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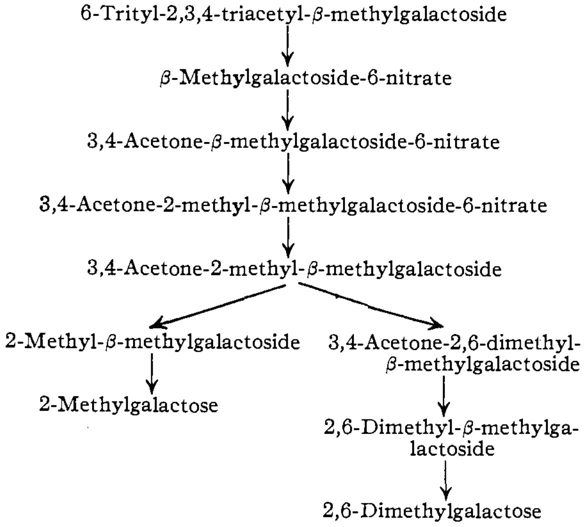
2-Methyl- and 2,6-Dimethylgalactose

BY JOHN WALTER HYDE OLDHAM AND DAVID JAMES BELL

For some years past, work in these Laboratories has required a knowledge of certain partially methylated derivatives of galactose. The preparation of 2,3-dimethylgalactose already has been described by Robertson and Lamb.[1] On this occasion, their work was repeated on the β-series and the same 2,3-dimethylgalactose was obtained and its identity confirmed by its conversion to 3-methylgalactosazone.

Greater interest, however, attaches to the results obtained by introducing an acetone residue into the 3,4-position of β-methylgalactoside, the β-form being chosen in view of the greater ease of crystallization displayed by compounds of this series. The preparation of monoacetone β-methylgalactoside as described by Micheel[2] was found to be attended by such practical difficulties as to render it unsuitable for large scale work. This difficulty, however, could be overcome by starting from a monosubstituted β-methylgalactoside A convenient compound was 6-trityl-2,3,4-triacetyl-β-methylgalactoside, which has been prepared by Müller.[3] Starting from this material, the scheme of reactions outlined below was carried out and crystalline compounds were obtained at each stage.



The constitutions of these substances were proved by the fact that the 2-methylgalactose gave a good yield of galactosazone and the 2,6-dimethyl galactose gave a good yield of 6-methylgalactosazone, both osazones being identified by mixed melting points with authentic specimens.

Experimental

β-Methylgalactoside-6-nitrate.—6-Trityl-triacetyl-β-methylgalactoside was prepared by Müller's method,[3] and was treated with 30% fuming nitric acid in chloroform at 0°. After five minutes, the chloroform solution was poured carefully into much crushed ice and water and the mixture was well shaken. The chloroform layer was removed and washed with ice-cold potassium bicarbonate solution until it was free from acid. After being dried over sodium sulfate, the solution was evaporated to dryness at a temperature not exceeding 50°. The residue, a mixture of triacetyl-β-methylgalactoside-6-nitrate and tritylcarbinol, was dissolved in benzene and the acetyl groups were saponified by the addition of sodium methoxide in sufficient methyl alcohol to keep the system homogeneous. After five minutes, the benzene solution was acidified with glacial acetic acid and extracted repeatedly with water until the extracts and the benzene solution showed no optical activity. It sometimes happened that a residual activity was observed in the benzene (which should contain nothing but the trityl residue), after the aqueous extracts had become inactive. When this activity was large, it was found advisable to dry the benzene layer again over sodium sulfate and to repeat the treatment with sodium methoxide and the extraction with water. The total extract was evaporated to dryness at a temperature not exceeding 50°. The residue was extracted with acetone and the solvent again evaporated below 50°. In this way 1.08 g. of β-methylgalactoside-6-nitrate was obtained from 1 g. of β-methylgalactoside, a yield of 87.8% of that theoretically obtainable. It crystallized from ethyl acetate in prisms melting at 106–107°. *Anal.* Calcd. for $C_7H_{13}O_8N$: OCH_3, 12.9; N, 5.86. Found: OCH_3, 12.8; N, 5.9. The substance showed $[\alpha]^{17}_D$ in ethyl alcohol $-5.0°$ for $c = 4.34$.

