product with water gave a colorless substance, identical with that compound decomposing at 290° and obtained by de Haan as stated above.

It is exceedingly difficult to procure any appreciable quantity of this dithioureinopentane. The greater ease by which the diureinopentane may be procured is, in one respect at least due to the practical insolubility of this latter product in acetylacetone.

For the kind assistance of Mr. Frank C. Vibrans upon the analytical data in this paper the author desires to express his indebtedness.

ANN ARBOR, MICHIGAN.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF COLUMBIA UNIVERSITY AND THE HARRIMAN RESEARCH LABORATORY. NO. 249.]

INOSITE AND PINITE AND SOME OF THEIR DERIVATIVES.

BY EDWARD G. GRIFFIN AND J. M. NELSON.

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Inosite and its derivatives possess considerable interest. The sugar itself is interesting, due to its wide occurrence in nature and possible important physiological functions, and also due to its close relationship in chemical constitution to the hexoses and some hydroaromatic compounds. The synthesis of the derivatives of inosite, when compared to the synthesis of the analogous derivatives of a substance like glucose, affords a comparison of the effect on the properties of a hexose in which the carbons are arranged in the form of a closed ring instead of an open chain. The derivatives might also prove valuable in the study and synthesis of many complex substances like phytin and some of the tannins, which yield, on decomposition, inosite or closely related products like phloroglucin and quinic acid, $C_6H_7(OH)_4COOH$.

Derivatives of inosite mentioned in literature prior to this investigation are: the hexacetate, hexabenzoate,[1] hexa- and trinitrates,[2] monobromopentacetate, two isomeric dibromotetraacetates, and mono- and dibromohydrins.[3] While this work was in progress, Müller published a second article describing a triacetate, three isomeric chlorohydrinpentacetates, a chlorohydrintriacetate, a chlorohydrin, two new isomeric inosites, which he called iso and ψ; and an iso-inosite hexacetate and tetrabenzoate.[4]

By the action of acetyl bromide on inosite the following products were obtained: Bromopentacetylcyclohexanpentol, $C_6H_6Br(OCOCH_3)_5$;[5] two

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[1] Maquenne, *Compt. rend.*, 104, 297 (1887).

[2] Vohl, *Ann.*, 101, 55 (1857).

[3] Müller, *J. Chem. Soc.*, 91, 1780 (1907).

[4] *J. Chem. Soc.*, 101, 2383 (1912).

[5] The names ascribed to the esters and derivatives of inosite mentioned in literature are sometimes not satisfactory, and for that reason the Geneva system of nomenclature has been adopted.

isomeric dibromotetracetylcyclohexantetrols, $C_6H_6Br_2(OCOCH_3)_4$, called α and β for distinction in name; dibromocyclohexantetrol, $C_6H_6Br_2(OH)_4$; dibromodiacetylcyclohexantetrol, $C_6H_6Br_2(OH)_2(OCOCH_3)_2$; dibromotriacetylcyclohexantetrol, $C_6H_6Br_2(OH)(OCOCH_3)_3$; and tribromotriacetylcyclohexantriol, $C_6H_6Br_3(OCOCH_3)_3$. The first four products mentioned were identical with those obtained by Müller by glacial acetic acid, hydrogen bromide and hexacetylcyclohexanhexol, although the melting points of three of them were different.

Acetyl chloride gave products, none of which appeared to be identical with those obtained by Müller. They are: chloropentacetylcyclohexanpentol, $C_6H_6Cl(OCOCH_3)_5$; α- and β-dichlorotetracetylcyclohexantetrol, $C_6H_6Cl_2(OCOCH_3)_4$; and dichlorocyclohexantetrol, $C_6H_6Cl_2(OH)_4$. Another substance, probably dichlorodiacetylcyclohexantetrol, $C_6H_6Cl_2(OH)_2(OCOCH_3)_2$, was also obtained.

Many additional organic acyl derivatives were also prepared. Besides hexacetylcyclohexanhexol and hexabenzoylcyclohexanhexol, two isomeric hexacetylcyclohexanhexols which have been distinguished in name by the prefixes, α and β; pentabenzoylcyclohexanhexol, $C_6H_6(OH)(OCOC_6H_5)_5$; tetrabenzoylcyclohexanhexol, $C_6H_6(OH)_2(OCOC_6H_5)_4$; hexanisylcyclohexanhexol, $C_6H_6(OCOC_6H_4OCH_3)_6$; pentanisylcyclohexanhexol, $C_6H_6(OH)(OCOC_6H_4OCH_3)_5$; hexacinnamoylcyclohexanhexol, $C_6H_6(OCOC_2H_2C_6H_5)_6$; two isomeric pentacinnamoylcyclohexanhexols, α and β, $C_6H_6(OH)(OCOC_2H_2C_6H_5)_5$; hexa-*m*-nitrobenzoylcyclohexanhexol, $C_6H_6(OCOC_6H_4NO_2)_6$; and penta-*m*-nitrobenzoylcyclohexanhexol, $C_6H_6(OH)(OCOC_6H_4NO_2)_5$, were obtained.

Up to the time of this investigation, no alkyl derivatives of inosite had been synthesized. By alkylation of inosite and subsequent purification by means of the intermediate alkyl acetyl derivatives, the following were obtained: monomethylcyclohexanhexol, $C_6H_6OCH_3(OH)_5$; a syrup, probably dimethylcyclohexanhexol, $C_6H_6(OCH_3)_2(OH)_4$; diethylcyclohexanhexol, $C_6H_6(OC_2H_5)_2(OH)_4$; and a syrup, probably monoethylcyclohexanhexol, $C_6H_6OC_2H_5(OH)_5$. Others were obtained as syrups, but so far not sufficiently pure to definitely decide on their true composition. The alkyl acetyl derivatives obtained were, pentacetylmethyl cyclohexanhexol, $C_6H_6OCH_3(OCOCH_3)_5$; tetracetyldimethylcyclohexanhexol, $C_6H_6(OCH_3)_2(OCOCH_3)_4$; pentacetylethylcyclohexanhexol, $C_6H_6OC_2H_5(OCOCH_3)_5$; tetracetyldiethylcyclohexanhexol, $C_6H_6(OC_2H_5)_2(OCOCH_3)_4$; and triacetyldimethylcyclohexanhexol, $C_6H_6(OCH_3)_2(OH)(OCOCH_3)_3$.

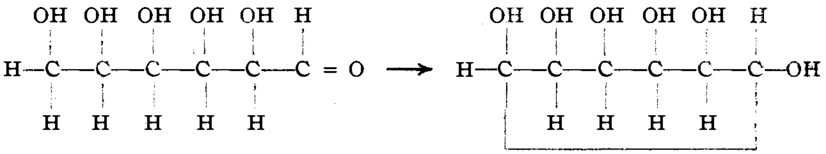
From pinite itself the following acyl derivatives were also prepared: pentacetylmethylcyclohexanhexol, $C_6H_6OCH_3(OCOCH_3)_5$; pentabenzoylmethylcyclohexanhexol, $C_6H_6OCH_3(OCOC_6H_5)_5$; pentanisylmethylcyclohexanhexol, $C_6H_6OCH_3(OCOC_6H_4OCH_3)_5$; and pentacinnamoylmethylcyclohexanhexol, $C_6H_5OCH_3(OCOC_2H_2C_6H_5)_5$.

Nitration and alkylation yielded syrups, which could not be crystallized and so far have not been identified.

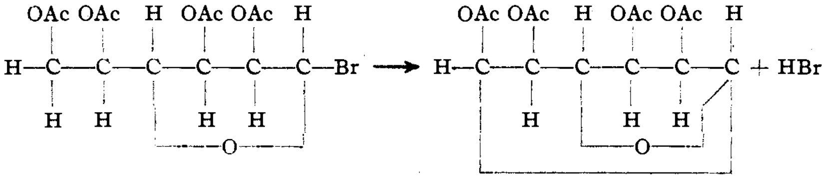
In treating pinite with acetyl bromide, as was done in the case of inosite, no halide esters of pinite were obtained but, instead, halide esters of inosite. This shows that the methoxy groups were attacked by the acetyl bromide as well. The following inosite esters were obtained: α- and β-dibromotetracetylcyclohexantetrol and dibromocyclohexantetrol.

