A Synthesis of Optically Active Key Intermediate for the Synthesis of Optically Active Thromboxanes

Hiroshi OHRUI and Sakae EMOTO

The Institute of Physical and Chemical Research, Wako-shi,
Saitama 351, Japan

Received May 2, 1977

An optically active key intermediate, methyl 2,4-dideoxy-4-*C*-carboxymethylene- α -D-*ribo*-hexopyranoside 2'→3 lactone (XII), for the syntheses of optically active Thromboxanes was prepared from D-glucose.

Recently, Hamberg and Samuelsson found a significant new branch in the arachidonic acid metabolism.¹⁾ The endoperoxide (PGG₂) which had previously been known to give the prostaglandins (*e.g.* PGE₂ and PGF₂) was found to give a new type of short lived, but extremely biologically active substance called Thromboxane A₂ (TXA₂).^{1,2)} This substance, of which half life in aqueous solution is 30 seconds, has a profound effect on certain smooth muscles and cells and appears to be an important early factors in Thrombosis. Thromboxane A₂ is rapidly converted to Thromboxane B₂ (TXB₂), of which little has been known regarding biological activity.

As a part of our studies on the stereoselective syntheses of biologically active compounds in optically active forms by use of asymmetric carbons of carbohydrates,³⁾ we have planned the synthesis of optically active Thromboxanes from D-glucose. Short after our project was started, two syntheses of

Thromboxane B₂ starting from the "Corey lactones" via the same key intermediate "lactone alcohol" have been reported by the Upjohn Company groups.^{4,5)} In this paper, we would like to describe the synthesis of the key intermediate "lactone alcohol" in an optically active form from D-glucose.⁶⁾

D-Glucose was converted to methyl 2,3-anhydro-4,6-O-benzylidene- α -D-allopyranoside (I) by the well established method.⁷⁾ The reduction of I with lithium aluminum hydride was carried out in a slightly modified method from the original method.⁸⁾ The change of the solvent from ether to tetrahydrofuran resulted in the raise of the yield of the desired 2-deoxy sugar (II) from 86% to almost quantitative. Treatment of II with benzyl chloride in the presence of powdered potassium hydroxide at 100°C for 4 hr gave a crystalline benzyl ether III, mp 95~96°C, in good yield. In order to assign the chemical shift of H-3 of III in the NMR spectrum, two other derivatives of II, 3-O-benzoate (IIIb) and 3-O-*p*-toluenesulfonate (IIIc), were prepared. The signals of H-3 of these compounds appeared as very similar multiplets but at very different chemical shifts. Therefore, the chemical shifts (δ values) of these three protons of III, IIIb and IIIc were easily assigned as 3.96, 5.54 and 4.89, respectively.

Treatment of III with 85% acetic acid overnight at room temperature gave a syrupy methyl 3-O-benzyl-2-deoxy- α -D-*ribo*-hexopyranoside (IV) in 73% yield. Partial benzoyl-

FIG. 1.

lation of **IV** with 1.2 equivalent of benzoyl chloride in a mixture of pyridine and dichloromethane (1:1, v/v) for 3 hr at 0°C and then overnight at room temperature gave two major products. They were purified by column chromatography on silicic acid with a mixture of benzene and ethyl acetate (10:1, v/v) as an eluent. The IR spectrum of the faster eluted compounds (12%) showed the absence of hydroxy group and its ¹H NMR spectrum showed the presence of two benzoyl groups. Therefore, this compound was assigned as methyl 3-O-benzyl-4,6-di-O-benzoyl-2-deoxy- α -D-ribo-hexopyranoside (**V**). The IR spectrum of the slower eluted compound showed the presence of both hydroxy and ester groups. The signal of the hydroxy group in its ¹H NMR spectrum appeared as a doublet indicating a secondary alcohol. Therefore, this compound was assigned as methyl 3-O-benzyl-6-O-benzoyl-2-deoxy- α -D-ribo-hexopyranoside (**VI**).

