R^2 = 9-Me, R^3 = H), 50834-58-7; **23** (R^1 = CH_2CO_2Et, R^2 = 6-Me, R^3 = 8-Me), 50609-65-9; **24** (R^1 = CO_2Et, R^2 = 6-Me), 70999-37-0; **24** (R^1 = CO_2Et, R^2 = 7-Me), 71165-64-5; **24** (R^1 = CO_2Et, R^2 = 8-Me), 71165-59-8; **24** (R^1 = CH_2CO_2Et, R^2 = 6-Me), 71165-44-1.

Supplementary Material Available: Detailed ^1H and ^{13}C NMR data for 6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]-pyrimidin-4-ones **1–22** are presented (3 pages). Ordering information is given on any current masthead page.

A Stereocontrolled Synthesis of Thienamycin from 6-Aminopenicillanic Acid[1]

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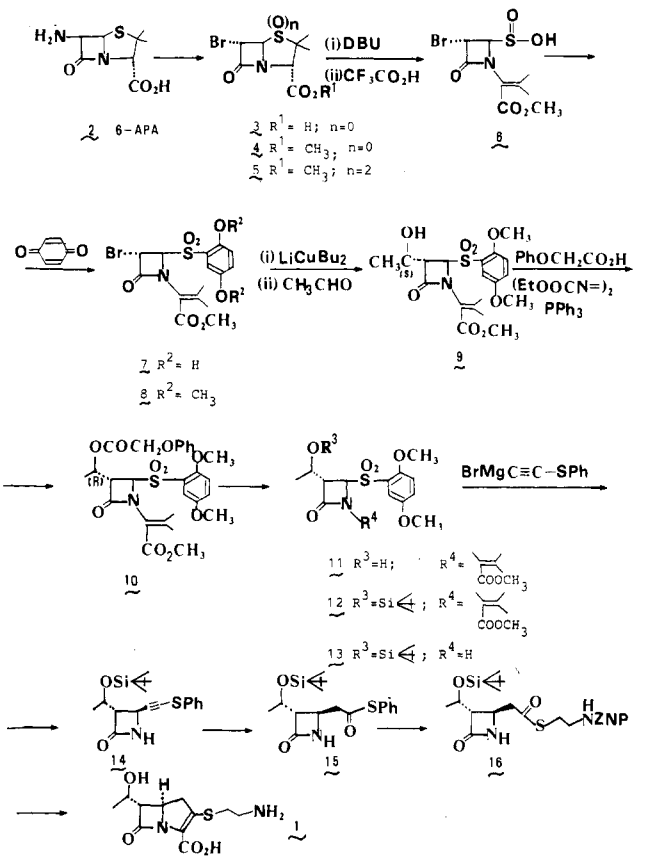
A stereocontrolled efficient synthesis of thienamycin (**1**) from 6-aminopenicillanic acid (6-APA) (**2**) was achieved. The thiazolidine ring of bromosulfone **3** was cleaved with DBU and the resulting sulfenic acid **4** was trapped with *p*-benzoquinone to give the sulfone **5**, which, after methylation, was transformed to the (hydroxyethyl)-azetidinone **6** in a stereocontrolled way. Carbon–carbon extension reaction of **6** at the 4-position with an acetylenic Grignard reagent, the following hydration, thiol ester exchange, and cyclization afforded natural thienamycin (**1**) in good yield.

Recently, much attention has been focused on thienamycin[2] since it has very high and broad activity against a variety of bacteria.[3] Syntheses of thienamycin and its analogues have been disclosed by a Merck group[4] and others.[5] Also conversion of penicillin to thienamycin[6] has been carried out since fermentation yields of thienamycin have been relatively low.[2] The purpose of our research was the synthesis of thienamycin utilizing inexpensive 6-aminopenicillanic acid (6-APA) whose thiazolidine ring can be cleaved off and reconstructed to the carbapenem nucleus. In this synthesis two major tasks need to be undertaken: (i) a carbon–carbon extension reaction at the 5- and 6-positions of 6-APA and (ii) stereocontrol of the three asymmetric centers in thienamycin. These problems were solved by careful analysis of the environments of the starting material and the target molecule and the formal total synthesis of thienamycin was achieved.