The object in the beginning of this investigation was the synthesis of inosite or compounds closely related to it. However, all the attempts proved unsuccessful, and their descriptions are only indicated briefly as follows:

1. Aldolization between the carbonyl and primary alcohol groups in glucose.



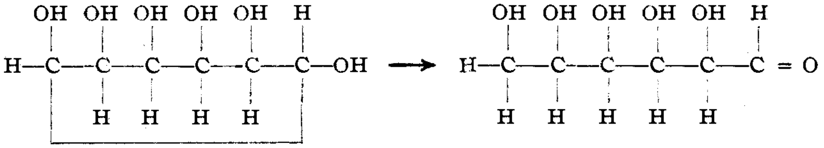
2. Removal of hydrogen bromide from bromotetracetyl glucose.



Attempts were also made to repeat the work of Rosenstiehl,[1] in which he claimed to have obtained sugars by treating benzene hexachloride with silver acetate, but no reaction was found to take place.

Neither was it possible to repeat the work of Carius,[2] who prepared a cyclic sugar, phenose, $C_6H_{12}O_6$, by the hydrolysis of benzene trichlorohydrin, $C_6H_6(Cl\ OH)_3$.

Having failed to obtain any information as to the stereo-configuration of inosite by tying up the end carbon atoms of an open chain hexose molecule, the opposite was undertaken. It was hoped to pass from inosite to a hexose by opening the ring as follows:



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[1] *Compt. rend.*, **54**, 178 (1862).

[2] *Ann.*, **136**, 323 (1866).

and thus the stereo-configuration might be established by noticing the particular hexose formed.

As yet, the identity of the products obtained has not been ascertained and will be further investigated.

Experimental Part.

Although the synthesis of inosite in this laboratory has thus far been unsuccessful, "steep water,"[1] a by-product obtained in the manufacture of corn products, has been found to offer a source for inosite in sufficient quantities for the study and preparation of several of its derivatives.

Procedure: In a vat containing 42 liters of "steep water," (sp. gr. 1.246) were poured 125 liters of boiling water containing 20 kg. of barium hydroxide. The precipitate was separated by means of a filter press and washed till the filtrate was colorless. The press cake obtained was transferred to a vat and stirred with 40 liters of water containing 12 kg. of commercial sulfuric acid. The dark red mixture was pumped through a filter press and washed with water till the filtrate totaled 100 liters. The solution was then evaporated to 12 liters, giving a heavy reddish black liquid (sp. gr. 1.484, b. p. 125°), containing approximately 33% sulfuric acid. This liquid was divided into eight portions of 1500 cc. each. A portion was placed in a tall meal jar and heated in a steam digestor under a pressure of 5 atmos. at 150° for 4 hours. The resulting black liquid was diluted with water, filtered from the carbonaceous material and thoroughly washed. The red solution was diluted to 9 liters, three equal portions of which were placed in large jars. To each were added 5 liters of a hot aqueous solution, containing 1300 g. of barium hydroxide, and the resulting curdy, grayish precipitate vigorously stirred. The precipitate was filtered through large fluted filter papers with parchmentized tips, and washed by boiling with water. The combined pale yellow filtrates were evaporated to 400 cc., yielding a dark, reddish green fluorescent liquid. While still hot, 1200 cc. of glacial acetic acid were added, which caused the inosite to separate on cooling. To complete the crystallization, the mixture was placed in the ice box over night. It was filtered by suction and washed with glacial acetic acid, which dissolved out the coloring matter, and finally with alcohol. A beautiful, white, crystalline product of practically pure inosite remained. Yield, 46 g.

The use of glacial acetic acid in precipitating the above solution was found to be very advantageous, since it removes the gums and coloring matter, which alcohol does not do. For the further purification of inosite, the following method was found to work satisfactorily: Fifty grams of crude inosite were dissolved in 200 cc. of water, a few drops of sulfuric

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[1] The steep water was kindly furnished by the Corn Products Refining Company. Its use as a source for the preparation of inosite was suggested by Dr. A. R. Rose, recently of the New York Agricultural Experiment Station.

acid added to remove any barium, the solution was concentrated to 75 cc. and alcohol added to turbidity. When cold, 200 cc. of alcohol and 50 cc. of ether were added and the mixture placed in the ice box over night. The inosite separated nearly quantitatively in little, feathery crystals, melting at 225°

Each of remaining seven portions were treated in the same manner. Some additional inosite was obtained from the acetic acid and alcoholic mother liquors, giving a total yield of 368 g.

Inosite, containing two molecules of water, crystallizes from water or dilute acetic acid in colorless rhombic prisms, melting at 225°, and charring slightly above this temperature. It is optically inactive and unfermentable.

Action of Acetyl Bromide on Inosite.

The fact that glucose and acetyl bromide yield bromotetracetyl glucose suggested that halide esters of inosite might be obtained in a similar manner. Accordingly, inosite was treated with acetyl bromide but only hexacetylcyclohexanhexol was obtained. It proved, however, to be an excellent method for the preparation of hexacetylcyclohexanhexol, giving better yields in a shorter time than by any of the methods heretofore used.

Acetylation of Inosite by means of Acetyl Bromide.—Three grams of dry inosite and 18 g. of acetyl bromide were gently heated together in a flask connected with a ground-in glass condenser. In ten minutes, a clear, red solution resulted which was slowly poured into water, whereupon a semicrystalline mass separated. The mass was filtered off and recrystallized from hot alcohol as a scaly crystalline product. Yield, 7 g. No lower acetylated derivatives were obtained from the mother liquors.

Since inosite is not easily decomposed by concentrated acids under pressure, the reaction was also carried out in a sealed tube. Under these conditions, however, no hexacetylcyclohexanhexol was obtained, but, instead, several bromo esters of inosite.

In a large glass tube, immersed in a freezing mixture in order to retard the reaction until the tube was sealed, 25 g. of inosite (dried at 110°) and 100 g. of acetyl bromide were placed. The sealed tube was heated for 6 hours at 120°. Care was taken in opening the tube to prevent loss of the contents due to frothing. The dark red syrup together with the glass tube, which was broken in pieces to regain the adhering syrup, was transferred to a flask and the mass evaporated in a vacuum on a water bath. The residue was taken up with a little absolute alcohol and again evaporated and finally crystallized from a large amount of alcohol. The crystals were dried on a porous plate and gave a yield of 18 g. and were designated (A). On evaporating the filtrate to half its volume by means of a current of air, a precipitate of smaller crystals gradually separated. These were filtered off and amounted to 12 g. (B). The dark red filtrate was further concentrated by a current of air to the point at which an oil began to form. Five grams of a crystalline precipitate (C) were obtained. The filtrate now measured about 75 cc. and on standing over night separated into two layers. The upper, a light red solution having a strong odor of ethyl acetate yielded 2 g. of a fine crystalline product (D). The lower layer was a black oil. This was combined with the filtrate from (D), alcohol and animal charcoal were added, and the mixture boiled for 6 hours. A pale yellow solution (E) was obtained, which did not crystallize. It was placed in the ice box over calcium chloride for a few days.

The various portions were mixtures and were best separated by fractional crystallization from alcohol. As there was no well-defined line of separation, the crystallization was carefully watched, and each kind of crystals filtered off as they formed. Two recrystallizations usually resulted in a constant melting point being obtained.

