"The Synthesis of Depsides and Products related to the Tannins with additional work."

by

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The numbers in brackets refer to references which for the sake of clarity and continuity are placed in a folder at the back of the book.

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Part I

The Synthesis of Depsides and products related to the Tannins.

Historical Introduction.

The tannins are defined as a class of amorphous, vegetable substances which are characterised by having an astringent taste, produce a blue or greencolour and precipitate with iron salts, are precipitated by gelatin, albumen and alkaloids, and form an insoluble and imputrescible compound called leather with animal membrane.

The tannins are widely distributed throughout the vegetable Kingdom. Galls are rich in tannin even up to 75%; the inner bark of certain trees is next most abundant especially the oak species; they are also found in leaves, unripe fruit, woods, roots, certain buds and flowers and occasionally in small quantity in seeds.

Many theories have been put forward to account for the presence of the tannins. It was observed that starch was always present with the tannins in barks; that tannins resembled resins; that when both tannins and resins were heated with caustic potash, they yielded the same or similar decomposition products. It was also noticed that tannin free seeds on germinating produced tannin. The tannin content of the tree varies with the time of the year, and in special cases with the amount of starch. Peacock determined the amount of tannin to be greatest in October and least in May, while the amount of starch present was greatest in March.

Experimental efforts to prove the theory that tannins result from the decomposition of starch have so far met with little success and the exact relation between tannins and resins has not been established.

Kraus maintained that all tannins were physiologically alike, but Reintzer disproved this view. Kraus, however, showed that carbon dioxide and light were essential for tannin formation in leaves, and that only green leaves could produce tannin. The outer leaves of a plant exposed to direct sunlight contain more tannin than the inner leaves. The tannin passes from the leaves to the branches then to the trunk and finally to the roots of the tree. Generally most tannin is found in the rhizome.

Darton, in 1881, expressed the generally accepted opinion that only one tannin existed, the difference in properties being due to impurities associated with the tannin in the plant. It is now well established that tannins from different sources frequently vary in composition and properties, and although it is difficult to obtain tannin in a reasonable state of purity, and whilst the number may not be so great as supposed, there is no doubt that three important classes exist.

Many tests were applied in the detection of tannins. Potassium dichromate forms a brown precipitate with nearly all tannins. Ammoniacal copper sulphate forms precipitates of varying colour although Procter maintained that this reagent did not precipitate the tannin of the Hungarian larch, and that it formed insoluble precipitates with compounds other than tannin. Allen recommended ammoniacal potassium ferricyanide which produces a deep red colour which finally turns brown. Alkaloids form white precipitates with tannins and a solution of iodine in aqueous potassium iodide mixed with dilute ammonia produces a brilliant red colour with tannin solutions even when very dilute.

Classifications.

The first attempt to classify the tannins was to divide them into two classes.

1. Iron greening tannins
2. Iron blueing tannins.

The first group give green precipitates with ferric salt solutions and the second group give blue precipitates with ferric salt solutions. This classification, however, fails, due to a modified colouring effect obtained in the presence of acid or organic impurity. Moreover an iron greening tannin can be changed to an iron blueing tannin by cautious addition of alkali. Stenhouse believed that tannins giving blue-black precipitates with ferric salt solutions were glucosides.

Wagner classified the tannins according to their method of formation.

1. Pathological tannins
   i.e. those which are formed by the sting of an insect on vegetable tissue.
2. Physiological tannins
   i.e. those which normally exist in plants.

The former class give blue precipitates, and the latter class either green or blue precipitates with iron salt solutions. He claimed that pathological tannins, as represented by gallotannic acid, existed only in pathological formations of certain species of oak and sumach. This classification was abandoned when it was discovered that gallotannic acid existed in some plants as a physiological tannin.

Böttinger by examining the action of bromine on aqueous tannin extracts and by estimating the bromine content in the precipitated bromo-compounds, grouped the tannins according to the amount of bromine absorbed by them

e.g.	Mangrove tannin	42·15%
	Hemlock bark tannin	43·6%
	Quebracho tannin	44·5%
	Mimosa tannin	49·36%

Many classifications have been suggested, the more important being

1. Colouration of ferric salts
2. Digestion with boiling dilute sulphuric acid.

In the second classification three reactions may be observed.

(a) The hydrolysis of the tannin with formation of gallic acid
(b) Precipitation of ellagic acid
(c) The gradual production of a red insoluble matter known as phlobaphene

According to Procter precipitation with bromine water indicates a "Catechol" or phlobatannin.

Various tests have been employed to distinguish the tannins.

Pine Wood Test.

If a deal shaving is moistened with a solution of phloroglucinol and then with hydrochloric acid, a deep-red-violet colour of phloroglucinol vanillein is produced. Resorcinol gives a blue-violet-colour. Gallotannin or ellagitannin do not react in this manner.

Diazobenzene chloride Test.

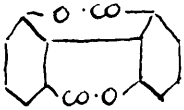
Solutions of certain tannins give, in presence of alkali or alkaline acetates, a red precipitate of azobenzene tannin. This indicates the presence of phloroglucinol or resorcinol. Again, gallotannin and ellagitannin do not react in this way.

Based mainly on the above tests a further classification was suggested.

1. Gallotannins
2. Ellagitannins
3. Catechol tannins.

However, Fischer and Freudenberg's synthetical tannins proved this classification imperfect at least when applied to the first group. Thus, whereas the term "Gallotannin" is only applicable to the "Pyrogallol" tannins and really only related to digallic acid and its derivatives, it is now known that diprotocatechuic acid, diresorcylic acid and digentisic acid, members of the same group, possess tannin properties.

In order to allow for new tannins which might be found or synthesised, it was thought advisable to name the second group after the parent body "Diphenyldimethylolid"



The name "Phlobatannin" was preferred to "Catechol" tannins for the third group because, as far as was known, all tannins belonging to this class yield, on acid hydrolysis, a red insoluble matter known as "Phlobaphene". The classification therefore resolved into—

1. Depside group
2. Diphenyldimethylolid group
3. Phlobatannin group.

This is the classification now in use.

Since this thesis deals only with the third group an example of groups one and two will suffice.

Gallotannin is typical of the first group.

Ellagitannin is the only natural product of the second group yet isolated.

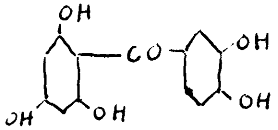
Phlobatannins.

The characteristic of this group is that on boiling with dilute mineral acid, "anhydride" or "phlobaphene" is precipitated. The group is sometimes known as the "Catechol" group because the majority of its members give a green colouration with ferric chloride and protocatechuic acid or catechol is one of the degradation products. The above statement is somewhat misleading because it infers that all members of this class are derived from diprotocatechuic acid.

$$(OH)_2\ C_6H_3CO{\cdot}O\ C_6H_3(OH)COOH$$

On hydrolysis, diprotocatechuic acid yields two molecules of protocatechuic acid without precipitation of phlobaphene. Moreover phlobaphene yielding tannins exist which do not contain the catechol nucleus e.g. Cyanomaclurin of Jakwood.

Böttinger and Etti suggested a benzophenone structure for tannins of this group e.g. Maclurin tannin



which, on boiling with dilute hydrochloric acid, yields rufimoric acid, a red insoluble phlobaphene-like mass.

Maiden and Smith claimed that Aromadendin, which apparently has a benzophenone structure, was similar to catechin. It is well to bear in mind that carboxylic acids of certain hydroxy benzophenones have strong mordant dye properties which are foreign to tannins of this group.

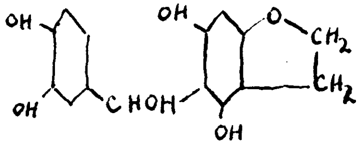
Many phlobatannins contain both phloroglucinol and catechol in their nucleii. It is curious to note that the bromo-derivatives, which are precipitated by the addition of bromine water, are easily accounted for if phloroglucinol or resorcinol is present, but even where these two compounds are absent so far as is known, the same result is obtained.

Fischer suggested that the phlobaphene reaction is to be assigned to the reactivity of the phloroglucinol group present in these substances. Coloured compounds have been prepared by the interaction of phloroglucinol with aldehydes and Counder united sugars and phloroglucinol in presence of gaseous hydrochloric acid. Again, by boiling dextrose with phloroglucinol in dilute hydrochloric acid, a brown-red precipitate closely resembling phlobaphene, can be produced. "Phlorotannin Red" is also interesting. It was prepared by heating phloroglucinol dicarboxylic acid to 160-175°

The presence of a depside group in the molecule is reported to confer tanning properties on the phlobatannins as generally acid hydrolysis yields protocatechuic acid as well as phlobaphene.

It was anticipated by Fischer and Freudenberg that these compounds would also possess a sugar nucleus.

Catechin, aca-catechin and cyanomaclurin, all crystalline products, are closely allied to phlobatannins. Kostanecki and Lampe assigned to catechin the constitution



Catechin, although not a tannin, gives the "pine wood" test and bromocatechuretin is precipitated with bromine water. Löwe and Etti state that catechin forms catechutannic acid which exists beside the tannin in the plant and possesses typical properties of phlobatannins. It is therefore deduced that tannins have evolved from substances of the catechin type and that Quebracho resin and Guarana catechin are intermediate products of the evolution.

Coca-tannic acid is the only member of this group obtained crystalline. The remaining members are all amorphous, faintly coloured compounds, the colour developing on continued exposure to light.

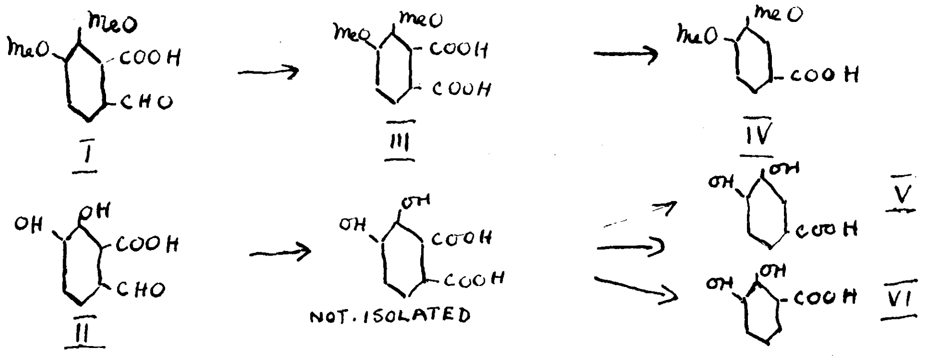
Numerous tannins of this group have been isolated, most of them showing the same reactions.

<u>Hemlock Tannin</u>.

This tannin is obtained from the bark of the Hemlock tree, and it is widely used for tanning purposes. Böttinger thought this tannin was related to Quercitannic acid of the oak, as, on heating with sulphuric or hydrochloric acid, the "anhydride", hemlock red is formed to which he assigns the formula $C_{40}H_{30}O_{17}$. With hydrochloric acid at 180° hemlock red evolves methyl chloride and the acetyl derivative $C_{40}H_{23}O_{17}(C_2H_3O_2)_7$ (based on the empirical formula $C_{20}H_{18}O_{10}$) but bromine gives a mixture of $C_{40}H_{20}Br_{10}O_{17}$ and $C_{40}H_{16}Br_{14}O_{17}$ Addition of bromine to Hemlock tannin extract precipitates the tetrabromo compound $C_{20}H_{14}Br_4O_{10}$ a yellow powder which yields the penta-acetyl derivative $C_{20}H_9Br_4O_{10}(C_2H_3O_2)_5$ and by further addition of bromine $C_{20}H_{12}Br_6O_{10}$.

Manning and Nierenstein (1) re-examined Böttinger's empirical formula $C_{20}H_{18}O_{10}$ for Hemlock tannin (based on the bromine content) and found that his product $C_{20}H_{14}O_{10}Br_4$ was not always produced. They obtained a series of compounds which varied in content of bromine from 40-48%. On alkaline hydrolysis brome-hemlock tannin yielded a substance $C_8H_7O_4Br$ which they called "monobromotsuginic acid" M.P 143-145°

This acid did not undergo further hydrolysis as did the hydrolysis product from Quebracho tannin by the same method. They assigned the constitution $COOH \cdot C_7 H_5 O Br OH$ to this acid. With alcoholic potash the tannin yielded protocatechuic acid but with barium hydroxide it yielded protocatechuic acid and 2:3 dihydroxy benzoic acid and a substance $C_{10} H_8 O_3$ which they thought to be an aldehyde. Methylated Hemlock tannin, (which was optically active) gave on alkaline hydrolysis, vanillic acid and a precipitate A which oxidised to hemipinic acid. Mild hydrolysis of A gave opianic acid. They therefore suggested the existence of noropianic acid II in the molecule because opianic acid I is found which probably explains the formation of hemipinic acid III and veratric acid IV from methylated Hemlock tannin and protocatechuic acid V and 2:3 dihydroxy benzoic acid VI from Hemlock tannin



Experimental

Estimation of acetone soluble tannin in Hemlock bark.

