Branched-chain Sugars. XXVIII. Synthesis of 2-*C*-Methyl-L-glyceraldehyde, 2-*C*-Methyl-D-erythrose, and 3-*C*-Methyl-L-erythrose Derivatives[1)]

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As synthons for the synthesis of bicyclomycin, the title compounds were derived from 1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose by the descendent method.

Recent advances in the chiral synthesis established the general recognition that monosaccharides are valuable sources of chiral synthons for optically active, non-sugar natural products.[2-4)] However, it seems likely that the strategy for the derivation of a desired synthon from a proper monosaccharide is still under development. As a part of the synthetic studies on branched-chain sugars, this paper describes the preparation of 2-*C*-methyl-L-glyceraldehyde, 2-*C*-methyl-D-erythrose, and 3-*C*-methyl-L-erythrose derivatives as synthons for the chiral synthesis of bicyclomycin[5)] (**1**) which contains a (1*S*,2*S*)-1,2,3-trihydroxy-2-methylpropyl group attached to a bicyclic 2,5-piperazinedione ring. After a few attemps, the aimed compounds were derived from 1,2-*O*-isopropylidene-3-*O*-benzyl-3-*C*-methyl-α-D-allofuranose,[6)] obtained from D-glucose *via* four-step conversions, by the descendent method.

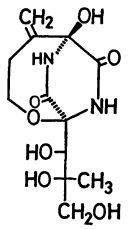
Results and Discussion

In general, two approaches, *i.e.* i) introduction of a methyl-branching into an appropriate tetrose or triose derivative and ii) decrement of carbon number from a higher carbon branched-chain sugar, are considered for the present synthesis.

Firstly, periodate oxidation of 2,5-di-*C*-methyl-L-iditol protected at 1,2,5,6-positions was considered to be the ideal method for the preparation of 2-*C*-methyl-L-glyceraldehyde derivatives, as the preparation of 2,3-*O*-isopropylidene-D-glyceraldehyde from 1,2:5,6-di-*O*-isopropylidene-D-mannitol has been well-known.[7)] For the protection of 1,6-positions of 3,4-*O*-isopropylidene-D-mannitol,[8)] the usual tritylation with triphenylmethyl chloride in pyridine gave the corresponding di-*O*-trityl derivative (**2**) in 74% yield. However, benzoylation with benzoyl chloride under similar conditions gave a mixture of di- (**4**), tri- (**5**), and tetrabenzoate (**6**) in the ratio of 2:2:1, together with a small amount of monobenzoate and the unchanged starting material. When the benzoylation was conducted in chloroform at 0 °C in the presence of pyridine, the desired **4** was selectively obtained in 80% yield. The structure of **2** and **4** was confirmed by the derivation into the corresponding 2,5-diacetates (**3** and **7**).

Oxidation of **4** with dimethyl sulfoxide (DMSO)–acetic anhydride gave only 5-*O*-acetyl-1,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-D-fructose (**8**) in 90% yield, but did not give the corresponding diketone. The structure of **8** was ascertained by the comparison of its NMR spectrum with that of the corresponding 5-*O*-benzoyl derivative (**9**) obtained by the similar oxidation of **5**. These compounds showed a characteristic larger geminal coupling constant (17.5 Hz) of H-1 and H-1′ protons. Attemped oxidation of **4** with DMSO–phosphorus pentaoxide[9)] gave a complex product from which the corresponding monoketone (**10**) was separated. All other oxidations with ruthenium tetraoxide, pyridimium chlorochromate,[10)] and potassium permanganate gave unsuccessful results. Moreover, NMR spectra of the reaction products obtained by the reactions of these monoketones with methylmagnesium iodide showed the presence of epimeric *C*-methyl (δ 1.25—1.15) derivatives in the ratios from 1:4 to 1:1. Therefore, this approach was given up.

Secondly, *C*-methylation of known 2,4-*O*-ethylidene-D-erythritol[11)] was considered. Partial benzoylation of the substrate with benzoyl chloride gave 1-*O*-benzoyl-2,4-*O*-ethylidene-D-erythritol (**11**) in 80% yield. However, oxidation of **11** with DMSO–trifluoroacetic an-



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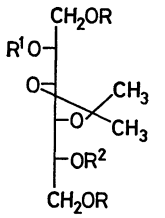
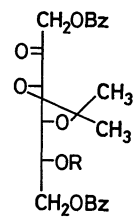
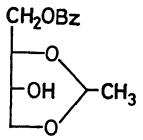


2 R=CPh$_3$, R^1=R^2=H
3 R=CPh$_3$, R^1=R^2=Ac
4 R=Bz, R^1=R^2=H
5 R=R^2=Bz, R^1=H
6 R=R^1=R^2=Bz
7 R=Bz, R^1=R^2=Ac



8 R=Ac
9 R=Bz
10 R=H



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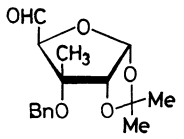
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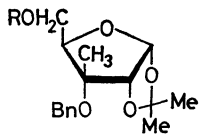
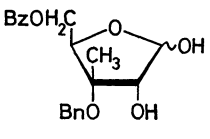

