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Conversion of D-Glucose into the β-Hydroxy-δ-lactone Moiety of Mevinic Acids and Congeners *via* D-Idose as a Key Chiral Intermediate

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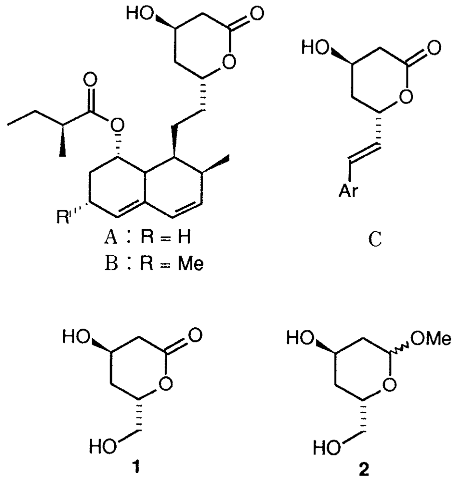
(4*R*,6*S*)-4-Hydroxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-one (1) and (4*R*,6*S*)-4-hydroxy-6-hydroxymethyl-2-methoxytetrahydropyran (2), chirons of the β-hydroxy-δ-lactone moiety of mevinic acids and congeners, were derived from 1,2,3,6-tetra-*O*-acetyl-α-D-idose (5), which is easily available from penta-*O*-acetyl-β-D-glucose (3).

Keywords idose; δ-lactone; mevinic acid; tetrahydropyran-2-one; tributyltin hydride; reductive deoxygenation; reductive rearrangement

Mevinic acids [*i.e.*, mevastatin (A)[1] and lovastatin (B)[2]] are potent inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, an enzyme involved in one of the early steps of cholesterol biosynthesis.[3] Lovastatin (B) and a 3-hydroxymevastatin derivative (pravastatin sodium) are members of a new class of hypocholesterolemic agents and are in clinical use. Numerous studies[4] on the structure–activity relationships of HMG-CoA reductase inhibitors have shown that the chiral δ-lactone moiety in mevinic acids is essential for strong hypocholesterolemic activity and various types of (4*R*,6*S*)-6-arylethenyl-4-hydroxy-3,4,5,6-tetrahydro-2*H*-pyran-2-one (C) retain the activity. Thus, synthesis of (4*R*,6*S*)-4-hydroxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-one (**1**) and (4*R*,6*S*)-4-hydroxy-6-hydroxymethyl-2-methoxytetrahydropyran (**2**), chirons of the δ-lactone moiety of mevinic acids and their congeners is of potential importance.

Among the published routes to the δ-lactone moiety, the conversion of a readily available carbohydrate such as D-glucose has been most studied. These conversions involve two deoxygenation reactions at C-2 and C-4 and an inversion of configuration at C-3 of D-glucose by various procedures.[5—9]

A special feature of our synthetic approaches to **1** and **2** is employment of 1,2,3,6-tetra-*O*-acetyl-α-D-idose (**5**) as a key chiral intermediate which is easily obtained from penta-*O*-acetyl-β-D-glucose (**3**).[10] The intermediate (**5**) appropriately sets up the 3(*R*)-configuration corresponding to the 4(*R*)-configuration of **1** and **2** and possesses a free C-4-hydroxy group, which is convenient for reductive deoxygenation.[11] For the deoxygenation at C-2, two methods are applicable: one is reductive rearrangement of 2-*O*-acetyl-1-halogenosugars[12] and the other is reductive elimination of 1-*O*-acetyl-2-halogenosugars (see Chart 2). Although the overall yields of the present approaches are not always superior to previously reported routes,[6] employment of **5** as a chiral pool made it possible to prepare **1** and **2** *via* comparatively few steps on a laboratory scale.[13]



A : R = H
B : R = Me

C

1

2

Chart 1

According to the modified Paulsen procedure,[10] the glucose (**3**) was allowed to react with antimony pentachloride to give the acetoxonium salt, which was subsequently treated with sodium acetate to give a mixture of D-idose derivatives (**4** and **5**) as rearranged products. Fortunately, the desired 4-hydroxy derivative (**5**) was obtained as a sole product upon treatment of the mixture of **4** and **5** with aqueous pyridine as a result of acetyl migration[14] (46.7% from **3**). After conversion of **5** to the 4-*O*-phenoxythiocarbonyl derivative (**6**), the reaction with tributyltin hydride resulted in smooth deoxygenation at C-4 of **5** to give the 4-deoxy derivative (**7**) (82% from **5**).