An accurately weighed quantity (about 25 grams) of finely divided Hemlock bark was weighed into a soxlet thimble, the thimble transferred to a soxlet apparatus and the tannin extracted with 50c·c acetone during 3 hours heating on a waterbath. After complete exhaustion of the tannin the solution was poured into an evaporating basin which had been previously weighed and the acetone was evaporated. The residual tannin was then weighed.

Estimation of Water soluble tannin in Hemlock bark.

An accurately weighed quantity of finely divided bark was extracted with 200c.c. water by the above method. After the extraction was complete (5 hours) the aqueous tannin solution was evaporated to dryness in an air oven at 125° and the percentage water soluble tannin estimated.

Estimation of the Sugar content of Hemlock bark.

The water soluble tannin residue was ground into a very fine state of division and 250c.c. 5% sulphuric acid added. The mixture was refluxed for 8 hours and then was filtered and thoroughly washed with water. The filtrate was made alkaline with dilute sodium hydroxide solution, boiled with animal charcoal to remove colouring matter and titrated with standard Fehling's solution.

In this manner the acetone soluble tannin, water soluble tannin and sugar content of Hemlock bark obtained from two sources were estimated. Two of the samples of bark came from the same source, but from trees of different age. The results are contained in the following table.

	Western I	Western II	Eastern
Acetone soluble tannin	22%	22·8%	14·2%
Water soluble tannin	13·8%	16·5%	12·58%
Sugar Content	5·18%	4·8%	4·2%

Methylation of Hemlock tannin.

Hemlock tannin (3·5 grams) was dissolved in a solution containing sodium hydroxide (6 grams) and water (45c·c) by shaking vigorously. The alkaline solution was then gently heated and a little dimethyl sulphate was added. As soon as the violent reaction commenced the heat was removed and the action was maintained by additions of small quantities of dimethyl sulphate. The contents of the flask were kept alkaline by adding 4 normal sodium hydroxide solution when necessary. A red solid separated from the solution and when it was completely precipitated the mixture was heated to boiling and allowed to cool. The solid was filtered and washed, first with dilute caustic soda to remove unchanged starting product and finally with water. It was then dissolved in the minimum quantity of acetone and poured into 4 times its own volume of water. The resultant precipitated methylated tannin was collected, washed with water and dried in a vacuum. Methylated Hemlock tannin had no definite melting point. It became sticky at 85° turned a black colour at 120° and decomposed at 132° It was an amorphous red coloured solid insoluble in water, but easily soluble in acetone and alcohol.

Analysis.

Carbon	Found C = 64·1%
Hydrogen	Found H = 5·32%

Methylation of Mimosa tannin.

Finely divided Mimosa tannin (10 grams) was dissolved by shaking in 50% sodium hydroxide solution. The solution became warm and a little dimethyl sulphate was added. A vigorous reaction ensued which was maintained by further additions of small quantities of dimethyl sulphate. The mixture was kept alkaline by adding a few drops of 50% sodium hydroxide solution when necessary. As before, a dark coloured solid separated from solution and when no further solid separated the reaction was assumed complete. The solid was collected washed with dilute alkali to remove unchanged tannin and then with water. It was then dried in vacuo. The faintly red amorphous methylated Mimosa tannin had no definite melting point, but decomposed at 130° It was insoluble in water, but easily soluble in acetone and alcohol.

Analysis.

Carbon	Found C = 66·6%
Hydrogen	Found H = 5·23%

Oxidation of methylated Hemlock tannin with aqueous potassium permanganate.

Fully methylated Hemlock tannin (6 grams) was ground into a very fine state of division and suspended in water (300c·c·) Potassium permanganate (25 grams) was added a little at a time the reaction being allowed to complete before further addition. It was necessary to heat for a short time to begin the oxidation. The mixture was kept agitated during the reaction. After cooling, sulphur dioxide was passed through the liquid until the manganese dioxide had entirely disappeared and a white precipitate had formed. This precipitate was collected, washed thoroughly with water and dried. On treatment with dilute mineral acid sulphur dioxide was evolved and a faintly red solid was obtained. It was filtered, washed with water free from acid and recrystallised from a mixture of benzene and ligroin in very fine red crystals melting above 360°. This product is evidently an aldehyde or ketone since it was obtained from its bisulphite product.

Analysis.

Carbon	Found C = 66·5%
Hydrogen	Found H = 5·5%

Oxidation of methylated Mimosa tannin with aqueous potassium permanganate.

Finely ground methylated Mimosa tannin (10 grams) was suspended in water (400c·c·) Potassium permanganate 40 grams) was added a little at a time and after all the potassium permanganate was decomposed the liquid was cooled and sulphur dioxide passed through it until the manganese dioxide was removed and a cream coloured precipitate remained. The precipitate was filtered and washed with water. It had no action with saturated sodium bicarbonate solution and was therefore not acidic. The product was subjected to further oxidation with potassium permanganate (8 grams) in the same way as before. The oxidation product which was isolated with sulphur dioxide, was collected, washed with water and recrystallised from alcohol in faintly red crystals M.P.170°

Analysis.

Carbon	Found C = 67·1%
Hydrogen	Found H = 5·30%

Oxidation of methylated Mimosa tannin with hydrogen peroxide.

Methylated Mimosa tannin (6 grams) was ground into a fine state of division and suspended in water (100c.c.) The mixture was heated on a waterbath with constant stirring and hydrogen peroxide (100c.c of 100 volumes) was added gently. In order to begin the reaction normal sodium hydroxide solution (25c.c.) was added. When the reaction was complete a further quantity of hydrogen peroxide (150c.c.) was added and the oxidation allowed to proceed on the waterbath. On the termination of the reaction the liquid was filtered to remove solid material, cooled and carefully acidified with dilute sulphuric acid. The resultant precipitate was filtered, washed with water and recrystallised from benzene in small red crystals which melted above 360° This compound slowly reacted with saturated sodium bicarbonate solution and therefore is acidic.

Analysis.

Carbon	Found C = 66.5%
Hydrogen	Found H = 5.37%

Oxidation of methylated Mimosa tannin. Perkin's method.

Methylated Mimosa tannin (5 grams) was dissolved in methyl alcohol (90c.c) and heated on a waterbath. Saturated potassium permanganate solution (100c.c.) was added drop by drop with constant stirring. When the oxidation was complete further quantities of methyl alcohol (50c.c.) and of saturated aqueous potassium permanganate (100c.c.) were added. On completion, the manganese dioxide was filtered and washed with boiling méthyl alcohol. The filtrate when cold was refiltered to remove any unchanged starting product which had separated during the cooling and the filtrate was poured into twice its volume of water and made just acid with dilute hydrochloric acid. A brown gelatinous solid precipitated. It was collected, washed with water and recrystallised from benzene in shining dark red plates M.P.208°

Analysis.

Carbon	Found C = 63·8%
Hydrogen	Found H = 5·42%

Summary

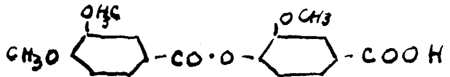
The yields obtained were very small generally 0·5 grams being obtained from 10 grams of starting product. Sufficient oxidation product which might be useful in establishing the molecular structure of phlobatannins cannot be obtained.

The Synthesis of Depsides and Polydepsides.

Depsides are closely related to tannins in that they possess tanning properties and the presence of a depside group is thought to confer tanning properties on the molecule. In order that they might be obtained in good yield and in the easiest possible manner an improved method of synthesis was exploited.

The existing method of synthesis consisted of condensing an acid chloride directly with the di-sodium salt of a hydroxy acid. The improved method consists briefly of condensing an acid chloride with the sodium salt of a hydroxy aldehyde and oxidising the resultant aldehyde with aqueous potassium permanganate in methyl alcoholic solution. This method possesses several advantages over the general method; there is no complication due to the simultaneous formation of depside and acid anhydride, separation of which is very difficult owing to the low solubility of the feebly acidic depside in sodium bicarbonate solution. The yields in all cases are very good and the method is of general application.

Two series of depsides are now described, one derived from anisoyl chloride and the other from veratroyl chloride. The positions of the substituents in the ring bearing the carboxyl group are indicated by the numbers 1, 2, 3 etc. and those in the other ring by the numbers $1'$, $2'$, $3'$ etc. e.g. diprotocatechuic acid trimethyl ether is named $3:3':4'$ trimethoxy - p-dibenzoic acid.



The constitution of the depsides is fixed by the mode of synthesis and confirmed by analysis. In order to prove conclusively that the free components of the depside namely anisic acid, veratric acid, p-hydroxy benzoic acid etc. were not present with the depside, it was tested for the characteristic colour reaction of phenolic acids with ferric chloride solution.

The condensation of the acid chloride with the sodium salt of the hydroxy aldehyde was usually quick, being generally completed after shaking them together for two hours at room temperature. On pouring into water, a crystalline precipitate of the aldehyde separated from solution. To ensure the absence of the free parent substances the aldehyde was obtained from alkaline solution and as a further precaution it was washed with dilute alkali. The aldehydes readily crystallised from dilute acetone or dilute alcohol giving yields of approximately 70% of the theoretical.

It was noticed during the course of this work that condensation was most difficult when the hydroxyl group of the hydroxy aldehyde occurred in the meta position, a much longer time being required to effect the condensation. Indeed 4' methoxy-m-dibenzaldehyde was only prepared after several attempts and with difficulty after shaking the component substances for eight hours at room temperature. When poured into water an oily solid separated which however was easily recrystallised.

The oxidation of the aldehyde to the acid was straightforward and presented little difficulty. The methyl alcoholic solution of the depside is poured into water and made slightly acid with dilute acetic acid. This experiment required considerable care owing to the easily hydrolysed nature of the product in acid solution. The resultant precipitate was recrystallised in every case with dilute acetone or dilute alcohol and the yields after purification were of the order of 70% of the theoretical.

When the benzoyloxy and the carboxyl groups were in the para position to one another the crude depside when precipitated with dilute acetic acid was gelatinous.

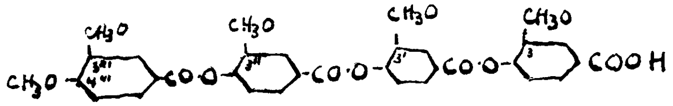
The described method was then extended to the synthesis of polydepsides by the repeated coupling of depside acid chloride with the sodium salt of a hydroxy aldehyde and oxidising the resultant aldehyde with aqueous potassium permanganate to the corresponding acid. In this way di -tri- and tetradepsides were prepared.

It would be well at this juncture to report an improvement in the method of oxidising the aldehyde. Previously it had been effected by oxidising the aldehyde in methyl alcoholic solution with aqueous potassium permanganate which was not entirely satisfactory due to the oxidation of the solvent and to the fact that the terminating point of the aldehyde oxidation could not be guaranteed with any degree of accuracy. The improved method consists of suspending the finely divided aldehyde in dilute potassium permanganate solution containing approximately an equal weight of permanganate as aldehyde to be oxidised. The mixture is heated on a waterbath at about 70° for twenty-four hours until the characteristic colour of the permanganate entirely vanished. The liquid is then cooled and sulphur dioxide is passed through it which simultaneously removed the manganese dioxide and precipitated the oxidation product. The method is additionally advantageous because sulphurous acid does not hydrolyse the depside. The acid is then collected, washed and recrystallised. The yields improved considerably as nothing was lost as previously in transferring and filtering.

As the series is ascended the application of the method becomes increasingly difficult due to the depside acid chloride becoming more and more sparingly soluble in acetone and finally becoming insoluble in cold acetone. Condensation is effected with the sodium salt of the hydroxy aldehyde, but since the polydepside separates immediately on formation from the solution, the completion of the reaction is indeterminate. Moreover difficulty is experienced in removing any free acid chloride from the polydepside.

All the polydepsides are crystalline, increase in molecular weight being generally accompanied by increase in melting point. They are insoluble in water, sparingly soluble to insoluble in acetone even when hot, as we ascend from didepside to tetradepside.

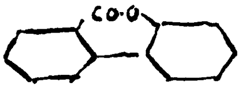
The nonenclature previously used has been extended e.g. tetraprotocatechuic acid pentamethyl ether is named $3:3':3'':3''':4'''$ pentamethoxy-p-p-p tetrabenzoic acid



It was thought that a depside group might be present in the molecular structure of phlobatannins and if so would probably be of the ellagic acid type. An investigation of the constitution of diphenylmethylolid was therefore instituted.

This compound has been described by several authors.

1. Richter (2) prepared diphenylmethylolid by distilling a mixture of finely divided sodium salicylate with phosphorus oxychloride in a retort and after removing the excess phosphorus oxychloride by distillation he obtained an oily distillate which boiled at 250-300° On subsequent treatment and purification a colourless crystalline product melting at 91° was obtained. He assigned to the compound the constitution

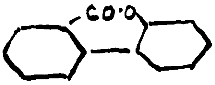


2. Graebe and Schestakow (3) prepared it by fusing hydroxy fluorenone with solid sodium hydroxide which resulted in the production of $2:2'$ dihydroxy diphenyl carboxylic acid and $2:6'$ dihydroxy diphenyl carboxylic acid and from the former they obtained diphenylmethylolid. They also repeated Richter's synthesis for comparison with their product and

although the two compounds closely resembled one another, the authors were not entirely satisfied. Furthermore they prepared diphenylmethylolid from anthranilic acid by diazotising and heating the diazonium sulphate with two parts of phenol on a waterbath.

