[CONTRIBUTION FROM THE DIVISION OF ORGANIC CHEMISTRY, SQUIBB INSTITUTE FOR MEDICAL RESEARCH]

The Partial Methylation of Methyl β-D-Xylopyranoside with Methyl Sulfate

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In connection with our study of O-tetramethylstreptamine[1] methyl trimethyl-β-D-xylopyranoside was needed. Instead of preparing this compound from β-methyl-D-xylopyranoside by the usual multiple treatment with methyl iodide and silver oxide,[2] we explored the use of the method of Holden and West[3] with dimethyl sulfate and sodium hydroxide which in other instances studied in our laboratory had given excellent yields of fully methylated sugars. However, the chloroform-extractable material obtained in a trial run amounted to only 20% of the starting product and consisted for the most part of a crystalline methyl dimethylxyloside m. p. 78°. The fully methylated product had evidently been lost by volatilization during the later stages (70–100°) of the reaction. By conducting the methylation under somewhat milder conditions in a closed vessel fitted with a reflux condenser there was obtained in good yield a mixture of methylated products the crystallizable part of which consisted again of the methyl dimethylxyloside m. p. 78°. The remainder could be conveniently and quantitatively separated into methyl 2,3,4-trimethyl-β-D-xyloside and dimethylated methyl xylosides by steam distillation.

The compound m. p. 78° was identified as methyl 2,4-dimethyl-β-D-xylopyranoside by the following reactions: On tosylation it yielded a monotosylate m. p. 76°, and on acid hydrolysis a crystalline dimethylxylose m. p. 118° which showed $[\alpha]_D$ −26° in chloroform and in water mutarotated to an equilibrium value of +24°, which is in the neighborhood of those reported for the sirupy 2,3- and 3,4-dimethyl-D-xyloses,[4,5] and the crystalline 2,4-dimethyl-β-D-xylopyranose[6] to be mentioned later. The phenylosazone (m. p. 158°) obtained from the dimethyl sugar contained only one methoxyl group, proving that the methyl group eliminated in its formation occupied position 2. The sugar was further characterized by the preparation of an anilide m. p. 157°, $[\alpha]_D$ −40° in ethyl acetate, which in ethyl acetate containing acetic acid attained an equilibrium rotation value of +85°. The sirupy dimethylxylonic lactone formed by bromine oxidation showed the characteristic fast mutarotation of a pyranolactone, and moreover on Purdie methylation yielded 2,3,-4-trimethylxylonic lactone. The dimethyl lactone was converted into two crystalline derivatives of the corresponding xylonic acid, namely, an amide m. p. 100° and a phenylhydrazide m. p. 144°. The amide was only very gradually attacked by periodic acid under conditions under which 2-tosyl-5-desoxyarabonamide[7] was readily cleaved. The phenylhydrazide consumed in rapid reaction 2 moles of periodic acid, but since a simple hydrazide, N-acetylphenylhydrazine, behaved in the same manner, it is clear that the xylose portion had remained unaffected. These findings, and the additional fact that the dimethylxylose itself proved to be inert toward periodate, show conclusively that the second methyl group in this compound occupies position 4.

It should be mentioned that a result seemingly inconsistent with the above conclusion was obtained in the periodate titration of the monomethylxylosazone derived from the dimethyl sugar. Since it is known that the phenylosazone grouping in glucosazone protects the linkage between carbon atoms 2 and 3 from cleavage by periodic acid,[7a] 4-methylxylosazone should not be attacked at all by this oxidant. Actually, a rapid uptake of periodate, which came to a standstill at between 1 and 2 molar equivalents, was observed. However, as it could be demonstrated that no formaldehyde is produced in this reaction, the 4-methyl structure is secure, and the observed uptake must be ascribed to an anomalous type of oxidation.

The methyl dimethylxyloside fraction remaining after steam distillation usually yielded additional small amounts of methyl 2,4-dimethyl-β-D-xyloside, and, on occasion, lower-melting crystalline products which were obviously mixtures containing the position-isomeric compounds. In one run the non-crystallizable part of the steam distillation residue was converted to a mixture of dimethylated xylonolactones. From the mutarotation characteristics of one of the lactone fractions it appeared that considerable amounts of the highly dextro rotatory 2,3-dimethyl-D-xylono-γ-lactone[4] were present. This was borne out by the fact that the sirupy amides prepared from the lactone mixtures rapidly consumed periodic acid equivalent to the presence of about 20% of the 2,3-dimethyl isomer.

