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속 보

L-Ascorbic Acid로부터 2-Deoxy-L-Ribose의 효과적인 합성

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Efficient Synthesis of 2-Deoxy-L-Ribose Starting from L-Ascorbic Acid

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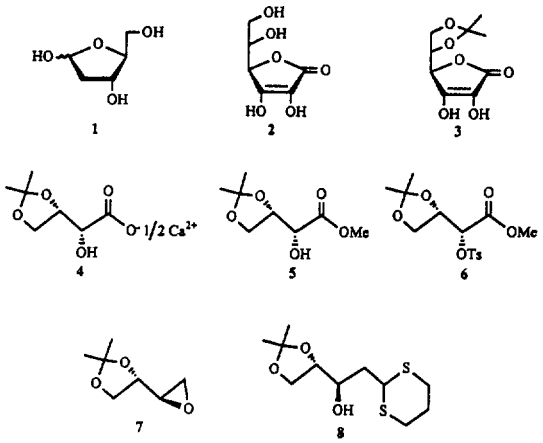
The chirality of the sugar-backbone units in natural nucleic acids is responsible for the formation of the high-order structure of the nucleic acids and for their functions as well. Organisms on the earth utilize only the D-sugar. Nevertheless, calculations[1] and other studies[2] suggest that modified nucleic acids based on L-sugar recognize complementary nucleic acids. Furthermore, oligonucleotides composed of 2-deoxy-L-ribose (2-deoxy-L-*erythro*-pentose **1**) show resistance to digestion by certain nucleases[2~4]. Enantio-DNA (DNA having 2-deoxy-L-ribose) and meso-DNA (DNA having an alternating sequence of L-sugar and D-sugar) are, therefore, valuable tools for studying protein-DNA interactions and are promising antisense agents[5~7]. In this regard, there still remains a need for the efficient synthetic method for 2-deoxy-L-ribose. Among a few known methods for the synthesis of **1**[8~10], only the glycal method developed by Deriaz *et al.*[9] has been used in practice. Herein we report a new efficient method for the synthesis of compound **1** starting from L-ascorbic acid (**2**).

L-Ascorbic acid (**2**) was converted to 5,6-O-isopropylidene derivative **3** in 95% yield by treatment with acetyl chloride in acetone[11]. Oxidation of **3** with hydrogen peroxide in the presence of calcium carbonate[12] afforded the threonic acid derivative **4**[13] in 72% yield. Compound **4** was transformed into the methyl ester **5**[13] in 95% yield with methyl iodide and sodium bicarbonate in dimethylacetamide. The secondary hydroxyl group of **5** was tosylated with tosyl chloride and triethylamine in methylene chloride to give compound **6**[14] in 90% yield. The reduction of tosylate **6** with sodium borohydride in methanol and subsequent epoxidation of the resulting 1,2-hydroxytosylate with potassium carbonate were carried out in one pot to afford epoxide **7**[15] in 63% yield. Reaction of compound **7** with lithiated 1,3-dithiane in THF at −40 ℃ provided white solid **8**[16] in 70% yield. To a solution of thioacetal **8** (0.18 g, 0.68 mmol) in water (16 m*l*)-acetone (16 m*l*) was added 1.0 N HCl (1.0 m*l*) at room temperature. After stirring for 30 min, HgO (0.66 g, 3.04 mmol) and $HgCl_2$ (0.80 g, 2.96 mmol) were added to the reaction mixture and the stirring continued for further 2 h at 40℃. The reaction mixture was filtered and acetone was removed *in vacuo*. To the remaining aqueous solution was added Na_2S (0.86 g, 3.56 mmol) and precipitated HgS was removed. The volume of aqueous solution was reduced to a half by freeze-drying. Isopropyl alcohol (20 m*l*) was added to the aqueous solution and precipitated sodium chloride was removed by filtration. The filtrate was evaporated to give a pale yellow syrup which was crystallized in vacuum after one week. Recrystallization of the



crude crystal from ethyl acetate gave pure 2-deoxy-L-ribose (**1**, 0.06 g, 70%)[17]. The overall yield of the present procedure is 18%. The present method is superior over Deriaz's glycal method[9] at least in two aspects: the overall yield and the cost of the starting material.

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14. Compound **6**: mp. 56~58 ℃; ^{1}H NMR (80 MHz, $CDCl_3$) δ 1.22 (s, 6H), 2.37 (s, 3H), 3.63 (s, 3H), 3.88~3.92 (m, 2H), 4.28~4.48 (m, 1H), 4.75~4.81 (d, 1H), 7.19~7.81 (2d, 4H).
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16. Compound **8**: mp. 71 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.36 (s, 3H), 1.17~2.10 (m, 4H), 2.21 (s, 1H), 2.76~2.84 (m, 5H), 3.85~4.03 (m, 3H), 4.19~4.24 (m, 1H).
17. Compound **1**: mp. 89℃ (lit.[9] 90 ℃); $[\alpha]_D$ +55.0° (c 0.27, H_2O) (lit.[9] +58°); ^{1}H NMR (200 MHz, D_2O) δ 1.64~2.50 (m, 2H), 3.57~4.42 (m, 4H), 5.30~5.65 (m, 1H).