13 R=H
14 R=Bz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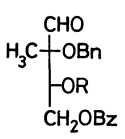
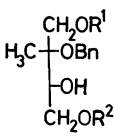
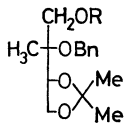
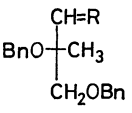
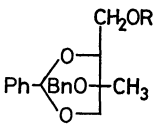
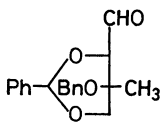

16 R=CHO
17 R=H


18 R^1=H, R^2=Bz
19 R^1=R^2=H
22 R^1=Bn, R^2=H


20 R=H
21 R=Bn


23 R=O
24 R=NNHCNH$_2$ (O)


25 R=Bz
26 R=H
27 R=CH$_2$SCH$_3$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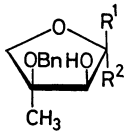
29 R^1=OMe, R^2=H
30 R^1=H, R^2=OMe

hydride[12] was unsuccessful, probably due to the accompanying β-elimination and also oxidation of the ethylidene group.[13]

From the aforementioned failed results, the descendent method from 1,2-*O*-isopropylidene-3-*O*-benzyl-3-*C*-methyl-α-D-allofuranose,[6] which seems to be the most certain, was thirdly adopted.

Periodate oxidation of the starting α-D-allofuranose gave 3-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-*ribo*-pentodialdofuranose (**12**) quantitatively. Reduction of **12** with sodium borohydride gave the corresponding α-D-ribofuranose (**13**) in 94% yield. The usual benzoylation of **13** gave the corresponding benzoate (**14**) in 95% yield. Partial hydrolysis of **14** with 70% acetic acid gave de-*O*-isopropylidenated product (**15**) in 96% yield. Periodate oxidation of **15** and successive reduction with sodium borohydride gave 4-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-D-erythritol (**18**) in 92% yield. The intermediary 4-*O*-benzoyl-2-*O*-benzyl-3-*O*-formyl-D-erythrose (**16**) could not be purified, but characterized by its NMR spectrum, and 4-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-D-erythrose (**17**) could be incidentally obtained as crystals from an incomplete reduction products. Treatment of **18** in methanol with a catalytic amount of sodium methoxide gave de-*O*-benzoylated product (**19**) in a good yield.

For the conversion of **19** into branched-chain sugars of L-series, periodate oxidation of **19** was tried. However, the product showed eight kinds of *C*-methyl signals in the NMR spectrum, indicating 2-*O*-benzyl-2-*C*-methyl-L-glyceraldehyde exists in polymeric states. Therefore, **19** was treated with acetone containing sulfuric acid catalyst to give the corresponding 3,4-*O*-isopropylidene derivative (**20**) in 70% yield. Successive benzylation of **20** with sodium hydride and benzyl chloride gave the 1-*O*-benzyl derivative (**21**) in 68% yield, which was partially hydrolyze into the corresponding de-*O*-isopropylidenate product (**22**) in 84% yield. Periodate oxidation of **22** gave the desired 2,3-di-*O*-benzyl-2-*C*-methyl-L-glyceraldehyde (**23**) quantitatively. Because **23** is stable at room temperature only for a few h, it was instantly characterized as the crystalline semicarbazone (**24**).

On the other hand, benzylidenation of **18** with dimethoxytoluene gave the corresponding benzylidene derivative (**25**) which was then converted into the de-*O*-benzoyl derivative (**26**) in a good yield, by treatment with sodium methoxide. Oxidation of **26** with DMSO–dicyclohexylcarbodiimide gave 3-*O*-benzyl-2,4-*O*-benzylidene-3-*C*-methyl-L-erythrose (**28**) and the corresponding methylthiomethyl ether (**27**) in 27 and 25% yield, respectively. The L-erythose derivative **28** was further characterized by the conversion into methyl 3-*O*-benzyl-3-*C*-methyl-α- and β-L-erythrofuranosides (**29** and **30**) by treatment with methanolic hydrogen chloride.

Thus, it was shown that the descendent method of a branched-chain hexose having a proper configuration provides certain pathways to various lower carbon branched-chain sugars of D- and L-series, by the combination of the protection of hydroxyl groups with an aldehyde or a ketone and periodate cleavage of carbon-chain.

Experimental

General Methods. Melting points were determined with a Mel-Temp melting point apparatus and not corrected. Evaporations were conducted under diminished pressure. Optical rotations were measured in a 0.5 dm tube with Carl Zeiss LEP-Al or JASCO DIP-4 polarimeter, using chloroform as a solvent unless otherwise stated. IR spectra were recorded with a Hitachi EPI-G2 grating spectrometer. NMR spectra were recorded with a JEOL JNM PS-100 spectrometer for solutions in chloroform-*d* containing tetramethylsilane as the internal reference. Chemical shifts and coupling constants were recorded in δ and Hz units, respectively, and IR frequencies in cm^{-1}.