In 1934 Robertson and Speedie[5] described a methyl dimethylxyloside (m. p. 61°, $[\alpha]_D$ −82°), to which they likewise attributed the methyl 2,4-dimethyl-β-D-xylopyranoside structure. They prepared this compound by a sequence of reactions involving first monotritylation of methyl β-

(1) O. Wintersteiner and A. Klingsberg, THIS JOURNAL, **70**, 885 (1948).

(2) A. Carruthers and E. L. Hirst, *J. Chem. Soc.*, **121**, 2299 (1922); F. P. Phelps and C. B. Purves, THIS JOURNAL, **51**, 2443 (1929).

(3) R. F. Holden and E. S. West, *ibid.*, **56**, 930 (1934).

(4) H. A. Hampton, W. N. Haworth and E. L. Hirst, *J. Chem. Soc.*, 1739 (1929).

(5) G. J. Robertson and T. H. Speedie, *ibid.*, 824 (1934).

(6) C. C. Barker, E. L. Hirst and J. K. N. Jones, *ibid.*, 783 (1946).

(7) J. Fried and D. Walz, unpublished results from this Laboratory.

(7a) E. Chargaff and B. Magasanik, THIS JOURNAL, **69**, 1459 (1947).

D-xylopyranoside, acetylation of the other two hydroxyl groups, replacement of the trityl by a nitrate group, deacetylation first with sodium methylate and then dimethylaniline, methylation according to Purdie, and finally reductive removal of the nitrate group with sodium amalgam. None of the intermediates except the diacetyl nitrate derivative were crystalline. The 2,4-position of the methylated hydroxyl groups in the final product was inferred from the fact that the monotosylate (m. p. 88°, $[\alpha]D$ −58.9° in chloroform) was not identical with either the monotosylate of the crystalline β-methyl-3,4-dimethylxylopyranoside described by the same authors, or with that of the sirupy methyl 2,3-dimethylxylopyranoside of Hampton, Haworth and Hirst.[4] Though it would appear from the rotation characteristics that the compound m. p. 61° belongs to the β-xylopyranoside series, a more direct proof for the location of the methylated hydroxyl groups would be desirable. Since neither the free sugar nor the lactone were prepared, any basis for correlating this product with compounds of known structure is lacking, so that the marked discrepancies between the melting points and rotations reported by Robertson and Speedie and those found by us cannot be explained at present. The possibility that our compound m. p. 78° is a mixture of dimethylated methyl xylopyranosides seems to be excluded by the fact that the lactone obtained from it directly by hydrolysis and oxidation, that is without isolation of the intermediate dimethylxylose, gave no evidence of being contaminated by either 2,3-dimethylxylono-γ-lactone[4] or 3,4-dimethylxylonolactone,[8] both of which exhibit quite different mutarotation characteristics.

On the other hand, there is little doubt that our dimethylxylose m. p. 118° is essentially identical with the 2,4-dimethylxylose m. p. 108° (equilibrium rotation in water +22°) which Barker, Hirst and Jones[6] obtained by methylation of methyl α,β-D-xylopyranoside with methyl iodide and thallous hydroxide. The structure of this product was deduced from the non-identity with the position-isomeric dimethylxyloses, the mutarotation of the lactone, and the negative Weerman test of the (sirupy) amide. The only other derivative reported by Barker, *et al.*, is the anilide, which showed a somewhat higher melting point (170°) and levorotation (−80°, in dioxane) than the anilide prepared by us. These differences are probably to be ascribed to the presence of a greater proportion of the α-anomer in our product, and the lower melting point of their dimethylxylose preparation can be similarly explained. On the other hand, the mutarotation data obtained on the respective lactones are in excellent agreement.

The findings of the British authors parallel ours also in that the 2,4-dimethyl isomer preponderated in the dimethylxyloside fraction. To explain the preferential formation of this isomer they reason that "the hydrogen atoms on the hydroxyl groups at C_2 and C_4 are most likely to be substituted since they are the greatest distance apart, and the thallium atoms in these positions are therefore least likely to interfere with each other." However, this concept is applicable only when, as in the procedure with thallous hydroxide, the metal salt of the starting glycoside is isolated prior to this reaction with the anhydrous methylating agent. In our case, where the reaction proceeded in aqueous sodium hydroxide solution and the hydroxyl groups of the glycoside were presumably in the charged anionic form, it is difficult to see how steric factors could have played any role in preventing salt formation at the third hydroxyl group in position 3. This group, since it is situated *trans* to the neighboring, more reactive, hydroxyl groups, does not appear to be subject to steric hindrance of any kind in the model. It would be interesting to ascertain by a similar study on methyl arabinoside whether the *cis* relationship of two hydroxyl groups in the pyranoside ring *per se* predisposes them to preferential attack by methylating agents.

