Synthesis of Optically Active Substituted Cyclohexenones from Carbohydrates by Catalytic Ferrier Rearrangement

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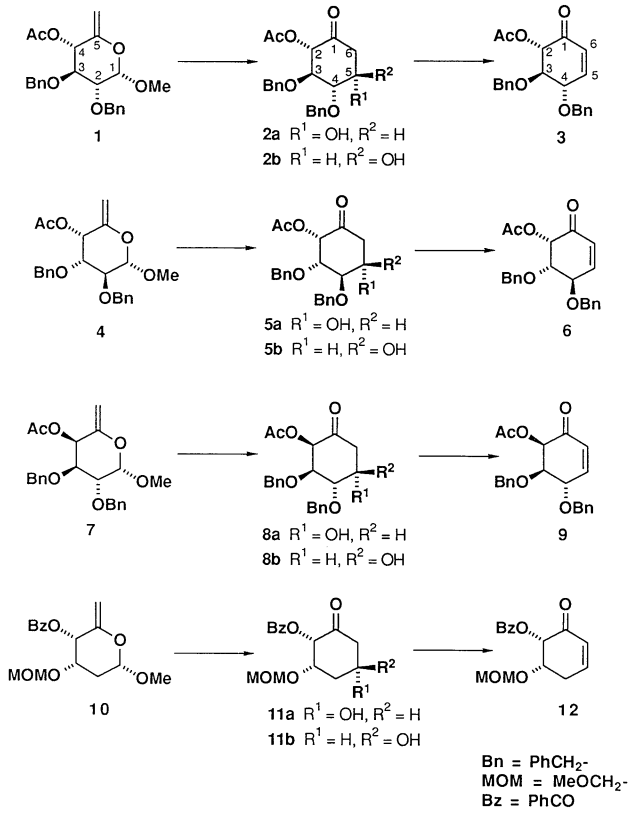
Conversion of hex-5-enopyranosides into substituted cyclohexanones (Ferrier rearrangement) was found to proceed efficiently with a catalytic amount of various mercury(II) salts at room temperature in a neutral solvent system. Among the mercury(II) salts tested, mercury(II) trifluoroacetate showed the highest activity. Four optically active cyclohexenones were prepared from hex-5-enopyranosides utilizing this method.

In 1979, Ferrier disclosed the efficient synthesis of chiral substituted cyclohexanones (2-deoxyinsoses) from hex-5-enopyranosides by the action of stoichiometric amount of mercury(II) chloride in hot aqueous acetone.[1] After this discovery, many reports concerning the mechanistic study,[2] application for syntheses of natural products,[3-8] and improved reaction conditions[5,9,10] have appeared so far. Lukacs and co-workers have reported that the Ferrier rearrangement proceeds with a catalytic amount (2 mol%) of mercury(II) sulfate in aqueous 1,4-dioxane containing sulfuric acid.[11] Recently, Adam has reported $PdCl_2$ or $Pd(OAc)_2$ also catalyzes conversion of hex-5-enopyranoside with an amino function at C-2 into 4-amino-2,4-dideoxyinosose in the solvent containing sulfuric acid.[12] Although this reaction is very useful and convenient for preparations of optically active cyclohexanones and/or cyclohexenones, sometimes difficulty is encountered in isolating the pure products due to the presence of excess Hg salts,[10] or in suppressing side reactions which might be caused by the acidic reaction conditions.[11,13]

During our study for the synthesis of natural products containing cyclohexane rings utilizing the Ferrier rearrangement,[14] we have investigated milder and simpler reaction conditions to avoid undesired side reactions such as β-elimination and aromatization. We report here our findings that the Ferrier rearrangement proceeds in high yields with a catalytic amount of various Hg(II) salts at room temperature in the neutral solvent system (acetone–water, without sulfuric acid), and the preparation of optically active cyclohexanones and cyclohexenones using this methodology.

The results of the catalytic Ferrier rearrangement of several hex-5-enopyranosides are shown in Table 1.

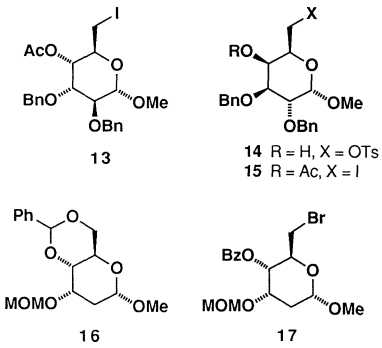


Scheme 1.