The oxidation of **VI** with ruthenium dioxide and sodium metaperiodate in a mixture of carbontetrachloride and water gave the ketone **VII**, which was treated directly with the ylide prepared from trimethylphosphonoacetate and *n*-butyl lithium in tetrahydrofuran at -30°C to give a 1:1 mixture of α,β -unsaturated esters **VIIIa** and **VIIIb** in a total yield of 60%. They were separated by a column chromatography on silicic acid with a mixture of benzene and ethyl acetate (10:1, v/v) as an eluent. The ¹H NMR spectra of **VIIIa** and **VIIIb** were shown in Figs. 2 and 3, respectively. As can be seen in Fig. 2, the benzyl protons of the faster eluted **VIIIa** appeared as AB type pattern. On the other hand, the benzyl protons of the slower eluted **VIIIb** appeared almost equivalent. These facts indicated that the benzyl group of **VIIIa** would be in the nearer position to the carbomethoxy group than that of **VIIIb**. Therefore, the compounds **VIIIa** and **VIIIb** were assigned as **E** and **Z** configuration respectively as shown in Fig. 4.

The catalytic reduction of **VIIIa** over 10% Pd-C in ethanol gave a main product **IX** and a very small amount of another product **X**. The main product **IX** changed slowly to **X** on

standing in solution. Several attempts to isolate **IX** in an analytically pure form were not successful because **IX** changed to **X** during purification process and was always contaminated with **X**. Therefore, the crude **IX** was treated directly with silicic acid in toluene at reflux to give the crystalline **X**, mp 102~103°C, in 83% yield. The IR spectrum of **X** showed the presence of both ester (1710 cm⁻¹) and lactone (1760 cm⁻¹) groups. The ¹H NMR spectrum of **X** showed the presence of benzoyl group and the absence of benzyl group. Therefore, compound **X** was assigned as methyl 6-O-benzoyl-2,4-dideoxy-4-C-carboxymethylene- α -D-ribo-hexopyranoside 2'→3 lactone and compound **IX** as methyl 6-O-benzoyl-2,4-dideoxy-4-C-carbomethoxymethylene- α -D-ribo-hexopyranoside.

On the other hand, the catalytic reduction of **VIIIb** under similar conditions gave a 1:1 mixture of **IX** and a new hydroxy ester **XI**, mp 77~78°C. The new hydroxy ester **XI** could not be lactonized under similar conditions as that lactonized **IX**. This fact indicated that the ester and the hydroxy groups should be in the *trans* relation on the pyranose ring. Therefore, the new hydroxy ester was assigned as methyl 6-O-benzoyl-2,4-dideoxy-4-C-carbomethoxymethylene- α -D-xylo-hexopyranoside (**XI**).

Treatment of **X** with 0.05 N sodium methoxide in methanol overnight at room temperature gave the syrupy lactone alcohol, methyl 2,4-dideoxy-4-C-carboxymethylene- α -D-ribo-hexopyranoside (**XII**), $[\alpha]_D^{20} + 100^\circ$ ($c=0.09$, CHCl₃), in 83% yield.

Treatment of **XII** with *p*-phenylbenzoyl chloride in pyridine gave the corresponding *p*-phenylbenzoate **XIII**, mp 149~150°C (*cf.* lit.^{4,9} mp 149.5~150°C), $[\alpha]_D^{20} + 48.6^\circ$ ($c=0.18$, CHCl₃).

The syntheses of optically active Thromboxanes from **XII** are now in progress in our laboratory.

EXPERIMENTAL

All melting points were not corrected. Optical rotations were measured with a Perkin-Elmer 141

polarimeter. ^1H NMR spectra were obtained using a Varian HA-100 spectrometer. Column chromatography was performed using 70–230 mesh Merck silica gel. Thin-layer chromatography was done using silica gel GF 254.

Methyl 4,6-O-benzylidene-2-deoxy- α -D-ribo-hexopyranoside (II)

To a suspension of I (79 g) in dry tetrahydrofuran (1000 ml) was added lithium aluminum hydride (6 g) with stirring at room temperature. The temperature of the reaction mixture was raised to about 50–60°C and the starting material went into solution completely. After the reaction mixture was stirred for 4 hr at the temperature, saturated aqueous sodium tartarate (200 ml) was added to it. The aqueous layer was separated and was extracted five times with ether (100 ml). The tetrahydrofuran layer and the ether extract were combined and evaporated under reduced pressure to give a crystalline mass. It was dissolved in dichloromethane (1000 ml) and the solution was washed with saturated aqueous ammonium chloride solution (200 ml). The organic layer was dried over Na_2SO_4 and evaporated *in vacuo* to give the crystalline II (80 g, quantitative). It was pure enough to be used for the next step.

