The Use of 1,3-Dithiane in a Regioselective Synthesis of a Novel 2-Alkyl-2-deoxy-D-arabinofuranose Branched-Chain Sugar

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Reactions of 1,3-dithiane with methyl 2,3-anhydro-5-*O*-trityl-α-D-ribofuranoside (**1a**) and methyl 2,3-anhydro-5-*O*-benzyl-α-D-ribofuranoside (**1b**) have been found to proceed in high yield and with completely regioselective nucleophilic attack at C_2. In the presence of sponge nickel catalyst, the dithiane adducts of **1a** and **1b** undergo facile dethiation to 2-deoxy-2-methyl-D-arabinofuranose sugars which are examples of a rare variety of fraudulent branched-chain sugars not readily available by chemical synthesis until now. In connection with this work a convenient new synthesis of **1b** was also developed.

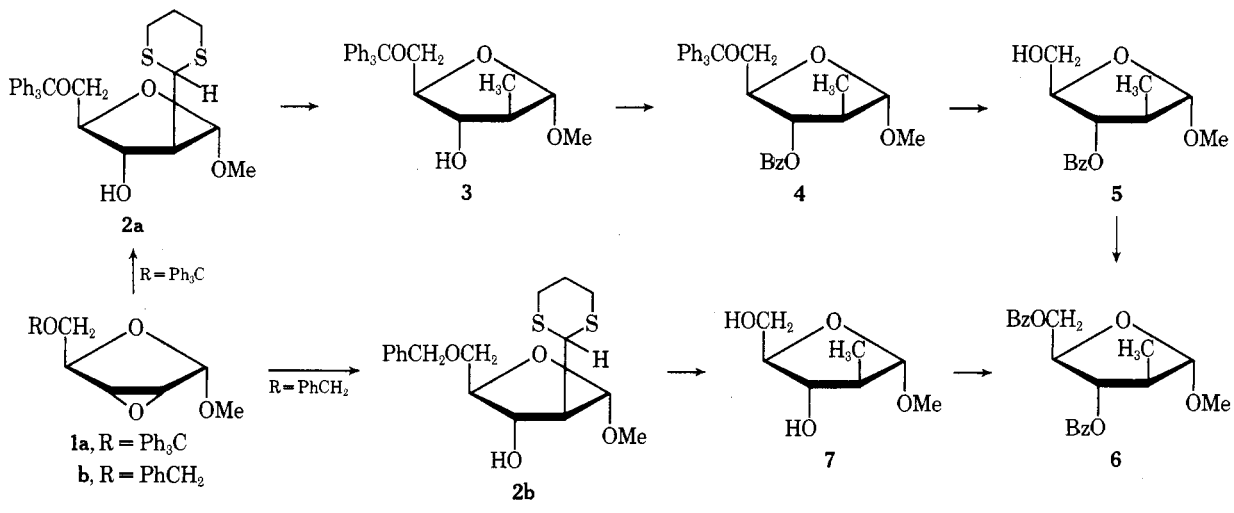
2-Alkyl-2-deoxypentofuranoses are a rare variety of fraudulent sugars which are of greatest synthetic interest as potential intermediates in nucleoside chemistry.[1,2] In this paper we wish to report the preparation of several heretofore unknown 2-deoxy-2-methyl-D-arabinofuranose derivatives by a method which takes advantage of the unexpected discovery that 1,3-dithiane adds to the epoxide ring in methyl 2,3-anhydro-5-*O*-trityl-α-D-ribofuranoside (**1a**)[3] and methyl 2,3-anhydro-5-*O*-benzyl-α-D-ribofuranoside (**1b**)[4] with completely regioselective attack at C_2, as shown in Scheme I. These results contrast sharply with the behavior of alkylmagnesium halides, which are known to give low yields and difficultly separable mixtures of 3-alkyl-3-deoxy and 2-alkyl-2-deoxy adducts on reaction with these 2,3-anhydro sugars.[5,6] The use of 1,3-dithiane offers a further advantage in that halohydrin by-products, a very significant source of difficulty in this and other Grignard reactions with epoxides,[7] cannot form. A number of papers describing the use of 1,3-dithiane with sugar epoxides[8] and ketones[9,10] have appeared in recent years, but this is the first instance in which this versatile reagent[11] has been employed successfully to cleave the epoxide ring in 2,3-anhydroribofuranose derivatives.

