and **2** arise from radical coupling[10] or radical displacement reactions, but evidence other than the isolation of **2** is not at hand at this time.

Experimental Section

The usual procedures[2,3] were used to obtain the results shown in Table II. An example follows.

Reaction of Ethyl Grignard Reagent and N-phenyl-N'-(*p*-toluenesulfonoxy)diimide N-Oxide.—To a solution of 5.84 g (20 mmoles) of the above tosylate in 100 ml of THF in a nitrogen atmosphere was added 8 ml of 3 *M* ethyl magnesium bromide in ether (Arapahoe Chemicals). The ether was swept out in the nitrogen stream and the solution was heated at 55° for 5 hr. After the usual hydrolysis procedure,[2] the organic residue was chromatographed on silica gel. Pentane–methylene chloride (2:1) eluted 0.57 g of N-phenyl-N'-ethyldiimide N-oxide; methylene chloride eluted 0.30 g of starting tosylate; and methylene chloride–ethyl acetate eluted 0.30 g of N-phenyl-N'-(2-tetrahydrofuryl)diimide N-oxide, a yellow oil.

(10) Such a mechanism would be similar to that reported for some carbon alkylations of nitro benzyl halides by 2-nitropropane salts: R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Am. Chem. Soc.*, **87**, 4520 (1966). We have not observed any significant amounts of radical coupling products in reactions of arylnitrosohydroxylamine tosylates or N'-fluorodiimide N-oxides and the lithium salt of 2-nitropropane. The N-fluoroazoxy materials did not react in these experiments, and, with the tosylate, 2,3-dimethyl-2,3-dinitrobutane (traces) appeared only at temperatures where thermal decomposition[9] may have given radical products.

Syntheses of 6-Deoxy-2,4-di-*O*-methyl-D-galactose (Labilose) and of 2,4-Di-*O*-methyl-D-galactose

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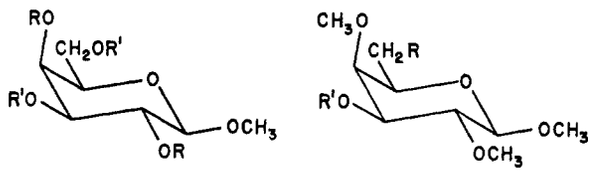
Labilomycin, an antibiotic which inhibits the growth of Gram-positive bacteria[2] and which is effective against certain tumor cells,[3] is produced by the microorganism *Streptomyces albosporeus*.[4] The antibiotic contains, as part of its structure,[5] a methylated sugar termed labilose, which has been shown[6] to be 6-deoxy-2,4-di-*O*-methyl-D-galactose. The preparation, in these laboratories, of methyl 3,6-di-*O*-mesyl-β-D-galactopyranoside (**1**)[7] (Chart I) in one stage from methyl β-D-galactopyranoside provided a convenient starting material for the synthesis of labilose.

Methylation of **1** gave methyl 3,6-di-*O*-mesyl-2,4-di-*O*-methyl-β-D-galactopyranoside (**2**)[7] which was reduced with lithium aluminum hydride in anhydrous tetrahydrofuran. Instead of the expected methyl β-D-labiloside, a mixture of methyl 2,4-di-O-methyl-β-D-galactopyranoside (**3**) and methyl 3,6-anhydro-2,4-di-*O*-methyl-β-D-galactopyranoside (**4**) was produced. The physical constants of both of these compounds agreed with those in the literature. The identity of **3** was confirmed by remesylation to the starting material (**2**). The synthesis of **3** as above, followed by hydrolysis to the free sugar, gave an alternative synthesis to that of Jeanloz[8] for 2,4-di-*O*-methyl-D-galactose which has been isolated several times[9-11] from the hydrolysis of methylated polysaccharides.

An attempt to prepare methyl 2,4,6-tri-*O*-methyl-β-D-galactopyranoside by treatment of **2** with sodium methoxide in methanol, as previously described,[12,13] gave a mixture of compounds indicating that nucleophilic attack at the C-6 atom is inhibited.[14] A similar inhibition would account for the results obtained in the above reduction.

The synthesis of methyl β-D-labiloside was accomplished by reduction of the intermediate 6-iodo compound. Treatment of **2** with sodium iodide in boiling methyl ethyl ketone effected displacement of the 6-mesyloxy group. Methyl 6-deoxy-6-iodo-3-*O*-mesyl-2,4-di-*O*-methyl-β-D-galactopyranoside (**5**) was isolated from the reaction mixture in 59% yield by silica gel column chromatography. Treatment of the 6-iodo derivative (**5**) with lithium aluminum hydride in anhydrous tetrahydrofuran gave crystalline methyl 6-deoxy-2,4-di-*O*-methyl-β-D-galactopyranoside (methyl β-D-labiloside) (**6**). The physical constants of **6** are in good agreement with those quoted by Akita, *et al.*,[6] for methyl β-D-labiloside.