3,4-O-Isopropylidene-1,6-di-O-triphenylmethyl-D-mannitol (2) and Its 2,5-Diacetate (3). To a solution of 3,4-*O*-isopropylidene-D-mannitol[8] (10 g, 45 mmol) in pyridine (30 ml) was added triphenylmethyl chloride (27 g, 96.9 mmol) portionwise, and the resulting solution was kept at room temperature for 2 d, poured into ice–water, and extracted with dichloromethane. The extract was washed successively with water, 0.1 M sulfuric acid, saturated aqueous sodium hydrogencarbonate, and water, and then evaporated. The residual syrup was crystallized from ethanol to give **2** as prisms in 74% (23.5 g) yield. Mp 174—175 °C; $[\alpha]_D^{24}$ +10.5° (*c* 1.0, MeOH).

Found: C, 79.25; H, 6.33%. Calcd for $C_{47}H_{46}O_6$: C, 79.86; H, 6.56%.

The usual acetylation of **2** (1.4 g, 2 mmol) in pyridine (2 ml) with acetic anhydride (4 ml) gave **3** as needles in 83% (1.3 g) yield. Mp 154—155 °C (ethanol); $[\alpha]_D^{22}$ −5.5° (*c* 1.0, MeOH); NMR: 7.5—7.1 (m, 30H, 6 Ph), 5.18 (dd, 2H, $J_{2,3}=J_{4,5}=4.5$, H-2 and 5), 3.98 (d, 2H, H-3 and 4), 3.30 (d, 4H, $J_{1,2}=J_{5,6}=4.7$, H-1,1′,6, and 6′), 2.09 (s, 6H, 2Ac), 1.15 (s, 6H, Ip).

Found: C, 76.82; H, 6.32%. Calcd for $C_{51}H_{50}O_5$: C, 77.45; H, 6.37%.

*Benzoylation of 3,4-*O*-Isopropylidene-*D*-mannitol.* To an ice-cooled solution of 3,4-*O*-isopropylidene-D-mannitol (22.2 g, 0.1 mol) in pyridine (100 ml) was added with stirring benzoyl chloride (29.5 g, 0.21 mol) dropwise. The mixture was kept at room temperature overnight, poured into ice-water, and extracted with dichloromethane. The usual processing of the extract and fractionation of the products on a column of silica gel with 50:1 benzene–acetone gave in turn tetra- (**6**), tri- (**5**), and dibenzoate (**4**) in 12% (7.65 g), 24% (12.8 g), and 24% (10.3 g) yield, respectively.

6: mp 120—122 °C; $[\alpha]_D^{24}$ −0.59° (*c* 0.8, MeOH); NMR: 8.0—7.8 and 7.6—7.2 (m, 20H, 4Ph), 5.61 (m, 2H, H-2 and 5), 4.75 (dd, 2H, $J_{1,2}=J_{5,6}=3.2$, $J_{1,1'}=J_{6,6'}=12.2$, H-1 and 6), 4.59 (d, 2H, $J_{2,3}=J_{4,5}=6.0$, H-3 and 4), 4.56 (dd, 2H, $J_{1',2}=J_{5,6'}=6.0$, H-1′ and 6′), 1.49 (s, 6H, Ip).

Found: C, 69.52; H, 5.32%. Calcd for $C_{37}H_{30}O_{10}$: C, 69.58; H, 5.37%.

5: mp 115—118 °C (prisms from EtOH); $[\alpha]_D^{24}$ +5.5° (*c* 0.7, MeOH). NMR and IR patterns were very similar to those of **4**.

Found: C, 67.25; H, 5.42%. Calcd for $C_{30}H_{30}O_9$: C, 67.40; H, 5.66%.

4: mp 96—97 °C; $[\alpha]_D^{20}$ +29.2° (*c* 0.4, MeOH); IR: 3400 (OH), 1720 and 1690 (C=O); NMR; 8.1—7.9 and 7.6—7.2 (m, 10H, 2Ph), 4.63 (bd, 2H, $J_{2,3}=J_{3,4}=11.0$, H-1 and 6), 4.5—4.3 (m, 2H, H-1′ and 6′), 3.97 (bs, 6H, H-2,3,4,5 and OH), 1.40 (s, 6H, Ip).

Found: C, 64.67; H, 6.09%. Calcd for $C_{23}H_{26}O_8$: C, 64.17; H, 6.09%.

The usual acetylation of **4** (200 mg, 0.59 mmol) in pyridine (10 ml) with acetic anhydride (10 ml) gave the corresponding diacetate (**7**) in 83% (198 mg) yield. Mp 75—76 °C (ethanol); $[\alpha]_D^{20}$ +21.1° (*c* 1.0, MeOH); IR: 1760—1720 (C=O); NMR: 8.1—7.9 and 7.6—7.3 (m, 10H, 2Ph), 5.33 (m, 2H, H-2 and 5), 4.68 (dd, 2H, $J_{1,2}=J_{5,6}=3.1$, $J_{gem}=12.0$, H-1 and 6), 4.43 (dd, 2H, $J_{1',2}=J_{5,6'}=6.7$, H-1′ and 6′), 4.24 (d, 2H, $J_{2,3}=J_{4,5}=4.6$, H-3 and 4), 2.07 (s, 6H, 2 OAc), 1.46 (s, 6H, Ip).

Found: C, 62.87; H, 5.84%. Calcd for $C_{27}H_{30}O_{10}$: C, 63.03; H, 5.88%.