Addition of the 5-*O*-trityl derivative **1a** in tetrahydrofuran to a solution of 1,3-dithian-2-yllithium in tetrahydrofuran at −30 to −20 °C, followed by stirring at 0 °C for 4 days under a nitrogen atmosphere, produced an 86% yield of the adduct **2a** after column chromatography on silica gel. The presence of the dithianyl moiety in **2a** was evident from the NMR spectrum, which contained new signals at τ 7.8–8.2 and 7.0–7.4 characteristic of the $-S(CH_2)_3S-$ protons and a peak at τ 6.1 corresponding to the lone –SCHS– proton. The coupling constant of 1.5 Hz for the anomeric proton signal at τ 4.98 was consistent with trans stereochemistry for the C_1 and C_2 protons.

On being heated in the presence of sponge nickel catalyst, compound **2a** underwent dethiation to the 2-deoxy-2-methyl derivative **3** in 95% yield. The structure of **3** was apparent from its lack of identity with a sample of methyl 3-deoxy-3-methyl-5-*O*-trityl-α-D-xylofuranoside prepared for comparison via the method of Jenkins and Walton.[5] The NMR spectrum of **3** showed the expected C_2-Me signal at τ 9.0 (d, J = 7.5 Hz), and in addition revealed an upfield shift of the C_1-H signal to τ 5.42 (d, J = 1.5 Hz) which was consistent with loss of the dithianyl moiety. The deshielding effect of the dithianyl group on C_1 H was in agreement with results found by Sepulchre and co-workers[8] in the pyranose series, though the size of the shift was smaller in the furanose derivatives. Thus, **3** had to be a 2-deoxy-2-methyl derivative, and was in fact the same as the compound that Jenkins and Walton[5] had isolated but not fully characterized in their work on the reaction of methylmagnesium chloride with **1a.**

Esterification of **3** with benzoyl chloride in pyridine afforded **4** (97% yield), and removal of the 5-*O*-trityl group from **4** with acetic acid in refluxing methanol gave methyl 3-*O*-benzoyl-2-deoxy-2-methyl-α-D-arabinofuranoside (**5**, 76% yield) as an oil whose infrared spectrum contained the requisite aromatic ester peak at 1725 cm^{-1} and whose NMR spectrum showed the C_2-Me and C_1-H protons at τ 8.8 (d, J = 7.5 Hz) and 5.25 (d, J = 1.5 Hz), respectively. Esterification of **5** with benzoyl chloride in pyridine proceeded quantitatively, giving **6** as an oil with the expected infrared and NMR spectral properties. Although all the intermediates in the sequence **2a** → **6** were oils, they could be purified readily by column chromatogray on silica gel with mixtures of benzene

Scheme I



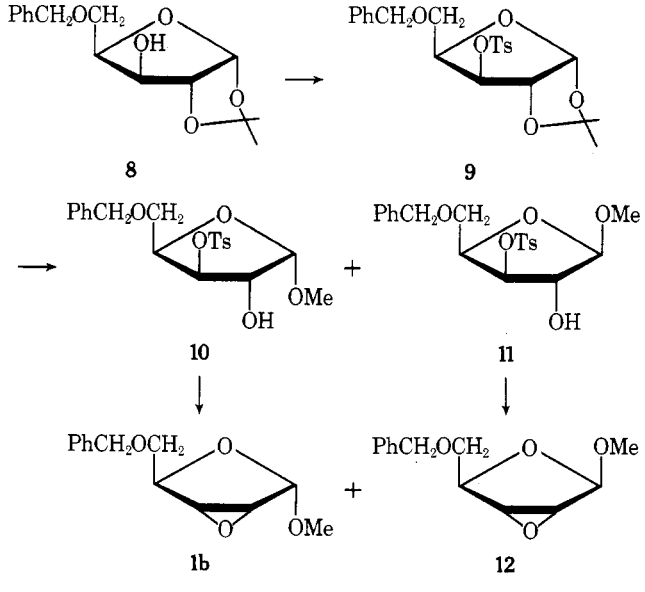
and ethyl acetate ranging in composition from 9:1 to 40:1 as eluents. The overall yield of **6** from **1a** (five steps) was 60%.