The 1-bromo derivative (**8**), which was quantitatively prepared by bromination of **7** using hydrogen bromide, was subjected to radical rearrangement leading to 1,3,6-tri-*O*-acetyl-2,4-dideoxy-β-D-idopyranose [(2*S*,4*R*,6*S*)-2,4-diacetoxy-6-acetoxymethyltetrahydropyran] (**9a**). Giese *et al.*[12] have shown that the reduction of 2-*O*-acylated or benzoylated glycosyl halides with low concentrations of tributyltin hydride provides 2-deoxysugars, and an important step in this radical chain reaction is the *cis*-selective migration of an ester group. Although the reductive rearrangement of 2-*O*-acylglucosyl bromides to 2-deoxy-α-D-glucoses proceeds in high yield, acylmannosyl bromide gives 2-deoxy-β-D-mannose with *cis*-selectivity in slightly lower yield, because the C–O bond at the anomeric center of the resulting 2-deoxysugar is situated in the less stable equatorial position.[12] In accordance with the previous observation, the *cis*-rearranged product (**9a**), which has β-configuration at the anomeric position was formed in moderate yield (60%) together with the debromination product (**14**) (40%) (reaction conditions: see the Experimental section). The structure of **9a** with the equatorial 2-acetoxy group in its preferred conformation was confirmed by nuclear magnetic resonance (NMR) spectral comparison with **9a**, which was previously prepared by an alternative route.[15] When the bromide (**11**) derived from **6** was treated with tributyltin hydride, a complex mixture of products was formed and **9a** was isolated in only a poor

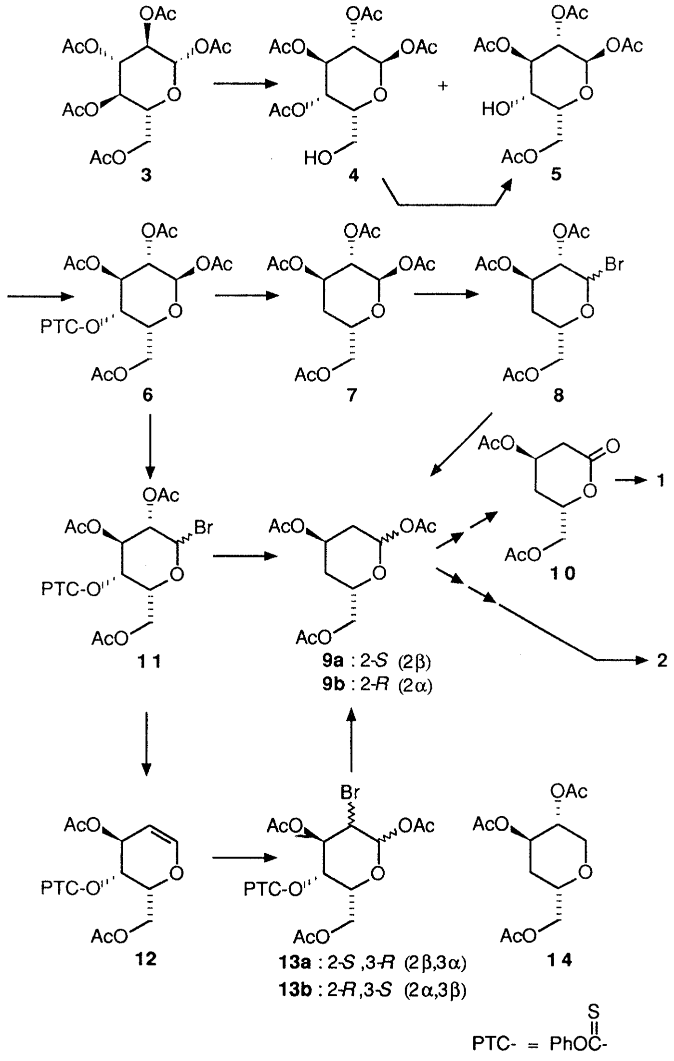


Chart 2

yield from the reaction mixture.