6-APA (**2**) was converted to the known methyl 6α-bromopenicillanate (**4**)[7] in 74% yield which was oxidized to the sulfone **5** with *m*-chloroperbenzoic acid. The thiazoline dioxide ring of compound **5** was cleaved with DBU according to Stoodley's method[8] to give the sulfenic acid salt which was transformed into the free acid **6** by neutralization with trifluoroacetic acid (Scheme I). Sulfenic acid **6** could be isolated and was characterized by its NMR spectrum. The intermediate sulfenic acid **6** was treated, without isolation, with *p*-benzoquinone to afford the sulfone **7**.[9] When this sulfenic acid salt (6-DBU salt) was trapped with methyl iodide, a mixture of the sulfone **17** and methyl sulfinate **18** was obtained, the ratio depending upon the reaction conditions. During this ring-opening reaction the stereochemistry of compound **7** was retained 3,4-trans, this being apparent from the coupling constant

Scheme I



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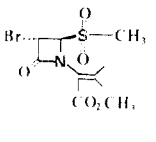

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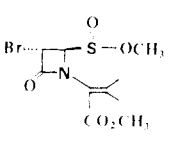

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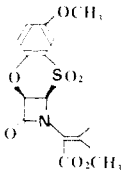
(2.0 Hz) determined from the NMR study. The dihydroxyphenyl sulfone **7** was methylated with dimethyl sulfate and potassium carbonate to furnish dimethoxyphenyl sulfone **8** in good yield. When the reaction conditions were not optimal in this reaction, a fair amount of tricyclic byproduct **19** was isolated.[10] Then bromo-



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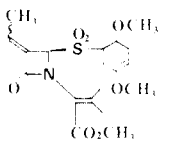

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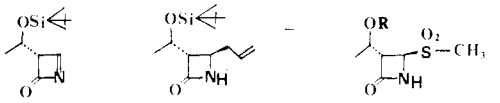
azetidinone **8** was treated with an excess of dibutylcopper lithium, followed by the addition of acetaldehyde to give the desired (hydroxylethyl)azetidinone **9** in good yield in which the ratio of isomer in the hydroxy part was estimated by NMR spectroscopy to be 90:10. Intervention of an enolate in this reaction was verified by the addition of water instead of acetaldehyde to furnish 3-non-substituted azetidinone. Formation of this kind of enolate starting from the bromo β-lactam using lithium dibutylcuprate is unusual; however, a related reaction has been reported[11] in the case of an aliphatic α-bromo ketone with other side reactions. Generation of this β-lactam enolate starting from 3-bromoazetidinone was accomplished only by the use of dibutylcopper lithium; methylmagnesium bromide or alkyllithium gave poor results. The configuration of the hydroxy part of the major isomer in compound **9** was determined to be *S* in the later reaction (vide infra). Since the configuration of the hydroxy group of **9** was opposite to that of thienamycin, the hydroxyethyl compound **9** was submitted to Mitsunobu reaction[12] using phenoxyacetic acid with ethyl diazocarboxylate and triphenylphosphine to afford the desired (phenoxyacetyl)oxy compound **10**. Other acids such as formic and acetic acid were also examined, but phenoxyacetic acid was found to be the best choice as the resulting phenoxy acetate was rapidly hydrolyzed to the free hydroxyl group in the following reaction and the dehydrated byproduct **20** in the Mitsunobu reaction was minimal. The phenoxyacetate **10** was hydrolyzed with a calculated amount of sodium hydroxide to yield the alcohol **11** and the hydroxy function was protected with the *tert*-butyldimethylsilyl group. Then the substituent of the nitrogen part of compound **12** was removed by reaction with potassium permanganate in the usual way[13] to afford the azetidinone **13**. Then the sulfone **13** was reacted with [(phenylthio)acetylene]magnesium bromide according to our method[14] to give [(phenylthio)ethynyl]azetidinone **14** in good yield. In this reaction when the hydroxy part was protected with the dimethyl-*tert*-butylsilyl grou, use of excess Grignard reagent can be avoided. The stereochemistry of the Grignard product **14** was found to be exclusively trans, suggesting participation of an intermediate such as the azetinone **21**. Thus, this carbon extension reaction at the 4-position of azetidin-2-one would be a kind of 1,4-addition reaction to the azetinone **21**.[15] This hypothesis was supported by starting