Table 1. Catalytic Ferrier Rearrangement of Some Hex-5-enopyranosides[a]

Run	Enopyranoside	Catalyst mol%	Time h	Products	Yield %	a/b[b]
1	**1**	$HgCl_2$ (10)	72	**2a, 2b**	97	6/1
2	**1**	HgO (10)	180	**2a, 2b**	94	6/1
3	**1**	$Hg(OAc)_2$ (10)	72	**2a, 2b**	96	8/1
4	**1**	$Hg(OCOCF_3)_2$ (10)	6	**2a, 2b**	96	8/1
5	**1**	$Hg(OCOCF_3)_2$ (5)	15	**2a, 2b**	96	8/1
6	**4**	$Hg(OCOCF_3)_2$ (10)	1	**5a, 5b**	79	1/4
7	**7**	$Hg(OCOCF_3)_2$ (10)	5	**8a, 8b**	91	4/1
8	**10**	$Hg(OCOCF_3)_2$ (10)	1.5	**11a, 11b**	86	1/19

a) All reactions were carried out at room temperature. b) Determined with 270 MHz ^{1}H NMR spectra.



Scheme 2.

Although reactions of methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α-D-*xylo*-5-enopyranoside (**1**)[7] with 10 mol% of $HgCl_2$, HgO, and $Hg(OAc)_2$ in acetone–water (2 : 1) at room temperature were sluggish, they afforded the cyclized products (**2a**) and (**2b**)[7] in high yields (Runs 1—3). On the other hand, use of $(CF_3CO_2)_2Hg$[15] as the catalyst (5 or 10 mol%) accelerated the reaction and gave (**2a**) and (**2b**) in high yield as well as in much shorter time (Runs 4 and 5). Reaction of hex-5-enopyranosides having D-*arabino* configuration (**4**, Run 6), prepared from compound **13** in one step, with 10 mol% of $(CF_3CO_2)_2Hg$ at room temperature also provided the corresponding cyclohexanones (**5a** and **5b**) in 79% yield. Similar reaction of compounds **7** possessing L-*arabino* configuration (Run 7), synthesized from compound **14** in 3 steps, afforded the products (**8a** and **8b**) which were enantiomers of **5b** and **5a**, in 91% yield. Treatment of 2-deoxy-D-*erythro*-hex-5-enopyranoside derivative (**10**, Run 8), obtained from compound **16** in 2 steps via compound **17**, under the same reaction condition gave the desired products (**11a** and **11b**).

These β-hydroxycylohexanones, (**2a**, **2b**), (**5a**, **5b**), (**8a**, **8b**), and (**11a**, **11b**) were effectively converted into the corresponding cyclohexenones (**3**,[16] **6**, **9**, and **12**) by the action of methanesulfonyl chloride and triethylamine in moderate-to-good yields, respectively. The compounds thus obtained would be useful precursors for syntheses of optically active cyclitols, aminocyclitols, and other natural products.

Therefore, use of $(CF_3CO_2)_2Hg$ as the catalyst is found to be very effective for the Ferrier rearrangement. The mild reaction conditions as well as the short reaction time using a small amount (5—10 mol%) of $(CF_3CO_2)_2Hg$ should allow us to apply this reaction to the synthesis of complex natural products having acid labile functions. Use of the catalytic amount of mercury(II) salt also makes the work-up procedure of this reaction quite easy.

Experimental

Melting points were determined on a Mitamura Riken micro hot stage and are uncorrected. ^1H NMR spectra were taken on JEOL GX 270 (270 MHz) or JEOL EX 90 (90 MHz) spectrometers in chloroform-*d* with tetramethylsilane as an internal standard. Specific rotations were measured in a 0.1 dm tube with a JASCO DIP-370 Digital Polarimeter. Mass spectra were taken on a JEOL JMS-DX 302 spectrometer with EI (70 eV) mode. IR spectra were recorded with a JASCO IR-810 spectrometer.

Organic solutions were dried over anhydrous sodium sulfate and concentrated below 40 °C under reduced pressure.

General Procedure for Catalytic Ferrier Rearrangement: To a stirred mixture of hex-5-enopyranoside (**1**, **4**, **7**, and **10**; 1 mmol) in acetone–water (2:1, 10 ml) at room temperature was added Hg(II) salt (0.05 or 0.1 mmol) and the mixture was stirred at room temperature for the period indicated in Table 1. The mixture was partially evaporated to remove acetone and extracted with ethyl acetate, and the extract was dried. Removal of the solvent left a residue, which was purified on a column of silica gel (ethyl acetate–toluene) to afford the products.