Methyl 3-O-benzyl-4,6-O-benzylidene-2-deoxy- α -D-ribo-hexopyranoside (III)

A mixture of II (27 g) and powdered potassium hydroxide (100 g) in benzyl chloride (300 ml) was stirred vigorously at 100°C for 3 hr. After the reaction mixture was cooled, water (200 ml) was added to it. It was extracted five times with ether (100 ml). The extracts were combined and washed with saturated ammonium chloride solution (300 ml). The ether and the excess benzyl chloride were evaporated under reduced pressure to give a crystalline mass. It was recrystallized from cyclohexane to give III (35 g, 95%), mp 95–96°C, $[\alpha]_D^{25} + 59.9^\circ$ ($c=1.0$, CHCl_3). *Anal.* Found: C, 71.00; H, 6.75. Calcd. for $\text{C}_{21}\text{H}_{24}\text{O}_6$: C, 70.76; H, 6.79%. NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.76–2.33 (2H, m, $J_{2,2'}=15$ Hz, H_2 , $\text{H}_{2'}$), 3.37 (3H, s, OCH_3), 3.50–3.87 (2H, m, H_6 , $\text{H}_{6'}$), 3.96 (1H, m, H_3), 4.20–4.63 (2H, m, H_4 , H_5), 4.72 (1H, d, $J=4$ Hz, H_1), 4.80 (2H, s, benzyl protons), 5.54 (1H, s, benzylidene proton), 7.16–7.66 (10H, m, aromatic protons).

Methyl 3-O-benzoyl-4,6-O-benzylidene-2-deoxy- α -D-ribo-hexopyranoside (IIIb)

To a solution of II (5.4 g) in pyridine (50 ml) was added benzoyl chloride (4.0 g) at 0°C. The mixture was stirred for 2 hr at 0°C and then overnight at room temperature. Water (100 ml) was added to the reaction mixture and the mixture was stirred for additional 1 hr. It was extracted three times with dichlorome-

thane (50 ml). The organic layer was successively washed with cold 3% H_2SO_4 (1000 ml), water (50 ml), saturated NaHCO_3 (50 ml) and then water (50 ml). The dichloromethane solution was dried over Na_2SO_4 and evaporated under reduced pressure to give a syrup (7.5 g). The syrup was purified by column chromatography on silicic acid (200 g) using a mixture of benzene and ethyl acetate (30:1, v/v) as an eluent to give a syrupy IIIb (7 g, 94%), $[\alpha]_D^{25} + 179.1^\circ$ ($c=0.15$, CHCl_3). *Anal.* Found: C, 67.92; H, 5.75. Calcd. for $\text{C}_{21}\text{H}_{22}\text{O}_6$: C, 68.09; H, 5.99%. NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.90–2.50 (2H, m, H_2 , $\text{H}_{2'}$), 3.35 (3H, s, OCH_3), 3.60–4.00 (2H, m, H_6 , $\text{H}_{6'}$), 4.20–4.70 (2H, m, H_4 , H_5), 4.76 (1H, d, $J=4$ Hz, H_1), 5.54 (1H, m, H_3), 5.60 (1H, s, benzylidene proton).

Methyl 4,6-O-benzylidene-2-deoxy-3-O-p-toluenesulfonyl- α -D-ribo-hexopyranoside (IIIc)

To a solution of II (5.4 g) in pyridine (50 ml) was added *p*-toluenesulfonyl chloride (5.0 g) at 0°C. The reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with dichloromethane (200 ml). The dichloromethane solution was successively washed with cold 3% H_2SO_4 (1000 ml), water (50 ml), saturated NaHCO_3 (50 ml) and again with water (50 ml). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure to give a crystalline mass (8 g). It was recrystallized from 2-propanol to give a crystalline IIIc (7.5 g, 90%), mp 119–120°C, $[\alpha]_D^{25} + 72.0^\circ$ ($c=0.8$, CHCl_3). *Anal.* Found: C, 59.60; H, 5.57; S, 7.58. Calcd. for $\text{C}_{21}\text{H}_{24}\text{SO}_7$: C, 59.99; H, 5.75; S, 7.62%. NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.80–2.60 (2H, m, H_2 , $\text{H}_{2'}$), 2.32 (3H, s, CH_3 -Ph), 3.36 (3H, s, OCH_3), 3.50–3.80 (2H, m, H_6 , $\text{H}_{6'}$), 4.10–4.44 (2H, m, H_4 , H_5), 4.74 (1H, d, $J=4$ Hz, H_1), 4.87 (1H, m, H_3), 5.45 (1H, s, benzylidene proton).