3,4-Acetone-β-methylgalactoside-6-nitrate.—β-Methylgalactoside-6-nitrate was dissolved in acetone containing 1% of dry hydrogen chloride and, after standing at 15–18° for twenty minutes, was poured into water containing an excess of ammonia and then extracted repeatedly with chloroform. The water layer was evaporated to dryness and the residue was again extracted with acetone. This treatment was repeated until the residue from the aqueous layer was negligible. The total chloroform solution was dried over sodium sulfate and evaporated to dryness at 100°. The product was recrystallized from methyl alcohol. In this way, 1.08 g. of β-methylgalactoside-6-nitrate gave 1.20 g. of needles melting at 103–104° and having $[\alpha]_D$ in chloroform $+0.0°$ for $c = 3.7$. *Anal.* Calcd. for $C_{10}H_{15}O_8N$: OCH_3, 11.1. Found: OCH_3, 11.0.

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[1] Robertson and Lamb, *J. Chem. Soc.*, 1321 (1934).
[2] Micheel, *Ber.*, **62**, 687 (1929).
[3] Müller, *ibid.*, **64**, 1820 (1931).

3,4-Acetone-2-methyl-β-methylgalactoside-6-nitrate.—On treating 3,4-acetone-β-methylgalactoside-6-nitrate with silver oxide and methyl iodide, a quantitative yield of the 2-methyl derivative was obtained. It crystallized from petroleum ether (b. p. 40–60°) in rhombs melting at 53–54°. *Anal.* Calcd. for $C_{11}H_{17}O_8N$: OCH_3, 21.3; N, 4.81. Found: OCH_3, 20.8; N, 4.87.

3,4-Acetone-2-methyl-β-methylgalactoside.—3,4-Acetone-2-methyl-β-methylgalactoside-6-nitrate was dissolved in alcohol. A considerable excess of a freshly prepared solution of sodium sulfide (made by saturating one half of a sodium hydroxide solution with hydrogen sulfide and adding the other half) was added and the mixture was boiled for twenty minutes during which it blackened. Water and potassium carbonate were added and the solution was extracted with chloroform until the extracts were inactive. On evaporation of the chloroform extracts 8.3 g. of crystalline compound was obtained from 10.2 g. of starting material, the yield being 96.5% of the theoretical amount. The product was recrystallized from a mixture of ether and petroleum ether (b. p. below 40°), in rosets of prisms melting at 75–76° and having $[\alpha]^{17}_{\mathrm{D}}$ in chloroform +7.16° for c = 4.0. *Anal.* Calcd. for $C_{11}H_{18}O_6$: OCH_3, 25.0. Found: OCH_3, 24.99.

2-Methyl-β-methylgalactoside.—A 5% solution of 3,4-acetone-2-methyl-β-methylgalactoside was made in water containing 5% acetic acid and the mixture was boiled until the rotation was constant. The solution was evaporated to dryness and the product, after recrystallization from ethyl acetate, was obtained in the form of needles which melted at 131–132° and showed $[\alpha]^{17}_{\mathrm{D}}$ in water +1.69° for c = 11.25. The yield was almost quantitative. *Anal.* Calcd. for $C_8H_{16}O_6$: OCH_3, 29.8; C, 46.15; H, 7.69. Found: OCH_3, 29.0; C, 46.0; H, 7.73.

2-Methyl-β-galactose.—Two grams of 3,4-acetone-2-methyl-β-methylgalactoside was boiled with 20 cc. of 5% hydrochloric acid and the specific rotation changed from 5.7° to a constant value of 92.3°, allowing for change in concentration. The solution was neutralized with pure lead carbonate, filtered and evaporated to dryness. The residue was extracted with boiling alcohol and the solvent was thereafter removed by evaporation at 100°. The product crystallized from ethyl alcohol in prisms or stout needles melting at 147–149°. The rotation in water changed from +53.0° after five minutes to a constant value of +82.6° after 2970 minutes, the concentration being 4.77. Further crops were obtained from the mother liquors. The yield was good. In view of the upward mutarotation, the β-configuration was assigned to the compound. *Anal.* Calcd. for $C_7H_{14}O_6$: OCH_3, 15.9; C, 43.3; H, 7.2. Found: OCH_3, 16.0; C, 43.1; H, 7.4.