2L-(2,4,5/3)- and 2L-(2,4/3,5)-2-*O*-Acetyl-3,4-di-*O*-benzyl-2,3,4,5-tetrahydroxycyclohexanone (2a) and (2b). Treatment of methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α-D-*xylo*-5-enopyranoside (**1**)[7] (398 mg) with mercury(II) trifluoroacetate (43 mg) in acetone–water afforded 370 mg (96%) of a mixture of **2a** and **2b** (8:1): $[\alpha]_D^{27}$ −24° (*c* 2.2, $CHCl_3$). The ^1H NMR data for the major isomer (**2a**) were identical with those reported in the literature.[7]

2L-(2,4/3)-2-*O*-Acetyl-3,4-di-*O*-benzyl-2,3,4-trihydroxy-5-cyclohexen-1-one (3). A mixture of **2a** and **2b** (8:1, 161 mg) was converted into compound **3** by the same procedure reported in the reference[14] to give 140 mg (91%) of **3** as a colorless syrup. The physical and spectral properties were all identical with those of the authentic sample.[14]

Methyl 4-*O*-Acetyl-2,3-di-*O*-benzyl-α-D-*arabino*-5-enopyranoside (4). A mixture of **13** (530 mg) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.30 ml) in toluene (6 ml) was heated at 80 °C for 3 h. The mixture was diluted with ethyl acetate and washed successively with diluted hydrochloric acid solution, saturated aqueous sodium hydrogencarbonate solution and brine, and dried. Evaporation of the solvent left a residue, which was purified on a column of silica gel (10 g) with acetone–hexane (1:6) to give 364 mg (91%) of compound **4** as a colorless syrup. $[\alpha]_D^{27}$+21° (*c* 0.25, $CHCl_3$); IR (neat) 1740 and 1660 cm^{-1}; ^1H NMR (270 MHz) δ=2.12 (3H, s, OAc), 3.60 (3H, s, OMe), 3.64 (1H, dd, $J_{2,3}$=9.2 Hz, $J_{3,4}$=3.3 Hz, H-3), 3.78 (1H, dd, $J_{1,2}$=6.2 Hz, H-2), 4.45 (1H, d, H-1), 4.58 (1H, d, *J*=11.7 Hz, benzyl), 4.67 (1H, bs, H-6), 4.70 (1H, d, *J*=11.7 Hz, benzyl), 4.73 (1H, d, *J*=11.0 Hz, benzyl), 4.80 (1H, bs, H-6′), 4.82 (1H, d, *J*=11.0 Hz, benzyl), 5.73 (1H, d, H-4), and 7.26—7.36 (10H, m, phenyl). Found: *m/z* 399.1808 ($M+H^+$). Calcd for $C_{23}H_{27}O_6$: 399.1808 (M+H).

2L-(2,3,5/4)- and 2L-(2,3/4,5)-2-*O*-Acetyl-3,4-di-*O*-benzyl-2,3,4,5-tetrahydroxycyclohexanone (5a) and (5b). Treatment of compound **4** (398 mg) with mercury(II) trifluoroacetate (43 mg) in acetone–water gave 303 mg (79%) of a mixture of **5a** and **5b** (1:4) as a colorless syrup. $[\alpha]_D^{27}$ −37° (*c* 0.95, $CHCl_3$); IR (neat) 3450 and 1750 cm^{-1}; ^1H NMR (270 MHz) for the major isomer (**5b**) δ=2.19 (3H, s, OAc), 2.20—2.30 (1H, m, H-6), 2.71—2.75 (2H, m, H-6′ and OH), 3.90 (1H, dd, $J_{3,4}$=4.0 Hz, $J_{4,5}$=3.7 Hz, H-4), 4.09 (1H, dd, $J_{2,3}$=3.3 Hz, H-3), 4.20—4.40 (1H, m, H-5), 4.51 and 4.60 (each 1H, 2d, *J*=12 Hz, benzyl), 4.70 (2H, d, *J*=12 Hz, benzyl), 5.60 (1H, d, H-2), and 7.30—7.35

(10H, m, phenyl). Found: m/z 384.1585 (M^+). Calcd for $C_{22}H_{24}O_6$: M, 384.1573.