Methyl 3-O-benzyl-2-deoxy- α -D-ribo-hexopyranoside (IV)

A solution of III (10 g) in 80% aqueous acetic acid (100 ml) was stirred overnight at room temperature. The solvent was evaporated under reduced pressure below 40°C to give a syrup (10 g). The syrup was purified by a column chromatography on silicic acid (250 g) using a mixture of CHCl_3 and MeOH (20:1, v/v) as an eluent. The fractions that contained the compound with $R_f=0.2$ (the same solvent system as the eluent) were collected. Evaporation of the solvent gave a syrupy IV (7.2 g, 95%), $[\alpha]_D^{25} + 161.9^\circ$ ($c=0.1$, CHCl_3). *Anal.* Found: C, 62.37; H, 7.35%. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_5$: C, 62.67; H, 7.51. NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.52–2.46 (2H, m, $J_{2,2'}=15$ Hz, H_2 , $\text{H}_{2'}$), 3.34 (3H, s, OCH_3), 3.60 (1H, m), 3.70–4.08 (4H, m), 4.40 and 4.80 (2H, 2d, $J=12$ Hz, benzyl protons), 4.80 (1H, d, $J=4$ Hz, H_1), 7.20–7.46 (5H, m, aromatic protons).

FIG. 2. NMR Spectrum of VIIIa.

FIG. 3. NMR Spectrum of VIIIb.

Methyl 6-O-benzoyl-3-O-benzyl-2-deoxy- α -D-ribohexopyranoside (VI)

To a solution of IV (8.0 g) in a mixture of pyridine and dichloromethane (1:1, v/v, 200 ml) was added benzoyl chloride (5.0 g) under cooling in an ice-water bath. The reaction mixture was stirred for 3 hr at 0°C and then overnight at room temperature. The mixture was diluted with dichloromethane (500 ml) and washed successively with cold 3% H₂SO₄ (2000 ml), saturated NaHCO₃ (100 ml) and then water (100 ml). The dichloromethane solution was dried over Na₂SO₄ and evaporated under reduced pressure to give a syrup (10 g). The syrup was submitted to a column chromatography on silicic acid (250 g) and eluted with a mixture of benzene and ethyl acetate (10:1, v/v). The fractions that had *R_f*=0.45 with the same solvent system gave a syrupy 4,6-O-benzoyl-3-O-benzyl-2-deoxy- α -D-ribohexopyranoside (V) (1.7 g, 12%), $[\alpha]_D^{20} + 137.8^\circ$ (*c*=0.8, CHCl₃). *Anal.* Found: C, 70.51;

H, 5.91. Calcd. for C₂₈H₂₈O₇: C, 70.57, H, 5.92. NMR $\delta_{Me_4Si}^{CDCl_3}$: 1.80~2.48 (2H, m, H₂, H_{2'}), 3.40 (3H, s, OCH₃), 4.14 (1H, m, H₃), 4.34~4.92 (5H, m, H₄, H₅, H₆, H_{6'}, benzyl protons), 5.25 (1H, dd, *J*_{3,4}=3 Hz, *J*_{4,5}=10 Hz, H₄). The fractions that contained the compound of *R_f*=0.2 gave a syrupy VI (7.0 g, 63%), $[\alpha]_D^{21} + 117.3^\circ$ (*c*=0.8, CHCl₃). *Anal.* Found: C, 67.75; H, 6.37. Calcd. for C₂₁H₂₄O₈: C, 67.73; H, 6.50%. NMR $\delta_{Me_4Si}^{CDCl_3}$: 1.60~1.90 (1H, m, *J*_{2,2'}=15 Hz, H₂), 2.22~2.46 (1H, m, H_{2'}), 2.75 (1H, d, *J*_{OH, H4}=10 Hz), 3.34 (3H, s, OCH₃), 3.62 (1H, td, *J*_{4,5}=3.9 Hz, H₄), 3.88 (1H, m, H₃), 4.22 (1H, m, H₅), 4.40 and 4.80 (2H, 2d, *J*=12 Hz, benzyl protons), 4.42~4.73 (2H, m, H₆, H_{6'}), 5.74 (1H, d, *J*=4 Hz, H₁), 7.20~7.64 (8H, m, aromatic protons), 7.96~8.13 (2H, m, aromatic protons). IR ν_{max}^{film} cm⁻¹: 3500 (OH), 1735 (CO).