Treatment of this substance with phenylhydrazine gave a good yield of an osazone melting at 200–202°. A mixture of the substance with galactosazone melted at the same temperature.

3,4-Acetone-2,6-dimethyl-β-methylgalactoside.— Methylation of 3,4-acetone-2-methyl-β-methylgalactoside with silver oxide and methyl iodide gave a product, which was recrystallized from petroleum ether (b. p. 40°), in the form of needles melting at 56–57° and showing $[\alpha]_{\mathrm{D}}$ in chloroform −4.46° for c = 6.95. *Anal.* Calcd. for $C_{12}H_{22}O_6$: OCH_3, 35.5. Found: OCH_3, 35.4.

2,6-Dimethyl-β-methylgalactoside.—3,4-Acetone-2,6-dimethyl-β-methylgalactoside was hydrolyzed in the manner already described for the hydrolysis of 3,4-acetone-2-methyl-β-methylgalactoside. The crude product crystallized from ether in needles melting at 45–46.5° and showing $[\alpha]^{17}_{\mathrm{D}}$ in chloroform −23.3° for c = 5.95. *Anal.* Calcd. for $C_9H_{18}O_6$: OCH_3, 41.9. Found: OCH_3, 41.8.

2,6-Dimethylgalactose.—3,4-Acetone-2,6-dimethyl-β-methylgalactoside was hydrolyzed by boiling with 2.5% hydrochloric acid until the rotation remained constant at 87° allowing for the change in concentration. The solution was neutralized with lead carbonate, filtered and evaporated to dryness. The residue was extracted with acetone and, on removal of the solvent, a sirup was obtained. This rapidly crystallized and, on being recrystallized, from dry ethyl acetate, separated in the form of stout needles melting at 128–130°. As an aqueous solution displayed upward mutarotation, changing from +46.8° after five minutes to a constant value of +87.5° after nine hundred and eighty-five minutes, the concentration being 6.25, the β-configuration was assigned to the compound. *Anal.* Calcd. for $C_8H_{16}O_6$: OCH_3, 29.28; C, 46.15; H, 7.69. Found: OCH_3, 29.5; C, 45.90; H, 7.60. Treatment with phenylhydrazine yielded a monomethylosazone which melted at 204–205°. A mixture of this compound and 6-monomethylgalactosazone, prepared as described by Freudenberg,[4] melted at the same temperature.

2,6-Dimethyl-β-methylgalactoside-3,4-dinitrate.—The low melting point of 2,6-dimethyl-β-methylgalactoside renders it unsuitable as a reference compound. It was treated with 30% fuming nitric acid in dry chloroform for ten minutes and then isolated in the manner already described. On evaporating the chloroform solution, a dinitrate was obtained and this crystallized from methyl alcohol in the form of needles melting at 88–88.5° and showing $[\alpha]^{17}_{\mathrm{D}}$ 3.47° for c = 6.9. *Anal.* Calcd. for $C_9H_{16}O_{10}N_2$: N, 8.97. Found: N, 8.76.

4,6-Benzylidene-β-methylgalactoside.—This compound was prepared from β-methylgalactoside by Freudenberg's method.[5] The yield was poor. The product crystallized from alcohol in needles melting at 200° and having $[\alpha]_{\mathrm{D}}$ in chloroform −35.1° for c = 2.0. *Anal.* Calcd. for $C_{14}H_{18}O_6$: OCH_3, 11.0. Found: OCH_3, 10.9.

4,6-Benzylidene-2-methyl-β-methylgalactoside.—2-Methyl-β-methylgalactoside was treated with benzaldehyde under Freudenberg's conditions.[5] The product separated from alcohol in needles melting at 169–170° and showing $[\alpha]^{17}_{\mathrm{D}}$ in chloroform −59.4°. *Anal.* Calcd. for $C_{15}H_{20}O_6$: OCH_3, 20.9; C, 60.8; H, 6.7. Found: OCH_3, 20.8; C, 60.5; H, 6.9.