According to the procedure previously reported,[16] **9a** was hydrolyzed in aqueous dioxane and subsequently oxidized with bromine to give the lactone (**10**). Deprotection of **10** to **1** was achieved by using diluted hydrochloric acid. The deprotection, however, was always accompanied with the formation of the (3*R*,5*S*)-3,5,6-trihydroxyhexanoic acid and (6*S*)-6-hydroxymethyl-5,6-dihydro-2*H*-pyran-2-one through hydrolysis of the lactone portion and elimination of the 4-acetoxy group in **10**, respectively. The acetal (**2**) was obtained in 74% yield from **9a** in the previously reported manner.[16] Thus, in the present trial, **2** is preferable to **1** as a synthetic intermediate for the HMG-CoA reductase inhibitors. The spectral data of **1**[17] and **2**[16] were identical with those of authentic samples.

When **11** was treated with zinc in acetic acid,[18] the gulal derivative (**12**) was obtained in 44% yield. *trans*-Addition of acetyl hypobromite (CH_3COOBr, prepared from *N*-bromosuccinimide and acetic acid) to **12** resulted in the formation of a stereoisomeric mixture of 2-acetoxy-3-bromopyran derivative (**13a** and **13b**) in 60% yield. Upon treatment of **13a** and **13b** with tributyltin hydride, **9a** and its anomer (**9b**) were obtained in 32% and 48% yields after chromatography as a result of the concurrent occurrence of debromination and deoxygenation. The product (**9a**) was identical with a sample prepared by the foregoing method. The structure of the anomer (**9b**) was confirmed by comparison of its NMR spectrum with that of **9b** described in the literature.[16]

The overall yield of the mixture of **9a** and **9b** (9.7% from **3**) obtained by this route, however, is inferior to that by the foregoing route (22.5% **9a** from **3**).

Experimental

Melting points were determined on a Yanagimoto melting-point apparatus and are uncorrected. ^1H-NMR spectra were determined with a Hitachi–Perkin-Elmer R-20B 60 MHz instrument and a JEOL JNM-GX270 NMR spectrometer, using tetramethylsilane in $CDCl_3$ or sodium 2,2-dimethyl-2-silapentane-5-sulfonate in $(CD_3)_2SO$ as an internal standard. Chemical shifts are reported in ppm (δ) and J values in Hz. Mass spectra were taken on a JEOL JMS-D300 machine operating at 70 eV. Elemetal analyses were carried out at the Microanalytical Laboratory of our University. Column chromatography was carried out on silica gel (Wako gel C-300).

1,2,3,6-Tetra-*O*-acetyl-α-D-idopyranose (5) A solution of antimony pentachloride (15 ml, 110 mmol) in dry dichloromethane (10 ml) was added dropwise to a stirred solution of penta-*O*-acetyl-*β*-D-glucopyranose (**3**) (31.2 g, 80 mmol) in dry dichloromethane (100 ml) at 0 °C under an argon atmosphere. The acetoxonium salt appeared within 10—15 min. After 1 h, the resulting salt was filtered through a glass filter, washed with dry dichloromethane (100 ml), and dried *in vacuo*. The salt was added to a aqueous solution of sodium acetate (36 g of sodium acetate was dissolved in 100 ml of water) with stirring at 0 °C for 15 min. The reaction solution was extracted with chloroform. The organic layer was washed with water and saturated aqueous sodium chloride, and dried over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure gave a syrup, which was a mixture of 1,2,3,4-tetra-*O*-acetyl-α-D-idopyranose (**4**) and 1,2,3,6-tetra-*O*-acetyl-α-D-idopyranose (**5**). The mixture was dissolved in 10% aqueous pyridine (100 ml) and left to stand at room temperature for 24 h. The solution was extracted with chloroform. The extract was washed with water, dil. HCl and water, and dried over anhydrous magnesium sulfate. Evaporation of the solvent under reduced pressure gave a syrup, which was triturated with dry ether to give 1,2,3,6-tetra-*O*-acetyl-α-D-idopyranose (**5**) as a white powder (13.0 g, 46.7%). This crude product was used in the next step without further purification. Recrystallization from ether gave a pure product (**5**), which was identified by comparison of its NMR spectra with those of an authentic sample.[10]