CHART I



1 R = H, R' = SO_2CH_3 **5** R = I, R' = SO_2CH_3

2 R = CH_3, R' = SO_2CH_3 **6** R = R' = H

3 R = CH_3, R' = H

Hydrolysis of the glycoside with sulfuric acid gave 6-deoxy-2,4-di-*O*-methyl-D-galactose (labilose) (**7**) as a white crystalline product with mp 131–134° and $[\alpha]_D$ +86° (water). The recorded values for natural labilose are mp 129°, $[\alpha]^{27}_D$ +82° (water).[6] The enantiomorph of labilose, 2,4-di-*O*-methyl-L-fucose, has been synthesized by Gardiner and Percival[15] and had mp 131–132°, $[\alpha]^{18}_D$ −85° (water).

The lithium aluminum hydride reduction of **2** in ether–benzene gave **6** directly in 60% yield. This difference in product owing to change in solvent, has been noted previously for reductions of other carbohydrate derivatives.[16]

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Experimental Section[17]

Lithium Aluminum Hydride Reduction of 2 in Tetrahydrofuran.—A solution of **2** (0.54 g) in anhydrous tetrahydrofuran (30 ml) was heated at 50° with lithium aluminum hydride (0.30 g) for 24 hr. Excess hydride was destroyed with ethyl acetate and water. After filtration, the residue was washed with tetrahydrofuran, and the filtrate and washings were combined and concentrated to give a crystalline residue. Recrystallization from ethyl acetate gave methyl 2,4-di-*O*-methyl-β-D-galactopyranoside (**3**) (0.12 g), mp 166–169°, $[\alpha]^{25}D$ −4.8° (*c* 1.3, water). Smith[10] reported mp 165–166° and $[\alpha]D$ 0° (water) for methyl 2,4-di-*O*-methyl-β-D-galactopyranoside. The nuclear magnetic resonance (nmr) spectrum was consistent with that expected for **3**.

Anal. Calcd for $C_9H_{18}O_6$: C, 48.64; H, 8.16. Found: C, 48.87; H, 7.91.

Fractionation of the mother liquors on a silica gel column with ethyl acetate as eluent gave an additional 0.02 g of **3** and a faster moving component identified as methyl 3,6-anhydro-2,4-di-*O*-methyl-β-D-galactopyranoside (**4**) (0.06 g). This compound was purified by sublimation to give long white needles of mp 82°, $[\alpha]^{25}D$ −74° (*c* 0.7, water). Haworth, *et al.*,[18] reported mp 83° and $[\alpha]D$ −77° (water) for **4**.

2,4-Di-*O*-methyl-D-galactose.—A solution of **3** in 1.5 *N* sulfuric acid was heated at 95° for 6 hr, cooled, and passed through a column of Duolite A-4 (OH^-) ion-exchange resin. The resultant aqueous solution was concentrated to a syrup which on thin layer chromatography (tlc) (methyl acetate) showed some starting material as well as product. After chromatography on silica gel with methyl acetate as eluent, crystalline 2,4-di-*O*-methyl-D-galactose was obtained with mp 105–105.5°. An infrared spectrum of this compound was identical with that of authentic 2,4-di-*O*-methyl-D-galactose.[19]

Methyl 6-Deoxy-6-iodo-3-*O*-mesyl-2,4-di-*O*-methyl-β-D-galactopyranoside (**5**).—A solution of methyl 3,6-di-*O*-mesyl-2,4-di-*O*-methyl-β-D-galactopyranoside (**2**)[7] (1.6 g) and sodium iodide (1.3 g) in methyl ethyl ketone was boiled under reflux for 7 days. Sodium mesylate was removed by filtration and the filtrate concentrated to a syrup. The syrup was dissolved in chloroform and insoluble sodium iodide was removed by filtration. The filtrate was again concentrated to a yellow syrup (2.0 g) which was shown to be composed of one product plus starting material [tlc, chloroform–ethyl acetate (3:7)]. Fractionation of the mixture by silica gel column chromatography (same solvent system) gave **5** (1.1 g) and starting material (**2**) (0.6 g after recrystallization from ethanol). The product (**5**) was recrystallized from ethanol, mp 100–101.5°, $[\alpha]^{25}D$ +20° (*c* 1.5, chloroform). The infrared and nmr spectra were consistent with the proposed structure.

Anal. Calcd for $C_{10}H_{19}IO_7S$: C, 29.25; H, 4.65; I, 30.95; S, 7.80. Found: C, 29.55; H, 4.75; I, 30.58; S, 8.05.