21 22 23

from the sulfone **13** which reacted with allylmagnesium chloride in the presence of CuCl or CuBr to afford the allylazetidinone **22** in higher yield compared to reaction in the absence of cuprous catalyst. Since the importance of cuprous catalyst in the 1,4-addition reaction of a Grignard reagent is well established,[16] the intermediacy of compound **21** might be definite. When the Grignard reaction was carried out starting from the methyl sulfone **23** instead of the aryl sulfone **13**, the yield of the expected product such as **14** or **22** was not good, indicating the poor ability of methyl sulfone as a leaving group. This was the reason why the sulfinic acid **6** was trapped with *p*-benzoquinone, which became a substituted benzene ring with excellent ability as a leaving moiety in the Grignard reaction. The thioacetylene **14** was hydrated by successive treatment with trifluoroacetic acid in methylene chloride and water to furnish the phenyl thio ester **15**, which was identical in all respects with an authentic sample prepared from L-threonine.[17] Thus the three asymmetric centers in compound **15** had the correct configuration for thienamycin, indicating that extension of the carbon–carbon bond at the 3- and 4-positions of the sulfone **8** took place stereospecifically in accord with our purpose. Next, the thio ester exchange reaction was successfully carried out by reaction of the thio ester with ((*p*-nitrobenzyloxy)carbonyl)cysteamine in methylene chloride at room temperature to furnish the desired compound **16**. The thio ester **16** had already been converted to thienamycin by our research chemists.[18] Thus, transformation of 6-APA to thienamycin was achieved with the following features: (i) the three asymmetric centers were constructed in a stereocontrolled way, (ii) all steps were performed in moderate to good yields, and (iii) extension of the carbon–carbon bond at the 3- and 4-positions of the β-lactam was carried out by new methods.

Experimental Section

Melting points are uncorrected. Proton NMR spectra were recorded on a Varian T-60 spectrometer. IR spectra were obtained on a Jasco IR A-2 spectrometer.

Methyl 6α-Bromo-1,1-dioxypenicillanate (5). To a stirred solution of **4**[7] (10.5 g, 36 mmol) in methylene chloride (300 mL) was added *m*-chloroperbenzoic acid (MCPBA) (18.5 g, 0.107 mmol) with ice cooling, and the reaction mixture was kept at room temperature overnight. After filtration, the filtrate was washed with 15% Na_2SO_3 solution, saturated $NaHCO_3$ solution, and saturated NaCl solution and dried over $MgSO_4$. After evaporation, the oily residue was dissolved in benzene (20 mL) and left at room temperature to give crystals, which were collected by filtration, washed with benzene twice, and dried to give 8.4 g of **5**. The filtrate was evaporated to give a foam, which was dissolved in

(10) ^1H NMR ($CDCl_3$) data of the compound **19**: δ 1.50 (3 H, s), 2.15 (3 H, s), 3.73 (3 H, s), 3.79 (3 H, s), 5.48 and 5.80 (2 H, AB quartet, J = 5.5 Hz), 7.16–7.46 (3 H, m).

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benzene–cyclohexane (1:1, 20 mL), and further cyclohexane was added to give another crop of crystals of **5** (0.40 g): mp 141–142 °C; IR (KBr) 1800, 1760, 1330, 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (3 H, s), 1.62 (3 H, s), 3.78 (3 H, s), 4.44 (1 H, s), 4.71 (1 H, d, J = 1.5 Hz), 5.17 (1 H, d, J = 1.5 Hz).