1,2,3,6-Tetra-*O*-acetyl-4-*O*-phenoxythiocarbonyl-α-D-idopyranose (6) Phenoxythiocarbonyl chloride (PTC-Cl) (2.32 ml, 13 mmol) was added dropwise to a mixture of **5** (3.48 g, 10 mmol) and 4-dimethylaminopyridine (DMAP) (2.44 g, 20 mmol) in dry acetonitrile (50 ml) at 0 °C under an argon atmosphere. The solution was stirred overnight at room temperature. The solvent was evaporated off under reduced pressure and the residue was purified by column chromatography on silica gel with benzene–ethyl acetate (10 : 1) to give 1,2,3,6-tetra-*O*-acetyl-4-*O*-phenoxythiocarbonyl-α-D-idopyranose (**6**) (4.80 g, 98%) as a colorless syrup. *Anal.* Calcd for $C_{21}H_{24}O_{11}S$: C, 52.06; H, 4.99. Found: C, 52.28; H, 5.12. ^1H-NMR ($CDCl_3$) δ: 7.39—7.01 (5H, m, O-Ph), 6.06 (1H, d, J = 1.0 Hz, H-1), 5.37 (1H, m, H-2), 5.28 (1H, t, J = 2.4 Hz, H-3), 4.85 (1H, m, H-4), 4.55 (1H, dt, J = 2.0, 6.4 Hz, H-5), 4.26 (2H, m, H-6 and H-6′), 2.09, 2.08, 2.07, 2.02 (each 3H, each s, each OAc).

1,2,3,6-Tetra-*O*-acetyl-4-deoxy-α-D-idopyranose (7) A solution of the idopyranose (**6**) (4.84 g, 10 mmol), α,α′-azobis(isobutyronitrile) (AIBN) (200 mg, 1.2 mmol), and tributyltin hydride (2 ml, 7.2 mmol) in distilled toluene (50 ml) was degassed with argon for 20 min, and then heated at 80 °C for 2 h. Tributyltin hydride (1 ml, 3.6 mmol) was further added twice at every third hour. Then the reaction solution was stirred for 1 h at the same temperature. The solution was diluted with acetonitrile, and washed three times with the same volume of hexane. The acetonitrile layer was evaporated under reduced pressure and the residue was triturated with dry ether. The resulting precipitate was collected by filtration and recrystallized from dry ether to give 2.72 g (82%) of 1,2,3,6-tetra-*O*-acetyl-4-deoxy-α-D-idopyranose (**7**), mp 92 °C. *Anal.* Calcd for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07. Found: C, 50.56; H, 6.11. ^1H-NMR ($CDCl_3$) δ: 6.03 (1H, d, J = 1.0 Hz, H-1), 5.02 (1H, dd, J = 1.0, 2.9 Hz, H-3), 4.81 (1H, t, J = 1.0 Hz, H-2), 4.32 (1H, m, H-5), 4.14 (2H, dd, J = 1.0, 5.9 Hz, H-6 and H-6′), 2.13 (3H, s, OAc), 2.12 (6H, s, OAc), 2.10 (3H, s, OAc), 2.00 (1H, ddd, J=2.9, 11.7, 14.6 Hz, H-4), 1.76 (1H, d, J=14.6 Hz, H-4′).