(8) S. P. James and F. Smith, *J. Chem. Soc.* 739 (1945).

Experimental

Methylation of Methyl β-D-Xyloside.—A solution of methyl β-D-xyloside (m.p. 155°, $[\alpha]^{26}D$ −64.7° in water, 13.6 g.) in water (10 cc.) was placed into a 500-cc. 3-neck reaction flask equipped with a mercury-sealed stirrer, reflux condenser, thermometer and two dropping funnels. After the addition of methyl sulfate (36.8 cc.) and carbon tetrachloride (50 cc.) the mixture was warmed to 55°. During the following dropwise addition, with stirring, of 60% sodium hydroxide solution (163 cc.) this temperature was maintained by outside cooling and regulation of the dropping rate. After about half of this volume had been added, cooling could be dispensed with, and the remainder of the solution was added at a rate of 3 drops per second. (Toward the end slight warming may be necessary to maintain the temperature at 55°.) Methyl sulfate (65 cc.) was then added dropwise in such a manner that the temperature remained around 55° during this period also (cooling). After all of the reagent had been added stirring was continued for thirty minutes at 55°. The mixture was allowed to come to room temperature, and after addition of sufficient water (*ca.* 90 cc.) to dissolve the sodium sulfate, was extracted with 900 cc. of chloroform in ten portions. The combined extracts were dried and concentrated *in vacuo* to a small volume (*ca.* 15 cc.). Ligroin (b.p. 90–100°) was added in small portions to faint turbidity (50 cc.). The crystalline product obtained on standing in the refrigerator (2.64 g.) yielded on recrystallization from warm ligroin substantially pure **methyl 2,4-dimethyl-β-D-xyloside**, m.p. 76–78°[9]; yield 2.31 g. or 14.5%. One more recrystallization raised the melting point to 77.5–78.5° (constant); $[\alpha]^{24}D$ −70 ± 1° (*c*, 1.0 in chloroform).

Anal. Calcd. for $C_8H_{16}O_5$: C, 49.99; H, 8.39; OCH_3, 48.4. Found: C, 50.20; H, 8.60; OCH_3, 48.4.

The combined mother liquors were taken to dryness. The residue (*ca.* 12 g.) was dissolved in water (150 cc.) and subjected to steam distillation.[10] Exhaustive extraction of the steam distillate (320 cc.) with chloroform yielded a partly crystalline product (7.9 g.) which on recrystallization from ligroin melted at 47–49°. Further recrystallization yielded methyl **2,3,4-trimethyl-β-D-xylo-**

(9) All melting points were taken in the capillary and are corrected for stem exposure.

(10) Fractional distillation *in vacuo* was not practicable because the products crystallized in the efferent parts of the distillation vessel.

pyranoside[2] m.p. 49–50°, $[\alpha]^{24}D$ −73° (*c*, 0.765 in chloroform).

Anal. Calcd. for $C_8H_{16}O_5$: C, 52.41; H, 8.79; OCH_3, 60.2. Found: C, 52.57; H, 8.93; OCH_3, 59.9.

The glycoside was converted to 2,3,4-trimethyl-D-xylose[2], m.p. 88–91°, $[\alpha]^{27}D$ + 62.5° (*c*, 1.0 in chloroform), and further to 2,3,4-trimethylxylonolactone[11] m.p. 52–53°.

The products not volatile with steam (3.1 g.) were recovered by extraction with chloroform. The oily residue on seeding gave an additional small amount (520 mg.) of impure methyl 2,4-dimethylxyloside (m.p. 67–71°). The remainder was distilled *in vacuo* (100–110° (0.5 mm.)), and yielded 2.33 g. of a sirup consisting of mixed methyl dimethylxylosides ($[\alpha]^{26}D$ − 69°; OCH_3, found, 48.0; calcd., 48.4) which was hydrolyzed and oxidized to the mixture of lactones described further below.

In another methylation experiment carried out as described above, in which the yield of methyl 2,4-dimethylxyloside was 17.4%, the non-steam distillable fraction of the mother liquor material afforded a crystalline mixture of methyl dimethylxylosides (m.p. 55–58°, $[\alpha]D$ −65°; OCH_3, 49.2) accounting for an additional 22% of the starting material. Hydrolysis of this material gave a crystalline product, from which, however, only a small amount of impure 2,4-dimethylxylose (m.p. 108°) could be eventually obtained.