(A) consisted of bromopentacetylcyclohexanpentol and α-dibromotetracetylcyclohexantetrol. (B) was a mixture of α- and β-dibromotetracetylcyclohexantetrols and a small amount of dibromotriacetylcyclohexantetrol. From (C) was obtained dibromotetracetylcyclohexantetrol and dibromodiacetylcyclohexantetrol. (D) consisted of only dibromodiacetylcyclohexantetrol. (E) yielded a small amount of tribromotriacetylcyclohexantriol, as a fine, white powder. The mother liquors from (E) after standing in the ice box for several weeks changed to an opaque mass. It was freed from adhering syrup by crushing on a porous plate. This crude product, which amounted to 15 g., was boiled with benzene, which dissolved the coloring material and any tribromotriacetylcyclohexantriol, and was finally obtained as a white powder which proved to be dibromocyclohexantetrol.

Bromopentacetylcyclohexanpentol, crystallizes from boiling alcohol in fine, indistinct crystals, melting sharply at 240°. It is soluble in chloroform, ether, acetone and benzene, and is insoluble in water, ligroin or methyl alcohol. It is optically inactive.

Calc. for $C_6H_6Br(OCOCH_3)_5$: Br, 17.66%; C, 42.38%; H, 4.64%. Found: Br, 17.72%; C, 42.23%; H, 4.69%.

α-Dibromotetracetylcyclohexantetrol, differs from its isomer in its crystalline form and is less soluble. It separates as scaly crystals from alcohol and as long, flat, colorless prisms from benzene. It melts at 225° to a colorless liquid. It is optically inactive.

Calc. for $C_6H_6Br_2(OCOCH_3)_4$: Br, 33.75%; C, 35.44%; H, 3.78%. Found: Br, 33.83; C, 35.35; H, 3.83.

β-Dibromotetracetylcyclohexantetrol, crystallizes best from alcohol, forming large, brilliant, rhombic prisms, melting at 130° to a clear, colorless liquid which forms a crystalline foliated solid on cooling. It is soluble in benzene, chloroform, ether, glacial acetic acid, and ethyl acetate, and insoluble in water. It is optically inactive.

Calc. for $C_6H_6Br_2(OCOCH_3)_4$: Br, 33.75%; C, 35.44%; H, 3.78%. Found: Br, 33.71; C, 35.29; H, 3.72.

Dibromotriacetylcyclohexantetrol, crystallizes from alcohol in small, slender prisms, m. p. 124°. On acetylation, it yields β-dibromotetracetylcyclohexantetrol.

Calc. for $C_6H_6Br_2(OH)(OCOCH_3)_3$: Br, 37.04%. Found: 37.20.

Dibromodiacetylcyclohexantetrol, crystallizes from alcohol in clusters of soft, white needles, melting at 214° with decomposition. It is soluble in alcohol, acetone and ethyl acetate, less soluble in ether or glacial acetic acid and insoluble in water, chloroform, and benzene. It is optically inactive.

Calc. for $C_6H_6Br_2(OH)_2(OCOCH_3)_2$: Br, 41.02%; C, 30.77%; H, 3.59%; Acetyl, 30.26%. Found: Br, 40.78 and 40.83; C, 30.59 and 30.88; H, 3.42 and 3.65; Ac,[1] 30.28 and 30.33.

On acetylation, dibromodiacetylcyclohexantetrol yields β-dibromotetracetylcyclohexantetrol.

Tribromotriacetylcyclohexantriol, crystallizes from benzene in microscopic plates, melting at 180°. It is soluble in alcohol, chloroform, benzene, acetone and glacial acetic acid and insoluble in water and in ligroin. It is optically inactive.

Calc. for $C_6H_6Br_3(OCOCH_3)_3$: Br, 48.48%; C, 29.09%; H, 3.33%. Found: Br, 48.36 and 48.29; C, 29.13 and 28.87; H, 3.49 and 3.12.

Dibromocyclohexantetrol, crystallizes from water in massive colorless prisms, melting at 216° with decomposition. It separates from hot ethyl acetate in small, shining prisms, and from alcohol in tufted crystals. It is soluble in benzene, chloroform, ether and amyl acetate. It is optically inactive.

Calc. for $C_6H_6Br_2(OH)_4$: Br, 59.29%; C, 23.53%; H, 3.27%. Found: Br, 59.29; C, 23.28; H, 3.35.

On acetylation, dibromocyclohexantetrol yields β-dibromotetracetylcyclohexantetrol.

It was found that four of the products prepared from acetyl bromide and inosite were identical with those obtained by Müller.[2] Since his method of procedure yielded a smaller number of esters, and since he mentions melting points for some of these compounds which are different from those observed in this laboratory, this part of his work was repeated.

Six grams of anhydrous hexacetylcyclohexanhexol and 20 g. of glacial acetic acid, saturated at 0° with hydrogen bromide, were heated in a sealed tube for 8 hours at 100°, and 8 hours at 150°. No pressure was noticed in opening the tube. The contents were divided into two portions. The products of one portion were separated according to the method of Müller, and the other, by the scheme adopted for acetyl bromide and inosite. Half the contents of the tube were emptied into water and the products which separated gradually solidified as a crystalline mass. This was extracted with cold alcohol which dissolved part of it. The insoluble residue was filtered off and the filtrate added to the water soluble portion. This mixture was evaporated in a vacuum to a thick syrup, water added, and boiled till solution took place. The clear liquid was concentrated and after standing in the ice box a few days a white powder separated. This was dried on porous plates and recrystallized from alcohol and finally from water, yielding large colorless prisms of dibromocyclohexantetrol, m. p. 216°.

[1] Correction made for halogen which was also saponified by the action of the sodium hydroxide.

[2] *J. Chem. Soc.*, **91**, 1780 (1907).

The insoluble residue was a mixture of products which, by repeated crystallization from alcohol, were obtained pure. The small, indistinct crystals separating first were bromopentacetylcyclohexanpentol, m. p. 240°. These were followed by scaly crystals of α-dibromotetracetylcyclohexantetrol, m. p. 225° (Müller, m. p. 235°) and then massive rhombic prisms of β-dibromotetracetylcyclohexantetrol, m. p. 130°. (Müller, m. p. 140°.) From the alcoholic mother liquors two kinds of crystals were obtained. They were mechanically separated and each recrystallized from alcohol; one, massive prisms of β-dibromotetracetylcyclohexantetrol, m. p. 130°, and the other, soft, white needles of dibromodiacetylcyclohexantetrol, m. p. 214°. The latter substance is similar in properties to one observed by Müller, but not isolated by him. Müller, by hydrolysis of the mother liquors resulting from the separation of the above-mentioned products, obtained bromocyclohexanpentol. Neither by means of Müller's method, nor with acetyl bromide could any product like this be obtained.

The second half of the reaction mixture was treated as in the scheme for the separation of the products formed by the action of acetyl bromide and inosite, *i. e.*, direct evaporation in a vacuum and fractional crystallization from alcohol. Bromopentacetylcyclohexanpentol, m. p. 240,° separated first; followed by α-dibromotetracetylcyclohexantetrol, m. p. 225°, and then β-dibromotetracetylcyclohexantetrol, m. p. 130°, and finally dibromodiacetylcyclohexantetrol, m. p. 214°. The dark red mother liquors after long standing over calcium chloride yielded dibromocyclohexantetrol, m. p. 216°. (Müller, m. p. 210°.) The presence of tribromotriacetylcyclohexantriol or bromocyclohexanpentol was not observed.

This latter scheme of separating the products gave better yields than Müller's method.

Heating inosite with acetyl bromide in a sealed tube above 120° for a longer period than 6 hours had some effect on the amount of the products formed. When the reaction was carried out at 150° for 8 hours, none of the bromopentacetylcyclohexanpentol, but more of the tribromotriacetylcyclohexantriol was obtained. The formation of a tetra-halide ester of inosite at even higher temperatures was not successful since carbonization took place above 160°.