3. Dobbie, Fox and Gauge (4) reported the formation of diphenylmethylolid by dry distilling silver diphenate. They obtained a light yellow crystalline solid meltingat 92° the bromo derivative of which corresponded with that prepared by Richter.

It is obvious from these syntheses that the constitution



assigned to diphenylmethylolid has not been satisfactorily established and it was deemed advisable to synthesise this compound in such a way that the manner of synthesis would fix the constitution.

The first method attempted was to couple ortho-iodophenol with ortho-iodo-benzoic acid in the presence of copper bronze. This condensation resulted in the formation of the three possible products, viz:-

1. 2:2' dihydroxy diphenyl
2. 2:2' dicarboxy diphenyl
3. diphenylmethylolid

It was expected that 2 hydroxy 2' carboxy diphenyl on formation would automatically lose a molecule of water and form diphenylmethylolid. It was proposed to separate these products in the following way:-

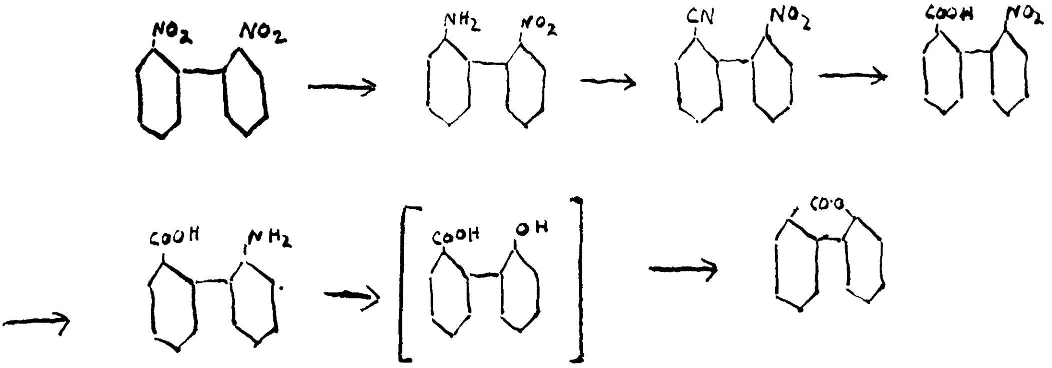
1. Remove 2:2' diphenic acid by extracting the ethereal solution of the mixture with saturated sodium bicarbonate solution and if diphenylmethylolid was not automatically formed as above, 2 hydroxy 2' carboxy diphenyl would also be extracted by the bicarbonate solution. The bicarbonate solution was acidified and the precipitated acid collected, washed and dried thoroughly. It was then dissolved in dry chloroform and treated in the cold with phosphorus pentoxide which would result in the formation of diphenic anhydride and diphenylmethylolid by removal of a molecule of water, assuming both acids present. After pouring into water and cooling, the liquid was extracted with sodium carbonate solution to remove the diphenic anhydride as the acid and the diphenylmethylolid would remain in the chloroformic solution. According to the authors who have reported on diphenylmethylolid, sodium carbonate does not effect hydrolysis. However, no diphenylmethylolid was isolated at this stage.

The mixture of diphenylmethylolid and 2:2' dihydroxy diphenyl was treated fractionally with increasingly strong alkali, but complete separation could not be effected.

2. A probable synthesis from 2:2' dinitrodiphenyl was next examined. It was proposed to reduce one of the nitro groups to form 2 amino 2' nitrodiphenyl and then replace the amino group with a nitrile group. The nitrile

on hydrolysis would yield 2 carboxy 2′ nitrodiphenyl. The second nitrogroup could then be reduced and by diazotising and subsequently boiling the diazonium solution diphenylmethylolid should be formed by elimination of a molecule of water. If water is not eliminated then dehydration by the method indicated above would result in the formation of the desired compound.

Scheme of Synthesis.

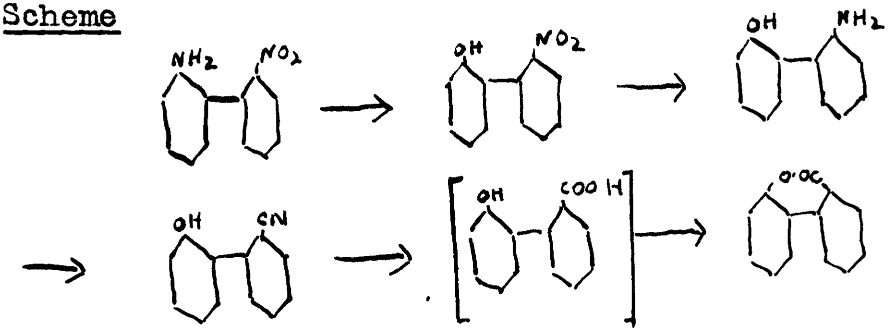


However, this scheme broke down due to the fact that sufficient nitrile could not be obtained.

A slight alteration in the above procedure was then tried. It had been found very difficult to diazotise 2 amino 2′ nitrodiphenyl and obtain from it a good yield of the corresponding nitrile by the Sandmeyer reaction, owing to the large excess mineral acid used in the diazotisation the subsequent neutralisation of which so increased the bulk of solution, that it was impossible to work with it. Diazotisation with amyl nitrite in alcoholic solution proved unavailing for even in moderate excess hydrochloric acid the corresponding diazo-amino product separated immediately from solution. Another method which failed was that of Hogson and Walker (5) - diazotisation of the compound in glacial acetic acid with a solution of sodium nitrite in concentrated sulphuric acid. Again the neutralisation of the free acid made the bulk of solution too great to work with.

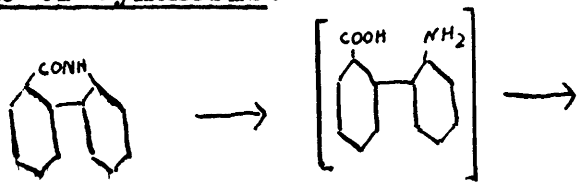
It was decided to diazotise the 2 amino - $2'$-nitrodiphenyl in a large excess of acid and by subsequent boiling replace the amino group with a hydroxyl group. It was then proposed to reduce the second nitro group and replace the resultant amino group with a nitrile group. On hydrolysis this product should yield diphenylmethylolid. Unfortunately, however, the 2 hydroxy-$2'$amino diphenyl could only be obtained in very small yield. Many methods of reduction were tried e.g. with tin and hydrochloric acid, with zinc and acetic acid, with titinous sulphate and with sodium polysulphide, but no satisfactory method was obtained. The failure to obtain this compound in bulk was thought due to a strong steric effect from the hydroxyl in the 2 position, and this seems borne out by the failure of attempts to acetylate the free hydroxyl group. This synthesis was therefore given up.

Scheme



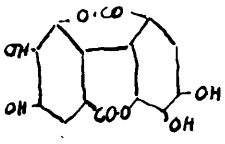
3. A third method was then tried. It was proposed to hydrolyse phenanthradone and by diazotising and boiling diphenylmethylolid would result. The hydrolysis was effected by heating phenanthradone with concentrated sulphuric acid on a waterbath until complete solution. Attempts to isolate the free amino-acid proved futile, but proof of the presence of the primary amine group was established by a characteristic test. The cold phenanthradone solution in concentrated sulphuric acid was diazotised in the ordinary way and on subsequently boiling the diazonium solution for three hours an oil separated. It was extracted with ether, the ether removed by distillation and the residue recrystallised from alcohol in faintly yellow coloured needles M.P.90°

Scheme of Synthesis.



This method of synthesis whilst useful in establishing the constitution of diphenylmethylolid is useless for its preparation in bulk.

4. It was deduced from the foregoing that if phenyl benzoate was distilled over red-hot pumice stone diphenylmethylolid might result. However, decomposition products only were obtained.

Ellagic Acid  has been prepared by various methods such as oxidising gallic acid with potassium persulphate, iodine or arsenic acid (6) and by oxidising protocatechuic aldehyde in a similar way. None of these methods give good yields, the last method giving the best results.

In order to synthesise ellagic acid cheaply, oxidation of piperonal with ammonium persulphate was exploited in the hope that the methylenedioxy derivative of ellagic acid would result. Hydrolysis of the two, three membered rings should then yield ellagic acid. A compound melting at 274° was obtained. At this time Pfeiffer (7) published a synthesis of protocatechuic aldehyde from piperonal which robbed the work of any potential value.

Experimental.

Simple Depsides.

Veratraldehyde

Reference (8)

This compound was prepared by methylating a strongly alkaline solution of vanillin with dimethyl sulphate according to the method of Perkin and Robinson.

Veratric Acid.

Veratraldehyde (20 grams) was dissolved by heating in dilute alkali (50c.c. dilute sodium hydroxide in 150c.c. water). A saturated aqueous potassium permanganate solution was added in small quantities until the oxidation was complete. After cooling, sulphur dioxide was passed through the solution which simultaneously removed the manganese dioxide and precipitated the veratric acid. The acid was collected, washed with water and thoroughly dried.

Yield 95% theoretical.

Veratroyl Chloride.

Dry veratric acid (1 molecule) was refluxed with thionyl chloride (1·5 molecules) on a waterbath for 3 hours until no sulphur dioxide or hydrochloric acid gas was evolved. The excess thionyl chloride was distilled at reduced pressure and the residue was recrystallised from ligroin.

Yield theoretical.

Diprotocatechuic-aldehyde-trimethyl ether (3:3′:4′trimethoxy-p-dibenzaldehyde).

Vanillin (1·52 grams- 1 molecule) was dissolved in the minimum quantity of acetone (15c.c.) and normal sodium hydroxide solution (10c.c.-1 molecule) added. Veratroyl chloride (2·1 grams-slight excess of 1 molecule) was dissolved in acetone (15c.c.) and the latter solution added to the former. The mixture was then shaken for 2 hours at room temperature to complete the condensation. The reaction mixture was poured in water (5 volumes) and left standing for some time. The solution was made alkaline to prevent contamination from the component substances. The solid aldehyde which separated as a crystalline precipitate from the alkaline solution was filtered, washed with dilute caustic soda solution and then with water and recrystallised from dilute alcohol in stout colourless needles M.P.124°

Yield - 90% of the theoretical.

Analysis.

Carbon Found C = 64·0%
$C_{17}H_{16}O_6$ requires C = 64·6%
Hydrogen Found H = 5·1%
$C_{17}H_{16}O_6$ requires H = 5·1%

Diprotocatechuic acid trimethyl ether (3:3′:4′ trimethoxy-p-dibenzoic acid)

To a boiling solution of diprotocatechuic-aldehyde trimethyl ether (6 grams) in methyl alcohol (100c.c.) saturated potassium permanganate solution (100c.c.) was added drop by drop. The liquid was filtered hot to remove precipitated manganese dioxide, cooled, and diluted with water (5 volumes) and made just acid with dilute acetic acid. Great care is necessary on adding the acetic acid because excess acid would result in the hydrolysis of the depside. The depside which settled out of solution during one hour was filtered, washed free from acid with water and recrystallised from dilute acetone in colourless plates or prisms M.P.216-218°

The yield was 90% of the theoretical.

The depside was very slowly soluble in sodium bicarbonate solution, but freely soluble in dilute caustic soda solution.

Analysis.

Carbon Found C = 61·3%

$C_{17}H_{16}O_{7}$ requires C = 61·5%

Hydrogen Found H = 4·9%

$C_{17}H_{16}O_{7}$ requires H = 4·8%

3′:4′ dimethoxy-o-dibenzaldehyde.

Salicylaldehyde (1·22 grams-1 molecule) was dissolved in acetone (15c·c·) and normal sodium hydroxide solution (10c.c.-1 molecule) added. Veratroyl chloride (2·1 grams - slight excess of 1 molecule) was dissolved in acetone (15c.c.) and the second solution added to the first. After shaking the mixture for 1½ hours at atmospheric temperature it was poured into water (5 volumes) and the solution was made alkaline with standard alkali if necessary. The resultant white precipitate was filtered, washed with water and recrystallised from dilute alcohol in very fine white needles M.P.102° The yield was 90% of the theoretical.

Analysis.

Carbon Found C = 66·3%

$C_{16}H_{14}O_5$ requires C = 67·1%

Hydrogen Found H = 5·0%

$C_{16}H_{14}O_5$ requires H = 4·9%

3′:4′ dimethoxy-o-dibenzoic acid

3′:4′ dimethoxy-o-dibenzaldehyde (1 gram) was dissolved in methyl alcohol (17 grams) by heating on a waterbath and saturated aqueous potassium permanganate (30c.c.) was carefully added. A further 10c.c. of methyl alcohol was then added and the precipitated manganese dioxide was filtered, washed thoroughly with boiling methyl alcohol and the filtrate allowed to cool. It was poured into water (5 volumes) and the depside was precipitated by adding a few drops of dilute sulphuric acid until the solution was just acid. The precipitate was collected, washed with water and recrystallised from dilute alcohol in fine white needles M.P.151-152°

The yield was 60% of the theoretical.