(*E*)-Methyl 6-*O*-benzoyl-4-*C*-carbomethoxymethylene-2,4-dideoxy- α -*D*-erythro-hexopranoside (**VIIIa**) and (*Z*)-methyl 6-*O*-benzoyl-4-*C*-carbomethoxymethylene-2,4-dideoxy- α -*D*-erythro-hexopranoside (**VIIIb**)

A mixture of **VI** (3.7 g), RuO_2 (300 mg), saturated NaHCO_3 (10 ml), NaIO_4 (10 g), CCl_4 (40 ml) and water (40 ml) was vigorously stirred for 5 hr. Isopropyl alcohol (10 ml) was added to the reaction mixture and the mixture was stirred for additional 15 min. The reaction mixture was diluted with dichloromethane (100 ml) and then filtered with the aid of celite. The filtrate was washed three times with water (50 ml) and then dried over Mg_2SO_4 . The solvent was evaporated under reduced pressure below 30°C and the resulting crude syrupy ketone (**VII**) (3.3 g) was directly used for the next reaction. To a solution of trimethylphosphonoacetate (3 g) in dry tetrahydrofuran (30 ml) was added *n*-BuLi (9 ml of 15% hexane solution) at -70°C under N_2 atmosphere. A solution of the crude ketone (3.3 g) in dry tetrahydrofuran (15 ml) was added dropwise to the ylide solution. The reaction temperature was raised gradually to about -30°C and kept for 2 hr at the temperature and then for 1 hr at 0°C . After saturated NH_4Cl solution (30 ml) was added to the reaction mixture, it was extracted five times with ether (250 ml). The ether solution was washed with saturated NH_4Cl solution (50 ml) and then dried over Na_2SO_4 . The solvent was removed under reduced pressure to give a syrup (4 g). The syrup was submitted to a column chromatography on silicic acid (100 g) and eluted with a mixture of benzene and ethyl acetate (50:1, v/v). The fractions that contained a compound of $R_f=0.5$ (benzene-ethyl acetate, 10:1, v/v) gave a syrupy **VIIIa** (1.25 g, 30% from **VI**), $[\alpha]_D^{21}+164.8^\circ$ ($c=0.2$, CHCl_3). *Anal.* Found: C, 67.55; H, 5.95. Calcd. for $\text{C}_{24}\text{H}_{28}\text{O}_7$: C, 67.59; H, 6.15%. IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1725 (CO), 1665 (C=C). NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.62 (1H, m, $J_{2,2'}=13$ Hz, H_2), 2.76 (1H, m, H_2'), 3.34 (3H, s, OCH_3), 3.70 (3H, s, COOCH_3), 4.30~4.98 (3H, m, H_6 , H_6'), 4.44 and 4.62 (2H, 2d, $J=12$ Hz, benzyl protons), 5.66 (1H, m, H_1), 6.18 (1H, m, vinyl proton), 7.20~7.71 (8H, m, aromatic protons), 7.94~8.10 (2H, m, aromatic protons). The fractions that contained a compound of $R_f=0.45$ gave a syrupy **VIIIb** (1.26 g, 30%), $[\alpha]_D^{21}+167.4^\circ$ ($c=0.8$, CHCl_3). *Anal.* Found: C, 67.55; H, 5.93. Calcd. for $\text{C}_{24}\text{H}_{28}\text{O}_7$: C, 67.59; H, 6.15%. IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1725 (CO), 1665 (C=C). NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.88~2.42 (2H, m, $J_{2,2'}=14$ Hz, H_2 , H_2'), 3.43 (3H, s, OCH_3), 3.64 (3H, s, COOCH_3), 4.44~4.63 (4H, m, H_6 , H_6' , benzyl protons), 4.82 (1H, d, $J=4$ Hz, H_8), 5.14 (1H, m, H_6), 5.50 (1H, t, $J=4$ Hz), 5.88 (1H, s, vinyl proton), 7.16~7.60 (8H, m, aromatic protons), 7.96~8.15 (1H, m, aromatic protons).