Besides the synthesis of these halogen esters of inosite some of their properties were studied to ascertain their behavior towards certain reagents. It was found that they were not affected by anhydrous aluminium chloride and dry benzene, nor by metallic sodium and ethyl bromide in ether, and only slightly affected by silver carbonate after long boiling in absolute methyl alcohol. Phenyl magnesium bromide in ether gave as final products, dark-colored resinous substances which were not identified, due to lack of material. It was hoped that by means of liquid ammonia, a halogen in dibromotetracetylcyclohexantetrol might be replaced by an amino group. The products of the reaction showed that saponification of the acetyl groups had taken place, since only dibromocyclohexantetrol was obtained. However, the reaction was not given a fair trial, since large amounts of impurities such as water, iron, pyridine, etc., were subsequently found to be present in the liquid ammonia.

Five grams of β-dibromotetracetylcyclohexantetrol were mixed with liquid ammonia in a thermos bottle. After standing 12 hours, the contents were emptied into a flask to evaporate off the ammonia. The resulting dark-colored residue was extracted first with cold alcohol and then with water. The water solution yielded 1 g. of dibromocyclohexantetrol, while from the alcohol solution, after boiling with animal charcoal, was obtained 2 g. of unchanged β-dibromotetracetylcyclohexantetrol.

Action of Acetyl Chloride on Inosite.

When H. Müller,[1] heated hexacetylcyclohexanhexol with glacial acetic acid saturated with hydrogen chloride he obtained several monochloro esters of inosite, together with two new isomeric inosites, which he called iso and ψ.

By using acetyl chloride none of the above products seemed to be formed, but, as was to be expected, chloro esters of inosite were obtained similar in properties to those resulting from the action of acetyl bromide. Furthermore, these chloro esters of inosite appear to be isomorphous with the analogous bromo esters, since the latter served in inoculating the solutions from which the former were crystallized.

Twenty grams of inosite (dried at 110°) and 80 g. of acetyl chloride were heated in a sealed tube at 140° for 6 hours. Care was taken in opening the tube to prevent loss of the contents, due to frothing. The syrup obtained was emptied into a flask together with the pieces of the crushed glass tube. Absolute alcohol was added and the mixture evaporated in a vacuum on a water bath. The dark brown syrupy residue was dissolved in 500 cc. of hot alcohol and filtered hot. After cooling, the crystalline product (A) which separated was filtered and the filtrate evaporated to half its volume, with a current of air. A second crystalline product (B) resulted and the filtrate evaporated as before until an oil began to form, giving a white precipitate (C). The reddish black solution was heated with animal charcoal yielding a pale yellow solution which did not crystallize. Instead, a syrup slowly separated which dissolved on heating, but formed again on cooling. The mixture was evaporated to a syrup (D) in a vacuum and dried over calcium chloride. This syrup weighed 32 g. or 80% of the total yield obtained.

(A), (B), and (C) were mixtures and were separated by fractional crystallization from alcohol. (A) gave chloropentacetylcyclohexanpentol and α-dichlorotetracetylcyclohexantetrol while (B) yielded α- and β-dichlorotetracetylcyclohexantetrols. From (C), by mechanical separation, β-dichlorotetracetylcyclohexantetrol and a minute amount of white needles melting at 107° were obtained. The latter substance is probably dichlorodiacetylcyclohexantetrol, since its properties are similar to those of dibromodiacetylcyclohexantetrol. Furthermore, like the latter sub-

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[1] *J. Chem. Soc.*, 101, 2383 (1912).

stance, it gave on acetylation the corresponding β-dichlorotetracetyl derivative. The syrup (D) was dichlorotriacetylcyclohexantetrol, which on hydrolysis with HCl gave dichlorocyclohexantetrol.

Chloropentacetylcyclohexanpentol crystallizes from hot alcohol in fine, indistinct crystals melting at 250°. It is soluble in benzene, chloroform and ether, and insoluble in water. It is optically inactive.

Calc. for $C_6H_6Cl(OCOCH_3)_5$: Cl, 8.70%; C, 47.00%; H, 5.14%. Found: Cl, 8.65; C, 46.87; H, 5.09.

α-Dichlorotetracetylcyclohexantetrol differs from its isomer in its crystalline form and is less soluble. It crystallizes from alcohol in shining scales, melting at 186° to a colorless liquid, which forms a crystalline mass on cooling. It is soluble in alcohol, chloroform, ethyl acetate, glacial acetic acid, benzene, ether and acetone, and insoluble in water and in ligroin. It is optically inactive.

Calc. for $C_6H_6Cl_2(OCOCH_3)_4$: Cl, 18.44%; C, 43.68%; H, 4.67%. Found: Cl, 18.37 and 18.25; C, 43.68; H, 4.75.

β-Dichlorotetracetylcyclohexantetrol crystallizes from alcohol in large, brilliant, rhombic prisms melting sharply at 118°. It is optically inactive.

Calc. for $C_6H_6Cl_2(OCOCH_3)_4$: Cl, 18.44%; C, 43.68%; H, 4.67%. Found: Cl, 18.42 and 18.50; C, 43.51; H, 4.60.

Dichlorotriacetylcyclohexantetrol distils at 216–217° at 2.3 mm. It is a colorless, brittle gum, soluble in alcohol, glacial acetic acid, ethyl acetate and hot water. For analysis, small portions were dried to a constant weight at 80° in a vacuum over sulfuric acid. It is optically inactive.

Calc. for $C_6H_6Cl_2(OH)(OCOCH_3)_3$: Cl, 20.70%; C, 41.91%; H, 4.67%; Acetyl, 50.00%. Found: Cl, 20.73 and 20.78; C, 41.75; H, 4.14; Ac, 50.13 and 50.05.

On acetylation with acetic anhydride β-dichlorotetracetylcyclohexantetrol, was formed. Dichlorotriacetylcyclohexantetrol in an alcoholic solution was hydrolized for 12 hours with hydrochloric acid. The chlorides were removed with silver carbonate, and the solution boiled with bone black, filtered and evaporated to a syrupy consistency. On inoculating with a crystal of dibromocyclohexantetrol and vigorously agitating the mixture, a crystalline mass of dichlorocyclohexantetrol separated. This was filtered, washed with ethyl acetate and recrystallized from alcohol. On acetylation, it gave β-dichlorotetracetylcyclohexantetrol.

Dichlorocyclohexantetrol crystallizes from alcohol in small, colorless prisms, melting at 221°. It is soluble in water and in alcohol; less soluble in ethyl acetate and insoluble in chloroform, ether and benzene.

Calc. for $C_6H_6Cl_2(OH)_4$: Cl, 32.72%, C, 33.18%; H, 4.61%. Found: Cl, 32.62; C, 33.30; H, 4.77.

Maquenne[1] prepared hexacetyl and hexabenzoylcyclohexanhexol by

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[1] *Compt. rend.*, 104, 297 (1887).

means of the acid chlorides. This suggested that other acyl derivatives of inosite might be obtained by employing other acid chlorides.

The method adopted was to mix powdered anhydrous inosite with quinoline in slight excess of that necessary to react with the calculated amount of acid chloride. The mixture was heated at 120° till solution was complete, usually half an hour. The resulting syrupy mass was dissolved in 100 cc. of chloroform and washed two or three times with dilute sulfuric acid. The pale yellow solution was concentrated to about 25 cc. and warm alcohol added to the point of precipitation. The products separated on cooling and were usually purified by fractional crystallization.

Hexa-, penta-, and tetra-acyl derivatives of inosite were thus obtained. The hexacyl derivatives were less soluble and the melting points lower than the corresponding pentacyl derivatives.

Benzoylation of Inosite.—Maquenne[1] by direct heating of inosite with benzoyl chloride and zinc chloride obtained hexabenzoylcyclohexanhexol and chlorotribenzoylcyclohexanpentol. By using quinoline, no chloro esters were obtained, but instead lower benzoyl derivatives of inosite.