In a reaction analogous to the dithianylation of **1a**, the 5-*O*-benzyl derivative **1b** was converted to **2b** in 87% yield. The structure of **2b** was again evident from the NMR spectrum, which contained dithiane peaks at τ 7.8–8.2, 7.0–7.4, and 6.1, and a C_1-H proton signal shifted downfield to τ 4.98 (d, J = 1.5 Hz) by the neighboring dithiane moiety. Treatment of **2b** with sponge nickel in refluxing ethanol led to the desired dethiation, but also resulted conveniently in cleavage of the 5-*O*-benzyl group to give methyl 2-deoxy-2-methyl-α-D-arabinofuranoside (**7**) in 77% yield. The absence of a 5-*O*-benzyl group in **7** was apparent from its thin layer chromatographic behavior (development required pure ethyl acetate rather than benzene–ethyl acetate mixtures, and spots had to be visualized by exposure to iodine vapor since they could not be detected under ultraviolet light), and by the NMR spectrum, which contained the expected C_2-Me and C_1-H signals at τ 8.9 (d, J = 7.5 Hz) and 5.38 (d, J = 1.5 Hz), respectively, but showed no aromatic proton absorption. Diesterification of **7** with benzoyl chloride in pyridine gave a 96% yield of **6** which was indistinguishable from the material prepared via the 5-*O*-trityl epoxide **1a**. The overall yield of **6** starting from **1b** (three steps) was 64%.

Although epoxide **1b** is a known compound,[4] the method of its synthesis deserves some discussion. Wright and coworkers[4] prepared **1b** by 5-O-alkylation of methyl 2,3-anhydro-α-D-ribofuranoside with benzyl bromide and silver oxide in *N,N*-dimethylformamide. They obtained the starting epoxide via the classical six-step route of Anderson and coworkers,[12] which begins with 1,2-*O*-isopropylidene-D-xylofuranose and involves separation of the α- and β-anomeric products formed in the last step by fractional vacuum distillation.

We developed an alternative procedure for the synthesis of **1b** which is shorter by one step and avoids the need for fractional distillation. The latter point was especially advantageous for work on a preparative scale because we had previously witnessed considerable decomposition of the high-boiling α anomer when large batches of the mixed α- and β-anomeric epoxides were subjected to vacuum distillation. The synthesis of compound **1b** via this alternative route is shown in Scheme II. 1,2-*O*-Isopropylidene-D-xylofuranose was 5-*O*-tosylated and the tosyl derivative allowed to react with sodium benzylate in hot benzyl alcohol as described by Kuzuhara and Emoto[13] in order to obtain 5-*O*-benzyl-1,2-*O*-isopropylidene-D-xylofuranose (**8**), the starting point in Scheme II. The 3-hydroxy group in **8** was tosylated, the resultant product (**9**) subjected to acid-catalyzed methanolysis, and the mixture of α- and β-anomeric derivatives **10** and **11** treated with sodium methoxide to effect closure of the epoxide ring. Following separation of the anomeric products **1b** and **12** by column chromatography on silica gel, the yield of pure **1b** starting from compound **8** was 18%. This was significantly more than one can expect to obtain via the earlier route,[4] and there were fewer steps.