Analysis.

Carbon Found C = 63·5%

$C_{16}H_{14}O_6$ requires C = 63·6%

Hydrogen Found H = 4·7%

$C_{16}H_{14}O_6$ requires H = 4·6%

3′:4′ dimethoxy-m-dibenzaldehyde.

To a solution containing m-hydroxy-benzaldehyde (1·2 grams-1 molecule) in acetone (15c.c.) and normal sodium hydroxide solution (10c.c.-1 molecule) was added a solution of veratroyl chloride (2·1 grams-slight excess of 1 molecule) dissolved in acetone (15c.c.) This mixture was shaken for 4 hours and then poured into water (5 volumes) the solution being made alkaline if necessary. On standing the aldehyde separated as a solid. It was filtered, washed with water and recrystallised from dilute alcohol in fine white needles M.P.120° The yield was 2·8 grams which is 75% of the theoretical.

Analysis.

Carbon	Found C =	66·2%
	$C_{16}H_{14}O_5$ requires C =	67·1%
Hydrogen	Found H =	5·0%
	$C_{16}H_{14}O_5$ requires H =	4·9%

3′:4′ dimethoxy-m-dibenzoic acid.

3′:4′ dimethoxy-m-dibenzaldehyde (2 grams) was dissolved in methyl alcohol (30c.c.) and raised to boiling. Saturated potassium permanganate solution (50c.c.) was added in small quantities the reaction being allowed to complete before further additions. The boiling liquid was filtered and the manganese dioxide was washed with boiling methyl alcohol. After cooling the filtrate was poured into water (5 volumes) and made acid with a few drops of dilute acetic acid. The precipitate which separated after a few hours was collected, washed free from dilute acetic acid with water and recrystallised from dilute acetone in plate crystals M.P.167° The yield was 95% of the theoretical.

Analysis.

Carbon Found C = 62·5%

$C_{16}H_{14}O_6$ requires C = 63·6%

Hydrogen Found H = 4·7%

$C_{16}H_{14}O_6$ requires H = 4·6%

3′:4′ dimethoxy-p-dibenzaldehyde

p-hydroxybenzaldehyde (2·4 grams-1 molecule) was dissolved in acetone (30c.c.) and normal caustic soda solution (20c.c-1 molecule) added. To this solution was added a solution of veratroyl chloride (4·2 grams-slight excess of 1 molecule) in acetone (30c.c.) and the mixture was shaken for 1 hour at room temperature. On pouring into water a thick white precipitate settled out almost immediately and after making the solution alkaline this precipitate was filtered, washed free from alkali with water, and it recrystallised from dilute alcohol in colourless needles M.P.109°. The yield was 85% of the theoretical.

Analysis.

Carbon Found C = 67·0%

$C_{16}H_{14}O_5$ requires C = 67·1%

Hydrogen Found H = 5·0%

$C_{16}H_{14}O_5$ requires H = 4·9%

3′: 4′ dimethoxy-p-dibenzoic acid

A boiling solution of 3′:4′ dimethoxy-p-dibenzaldehyde (2 grams) in methyl alcohol (30c.c.) was oxidised by adding small quantities of saturated potassium permanganate solution (in all 50c.c.) The precipitated manganese dioxide was separated from the hot solution by filtering. The filtrate when cold was poured into water (5 volumes) and made just acid as before with dilute acetic acid. A gelatinous precipitate resulted. After standing for 24 hours this precipitate was collected, washed with water free from acid, and it recrystallised from dilute acetone in hair-like needles M.P.211-212° The yield was 70% of the theoretical.

Analysis.

Carbon Found C = 62·8%

$C_{16}H_{14}O_6$ requires C = 63·6%

Hydrogen Found H = 4·60%

$C_{16}H_{14}O_6$ requires H = 4·64%

Anisoyl Chloride.

Anisic acid (1 molecule) was refluxed with thionyl chloride (2 molecules) on a waterbath until there was no further evolution of sulphur dioxide or hydrochloric acid gas (time 3 hours). The excess thionyl chloride was distilled off and the residue was distilled under reduced pressure. On cooling the distillate solidified M.P.22° The yield was 98% of the theoretical.

4' methoxy-o-dibenzaldehyde.

Salicylaldehyde (2·2 grams-1 molecule) was dissolved in the minimum quantity of acetone (15c.c.) and normal sodium hydroxide solution (20c.c.-1 molecule) was added. Anisoyl chloride (3·4 grams- slight excess of 1 molecule) dissolved in acetone (15c.c.) was added to the first solution and the mixture was shaken for 4 hours at room temperature. The reaction mixture was then poured into water (6-7 volumes) and the solution made slightly alkaline with standard caustic soda. The precipitate which separated on standing overnight was filtered, washed with water free from alkali and it recrystallised from dilute alcohol in colourless prisms M.P.85° The yield was 60% of the theoretical.

Analysis.

Carbon	Found	C = 69·0%
	$C_{15}H_{12}O_4$ requires	C - 70·4%
Hydrogen	Found	H = 4·7%
	$C_{15}H_{12}O_4$ requires	H = 4·7%

4' methoxy-o-dibenzoic acid

4'methoxy-o-dibenzaldehyde (3 grams) was dissolved in methyl alcohol (30c.c.) by heating on a waterbath. Saturated potassium permanganate was added in small quantities the reaction being allowed to complete between each addition. A slight excess on that required to oxidise the aldehyde was used. The manganese dioxide was filtered and washed with boiling methyl alcohol. The cold filtrate was then poured into water (4-5 volumes) and made slightly acid with a few drops of dilute sulphuric acid. The precipitated depside was allowed to settle and it was then filtered and washed with water. It recrystallised from dilute alcohol in colourless needles M.P.132° giving a yield of 70% of the theoretical.

Analysis.

Carbon Found C = 65·2%

$C_{15}H_{12}O_5$ requires C = 66·2%

Hydrogen Found H = 4·5%

$C_{15}H_{12}O_5$ requires H = 4·4%

4' methoxy-m-dibenzaldehyde.

To a solution of m-hydroxy benzaldehyde (2·2 grams-1 molecule) in acetone (15c.c.) and normal sodium hydroxide solution (20c.c.-1 molecule) was added a solution of anisoyl chloride (3·4 grams - slight excess of 1 molecule) in acetone (15c.c.) and the mixture was shaken for 16 hours at room temperature. It was then poured into water (5 volumes made slightly alkaline by addition of standard caustic soda solution and after standing for 24 hours an oily solid separated from solution. The supernatent liquid was poured off and the residue was washed several times by decantation with water. It recrystallised from dilute alcohol in fine white needles M.P.102° The yield was 60% of the theoretical.

Analysis.

Carbon Found C = 69·8%

$C_{15}H_{12}O_4$ requires C = 70·4%

Hydrogen Found H = 4·8%

$C_{15}H_{12}O_4$ requires H = 4·7%

4' methoxy-m-dibenzoic acid.

A boiling solution of 4' methoxy-m-dibenzaldehyde (3 grams) dissolved in methyl alcohol (20c.c.) was oxidised by adding saturated aqueous potassium permanganate (30c.c.)

in small quantities at a time. The solution was filtered hot and the manganese dioxide was washed with boiling methyl alcohol. The filtrate after cooling was poured into water (4 volumes) and made slightly acid with dilute sulphuric acid. After standing for several hours the depside separated from solution. It was collected, washed free from acid with water, and it recrystallised from dilute alcohol in white hair-like needles M.P.196° The yield was 80% of the theoretical.

Analysis.

Carbon Found C = 66·1%

$C_{15}H_{12}O_5$ requires C = 66·2%

Hydrogen Found H = 4.45%

$C_{15}H_{12}O_5$ requires H = 4.4%

4',4' methoxy-p-dibenzaldehyde

p-hydroxy benzaldehyde (2·2 grams-1 molecule) was dissolved in acetone (15c.c.) and normal sodium hydroxide solution (20c.c.-1 molecule) was added. A solution of anisoyl chloride (3·4 grams- slight excess of 1 molecule) in acetone (15 c.c.) was mixed with the first solution and the whole was shaken at room temperature for 1 hour. The reaction mixture was then poured into water (4 volumes) and made slightly alkaline. The aldehyde separated almost immediately from the alkaline solution. It was filtered, washed with water and recrystallised from dilute alcohol giving colourless prisms M.P.113° The yield was 70% of the theoretical.

Analysis.

Carbon Found C = 69·7%

$C_{15}H_{12}O_4$ requires C = 70·4%

Hydrogen Found H = 4·7%

$C_{15}H_{12}O_4$ requires H = 4·7%

4' methoxy-p-dibenzoic acid.

4' methoxy-p-dibenzaldehyde (3 grams) was dissolved in boiling methyl alcohol (20c.c.). Saturated potassium permanganate solution (30c.c.) was added in small quantities the oxidation being allowed to complete before further additions. The liquid was filtered hot and the manganese dioxide was washed with hot methyl alcohol. After cooling the filtrate was poured into water (4 volumes) and made just acid with dilute sulphuric acid. After standing overnight a gelatinous solid separated from solution. It was filtered, washed with water and recrystallised from dilute alcohol in fine white hair-like needles M.P.212° The yield was 70% of the theoretical.

Analysis.

Carbon Found C = 65·5%

$C_{15}H_{12}O_5$ requires C = 66·2%

Hydrogen Found H = 4·4%

$C_{15}H_{12}O_5$ requires H = 4·4%

3:4' dimethoxy-p-dibenzaldehyde

Vanillin (3·04 grams-1 molecule) was dissolved in the minimum quantity of acetone (15c.c.) and normal sodium hydroxide solution (20c.c.-1 molecule) added. Anisoyl chloride (3·42 grams- slight excess of 1 molecule) dissolved in the minimum quantity of acetone was mixed with the above solution and the whole was shaken for 1 hour at room temperature. It was then poured into water and after making the solution slightly alkaline with standard alkali, the aldehyde precipitated almost immediately. It was collected, washed with water and recrystallised from dilute alcohol in small colourless prisms M.P.136° The yield was 85% of the theoretical.

Analysis.

Carbon Found C = 66·8%

$C_{16}H_{14}O_5$ requires C = 66·3%

Hydrogen Found H = 5·0%

$C_{16}H_{14}O_5$ requires H = 5·0%

3: 4' dimethoxy-p-dibenzoic acid.

3: 4' dimethoxy-p-dibenzaldehyde (2 grams) was dissolved in methyl alcohol (20c.c.) and raised to boiling. Saturated aqueous potassium permanganate (30c.c.) was added in small quantities at a time. The boiling liquid was filtered to remove the precipitated manganese dioxide which was washed thoroughly with hot methyl alcohol. The cold filtrate was then poured into water (5 volumes) and the solution was made slightly acid with dilute acetic acid. The gelatinous solid which separated from solution after standing overnight was filtered, washed with water and recrystallised from dilute acetone in colourless plates M.P.171° The yield was 80% of the theoretical.

Analysis.

Carbon Found C = 63·2%

$C_{16}H_{14}O_6$ requires C = 62·8%

Hydrogen Found H = 4·8%

$C_{16}H_{14}O_6$ requires H = 4·6%

Polydepsides.

The improved method of oxidising the aldehyde to the depside.

3:3′:4′ trimethoxy-p-dibenzaldehyde (8 grams) was ground into a very fine state of division with a little water and was suspended in dilute potassium permanganate solution (8 grams potassium permanganate in 600c.c.water) The mixture was heated on a waterbath at 70° until decomposition of the potassium permanganate was complete (time 24 hours). It was allowed to cool and sulphur dioxide was passed through the liquid until no manganese dioxide remained and the depside was totally precipitated. The precipitate was collected, washed with water and recrystallised from acetone. The yield was 90% of the theoretical.

3:3′:4′ trimethoxy-p-dibenzoyl chloride

3:3′:4′ trimethoxy-p-dibenzoic acid (8 grams-1 molecule) and thionyl chloride (6 grams-2 molecules) were refluxed on a waterbath until there was no further evolution of sulphur dioxide or hydrochloric acid gas (time 2 hours). The solid acid passed completely into solution. The excess thionyl chloride was distilled off at reduced pressure and the residue was dissolved in chloroform, filtered and precipitated with ligroin. The precipitate was collected, thoroughly dried in a vacuum and recrystallised from a mixture of acetone and ligroin in light yellow needles M.P.129° Mixed melting point with the acid gave M.P.105-109° The yield was 7·1 grams.

Analysis.