Two grams of inosite, 10 g. of quinoline and 10 g. of benzoyl chloride were heated in a flask for half an hour at 120°. The orange red syrup obtained was dissolved in 100 cc. of chloroform and washed two or three times with 10% sulfuric acid, and then once with water. The light yellow solution was evaporated to 25 cc. and 100 cc. of alcohol added. A white crystalline precipitate of pentabenzoylcyclohexanhexol separated. The filtrate was concentrated to 50 cc. After standing in the ice box for 12 hours, 4 g. of hexabenzoylcyclohexanhexol were obtained in the form of crystals. When the alcoholic mother liquors were poured into water, a small amount of an amorphous product separated and proved to be the tetrabenzoyl derivative. They were obtained pure by recrystallization from other solvents.

Hexabenzoylcyclohexanhexol crystallizes from hot alcohol in microscopic crystals, m. p. 258°. It is soluble in benzene, glacial acetic acid and chloroform, slightly soluble in alcohol or ether, and insoluble in water.

Calc. for $C_6H_6(OCOC_6H_5)_6$: C, 71.64%; H, 4.34%. Found: C, 71.41; H, 4.42.

Pentabenzoylcyclohexanhexol crystallizes from benzene in large transparent prisms, m. p. 269°. It is soluble in chloroform, acetone, ethyl acetate, glacial acetic acid, and in benzene, insoluble in water, ligroin and in ether.

Calc. for $C_6H_6(OH)(OCOC_6H_5)_5$: C, 70.29%; H, 4.57%. Found: C, 70.39 and 70.29; H, 4.68 and 4.71.

Tetrabenzoylcyclohexanhexol separates from a mixture of chloroform and alcohol as a white amorphous powder, m. p. 231°.

Calc. for $C_6H_6(OH)_2(OCOC_6H_5)_4$: C, 68.46%; H, 4.69%. Found: C, 68.41; H, 4.55.

Anisylation of Inosite.—Two grams of dry inosite, 20 g. of quinoline and 11.5 g. of anisyl chloride were mixed in a flask and heated for half an hour at 120°. The resulting pale brown syrup was dissolved in 100 cc. of chloroform and washed twice with 10% sulfuric acid, and once with water. The yellow solution was concentrated to 25 cc. and 50 cc. of hot alcohol added. On cooling, a mixture of hexa- and pentanisyl-

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[1] *Loc. cit.*

cyclohexanhexol separated, and was dried on a porous plate. This crude product amounted to 7 g. It was dissolved in a hot mixture of equal volumes of chloroform and alcohol, which gave on cooling hexanisylcyclohexanhexol. From the mother liquors pentanisylcyclohexanhexol was obtained.

The hexanisyl derivative crystallizes from a mixture of equal volumes of chloroform and alcohol in fine, white prisms, melting at 225°. It is soluble in chloroform, difficultly soluble in acetone or in ethyl acetate, and insoluble in alcohol, ether, benzene or in water. It is optically inactive.

Calc. for $C_6H_6(OCOC_6H_4OCH_3)_6$: C, 65.86%; H, 4.88%. Found: C, 65.81 and 66.09; H, 5.15 and 4.94.

The pentanisyl derivative crystallizes from a mixture of chloroform and alcohol in microscopic needles, melting at 251°. It is soluble in chloroform, less so in acetone, and insoluble in alcohol, water or in ether.

Calc. for $C_6H_6(OH)(OCOC_6H_4OCH_3)_5$: C, 64.94%; H, 4.94%. Found: C, 64.80 and 64.93; H, 4.80 and 5.01.

Cinnamoylation of Inosite.—Two grams of anhydrous inosite, 20 g. of quinoline, and 12 g. of cinnamoyl chloride (prepared by distilling a solution of cinnamic acid and phosphorus trichloride in a vacuum of 21 mm. at 145°), were mixed in a flask and heated for half an hour at 120°. The resulting orange-red syrup was dissolved in 100 cc. of chloroform and washed three times with 10% sulfuric acid and once with water. The pale yellow chloroform solution was concentrated to 25 cc. and hot alcohol was added till a turbidity formed. On cooling an amorphous product separated. 200 cc. of alcohol were added and the mixture set away in the ice box for 12 hours. The resulting mixture was filtered. The residue was dried on a porous plate giving 6 g. of a white powder. It consisted of two substances, hexa- and α-pentacinnamoylcyclohexanhexol, which were separated by fractional crystallization from a mixture of equal volumes of chloroform and alcohol. A third product, β-pentacinnamoylcyclohexanhexol, was obtained from the mother liquors in the form of an amorphous product contaminated with a syrup. It was purified by pressing out on porous plates and crystallizing from hot alcohol.

The hexacinnamoyl compound crystallizes from a mixture of chloroform and alcohol in clusters of fine needles, m. p. 199°. It is soluble in chloroform or in acetone, and insoluble in water, ether, alcohol, or in benzene.

Calc. for $C_6H_6(OCOC_2H_2C_6H_5)_6$: C, 75.20%; H, 5.00%. Found: C, 75.19 and 75.20; H, 5.32 and 5.31.

The α-pentacinnamoyl derivative crystallizes from chloroform and alcohol in microscopic prisms, m. p. 271°. It is soluble in chloroform or in acetone, and insoluble in water, ether, alcohol, or in benzene. It is optically inactive.

Calc. for $C_6H_6(OH)(OCOC_2H_2C_6H_5)_5$: C, 73.73%; H, 5.06%. Found: C, 73.58 and 73.50; H, 5.18 and 5.06.

The β-pentacinnamoyl derivative is a white, amorphous powder, m. p. 125°. It is soluble in chloroform, benzene or in alcohol, and insoluble in methyl alcohol, ether or in water.

Calculated for $C_6H_6(OH)(OCOC_2H_2C_6H_5)_5$: C, 73.73%; H, 5.06%. Found: C, 73.58; H, 5.16.

m **Nitrobenzoylation of Inosite.**—Two grams of anhydrous inosite, 18 g. of quinoline and 14 g. of metanitrobenzoyl chloride were dissolved by heating at 120° for half hour. The resulting pale brown solution was taken up in 100 cc. of chloroform and washed two or three times with dilute sulfuric acid and once with water. The solution was concentrated to 40 cc. and 10 cc. of hot alcohol added. On cooling, a red syrup separated which changed to a crystalline mass on standing in the ice box over night. The mass was dried on porous plates, pulverized, and the color removed by boiling with alcohol. Eight grams of hexa-*m*-nitrobenzoylcyclohexanhexol were obtained in the form of an insoluble, white powder. The mother liquors gave a small amount of penta *m*-nitrobenzoylcyclohexanhexol.

The penta-*m*-nitrobenzoyl derivative separates as a white powder from amyl alcohol, m. p. 226°. It is soluble in chloroform or in acetone, and insoluble in water, alcohol, ligroin, or in ether.

Calc. for $C_6H_6(OH)(OCOC_6H_4NO_2)_5$: C, 53.19%; H, 2.92%. Found: C, 53.00; H, 2.75.

The hexa-*m*-nitrobenzoyl compound crystallizes from ethyl acetate in fine, shining needles, m. p. 217°. It is soluble in chloroform or in acetone; slightly soluble in ethyl acetate or in benzene; and insoluble in water, ether, or in alcohol.

Calc. for $C_6H_6(OCOC_6H_4NO_2)_6$: C, 53.63%; H, 2.80%. Found: C, 53.81 and 53.75; H, 3.02 and 2.77.

Action of Chlorocarbonic Acid Ester on Inosite.—Carbonates of inosite are probably formed by heating inosite with chlorocarbonic acid ester and quinoline, and are insoluble in anhydrous solvents. The product obtained is a hygroscopic syrup soluble in alcohol but at the same time inosite is formed. This may be due to alcoholysis having taken place. Acetylation of the syrup yields a mixture of two isomeric hexacetylcyclohexanhexols, which were named α and β, and which are both different from the hexacetylcyclohexanhexol, obtained by direct acetylation of inosite.