Scheme II



It is of interest to note that Anderson and co-workers[12] obtained a mixture of α- and β-anomeric products when they subjected 1,2-*O*-isopropylidene-5-*O*-methoxycarbonyl-D-xylofuranose to acetolysis followed by methanolysis, but the preponderant product had the β-anomeric configuration. This could be attributed to anchimeric assistance by the 2-acetoxy substituent, and Montgomery and Clayton[14] have in fact taken advantage of this phenomenon in developing a modified procedure which yields a β anomer exclusively. Whereas the use of a 5-*O*-methoxycarbonyl blocking group necessitates a separate acetolysis step prior to methanolysis (in order to achieve selective removal of the 1,2-*O*-isopropylidene group under mild conditions that leave the 5-*O*-methoxycarbonyl group intact),[12] the 5-*O*-benzyl derivative **8** can be methanolyzed *directly* because the 5-*O*-benzyl group is not affected by boiling 1% methanolic HCl. The stereochemical consequence of going from the 5-*O*-methoxycarbonyl to the 5-*O*-benzyl series is thus a significant one, in that the α/β anomeric ratio in the methanolysis step is no longer under the influence of a 2-acetoxy neighboring group.

The regioselectivity of 1,3-dithiane addition to epoxides **1a** and **1b** was not predictable a priori, and in fact we had expected by analogy with reactions of Grignard reagents[5,6] and other nucleophiles[3,12,15–17] with these epoxides that addition might take place partly, if not mainly, at C_3. The surprising lack of C_3 attack in both **1a** and **1b** is probably due to a steric effect, since the bulky dithiane molecule must approach the furanose ring from the β side where it encounters interference from the 5-*O*-trityl and 5-*O*-benzyl groups, respectively.

In summary, the work reported here offers further evidence of the usefulness of 1,3-dithiane as a synthetic reagent in sugar chemistry. The regioselectivity of attack at C_2 of the ribofuranose ring can be exploited in a number of ways. These might include, for example, the use of 2-substituted 1,3-dithianes or the conversion of the dithianyl moiety in the sugar adducts to a formyl group, which could then be elaborated into a variety of other side chain functionalities.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 137B double beam recording spectrophotometer, and NMR spectra were determined by means of a Varian T-60A instrument, tetramethylsilane being used as a reference standard. Thin layer chromatography was performed on 250-μ Analtech silica gel GF glass plates which were dried in an oven for 30 min prior to use. Spots were visualized under 254-nm ultraviolet light. Column chromatography was carried out on Baker 5-3405 silica gel (60–200 mesh). 1,3-Dithiane was obtained from Aldrich Chemical Co., Milwaukee, Wis., and 1,2-*O*-isopropylidene-D-xylofuranose was from Pfanstiehl Laboratories, Inc., Waukegan, Ill. Davison sponge nickel, the use of which in dethiation has been described previously in detail,[18] was obtained as a slurry in water from Monsanto Chemical Co., St. Louis, Mo., and was washed with ethanol prior to use. Microchemical analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Methyl 2-Deoxy-2-(1′,3′-dithian-2′-yl)-5-*O*-trityl-α-D-arabinofuranoside (2a). *n*-Butyllithium (17.8 ml of 2.3 M solution in hexane, 0.04 mol) was added with stirring, under a nitrogen atmosphere, to a solution of 1,3-dithiane (4.8 g, 0.04 mol) in dry tetrahydrofuran (50 ml) at −40 °C (bath temperature), and stirring was continued at −30 to −20 °C for 2.5 h. A solution of epoxide **1a** (1.94 g, 0.005 mol) in dry tetrahydrofuran (50 ml) was added dropwise with