An attempt to increase the yield of pure 2,4-dimethyl isomer by conducting the methylation at 35–40° failed, as all the crystalline products isolated from the dimethylated fractions consisted of inseparable mixtures.

Methyl 2,4-Dimethyl-3-tosyl-β-D-xyloside.—To an ice-cold solution of methyl 2,4-dimethyl-β-D-xyloside (192 mg.) in pyridine (2.5 cc.) tosyl chloride (380 mg.) dissolved in chloroform (1 cc.) was slowly added. After standing at room temperature for forty-eight hours the product was recovered by chloroform extraction in the usual way. Crystallization of the oily residue (306 mg.) from ethyl acetate–hexane yielded plates (200 mg., m.p. 74–75°). The pure substance melted at 75–76°; $[\alpha]^{28}D$ + 28.8° (*c*, 1.06 in chloroform).

Anal. Calcd. for $C_{15}H_{22}O_7S$: C, 52.02; H, 6.40; S, 9.25. Found: C, 52.04; H, 6.59; S, 9.48.

2,4-Dimethyl-D-xylose.—A solution of methyl 2,4-dimethyl-β-D-xyloside (0.50 g.) in 0.6 *N* hydrochloric acid (13 cc.) was heated on the steam-bath till $[\alpha]^{26}D$ became constant at +23° (six hours). After removal of the chlorine ions with silver carbonate and of excess silver with hydrogen sulfide the solution was lyophilized. The partly crystalline residue (335 mg.), was recrystallized to constant melting point from ethyl acetate. 2,4-Dimethylxylose forms long fine needles melting at 116–118°; $[\alpha]^{25}D$ −26° (*c*, 0.95 in chloroform). A 3.0% solution in water showed $[\alpha]^{25}D$ +9.4° after five minutes and +24.7° after fifty minutes (constant).

Anal. Calcd. for $C_7H_{14}O_5$: C, 47.18; H, 7.92; OCH_3, 34.8. Found: C, 47.04; H, 7.82; OCH_3, 35.7.

An aqueous solution of the compound did not consume any periodate within a four-hour period. (Potassium paraperiodate was used in this and all other titrations.)

The anilide was prepared by refluxing a solution of the sugar (89 mg.) with aniline (623 mg.) in absolute ethanol (3 cc.) for two and one-half hours. The residue obtained after removal of the solvents was crystallized from ethyl acetate (0.7 cc.) and a few drops of pentane (23 mg., m. p. 144–145°). Two recrystallizations raised the melting point to 155–157°; $[\alpha]^{27}D$ −40° (*c*, 0.695 in ethyl acetate).

Anal. Calcd. for $C_{13}H_{19}O_4N$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.77; H, 7.61; N, 5.28.

A 0.74% solution in ethyl acetate containing 4% acetic acid showed rapid mutarotation from $[\alpha]^{27}D$ −7° (five minutes) to the equilibrium value +87° (two hours). The corresponding figures for another, independently prepared sample (m. p. 148–151°), $[\alpha]^{26}D$ −40° in ethyl acetate) were −56 and +85°, respectively.

4-Methyl-D-xylosazone.—2,4-Dimethyl-D-xylose (180 mg.) was dissolved in water (5 cc.), and acetic acid (0.25 cc.) and phenylhydrazine (0.5 cc.) were added. The solution was heated on a steam-bath for one and one-half hours while a slow stream of carbon dioxide was passed through it, and the water lost by evaporation was replaced from time to time. After cooling, the solution was extracted with benzene. The red oil obtained on evaporation of the dried benzene extract (454 mg.) could not be crystallized. It was dissolved in benzene and chromatographed on a column of acetic acid–washed alumina (1 × 20 cm.). After elution of pigmented amorphous material with benzene (300 cc.) and of some colorless crystalline material, probably acetylphenylhydrazine, with benzene–ether 3:1 (350 cc.), the crude osazone (153 mg.) was recovered by washing with benzene containing 3% of ethanol (250 cc.). Several recrystallizations from ethyl acetate–hexane 2:1 yielded small yellow needles melting at 158–158.5°; $[\alpha]^{26}D$ +25° → 0° (constant) in twenty-one hours (*c*, 0.91 in pyridine–ethanol 2:3).