Chlorine Found Cl = 10·41%

$C_{17}H_{15}O_6Cl$ requires Cl = 10·12%

3:3′:3″:4″tetramethoxy-p-p-tribenzaldehyde

Vanillin (3 grams-1 molecule) was dissolved in acetone (30c.c.) and normal sodium hydroxide solution (20c.c.-1 molecule) was added. 3:3′:4′ trimethoxy-p-dibenzoyl chloride (7·0 grams-1 molecule) was added to the above solution and the mixture was shaken for 4 hours at room temperature. During the shaking a solid separated from the solution; it was filtered, washed free from alkali with water and recrystallised from aqueous acetone yielding 8 grams of fine needle crystals M.P.159°

Analysis.

Carbon Found C = 61·7%

$C_{25}H_{22}O_9 \cdot H_2O$ requires C = 62·0%

Hydrogen Found H = 5·0%

$C_{25}H_{22}O_9 \cdot H_2O$ requires H = 5·0%

3:3′:3″:4″ tetramethoxy-p-p-tribenzoic acid

3:3′:3″:4″tetramethoxy-p-p-tribenzaldehyde (7 grams) was ground into a very fine state of division and suspended in a dilute solution of potassium permanganate (5 Grams in 400c.c. warm water) and allowed to oxidise on a waterbath for 24 hours by which time the oxidation was complete. The depside was obtained by passing sulphur dioxide through the cold liquid until the solid was completely precipitated and no manganese dioxide remained. The acid was collected, washed with water and recrystallised from dilute acetone in small needles M.P.251-252° The yield was 4 grams.

Analysis.

Carbon Found C = 61·5%

$C_{25}H_{22}O_{10}$ requires C = 62·2%

Hydrogen Found H = 4·7%

$C_{25}H_{22}O_{10}$ requires H = 4·6%

3:3′:3″:4″tetramethoxy-p-p-tribenzoyl chloride

Finely ground 3:3′:3″:4″tetramethoxy-p-p-tribenzoic acid (3 grams-1 molecule) was refluxed on a waterbath for 3 hours with thionyl chloride (10c.c.-2 molecules) until the solid had passed wholly into solution and there was no further evolution of sulphur dioxide or hydrochloric acid gas. The excess thionyl chloride was distilled off under reduced pressure and the residue was recrystallised from dry acetone in faintly yellow needles M.P.171° (with decomposition) A theoretical yield was obtained.

Analysis.

Chlorine Found Cl = 7·2%

$C_{25}H_{21}O_9Cl$ requires Cl = 7·1%

3:3′:3″:3‴:4‴pentamethoxy-p-p-p-tetrabenzaldehyde

A mixture containing vanillin (0·38 grams-1 molecule) dissolved in acetone (30c.c.) and normal sodium hydroxide solution (2·5c.c.-1 molecule) and 3:3′:3″:4″tetramethoxy-p-p-tribenzoyl chloride (1·16 grams-1 molecule) in acetone (150c.c.) was shaken for 20 hours at room temperature. During the agitation a solid precipitated from solution; it was filtered, washed with boiling acetone to remove any unchanged depside acid chloride and then recrystallised from glacial acetic acid in very minute crystals M.P.249° The yield was 65% of the theoretical.

Analysis.

Carbon Found C = 63·5%

$C_{33}H_{28}O_{12}$ requires C = 64·3%

Hydrogen Found H = 4·7%

$C_{33}H_{28}O_{12}$ requires H = 4·55%

3:3′:3″:3‴:4‴pentamethoxy-p-p-p-tetrabenzoic acid

3:3′ :3″ :3‴:4‴pentamethoxy-p-p-p-tetrabenzaldehyde (0·5 grams) was ground into a fine state of division and suspended in a dilute solution of potassium permanganate (0·8 grams in 100c.c. warm water) and allowed to oxidise on a waterbath until the reaction was complete (time 36 hours). After cooling, sulphur dioxide was passed through the liquid until no manganese dioxide remained and the depside was completely precipitated. It was allowed to settle, filtered and washed with water. Finally it was recrystallised from a mixture of tetrachlorethane and alcohol in very small crystals M.P.327°

Analysis.

Carbon Found C = 61·3%

$C_{33}H_{28}O_{13}$ requires C = 62·7%

Hydrogen Found H = 4·5%

$C_{33}H_{28}O_{13}$ required H = 4·4%

$4'$ methoxy-p-dibenzoyl chloride

$4'$ methoxy-p-dibenzoic acid (1 molecule) was refluxed with thionyl chloride (2 molecules) on a waterbath until the solid had completely passed into solution (time 3 hours). The reaction was then completed. The excess thionyl chloride was removed by distillation at reduced pressure and the residue was recrystallised from a mixture of acetone and ligroin in colourless needles M.P.138° The yield was 95% of the theoretical.

Analysis.

Chlorine		Found Cl = 11·8%
	$C_{15}H_{11}O_4Cl$	requires Cl = 12·2%

3: $4''$ dimethoxy-p-p-tribenzaldehyde

Vanillin (3 grams-1 molecule) was dissolved in acetone (30c.c.) and normal sodium hydroxide solution (20c.c.-1 molecule) added. To this solution was added $4'$ methoxy-p-dibenzoyl chloride (5·2 grams-1 molecule) and the mixture was shaken for 5 hours at room temperature. The solid which had separated during the shaking was filtered, washed with dilute caustic soda and then with water and finally recrystallised from dilute acetone in minute needles M.P.152° The yield was 65% of the theoretical yield.

Analysis.

Carbon		Found C = 67·7%
	$C_{23}H_{18}O_7$	requires C = 68·0%
Hydrogen		Found H = 4·6%
	$C_{23}H_{18}O_7$	requires H = 4·4%

$3:4''$ dimethoxy-p-p-tribenzoic acid

$3:4'$ dimethoxy-p-p-tribenzaldehyde (3 grams) was carefully ground into a very finely divided powder and suspended in a dilute solution of potassium permanganate (3 grams in 300c.c. warm water). The solution was heated on a waterbath for 24 hours until the potassium permanganate was completely decomposed. The liquid was cooled and sulphur dioxide was passed through it until the depside was precipitated. The solid product was filtered, washed with water and recrystallised from dilute acetone in very small crystals M.P.251-252°

Analysis.

Carbon Found C = 64·6%

$C_{23}H_{18}O_8$ requires C = 65·4%

Hydrogen Found H = 4·4%

$C_{23}H_{18}O_8$ requires H = 4·3%

$3:4''$ dimethoxy-p-p-tribenzoyl chloride

$3:4'$ dimethoxy-p-p-tribenzoic acid (1 molecule) was refluxed with thionyl chloride (1·5 molecules) on a waterbath until there was no further evolution of sulphur dioxide or hydrochloric acid gas. After removing the excess thionyl chloride by distillation at reduced pressure the residue was recrystallised from dry acetone M.P.155°

Analysis.

Chlorine Found Cl = 8·25%

$C_{23}H_{17}O_7Cl$ requires Cl = 8·05%

Synthesis of Diphenylmethylolid.

O-Chloromercuriphenol

Reference (9)

This compound was prepared by heating phenol to 170°, adding mercuric acetate, and pouring the mixture into boiling water. The product was then precipitated with sodium chloride solution.

O-iodophenol

Reference (10)

Prepared by treating a suspension of o-chloromercuriphenol in chloroform with iodine and after removal of the precipitated inorganic material,the product is obtained by distilling under reduced pressure.

Condensation of o-iodophenol with o-iodobenzoic acid.

O-iodophenol (1 molecule) and o-iodobenzoic acid (1 molecule) were dissolved in alcohol and excess of copper bronze was added. The mixture was heated under reflux on a waterbath for 3 hours during which time copper iodide settled out. After cooling the liquid was filtered to separate excess copper bronze and copper iodide and the filtrate was distilled to remove the alcohol. The residue was taken up in ether and the ethereal solution A was extracted with saturated sodium bicarbonate solution in order to extract 2:2′ diphenic acid and possibly 2 hydroxy-2′ carboxy diphenyl. After separating the layers the alkaline one was acidified with dilute hydrochloric acid and the resultant precipitate was filtered, washed with water to remove mineral acid and dried for 2 days at 105°. It was then dissolved in dry chloroform and treated in an ice bath with phosphoric anhydride until the violent reaction ceased. The mixture was then heated on a waterbath for 1 hour. After cooling, water was carefully added and the mixture was extracted with ether. The ethereal solution was shaken up with saturated sodium carbonate solution to remove the diphenic anhydride which would be hydrolysed. The alkaline layer was acidified and the resultant precipitate was collected, washed with water and recrystallised from alcohol. It was identified as $2:2'$ diphenic acid by its melting point. The ethereal layer was distilled, but no diphenylmethylolid was obtained. The ethereal extract A was treated with increasingly strong solutions of alkali to try and effect a separation of $2:2'$ dihydroxy diphenyl and diphenylmethylolid, but a proper separation could not be obtained.

2·2' dinitrodiphenyl.

Reference (11)

100 grams o-chloronitrobenzene were heated at boiling for 30 minutes with 50 grams of copper bronze. The mixture was then extracted with alcohol from which the compound crystallised. Yield 50%.

2 Amino-2' nitrodiphenyl hydrochloride

Reference (12)

An ammoniacal alcoholic solution of $2:2'$ dinitrodiphenyl was reduced by passing sulphuretted hydrogen through it. The red Oil which separated was extracted with ether, the ethereal solution dried and the amine was precipitated with hydrogen chloride. Yield 10%.

A better method for the preparation of the above product was devised. 6·2 grams 2:2' dinitrodiphenyl were dissolved in 250c.c. alcohol and raised to boiling on a waterbath. To this solution was added an equimolecular boiling solution of sodium trisulphide (7·2 grams sodium sulphide crystals; 1·9 grams powdered sulphur and 0·1c.c. methylated spirits). The whole was then refluxed for 2 hours and then poured into twice its volume of water. The amine was extracted with ether, the ether layer dried over potassium carbonate, and the amine hydrochloride precipitated by means of hydrogen chloride. It was then recrystallised from alcohol giving faintly yellow needles M.P.220°(with decomposition). Yield 3·2 grams.

Analysis.

Gives H Cl = 14·10%

$C_{12}H_{13}N_2O_2 \cdot HCl$ Requires H Cl = 14·42%

2 cyano-2' nitrodiphenyl.

2 amino-2' nitrodiphenyl (3 grams-1 molecule) was diazotised with 50% sulphuric acid (3·5 grams-2·5 molecules) and 10% sodium nitrite solution (1 gram sodium nitrite in 10c.c. water). Potassium cyanide (4·5 grams) dissolved in an equal weight of water was poured into the neutralised diazonium solution and copper bronze (2 grams) was added in small quantities at a time, the violent reaction being allowed to subside before making further additions. After diluting with water, the product and excess copper were

filtered and dried. The product was separated by dissolving in ether and filtering. On evaporation of the ether a dark red solid was obtained. Only a trace of product was yielded.

4·2 grams 2 amino-2′nitrodiphenyl hydrochloride were suspended in 5 grams hydrochloric acid and 15 c.c. water and the mixture boiled. The suspension was then cooled rapidly in an ice bath and diazotised with a solution of 1·6 grams sodium nitrite in 8c.c. water. The diazonium solution was then filtered and the excess acid neutralised with dilute caustic soda. Ice was added at this point to keep down the temperature. The diazonium solution was added to the Sandmeyer reagent which was prepared from 10 grams copper sulphate in 20c.c. water and 11 grams potassium cyanide in 10c.c. water. After heating for 15 minutes on the water-bath the product was steam distilled. The distillate on extraction with ether yielded a solid which crystallised from dilute alcohol in glistening flakes M.P.89° Only sufficient product to take a melting point was obtained.

An attempt was made to carry out the diazotisation according to the instructions of Hogson and Walker (5). 5 grams 2 amino 2′nitrodiphenyl hydrochloride were dissolved in the minimum quantity of glacial acetic acid and the solution cooled rapidly to room temperature. This solution was slowly added to a solution of 1·2 grams sodium nitrite in 7c.c. concentrated sulphuric acid with constant stirring. Ice was then added and the diazonium solution was neutralised with dilute sodium hydroxide. However on treatment with the Sandmeyer reagent no yield was obtained.

5 grams 2 amino-2' nitrodiphenyl hydrochloride were dissolved in 20c.c. alcohol saturated with hydrogen chloride and cooled to 30-35°C. 3 grams freshly prepared amyl nitrite were added drop by drop with constant stirring but the corresponding diazo-amino compound immediately separated.

2 Hydroxy-2' nitrodiphenyl.

5 grams 2 amino 2' nitrodiphenyl hydrochloride were heated to boiling in 20c.c. concentrated hydrochloric acid whence a little of the solid passed into solution. Ice was then added and the suspension was diazotised with 5 grams sodium nitrite in 20c.c. water. The diazonium solution was filtered and heated to boiling which caused the separation of a very dark red oil which solidified on cooling. It was filtered, washed with water and recrystallised in light brown needles M.P.102° from dilute alcohol. Yield 2·8 grams.

Analysis.

Gives N = 6·3%

$C_{12}H_9O_3N$ Requires N = 6·55%

2 hydroxy-2' amino diphenyl hydrochloride.

