Synthesis of (3R,4R,5R)-1-(tert-Butoxycarbonyl)-3,4-isopropylidenedioxy-5-methoxymethyl-2-pyrrolidinone from (S)-Pyroglutaminol

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(3R,4R,5R)-1-(tert-Butoxycarbonyl)-3,4-isopropylidenedioxy-5-methoxymethyl-2-pyrrolidinone (6), a useful chiral intermediate for the preparation of calycins, was synthesized starting from (S)-pyroglutaminol via the O-methylation of 1c with diazomethane in the presence of fluoboric acid and cis-dihydroxylation of the x,y-unsaturated lactam (4) as the key reactions.

Keywords: (S)-pyroglutaminol; calycinin; chiral synthesis; fluoboric acid; O-methylation; cis-dihydroxylation

Earlier we have reported the synthesis of optically active polyhydroxylated amines by employing cis-dihydroxylation of x,y-unsaturated lactams derived from chiral (S)- and (R)-pyroglutamic acid.1) Recently, Smith, III et al.2) and Shioiri et al.3) have reported the synthesis of (3R,4R,5R)-1-(tert-butoxycarbonyl)-3,4-isopropylidenedioxy-5-methoxymethyl-2-pyrrolidinone (6), a useful intermediate for the preparation of calycins,4) from D-isoascorbic acid and from (S)-pyroglutaminol respectively. In these procedures the p-methoxybenzyl group was used as the lactam N-protecting group for the O-methylation of the alcohol, and then the p-methoxybenzyl group was replaced with a tert-butoxycarbonyl group. In a continuation of our studies on the utility of chiral pyrogulatolic acid derivatives for natural product synthesis, we describe here a synthesis of 6 from (S)-1-(tert-butoxycarbonyl)-5-hydroxymethyl-2-pyrrolidinone (1c).

Compound 1c (mp 91—92°C; [α]D20 = 68° (c = 1, CHCl3), lit.5) mp 98—99°C, [α]D25 = 63° (c = 0.61, CHCl3) was prepared from either (S)-pyroglutaminol (1a)6) or (S)-1-(tert-butoxycarbonyl)-5-trityloxyethyl-2-pyrrolidinone (1d).14) Successive treatment of 1a with tert-butyldimethylsilyl chloride, di-tert-butyl dicarbonate, and tetrahydroammonium fluoride gave 1c in 76% overall yield. Acid hydrolysis of 1d with concentrated HCl-methanol (1:50) at 30—35°C gave 1c in 48% yield. Treatment of 1c with sodium hydride in tetrahydrofuran (THF)-N,N-dimethylformamide (DMF) (1:1) followed by addition of methyl iodide did not afford the O-methyl compound 2, while the reaction with a large excess of methyl iodide and silver oxide gave a mixture of 2 (about 15%) and an inseparable by-product with 35% recovery of the starting alcohol 1c. However, when treated with diazomethane in the presence of fluoboric acid7) in methylene chloride at 0°C, 1c furnished the O-methyl compound 2 in 74% yield.

Then, selenenylation of 2 using lithium disopropylamide (LDA) and phenylselenenyl chloride afforded a diastereomeric mixture of the 3-phenylseleno-2-pyrrolidinone derivative 3 (2.5:1 by 1H-NMR) in 63% yield. Treatment of 3 with 30% H2O2 in ethyl acetate gave the x,y-unsaturated lactam 4 in 73% yield. The lactam 4 was also obtained from 7a,14a) a major diastereomer synthesized from 1d by selenenylation with LDA and phenylselenenyl bromide. Acid hydrolysis of 7a with concentrated HCl-methanol (1:50) at 35°C followed by O-methylation with diazomethane in the presence of fluoboric acid and subsequent deselenenylation provided 4 in 26% yield. cis-Dihydroxylation of 4 with a catalytic amount of OsO4 in the presence of N-methylmorpholine N-oxide in aqueous acetone produced the diol 5 in 68% yield as a single diastereomer. Protection of the cis-diol in 5 with an isopropylidene group provided 6 ((α)D20 = 91.1° (c = 1, CHCl3), lit.5) [α]D25 = 92.3° (c = 1, CHCl3)) in 80% yield. Its spectral data (1H-NMR and IR) were identical with those reported.3)

Thus, O-methylation of 1c with diazomethane and fluoboric acid provided a facile route to 6.

Experimental

Melting points were measured on a Yanagimoto micro melting point apparatus and are not uncorrected. Infrared (IR) spectral measurements were performed on a JASCO FT-IR spectrophotometer. Proton and carbon-13 nuclear magnetic resonance (1H- and 13C-NMR) spectra were measured with a JEOL JNM FX-100 (100 MHz) spectrometer. Data were recorded in parts per million (ppm) downfield from internal tetramethylsilane (TMS). The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Optical rotations were determined with a JASCO DIP-360 digital polarimeter. Mass spectra (MS) were recorded with JOEL JMS-D302 and JOEL JMS-HX110 mass spectrometers. Organic extracts were dried over MgSO4 before vacuum evaporation.

Chart 1

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0°C for 12 h. After dialysis with AcOEt-benzene (3:1, 300 ml), the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation gave a crude silyl ether (1.5 g, yield quant.), which was treated with diisobutyl dicarbonate (2.88 g, 13.2 mmol) in CHCl₃ (30 ml) at room temperature for 5 h. After removal of the volatiles in vacuo, the residue was purified by column chromatography (silica gel, AcOEt:hexane = 1:1) to afford 1b (1.75 g, yield 81%) as an oil. [α]D 23 ± 68.5° (c = 0.7, CHCl₃) (lit. [α]D 23 ± 61° (c = 1.1, CHCl₃)), IR νcm⁻¹: 1787, 1753, 1712. ¹H-NMR (CDCl₃): 0.015 (6H, br, s, 2 × CH₃), 0.85 (9H, s, tert-Bu), 1.50 (9H, s, tert-Bu), 1.81–2.91 (4H, m, 2 × CH₂), 3.65 (1H, dd, J = 2.3, 10.3Hz), 3.91 (1H, dd, J = 3.8, 10.3Hz), 4.16 (m, 1H, CH), MS m/z: 329 (M⁺).

Preparation of 4 from (3R,5S)-1-(tert-Butylocarbonyl)-3-phenylseleno-5-trityloxymethyl-2-pyrrolinone (7a) (3R,5S)-1-(tert-Butylocarbonyl)-5-seleno-phenylseleno-2-pyrrolinone (7b) was obtained from 7a in 71% yield as an oil after column chromatography (silica gel, AcOEt:hexane = 3:2) in the same manner as described above for the preparation of 4 from 1b.

Preparation of 5 from (3R,5R)-1-(tert-Butylocarbonyl)-5-seleno-phenylseleno-2-pyrrolinone (7c) was obtained from 7b in 64% yield as an oil after column chromatography (silica gel, AcOEt:hexane = 1:1) in the same manner as described above for the preparation of 4 from 1d.

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References and Notes