continued cooling (−40 °C) and after 2 h at −30 to −20 °C the mixture was left to stir at 0 °C under nitrogen for 4 days, at which time TLC analysis showed complete absence of starting material. The reaction mixture was poured into ice water (200 ml), the product was extracted with ether (4 × 75 ml), and the combined ether extracts were washed with saturated sodium chloride (2 × 75 ml), dried over anhydrous magnesium sulfate, and evaporated. Chromatography of the oily residue on silica gel with 19:1 benzene–ethyl acetate gave an oily solid (2.1 g, 86%): ir (KCl) ν 3450 cm^{-1} (OH); NMR ($CDCl_3$) τ 7.8–8.2 (m, SCH_2CH_2), 7.0–7.4 (m, SCH_2CH_2), 6.6 (s, MeO), 6.4–6.6 (m, C_5 H), 6.1 (s, SCHS), 5.8–6.0 (m, C_2 H, C_3 H, and C_4 H), 4.98 (d, J = 1.5 Hz, C_1 H), 2.2–3.0 (m, aromatic protons).

Anal. Calcd for $C_{29}H_{32}O_4S_2$: C, 68.47; H, 6.34. Found: C, 68.46; H, 6.28.

Methyl 2-Deoxy-2-methyl-5-*O*-trityl-α-D-arabinofuranoside (3). A mixture of compound **2a** (1.6 g, 0.0032 mol) and Davison sponge nickel (45 g)[18] in absolute ethanol (450 ml) was stirred under reflux for 4 h, cooled to room temperature, and filtered. The filter cake was washed repeatedly with ethanol, and the combined filtrate and wash solutions were evaporated unde reduced pressure. The residue was dissolved in chloroform (300 ml), and a small amount of insoluble material was filtered off. Evaporation of the chloroform extract and chromatography of the oily residue on silica gel with 19:1 benzene–ethyl acetate gave compound **3** as a colorless glass (1.2 g, 95%): R_f 0.38 (9:1 benzene–ethyl acetate); NMR ($CDCl_3$) τ 9.0 (d, J = 7.5 Hz, C_2 Me), 7.8–8.0 (m, C_2 H), 6.4–7.0 (complex m, C_5 H), 6.6 (s, MeO), 5.8–6.1 (m, C_3 H and C_4 H), 5.42 (d, J = 1.5 Hz, C_1 H), 2.4–2.9 (m, aromatic protons).

Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.20; H, 6.88. Found: C, 77.15; H, 6.88.

Methyl 3-*O*-Benzoyl-2-deoxy-2-methyl-5-*O*-trityl-α-D-arabinofuranoside (4). Compound **3** (4.1 g, 0.01 mol) was dissolved in dry pyridine (82 ml), benzoyl chloride (2.6 ml) was added dropwise with stirring, and the mixture was stirred at room temperature overnight. A few drops of water were added to dissolve the dense precipitate of pyridine hydrochloride, the solution was poured into ice water (150 ml), and the product was extracted with three portions of chloroform. The combined organic layers were washed successively with water, cold 4% hydrochloric acid, and saturated sodium bicarbonate, rinsed again with water, dried over anhydrous magnesium sulfate, and evaporated to a syrup. On removal of the last traces of pyridine via repeated azeotropic distillation with toluene, compound **4** was isolated as an amber-colored glass (5 g, 97%): R_f 0.42 (40:1 benzene–ethyl acetate); ir (thin film) ν 1725 cm^{-1} (C=O).

Anal. Calcd for $C_{33}H_{32}O_5$: C, 77.93; H, 6.34. Found: C. 77.72; H, 6.38.

Methyl 3-*O*-Benzoyl-2-deoxy-2-methyl-α-D-arabinofuranoside (5). A solution of compound **4** (5 g, 0.01 mol) in acetic acid (35 ml), water (25 ml), and methanol (20 ml) was stirred under reflux for 16 h, cooled, and evaporated to dryness under reduced pressure. After removal of all the acetic acid by repeated azeotropic distillation with methanol, the residue was chromatographed on silica gel (120 g) with 19:1 benzene–ethyl acetate as the eluent. Compound **5** was isolated as a colorless oil (2 g, 76%): R_f 0.28 (4:1 benzene–ethyl acetate); ir (thin film) ν 1725 cm^{-1} (C=O); NMR ($CDCl_3$) τ 8.8 (d, J = 7.5 Hz, C_2 Me), 7.3–7.7 (m, C_2 H), 6.6 (s, MeO), 5.9–6.1 (broad s, C_5 H), 5.5–5.9 (m, C_4 H), 5.25 (d, J = 1.5 Hz, C_1 H), 4.9–5.1 (m, C_3 H), 1.8–2.7 (complex m, aromatic protons).

Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.33; H, 6.96.

Methyl 5-*O*-Benzyl-2-deoxy-2-(1′,3′-dithian-2′-yl)-α-D-arabinofuranoside (2b). Epoxide **1b** (1.2 g, 0.005 mol) was allowed to react with 1,3-dithian-2-yllithium (0.04 mol) in dry tetrahydrofuran as in the preparation of compound **2a**, except that the reaction mixture was stirred for 3 h at −30 to −20 °C and then for 3 days at 0 °C. Column chromatography on silica gel with mixtures of petroleum ether (bp 30–60 °C) and ether gave compound **2b** as a yellow oil (1.55 g, 87%): ir (thin film) ν 3500 cm^{-1} (OH); NMR ($CDCl_3$) τ 7.8–8.2 (m, SCH_2CH_2), 7.0–7.4 (m, SCH_2CH_2), 6.6 (s, MeO), 6.2–6.4 (m, C_5 H), 6.1 (s, SCHS), 5.7–5.9 (m, C_2 H, C_3 H, and C_4 H), 5.4 (s, $PhCH_2$), 4.98 (d, J = 1.5 Hz, C_1 H), 2.6 (aromatic protons).

Anal. Calcd for $C_{17}H_{24}O_4S_2$: C, 57.27; H, 6.79; S, 17.99. Found: C, 57.35; H, 6.84; S, 17.85.

Methyl 2-Deoxy-2-methyl-α-D-arabinofuranoside (7). Treatment of compound **2b** (0.7 g, 0.002 mol) directly with Davison sponge nickel in boiling ethanol for 5 h, as in the synthesis of compound **3**, gave **7** as a colorless oil (0.25 g, 77%) whose properties were consistent with simultaneous dethiation and de-O-benzylation: R_f 0.42 (ethyl acetate, spot visualized by exposure to iodine vapor); NMR ($CDCl_3$) τ 8.9 (d, J = 7.5 Hz, C_2 Me), 7.8–8.0 (broad m, C_2 H), 6.6 (s, MeO), 5.8–6.4 (broad m, C_3 H, C_4 H, and C_5 H), 5.38 (d, J = 1.5 Hz, C_1 H).

Anal. Calcd for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.88; H, 8.68.

Methyl 3,5-Di-*O*-benzoyl-2-deoxy-2-methyl-α-D-arabinofuranoside (6). Method A. A solution of compound **5** (2 g, 0.0075 mol) in dry pyridine (60 ml) was treated with benzoyl chloride (2 ml), the mixture was stirred at room temperature overnight and poured into ice water, and the product was extracted with several portions of chloroform and worked up as in the synthesis of compound **4**. After chromatography on silica gel (80 g) with 39:1 benzene–ethyl acetate as the eluent, compound **6** was isolated as a colorless oil (2.8 g, 100%): R_f 0.46 (19:1 benzene–ethyl acetate); ir (thin film) ν 1725 cm^{-1} (C=O); NMR ($CDCl_3$) τ 8.8 (d, J = 7.5 Hz, C_2 Me), 7.4–7.8 (m, C_2 H), 6.6 (s, MeO), 5.2–5.6 (complex m, C_4 H and C_5 H), 5.19 (d, J = 1.5 Hz, C_1 H), 4.9–5.1 (m, C_3 H), 1.8–2.8 (complex m, aromatic protons).

Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 68.01; H, 5.96).

