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Crystalline Triphenylmethyl Derivatives of β-Methyl-d-xyloside[1]

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In a previous paper[2] it was reported, principally from polarimetric changes, that triphenylmethyl chloride reacts with β-methyl-*d*-xyloside in dry pyridine solution. As stated, this reaction receives an explanation only on the basis that (1) triphenylmethyl chloride may react with secondary hydroxyl groups, which is contrary to the views of most investigators,[3] or (2) that a ring shift occurs in the condensation reaction or (3) that β-methyl-*d*-xyloside does not possess the 1,5-ring structure generally accepted. The further investigation of this reaction has led to the isolation of two crystalline isomeric di-triphenylmethyl-β-methyl-*d*-xylosides and two crystalline di - acetyl - mono - triphenylmethyl - β - methyl-*d*-xylosides, which are now described.

The first di-triphenylmethyl-β-methyl-*d*-xyloside, which is separated readily from the second isomer by recrystallization from alcohol, melts at 238–240° (corr.) and shows $[\alpha]_D^{20}$ −55.5° in pyridine, while the second isomer melts at 162.5–163° (corr.) and shows $[\alpha]_D^{20}$ −22.5° in pyridine. Although a crystalline mono-triphenylmethyl-β-methyl-*d*-xyloside has not been obtained, the acetylation of the sirupy portion of the reaction product has yielded two crystalline isomeric diacetyl - mono - triphenylmethyl - β - methyl-*d*-xylosides, the first isomer melting at 169–170° (corr.) and showing $[\alpha]_D^{20}$ −15.7° in chloroform, while the second isomer melts at 125–127° (corr.) and shows $[\alpha]_D^{20}$ −49.1° in chloroform. These results show clearly that triphenylmethyl chloride has entered into reaction with the secondary hydroxyl groups in the β-methyl-*d*-xyloside molecule and that under the conditions of our experiments this reagent is not specific for primary hydroxyl groups. The reaction was carried out at 20° over a period of fourteen days or at 100° for a shorter time.

We wish to express our thanks to Dr. F. H. Goldman of this Laboratory who has kindly made combustions and methoxyl analyses of the compounds.

(1) Publication authorized by the Surgeon General of the U. S. Public Health Service.

(2) Hockett and Hudson, THIS JOURNAL, **53**, 4456 (1931).

(3) Helferich and Becker, *Ann.*, **440**, 1 (1924); Helferich, Moog and Jünger, *Ber.*, **58**, 872 (1925); Josephson, *Ann.*, **472**, 230 (1929); *Ber.*, **62**, 313 (1929); Pacsu, THIS JOURNAL, **53**, 3099 (1931); F. Valentin, *Coll. Czechoslov. Chem. Comm.*, **3**, 499 (1931). Compare Oldham and Rutherford, THIS JOURNAL, **54**, 366 (1932).

Experimental Part

A solution of 26.5 g. of pure β-methyl-*d*-xyloside ($[\alpha]_D^{20}$ −65.6° in water) and 66 g. of triphenylmethyl chloride in 220 cc. of pure dry pyridine was kept at 20° for fourteen days, when the rotation had become practically constant. Distilled water was added dropwise until the crystals which had separated were nearly dissolved, the turbid solution was seeded with triphenylcarbinol and cooled in ice water for three hours. The crystals were filtered off, washed first with 95% pyridine and then with distilled water, the pyridine washing being combined with the mother liquor. The dried crystals (15.5 g.) were identified as triphenylcarbinol by the melting point of 161–162° and a mixed melting point with authentic triphenylcarbinol. Another crop of triphenylcarbinol (10 g.) was separated from the filtrate by adding distilled water to turbidity, seeding with triphenylcarbinol and cooling in the refrigerator for several hours. The mother liquor was poured into about 3500 cc. of ice water, which precipitated a gum. After standing in the refrigerator for several days the aqueous layer was decanted and the gum was washed thoroughly with distilled water. It was dissolved in 250 cc. cold 95% alcohol and after starting crystallization by scratching and shaking, it was kept at about 25° for two days with occasional shaking and the crystals were filtered off, washed with cold 95% alcohol and dried in an evacuated desiccator over calcium chloride. The crystals weighed 6.8 g. and gave $[\alpha]_D^{20}$ −26.7° in pyridine. A second crop of crystals (1.3 g.) was obtained from the filtrate by adding distilled water to turbidity and allowing the solution to evaporate spontaneously for about ten days with occasional stirring. Since the remainder of the product showed little tendency to crystallize, the solvent was distilled off under reduced pressure and the residual sirup was acetylated as described under isomeric di-acetyl-mono-triphenylmethyl-β-methyl-*d*-xylosides. The crystalline material was shown to be a mixture of two isomeric di-triphenylmethyl-β-methyl-*d*-xylosides, which were separated readily by a fractional crystallization from absolute ethyl alcohol. Most of the first isomer separated from the alcohol solution in the first crop as small well-developed square or rectangular prisms which weighed 0.8 g. and melted at 229–234°. The second isomer constituted the bulk of the material and was easily separated from the small amount of the first isomer remaining in the mother liquor. One recrystallization of the first isomer from 95% alcohol gave characteristic colorless prisms which, after drying to constant weight in a high vacuum at 80°, melted at 238–240° (corr.) and showed $[\alpha]_D^{20}$ −55.5° in pyridine (0.2386 g. of substance, 25 cc. of solution in pyridine, 2-dm. tube; rotation, 1.06° to the left). Although the quantity of the first isomer available was not sufficient to recrystallize further, the large difference in solubility of the two isomers