Anal. Calcd for $C_9H_{12}NO_5SBr$: C, 33.12; H, 3.68; N, 4.29; Br, 24.50; S, 9.82. Found: C, 33.35; H, 3.69; N, 4.25; Br, 24.40; S, 9.83.

3(*S*)-Bromo-4(*R*)-[(2,5-dihydroxyphenyl)sulfonyl]-1-[1-(methoxycarbonyl)-2-methyl-1-propen-1-yl]azetidin-2-one (7). To a solution of **5** (6.5 g, 20 mmol) in THF (70 mL) was added a solution of DBU (2.74 g, 24 mmol) in THF (15 mL) at 0–5 °C, and the reaction mixture was stirred at 0–5 °C for 1 h. Then a solution of CF_3COOH (2.74 g, 24 mmol) in THF (6 mL) was added at 0–5 °C and stirring was continued for 10 min at 0–5 °C. Then a solution of *p*-benzoquinone (2.38 g, 22 mmol) in THF (25 mL) was added at 0–5 °C and the mixture was kept at room temperature overnight. The solution was diluted with AcOEt (600 mL), washed successively with water (once), 2% HCl solution (once), water (once), saturated $NaHCO_3$ solution (once), water (once), and saturated NaCl solution (once), and dried over $MgSO_4$. After evaporation of the solvents the oily residue was dissolved in a small amount of EtOH and again evaporated. The resulting oil was dissolved in EtOH (20 mL), to which water (40 mL) was added dropwise. The result was then allowed to stand at room temperature to give crystals. The crystals were collected by filtration, washed with EtOH–H_2O (1:2) twice, and dried to give **7** (6.80 g, 78%): mp 180–181 °C; IR (KBr) 3300, 1790, 1730, 1440, 1320, 1140 cm^{-1}; ^1H NMR ($CDCl_3$ + CD_3OD + D_2O) δ 2.04 (3 H, s), 2.18 (3 H, s), 3.68 (3 H, s), 5.31 (1 H, d, J = 2.0 Hz), 5.59 (1 H, d, J = 2.0 Hz), 6.94–7.35 (3 H, m).

Anal. Calcd for $C_{15}H_{16}BrNO_7S$: C, 41.45; H, 3.68; N, 3.22; Br, 18.40; S, 7.32. Found: C, 41.61; H, 3.62; N, 3.21; Br, 18.58; S, 7.29.

3(*S*)-Bromo-4(*R*)-[(2,5-dimethoxyphenyl)sulfonyl]-1-[1-(methoxycarbonyl)-2-methyl-1-propen-1-yl]azetidin-2-one (8). To a stirred solution of **7** (5.50 g, 12.7 mmol) in acetone (80 mL) was added K_2CO_3 (9.63 g, 69.8 mmol) at 0–5 °C, followed by dropwise addition of dimethyl sulfate (7.99 g, 63.5 mmol) at 0–5 °C. The reaction mixture was stirred at room temperature for 2.5 h. To this mixture was added AcOH (3.5 mL) at room temperature to destroy the excess dimethyl sulfate, and stirring was continued at room temperature for 1 h. The mixture was diluted with AcOEt (300 mL) and washed successively with water, saturated $NaHCO_3$ solution, and saturated NaCl solution, and dried over $MgSO_4$. After evaporation, the residue was chromatographed on silica gel. Elution with benzene-AcOEt (4:1) gave **8** (5.46 g, 94%) as crystals: mp 128–130 °C; IR (KBr) 1800, 1740, 1500, 1320, 1200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.96 (3 H, s), 2.03 (3 H, s), 3.71 (3 H, s), 3.79 (3 H, s), 3.92 (3 H, s), 5.31 (1 H, d, J = 1.8 Hz), 5.53 (1 H, d, J = 1.8 Hz), 6.80–7.50 (3 H, m).

Anal. Calcd for $C_{17}H_{20}BrNO_7S$: C, 44.13; H, 4.33; N, 3.03; Br, 17.28; S, 6.92. Found: 44.10; H, 4.31; N, 3.08; Br, 17.32; S, 7.13.

