹⁶, tri-*n*-butyltin hydride¹⁷, and sodium bisulfite¹⁸. Reduction of methyl or benzyl 6-bromo-6-(1-hydroxyethyl)penicillanate by Zn-AcOH, Zn-AcOH-MeOH or tri-*n*-butyltin hydride gave very poor yields (less than 50%). However, reduction of **6a** (or **6a** and **6b**) with Zn-NH₄OH-NH₄Cl-acetone provided the desired product, methyl (6*S*)-6-[(1*R*)-1-hydroxyethyl]penicillanate(**7a**) in a high yield (**6a** gave **7a** in 97% yield). The reductive debromination procedure involving tri-*n*-butyltin hydride or sodium bisulfite has been reported particularly for the conversion of the 6,6-dibromopenams to the 6-bromopenams^{17,18}. Dissolving metal reduction process for the removal of the C-6 bromine atom(s) on a penicillin nucleus was also reported¹⁹. The zinc-silver couple reduction of **6** in methanol gave **7a** in 65% yield. The relative ratio of the *trans* to the *cis* isomer of benzyl 6-(1-hydroxyethyl)penicillanate was 94:6. Recently a new reduction method, in which Zn-NH₄OAc in THF solution was employed, for the reduction of methyl 6,6-dibromopenicillanate to methyl penicillanate in 90% yield was reported²⁰. A similar reduction with Zn-AcOH in acetonitrile gave much poor yield due to the decomposition of the reactant²⁰. Our dissolved metal reduction method gave almost exclusively the desired *trans* isomer. The protection of the hydroxy group in **7a** was achieved by treatment with β,β,β-trichloroethyl chloroformate in methylene chloride at 0°C or with *t*-butyldimethylsilyl chloride and triethylamine in DMF at room temperature to give **7b** and **7c**, respectively. Crystallization of methyl (6*S*)-6-[(1*R*)-1-(β,β,β-trichloroethoxycarbonyloxy)ethyl]penicillanate (**7b**) was achieved in cold 2-propanol. Repeated experiments of the



Scheme 1.



Scheme 2.

whole process for the preparation of **7b** as a crystalline form from 6-APA gave 40–50% overall yields.

The ring cleavage²¹ of the thiazolidine rings in protected 6-(1-hydroxyethyl)penicillanate derivatives (**7b** and **7c**) was achieved by addition of **7b** or **7c** in the mixture of mercury(II) acetate, acetic acid and acetic anhydride maintained at 90°C to give the expected product **8a** or **8b**, respectively. Derivatives of 4-acetoxy-3-(1-hydroxyethyl)azetidino-2-one (**8a** and **8b**) were further oxidized with permanganate to remove the side chain at the N- position to afford the desired 4-acetoxy-3-(1-hydroxyethyl)azetidino-2-one derivatives, **3a** and **3b**, respectively²². When the thiazolidine ring of methyl 6-(1-hydroxyethyl)penicillanate was cleaved by treatment of mercury(II) acetate and by oxidation with permanganate, 4-acetoxy-3-(1-acetoxymercurioxyethyl)azetidino-2-one(**9**) was isolated.

Experimental

Melting points were determined on a Fisher-Johns melting point apparatus and were uncorrected. Infrared spectra were recorded with Perkin Elmer 710 spectrophotometer. The NMR spectra were recorded on a Varian EM-360A spectrometer with tetramethylsilane(TMS) as an internal standard. Chemical shifts were reported in parts per million (ppm) relative to TMS. Optical rotation values were obtained by using Jasco Model DIP-360 Digital Polarimeter with a Na lamp (589 nm) as the light source. The progress of reaction was generally followed by TLC on DC-Alufolien Kieselgel 60F (Art. 5554) silica gel plates using iodine or ceric sulfate spray followed by heating to detect spots. Column chromatography was performed with Merck Kieselgel 60G (70–230 mesh ASTM). Tetrahydrofuran was freshly distilled over sodium with benzophenone. Anhydrous acetic acid was obtained by distillation of pre-refluxed glacial acetic acid with P₂O₅ or of pre-distilled glacial acetic acid with benzene as an azeotrope. Methanol was distilled over magnesium metal. Methylene chloride and triethylamine were distilled over calcium hydride.