in alcohol makes it probable that it was obtained pure. The triphenylmethyl group was determined by the method of Valentin.[3] The sample (0.1384 g.) was dissolved in 2 cc. of sulfuric acid (sp. gr. 1.84), the solution was poured quickly into 50 cc. of distilled water and left for thirty minutes. The triphenylcarbinol was collected on a weighed Gooch crucible, washed with distilled water and dried to constant weight at 110°. The yield of triphenylcarbinol was 0.1106 g. or 99.6% of the amount calculated for di-triphenylmethyl-β-methyl-*d*-xyloside.

Anal. Calcd. for $C_{44}H_{40}O_5$: C, 81.44; H, 6.22. Found: C, 81.06; H, 6.30.

The first isomer is soluble in warm chloroform, difficultly soluble in cold pyridine, slightly soluble in hot absolute alcohol and cold ether and insoluble in water.

The second isomer, after recrystallization to constant rotation from absolute alcohol and drying to constant weight in a high vacuum at 76°, melted at 162.5–163° (corr.) and gave $[\alpha]_D^{20}$ −22.5° in pyridine (0.2772 g. of substance, 25 cc. of solution in pyridine, 2-dm. tube; rotation, 0.50° to the left). In a triphenylmethyl analysis 0.1370 g. of substance gave 0.1088 g. of triphenylcarbinol or 99.0% of the amount calculated for di-triphenylmethyl-β-methyl-*d*-xyloside. In a repetition of the analysis 0.1131 g. of substance gave 0.0894 g. of triphenylcarbinol or 98.5% of the theoretical amount.

Anal. Calcd. for $C_{44}H_{40}O_5$: C, 81.44; H, 6.22; OCH_3, 4.8. Found: C, 81.10, 81.13; H, 6.33, 6.31; OCH_3, 4.9, 5.0.

The second isomer is insoluble in water and difficultly soluble in cold pyridine and hot absolute alcohol, but is considerably more soluble in alcohol than the first isomer. It usually crystallizes from absolute alcohol as clusters of pale yellow stout prismatic needles, but at times was observed to crystallize as individual slender prisms.

Isomeric Di-acetyl-mono-triphenylmethyl-β-methyl-*d*-xylosides.—The sirupy portion of the product of the reaction of triphenylmethyl chloride with β-methyl-*d*-xyloside was acetylated by dissolving it in a mixture of 200 cc. of acetic anhydride and 200 cc. of pyridine at 0° and keeping the solution in the refrigerator for about seventeen hours. It was poured into about 3500 cc. of ice water which was then nearly neutralized with sodium bicarbonate. After stirring awhile the precipitated sirup crystallized and the crystals were filtered off and washed thoroughly with distilled water. By a fractional crystallization from 95% alcohol two isomeric di-acetyl-mono-triphenylmethyl-β-methyl-*d*-xylosides were isolated, most of the first isomer separating almost pure in the first two crops (yield, 27 g.). The nearly pure second isomer was obtained from the mother liquor by concentrating the solution under reduced pressure, cooling in ice water and adding petroleum ether to turbidity (yield, 9 g.). After recrystallizing the first isomer to constant rotation from absolute alcohol and drying in an evacuated desiccator over calcium chloride, it melted at 169–170° (corr.) and showed $[\alpha]_D^{20}$ −15.7° in chloroform (0.6130 g. of sample, 25 cc. of solution in chloroform, 2-dm. tube; rotation, 0.77° to the left). In a triphenylmethyl determination 0.1702 g. of substance gave 0.0895 g. of triphenylcarbinol or 99.1% of the amount calculated for di-acetyl-mono-triphenylmethyl-β-methyl-*d*-xyloside. In a repetition of the analysis 0.1563 g. of substance gave 0.0825 g. of triphenylcarbinol or 99.5% of the theoretical amount.