3 grams 2 hydroxy-2' nitrodiphenyl were dissolved in 20c.c. alcohol and 20c.c. glacial acetic acid added. The solution was heated on a waterbath and 10 grams zinc dust

were added in small quantities at a time. After 30 minutes the reduction was completed and after filtration and cooling sulphuretted hydrogen gas was passed into the solution until the zinc was completely precipitated as sulphide. The precipitate was filtered and washed with water. The filtrate was then made alkaline with solid sodium bicarbonate and extracted with ether. The ethereal layer was evaporated to dryness and the residue was treated with water to remove sodium acetate. The residue was now taken up in ether, the ethereal solution dried over potassium carbonate and hydrogen chloride gas passed through it. Only a trace of amine hydrochloride was obtained.

Reduction of the aforementioned compound in alcoholic solution, with titanous sulphate in acid solution, in an atmosphere of carbon Dioxide, was next attempted, but the rapid hydrolysis of the tinanic sulphate during the extraction prevented the isolation of the product owing to the impossibility of obtaining an ether separation from the voluminous precipitate of tinanic hydroxide.

An alcoholic solution of 2 hydroxy-2′ nitrodiphenyl (2 grams in 10c.c. alcohol) was heated to boiling and a solution of sodium trisulphide added. The mixture was allowed to reflux for 2 hours and was then poured into water and extracted with ether. The ethereal solution was dried over potassium carbonate and after filtration hydrochloric acid gas was passed through the solution until all the amine had precipitated as hydrochloride. The solid was separated and recrystallised from dilute alcohol in white needles M.P.240° (with decomposition). Yield 0·5 grams.

Gives H Cl = 15·92%

$C_{12}H_{11}ON \cdot HCl$ requires H Cl = 16·1%

4 grams 2 hydroxy 2' nitrodiphenyl were mixed with 20 grams stannous chloride and 100c.c. glacial acetic acid saturated with hydrogen chloride were added. The whole was boiled on a waterbath for 2 hours and again saturated with hydrogen chloride. It was then boiled for 1 hour. The solution was poured into an equal volume of water and saturated with sulphuretted hydrogen to precipitate the tin; the tin sulphide was filtered and the filtrate was made alkaline with sodium bicarbonate. The solution was then extracted with ether and the ethereal solution dried over potassium carbonate. After filtration the solution was saturated with hydrogen chloride and the amine hydrochloride filtered.

Benzanalide.

Reference (13)

This compound was prepared by heating molecular proportions of benzoyl chloride and acetanalide in an oil bath to 150°

Phenanthadone.

Reference (14)

When benzanalide is distilled over red-hot pumice stone phenanthradone results. For its preparation a brass flask with a long iron side-arm was used. The side-arm was closely packed with chips of pumice stone and a glass distilling flask,attached by asbestos string to the side-arm,acted as receiver. The brass flask which contained the benzanalide was heated strongly to distil the vapour through the pumice stone. A very small yield (about 1%) of phenanthradone resulted. Most of the benzanalide escaped unchanged as a dense smoke through the side-arm of the receiver. Difficulty is experienced preventing the choking of the apparatus.

Hydrolysis of Phenanthradone.

Phenanthradone (2 grams) was just covered with concentrated sulphuric acid and the mixture was heated on a waterbath until the solid had completely dissolved (time 1½ hours). The hydrolysis was then effected and proved by obtaining a positive test for a primary amine. The resultant amino acid could not be isolated by such methods as

(a) almost neutralising the diluted solution and extracting with ether

(b) almost neutralising with sodium carbonate and precipitating with sodium acetate

(c) by the buffer solution method.

Diphenylmethylolid.

The hydrolysed solution was diluted with 4 times its volume of water and cooled in ice. It was then diazotised with 1 molecule sodium nitrite solution and the diazonium solution was boiled for 3 hours. When cold it was extracted with ether and the ethereal solution when dried was distilled to remove the ether. The dark coloured residue was recrystallised from alcohol M.P.90° The light yellow needles were insoluble in sodium bicarbonate solution. Yield 0·5 grams.

Phenyl benzoate.

Reference (15)

This compound was prepared by condensing equimolecular quantities of phenol and benzoyl chloride with sodium hydroxide solution. The product was recrystallised from alcohol.

Phenyl benzoate was distilled through red-hot pumice stone in the manner previously described, but only decomposition products resulted.

Oxidation of Piperonal.

Piperonal (8 grams) was dissolved in concentrated sulphuric acid (15c.c.) by gently heating and when cold ammonium persulphate (15 grams) was added gradually, the reaction flask being immersed in ice to prevent sudden rise in temperature. After standing overnight the contents were poured into a large volume of water (1 litre) and the resultant dark coloured precipitate was filtered and washed with water. It was then extracted with boiling alcohol and filtered. The residue was recrystallised from pyridine M.P.274°(A). The alcohol extract on concentration deposited slate coloured crystals M.P.242°(B).

Analysis (A)

Carbon Found C = 57·9%

Hydrogen Found H = 2.1%

Summary.

The described syntheses of depsides prove that the method applied to the preparation of didepsides is of general application. The depsides are obtained in good yield in a comparatively easy manner. The manipulation becomes increasingly difficult as the series is ascended from di- to tetra-depsides.

All the compounds are crystalline the structure becoming more indeterminate the higher the molecular weight of the substance.

The constitution of diphenylmethylolid has been proved although the synthesis is of no value for obtaining the compound in bulk.

The Depside Esters of Polyhydric Phenols.

Dr. Russell found that Hemlock tannin on degradation yielded pyrogallol and protocatechuic acid. The simplest structure which would yield these degradation products would therefore be the depside ester of a polyhydric phenol. A series of these compounds was prepared for comparison with fully methylated Hemlock and Mimosa tannins.

In the preparation of the didepside esters, the depside acid chloride was shaken with the requisite quantity of sodium phenoxide in acetone solution from 3-16 hours at room temperature. Since both didepside and phenol are soluble in alkali that part of the reaction mixture which is insoluble in alkali when all acid chloride has disappeared is the required ester. Tridepsides, however, offer some difficulty in that they are sparingly soluble in acetone. The tridepside esters were isolated by washing the reaction mixture free from depside acid chloride with boiling acetone.

All the depside esters are crystalline; with increase in molecular weight there is an increase in melting point and greater difficulty of crystallisation. Acid hydrolysis produces the parent substances without other decomposition.

In all cases where atmospheric oxygen interfered with the course of the reaction due to oxidation of the polyhydric phenol in alkaline solution the experiments were carried out in an atmosphere of nitrogen.

Experimental.

Quinol bis (3:3':4' trimethoxy-p-dibenzoyl) ether.

Solutions of quinol (0·5 grams-1 molecule) dissolved in 20c.c. acetone and normal sodium hydroxide solution (2 molecules) and of 3:3':4' trimethoxy-p-dibenzoyl chloride (3·5 grams - slight excess of 2 molecules) in acetone (20c.c.) were mixed and shaken for 6 hours at room temperature. The reaction mixture was poured into water and the solution made slightly alkaline. The precipitated product was collected, washed with water and recrystallised from chloroform in colourless needles M.P.229°

Analysis.

Carbon		Found C = 64·5%
	$C_{40}H_{34}O_{14}$	Requires C = 65·0%
Hydrogen		Found H = 4·6%
	$C_{40}H_{34}O_{14}$	Requires H = 4·6%

Quinol bis (3':4' dimethoxy-p- dibenzoyl) ether.

Quinol (0·5 grams-1 molecule) was dissolved in acetone (20c.c.) and normal sodium hydroxide solution (2 molecules) added. A solution of 3':4' dimethoxy-p-dibenzoyl chloride (3·5 grams- slight excess of 2 molecules) in acetone (20c.c.) was mixed with the first solution and after shaking for 5 hours at room temperature the mixture was poured into water and the solution made slightly alkaline if necessary. The precipitate, which separated from the solution, was filtered, washed with water and recrystallised from a mixture of alcohol and chloroform in colourless crystals M.P.232°

Analysis.

Carbon Found C = 66·7%

$C_{38}H_{30}O_{12}$ requires C = 67·3%

Hydrogen Found H = 4·3%

$C_{38}H_{30}O_{12}$ requires H = 4·4%

Catechol bis (3′:4′ dimethoxy-p-dibenzoyl) ether.

To a solution containing catechol (0·5 grams-1 molecule) in acetone (20c.c.) and normal sodium hydroxide solution (2 molecules) was added a solution of 3′:4′ dimethoxy-p-dibenzoyl chloride (3·5 grams- slight excess of 2 molecules) dissolved in acetone (20c.c.). The mixture was shaken for four hours and then poured into water and made slightly alkaline. The resultant precipitate was filtered, washed with water and recrystallised from chloroform in minute crystals M.P.175 °

Analysis.

Carbon Found C = 66·5%

$C_{38}H_{30}O_{12}$ requires C = 67·3%

Hydrogen Found H = 4·35%

$C_{38}H_{30}O_{12}$ requires H = 4·4%

Resorcinol bis(3′:4′dimethoxy-p-dibenzoyl) ether.

3′: 4′dimethoxy-p-dibenzoyl chloride (3·5 grams - slight excess of 2 molecules) was mixed with a solution of resorcinol (0·5 grams-1 molecule) and normal sodium hydroxide solution (2 molecules) dissolved in acetone (40c.c.) and after the mixture had been shaken for 3 hours at ordinary temperature it was poured into water from which solution a solid separated on standing. To prevent contamination of the free components the solid was obtained from alkaline solution. It was filtered, washed first with dilute alkali and then with water and recrystallised from chloroform in small white needles M.P.194°

Analysis.

Carbon Found C = 66·8%

$C_{38}H_{30}O_{12}$ requires C = 67·3%

Hydrogen Found H = 4·35%

$C_{38}H_{30}O_{12}$ requires H = 4·4%

Resorcinol bis (4'methoxy-p-dibenzoyl) ether.

Resorcinol (0·5 grams-1 molecule) was dissolved in acetone (20c.c.) and normal sodium hydroxide solution (2 molecules) added. This solution was mixed with a solution of 4'methoxy-p-dibenzoyl chloride (3 grams - slight excess of 2 molecules) dissolved in acetone (20c.c.) and the mixture was shaken for 6 hours at room temperature. On pouring into water the product precipitated. After making the solution slightly alkaline the precipitate was collected, washed with water and recrystallised from dilute acetone in small colourless crystals M.P.154°

Analysis.

Carbon Found C = 69·3%

$C_{36}H_{26}O_{16}$ requires C = 70·0%

Hydrogen Found H = 4·4%

$C_{36}H_{26}O_{16}$ requires H = 4·2%

Quinol bis (4'methoxy-p-dibenzoyl) ether.

This compound was prepared by mixing a solution of quinol (0·5 grams-1 molecule) in acetone (20c.c.) and normal sodium hydroxide solution (2 molecules) with a solution of $4'$ methoxy-p-dibenzoyl chloride (3 grams - slight excess of 2 molecules) in acetone (20c.c.) and shaking the mixture for 6 hours at room temperature. The product which separated on pouring into water, was collected, washed with water and recrystallised from dilute acetone in colourless plates M.P.230°

Analysis.

Carbon Found C = 71%

$C_{36}H_{26}O_{16}$ requires C = 70%

Hydrogen Found H = 4·25%

$C_{36}H_{26}O_{16}$ requires H = 4·2%

Quinol bis (3:$4''$ dimethoxy-p-p-tribenzoyl) ether.

A solution of quinol (0·5 grams-1 molecule) dissolved in acetone (20c.c.) and normal sodium hydroxide (10c.c.-2 molecules) was mixed with a very fine suspension of 3:$4''$dimethoxy-p-p-tribenzoyl chloride (3·4 grams-2 molecules) in acetone (100c.c.). The mixture was shaken for 24 hours at room temperature and then diluted with water (500c.c.). After making slightly alkaline the precipitated solid was collected, washed with water free from alkali, and then with boiling acetone to remove unchanged depside acid chloride. It recrystallised in fine white needles from a mixture of tetrachlorethane and acetone M.P.278-279°

Analysis.

Carbon Found C = 66·7%

$C_{52}H_{38}O_{16}$ requires C = 68·0%

Hydrogen Found H = 4·3%

$C_{52}H_{38}O_{16}$ requires H = 4·1%

Summary.

The depside esters of polyhydric phenols become increasingly difficult to prepare the higher the molecular weight of the depside used to condense with the phenol. The insolubility of the higher depside acid chlorides in cold acetone makes it difficult to separate them from the esters.

All the depside esters of polyhydric phenols are crystalline, colourless or white and possess a definite melting point. They are insoluble in water, sparingly soluble to insoluble in acetone, and very sparingly soluble in alcohol. They are easily hydrolysed into their components.

Fully methylated phlobatannins are amorphous, faintly red, compounds of no well defined melting point. They are insoluble in water, easily soluble in acetone, and alcohol, and yield on hydrolysis the insoluble phlobaphene.

Depside esters of dihydric phenols therefore show no resemblance to fully methylated phlobatannins.