(2*S*,4*R*,6*S*)-2,4-Diacetoxy-6-acetoxymethyltetrahydropyran (1,3,6-Tri-*O*-acetyl-2,4-dideoxy-*β*-D-idopyranose) (9a) and (3*S*,4*R*,6*S*)-3,4-Diacetoxy-6-acetoxymethyltetrahydropyran (14) a): A 30% acetic acid solution of HBr (3 ml) was added to a solution of **7** (996 mg, 3 mmol) in acetic acid (2 ml) with stirring at room temperature. After 20 min, the straw-colored solution was taken up in dichloromethane (50 ml) and the mixture was washed twice with ice water, cold 1 M sodium bicarbonate, and water, then dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give 2,3,6-tri-*O*-acetyl-4-deoxy-D-idopyranosyl bromide (**8**) as a light yellow syrup. To a solution of the above-obtained product (**8**) and AIBN (50 mg, 0.3 mmol) in distilled toluene (200 ml), 0.2 ml of tributyltin hydride was added dropwise every 5 min twelve times at 80 °C under an argon atmosphere. The mixture was stirred for 2 h and the solvent was evaporated off under reduced pressure. The residue was dissolved in acetonitrile and the solution was washed three times with the same volume of hexane. The acetonitrile layer was evaporated under reduced pressure and the residue was chromatographed on silica gel with benzene–ethyl acetate (5 : 1) to give two products, **9a** and **14**, in 60%, 40% yields, respectively. (2*S*,4*R*,6*S*)-2,4-Diacetoxy-6-acetoxymethyltetrahydropyran (**9a**); syrup, *Anal.* Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.92; H, 6.87. ^{1}H-NMR ($CDCl_3$) δ: 6.00 (1H, dd, J=9.8, 2.5 Hz, H-2), 5.32 (1H, t, J=3.4 Hz, H-4), 4.18—4.11 (3H, m, H-6 and $C\underline{H}_2$–OAc), 2.11, 2.09, 2.08 (each 3H, each s, each OAc), 2.02—1.50 (4H, m, H-3, H-3′, H-5, H-5′). (3*S*,4*R*,6*S*)-3,4-Diacetoxy-6-acetoxymethyltetrahydropyran (**14**); syrup, *Anal.* Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.64; H, 6.77. ^{1}H-NMR ($CDCl_3$) δ: 5.05 (1H, d, J=2.9 Hz, H-4), 4.67 (1H, d, J=2.0 Hz, H-3), 4.20—3.80 (5H, m, H-2, H-2′, H-6, $C\underline{H}_2$–OAc), 2.13 (9H, s, 3×OAc), 1.92 (1H, ddd, J=2.9, 11.7, 14.1 Hz, H-5), 1.73 (1H, d, J=14.1 Hz, H-5′).

b): A 30% acetic acid solution of HBr (3 ml) was added to a solution of **6** (1.46 g, 3 mmol) in acetic acid (2 ml) with stirring at room temperature. After 20 min, the solution was taken up in dichloromethane (50 ml) and the mixture was washed twice with ice water, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to give 2,3,6-tri-*O*-acetyl-4-*O*-phenoxythiocarbonyl-D-idopyranosyl bromide (**11**) as a syrup. To a solution of the above product (**11**) and AIBN (100 mg, 0.6 mmol) in distilled toluene (200 ml), 0.3 ml of tributyltin hydride was added dropwise every 5 min twelve times. The mixture was stirred for 2 h and the solvent was evaporated off under reduced pressure. The residue was dissolved in acetonitrile and the solution was washed three times with the same volume of hexane. The acetonitrile layer was evaporated under reduced pressure and the residue was chromatographed on silica gel with benzene–ethyl acetate (5 : 1) to give a mixture of (2*S*,4*R*,6*S*)-2,4-diacetoxy-6-acetoxymethyltetrahydropyran (**9a**) (9.3%) and (3*S*,4*R*,6*S*)-3,4-diacetoxy-6-acetoxymethyltetrahydropyran (**14**) (60%). The two products could not be separated by further column chromatography and the yields were determined from the integrals of the NMR signals.