3(*S*)-[1(*S*)-Hydroxyethyl]-4(*R*)-[(2,5-dimethoxyphenyl)sulfonyl]-1-[1-(methoxycarbonyl)-2-methyl-1-propen-1-yl]azetidin-2-one (9). To a stirred suspension of cuprous iodide (5.93 g, 31.15 mmol) in THF (100 mL) was added a solution of *n*-BuLi (15% solution in *n*-hexane, 37.6 mL, 62.3 mmol) at −18 to −20 °C. After being stirred at −20 °C for 20 min, the mixture was cooled to −78 °C (bath temperature) and a solution of **8** (3.55 g, 7.68 mmol) in dry THF (35 mL) was added. After being stirred at −78 °C for 40 min, acetaldehyde (4.11 g, 93.2 mmol) was added at the same temperature. The reaction mixture was stirred at −78 °C for 1 h. A solution of $(NH_4)_2SO_4$ (15.9 g) in water (120 mL) and AcOEt (100 mL) was added at −78 °C and well stirred at room temperature. The mixture was filtered through Celite and the aqueous layer was extracted with AcOEt (twice). The combined organic layers were washed with saturated NaCl solution, dried over $MgSO_4$, and evaporated to give an oil (3.9 g). This oil was chromatographed on silica gel and elution with benzene–AcOEt (1:1) gave **9** (1.53 g, (46.6%) as crystals: mp 141–142 °C; IR (KBr) 3520, 1780, 1710, 1500, 1310, 1280, 1145 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (3 H, d, J = 6.4 Hz), 1.92 (6 H, s), 2.33 (1 H, bd, J = 5.0 Hz), 3.67 (3 H, s), 3.79 (3 H, s), 3.94 (3 H, s), 3.55–4.06 (1 H, m), 5.05–5.42 (1 H, m), 5.48 (1 H, d, J = 2.4 Hz), 6.75–7.35 (3 H, m).

Anal. Calcd for $C_{19}H_{25}NO_8S$; C, 53.34; H, 5.85; N, 3.28; S, 7.48. Found: C, 53.35; H, 5.85; N, 3.32; S, 7.57.

3(*S*)-[1(*R*)-[[(Phenoxymethyl)carbonyl]oxy]ethyl]-4-(*R*)-[(2,5-dimethoxyphenyl)sulfonyl]-1-[1-(methoxycarbonyl)-2-methyl-1-propen-1-yl]azetidin-2-one (10). A mixture of **9** (1.40 g, 3.28 mmol), triphenylphosphine (1.72 g, 6.55 mmol), and phenoxyacetic acid (1.0 g, 6.55 mmol) was dried in vacuo at room temperature for 1 h. Then the mixture was dissolved in dry THF (40 mL) and cooled to −5 °C with an ice–salt bath. To the solution was dropwise added a solution of diethyl azodicarboxylate (1.14 g, 6.55 mmol) in THF (8 mL) at −5 to −3 °C during 40 min. After the addition the reaction mixture was stirred at −8 to −5 °C for 30 min and kept at room temperature overnight. The solution was diluted with AcOEt (50 mL) and washed with saturated $NaHCO_3$ solution (twice) and saturated NaCl solution (twice), dried over $MgSO_4$, and evaporated to give an oil, which was chromatographed on silica gel (40 g). Elution with benzene–AcOEt (5:1) gave **10** (1.09 g, 59.3%) as crystals: mp 119–120 °C; IR (KBr) 1785, 1760, 1710, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52 (3 H, d, J = 6.5 Hz), 1.92 (6 H, s), 3.68 (3 H, s), 3.77 (6 H, s), 3.75–4.20 (1 H, m), 4.65 (2 H, s), 5.64 (1 H, d, J = 2.4 Hz), 5.42–5.79 (1 H, m), 6.75–7.38 (8 H, m).