When the benzoylation of 3,4-*O*-isopropylidene-D-mannitol (5 g, 22.5 mmol) with benzoyl chloride (6.6 g, 47 mmol) was performed in chloroform (50 ml) at 0 °C in the presence of pyridine (3.3 g, 78 mmol), **4** was selectively obtained in 80% (7.75 g) yield.

5-O-Acetyl-1,6-di-O-benzoyl-3,4-O-isopropylidene-D-fructose (8). A solution of **4** (1.5 g, 3.5 mmol) in dimethyl sulfoxide (DMSO, 35 ml) and acetic anhydride (25 ml) was kept at room temperature overnight, and then evaporated. The residual syrup was extracted with dichloromethane. The usual processing of the extract and purification of the product on a column of silica gel with 50:8 petroleum ether–benzene gave syrupy **8** (1.47 g, 89.7%) which was crystallized from hexane. Mp 54—56 °C; $[\alpha]_D^{22}$ +0.67° (*c* 1.13, acetone); IR: 1760—1720 (C=O); NMR: 8.1—7.9 and 7.6—7.3 (m, 10H, 2 Ph), 5.46 (m, 1H, H-5), 5.28 and 5.08 (ABq, 2H, $J=17.5$, H-1 and 1′), 4.8—4.2 (m, 4H, H-3,4,6, and 6′), 2.08 (s, 3H, OAc), 1.46 (s, 6H, Ip).

Found: C, 63.50; H, 5.72%. Calcd for $C_{25}H_{26}O_9$: C, 63.82; H, 5.72%.

1,5,6-Tri-O-benzoyl-3,4-O-isopropylidene-D-fructose (9). Compound **5** (4.3 g, 8 mmol) was oxidized with DMSO (75 ml) and acetic anhydride (50 ml) as above. Purification of the product gave syrupy **9** (4.2 g) quantitatively, which was crystallized from ethyl acetate–ligroine. Mp 129—130 °C; $[\alpha]_D^{22}$ +15.5° (*c* 1.4, acetone); IR: 1740—1710 (C=O); NMR: 8.1—7.9 and 7.6—7.2 (m, 15H, 3 Ph), 5.69 (m, 1H, H-5), 5.31 and 5.10 (ABq, 2H, $J=17.5$, H-1 and 1′), 4.73 (dd, 1H, $J_{5,6}=4.0$, $J_{6,6'}=12.5$, H-6), 4.72 (d, 1H, $J_{2,3}=4.2$, H-3), 4.69 (t, 1H, H-4), 4.54 (q, 1H, $J_{5,6'}=6.3$, H-6′), 1.45 (s, 6H, Ip).

Found: C, 67.24; H, 5.32%. Calcd for $C_{30}H_{28}O_9$: C, 67.66; H, 5.30%.

1,6-Di-O-benzoyl-3,4-O-isopropylidene-D-fructose (10). To an ice-cooled mixture of phosphorus pentaoxide (5 g) and DMSO (50 ml) was added with stirring a solution of **4** (6 g, 14 mmol) in DMSO (40 ml), and the resulting solution was kept at room temperature overnight, poured into excess aqueous sodium hydrogencarbonate, and extracted with dichloromethane. The usual processing of the extract gave a syrup (4.8 g) which showed four spots on TLC, excepting a small amount of the starting material. Separation of the syrup on a column of silica gel with 8:1 benzene–acetone gave **10** as the second polar fraction in 19% (1.15 g) yield. NMR spectrum of the most nonpolar fraction indicated that it is a monobenzoyl derivative. Mp 90—91 °C; NMR: 8.2—8.0 and 7.7—7.3 (m, 10H, 2Ph), 5.31 and 5.21 (ABq, 2H, $J=17.5$, H-1 and 1′), 4.75—4.3 (m, 4H, H-3,4,6, and 6′), 4.14 (m, 1H, H-5), 3.0 (bs, 1H, OH), 1.50 and 1.46 (each s, 6H, Ip).

Found: C, 66.18; H, 5.25%. Calcd for $C_{25}H_{24}O_8$: C, 66.36; H, 5.35%.

1-O-Benzoyl-2,4-O-ethylidene-D-erythritol (11). The usual benzoylation of 2,4-*O*-ethylidene-D-erythritol[11] (3.16 g, 20 mmol) in pyridine (20 ml) with benzoyl chloride (3.08 g, 22 mmol) at 0 °C gave **11** as crystals in 80% (4.58 g) yield. Mp 103—105 °C; $[\alpha]_D^{26}$ +13.4° (*c* 1.0); NMR: 8.2—8.0 and 7.7—7.3 (m, 5H, Ph), 4.77 (dd, 1H, $J_{1,2}=3.0$, $J_{1,1'}=12.0$, H-1), 4.50 (q, 1H, $J=5.0$, CHMe), 4.44 (dd, $J_{1',2}=2.0$, H-1′), 4.15 (dd, $J_{3,4e}=2.6$, $J_{4e,4a}=10.0$, H-4e), 3.75—3.55 (m, 2H, H-2 and 3), 3.48 (t, 1H, H-4a), 3.02 (s, 1H, OH), 1.36 (d, 3H, CMe).