4,6-Benzylidene-2,3-dimethyl-β-methylgalactoside.—Methylation of both 4,6-benzylidene-β-methylgalactoside and 4,6-benzylidene-2-methyl-β-methylgalactoside, with methyl iodide and silver oxide, yielded the same dimethyl derivative. It crystallized from a mixture of ether and petroleum ether (b. p. 60–80°), in needles melting at 148° and having $[\alpha]_{\mathrm{D}}$ in chloroform +18.0°. *Anal.* Calcd. for $C_{16}H_{22}O_6$: OCH_3, 30.0. Found: OCH_3, 30.0.

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[4] Freudenberg, *Ber.*, **59**, 100 (1926).

[5] Freudenberg, *ibid.*, **61**, 1750 (1928).

2,3-Dimethylgalactose.—4,6-Benzylidene-2-methyl-β-methylgalactoside was boiled with 8% aqueous hydrochloric acid for three-quarters of an hour. The system was neutralized with barium carbonate, evaporated to dryness and the residue was extracted with acetone. When the solution was evaporated, a sirup was obtained. This product, on treatment with phenylhydrazine, yielded an osazone melting at 176–179°. A mixture of this compound and a specimen of 3-monomethylgalactosazone prepared by Robertson and Lamb[1] melted at the same temperature.

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Summary

The present paper describes the preparation and properties of 2-monomethylgalactose and 2,6-dimethylgalactose and their respective β-methylgalactosides. In addition, benzylidene-β-methylgalactoside and its methylated derivatives are described.

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Oxidation in the Terpene Series. I. Action of Lead Tetraacetate and of Red Lead and Acetic Acid on Pinene, Dipentene, alpha-Terpinene and Terpinolene

BY KYLE WARD, JR.

The action of lead tetraacetate on the double bond has been studied by Criegee,[1] who found the product to be a mixture of acetates derived partly from the glycols obtained by hydroxylation of the double bond and partly from unsaturated alcohols in which a hydrogen in the beta-position to the double bond has been oxidized. In some cases dehydrogenation may occur, while in others the acetates are oxidized further to glycolic acid esters.

In Criegee's paper he predicted for the simpler terpenes a behavior similar to that of cyclohexene. However, his own findings show such marked differences in the behavior of different unsaturated compounds in this reaction that a study of the terpenes does not seem out of place. As will be seen later, his prediction holds good in a general way although the complex nature of the terpenes causes certain differences.

The present paper describes the general action of this reagent on four common terpenes: pinene, dipentene, alpha-terpinene and terpinolene. The main products, which are being further investigated, are shown to be acetates of mono-alcohols of the general formula $C_{10}H_{15}OH$ and of glycols of the formula $C_{10}H_{16}(OH)_2$.

To eliminate separate preparation and isolation of the lead tetraacetate, a modified procedure was investigated. The terpene was dissolved in acetic acid and oxidized by means of red lead. Here the lead tetraacetate formed from red lead and acetic acid may be expected to react at once with the terpene. Very similar products are formed in this way to those formed by the lead tetraacetate oxidation. The ratio of low-boiling to high-boiling acetates is much higher when lead tetraacetate is used, however, and there is some evidence that the products may differ in some cases, because the ester number of the higher-boiling acetate fraction is generally higher where lead tetraacetate is used. Such differences are to be expected because a number of factors differ where red lead and acetic acid are used. Some of these factors include the acidity of the solution, the introduction of water from the reaction of red lead and acid, and the presence of a solid phase with each addition of red lead.

Moreover, inactive sobrerol (pinol hydrate) was definitely identified as the main product from the oxidation of pinene with red lead and acetic acid, whereas it is obtained with lead tetraacetate only in acetic acid solution and then in low yield.

All of the esters, as well as the products obtained from them, are liquid, excepting the pinol hydrate previously mentioned. They are colorless or pale yellow in color and are usually very fragrant. The odor of lower esters resembles that of the esters of known terpene alcohols, such as bornyl and menthyl acetates. The higher esters have a much fainter odor.

The purpose of this preliminary work did not touch on the mechanism of the reaction, but there are a few points which may be mentioned, although further work must be done to clear them

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(1) Criegee, *Ann.*, **481**, 263 (1930).