Anal. Calcd for $C_{27}H_{31}O_{10}NS$: C, 57.74; H, 5.56; N, 2.49; S 5.71. Found: C, 57.86; H, 5.50; N, 2.64; S, 5.86.

3(*S*)-[1(*R*)-Hydroxyethyl]-4(*R*)-[(2,5-dimethoxyphenyl)sulfonyl]-1-[1-(methoxycarbonyl)-2-methyl-1-propen-1-yl]azetidin-2-one (11). The phenoxyacetate **10** (1.0 g, 1.78 mmol) was dissolved in dry THF (12 mL) and methanol (30 mL) and cooled to −3 °C. To the solution was added a solution of CH_3ONa (0.106 g, 1.96 mmol) in MeOH (5 mL) at −3 to −1 °C over a period of 20 min. The solution was stirred at −3 °C for 1 h. Acetic acid (143 mg, 2.4 mmol) was added and about 60% of the solvents were removed by distillation under reduced pressure at 25 °C. The resulting solution was diluted with AcOEt (60 mL) and washed with water, saturated $NaHCO_3$ solution, and saturated NaCl solution, dried ($MgSO_4$), and concentrated to give a crystalline substance. This compound was triturated with hexane (5 mL) and collected by filtration and washed well with hexane to give **11** (0.72 g, 94.8%): mp 157–158 °C; IR (KBr) 3520, 1780, 1730, 1500, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (3 H, d, J = 6 Hz), 1.92 (6 H, s), 2.25 (1 H, br s), 3.62 (3 H, s), 3.78 (3 H, s), 3.89 (3 H, s), 3.72–4.03 (1 H, m), 4.24–4.50 (1 H, m), 5.62 (1 H, d, J = 2.4 Hz), 6.81–7.42 (3 H, m).

Anal. Calcd for $C_{19}H_{25}NO_7S$: C, 53.34; H, 5.85; N, 3.27; S, 7.48. Found: C, 53.40; H, 5.81; N, 3.27; S, 7.45.

3(*S*)-[1(*R*)-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4(*R*)-[(2,5-dimethoxyphenyl)sulfonyl]-1-[1-(methoxycarbonyl)-2-methyl-1-propen-1-yl]azetidin-2-one (12). To a solution of alcohol **11** (650 mg, 1.52 mmol) in dimethylformamide (8 mL) was added *tert*-butyldimethylsilyl chloride (573 mg, 3.8 mmol) and 4-(dimethylamino)pyridine (464 mg, 3.8 mmol) at 10 °C. The reaction mixture was stirred at room temperature overnight. The mixture was diluted with AcOEt and washed (water, saturated $NaHCO_3$ solution, saturated NaCl solution), dried ($MgSO_4$), and evaporated to give an oil. By preparative layer chromatography (SiO_2, 2:1 benzene–AcOEt) **12** was isolated as crystals (807 mg, 98.0%): mp 61–63 °C: IR (KBr) 2990, 1735, 1500, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (3 H, s), 0.12 (3 H, s), 0.90 (9 H, s), 1.32 (3 H, d, J = 6.0 Hz), 1.98 (6 H, s), 3.56 (3 H, s), 3.78 (3 H, s), 3.81 (1 H, dd, J = 2.4, 4.6 Hz), 3.92 (3 H, s), 4.10–4.50 (1 H, m), 5.70 (1 H, d, J = 2.4 Hz), 6.85–7.45 (3 H, m).

Anal. Calcd for $C_{25}H_{39}O_8NSSi$: C, 55.38; H, 7.20; N, 2.58; S, 5.91. Found: C, 55.18; H, 7.31; N, 2.57; S, 5.95.