Found: C, 58.02; H, 6.10%. Calcd for $C_{13}H_{16}O_5$: C, 58.20; H, 6.01%.

3-O-Benzyl-1,2-O-isopropylidene-3-C-methyl-α-D-ribo-pentodialdofuranose (12). A solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose[6] (10 g, 30.8 mmol) and sodium periodate (7.0 g, 32.7 mmol) in aqueous acetic acid (1:1, 60 ml) was stirred for 30 min at room temperature, diluted with water (60 ml), and then extracted with chloroform. The usual processing of the extract gave **12**, quantitatively. Mp 74—76 °C (ether–petroleum ether); $[\alpha]_D^{22}$ +55.5° (*c* 1.1); IR: 1745 (CHO); NMR: 9.67 (s, 1H, CHO), 7.3 (m, 5H, Ph), 5.85 (d, 1H, $J_{1,2}=4.0$, H-1), 4.64 (s, 3H, H-4 and CH_2Ph), 4.38 (d, 1H, H-2), 1.60 (s, 3H, CMe), 1.40 and 1.29 (each s, 6H, Ip).

Found: C, 65.47; H, 7.01%. Calcd for $C_{16}H_{20}O_5$; C, 65.74; H, 6.90%.

3-O-Benzyl-1,2-O-isopropylidene-3-C-methyl-α-D-ribofuranose (13). To an ice-cooled solution of **12** (8.87 g, 30.3 mmol) in aqueous methanol (1:1, 160 ml) was added sodium borohydride (1.15 g, 30.4 mmol) portionwise, and the mixture

was stirred for 3 h, neutralized with 0.1 M hydrochloric acid, evaporated, and the residue was extracted with chloroform. The usual processing of the extract and crystallization and recrystallization of the product from ether–petroleum ether and ethanol–hexane gave **13** (8.58 g, 94%) as needles. Mp 65—66 °C; $[\alpha]_D^{22}$ +46.3° (*c* 0.99); NMR: 7.3 (m, 5H, Ph), 5.72 (d, 1H, $J_{1,2}$=3.6, H-1), 4.51 (s, 2H, CH_2Ph), 4.22 (d, 1H, H-2), 4.15 (dd, 1H, H-4), 3.74 (dd, 1H, $J_{4,5}$=4.0, $J_{5,5'}$=12.5, H-5), 3.60 (dd, 1H, $J_{4,5'}$=7.0, H-5′), 2.81 (bs, 1H, OH), 1.56 (s, 3H, CMe), 1.31 and 1.14 (each s, 6H, Ip).

Found: C, 65.34; H, 7.47%. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53%.

*5-O-Benzoyl-3-O-benzyl-1,2-O-isopropylidene-3-C-methyl-α-D-ribofuranose (**14**).* To an ice-cooled solution of **13** (10g, 34 mmol) in pyridine (100 ml) was added dropwise benzoyl chloride (5.25 g, 37.3 mmol) with stirring, and the mixture was kept for 1 h at room temperature, poured into ice–water, and then extracted with chloroform. The usual processing of the extract and recrystallization of the product from ether–petroleum ether gave **14** as needles (12.7 g, 95%). Mp 84—85 °C; $[\alpha]_D^{22}$ +12.5° (*c* 1.55); IR: 1720 (ester); NMR: 8.1—7.9 and 7.6—7.4 (m, 10H, 2Ph), 5.70 (d, 1H, $J_{1,2}$= 4.0, H-1), 4.55 (s, 2H, CH_2Ph), 4.3—4.5 (m, 3H, H-4, 5, and 5′), 4.23 (d, 1H, H-2), 1.60 (s, 3H, CMe), 1.33 and 1.21 (each s, 6H, Ip).

Found: C, 69.04; H, 6.50%. Calcd for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58%.

*5-O-Benzoyl-3-O-benzyl-3-C-methyl-D-ribofuranose (**15**).* A solution of **14** (5.28 g, 13.3 mmol) in acetic acid (70%, 60 ml) was refluxed for 2 h, diluted with water, and extracted with chloroform. The usual processing of the extract and purification of the product on a column of silica gel with 8:1 benzene–acetone gave pure **15** as a syrup in 96% (4.56 g) yield. $[\alpha]_D^{22}$ +36.3° (*c* 1.67).

Found: C, 66.70; H, 6.35%. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19%.

*4-O-Benzoyl-2-O-benzyl-2-C-methyl-D-erythritol (**18**).* To a solution of **15** (1.11 g, 3.1 mmol) in methanol (5 ml) was added a solution of sodium periodate (0.8 g, 3.7 mmol) in water (5 ml), and the resulting suspension was stirred for 30 min at room temperature, neutralized with sodium hydrogencarbonate and then extracted with chloroform. The usual processing of the extract gave 4-*O*-benzoyl-2-*O*-benzyl-3-*O*-formyl-2-*C*-methyl-D-erythrose (**16**, 0.84 g, 83%) as a syrup, but it could not be purified on a column of silica gel. However, the crude product gave reasonable NMR spectrum as follows. NMR: 9.63 (s, 1H, CHO), 8.10 (s, 1H, OCHO), 8.0—7.9 and 7.6—7.2 (m, 10H, 2Ph), 5.74 (dd, 1H, H-3), 4.62 (dd, 1H, $J_{3,4}$=4.0, $J_{4,4'}$=12.0, H-4), 4.60 and 4.52 (ABq, 2H, J=12.5, CH_2Ph), 4.51 (q, 1H, $J_{3,4'}$=7.4, H-4′), 1.49 (s, 3H, CMe).