Preparation of 6,6-dibromopenicillanic acid(5a) from 6-APA (4). A round bottomed flask containing a magnetic stirring bar and bromine (5.9 g, 76 mmol) in methylene chloride (50 ml) was cooled to about 0°C in an ice-salt water bath. Sulfuric acid (2.5*N*, 20 ml) and sodium nitrite (3.5 g, 50 mmol) were added in sequence. Then, 6-APA(**4**) (5.4 g, 25 mmol) was added portion by portion over a period of 50 min while maintaining the temperature of the reaction mixture at -5° - 0°C. The resultant dark red solution was stirred further at 0°C for 45 min. The reaction mixture was decolorized with sodium sulfite (1*M*, 40 ml) by dropwise addition at 5° - 15°C over a period of 15 min. When the bromine color was discharged, the organic layer was separated and the aqueous layer was extracted further with methylene chloride (2 × 20 ml). The combined organic extract was washed with 20 ml of 5% aqueous NaCl, dried over anhydrous sodium sulfate, and evaporated under vacuum to give 7.6 g (85%) of a yellow crystal (**5a**) which was recrystallized from benzene: mp 150°C; ¹H NMR(CDCl₃) δ 5.87 (s, 1H), 4.63 (s, 1H), 1.65 (s, 3H) and 1.56 (s, 3H); IR (KBr) 3300, 1780, 1760 cm⁻¹.

Methylation of 6,6-dibromopenicillanic acid (5a). Diazomethane was prepared from *N*-nitroso-*N*-methylurea by the reported procedure²³. *N*-Nitroso-*N*-methylurea (2.69 g, 25 mmol) was added to the ether-50% aqueous KOH solu-

tion (cooled in ice-water bath) and the flask was shaken frequently. Then the diazomethane solution which was dried over KOH pellets was mixed with the ether solution of 6,6-dibromopenicillanic acid (7.2 g, 20 mmol). After the reaction mixture was shaken for 20 min, it was evaporated to give 6.9 g (93%) of pale yellow crystals (**5b**): mp 95°C (benzene); ¹H NMR(CDCl₃) δ 5.89 (s, 1H), 4.65 (s, 1H), 3.88 (s, 3H), 1.69 (s, 3H), 1.52 (s, 3H); IR (KBr) 1780, 1740 cm⁻¹; [α]_D = 141.7 deg. (c = 0.935).

Preparation of methyl 6-bromo-6-(1-hydroxyethyl)penicillanate (6a). To a stirred solution of methyl 6,6-dibromopenicillanate (**5b**, 200 mg, 0.54 mmol) in 5 ml of dry THF at -78°C under nitrogen gas was added dropwise 200 μl (0.65 mmol) of ethereal methylmagnesium bromide solution. The mixture was stirred for 30 min at -78°C and acetaldehyde (140 μl, 2.70 mmol) was added. After the mixture was stirred further for 30 min, the solution was warmed up to 0°C, quenched with aqueous NH₄Cl solution (5%, 5 ml), and partitioned between ethyl acetate and water. The organic layer was separated, washed with 5% aqueous NaCl solution, dried over sodium sulfate, filtered, and evaporated. Column chromatography of the colorless oily residue on a silica gel column by elution with benzene-ethyl acetate (9:1) gave 163 mg (90%) of methyl 6-bromo-(1-hydroxyethyl)penicillanate(**6**). The (6*S*) isomer was crystallized from ethyl acetate and hexane (60%): mp 114°C; ¹H NMR (CDCl₃) δ 5.56 (s, 1H), 4.50 (s, 1H), 4.18 (m 1H), 3.73 (s, 3H), 2.65 (s, 1H), 1.54 (s, 3H), 1.34 (s, 3H), 1.18 (d, *J* = 5 Hz, 3H); IR (Neat) 3700–3300, 1790, 1740 cm⁻¹; [α]_D = 144.8 deg. (c = 0.259).

