SUMMARY

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Phenols are very reactive and they undergo a large number of reactions to give products of industrial, agricultural, medicinal and other importance. Extensive work has therefore been done on these substances. They have also been the starting materials for the synthesis of different types of heterocyclic compounds. The studies on biphenols and hydroxy derivatives of diphenyl methane, benzophenone and diphenyl sulfone are comparatively meagre. Investigations on the electrophilic substitutions in these compounds and the synthesis of oxygen heterocycles from these compounds has been going on in these laboratories and the present investigation deals with the synthesis of bichromonyl, biflavonyl, bicoumarinyl and bibenzofuranyl derivatives from the above phenolic compounds.

Chapter I deals with the synthesis of symmetrical bichromonyl derivatives from dihydroxy derivatives of diphenyl, diphenyl methane, benzophenone and diphenyl sulfone through cyanoethylation.

A large number of chromones having substituents in 2-position are known, but very few chromones without any substituent in the heterocyclic ring are known. There are only a couple of methods available for the synthesis of such compounds and the yields of the chromones are rather poor. It was therefore thought of interest to synthesise some bichromonyl derivatives through cyanoethylation.

Cyanoethylation of phenols affords a convenient method for the synthesis of chromones without any substituent in the heterocyclic ring. The intermediate cyanoethoxy derivatives can be hydrolysed to the corresponding acids which om cyclisation with PPA afford the chromanones which can be dehydrogenated with palladium on charcoal to the chromones. Using this approach 8,8'-bichromonyl, 6,6'-bichromonyl, 8,8'-bichromonyl methane, 6,6'-bichromonyl methane, 6,6'-bichromonyl ketone and 6,6'-bichromonyl sulfone have now been synthesised. Various catalysts such as cupric oxide, cuprous chloride, sodium hydroxide, sodium methoxide and Triton B have been tried out for cyanoethylation. The best results were obtained with cupric oxide except in the case of 4,4'-dihydroxydiphenyl which gave the highest yield with sodium hydroxide (10 %).

2,2'-Dihydroxydiphenyl on reaction with acrylonitrile in the presence of cupric oxide gave 2,2'-di(β-cyanoethoxy)diphenyl which on hydrolysis with conc. hydrochloric acid gave the corresponding acid. This was cyclised in the presence of polyphosphoric acid to

8,8'-bichromanomyl which dehydrogenated in the presence of palladium on charcoal in the boiling diphenyl ether to 8,8'-bichromonyl. It gave on heating with alkali a dihydroxy diacetyl derivative to which the 2,2'-dihydroxy-3,3'-diacetyldiphenyl structure is assigned as it gave a blue colouration with alcoholic ferric chloride and a di(2,4-dinitrophenylhydrazone). Incidentally this provides a method for the preparation of this compound as Friedel-Crafts acetylation of 2,2'-dihydroxydiphenyl or Fries migration of 2,2'-diacetoxydiphenyl gives the 5,5'-diacetyl derivative. Through a similar series of reactions 6,6'-bichromonyl has been synthesised from 4,4'-dihydroxydiphenyl. It gave on hydrolysis with alkali the known 3,3'-diacetyl-4,4'-dihydroxydiphenyl.

2,2'-Dihydroxydiphenyl methane on cyanoethylation gave 2,2'-di(β-cyanoethoxy)diphenyl methane which on hydrolysis, cyclisation and dehydrogenation gave 8,8'-bichromonyl methane. On alkaline hydrolysis it gave 2,2'-dihydroxy-3,3'-diacetyldiphenyl methane which gave a violet colouration with alcoholic ferric chloride and a di(2,4-dinitrophenylhydrazone) derivative. This provides a method for the preparation of this compound as Friedel-Crafts acetylation of 2,2'-dihydroxydiphenyl methane and Fries migration of 2,2'-diacetoxydiphenyl methane gives the 5,5'-diacetylderivative. 4,4'-Dihydroxydiphenyl methane on cyanoethylation in the presence of cupric oxide gave

4,4'-di(β-cyanoethoxy)diphenyl methane, previously prepared by Holsten using a mixture of sodium-tert-butoxide and cuprous chloride as the catalyst. On hydrolysis it gave the corresponding dicarboxylic acid which could not be cyclised with PPA. Its acid chloride on heating with anhydrous aluminium chloride however, gave 6,6'-bichromanonyl methane which on dehydrogenation as before gave 6,6'-bichromonyl methane. On alkaline hydrolysis it gave the known 3,3'-diacetyl-4,4'-dihydroxydiphenyl methane. Through a similar sequence of reactions 4,4'-dihydroxybenzophenone and 4,4'-dihydroxydiphenyl sulfone were converted into 6,6'-bichromonyl ketone and 6,6'-bichromonyl sulfone respectively. On hydrolysis with alkali they gave the known 3,3'-diacetyl-4,4'-dihydroxybenzophenone and 3,3'-diacetyl-4,4'-dihydroxydiphenyl sulfone respectively.