Anal. Calcd. for $C_{18}H_{22}O_3N_4$: C, 63.14; H, 6.47; N, 16.4; OCH_3, 9.06. Found: C, 63.32; H, 6.56; N, 16.6; OCH_3, 10.24, 9.94.

For measuring the periodate consumption, weighed samples (*ca.* 4 mg.) of the osazone were dissolved in ethanol (5 cc.), and 0.0128 *M* aqueous potassium paraperiodate (5 cc.) was added. Aliquots (2 cc.) were withdrawn at intervals for the determination of the residual oxidizing capacity with 0.01 *N* thiosulfate. The total oxidizing capacity of the reagent in 50% ethanol was determined at the same intervals to eliminate possible errors due to the presence of the alcohol. The figures obtained in two different runs were not consistent. Molar equivalents consumed: (1) 0.67 (four min.); 0.86 (twenty-five min.); 1.05 (one and one-half hours, constant to nineteen hours); (2) 1.52 (four min.); 1.69 (forty-five min., constant to nineteen hours).

In order to ascertain whether or not formaldehyde was produced in the reaction the osazone (60 mg.) was treated with paraperiodic acid and the volatile products were tested with dimedon as described by Karrer and Pfaehler.[12] A reaction occurred, as evidenced by the formation of a yellow precipitate, but no formal-dimedon was obtained. Glucosazone (60 mg.) subjected to the same procedure gave 48% of formal-dimedone, m. p. 186–187°.

2,4-Dimethyl-xylonolactone.—The procedure of Haworth and Westgarth[11] for the oxidation of 2,3,4-trimethylxylose was employed, as 2,4-dimethylxylose proved to be rather resistant to bromine oxidation at room temperature. Methyl 2,4-dimethyl-β-D-xyloside (2.31 g.) was hydrolyzed with 3% hydrobromic acid (24 cc.) at 85° for one hour. Heating was continued for a total of ten hours at 75° while bromine (3.0 cc.) was added in small portions. The Fehling reaction at this point was only slightly positive. The reaction mixture was worked up in the usual manner by removal of the excess bromine by aeration and of the bromide ions with silver carbonate. The residue of the filtered solution was repeatedly extracted with dry ether. The extracted material (1.82 g.) was heated for two hours on the steam-bath to complete lactone formation, and then distilled at 105–125° (0.1 mm.), yielding 1.23 g. of a sirup ($n^{27}D$ 1.4652; OCH_3: Found, 35.1; calcd., 35.2). Mutarotation in water (*c*, 1.02): −13.2° (seven min.), −9.3° (fifty min.), −5.8° (three hours), +26.8° (twenty-four hours), +29.5° (forty-eight hours, constant), in good agreement with the data of Barker, Hirst and Jones[6] (−15° → +30°).

A portion (150 mg.) of the lactone was methylated with methyl iodide (10 cc.) and silver oxide (0.98 g.) in the usual way. Removal of the reagent and extraction of the residue with chloroform yielded a sirup (162 mg.) from which on crystallization from benzene–pentane 2,3,4-

(11) W. N. Haworth and G. C. Westgarth, *J. Chem. Soc.*, 880 (1926).

(12) P. Karrer and K. Pfaehler, *Helv. Chim. Acta*, **17**, 766 (1934).

trimethylxylonolactone (99 mg., m. p. 50–52°) was obtained. The purified product melted at 52–54° and did not depress the melting point of an authentic specimen.

2,4-Dimethyl-D-xylonamide.—The amide was prepared from the lactone (331 mg.) with methanol (5.0 cc.) saturated at 0° with ammonia. After standing for three days at room temperature the mixture was taken to dryness. Since the sirupy product could not be induced to crystallize, it was dissolved in water and treated with charcoal. The filtered solution was lyophilized, and the residue (309 mg.) extracted with warm ethyl acetate (10 cc.). The extract on cooling to room temperature deposited crystals (160 mg., m. p. 95–97°) which were purified by recrystallization from the same solvent; rods, m. p. 98–100°, $[\alpha]^{26}D$ + 51° (*c*, 1.00 in water).

Anal. Calcd. for $C_7H_{15}O_5N$: C, 43.51; H, 7.82; N, 7.25; OCH_3, 32.1. Found: C, 43.41; H, 7.56; N, 6.95; OCH_3, 32.2.

The amide consumed no periodate over a two-hour period, but after this time was attacked at a slow rate (0.14 and 0.83 molar equivalents after five and one-half and twenty-four hours, respectively).