Reduction of methyl 6-bromo-6-(1-hydroxyethyl)penicillanate(6). Methyl 6-bromo-6-(1-hydroxyethyl)penicillanate(**6**) (200 mg, 0.60 mmol) was dissolved in acetone (0.8 ml) and zinc dust (60 mg, 0.9 mmol) was added. The mixture was maintained at the temperature between 0°C and -10°C. To this mixture 0.42 ml of water and 0.8 ml of ammonia water (29%) was added with stirring. Then, ammonium chloride (60 mg, 1.1 mmol) dissolved in 0.2 ml of water was added dropwise while maintaining the temperature of the reaction mixture at -5°-10°C and it was stirred further for 30 min. Then, it was filtered through Celite, and the filter cake was washed with methylene chloride (2 × 20 ml). The combined filtrate was transferred to a separatory funnel, diluted with water (50 ml), and adjusted the pH with concentrated hydrochloric acid to 2.0. The organic layer was separated and the aqueous layer was further extracted with methylene chloride (2 × 20 ml). The combined organic layer was washed with aqueous NaHCO₃ (5%, 40 ml) and aqueous NaCl (5%, 20 ml), dried over sodium sulfate, and evaporated. Chromatography of the residue on a silica gel column by elution with methylene chloride-ethyl acetate (9:1) gave 145 mg (97%) of methyl (6*S*)-6-[(1*R*)-1-hydroxyethyl]penicillanate(**7a**): ¹H NMR (CDCl₃) δ 5.33 (d, *J* = 2 Hz, 1H), 4.48 (s, 1H), 4.25 (m, 1H), 3.76 (s, 3H), 3.30 (dd, *J* = 6 Hz and *J* = 2 Hz, 1H), 2.15 (s, 1H), 1.63 (s, 3H), 1.45 (s, 3H), 1.33 (d, *J* = 6 Hz, 3H); IR (Neat) 3700–3200, 1770, 1750 cm⁻¹.

Preparation of methyl (6*S*)-6-[(1*R*)-1-(β,β-trichloroethoxycarbonyloxy)ethyl]penicillanate(7b). In a round bottomed flask **7a** (500 mg, 1.9 mmol) was dissolved in 15 ml of dry methylene chloride. The solution was cooled to 0°C under nitrogen flow and charged 0.33 ml (4.0 mmol) of pyridine and β,β,β-trichloroethyl chloroformate (510 mg, 2.4 mmol) was added dropwise over a period of 15 min. The temperature

of the reaction mixture was maintained at 0° - 4°C. After completion of the addition, the reaction mixture was stirred further for 30 min. The reaction mixture was diluted with methylene chloride and washed twice with cold 10% aqueous phosphoric acid (20 ml), once with cold 10% aqueous sodium bicarbonate (20 ml) and finally twice with 50 ml of water. The organic layer was dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated to give a yellow oil. Chromatography of the residue on a silica gel column by elution with chloroform afforded 770 mg (93%) of **7b**. The oil was dissolved in 2-propanol with warming and the solution was seeded with a pure crystal and then allowed to stand overnight at 5°C in a refrigerator. The crystal was separated to give 300 mg (40%) of the methyl (6*S*)-6-[(1*R*)-1-(β,β,β -trichloroethoxycarbonyloxy)ethyl]penicillanate(**7b**): mp 77-78°C; ¹H NMR(CDCl₃) δ 5.32 (d, *J*=2 Hz, 1H), 5.30 (m, 1H), 4.83 (s, 2H), 4.52 (s, 1H), 3.80 (s, 3H), 3.53 (dd, *J*=8 Hz and *J*=2 Hz, 1H), 1.65 (s, 3H), 1.50 (d, *J*=6 Hz, 3H); IR (Neat) 1800, 1790, 1770 cm⁻¹; [α]_D = 19.5 deg. (*c*=0.041)