To an ice-cooled solution of syrupy **16** (0.84 g, 2.56 mmol) in methanol (5 ml) and water (10 ml) was added sodium borohydride (110 mg, 2.9 mmol) with stirring. After stirring at room temperature for 3 h, the reaction mixture was neutralized with 0.1 M hydrochloric acid, and filtered. The filtrate was evaporated, and the residue was extracted with chloroform. The usual processing of the extract and purification of the product on a column of silica gel with 3:1 benzene–acetone gave pure **18** in 92% (0.78 g) yield. $[\alpha]_D^{22}$ +9.1° (*c* 1.03); NMR: 8.1—7.9 and 7.6—7.4 (m, 10H, 2 Ph), 4.66 (dd, 1H, H-4′), 4.57 (s, 2H, CH_2Ph), 4.43 (dd, 1H, $J_{4,4'}$=11.6, H-4), 4.17 (dd, 1H, $J_{3,4'}$=2.6, $J_{3,4}$=7.6, H-3), 3.77 (s, 2H, H-1 and 1′), 1.32 (s, 3H, CMe).

Found: C, 68.62; H, 6.95%. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71%.

In one instance, fractionation of the incomplete reduction product on a column of silica gel with 3:1 hexane–ethyl acetate gave 4-*O*-benzoyl-2-*O*-benzyl-2-*C*-methyl-D-erythrose (**17**) as crystals. Mp 97—98 °C (ether–ligroine); $[\alpha]_D^{22}$ +26.8° (*c* 0.98); IR: 3500 (OH), 1740 and 1700 (C–O); NMR: 9.71 (s, 1H, CHO), 8.1—7.9 and 7.6—7.1 (m, 10H, 2 Ph), 4.7—4.4 (m, 4H, H-4,4′ and CH_2Ph), 4.24 (dd, 1H, $J_{3,4}$=5.6, $J_{3,4'}$=9.2, H-3), 2.98 (bs, 1H, OH), 1.50 (s, 3H, CMe).

Found: C, 69.47; H, 6.04%. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14%.

*2-O-Benzyl-2-C-methyl-D-erythritol (**19**).* A solution of **18** (12 g, 36.3 mmol) in methanol (100 ml) containing a catalytic amount of sodium methoxide was stirred for 3 h at room temperature, neutralized with 0.1 M hydrochloric acid, and then evaporated. The residual syrup was purified on a column of silica gel with 2:1 benzene–acetone to give pure **19** as a syrup (6.1 g, 74%). $[\alpha]_D^{22}$ +8.7° (*c* 1.89); IR: 3600—3100 (OH); NMR: 7.3 (m, 5H, Ph), 4.42 (s, 2H, CH_2Ph), 3.80 (dd, 1H, H-3), 3.78 (dd, 1H, $J_{3,4}$=2.6, H-4), 3.64 (bs, 3H, 3 OH), 3.57 (s, 2H, H-1 and 1′), 3.50 (dd, 1H, $J_{3,4'}$=8.0, $J_{4,4'}$=11.6, H-4′), 1.08 (s, 3H, CMe).

Found: C, 64.00; H, 8.12%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%.

*2-O-Benzyl-3,4-O-isopropylidene-2-C-methyl-D-erythritol (**20**).* A solution of **19** (5.5 g, 24.3 mmol) in dry acetone (60 ml) containing concd sulfuric acid (1 ml) was stirred for 2 d at room temperature, poured into aqueous sodium hydrogencarbonate, and extracted with ether. The usual processing of the extract and purification of the product on a column of silica gel with 8:1 benzene–acetone gave **20** as crystals in 70% (4.5 g) yield. Mp 42—43 °C (methanol–hexane); $[\alpha]_D^{22}$ +13.2° (*c* 1.02); NMR: 7.3 (m, 5H, Ph), 4.56 and 4.62 (ABq, 2H, J=11.0, CH_2Ph), 4.26 (dd, 1H, $J_{3,4}$=6.0, $J_{4,4'}$=7.6, H-4), 4.1—3.9 (m, 2H, H-3 and 4′), 3.65 (s, 2H, H-1 and 1′), 2.21 (bs, 1H, OH), 1.45 (s, 3H, CMe), 1.24 and 1.35 (each s, 6H, Ip).

Found: C, 67.86; H, 8.44%. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%.