Methyl 6-Deoxy-2,4-di-*O*-methyl-β-D-galactopyranoside (Methyl β-D-Labiloside) (**6**).—A solution of **5** (0.95 g) in anhydrous tetrahydrofuran (60 ml) was boiled under reflux with lithium aluminum hydride (0.70 g) for 7 hr. Excess lithium aluminum hydride was destroyed with ethyl acetate and water, and the residue was removed by filtration. The combined filtrate and washings were concentrated to yield a syrup which partially crystallized. Recrystallization from hexane gave **6** (0.12 g), mp 111°, $[\alpha]^{25}D$ −19° (*c* 1.3, chloroform).

Anal. Calcd for $C_9H_{18}O_5$: C, 52.41; H, 8.80. Found: C, 52.86; H, 8.97.[20]

6-Deoxy-2,4-di-*O*-methyl-D-galactose (Labilose) (**7**).—A solution of **6** (0.05 g) in 1 *N* sulfuric acid was heated at 95° for 3 hr, cooled, and neutralized with barium hydroxide. Barium sulfate was removed by filtration and the aqueous solution was concentrated to a syrup which was extracted with ether. Concentration of the ether extracts gave a syrup which crystallized on addition of hexane. Recrystallization from ether–hexane gave **7** (0.02 g), mp 131–134°, $[\alpha]^{25}D$ +94° (3 min) → +86° (final, water), $R_{glucose}$ 3.2 in 1-butanol–pyridine–water (10:3:3).

Anal. Calcd for $C_8H_{16}O_5$: C, 49.99; H, 8.39. Found: C, 50.25; H, 8.48.

Lithium Aluminum Hydride Reduction of 2 in Ether–Benzene.—A solution of **2** (0.54 g) and lithium aluminum hydride (0.30 g) in a mixture of ether (20 ml) and benzene (10 ml) was boiled under reflux for 24 hr. Tlc (ethyl acetate) indicated incomplete reaction. More lithium aluminum hydride (0.30 g) was added and the heating was continued for 48 hr. Tlc (ethyl acetate) now showed only methyl β-D-labiloside plus a trace of **4**. The product crystallized after the usual isolation procedure and was recrystallized from hexane to give **6** (0.18 g, 60%). This product was shown to be identical with **6** obtained by the previous procedure.

Registry No.—**7**, 10123-01-0; 2,4-di-*O*-methyl-D-galactose, 4301-53-1; **3**, 7801-09-4; **5**, 7801-10-7; **6**, 3006-40-4.

(17) All melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer and nmr spectra were recorded on a Varian A-60 spectrometer. Silica gel column chromatography was performed on a silica gel, grade 950, 60–200 mesh from the Davison Co., Baltimore 3, Md. The microanalyses were done by Mr. C. DiPietro and the nmr spectra by Mr. F. H. Bissett, both of these laboratories.

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(19) The authors wish to thank Professor J. K. N. Jones for a sample of 2,4-di-*O*-methyl-D-galactose.

(20) Repeated vigorous drying of the sharp-melting, chromatographically pure material failed to remove all of the occluded hexane (recrystallization solvent) as demonstrated by the nmr analysis and the slightly high carbon analysis.

An Improved Synthesis of 9-β(-D-Arabinofuranosyl)-2-chloroadenine[1]

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The 9-β-D-arabinofuranosyl derivative of 2-chloroadenine (**1**) was previously prepared by Reist and Goodman[2] in an over-all yield of ~20% by the fusion of D-xylofuranose tetraacetate with 2,6-dichloropurine followed by preferential ammonolysis of the 6-chloro group and conversion to the 3′,5′-*O*-isopropylidene derivative of 2-chloro-9-β-D-xylofuranosyladenine which was subsequently methanesulfonated in the 2′ position and the isopropylidene blocking group removed by treatment with aqueous acetic acid. The resulting 2′-methanesulfonate on treatment with sodium methoxide yielded 2-chloro-9-(2,3-anhydro-β-D-lyxofuranosyl)adenine which was converted to **1** on warming with sodium acetate in dimethylformamide. It has been pointed out[2] that the above indirect method of synthesis with an acylated carbohydrate moiety was made necessary by the directing influences stated in the trans rule,[3] wherein use of an acylated arabinofuranose derivative would be expected to yield the undesired α anomer in this instance. Continued interest in the biological activity of **1** prompted the investigation of an adaptation of the Glaudemans and Fletcher[4] synthesis of 9-(β-D-arabinofuranosyl)adenine, wherein the directive influences of participating acyl groups on the sugar component in the nucleoside synthesis were obviated

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