Silylation of methyl (6*S*)-6-[(1*R*)-1-hydroxyethyl]penicillanate(7a**) with *t*-butyldimethylsilyl group.** To a mixture of **7a** (200 mg, 0.8 mmol) and *t*-butyldimethylchlorosilane (140 mg, 1 mmol) in 5 ml of dry DMF was added triethylamine (220 μ l, 1.6 mmol) and it was stirred under nitrogen at room temperature for 10 hr. Saturated ammonium chloride solution (30 ml) was added and the reaction mixture was extracted with methylene chloride (3 \times 20 ml). The combined organic extract was washed with water (2 \times 20 ml), dried over anhydrous sodium sulfate, filtered, and evaporated. Chromatography of the residue on a silica gel column by eluting with methylene chloride gave 250 mg (86%) of methyl (6*S*)-6-[(1*R*)-1-(*t*-butyldimethylsilyloxy)ethyl]penicillanate (**7c**): ¹H NMR(CDCl₃) δ 5.33 (d, *J*=2 Hz, 1H), 4.49 (s, 1H), 4.35 (m, 1H), 3.79 (s, 3H), 3.30 (dd, *J*=5 Hz and *J*=2 Hz, 1H), 1.67 (s, 3H), 1.48 (s, 3H), 1.26 (d, *J*=7 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); IR (Neat) 1770, 1750 cm⁻¹; [α]_D = 149.8 deg. (*c*=0.243).

Triazolidine ring cleavage of **7b by mercury(II) acetate.** To a solution of acetic anhydride (0.5 ml) in acetic acid (20 ml) was added mercury(II) acetate (630 mg, 2 mmol) with stirring at 85°C and added dropwise compound **7b** (450 mg, 1.0 mmol) dissolved in dry acetic acid (5 ml). After stirring for 5 min, the reaction mixture was turned to white. The resultant mixture was stirred further for 45 min. The acetic acid was evaporated at 40°C (bath temp) and the residue obtained was diluted with methylene chloride (100 ml). The solution was filtered through Celite. The filtrate was washed with 5% aqueous NaHCO₃ (30 ml) and 5% aqueous NaCl (30 ml). The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to give a yellow oil. Chromatography of the residue on a silica gel column by elution with methylene chloride afforded 400 mg (85%) of **8a**: ¹H NMR(CDCl₃) δ 6.32 (d, *J*=2 Hz, 1H), 5.35 (m, 1H), 4.84 (s, 2H), 3.84 (s, 3H), 3.53 (dd, *J*=6 Hz and *J*=2 Hz, 1H), 2.28 (s, 3H), 2.1 (s, 3H), 2.0 (s, 3H), 1.51 (d, *J*=7 Hz, 3H); IR (Neat) 1800, 1760, 1740, 1650 cm⁻¹; [α]_D = 6.7 (*c*=0.150).

Thiazolidine ring cleavage of **7c by mercury(II) acetate.** To a solution of acetic anhydride (0.5 ml) in dry acetic acid (30 ml) was added mercury(II) acetate (330 mg, 1.0 mmol) with stirring at 85°C and added dropwise compound **7c** (200 mg, 0.5 mmol) dissolved in dry acetic acid (10 ml). After 5 min the reaction mixture was turned to white. The resul-

tant mixture was stirred for 45 min and then cooled to room temperature. The solvent was evaporated at 40°C (bath temp.). The residue was dissolved in methylene chloride (100 ml) and filtered through Celite. The methylene chloride solution was washed with 5% aqueous NaHCO₃ (30 ml) and 5% aqueous NaCl (30 ml). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to give a residue. Chromatography of the residue on a silica gel with methylene chloride-ethyl acetate (8:2) afforded 180 mg (90%) of **8b**: ¹H NMR (CDCl₃) δ 6.20 (d, *J*=2 Hz, 1H), 4.15 (q, *J*=6 Hz, 1H), 3.75 (s, 3H), 3.18 (dd, *J*=6 Hz and *J*=2 Hz, 1H), 2.18 (s, 3H), 2.03 (s, 3H), 1.92 (s, 3H), 1.30 (d, *J*=6 Hz, 3H), 0.90 (s, 9H), 0.10 (s, 6H); IR (Neat) 1790, 1760, 1730 cm⁻¹.