Two grams of finely pulverized anhydrous inosite were thoroughly mixed with 10 g. of quinoline. Eight grams of chlorocarbonic acid ethyl ester were slowly added, keeping the mixture cold. After the frothing had ceased, the mixture was warmed until complete solution had taken place. The resulting dark-colored syrup was extracted with hot chloroform to remove the coloring material. After decanting off the chloroform, a white, hygroscopic syrup remained which was kept in a desiccator over sulfuric acid. The syrup was dissolved in acetic anhydride containing two drops of sulfuric acid, and the solution poured into water, from which an oil separated which gradually solidified. The white, amorphous mass thus obtained was washed with water and dissolved in hot alcohol. On cooling, a crystalline mass consisting of two acetylated products separated. By fractional crystallization from alcohol the α-hexacetylcyclohexanhexol was obtained, followed by the β-hexacetylcyclohexanhexol.

To determine the acetyl number a weighed amount (0.15–0.20 g.) was dissolved in 35 cc. of methyl alcohol in a flask connected with a ground-in reflux condenser, surmounted by a bent tube filled with soda lime. Thirty cubic centimeters of 0.1 *N* sodium hydroxide were added and the solution warmed on the water bath for 2 hours—5 hours for substances containing halogen—and titrated with 0.1 *N* hydrochloric acid, using phenolphthalein as an indicator.

α-Hexacetylcyclohexanhexol crystallizes from alcohol in small, flat prisms melting sharply at 212°. It is soluble in chloroform, benzene and in glacial acetic acid; less soluble in ether and in methyl alcohol, and insoluble in water. It is optically inactive. On hydrolysis with methyl alcohol and sodium hydroxide it yielded inosite.

Calc. for $C_6H_6(OCOCH_3)_6$: C, 50.00%; H, 5.55%; Ac, 81.94%. Found: C, 50.06 and 50.01; H, 5.56 and 5.72; Ac, 81.73 and 81.80.

β-Hexacetylcyclohexanhexol crystallizes from alcohol in microscopic prisms melting at 200°. It is soluble in ether, benzene, chloroform and in glacial acetic acid, and insoluble in water or in ligroin. It is optically inactive. On hydrolysis with methyl alcohol and sodium hydroxide it yielded inosite.

Calc. for $C_6H_6(OCOCH_3)_6$: C, 50.00%; H, 5.55%; Ac, 81.94%. Found: C 50.03 and 50.15; H, 5.68 and 5.79; Ac, 82.17 and 81.90.

On one occasion, α-hexacetylcyclohexanhexol changed over to β-hexacetylcyclohexanhexol. This interesting transformation could not be repeated although several attempts were made.

In order to study the relation of hexacetylcyclohexanhexol to α- and β-hexacetylcyclohexanhexols, it was warmed with quinoline and chlorocarbonic acid ester but no change took place. Also, it remained unchanged when treated with acetic anhydride saturated with hydrogen chloride.

It is stated by Fick[1] that a pentacetate, m. p. 216°, and a tetracetate have been obtained on short heating of inosite with acetic anhydride. In repeating the work, hexacetylcyclohexanhexol, m. p. 126°, was the only crystalline body obtained. The mother liquors gave a syrup, probably lower acetyl derivatives.

Lower acetyl derivatives of inosite in the form of syrups and the hexacetyl derivatives, m. p. 212°, were obtained by Maquenne,[2] on heating inosite with acetyl chloride. The work was repeated by the same method used for the formation of acyl derivatives in the presence of quinoline as mentioned above. A poor yield of hexacetylcyclohexanhexol, in addition to a small amount of a hygroscopic syrup, was obtained. This syrup is probably a lower acetylated derivative, since it is soluble in chloroform and in alcohol, and insoluble in water. Being unimportant, it was not investigated.

Hexacetylcyclohexanhexol crystallizes from toluene in monoclinic prisms, melting sharply at 216°, to a clear, colorless liquid, which solidifies on cooling. It sublimes at 200° and boils in a vacuum (2.5 mm.)

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[1] *Chem. Zentr.*, 1887, 452.

[2] *Bull. soc. chim.*, 48, 58 (1887).

at 234°. Saponification with liquid ammonia or with boiling alcoholic barium hydroxide gives inosite.

Calc. for $C_6H_6(OCOCH_3)_6$: C, 50.00%; H, 5.55%. Found: C, 50.04; H, 5.64.

Action of Liquid Ammonia on Hexacetylcyclohexanhexol.—The replacement of the acetyl groups with amino groups by means of liquid ammonia was undertaken. Only saponification of the acetyl groups took place with the production of inosite.

In a thermos bottle containing 50 cc. of liquid ammonia, 5 g. of the dry finely powdered compound were slowly added with stirring. After standing for 12 hours, the contents of the thermos bottle were emptied into a short-necked flask, the ammonia evaporating in about two hours. A brown residue resulted, which was extracted with alcohol. The alcohol solution gave a small amount of unchanged substance, but no intermediate acetylated derivatives could be obtained. The residue was dissolved in water, boiled with animal charcoal, and filtered. The filtrate was evaporated to 5 cc. and 30 cc. of alcohol added. The crystalline precipitate which formed was recrystallized from hot 80% alcohol, yielding 2 g. of inosite, m. p. 225°.

Alkylation of Inosite.

The occurrence of methyl ethers of inosite in nature suggested the alkylation of inosite. Of the many reagents employed for the alkylation of hydroxyl groups, dialkyl sulfate and a hot, 25% solution of sodium hydroxide was the only one which proved successful in the alkylation of inosite. The alkyl inosites obtained were of course optically inactive, and therefore it is impossible to say whether they are identical with the natural ethers which are active.

Unchanged inosite was obtained from heating inosite with diazomethane; a 15% alcohol solution of potassium hydroxide and methyl iodide; silver oxide, methyl alcohol, and methyl iodide, and also in a sealed tube; absolute methyl alcohol and hydrogen chloride in a sealed tube; and dimethyl sulfate with quinoline, and with pyridine.

Methylation of Inosite.—Ten grams of inosite were dissolved in 130 cc. of a 25% sodium hydroxide solution, heated to boiling, and 50 g. of dimethyl sulfate slowly added. The mixture was boiled for 24 hours, neutralized with a few drops of sulfuric acid and diluted with water. It was boiled with an excess of barium hydroxide, cooled, filtered, and the excess of barium hydroxide removed with carbon dioxide. The resulting pale yellow solution was acidified with acetic acid and boiled.

Any unchanged inosite was separated as the lead salt, $2C_6H_{12}O_6.5PbO$, by making the solution ammoniacal and then adding 50 cc. of a saturated solution of basic lead acetate, followed by 50 cc. of methyl alcohol. The addition of the alcohol causes the gelatinous mass to settle as a fine, white precipitate which is more easily filtered. The lead salts were decomposed with hydrogen sulfide and the resulting solution evaporated to 10 cc. Upon the addition of alcohol, 3 g. of inosite were obtained.

The lead salts in the original filtrate were precipitated with hydrogen sulfide. After boiling off the hydrogen sulfide the filtrate was concentrated on the water bath to a syrupy consistency. The syrupy mass was dried at 100° in a vacuum over sulfuric acid. The resulting hard, hygroscopic product was pulverized, emptied into 100 cc. of acetic anhydride, containing a few drops of sulfuric acid, and the mixture heated for an hour. After cooling, the mixture was filtered. The dark red solution was evaporated to a syrup, dissolved in alcohol and evaporated a second time. The syrupy residue was extracted with chloroform, filtered, and the chloroform distilled off. The dark-colored syrup thus obtained was dissolved in alcohol, boiled with animal charcoal, and filtered. The solution was evaporated to a pale yellow syrup, extracted with ether, and decanted from the tetracetyldimethylcyclohexanhexol which remained undissolved. From the ethereal solution, silky needles of pentacetylmethylcyclohexanhexol slowly separated. The mother liquors gave a yellow syrup, triacetyldimethylcyclohexanhexol, which was equal to 70–80% of the total yield obtained. Monomethylcyclohexanhexol was prepared by heating 2 g. of pentacetylmethylcyclohexanhexol with an aqueous solution containing 4 g. barium hydroxide. A slight excess of sulfuric acid was added and the mixture filtered. The filtrate was concentrated to a syrupy consistency and absolute alcohol added with stirring. A small amount of monomethylcyclohexanhexol separated as a white, amorphous mass. The alcoholic filtrate yielded a syrupy, optically inactive and which has not been identified.