2,4-Dimethyl-D-xylonic Acid Phenylhydrazide.—A mixture of the lactone (320 mg.) and phenylhydrazine (197 mg.) was heated on the steam-bath for one hour. Since the orange-colored, viscous product failed to crystallize, it was dissolved in ethylene chloride (5 cc.) and chromatographed on a small column of alumina (1 × 15 cm.). While washing with ethylene chloride (200 cc.) removed only pigmented impurities, the subsequent eluates with the same solvent containing 3% ethanol (150 cc.) and 10% ethanol (100 cc.) yielded the phenylhydrazide, which crystallized on addition of ethyl acetate. The combined crystalline material (363 mg., m. p. 142–144°) was recrystallized twice from the same solvent, blocks, m. p. 143.5–144.5°, $[\alpha]^{26}D$ + 47° (*c*, 0.98 in ethanol).

Anal. Calcd. for $C_{13}H_{20}O_5N_2$: C, 54.92; H, 7.09; N, 9.85; OCH_3, 21.8. Found: C, 54.73; H, 6.79; N, 10.14; OCH_3, 21.7.

The consumption of periodate was as follows (in molar equivalents): five min., 1.44; fifteen min., 1.80; four and one-half hours, 1.85; twenty-two hours, 1.99. Acetylphenylhydrazine behaved in a similar manner: five min., 1.62; twenty min., 1.78; three hours, 1.85; twenty hours, 2.17.

Lactone and Amide Fractions from Methyl Dimethylxyloside Mixture.—A portion (2.0 g.) of the mixture of methyl dimethylxylosides remaining after steam distillation (see above) was hydrolyzed and oxidized with bromine as described for the pure 2,4-dimethyl isomer, except that it was found necessary to employ larger amounts of bromine (6.5 cc.) and a longer heating period (twenty-six hours). The material finally recovered by ether extraction (1.3 g.) was heated at 75–80° at 12 mm. for one hour and then distilled fractionally *in vacuo*. Two main fractions were collected: I, 533 mg., b. p. 105–110° (0.05 mm.) and II, 469 mg., b. p. 125–130° (0.05 mm.). The mutarotation data were as follows: Fraction I (*c*, 1.14 in water): ten min., −5.3°; one hour, −4.2°; seven hours, −2.0°; twenty-four hours, +8.9°; thirty-four hours, +15.5°; fifty-four hours, +13.7. Fraction II (*c*, 0.99 in water): one hour, + 10.6°; four hours, +15.6; twenty-five hours, +34°; ninety-eight hours, +41° (constant).

The sirupy amides were prepared from both fractions in the usual fashion. Amide mixture II, but not I, gave on seeding with 2,4-dimethylxylonamide a small amount of crystalline material, which after purification melted at 93–95°. Both amide mixtures consumed periodate at a rapid rate:

Time		5 min.	3 hours	20 hours
Molar equivalents of	I	0.11	0.18	0.19
periodate consumed	II	.23	.22	.27

Since 2,3-dimethylxylonamide is the only isomer which should be attacked by periodate, the above figures may be taken as indicating the presence of about 20% of the corresponding methyl xyloside in the original mixture. This is also borne out by the high positive equilibrium rotation value of lactone fraction II, since 2,3-dimethyl-D-xylono-γ-lactone[4] is strongly dextrorotatory and mutarotates very slowly (+97° → + 86° (forty-eight hours) → +69° (384 hours)). Apparently Fraction II consisted mainly of a mixture of the 2,3- and 2,4-isomers (isolation of the amide of the latter), while the mutarotation data of Fraction I and the failure of the corresponding amide mixture to yield 2,4-dimethyl-xylonamide are consistent with the properties to be expected of a mixture containing mainly the 2,3- and 3,4-dimethyl isomers (3,4-dimethyl-D-xylonolactone[5] mutarotates from −56° to −27° in sixty-five hours).

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Summary

Methyl-β-D-xyloside on methylation with methyl sulfate yields besides methyl 2,3,4-trimethyl-β-D-xyloside a mixture of methyl dimethylxylosides, which can be conveniently separated from the trimethyl derivative by virtue of the fact that only the latter is volatile with steam. Methyl 2,4-dimethyl-β-D-xyloside m. p. 78°, which can be obtained in 15–20% yield directly from the reaction mixture, preponderates among the dimethylated compounds. It was identified by conversion, *via* the free sugar, to a monomethyl-D-xylosazone, and by the behavior toward periodate of the crystalline amide and phenylhydrazide of the corresponding xylonic acid. Indirect evidence for the occurrence also of the 2,3-dimethyl isomer in the dimethylated fraction is presented.

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