Method B. Benzoyl chloride (1 ml) was added dropwise with stirring to a solution of diol **7** in dry pyridine (30 ml), and after overnight stirring at room temperature the mixture was worked up as in the synthesis of compound **4**. Chromatography on silica gel with 39:1 benzene–ethyl acetate as the eluent gave a colorless oil (0.5 g, 96%) whose ir and NMR spectra were indistinguishable from those of the product obtained by method A.

Methyl 2,3-Anhydro-5-*O*-benzyl-α-D-ribofuranoside (1b) and Methyl 2,3-Anhydro-5-*O*-benzyl-β-D-ribofuranoside (12). A solution of compound **8** (16.8 g, 0.06 mol)[13] and *p*-toluenesulfonyl chloride (15 g, 0.079 mol) in pyridine (102 ml) was heated at 60–70 °C for 6 h in a flask protected from moisture. The mixture was cooled and poured into ice water (500 ml), and the product was extracted with chloroform (4 × 100 ml). The combined organic layers were washed with ice-cold 1% sulfuric acid, rinsed to neutrality with water, dried over anhydrous magnesium sulfate, and evaporated to a brown syrup (20 g, 87%). A solution of this material (**9**, 50 g, 0.15 mol) in 1% methanolic hydrogen chloride (1200 ml) was refluxed for 5 h, cooled, neutralized carefully with sodium bicarbonate, filtered, and evaporated under reduced pressure. The residue was taken up in water and the solution extracted with chloroform (4 × 90 ml). The combined extracts were dried over anhydrous magnesium sulfate and evaporated to a brown syrup (44 g, 82%) consisting of a mixture of **10** and **11**. This mixture (44 g, 0.11 mol) was dissolved directly in dry methanol (67 ml), to which was then added an ice-cold solution of sodium methoxide (6.4 g, 0.12 mol) in methanol (56 mol). After 4 days in a stoppered flask at about 5 °C the mixture was treated with Celite (5 g) and filtered, the filter cake was washed with methanol, and the combined filtrate and washings were neutralized with glacial acetic acid and evaporated under reduced pressure. The residue was taken up in water and the solution extracted with chloroform (4 × 90 ml). The combined extracts were dried over magnesium sulfate and evaporated, and the residue was chromatographed on a silica gel column with mixtures of petroleum ether (bp 30–60 °C) and ether ranging in composition from 9:1 to 8:2. The separation of compounds **1b** and **12** was monitored by thin layer chromatography on silica gel, with 19:6 petroleum ether–ether as the developing solvent. The faster moving product (10.9 g, 43%) was compound **12**:[19] R_f 0.33; NMR $CDCl_3$) τ 6.7 (s, MeO), 6.2–6.5 (complex m, C_3 H, C_4 H, and C_5 H), 5.7 (dd, C_2 H), 5.5 (d, $PhCH_2$), 5.13 (s, C_1 H), 2.7 (s, aromatic protons).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83. Found: C, 65.92; H, 6.86.

The slower component (6.3 g, 25%) was compound **1b**:[4] R_f 0.14; NMR ($CDCl_3$) τ 6.5 (s, MeO), 6.2–6.6 (complex m, C_3 H, C_4 H, and C_5 H), 5.6 (t, J = 3.0 Hz, C_2 H), 5.5 (s, $PhCH_2$), 4.86 (s, C_1 H), 2.7 (s, aromatic protons).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.08; Found: C, 65.83; H, 6.79.

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Registry No.—**1a,** 40147-69-1; **1b,** 20187-72-8; **2a,** 59906-69-3; **2b,** 59906-70-6; **3,** 59906-71-7; **4,** 59906-72-8; **5,** 59906-73-9; **6,** 59906-74-0; **7,** 59906-75-1; **8,** 2592-42-9; **10,** 59906-76-2; **11,** 59906-77-3; **12,** 20535-09-5; 1,3-dithiane, 505-23-7; benzoyl chloride, 98-88-4; *p*-toluenesulfonyl chloride, 98-59-9.