Methyl 6-*O*-benzoyl-4-*C*-carboxymethylene-2,4-dideoxy- α -*D*-ribo-hexopyranoside 2'→3 lactone (**X**)

A mixture of **VIIIa** (1 g) and 10% Pd-C (1 g) in ethanol (100 ml) was shaken under H_2 atmosphere for 2 hr at room temperature. After the catalyst was filtered off, the solvent was evaporated under reduced pressure to give a syrup (1 g). The syrup was dissolved in toluene (50 ml) and silicic acid (5 g) was added to the solution. The mixture was refluxed gently for 5 hr and then cooled to room temperature. The silicic acid was filtered off and the filtrate was evaporated under reduced pressure to give a crystalline mass. It was recrystallized from a mixture of hexane and ether to give **X** (590 mg, 83%), mp $102\sim103^\circ\text{C}$, $[\alpha]_D^{21}+65.0^\circ$ ($c=0.2$, CHCl_3). *Anal.* Found: C, 62.63; H, 5.73. Calcd. for $\text{C}_{16}\text{H}_{18}\text{O}_8$: C, 62.74; H, 5.92%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1760 (CO), 1710 (CO). NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 2.10~2.80 (5H, m, H_2 , H_2' , H_4 , CH_2CO), 3.34 (3H, s, OCH_3), 4.01 (1H, m, H_6), 4.44 (2H, m, H_6 , H_6'), 4.68 (1H, m, H_8), 4.86 (1H, t, $J=4$ Hz), 7.34~7.68 (3H, m, aromatic protons), 8.00~8.09 (2H, m, aromatic protons).

Methyl 6-*O*-benzoyl-4-*C*-carbomethoxymethylene-2,4-dideoxy- α -*D*-xylo-hexopyranoside (**XI**)

A mixture of **VIIIb** (1 g) and 10% Pd-C (1 g) in ethanol (100 ml) was shaken under H_2 atmosphere for 2 hr at room temperature. The catalyst was filtered off and the filtrate was evaporated under reduced pressure to give a syrup (1 g). The syrup was dissolved in toluene (100 ml) and the solution was gently refluxed

FIG. 4.

in the presence of silicic acid (5 g) for 5 hr. After the silicic acid was filtered off, the filtrate was evaporated under reduced pressure to give a syrup (1 g). The syrup was submitted to a column chromatography on silicic acid (100 g) and eluted with a mixture of hexane and ether (3:1, v/v). The fractions that contained a compound with $R_f=0.15$ (hexane: ether=3:1, v/v) gave crystalline XI (320 mg, 40%), mp $77\sim78^\circ\text{C}$, $[\alpha]_D^{25}+97.2^\circ$ ($c=0.1$, CHCl_3). *Anal.* Found: C, 60.23; H, 6.47. Calcd. for $\text{C}_{17}\text{H}_{22}\text{O}_7$: C, 60.34; H, 6.55%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3550 (OH), 1735 and 1710 (CO). NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.82~2.78 (5H, m, H_2 , H_2' , H_4 , CH_2CO), 3.37 (3H, s, OCH_3), 3.63 (3H, s, COOCH_3), 3.86 (1H, m, H_3), 4.37 (2H, m, H_6 , H_6'), 4.60 (1H, m, H_5), 4.75 (1H, m, H_1), 7.32~7.70 (3H, m, aromatic protons), 7.96~8.14 (2H, m, aromatic protons). The fractions that contained a compound with $R_f=0.08$ gave X (320 mg, 40%).

Methyl 4-C-carboxymethylene-2,4-dideoxy- α -D-ribo-hexopyranoside 2'→3 lactone (XII)

A solution of X (1 g) in 0.05 N methanolic sodium methoxide (100 ml) was stirred overnight at room temperature. Acetic acid (5 ml) was added to the reaction mixture and the solvent was removed under reduced pressure to give a syrup (1 g). The syrup was purified by column chromatography on silicic acid (50g) using a mixture of CHCl_3 and MeOH (20:1, v/v) as an eluent to give a syrupy XII (550 mg, 83%), $[\alpha]_D^{21}+100^\circ$ ($c=0.09$, CHCl_3). *Anal.* Found: C, 53.18; H, 6.98. Calcd. for $\text{C}_9\text{H}_{14}\text{O}_5$: C, 53.46; H, 6.89%. IR $\nu_{\text{max}}^{\text{NaCl}}$ cm^{-1} : 3500 (OH), 1760 (CO). NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 1.92~2.86 (6H, m, OH, H_2 , H_2' , H_4 , CH_2CO), 3.34 (3H, s, OCH_3), 3.50~3.90 (3H, m, H_5 , H_6 , H_6'), 4.66 (1H, m, H_3), 4.85 (1H, m, H_1).