*1,2-Di-O-benzyl-3,4-O-isopropylidene-2-C-methyl-D-erythritol (**21**).* To a solution of **20** (4.5 g, 16.9 mmol) in *N*,*N*-dimethylformamide (20 ml) was added sodium hydride (0.9 g) with stirring portionwise, and the mixture was kept at room temperature for 1 h. Benzyl chloride (3.2 g, 25.3 mmol) was further added dropwise to the above mixture with stirring, and the reaction mixture was stirred for 12 h, poured into water (50 ml), and then extracted with ether. The usual processing of the extract and purification of the product on a column of silica gel with 10:1:20 benzene–ethyl acetate–hexane gave **21** as a syrup in 68% (4.1 g) yield. $[\alpha]_D^{22}$ +2.8° (*c* 2.88); NMR: 7.3 (m, 10H, 2Ph), 4.53 and 4.57 (each s, 4H, $2CH_2Ph$), 4.30 (dd, 1H, $J_{3,4}$= 6.0, $J_{4,4'}$=8.0, H-4), 4.1—3.9 (m, 2H, H-3 and 4′), 3.49 and 3.56 (ABq, 2H, J=10.0, H-1 and 1′), 1.43 (s, 3H, CMe), 1.25 and 1.34 (each s, 6H, Ip).

Found: C, 74.18; H, 7.80%. Calcd for $C_{22}H_{27}O_4$: C, 74.13; H, 7.92%.

*1,2-Di-O-benzyl-2-C-methyl-D-erythritol (**22**).* A solution of **21** (3.65 g, 10.2 mmol) in acetic acid (70%, 30 ml) was stirred at room temperature for 72 h, diluted with water and then extracted with chloroform. The usual processing of the extract and purification of the product on a column of silica gel with 8:1 benzene–acetone gave **22** as a syrup in 84% (2.71 g) yield. $[\alpha]_D^{22}$ −7.5° (*c* 1.72); NMR: 7.3 (m, 10H, 2Ph), 4.52 (s, 4H, $2CH_2Ph$), 3.7—3.9 (m, 3H, H-3,4, and 4′), 3.55 and 3.60 (ABq, 2H, J=11.0, H-1 and 1′), 3.02 and 2.64 (each bs, 2H, 2OH), 1.30 (s, 3H, CMe).

Found: C, 71.60; H, 7.47%. Calcd for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65%.

*2,3-Di-O-benzyl-2-C-methyl-L-glyceraldehyde (**23**).* To a solution of **22** (388 mg, 1.23 mmol) in methanol (5 ml) was added a solution of sodium periodate (299 mg, 1.39 mmol) in water (5 ml), and the mixture was stirred at room temperature for 40 min, neutralized with sodium hydrogencarbonate, and then filtered. Methanol in the filtrate was evaporated and the water layer was extracted with ether. The usual processing of the extract gave **23** as a syrup in 95% (332 mg) yield. IR: 1730 (CHO); NMR: 9.69 (s, 1H, CHO), 7.3 (m, 10H, 2Ph), 4.50 and 4.55 (ABq, 2H, J=10.8, CH_2Ph), 4.51 (s, 2H, CH_2Ph), 3.61 and 3.67 (ABq, 2H, J=9.6, H-3 and 3′), 1.34 (s, 3H, CMe).

*2,3-Di-O-benzyl-2-C-methyl-L-glyceraldehyde Semicarbazone (**24**).* To a solution of **23** (200 mg, 0.7 mmol) in methanol (0.5 ml) was added semicarbazide hydrochloride (78.1 mg, 0.7 mmol), and the mixture was scrached with glass rod to produce crystals (193 mg, 80%) which were recrystallized from benzene. Mp 108—109 °C; $[\alpha]_D^{22}$ +13.2° (*c* 0.68); IR: 1690 (amide); NMR: 10.04 (s, 1H, NH), 7.3 (m, 10H, 2Ph), 7.16 (s, 1H, CH=N), 5.99 (s, 2H, NH_2), 4.50 and 4.39 (each s, 4H, $2CH_2Ph$), 3.54 (s, 2H, H-3), 1.41 (s, 3H, CMe).

Found: C, 66.29; H, 6.22; N, 12.54%. Calcd for $C_{19}H_{23}O_3N_3$: C, 66.84; H, 6.79; N, 12.31%.

*1-O-Benzoyl-3-O-benzyl-2,4-O-benzylidene-3-C-methyl-L-erythritol (**25**).* A solution of **18** (3.1 g, 9.4 mmol), dimethoxytoluene (1.71 g, 11.3 mmol), and catalytic amount of *p*-toluenesulfonic acid (170 mg, 0.89 mmol) in *N,N*-dimethylformamide (5 ml) was stirred at room temperature for 3 h, and then methanol produced was removed for 3 h under diminished pressure. The reaction mixture was neutralized with aqueous sodium hydrogencarbonate, evaporated, and the residual syrup was extracted with ether. The usual processing of the extract gave crystals which were recrystallized from methanol. Yield, 1.8 g (52%); mp 110—111 °C; $[\alpha]_D^{22}$ +58.4° (*c* 1.88); NMR: 8.1—7.9 and 7.6—7.2 (m, 15h, 3Ph), 5.57 (s, 1H, CHPh), 4.73 (dd, 1H, $J_{1,2}$=2.0, $J_{1,1'}$=11.6, H-1), *ca.* 4.52 and 4.57 (ABq, 2H, CH_2Ph), 4.42 (dd, 1H, $J_{1',2}$=8.4, H-1′), 4.41 and 3.87 (ABq, 2H, J=11.0, H-4 and 4′), 4.34 (dd, 1H, H-2), 1.60 (s, 3H, CMe).