(4*R*,6*S*)-4-Hydroxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-one (1) According to the previously reported method,[16] **9a** was hydrolyzed and oxidized to give (4*R*,6*S*)-4-acetoxy-6-acetoxymethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-one (**10**) (122 mg, 82%) as a syrup. This product was identified by comparison of its NMR spectra with those of an authentic sample.[16] A solution of **10** (280 mg, 1.2 mmol) and 2 N HCl (5 ml) was stirred at room temperature for 24 h and then adjusted to pH 3 with a saturated aqueous solution of sodium bicarbonate. The solution was further stirred at room temperature for 24 h and evaporated under reduced pressure. The residue was chromatographed on silica gel with chloroform–methanol (10 : 1) to give three products. (4*R*,6*S*)-4-Hydroxy-6-hydroxymethyl-3,4,5,6-tetrahydro-2*H*-pyran-2-one (**1**) (40 mg, 23%); syrup. This product was identified by comparison of its NMR spectra with those of an authentic sample.[17] (3*R*,5*S*)-3,5,6-Trihydroxyhexanoic acid (38 mg, 22%); ^{1}H-NMR [$(CD_3)_2SO$] δ: 4.18 (1H, m, H-3), 3.70 (1H, m, H-5), 3.42 (2H, d, J=5.4 Hz, H-6 and H-6′), 2.52 (2H, dd, J=4.4, 12.7 Hz, H-2 and H-2′), 2.80—2.50 (2H, m, H-4 and H-4′). (6*S*)-6-Hydroxymethyl-5,6-dihydro-2*H*-pyran-2-one (8 mg, 5%); ^{1}H-NMR ($CDCl_3$) δ: 6.89 (1H, m, H-4), 5.95 (1H, ddd, J=1.0, 2.9, 9.8 Hz, H-3), 4.49 (1H, m, H-6), 3.80 (1H, dd, J=3.4, 12.5 Hz, one H of $-C\underline{H}_2$–OH), 3.68 (1H, dd, J=4.9, 12.5 Hz, one H of $-C\underline{H}_2$–OH), 2.52 (1H, m, H-5), 2.27 (1H, m, H-5′)

(2*S*,3*R*,4*R*,5*S*,6*R*)-2,4-Diacetoxy-6-acetoxymethyl-3-bromo-5-phenoxythiocarbonyloxytetrahydropyran (1,3,6-Tri-*O*-acetyl-2-bromo-2-deoxy-4-*O*-phenoxythiocarbonyl-*β*-D-gulopyranose) (13a) and (2*R*,3*S*,4*R*,5*S*,6*R*)-2,4-Diacetoxy-6-acetoxymethyl-3-bromo-5-phenoxythiocarbonyloxytetrahydropyran (1,3,6-Tri-*O*-acetyl-2-bromo-2-deoxy-4-*O*-phenoxythiocarbonyl-*β*-D-idopyranose) (13b) A solution of $CuSO_4 \cdot 5H_2O$ (747 mg) in water (4 ml) was added to a mixture of sodium acetate (13.1 g) and zinc powder (7.2 g) in water (10 ml) and acetic acid (13 ml) under ice-salt cooling. A solution of **11** (10.2 g, 20 mmol) in acetic acid (10 ml) was dropped into the above solution for about 1 h under stirring with a mechanical stirrer at −10—−20 °C. After the addition, the mixture was further stirred for 3h, then filtered through Celite, and washed with 50% aqueous acetic acid. The combined filtrate was extracted with chloroform, and the organic layer was washed with cooled water, saturated aqueous solution of sodium bicarbonate, and water. The solution was dried over anhydrous magnesium sulfate and evaporated under reduced pressure to give a syrupy product. Purification by column chromatography on silica gel with benzene–ethyl acetate (10 : 1) gave 3,6-di-*O*-acetyl-2-deoxy-4-*O*-phenoxythiocarbonyl-D-xylohex-1-enitol (**12**) (3.19 g, 43.6%); ^{1}H-NMR ($CDCl_3$) δ: 7.45—7.12 (5H, m, O-Ph), 6.69 (1H, d, J=5.9 Hz, H-1), 5.58 (1H, m, H-4), 5.21 (1H, dd, J=2.4, 5.9 Hz, H-3), 5.13 (1H, dt, J=1.4, 5.9 Hz, H-2), 4.50—4.32 (3H, m, H-5, H-6, H-6′), 2.12 (6H, s, 2×OAc).