Anal. Calcd. for $C_{29}H_{30}O_7$: C, 70.99; H, 6.17; OCH_3, 6.3; CH_3CO, 17.55. Found: C, 70.81, 71.10; H, 6.15, 6.29; OCH_3, 5.9, 6.3; CH_3CO,[4] 17.41, 17.12.

The first isomer is readily soluble in chloroform, soluble in warm ether and acetone, difficultly soluble in absolute alcohol and insoluble in water. It crystallizes from absolute alcohol as clusters of short stout colorless prisms.

The second isomer was recrystallized to constant rotation from absolute alcohol from which it crystallized as long colorless prismatic needles which, after drying to constant weight in a high vacuum at 70°, melted at 125–127° (corr.) and gave $[\alpha]_D^{20}$ −49.1° in chloroform (0.4808 g. of sample, 25 cc. of solution in chloroform, 2-dm. tube; rotation, 1.89° to the left). When the crystals were dried in an evacuated desiccator over calcium chloride, the compound showed the lower $[\alpha]_D^{20}$ −45.9° in chloroform due to combined alcohol. On drying this material to constant weight in a high vacuum at 70° it lost 5.2% in weight compared with 4.5% calculated for one-half molecule of crystal alcohol. An alcohol-free sample (0.2019 g.) yielded 0.1065 g. of triphenylcarbinol or 99.4% of the theoretical for di-acetyl-mono-triphenylmethyl-β-methyl-*d*-xyloside.

Anal. Calcd. for $C_{29}H_{30}O_7$: C, 70.99; H, 6.17; OCH_3, 6.3; CH_3CO, 17.55. Found: C, 70.87, 71.13; H, 6.19, 6.22; OCH_3, 6.4, 6.5; CH_3CO, 17.59, 17.60.

The second isomer is insoluble in water, readily soluble in chloroform and considerably more soluble in absolute alcohol than the first isomer.

Besides the two pure isomers described, there was obtained from the mother liquor of crystallization of the crude acetylated product about 4.5 g. of crystals in fractions showing $[\alpha]_D^{20}$ −3 to −10° in chloroform, the remainder of the material being a sirup. The possibility of the presence of other acetates was not investigated further since it was unnecessary for the purpose of this research.

Reaction of Triphenylmethyl Chloride with β-Methyl-*d*-xyloside at 100°.—A solution of 6 g. of pure β-methyl-*d*-xyloside and 15 g. of triphenylmethyl chloride in 50 cc. of pure dry pyridine was heated on the steam-bath for one and one-half hours. From the reaction solution there was separated, by a procedure similar to that already outlined, 0.4 g. of small square prisms melting at 235–240° with $[\alpha]_D^{20}$ −54.8° in pyridine and 1.8 g. of crystals melting at 155–158° and showing $[\alpha]_D^{20}$ −23.6° in pyridine. The experiment was not completed, but it is apparent that the products isolated are the two previously described isomeric ditriphenylmethyl-β-methyl-*d*-xylosides.

Summary

The reaction of triphenylmethyl chloride with β-methyl-*d*-xyloside in dry pyridine solution at 20° yields two crystalline isomeric di-triphenylmethyl-β-methylxylosides and a sirup. Acetylation of the sirup gives two crystalline isomeric

(4) The acetyl analyses given in this paper were carried out by Kunz's method. Kunz and Hudson, THIS JOURNAL, **48**, 1932 (1926).

di - acetyl - mono - triphenylmethyl - β - methyl-*d*-xylosides. These results show that triphenylmethyl chloride reacts with the secondary hydroxyl groups in the β-methyl-*d*-xyloside molecule.