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Polysaccharide Sequencing by Mass Spectrometry: Chemical Ionization Spectra of Permethyl Glycosylalditols[1]

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Chemical ionization (CI) mass spectra with isobutane and isobutane/ammonia as the reagent gases are reported for the six permethylated glucosylalditols and for two permethylated biosylalditols. Intense peaks corresponding to MH^+ or $(M + NH_4)^+$ were observed in all cases. In the isobutane CI spectra the ratio of abundances for the alditol ions that were formed by cleavage of the glycosidic bond on the alditol or glucosyl side of the glycosidic oxygen depended strongly on the position of the glycosidic linkage. When the linkage was 1→6, 1→2, 1→4, and 1→3 the ratio of intensities for the altitol$^+$ (A^+) and alditol hydrate$^+$ (AOH_2^+) ions were respectively 0.72, 0.37, 0.17, and 0.06. The fragmentation of a biosylalditol (**7**) was clearly consistent with the relative intensities for the A^+ and AOH_2^+ ions anticipated from the disaccharide results. The ratio of A^+ to AOH_2^+ was 0.16 for this 1→4 linked alditol.

Determination of the structure of oligosaccharides by mass spectrometry is directly analogous to the problem of sequencing polypeptides by the same technique. However, in the case of carbohydrates the details of the structure are considerably more subtle. Ideally one would like to obtain information about the molecular weight, subunit structure, and position sequence. Fortunately conventional techniques will give reliable information concerning subunit structure in unknown oligosaccharides. The information that must be obtained from the mass spectrum is thus reduced to molecular weight and structure and position sequence. Chemical ionization (CI) mass spectra of oligosaccharide peracetates using ammonia/isobutane[2] and isobutane[3] alone as reagent gases have been investigated in this regard.

The primary reagent ion in isobutane CI mass spectra is the *tert*-butyl cation ($C_4H_9^+$).[4] Proton transfer from this ion is considerably more exothermic than proton transfer from the ammonium ion or attachment of NH_4^+ to a molecule. The ammonium ion is the dominant reagent ion in ammonia/isobutane CI mass spectra.[2,5] The higher exothermicity of ionization in isobutane CI mass spectra results in extensive fragmentation of oligosaccharide peracetates so that the spectra resembled the electron ionization (EI) mass spectra of these molecules in many details.[3] In particular the intensity of ions with masses near the molecular weight of the molecule were quite low in both EI and isobutane CI mass spectra.

It has been possible to obtain sequence information from EI mass spectra of permethylated sugars.[6] The low intensity of the high mass ions is a distinct disadvantage in these cases and the high energies associated with the ionization process tend to cloud the structural information in the spectra.

Ammonia/isobutane chemical ionization mass spectra of oligosaccharide peracetates gave molecular weight and structure sequence information for di-, tri-, and tetrasaccharides.[2] The dominant fragment ions in these spectra corresponded to ammonium ion attachment to thermolysis fragments. The thermolysis fragments reliably produced information concerning the masses of the subunits and their sequence. However, it has not yet been possible to determine positions for the subunits in the chain from these spectra.

The permethyl derivatives of oligosaccharides are considerably less polar and more volatile than their acetate analogues. Thus it seemed reasonable to expect[2] that these derivatives might be used to give position sequence information in CI mass spectra. We have used the permethylated alditol derivatives because reduction of the carbonyl terminus of the oligosaccharide prior to methylation unequivocally tags the reducing end of the sugar for sequence analysis.

In this report we discuss the isobutane and ammonia/isobutane CI mass spectra of six permethylated glycosylalditols and two permethylated biosylalditols. The numerical designations, names, and molecular weights for these compounds are indicated in Table I.

Results and Discussion

Isobutane CI Spectra. The major ions in the isobutane CI mass spectra of the glucosylalditols, **1–6**, are presented in Table II. The most intense ion in every case corresponded to the protonated molecule. All six of the compounds in Table II showed very similar fragmentation patterns. Probable structures for the major ions and routes for their formation are illustrated for permethyl-2-*O*-β-D-glucopyanosyl-D-glu-