3(*S*)-[1(*R*)-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4(*R*)-[(2,5-dimethoxyphenyl)sulfonyl]azetidin-2-one (13). To a stirred solution of the olefine **12** (700 mg, 1.29 mmol) in acetone (30 mL) were added acetic acid (620 mg, 10.34 mmol) and a solution of $KMnO_4$ (612 mg, 3.88 mmol) in water (15 mL) at 5–7 °C. The reaction mixture was stirred under ice cooling for 24 h and diluted with AcOEt (50 mL). Then Na_2SO_3 was added until the violet color disappeared. The whole mixture was filtered through Celite. To the filtrate were added AcOEt (50 mL) and water (30 mL), and the resulting mixture was stirred well. The aqueous layer was separated and extracted with AcOEt once. The combined organic layers were washed (saturated $NaHCO_3$ solution, saturated NaCl solution), dried ($MgSO_4$), and evaporated to give a solid substance. Purification of this compound by preparative layer chromatography (SiO_2, 10:1 benzene–AcOEt) afforded **13**

(421 mg, 58.7%), as crystals: mp 163–164 °C; IR (KBr) 3350, 1790, 1760, 1500, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (3 H, s), 0.07 (3 H, s), 0.86 (9 H, s), 1.14 (3 H, d, J = 6.6 Hz), 3.64 (1 H, dd, J = 2.0, 2.9 Hz), 3.80 (3 H, s), 3.93 (3 H, s), 4.00–4.35 (1 H, m), 5.18 (1 H, d, J = 2.0 Hz), 6.74 (1 H, br s), 6.92–7.48 (3 H, m).

Anal. Calcd for $C_{19}H_{31}O_6NSSi$: C, 53.12; H, 7.27; N, 3.26; S, 7.46. Found: C, 53.10; H, 7.33; N, 3.54; S, 7.49.

3(*S*)-[1(*R*)-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4(*S*)-[(phenylthio)ethynyl]azetidin-2-one (14). To a stirred solution of (phenylthio)acetylene [268 mg, 2 mmol, 0.59 mL of PhSC≡CH solution in *n*-hexane (3.4 mol/L)] in dry THF (2 mL) was dropwise added 0.67 mL (2 mmol) of ethylmagnesium bromide solution (3 mol/L solution in ether) in dry THF (2 mL) at −40 °C under nitrogen. The mixture was stirred at room temperature for 30 min. The mixture was again cooled at −40 °C, and azetidinone **13** (215 mg, 0.5 mmol) in dry THF (2 mL) was dropwise added. After stirring at room temperature for 1 h, water (10 mL) and 5% HCl solution (1 mL) were added at 0–5 °C and extracted with EtOAc (50 mL, twice). The extracts were washed (water, saturated $NaHCO_3$ solution, water, saturated NaCl solution), dried ($MgSO_4$), and evaporated to give an oily residue. Purification of this oil by preparative layer chromatography gave **14** (145 mg, 80.3%) as crystals: mp 78–79 °C; IR (KBr) 3100, 2180, 1770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (6 H, s), 0.88 (9 H, s), 1.25 (3 H, d, J = 6.0 Hz), 3.36 (1 H, dd, J = 2.6, 3.1 Hz), 4.10–4.40 (1 H, m), 4.58 (1 H, d, J = 2.6 Hz), 6.18 (1 H, br s), 7.12–7.50 (5 H, m).

Anal. Calcd for $C_{19}H_{27}NO_2SSi$: C, 63.07; H, 7.42; N, 3.87; S, 8.85. Found: C, 63.15; H, 7.58; N, 3.94; S, 9.12.

3(*S*)-[1(*R*)-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4(*R*)-[[(phenylthio)carbonyl]methyl]azetidin-2-one (15). To a stirred solution of 4-acetylenic azetidinone **14** (100 mg, 0.28 mmol) in methylene chloride (2 mL) was added trifluoroacetic acid (158 mg, 1.38 mmol) at room temperature. After 30 min of stirring, the mixture was evaporated under reduced pressure to give an oily residue. This oil was dissolved in AcOEt (20 mL) to which was added water (5 mL), and the solution was stirred at room temperature for 5 min. The organic layer was separated, washed (saturated $NaHCO_3$ solution, saturated NaCl solution), dried ($MgSO_4$), and evaporated to afford a solid substance. Purification of this crude compound by preparative layer chromatography gave **15** (67.2 mg, 64.0%) as crystals: mp 95–98 °C; IR (Nujol) 3175, 3110, 1765, 1725, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (6 H, s), 0.87 (9 H, s), 1.19 (3 H, d, J = 6.0 Hz), 2.25 (3 H, m), 3.70–4.33 (2 H, m), 6.20 (1 H, br s), 7.35 (5 H, s); $[\alpha]^{24}_D$ +41.8° (c 1.6, $CHCl_3$).