2L-(2,3/4)-2-*O*-Acetyl-3,4-di-*O*-benzyl-2,3,4-trihydroxy-5-cyclohexen-1-one (6). To a solution of a mixture of **5a** and **5b** (1:4, 39 mg) in dichloromethane (1.5 ml) were added triethylamine (0.15 ml) and methanesulfonyl chloride (0.023 ml). After stirring at room temperature for 15 min, the mixture was diluted with dichloromethane and washed successively with 0.25 mol dm^{-3} aqueous sulfuric acid and water, and dried. Evaporation of the solvent left a syrup, which was purified on a column of silica gel (1 g) with ethyl acetate–toluene (1:15) to afford **6** (29 mg, 79%) as a colorless syrup. $[\alpha]_D^{27}$ −92° (c 1.36, $CHCl_3$); IR (neat) 1750 and 1700 cm^{-1}; ^{1}H NMR (270 MHz) δ=2.19 (3H, s, OAc), 4.12—4.18 (2H, m, H-3 and 4), 4.55, 4.57, 4.64, and 4.70 (each 1H, 4d, J=12.1 Hz, benzyl), 5.84 (1H, d, $J_{5,6}$=2.6 Hz, H-6), 6.10 (1H, d, $J_{2,3}$=10.3 Hz, H-2), 6.74 (1H, ddd, $J_{3,4}$=4.6 Hz, $J_{3,5}$=1.8 Hz H-5), and 7.29—7.33 (10H, m, phenyl). Found: C, 72.07; H, 6.11%. Calcd for $C_{22}H_{22}O_5$: C, 72.12; H, 6.05%.

Methyl 4-*O*-Acetyl-2,3-di-*O*-benzyl-6-deoxy-β-L-*arabino*-hex-5-enopyranoside (7). A mixture of **15** (31 mg) and DBU (0.035 ml) in toluene (1 ml) was heated at 80 °C for 2 d. The mixture was worked up similarly as described for a preparation of compound **4** to give **7** (13 mg, 57%) as a colorless syrup. $[\alpha]_D^{27}$ +28° (c 0.79, $CHCl_3$); IR (neat) 1740 and 1660 cm^{-1}; ^{1}H NMR (270 MHz) δ=2.10 (3H, s, OAc), 3.42 (3H, s, OMe), 3.94 (1H, dd, $J_{1,2}$=3.3 Hz, $J_{2,3}$=9.9 Hz, H-2), 4.06 (1H, dd, $J_{3,4}$=3.7 Hz, H-3), 4.61 (1H, d, J=11.7 Hz, benzyl), 4.68 and 4.71 (each 1H, 2d, J=9.2 Hz, benzyl), 4.72 (2H, bs, H-6 and 6′), 4.75 (1H, d, H-1), 4.87 (1H, d, J=11.7 Hz, benzyl), 5.80 (1H, d, H-4), and 7.33 (10H, m, phenyl). Found: C, 69.17; H, 6.61%. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58%.

2D-(2,3/4,5)- and 2D-(2,3,5/4)-2-*O*-Acetyl-3,4-di-*O*-benzyl-2,3,4,5-tetrahydroxycyclohexanone (8a) and (8b). Treatment of compound **7** (398 mg) with mercury(II) trifluoroacetate (43 mg) in acetone–water gave 349 mg (91%) of a mixture of **8a** and **8b** (4:1) as a colorless syrup: $[\alpha]_D^{28}$ +45° (c 0.48, $CHCl_3$). The IR and ^{1}H NMR spectra were identical with those of compound **5b** and **5a**. Found: C, 69.02; H, 6.49%. Calcd for $C_{22}H_{24}O_6$: C, 68.74; H, 6.29%.

2D-(2,3/4)-2-*O*-Acetyl-3,4-di-*O*-benzyl-2,3,4-trihydroxy-5-cyclohexen-1-one (9). A mixture of **8a** and **8b** (4:1, 14 mg) was treated similarly as described for a preparation of compound **6** to afford **9** (9.6 mg, 71%) as a colorless syrup. $[\alpha]_D^{27}$ +91° (c 0.48, $CHCl_3$). The IR and ^{1}H NMR spectra of **9** were all identical with those of compound **6**. Found: C, 71.79; H, 6.07%. Calcd for $C_{22}H_{22}O_5$: C, 72.12; H, 6.05%.

Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-methoxymethyl-α-D-*erythro*-hex-5-enopyranoside (10). A mixture of **17** (522 mg) and DBU (0.50 ml) in toluene (15 ml) was heated at 90 °C for 8 h. The mixture was worked up similarly as described for a preparation of compound **4** to afford **10** (378 mg, 91%) as a colorless syrup. $[\alpha]_D^{29}$ +79° (c 0.73, $CHCl_3$); IR (neat) 1740 and 1670 cm^{-1}; ^{1}H NMR (270 MHz) δ=2.14—2.56 (2H, m, H-2 and 2′), 3.33 and 3.58 (each 3H, 2s, OMe), 4.06 (1H, ddd, $J_{2,3}$=4.8 Hz, $J_{2',3}$=9.5 Hz, $J_{3,4}$=3.5 Hz, H-3), 4.66 and 4.75 (each 1H, 2d, J=7.0 Hz, methylene), 4.68 (1H, dd, $J_{1,2}$=3.7 Hz, $J_{1,2'}$=10.6 Hz, H-1), 4.79 (1H, s, H-6), 4.83 (1H, bs, H-6′), 5.75 (1H, d, H-4), and 7.44—8.11 (5H, m, phenyl). Found: C, 62.46; H, 6.35%. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54%.

2L-(2,3,5/0)- and 2L-(2,3/5)-2-*O*-Benzoyl-3-*O*-methoxymethyl-2,3,5-trihydroxycyclohexanone (11a) and (11b). Treatment of compound **10** (308 mg) with mercury(II) trifluoroacetate (43 mg) in acetone–water gave 253 mg (86%) of a mixture of **11a** and **11b** (1:19) as a colorless syrup. $[\alpha]_D^{27}$ −37° (c 1.1, $CHCl_3$); IR (neat) 3450, 1750, and 1730 cm^{-1}; ^{1}H NMR (270 MHz) for the major isomer (**11b**) δ=2.02 (1H, ddd, $J_{3,4}$=2.2 Hz, $J_{4,5}$=11.2 Hz, $J_{4,4'}$=13.4 Hz, H-4), 2.14 (1H, b, OH), 2.54 (1H, m, H-4′), 2.60 (1H, dd, $J_{5,6}$=10.7 Hz, $J_{6,6'}$=13.7 Hz, H-6), 2.95 (1H, ddd, $J_{5,6'}$=4.9 Hz, $J_{4',6}$=2.4 Hz, H-6′), 3.39 (3H, s, OMe), 4.36—4.47 (2H, m, H-3 and 5), 4.74 and 4.79 (each 1H, 2d, J=6.5 Hz, methylene), 5.52 (1H, d, $J_{2,3}$=2.9 Hz, H-2), and 7.43—8.08 (5H, m, phenyl). Found: m/z 294.1104 (M^+). Calcd for $C_{15}H_{18}O_6$: M, 294.1104.

2L-(2,3/0)-2-*O*-Benzoyl-3-*O*-methoxymethyl-2,3-dihydroxy-5-cyclohexen-1-one (12). To a mixture of **11a** and **11b** (1:19, 48 mg) in dichloromethane (2 ml) at 0 °C were added methanesulfonyl chloride (33 μl) and triethylamine (0.158 ml). After stirring at room temperature for 90 min, the reaction mixture was treated similarly as described for a preparation of compound **6** to afford **12** (43 mg, 95%) as a crystalline residue. Mp 118—119 °C (from ethanol); $[\alpha]_D^{25}$ −12° (c 0.97, $CHCl_3$); IR (KBr) 1730 and 1695 cm^{-1}; ^{1}H NMR (270 MHz) δ=2.86 (2H, m, H-4 and 4′), 3.35 (3H, s, OMe), 4.53 (1H, dddd, $J_{3,4}$=4.4 Hz, $J_{3,4'}$= 2.9 Hz $J_{2,3}$=2.6 Hz, $J_{3,5}$=1.8 Hz, H-3), 4.73 and 4.78 (each 1H, 2d, J=7.0 Hz, methylene), 5.76 (1H, d, H-2), 6.19 (1H, ddd, $J_{4,6}$=$J_{4',6}$=1.8 Hz, $J_{5,6}$=9.9 Hz, H-6), 6.86 (1H, dddd, $J_{4,5}$=$J_{4',5}$=4.3 Hz, H-5), and 7.46—8.12 (5H, m, phenyl). Found: C, 64.92; H, 5.87%. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84%.