The Reduction Products of Chalkones.

Chalkone (Benzalacetophenone) was reduced with zinc dust and alcoholic glacial acetic acid which resulted in the production of a white, hair-like needle crystalline compound melting at 192° It was seen from the literature that this product was unknown. Estimation of its molecular weight proved it to be bimolecular. It formed a dibromide on treatment with bromine and a monobromo-hydride on treatment with hydrobromic acid. Moreover it was easily oxidised with aqueous potassium permanganate and gave the characteristic colour reaction for unsaturated compound with tetranitromethane. This proved that the produce was unsaturated and contained at least one double bond. Absence of free ketone groups was established by the non-formation of a phenyl hydrazone or semi-carbazone.

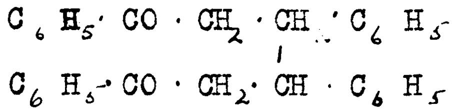
The following list gives the possible products which theoretically could be obtained by reducing chalkone.

Group I

1. $C_6H_5 \cdot CO \cdot CH_2 \cdot CH_2 \cdot C_6H_5$ (16) M.P. 72-73°
2. $C_6H_5 \cdot CHOH \cdot CH_2 \cdot CH_2 \cdot C_6H_5$ (17) B.P. 331°
3. $C_6H_5 \cdot CHOH \cdot CH{=}CH \cdot C_6H_5$ (18) M.P. 57°

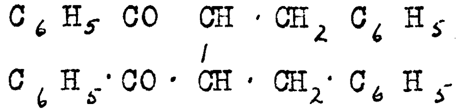
It cannot be any of the above compounds since the chalkone reduction product is bimolecular and moreover it differs in all other respects.

Group II

1.


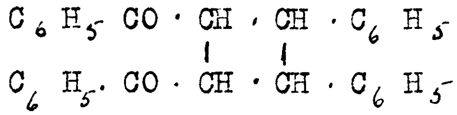
$$\begin{array}{lcl} C_6H_5\cdot CO\cdot CH_2\cdot & CH & \cdot C_6H_5 \\ & | & \\ C_6H_5\cdot CO\cdot CH_2\cdot & CH & \cdot C_6H_5 \end{array}$$

(19) M.P.267

2.


$$\begin{array}{lcl} C_6H_5\ CO & CH & \cdot CH_2\ C_6H_5 \\ & | & \\ C_6H_5\cdot CO\cdot & CH & \cdot CH_2\cdot C_6H_5 \end{array}$$

unknown

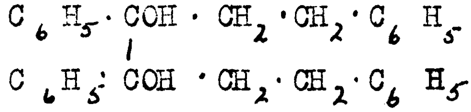
3.


$$\begin{array}{lcccl} C_6H_5\cdot CO\cdot & CH & \cdot & CH & \cdot C_6H_5 \\ & | & & | & \\ C_6H_5\cdot CO\cdot & CH & \cdot & CH & \cdot C_6H_5 \end{array}$$

(20) M.P.134

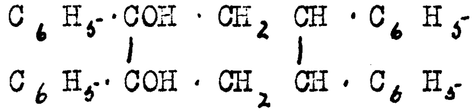
It cannot be any of this second group of compounds since it contains no free ketone groups.

GroupIII

1.


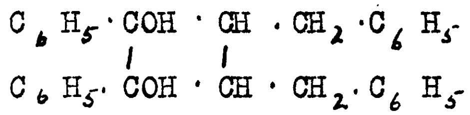
$$\begin{array}{lcl} C_6H_5\cdot & COH & \cdot CH_2\cdot CH_2\cdot C_6H_5 \\ & | & \\ C_6H_5\cdot & COH & \cdot CH_2\cdot CH_2\cdot C_6H_5 \end{array}$$

unknown

2.


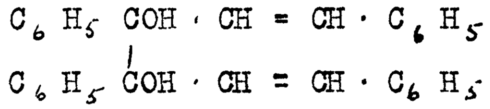
$$\begin{array}{lcccl} C_6H_5\cdot & COH & \cdot CH_2 & CH & \cdot C_6H_5 \\ & | & & | & \\ C_6H_5\cdot & COH & \cdot CH_2 & CH & \cdot C_6H_5 \end{array}$$

(21) M.P.211

3.


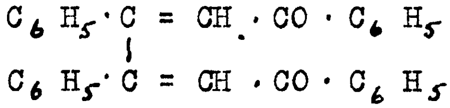
$$\begin{array}{lcccl} C_6H_5\cdot & COH & \cdot & CH & \cdot CH_2\cdot C_6H_5 \\ & | & & | & \\ C_6H_5\cdot & COH & \cdot & CH & \cdot CH_2\cdot C_6H_5 \end{array}$$

unknown

4.


$$\begin{array}{lcl} C_6H_5 & COH & \cdot CH = CH\cdot C_6H_5 \\ & | & \\ C_6H_5 & COH & \cdot CH = CH\cdot C_6H_5 \end{array}$$

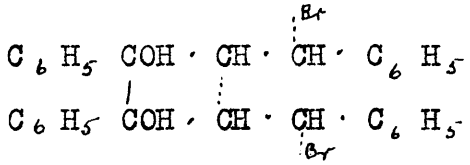
Of this group the product obtained by reducing chalkone with zinc dust and alcoholic glacial acetic acid cannot be 1 as it is completely saturated. It differs from 2. It is easily oxidisable and therefore cannot be 3. The evidence seems to point to 4, as the constitution of the compound. It is known that by reducing aromatic ketones by this method bimolecular compounds are obtained whose structure is regular. It would be strange if one of the double bonds were saturated and not the other. Yet if the structure 4 is to be assigned to the product melting at 192° a tetrabromide and a dibromohydride should be obtained. However, such a tetrabromide might be difficult to form or again it might be decomposed immediately on formation. This theory seems to be enhanced by the work of Lehmann (22) who found that the tetrabromide of



$$\begin{array}{l} C_6H_5\cdot C = CH\cdot CO\cdot C_6H_5 \\ \qquad\;\; | \\ C_6H_5\cdot C = CH\cdot CO\cdot C_6H_5 \end{array}$$

was very unstable and decomposed as soon as it was formed. He also found that on attempting to recrystallise this tetrabromide the dibromide resulted.

Again it is possible that the bromine adds on as follows:-



$$\begin{array}{l} C_6H_5\;COH\cdot CH\cdot \overset{Br}{CH}\cdot C_6H_5 \\ \qquad\quad\;\; | \qquad\;\; \vdots \\ C_6H_5\;COH\cdot CH\cdot \underset{Br}{CH}\cdot C_6H_5 \end{array}$$

with formation of a cyclobutane or alternatively a cyclohexane ring. The reduction products of some 2 hydroxy chalkones were examined. This part of the work was done on the advice of Dr. Russell.

Experimental.

Chalkone.

Reference (23)

Was prepared by condensing equimolecular proportions of acetophenone and benzaldehyde with sodium ethylate.

The Reduction of Chalkone.

Chalkone (5 grams), alcohol (100c.c.) and glacial acetic acid (15c.c.) were brought to boiling on a waterbath and zinc dust (2 grams) were added a pinch at a time, no further additions being made until the reaction had subsided. A white solid separated from the hot solution. After cooling, the solid was collected, washed free from acid with water and recrystallised in fine white needles M.P.192° from a large volume of alcohol. Yield 3 grams. This compound was soluble in chloroform and glacial acetic acid, sparingly soluble in alcohol, benzene, toluene and ether, and insoluble in acetone.

Analysis.

Carbon Found C = 85·9%

$C_{30}H_{26}O_2$ requires C = 86·1%

Hydrogen Found H = 6·3%

$C_{30}H_{26}O_2$ requires H = 6·22%

Molecular Weight determination of the Reduction product.

By elevation of the Boiling Point (Benzene) 446

By depression of the Freezing Point (Benzene) 442, 458

Bromination of Reduced Chalkone.

3 grams of Reduction product were dissolved in chloroform (50c.c.) and excess bromine (3c.c.) was added. The mixture was heated on a waterbath under reflux for 2 hours. After cooling the excess bromine was removed by washing the chloroformic solution with very dilute caustic soda solution and then several times with water. After drying the solution in chloroform over calcium chloride the chloroform was distilled off and the dark brown residue recrystallised from dilute alcohol in almost colourless needles M.P.106° The

yield was 2 grams.

Analysis.

Bromine Found Br = 27·5%
$C_{30}H_{26}O_2Br_2$ requires Br = 27·6%

Monobromohydride of Reduced Chalkone.

3 grams of reduced chalkone were dissolved in chloroform 50c.c. and a saturated solution of hydrobromic acid in glacial acetic acid (50c.c.) was added and the mixture thoroughly mixed by shaking. A deep red colour formed almost immediately and after standing for 30 minutes the liquid was extracted four times with water. The chloroform layer after drying was distilled to remove the solvent and the residue recrystallised from alcohol in small white plates M.P.114° The yield was 1 gram.

Analysis.

Bromine Found Br - 16·5%
$C_{30}H_{27}O_2Br$ requires Br = 16·1%

Gallacetophenone (2:3:4 trihydroxy acetophenone)

Reference (24)

This compound was prepared by heating together one part of pyrogallol and 1·5 parts each of glacial acetic acid and fused zinc chloride at 140° for 30 minutes. The product was isolated by pouring into water.

Gallacetophenone dimethyl ether.

Reference (25)

A strongly alkaline solution of gallacetophenone was methylated with dimethyl sulphate which resulted in the formation of a mixture of the di- and tri-methyl ethers. These were separated by pressing on porous tile.

2 hydroxy 3:4:4′ trimethoxy chalkone.

Gallacetophenone dimethyl ether (2 grams-1 molecule) and anisaldehyde (1·7 grams- slight excess of 1 molecule) were dissolved in alcohol (12·5c.c.) by gently heating. When cold 50% sodium hydroxide solution (5 grams) was added slowly with constant shaking. The mixture was heated just to boiling and after cooling was poured into water (150c.c.) and the solution was acidified with dilute sulphuric acid. The resultant yellow precipitate was collected, washed with water and recrystallised from dilute alcohol in fine orange-yellow needles M.P.133° Yield 3 grams.

Analysis.

Carbon		Found C = 68·1%
	$C_{18}H_{18}O_5$	requires C = 68·8%
Hydrogen		Found H = 5·78%
	$C_{18}H_{18}O_5$	requires H = 5·74%

2 hydroxy 3:4:3′:4′ tetramethoxy chalkone.

2 hydroxy 3:4 dimethoxy acetophenone (2 grams-1 molecule) and Veratraldehyde (1·7 grams-1 molecule) were dissolved in 10c.c. alcohol by gently heating. 50% caustic soda solution (5 grams) were added slowly with constant shaking and the mixture was then heated to boiling. The deep red solution on cooling was poured into water and acidified with dilute sulphuric acid and the resultant yellow precipitate was filtered, washed with water and recrystallised from dilute alcohol in fine orange-yellow needles M.P.124° The yield was

3 grams.

Analysis.

Carbon Found C = 65·2%

$C_{19}H_{20}O_6$ requires C = 66·3%

Hydrogen Found H = 5·80%

$C_{19}H_{20}O_6$ requires H = 5·82%

2 hydroxy 3:4 dimethoxy 3′:4′ methylenedioxy chalkone.

2 hydroxy 3:4 dimethoxy acetophenone (2 grams-1 molecule) and piperonal (1·8 grams- slight excess of 1 molecule) were dissolved in alcohol 12·5c.c. 50% caustic potash solution (1:1) was added and after shaking the mixture was raised to boiling. After cooling it was poured into water and acidified with dilute sulphuric acid. The resultant yellow precipitate was collected, washed with water and recrystallised from alcohol in yellow needles M.P.168° The yield was 98% of the theoretical.

Analysis.

Carbon Found C = 65·8%

$C_{18}H_{16}O_6$ requires C = 66·1%

Hydrogen Found H = 5·0%

$C_{18}H_{16}O_6$ requires H = 4·85%

Resacetophenone.

Reference (26)

Was prepared by heating 1 part resorcinol with 1·5 parts glacial acetic acid and 1·5 parts of fused zinc chloride for 30 minutes at 140-145°

2:4 dihydroxy 4′ methoxy chalkone.

Anisaldehyde (1.5 grams-1 molecule), resacetophenone

1·5 grams-1 molecule) and alcohol 12c.c. were heated until solution and after cooling 50% caustic soda solution (7 grams) was added. The mixture was then boiled on a waterbath for 15 minutes, cooled and poured into water. On acidifying a yellow precipitate was obtained; it was collected, washed with water and recrystallised from dilute alcohol in light yellow needles M.P.143° The yield was 2·5 grams.

Analysis.

Carbon Found C = 70·9%

$C_{16}H_{14}O_4$ requires C = 71·2%

Hydrogen Found H = 5·25%

$C_{16}H_{14}O_4$ requires H = 5·18%

2:4:4' trihydroxy chalkone.