Monomethylcyclohexanhexol crystallizes from hot alcohol in microscopic prisms, melting at 204°. It is soluble in water, less soluble in alcohol and insoluble in ether.

Calc. for $C_6H_6OCH_3(OH)_5$: C, 43.30%; H, 7.22%. Found: C, 43.42; H, 7.38.

Pentacetylmethylcyclohexanhexol, crystallizes from ether in long, white needles, melting at 141°. It is soluble in alcohol, benzene, glacial acetic acid, chloroform, and ethyl acetate. The crystals when exposed to the air for some time take up one and one-half molecules of water, and then melt at 96°. In a vacuum over sulfuric acid they lose this water and melt at 141°. It is optically inactive.

Calc. for $C_6H_6OCH_3(OCOCH_3)_5 + 1^1/_2H_2O$: H_2O = 6.26%; 0.6789 g. subs. lost 0.0422 g. of water = 6.22%.

Calc. for $C_6H_6OCH_3(OCOCH_3)_5$: C, 50.49%; H, 5.94%; Ac, 73.02%. Found: C, 50.52 and 50.47; H, 6.10 and 6.01; Ac, 73.01 and 72.88.

Tetracetyldimethylcyclohexanhexol, crystallizes from alcohol in small prisms, which melt at 223° and sublime unchanged above 300°. It is soluble in benzene, chloroform, alcohol, ethyl acetate and acetone, difficultly soluble in ether, and insoluble in water and in ligroin.

Calculated for $C_6H_6(OCH_3)_2(OCOCH_3)_4$: C, 51.06%; H, 6.38%; Ac, 62.77%. Found: C, 51.05 and 50.93; H, 6.38 and 6.31; Ac, 62.45 and 62.52.

On hydrolysis with an alcoholic solution of barium hydroxide, a syrup soluble in water was obtained which is probably a dimethylcyclohexanhexol.

Triacetyldimethylcyclohexanhexol is a syrup which could not be crystallized. It distils at 212–213°, and 2.5 mm. pressure. It is soluble in alcohol, acetone, ethyl acetate and glacial acetic acid; slightly soluble in hot water. Portions for analysis were dried to constant weight in a vacuum over sulfuric acid at 100°.

Calculated for $C_6H_6(OCH_3)_2OH(OCOCH_3)_3$: C, 50.30%; H, 6.56%; Ac, 53.00%. Found: C, 50.48 and 50.34; H, 6.59 and 6.64; Ac, 52.85 and 52.73.

On hydrolysis with barium hydroxide solution, an unidentified syrup was obtained which will be further investigated.

Ethylation of Inosite.—Thirty-five grams of diethyl sulfate were slowly dropped into a boiling solution of 10 g. of inosite and 70 cc. of 25% sodium hydroxide. The boiling was continued for 48 hours and the sodium sulfate which separated was filtered off. The yellow solution was concentrated to a thick paste on the water bath and then dried in a vacuum over sulfuric acid at 100°. The resulting hygroscopic mass was pulverized and emptied into a flask containing 50 cc. of acetic anhydride and 2 drops of sulfuric acid. The mixture was heated for an hour, cooled and filtered. The filtrate was evaporated to a syrup, dissolved in alcohol and again evaporated. The syrupy mass was extracted with chloroform and the chloroform distilled off. The dark-colored syrup thus obtained was dissolved in alcohol, boiled with animal charcoal and filtered. The resulting pale yellow solution was evaporated to a syrup and dissolved in boiling ether. On cooling, small prisms of tetracetyldiethylcyclohexanhexol separated. As the ether gradually evaporated, soft, white needles of pentacetylethylcyclohexanhexol crystallized. The mother liquors gave a syrup equal to 70–80% of the total yield. This pale yellow syrup on hydrolysis yielded another syrup which has not been identified.

Pentacetylethylcyclohexanhexol crystallizes from ether in long, white needles melting at 128°. It is soluble in chloroform, alcohol, glacial acetic acid, acetone and in benzene. It is optically inactive.

Calc. for $C_6H_6OC_2H_5(OCOCH_3)_5$: C, 51.67%; H, 6.22%; Ac, 70.58%. Found: C, 51.54 and 51.60; H, 6.19 and 6.04; Ac, 70.41 and 70.46.

Tetracetyldiethylcyclohexanhexol crystallizes from alcohol in small prisms melting at 212°, and subliming unchanged above 300°. It is soluble in benzene, chloroform, acetone, and in ethyl acetate, slightly soluble in ether, and insoluble in ligroin or in water. It is optically inactive.

Calc. for $C_6H_6(OC_2H_5)_2(OCOCH_3)_4$: C, 53.46%; H, 6.94%; Ac, 58.42%. Found: C, 53.48 and 53.46; H, 7.01 and 6.93; Ac, 58.31 and 58.65.

An alcoholic solution of tetracetyldiethylcyclohexanhexol was heated with a slight excess of barium hydroxide, sulfuric acid added, and the solution concentrated to a thick syrup. Absolute alcohol was added and on agitating the mixture, diethylcyclohexanhexol was separated.

Diethylcyclohexanhexol crystallizes from hot alcohol in small, shining prisms, which melt at 212°. It is soluble in water and insoluble in ether or in benzene.

Calculated for $C_6H_6(OC_2H_5)_2(OH)_4$: C, 50.67%; H, 8.69%. Found: C, 50.78; H, 8.67.

Derivatives of Pinite.

Preparation of Pinite.—Pinite is obtained from the roots of the "Pinus Lambertina," a species of Californian pine tree, in the form of a dark-colored granular substance with an aromatic odor, mixed with resinous material and pine needles. It was purified in the following manner:

One hundred grams of the crude pinite were dissolved in 250 cc. of water and the volatile resins distilled with steam. The solution was evaporated to a syrupy consistency, dissolved in warm alcohol and filtered. The dark-red filtrate was transferred to a bowl and set away in the ice box. Crystals, which adhered tenaciously to the sides of the bowl, separated. They were pulverized, dried on porous plates and recrystallized from hot alcohol. After remaining in the ice box for several weeks, another crop of crystals was obtained from the black mother liquors. A total yield of 71 g. of pinite was obtained. It gave the Scherer test.

Pinite, monomethylcyclohexanhexol, $C_6H_6OCH_3(OH)_5$, crystallizes from methyl alcohol in small, white prisms, which melt sharply at 186°. It sublimes unchanged above 200° giving fine, colorless needles. It crystallizes from water with difficulty. It is insoluble in absolute alcohol or in ether. The optical rotation was determined by dissolving 0.6950 g. of the anhydrous substance in 100 cc. of water, from which the air had been expelled. This gave $[\alpha]_D^{25} = +65.3°$. This rotation approaches nearest $[\alpha]_D^{22} = +65.5°$, the value determined by Maquenne.[1] Other investigators give[2] $[\alpha]_D^{20} = +65.0°$; and[3] $[\alpha]_D^{20} = +65.7°$.

Previous to this investigation, no crystalline acyl derivatives of pinite had been prepared. The acetyl and benzoyl derivatives were obtained by direct heating with the acid chloride, while the anisyl and cinnamoyl ethers required the presence of quinoline.