Permanganate oxidation of **8a to **3a**.** Compound **8a** (200 mg, 0.7 mmol) was dissolved in acetone (6 ml)-water (0.8 ml) solution and 0.2 ml of phosphate buffer (1M, pH=7.0) was added. Then, potassium permanganate (100 mg, 0.7 mmol) was added and the mixture was stirred at room temperature. After stirring for 30 min, more KMnO₄ (100 mg, 0.7 mmol) was added and stirred further for 30 min. After completion of the reaction, the mixture was diluted with ethyl acetate and stirred for 2 min. The reaction mixture was filtered through Celite and treated with sodium thiosulfate. The ethyl acetate solution was washed with 5% aqueous NaCl (20 ml) and water (30 ml), dried over sodium sulfate, and evaporated to give a colorless oil. The residue was chromatographed on a silica gel column by eluting with methylene chloride to give 200 mg (91%) of (3*R*,4*R*)-4-acetoxy-3-[(1*R*)-1-(β,β,β -trichloroethoxycarbonyloxy)ethyl]azetidino-2-one(**3a**): ¹H NMR(CDCl₃) δ 7.30 (broad s, 1H), 5.98 (d, *J*=2 Hz, 1H), 5.30 (m, 1H), 4.81 (s, 2H), 3.42 (dd, *J*=7 Hz and *J*=2 Hz, 1H), 2.10 (s, 3H), 1.53 (d, *J*=7 Hz, 3H); IR (Neat) 3420, 1800, 1770 cm⁻¹; [α]_D = 15.3 deg. (*c*=0.326).

Permanganate oxidation of **8b to **3b**.** Compound **8b** (200 mg, 0.5 mmol) was dissolved in acetone (6 ml)-water (0.8 ml) solution and 0.1 ml of phosphate buffer (1M, pH = 7.0) was added. Then, KMnO₄ (80 mg, 0.5 mmol) was added portion by portion and stirred for 20 min. Presence of the starting material or the excess of KMnO₄ was checked by TLC or by examination of the color of the solution after the MnO₂ was settled. More KMnO₄ (80 mg, 0.5 mmol) was added and stirred further for 30 min. The reaction mixture was diluted with ethyl acetate (50 ml) and filtered through Celite and the filter cake was washed with ethyl acetate. The filtrate was treated with solid sodium thiosulfate to destroy excess KMnO₄. The ethyl acetate solution was separated, washed with 5% aqueous NaCl (20 ml) and water (30 ml), dried over sodium sulfate, and evaporated under vacuum. The residue was chromatographed on a silica gel column by elution with methylene chloride to give 120 mg (88%) of (3*R*, 4*R*)-4-acetoxy-3-[(1*R*)-1-(*t*-butyldimethylsilyloxy)ethyl]azetidino-2-one(**3b**): mp 104°C; ¹H NMR (CDCl₃) δ 6.86 (broad s, 1H), 5.75 (d, *J*=1.5 Hz, 1H), 4.0 (m, 1H), 3.15 (dd, *J*=4 Hz and 1.5 Hz, 1H), 2.09 (s, 3H), 1.24 (d, *J*=6 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 6H); IR (KBr) 3600-3100, 1790, 1750 cm⁻¹; [α]_D = 8.51 deg. (*c*=0.27).

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A Theory of Polymer Adsorption from Solution

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A statistical thermodynamical treatment for polymer adsorption from solution is presented. The canonical partition function for the polymer solution in the presence of a surface or an impermeable interface is formulated on the basis of usual quasi-crystalline lattice model, Bragg-Williams approximation of random mixing, and Pak's simple treatment of liquid. The present theory gives the surface excess Γ_{sc} and the surface coverage ϕ_s of the polymer as a function of the chain length x , the Flory-Huggins parameter χ , the adsorption energy parameter χ_s , and polymer concentration v_2 . Present theory is also applicable to the calculation of interfacial tension of polymer solution against water. For the idealized flexible polymer, interfacial tensions according to our theory fit good to the experimental data to the agreeable degrees.

Introduction

The adsorption of polymer molecules at an interface from polymer solution is of great importance both in theoretical and practical aspects. It plays an essential role in colloid science, such as adhesion, flocculation, stabilization and destabilization of colloid particles by polymeric additives. One of the important features which are quite different from those of the adsorption of small molecules from monomeric liquid mixtures is that the number of conformations displayed by a flexible

polymer at an interface increases tremendously with chain length of the polymer. Since even in the very dilute solutions the segment concentration near the surface may be very high, the interaction between the segments can not be neglected. In addition, during the adsorption of polymer molecules at a surface, the conformation of the molecule changes considerably, and the initial conformation depends largely on the nature of the solvent, the temperature, the concentration of the solution, and other factors.

The nature of the solvent is one of the most important fac-