Resacetophenone (1·5 grams-1 molecule), p-hydroxy benzaldehyde (1·2 grams-1 molecule) and alcohol (12c.c.) were heated to solution and 50% sodium hydroxide solution (7 grams) was added slowly. After shaking the mixture was heated at boiling until a deep red colour developed (time 45 minutes). It was cooled, poured into water and acidified. The chalkone precipitate was filtered, washed with water and recrystallised from dilute alcohol in fine yellow needles M.P.186° The yield was 2·5 grams.

Reduction of 2 hydroxy 3:4:4' trimethoxy chalkone.

2 hydroxy 3:4:4' trimethoxy chalkone (3 grams) was dissolved in alcohol (30c.c.) and glacial acetic acid (10c.c.) was added. To this mixture was added zinc dust (6 grams) in small quantities at a time and the whole was refluxed for 2

hours. On cooling the mixture was poured into 250c.c. water and after standing for 24 hours a cream coloured solid separated. It was collected, washed with water and redissolved in the minimum quantity of alcohol and reprecipitated with water. An amorphous solid M.P.89° was obtained.

Analysis.

Carbon Found C = 68·7%
$C_{36}H_{36}O_{10}$ requires C = 68·4%
Hydrogen Found H = 6·46%
$C_{36}H_{36}O_{10}$ requires H = 6·33%

Reduction of 2 hydroxy chalkones.

Two experiments were run together in exactly similar types of apparatus of equal internal volume, one containing the chalkone whilst the second was regarded as a blank estimation. The difference between the volumes of hydrogen at N.T.P. gave the volume of hydrogen absorbed during reduction.

About 0·2 grams 2 hydroxy chalkone was weighed accurately into a test-tube and dissolved in 4c.c. alcohol. 3 grams of zinc dust and 10c.c. of 20% alcoholic glacial acetic acid were added, the acid being measured from a burette. In the blank experiment 3 grams of zinc dust, 4c.c. alcohol and 10c.c. of 20% alcoholic glacial acetic acid solution were added to the test-tube. These test-tubes were then attached to condensers which led to nitrometers. Both test-tubes were heated in the same waterbath to ensure equal temperatures.

The experiment lasted for 1½ hours and then the readings on the nitrometers were noted. The difference in volume was then corrected for normal temperature and pressure.

Table of Results.

NAME OF CHALKONE	WEIGHT OF CHALKONE (GRAMS.)	VOLUME OF 20% ALCOHOLIC GLACIAL ACETIC ACID	VOLUME OF H_2 ABSORBED	Volume. Required.	
				IF BIMOLECULAR	IF MONOMOLECULAR
2 HYDROXY 3:3':3'' TRIMETHOXY-CHALKONE	(1) 0·2094 (2) 0·1935	10c.c. 10c.c.	6·4c.c. 5·85c.c.	4·4c.c. 6·85c.c.	14·8c.c. 13·4c.c.
2 HYDROXY 3:4:3':4' TETRAMETHOXY-CHALKONE	0·1434	10c.c.	48c.c.	4·82c.c.	9·63c.c.
2:4 DIHYDROXY 4' METHOXY-CHALKONE	0·0530	10c.c.	2·13c.c.	2·21c.c.	4·42c.c.
2:4:4' TRIHYDROXY-CHALKONE	0·1046	10c.c.	4·34c.c.	4·58c.c.	9·16c.c.
2 HYDROXY 3:4 DIMETHOXY-3':4' METHYLENEDIOXY-CHALKONE	0·0914	10c.c.	2·8c.c.	3·13c.c.	6·26c.c.

Complete Review of Results.

Little light is thrown on the constitution of phlobatannins by the examination of their oxidation products due to the yields obtained being so small that further examination was impossible. Acid oxidising agents or mixtures cannot be used owing to the precipitation of the insoluble phlobaphene. The only conclusion which is arrived at, is, that methylated phlobatannins yield an aldehyde or ketone, since a bisulphite product was isolated, and an acid. The acid might possibly result from the further oxidation of the aldehyde or ketone, but no definite proof is available. Manning and Nierenstein isolated hemipinic acid but evidence of this acid was not obtained in this work.

Depsides which are closely allied to tannins have been synthesised by an improved method which offers little trouble and yields the compounds in bulk. The full benefit of the method is obtained in the synthesis of polydepsides. The constitution of diphenylmethylolid has been established by the mode of synthesis although the method is of no value for obtaining this compound in quantity.

Depside esters of polyhydric phenols which yield on hydrolysis similar degradation products to those obtained from phlobatannins show practically no resemblance to them. The method of synthesis was the same as that applied to depsides and indicates the extension of the method.

When chalkones are reduced with zinc dust and alcoholic glacial acetic acid bimolecular compounds are obtained.

Part II

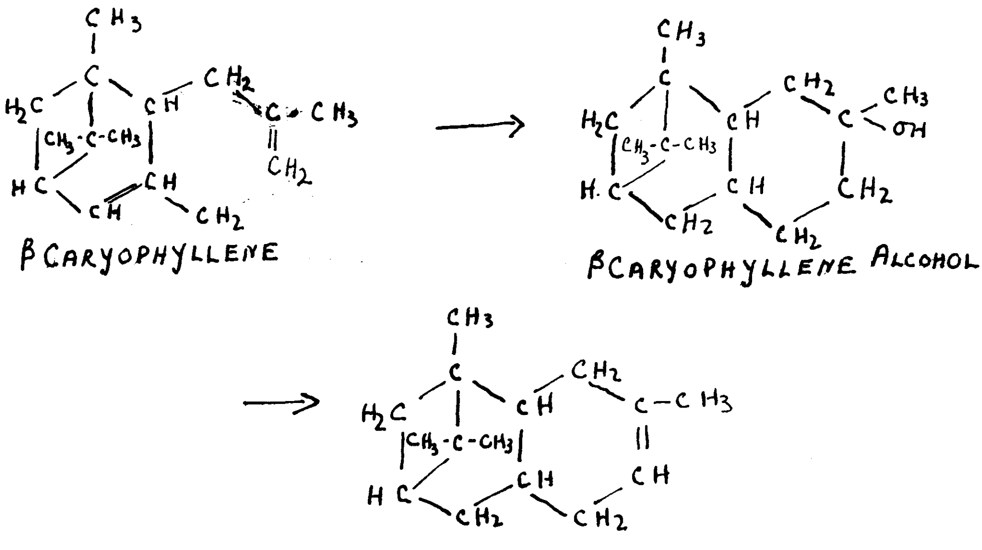
Experiments with β Caryophyllene.

Sesquiterpenes.

Experiments with Caryophyllene.

Introduction.

β Caryophyllene is a dicyclic sesquiterpene $C_{15}H_{24}$ which yields on hydration with concentrated sulphuric acid and ether two products (1) a solid alcohol called β Caryophllene alcohol and (2) a light yellow oil Clovene. Clovene has been proved to be a tricyclic sesquiterpene. To account for this reaction Henderson (27) suggested the following scheme


β CARYOPHYLLENE
β CARYOPHYLLENE ALCOHOL
CLOVENE.

On oxidising clovene with a mixture of chromic and acetic acids two products are again obtained (I) a white crystalline acid M.P.189° called Clovenic acid and (II) light yellow neutral oil. It was naturally thought that this latter product was partially oxidised clovene, but no derivatives of aldehyde, ketone etc. could be isolated.

Theoretical.

It was decided to examine the neutral oil for possible formation of a hydration compound. This premise is feasable when one considers that a mixture of sulphuric and acetic acids had been used as the hydrating agent, previous to the use of the sulphuric acid-ether method. If the chromic acid-acetic acid mixture used for the oxidation of the clovene is looked upon in the light of a hydration mixture and not as an oxidising agent, one would reasonably expect to obtain a corresponding product. The view that the oxidation mixture could act also as a hydration mixture was proved by dehydrating the neutral oil with the resultant formation of clovene. The purified oil was dissolved in dry chloroform, treated with phosphorus pentoxide and the product isolated proved to be clovene. The same experiment was applied to the resinous residue, the non-volatile in steam part, obtained in the preparation of clovene from β Carophyllene and again clovene resulted, thus proving that it also was a hydration product.

Clovenic acid is a white crystalline solid. It is a dibasic acid, completely saturated since it does not react like typically unsaturated compounds. It should be easily brominated, but so far the bromination has not been effected.

An attempt was made to separate possible cis-trans isomers but without success. Aschan's method, that of treating the acid with glacial acetic and concentrated hydrochloric acids and several variations of it proved ineffective.

The acid was dissolved in a large volume of alcohol and allowed to crystallise slowly. A first and second crops of crystals were refluxed with acetic and hydrochloric acids for 12 hours. After removing the glacial acetic and hydrochloric acids the residue was dissolved in ether and extracted with sodium carbonate solution. In this way the free acid was separated from any anhydride which remained in solution in the ether. However, on retreatment of the separated acid some of the previous anhydride was obtained.

Experimental.

Hydration of β Caryophyllene.

Reference (28)

β Caryophyllene was hydrated with a mixture of concentrated sulphuric acid and dry ether in the cold. The mixture was extracted with saturated sodium carbonate solution and the oil layer separated. On steam distilling, clovene comes over first followed by β Caryophyllene alcohol. A non-volatile product remains in the distillation flask. The Clovene is separated from β Caryophyllene alcohol by freezing and filtering off the clovene from the solid alcohol.

Oxidation of Clovene.

Reference (29)

Redistilled Clovene was oxidised by chromic acid in glacial acetic acid solution in the cold. Two products were obtained an acid Clovenic acid and a neutral oil. These were separated by extracting an ethereal solution of the mixture with alkali.

Dehydration of the Neutral Oil.

The neutral oil which distilled at 165 - 190° at 13 millimetres pressure was dissolved in an equal weight of specially dried chloroform. A quantity of phosphorus pentoxide equal to twice the weight of oil present was carefully added in small parts at a time. The reaction was comparatively slow at first and after the entire dehydrating agent had been added, the mixture was heated on the waterbath for 3 hours. The now deep red solution was carefully diluted with water which caused the formation of two layers. The oil layer was separated, extracted with ether and the ethereal solution was washed with water. The ether was next evaporated and the residue distilled under reduced pressure. A light yellow oil which distilled at 124° C under 13 millimetres pressure proved to be clovene from the determination of its physical constants. Yield 28%.

Dehydration of the Resinous Residue.

The resinous residue from the steam distillation of clovene was treated as follows:-

100 grams residue was dissolved in 65c.c. chloroform and dried by shaking over calcium chloride for 12 hours. After filtration 50 grams phosphoric anhydride were added a little at a time. A violent action ensued. After the reaction had subsided the solution was heated for 2 hours under reflux. After cooling, water was carefully added and the oil layer separated. The oil layer was dissolved in ether and placed in the refrigerator to separate any

β Caryophyllene alcohol. After evaporation of the ether, the oil was filtered and the filtrate distilled under reduced pressure. It distilled at 125 - 127° at 15 millimetres pressure and proved to be clovene from the determination of its physical constants. Yield 25%.

Treatment of Clovenic Acid.

1·5 grams clovenic acid were dissolved in 4·5c.c. glacial acetic acid and 4·5c.c. concentrated hydrochloric acid. The mixture was heated in a sealed tube at 170-180° for 1½ hours. It was then transferred to a beaker and evaporated to dryness. 10c.c. acetyl chloride were now added to the residue and after the violent reaction had subsided the mixture was heated for 2 hours on the waterbath at 30° The solvent was then removed in vacuo and the residue dissolved in ether. The ethereal solution was extracted with sodium carbonate solution and after separation the ether was evaporated and the weight of residual anhydride determined. The sodium carbonate layer was acidified and the resultant precipitate was washed, dried and weighed. The result showed that about 60% anhydride was obtained. However, on retreating the remaining acid a further quantity of the same anhydride as that obtained at the first attempt resulted. The method was therefore abandoned.

Second Method.

1·5 grams clovenic acid were mixed with 6c.c. concentrated hydrochloric acid and 12c.c. glacial acetic acid and the whole refluxed for 12 hours. After the solvent was evaporated the residue was dissolved in ether and extracted with sodium carbonate solution. The ethereal layer was separated, the ether removed and the residue weighed. Yield of anhydride = 45%. The sodium carbonate extract was acidified and the resulting acid again subjected to the same treatment as above. This time 52% anhydride was obtained.

Third Method.

2·5 grams clovenic acid were dissolved in 250c.c. alcohol and allowed to crystallise slowly. The first crop of crystals was removed and the solution was concentrated. A second crop of crystals was thus obtained. These crops of crystals were subjected to the treatment described in the second method and the first crop of crystals yielded on one treatment 52% anhydride and on retreatment 54% anhydride. The second crop crystals yielded on first treatment 90% anhydride and on the second treatment anhydride only resulted.

Summary.

It has been proved that the neutral oil obtained from the oxidation of Clovene by chromic acid in glacial acetic acid is a hydration product. The resin obtained in the preparation of Clovene can also be dehydrated to yield Clovene.

Attempts to separate isomers of clovenic acid proved unsuccessful.

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