Acetylation of Pinite.—Maquenne[4] obtained, on heating pinite with acetic anhydride and zinc chloride, a white, amorphous mass which he called pinite acetate. The work was repeated, and the amorphous mass obtained, which however could not be crystallized. A crystalline pentacetyl derivative of pinite was finally prepared by employing acetyl bromide.

Three grams of pulverized pinite (dried at 110°) and 15 g. of acetyl bromide were placed in a round-bottomed flask connected with a long ground-in glass tube, and gently warmed for half an hour. Hydrogen bromide was given off as the pinite slowly dissolved. The reddish yellow solution was emptied into cold water and settled as an oil, which gradually turned to a white syrup. The syrup was dissolved in alcohol and hot water added till a turbidity formed. On cooling, a fine, white precipitate separated and was filtered. It was recrystallized from 80% methyl alcohol, giving 5 g. of pentacetylmethylcyclohexanhexol.

Pentacetylmethylcyclohexanhexol crystallizes from 80% alcohol in clusters of fine prisms, melting at 98° to a clear liquid. It is insoluble in water, but readily soluble in alcohol, methyl alcohol, glacial acetic acid, benzene, ether, chloroform, acetone and ethyl acetate, $[\alpha]_D^{20} = -9.67°$.

Calc. for $C_6H_6OCH_3(OCOCH_3)_5$: C, 50.49%; H, 5.94%; Ac, 73.02%. Found: C, 50.50 and 50.41; H, 5.81 and 6.09; Ac, 73.30 and 73.11.

On hydrolysis with 50% methyl alcohol solution of barium hydroxide, pinite, m. p. 186°, was obtained.

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[1] *Ann. chim. phys.*, [6] 22, 264 (1891).

[2] Seidel, Thesis des Dorpat.

[3] Girard and Combes, *Compt. rend.*, 110, 84 (1890).

[4] *Loc. cit.*

Benzoylation of Pinite.—Three grams of pulverized anhydrous pinite and 11 g. of benzoyl chloride were placed in a round-bottomed flask connected with a long ground-in glass tube, and heated to boiling for fifteen minutes. To the resulting pale brown solution water was added giving a gummy product. This mixture was heated for an hour, after which a hard, white mass separated out. The water was decanted off and the mass dissolved in boiling absolute alcohol and water added till a precipitate formed. On cooling, a gummy, white mass separated which was filtered off and dried on porous plates. The resulting hard mass was pulverized, dissolved in boiling 80% methyl alcohol and yielded, on cooling, 7 g. of a white, amorphous precipitate of pentabenzoylmethylcyclohexanhexol.

Pentabenzoylmethylcyclohexanhexol separates as a white, amorphous powder, m. p. 97°. It is soluble in alcohol, methyl alcohol, benzene, ether, chloroform, and in glacial acetic acid, and insoluble in water and in ligroin. $[\alpha]_D^{20} = +32.3°$.

Calculated for $C_6H_6OCH_3(OCOC_6H_5)_5$: C, 70.59%; H, 4.76%. Found: C, 70.50 and 70.44; H, 4.76 and 4.73.

A methyl alcoholic solution of this compound was boiled for twenty-four hours with barium hydroxide. An excess of sulfuric acid was then added and the filtrate evaporated to nearly a syrup. On the addition of alcohol a precipitate of pinite, m. p. 186°, resulted.

Anisylation of Pinite.—Three grams of pinite, 11 g. of quinoline, and 13 g. of anisylchloride were heated in a flask for half an hour at 120°. The resulting pale brown solution was dissolved in 100 cc. of chloroform and washed two or three times with a 10% solution of sulfuric acid and once with water. The pale yellow chloroform solution was evaporated to 25 cc. and 100 cc. of hot alcohol added. On cooling, 4 g. of long, white needles of pentanisylmethylcyclohexanhexol crystallized.

Pentanisylmethylcyclohexanhexol crystallizes from alcohol in long, white needles, m. p. 101°. It is soluble in alcohol, methyl alcohol, glacial acetic acid, chloroform, and in benzene. It is insoluble in water. $[\alpha]_D^{20} = \pm 0.0°$.

Calc. for $C_6H_6OCH_3(OCOC_6H_4OCH_3)_5$: C, 65.29%; H, 5.09%. Found: C, 65.29 and 65.19; H, 4.93 and 5.06.

Cinnamoylation of Pinite.—Three grams of pinite, 12 g. of quinoline, and 12 g. of cinnamoyl chloride were heated together for half an hour at 120°. The dark orange-colored syrup was dissolved in 100 cc. of chloroform and washed three times with 10% sulfuric acid and once with water. The pale yellow chloroform solution was concentrated to 25 cc. and 100 cc. of alcohol added. On standing over night a yellow syrup settled, which was dissolved in the least amount of glacial acetic acid and then poured into 50% alcohol. Six grams of pentacinnamoylmethylcyclohexanhexol, in the form of a yellow, amorphous mass was obtained, which was purified by repeating the operation several times. A yield of 4.5 g. of the purified substance was finally obtained.

Pentacinnamoylmethylcyclohexanhexol slowly separates from hot absolute alcohol as a white, amorphous powder, m.p. 105°. It is soluble in benzene, chloroform, ethyl acetate, glacial acetic acid, and in acetone; slightly soluble in alcohol, and insoluble in water and in methyl alcohol. $[\alpha]_D^{20} = +41.2°$.

Calc. for $C_6H_6OCH_3(OCOC_2H_2C_6H_5)_5$: C, 74.00%; H, 5.21%. Found: C, 74.13 and 74.06; H, 5.34 and 5.46.

Nitration of Pinite.—One gram of anhydrous pinite was dissolved in a mixture of 5 cc. of fuming nitric acid and 10 cc. of sulfuric acid. The colorless oil which separated was poured into water. The white syrup which gradually formed was purified by dissolving in alcohol and pouring into water. The syrup which separated was soluble in alcohol, methyl alcohol, ethyl and amyl acetates, acetone, ether, benzene, pyridine, chloroform, carbon disulfide and in glacial acetic acid, but did not crystallize. It was insoluble in ligroin and in water. It possessed a bitter taste, easily decomposed on heating, and exploded when struck with a hammer.

Action of Acetyl Bromide on Pinite.—By the action of acetyl bromide on pinite in a sealed tube, dibromo esters of inosite were obtained. This shows that the methoxy group was also effected by the acid bromide.

Five grams of pinite (dried at 110°) and 19 g. of acetyl bromide were placed in a sealed tube. After remaining 72 hours at room temperature, a dark red solution resulted. This was emptied into water and an oil separated which gradually solidified. The mass was filtered, dissolved in hot alcohol, and on cooling separated as a fine, crystalline substance. This proved to be a mixture, which was separated by fractional crystallization from alcohol. Scaly crystals of α-dibromotetracetylcylcohexantetrol and large prisms of β-dibromotetracetylcyclohexantetrol were obtained. The water solution obtained above was evaporated to 50 cc. and combined with the alcoholic mother liquors and the mixture boiled with animal charcoal for five hours. The resulting pale yellow solution was concentrated to 25 cc. and set away in the ice box over calcium chloride for several days. Colorless, prismatic crystals of dibromocyclohexantetrol, m. p. 216°, were obtained.

On analysis, α-dibromotetracetylcyclohexantetrol gave Br = 33.80%; calc. for $C_6H_6Br_2(OCOCH_3)_4$: 33.75%.

β-Bromotetracetyl glucose containing a trace of impurity readily decomposes. This was noticeable in the case of the halide esters of inosite but to a lesser extent.

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TEMPERATURE COEFFICIENTS AND THE EFFECTS OF ACIDS, BASES AND SALTS IN REACTION VELOCITIES OF THE TRIPHENYLMETHANE DYES.

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1. Introduction.

The study of color changes among acid and basic derivatives of triphenylmethane has engaged the attention of many investigators.

As early as 1888 Nietzki[1] attributed a quinoid structure to the colored

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[1] *Organische Farbstoffe*, 1888.