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An Investigation of Certain Derivatives of Alkyl γ-Oxalylcrotonates

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In connection with certain work which was being done in this Laboratory, an attempt was made to synthesize ethyl α-oxalyl-vinylacetate, $CH_2{=}CHCH(COCOOC_2H_5)COOC_2H_5$, by the condensation of ethyl vinylacetate and ethyl oxalate in the presence of sodium. The substances reacted readily, hydrogen was evolved and a yellow sodium derivative was formed. However, the free ester which was obtained when an aqueous solution of the sodium derivative was acidified, was not ethyl vinyl-α-oxalylacetate, but was, instead, ethyl γ-oxalylcrotonate, $C_2H_5OOCC(OH){=}CHCH{=}CHCOOC_2H_5$, which previously had been prepared by Prager,[1] by the condensation of ethyl crotonate and ethyl oxalate. Apparently, under the conditions of the reaction, ethyl vinylacetate rearranged to ethyl crotonate which then reacted normally to give ethyl γ-oxalylcrotonate.[2]

$$CH_2{=}CHCH_2COOC_2H_5 \longrightarrow CH_3CH{=}CHCOOC_2H_5$$

$$CH_3CH{=}CHCOOC_2H_5 + (COOC_2H_5)_2 + Na \longrightarrow C_2H_5OOCC(ONa){=}CHCH{=}COOC_2H_5 + {}^1/_2H_2 + C_2H_5OH$$

As comparatively little work has been done on ethyl γ-oxalylcrotonate, it was thought desirable to make a further study of this interesting compound, particularly of its O-acyl derivatives. Lapworth[3] prepared γ-oxalylcrotonic acid, $HOOCCH{=}CHCH_2COCOOH$ by careful alkaline hydrolysis of the sodium derivative of ethyl γ-oxalylcrotonate. This compound was described as a bright yellow microcrystalline substance which melted with decomposition at about 190°. It was regarded by Lapworth as probably a mixture of tautomeric forms. The ethyl γ-oxalylcrotonates which we obtained by the condensation between either ethyl vinylacetate or ethyl crotonate, with ethyl oxalate were hydrolyzed by a slight modification of the process used by Lapworth. γ-Oxalylcrotonic acid was obtained in the form of a colorless, crystalline compound which melted sharply with decomposition at 212°. When it was oxidized with 30% hydrogen peroxide according to the method of Holleman,[4] it reacted as a normal α-ketonic acid, and glutaconic acid was formed in good yield.

$$HOOCCH{=}CHCH_2COCOOH + H_2O_2 \longrightarrow HOOCCH{=}CHCH_2COOH + H_2O + CO_2$$

Although it has long been generally accepted that ethyl oxalylcrotonate and its sodium salt have the enol structure,[1,3] until recently no O-acyl derivatives of this substance have been prepared. Börsche and Manteuffel[5] prepared ethyl O - acetyl - γ - oxalylcrotonate, $C_2H_5OOCC(OCOCH_3){=}CHCH{=}CHCOOC_2H_5$, by the action of acetic anhydride on the potassium salt of ethyl γ-oxalylcrotonate. They showed that this compound could be reduced catalytically in the presence of colloidal palladium to diethyl α-acetoxyadipate, $C_2H_5OOC(OCOCH_3)CH_2CH_2CH_2 - COOC_2H_5$. We have prepared ethyl O-carbethoxy-γ-oxalylcrotonate, $C_2H_5OOCC(OCOOC_2H_5){=}CHCH{=}CHCOOC_2H_5$, by the action of ethyl chlorocarbonate on the sodium derivative of ethyl γ-oxalylcrotonate.

In a similar manner, methyl-O-carbomethoxy-γ-oxalylcrotonate, $CH_3OOCC(OCOCH_3){=}CHCH{=}CH{-}COOCH_3$, was prepared from methyl chlorocarbonate and methyl-γ-oxalylcrotonate, which in turn had been made in the normal manner by the condensation of methyl crotonate with methyl oxalate. The alkyl O-carbalkoxy-γ-oxalylcrotonates prepared were reduced catalytically at room temperature in a solution of methyl alcohol in the presence of a platinum catalyst.[6] Approximately two and a half moles of hydrogen were absorbed and the principal product obtained was dialkyl adipate. Possibly the formation of car-

(1) Prager, *Ann.*, **338**, 375 (1905).

(2) Another mechanism for this reaction is suggested by the recent work of Borsche and Manteuffel, *Ann.*, **505**, 179 (1933).

(3) Lapworth, *J. Chem. Soc.*, **79**, 1279 (1901).

(4) Holleman, *Rec. trav. chim.*, **23**, 169 (1904).

(5) Börsche and Manteuffel, *Ber.*, **65**, 871 (1932).

(6) Adams and Voorhees, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1928, Vol. VIII, p. 10.