N-Bromosuccinimide (1.41 g, 7.92 mmol) was added to a solution of the gulal derivative (**12**) (2.67 g, 7.2 mmol) in acetic acid (15 ml). The mixture was stirred for 5 h at room temperature and extracted with chloroform. The extract was washed with water, a saturated aqueous solution of sodium bicarbonate, and water, and dried over anhydrous magnesium sulfate. The solvent was evaporated off under reduced pressure and the residue was chromatographed on silica gel with benzene–ethyl acetate (10 : 1) to give two main products (**13a** and **13b**). (2*S*,3*R*,4*R*,5*S*,6*R*)-2,4-Diacetoxy-6-acetoxymethyl-3-bromo-5-phenoxythiocarbonyloxytetrahydropyran (**13a**) was obtained in 24% yield as a syrup; ^{1}H-NMR ($CDCl_3$) δ: 7.47—7.12 (5H, m, O-Ph), 6.07 (1H, d, J=9.3 Hz, H-2), 5.70 (1H, dd, J=3.5, 3.9 Hz, H-4), 5.49 (1H, dd, J=1.5, 3.5 Hz, H-5), 4.49 (1H, dt, J=1.5, 5.8 Hz, H-6), 4.37—4.29 (2H, m, H-3 and one H of $-C\underline{H}_2$–OAc), 4.18 (1H, dd, J=6.8, 11.8 Hz, one H of $-C\underline{H}_2$–OAc), 2.23, 2.20, 2.09 (each 3H, each s, each OAc). (2*R*,3*S*,4*R*,5*S*,6*R*)-2,4-Diacetoxy-6-acetoxymethyl-3-bromo-5-phenoxythiocarbonyloxytetrahydropyran (**13b**) was obtained in 36% yield as a syrup; ^{1}H-NMR ($CDCl_3$) δ: 7.46—7.12 (5H, m, O-Ph), 6.33 (1H, d, J=2.4 Hz, H-2), 5.64 (1H, m, H-4), 4.90 (1H, dd, J=1.0, 2.5 Hz, H-5), 4.45—4.30 (3H, m, H-6 and $-C\underline{H}_2$–OAc), 4.08 (1H, m, H-3), 2.15, 2.14, 2.11 (each 3H, each s, each OAc).

(2*S*,4*R*,6*S*)-2,4-Diacetoxy-6-acetoxymethyltetrahydropyran (1,3,6-Tri-*O*-acetyl-2,4-dideoxy-*β*-D-idopyranose) (9a) and (2*R*,4*R*,6*S*)-2,4-Diacetoxy-6-acetoxymethyltetrahydropyran (1,3,6-Tri-*O*-acetyl-2,4-dideoxy-*α*-D-idopyranose) (9b) A solution of the mixture of **13a** and **13b** (2.19 g, 4.3 mmol), AIBN (100 ml, 0.6 mmol), and tributyltin hydride (2.5 ml, 9 mmol) in distilled toluene (50 ml) was degassed with argon for 20 min, and then heated at 80 °C for 2 h. Tributyltin hydride (1 ml, 3.6 mmol) was further added and the solution was stirred for 1 h at the same temperature. The solution was diluted with acetonitrile, and washed with hexane. The acetonitrile layer was evaporated under reduced pressure and the residue was chromatographed on silica gel with benzene–ethyl acetate (5 : 1) to give a mixture of **9a** and its anomer (**9b**) (997 mg, 80%). (2*R*,4*R*,6*S*)-2,4-Diacetoxy-6-acetoxymethyltetrahydropyran (**9b**) was isolated as a syrup, *Anal.* Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.62; H, 6.88. ^{1}H-NMR ($CDCl_3$) δ: 6.18 (1H, d, J=3.4 Hz, H-2), 5.15 (1H, m, H-4), 4.38 (1H, m, H-6), 4.11 (2H, m, $-C\underline{H}_2$–OAc), 2.15—1.70 (4H, m, H-3, H-3′, H-5, H-5′), 2.09 (9H, s, 3×OAc).

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