Methyl 4-*O*-Acetyl-2,3-di-*O*-benzyl-6-deoxy-6-iodo-α-D-altropyranoside (13). To a solution of methyl 2,3-di-*O*-benzyl-6-deoxy-6-iodo-α-D-altropyranoside[14] (200 mg) in pyridine (1.5 ml) was added acetic anhydride (1.5 ml), and the mixture was stirred at room temperature overnight. The reaction mixture was concentrated and co-distilled with toluene several times to give a residue, which was purified on a column of silica gel (10 g) with acetone–toluene (1:40) to afford **13** (210 mg, 97%) as a colorless syrup. $[\alpha]_D^{27}$ +21° (c 0.25, $CHCl_3$); IR (neat) 1740 cm^{-1}; ^{1}H NMR (90 MHz) δ=2.02 (3H, s, OAc), 3.17 (1H, dd, $J_{5,6}$=9.8 Hz, $J_{6,6'}$=13.0 Hz, H-6), 3.36 (1H, dd, $J_{5,6}$=4.0 Hz, H-6′), 3.49 (3H, s, OMe), 3.65 (1H, dd, $J_{1,2}$=2.5 Hz, $J_{2,3}$=5.2 Hz, H-2), 3.88 (1H, dd, $J_{3,4}$=4.0 Hz, H-3), 4.10 (1H, ddd, $J_{4,5}$=8.6 Hz, H-5), 4.42 and 4.59 (each 1H, 2d, J=12.0 Hz, benzyl), 4.57 (2H, s, benzyl), 4.68 (1H, d, H-1), 5.00 (1H, dd, H-4), and 7.20—7.43 (10H, m, phenyl). Found: m/z 527.0925 ($M+H^+$). Calcd for $C_{23}H_{28}O_6I$: 527.0931 (M+H).

Methyl 2,3-Di-*O*-benzyl-6-*O*-tosyl-α-D-galactopyranoside (14). A mixture of methyl 2,3-di-*O*-benzyl-α-D-galactopyranoside[17] (255 mg), *p*-toluenesulfonyl chloride (470 mg) and 4-dimethylaminopyridine (8 mg) in pyridine (4.5 ml) was stirred at room temperature for 16 h. The mixture was diluted with ethyl acetate and then washed successively with diluted hydrochloric acid and brine, and dried. Removal of the solvent gave a residue, which was purified on a column of silica gel (10 g) with ethyl acetate–toluene (1:5) to afford **14** (365 mg, 100%) as a colorless syrup. $[\alpha]_D^{24}$ +37° (c 1.9, $CHCl_3$); IR (neat) 3500 and 1360 cm^{-1}; ^{1}H NMR (90 MHz) δ=2.42 (3H, s, $PhC\underline{H}_3$), 3.32 (3H, s, OMe), 3.72—4.24 (6H, m, H-2,3,4,5,6 and 6′), 4.59 (1H, d, $J_{1,2}$=3.0 Hz, H-1), 4.60 and 4.63 (each 1H, 2d, J=12.0 Hz, benzyl), 4.80 (2H, d, J=12 Hz, benzyl), and 7.33—7.38 (14H, m, phenyl). Found: C, 63.39; H, 5.86%. Calcd for $C_{28}H_{32}O_8S$: C, 63.62; H, 6.10%.

Methyl 4-*O*-Acetyl-2,3-Di-*O*-benzyl-6-deoxy-6-iodo-α-D-

galactopyranoside (15). A mixture of **14** (202 mg) and sodium iodide (172 mg) in *N,N*-dimethylformamide (1 ml) was heated at 80 °C for 4 d. The mixture was diluted with ethyl acetate and washed with water, and dried. Evaporation of the solvent left a residue, which was then treated with acetic anhydride (1.8 ml) and pyridine (3.6 ml) at room temperature overnight. The mixture was concentrated and diluted with ethyl acetate, and washed successively with diluted hydrochloric acid, saturated aqueous sodium hydrogencarbonate solution and brine, and dried. Evaporation of the solvent gave a syrup, which was purified on a column of silica gel (4.2 g) with ethyl acetate–hexane (1:9) to afford **15** (139 mg, 70%) as a colorless syrup. $[\alpha]_D^{25}$ +65° (*c* 0.54, $CHCl_3$); IR (neat) 1740 cm^{-1}; ^1H NMR (270 MHz) δ=2.13 (3H, s, OAc), 3.11 (2H, m, H-6 and 6'), 3.46 (3H, s, OMe), 3.75 (1H, dd, $J_{1,2}$=3.7 Hz, $J_{2,3}$=9.9 Hz, H-2), 3.96 (1H, dd, $J_{3,4}$=4.0 Hz, H-3), 4.00 (1H, ddd, $J_{5,6}$=2.9 Hz, $J_{5,6'}$=8.1 Hz, $J_{4,5}$=1.8 Hz, H-5), 4.57 (1H, d, *J*=11.4 Hz, benzyl), 4.64 (1H, d, *J*=12.1 Hz, benzyl), 4.67 (1H, d, H-1), 4.73 (1H, d, *J*=11.4 Hz, benzyl), 4.84 (1H, d, *J*=12.1 Hz, benzyl), 5.59 (1H, dd, H-4), and 7.26—7.35 (10H, m, phenyl). Found: 526.0857 (M^+). Calcd for $C_{23}H_{27}O_6I$: M, 526.0853.