6-O-p-Phenylbenzoyl-4-C-carboxymethylene-2,4-dideoxy- α -D-ribo-hexopyranoside (XIII)

To a solution of XII (500 mg) in pyridine (5 ml) was added *p*-phenylbenzoyl chloride (1.5 g) at 0°C . The mixture was stirred overnight at room temperature and then poured into a cold saturated NaHCO_3 solution (10 ml). The mixture was extracted three times with dichloromethane (50 ml). The organic layer was successively washed with cold 3% H_2SO_4 (50 ml), water (10 ml), saturated NaHCO_3 (10 ml) and then water (10 ml). The dichloromethane solution was dried over Na_2SO_4 and evaporated under reduced

pressure to give a crystalline XIII (880 mg, 93%). It was recrystallized from MeOH, mp $149\sim150^\circ\text{C}$, $[\alpha]_D^{20}+48.6^\circ$ ($c=0.18$, CHCl_3). *Anal.* Found: 69.06; H, 5.50. Calcd. for $\text{C}_{22}\text{H}_{22}\text{O}_6$: C, 69.10; H, 5.80%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1760 and 1710 (CO). NMR $\delta_{\text{Me}_4\text{Si}}^{\text{CDCl}_3}$: 2.08~2.84 (5H, m, H_2 , H_2' , H_4 , CH_2CO), 3.36 (3H, s, OCH_3), 4.02 (1H, m, H_6), 4.40~4.52 (2H, m, H_6 , H_6'), 4.69 (1H, m, H_3), 4.87 (1H, t, $J=4$ Hz), 7.32~7.76 (8H, m, aromatic protons), 8.04~8.18 (2H, m, aromatic protons).

Acknowledgement. The authors wish to express their thanks to Dr. H. Homma and his collaborators for elemental analyses and Mr. J. Uzawa and Mrs. T. Chigimatsu for measurement of NMR spectra.

REFERENCES

- 1) M. Hamberg and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.*, **71**, 3400 (1974).
- 2) M. Hamberg, J. Svensson and B. Samuelsson, *ibid.*, **72**, 2994 (1975).
- 3) (a) (+)-Oxybiotin: H. Ohroi, H. Kuzuhara and S. Emoto, *Agric. Biol. Chem.*, **35**, 752 (1971) (b) (+)-Dethiobiotin: H. Kuzuhara, H. Ohroi and S. Emoto, *ibid.*, **35**, 8 (1971) (c) (+)-Biotin: H. Ohroi and S. Emoto, *Tetrahedron Lett.*, **32**, 2765 (1975) (d) (+)- and (−)-Avenaciolide: H. Ohroi and S. Emoto, *ibid.*, **42**, 3667 (1975) (e) (S)-(−)-Frontalin: H. Ohroi and S. Emoto, *Agric. Biol. Chem.*, **40**, 2267 (1976).
- 4) N. A. Nelson and R. W. Jackson, *Tetrahedron Lett.*, **37**, 3275 (1976).
- 5) R. C. Kelly, I. Schletter and S. J. Stein, *ibid.*, **37**, 3279 (1976).
- 6) After we have finished this work, a brief communication about the synthesis of optically active Thromboxane B_2 from D-glucose was reported by S. Hanessian and P. Lavalley in *Can. J. Chem.*, **55**, 562 (1977).
- 7) R. L. Whistler and M. L. Wolfrom, *Methods Carbohydr. Chem.*, **1**, 107 (1962).
- 8) D. A. Prins, *J. Am. Chem. Soc.*, **70**, 3955 (1948).
- 9) Judging from the identity of the melting points of the two compounds, the lactone prepared by the Upjohn Company group would be optically active. However, the data concerning the optical rotation and the absolute configuration of the compound have not been reported by them.