Found: C, 74.92; H, 6.35%. Calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26%.

*3-O-Benzyl-2,4-O-benzylidene-3-C-methyl-L-erythritol (**26**).* A solution of **25** (1.3 g, 3.1 mmol) in methanol containing a catalytic amount of sodium methoxide was stirred at room temperature for 2 h, neutralized with 0.1 M hydrochloric acid, evaporated, and the resulting sirup was extracted with chloroform. The usual processing of the extract and purification of the product on a column of silica gel with 1:3 ethyl acetate–hexane gave pure **26** as a syrup in 93% (862 mg) yield. $[\alpha]_D^{22}$ +12.9° (*c* 1.46); NMR: 7.4 (m, 10H, 2Ph), 5.51 (s, 1H, CHPh), 4.44 and 4.56 (ABq, 2H, J=10.4, CH_2Ph), 3.6—4.3 (m, 5H, H-1,1′,3,4, and 4′), 2.18 (bs, 1H, OH), 1.53 (s, 3H, CMe).

Found: C, 72.43; H, 7.07%. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05%.

*3-O-Benzyl-2,4-O-benzylidene-3-C-methyl-L-erythrose (**28**).* To a solution of **26** (335 mg, 1.12 mmol) in DMSO (3 ml) containing catalytic amount of pyridine and phosphoric acid was added dicyclohexylcarbodiimide (500 mg), and the mixture was stirred at room temperature for 24 h, poured into ice–water, and extracted with ether. The usual processing of the extract and fractionation of the products on a flash column with 1:7 ethyl acetate–hexane gave **28** (91 mg, 27%), together with 3-*O*-benzyl-2,4-*O*-benzylidene-3-*C*-methyl-1-*O*-methylthiomethyl-L-erythritol (**27**: 100 mg, 25%) and the starting material (67 mg, 20%).

28: mp 81—82 °C; $[\alpha]_D^{22}$ +73.7° (*c* 0.93); IR: 1735 (CHO); NMR: 9.78 (s, 1H, CHO), 7.3 (m, 10H, 2Ph), 5.50 (s, 1H, CHPh), 4.88 and 4.64 (ABq, 2H, J=11.4, CH_2Ph), 4.33 (s, 1H, H-2), 3.86 and 4.12 (ABq, 2H, J= 10.2, H-4 and 4′), 1.60 (s, 3H, CMe).

Found: C, 73.09; H, 6.41%. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45%.

27: syrup; $[\alpha]_D^{22}$ +53.7° (*c* 0.3); NMR: 7.29 (m, 10H, 2Ph), 5.51 (s, 1H, CHPh), 4.67 (s, 2H, OCH_2S), 4.58 and 4.46 (ABq, 2H, J=12, CH_2Ph), 4.07 (t, 1H, $J_{1,2}=J_{1,1'}$= 10.0, H-1), 3.84 (dd, 1H, $J_{1',2}$=8.0, H-2), 4.00 and 3.82 (ABq, 2H, J=11.5, H-4 and 4′), 3.65 (dd, 1H, H-1′), 2.11 (s, 3H, SMe), 1.51 (s, 3H, CMe).

Found: C, 67.02; H, 6.95; S, 8.28%. Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 7.00; S, 8.56%.

*Methyl 3-O-Benzyl-3-C-methyl-α-L-erythrofuranoside (**29**) and Its β-Anomer (**30**).* A solution of **28** (110 mg, 0.35 mmol) in methanolic hydrogen chloride (1%, 3 ml) was refluxed for 3 h, neutralized with sodium hydrogencarbonate, evaporated, and the residue was extracted with chloroform. The usual processing of the extract and fractionation of the product on a preparative TLC with 1:5 ethyl acetate–hexane gave the corresponding α-(**29**: 4.1 mg, 4.9%, R_f 0.29) and β-glycosides (**30**: 34.7 mg, 41%, R_f 0.39) as syrups.

29: $[\alpha]_D^{22}$ −82.9° (*c* 1.03); NMR: 7.3 (m, 5H, Ph), 4.89 (d, 1H, J=4.8, H-1), 4.63 and 4.52 (ABq, 2H, J=11.0, CH_2Ph), 4.12 and 3.66 (ABq, 2H, J=9.8, H-4 and 4′), 3.84 (dd, 1H, $J_{2,OH}$=10.4, H-2), 3.48 (s, 3H, OMe), 3.00 (d, 1H, OH), 1.48 (s, 3H, CMe).

30: $[\alpha]_D^{22}$ +99.5° (*c* 1.74); NMR: 7.3 (m, 5H, Ph), 4.86 (d, 1H, J=2.4, H-1), 4.52 (s, 2H, CH_2Ph), 4.12 and 3.77 (ABq, 2H, J=10.1, H-4 and 4′), 3.79 (dd, 1H, $J_{2,OH}$= 7.8, H-2), 3.42 (s, 3H, OMe), 3.07 (d, 1H, OH), 1.50 (s, 3H, CMe).

Found for **30**: C, 65.32; H, 7.59, and for **31**: C, 65.20; H, 7.69%. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%.

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