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*O*-methoxymethyl-α-D-ribopyranoside (16). A mixture of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-ribopyranoside[18] (1.00 g), chloromethyl methyl ether (0.57 ml) and *N,N*-diisopropylethylamine (2.62 ml) in dichloromethane (20 ml) was heated under reflux overnight. The mixture was diluted with dichloromethane and washed successively with diluted hydrochloric acid, saturated aqueous sodium hydrogencarbonate solution and brine, and dried. Concentration of the mixture afforded a residue, which was purified on a column of silica gel (30 g) with ethyl acetate–toluene (1:8) to give **16** (1.15 g, 86%) as needles. Mp 53—53.5 °C (from ether–petroleum ether); $[\alpha]_D^{27}$ +95° (*c* 1.0, $CHCl_3$); ^1H NMR (270 MHz) δ=2.00 (1H, ddd, $J_{1,2}$=4.4 Hz, $J_{2,3}$=4.0 Hz, $J_{2,2'}$=15.0 Hz, H-2), 2.19 (1H, ddd, $J_{1,2'}$=0.7 Hz, $J_{2',3}$=2.6 Hz, H-2'), 3.39 (6H, s, OMe), 3.65 (1H, dd, $J_{3,4}$=2.9 Hz, $J_{4,5}$=8.4 Hz, H-4), 3.70 (1H, dd, $J_{5,6}$=$J_{6,6'}$=12.1 Hz, H-6), 4.19 (1H, ddd, H-3), 4.26—4.37 (2H, m, H-5 and 6'), 4.71 (1H, dd, H-1), 4.76 and 4.85 (each 1H, 2d, *J*=7.0 Hz, methylene), 5.55 (1H, s, PhCH), and 7.31—7.56 (5H, m, phenyl). Found: C, 62.07; H, 6.96%. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15%.

Methyl 6-Bromo-4-*O*-benzoyl-2,6-dideoxy-3-*O*-methoxymethyl-α-D-ribopyranoside (17). A mixture of **16** (1.0 g), *N*-bromosuccinimide (599 mg), 1,1,2,2-tetrachloroethane (1.6 ml), and barium carbonate (332 mg) in carbon tetrachloride (20 ml) was heated at 90 °C for 4 h. After cooling, the insoluble matter was removed by filtration and washed with chloroform. The filtrate was concentrated to give a residue, which was dissolved in ethyl acetate and washed with water, and dried. Evaporation of the solvent left a residue, which was purified on a column of silica gel (80 g) with acetone–hexane (1:16) to afford **17** (1.13 g, 90%) as a colorless syrup. $[\alpha]_D^{27}$ +129° (*c* 1.5, $CHCl_3$); IR (neat) 1720 cm^{-1}; ^1H NMR (90 MHz) δ=1.87—2.40 (2H, m, H-2 and 2'), 3.24 and 3.46 (each 3H, 2s, OMe), 3.36—3.73 (2H, m, H-6 and 6'), 4.22—4.58 (2H, m, H-3 and 5), 4.57 and 4.73 (each 1H, 2d, *J*=7.0 Hz, methylene), 4.84 (1H, m, H-1), 5.02 (1H, dd, $J_{3,4}$=3.4 Hz, $J_{4,5}$=10.0 Hz, H-4), and 7.39—8.12 (5H, m, phenyl). Found: C, 49.60; H, 5.28%. Calcd for $C_{16}H_{21}O_6Br$: C, 49.37; H, 5.44%.

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