Anal. Calcd for $C_{19}H_{29}NO_3SSi$: C, 60.09; H, 7.64; N, 3.69; S, 8.43. Found: C, 60.04; H, 7.73; N, 3.71; S, 8.56.

3(*S*)-[1(*R*)-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4(*R*)-[[[[2-[[(*p*-nitrobenzyloxy)carbonyl]amino]ethyl]thio]carbonyl]methyl]azetidin-2-one (16). To a stirred solution of thiol ester **15** (379 mg, 1.0 mmol) in methylene chloride (5 mL) were added 2-[[(*p*-nitrobenzyloxy)carbonyl]amino]ethanethiol (512 mg, 2.0 mmol) and triethylamine (101 mg, 1.0 mmol) at room temperature, and the solution was kept at room temperature overnight. The mixture was evaporated under reduced pressure to give an oily residue, which was purified by preparative layer chromatography to afford **16** (515 mg, 98%) as an oil: IR (Nujol) 3250, 1760, 1740, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (6 H, s), 0.86 (9 H, s), 1.16 (2 H, d, J = 6.0 Hz), 2.70–3.70 (7 H, m), 3.90–4.25 (2 H, m), 5.20 (2 H, s), 5.55 (1 H, m), 6.65 (1 H, br s), 7.51 (2 H, d), 8.22 (2 H, d).

Anal. Calcd for $C_{23}H_{35}N_3O_7SSi$: C, 52.54; H, 6.71, N, 7.99. Found: C, 52.16; H, 6.92; N, 8.20.

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Registry No. 1, 59995-64-1; 4, 34800-34-5; 5, 98114-06-8; 7, 99765-22-7; 8, 99765-23-8; 9, 99827-42-6; 10, 99765-24-9; 11, 99827-43-7; 12, 99765-25-0; 13, 99765-26-1; 14, 90629-36-0; 15, 90628-93-6; 16, 90628-97-0; 19, 99765-27-2; CH_3CHO, 75-07-0; $PhOCH_2CO_2H$, 122-59-8; PhSC≡CH, 6228-98-4; *p*-$NO_2C_6H_4CH_2OC(O)NH(CH_2)_2SH$, 65750-59-6; *p*-benzoquinone, 106-51-4.

Notes

Iodosobenzene Diacetate, an Efficient Reagent for the Oxidative Decarboxylation of Carboxylic Acids

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The oxidative decarboxylation of organic acids with concomitant replacement by a halogen (halodecarboxylation), through a radical intermediate, in the Hunsdiecker[1] or modified Hunsdiecker[2] reaction comprises an extremely useful and selective procedure for the syntheses of halogenated organic substances. The oxidative elimination of the intermediate radicals to give olefins is an interesting variation of the decarboxylation reaction of acids, which is usually accomplished with lead tetraacetate (LTA)/$Cu(OAc)_2$.[2a]

Particularly, iododecarboxylation of carboxylic acids to alkyl iodides has been effected by reaction of the free acid with *tert*-butyl hypoiodite[2a,b] or with combinations of LTA[2a,b] or mercuric oxide[2c] with iodine and also treating the silver carboxylate with iodine.[2d] It is known that several other oxidizing metal ions such as Ce^{IV}, Mn^{III}, Co^{III}, and Tl^{III} can also effect the decarboxylation of acids.[2e,3]

We have recently reported[4] the functionalization of nonactivated carbon atoms, through intramolecular hydrogen abstraction by alkoxy radicals generated by photolysis of the corresponding alcohols in the presence of iodosobenzene diacetate (IBDA)[5] and iodine. Inasmuch

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