The I.R.spectra of the bichromanonyls, bichromonyls and the diacetyl derivatives obtained on hydrolysis showed the characteristic peak for the carbonyl group and the U.V.spectra of the bichromanonyls and bichromonyls gave the characteristic λ max. U.V.spectra were taken either in dioxan or in chloroform.

Chapter II deals with the synthesis of some oxygen heterocycles such as bicoumarinyls and biflavonyls from the appropriate derivatives of diphenyl methane and diphenyl sulfone. 4,4'-Dihydroxydiphenyl methane on condensation with ethyl acetoacetate in the presence of

80 % sulfuric acid gave bi(4-methyl-6-coumarinyl)methane. 2,2'-Dihydroxydiphenyl methane and 4,4'-dihydroxydiphenyl sulfone did not condense with ethyl acetoacetate in the presence of different condensing agents such as, conc. sulfuric acid, phosphorus pentoxide and anhydrous aluminium chloride. 3,3'-Diformyl-4,4'-dihydroxydiphenyl methane on condensation with diethyl malonate in the presence of piperidine gave bi(3-carbethoxy-6-coumarinyl)methane which on hydrolysis and decarboxylation gave bi(6-coumarinyl) methane which was also obtained by the Perkin acetylation of the above formyl derivative.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl methane was obtained by the Fries migration of 4,4'-diacetoxydiphenyl methane. Its structure was proved by the oxidation of its dimethyl ether to the known 3,3'-dicarboxy-4,4'-dimethoxybenzophenone.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl methane on condensation with diethyl carbonate in the presence of pulverised sodium gave bi(4-hydroxy-6-coumarinyl)methane.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl methane was converted into its dibenzoyloxy derivative which was subjected to Baker-Venkataraman rearrangement. The β-diketone obtained was cyclised using sulfuric acid-acetic acid mixture to bi(6-flavonyl)methane. The same bi(6-flavonyl) methane was obtained when 3,3'-diacetyl-4,4'-dihydroxydiphenyl methane was subjected to Kostanecki-Robinson benzoylation by heating with sodium benzoate and benzoic anhydride.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl methane on condensation with anisaldehyde in the presence of alcoholic potassium hydroxide gave the bi(6'-hydroxy-4-methoxy-3'-chalconyl) methane. This bichalconyl derivative on heating with selenium dioxide in iso-amyl alcohol gave bi(4'-methoxy-6-flavonyl) methane.

3,3'-Diformyl-4,4'-dimethoxydiphenyl methane on condensation with o-hydroxy acetophenone in the presence of alcoholic potassium hydroxide gave bi(2'-hydroxy-6-methoxy-3-chalconyl)methane which on refluxing with selenium dioxide in iso-amyl alcohol gave bi(6'-methoxy-3'-flavonyl) methane.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl sulfone was prepared by the Fries migration of 4,4'-diacetoxydiphenyl sulfone. Its structure was established by the oxidation of its dimethyl ether to the corresponding known 3,3'-dicarboxy-4,4'-dimethoxydiphenyl sulfone. The same hydroxy ketone was also prepared by the oxidation of the known 3,3'-diacetyl-4,4'-dihydroxydiphenyl sulfide with hydrogen peroxide in acetic acid.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl sulfone did not undergo condensation when refluxed with diethyl carbonate in the presence of pulverised sodium.

3,3'-Diacetyl-4,4'-dihydroxydiphenyl sulfone on condensation with benzaldehyde in the presence of alcoholic potassium hydroxide gave bi(6'-hydroxy-3'-chalconyl) sulfone which on methylation gave its dimethoxy derivative and on refluxing with selenium dioxide in iso-amyl alcohol gave bi(6-flavonyl) sulfone.

Chapter III deals with the work on the synthesis of bibenzofuranyl methane and sulfone derivatives. 3,3'-Diacetyl-4,4'-dihydroxydiphenyl methane was condensed with ethyl bromoacetate and the resulting diester was hydrolysed to the corresponding dicarboxylic acid. This cyclised to give bi(3-methyl-5-benzofuranyl)methane. Similarly bi(3-methyl-5-benzofuranyl) sulfone was prepared from 3,3'-diacetyl-4,4'-dihydroxydiphenyl sulfone.

3,3'-Diformyl-4,4'-dihydroxydiphenyl methane was condensed with diethyl bromomalonate when bi(2-carbethoxy-5-benzofuranyl)methane was obtained which was hydrolysed and decarboxylated to bi(5-benzofuranyl)methane.

4,4'-Dihydroxydiphenyl sulfone was converted into its diallyl ether by condensing with allyl bromide. This diallyl ether on Claisen rearrangement gave 3,3'-diallyl-4,4'-dihydroxydiphenyl sulfone. This was acetylated, brominated and subjected to the action of alcoholic potassium hydroxide when the desired bi(2-methyl-5-benzofuranyl) sulfone was obtained. Through a similar sequence of reactions bi(2-methyl-5-benzofuranyl) and bi (2-methyl-5-benzofuranyl)ketone were prepared from 4,4'-dihydroxydiphenyl and 4,4'-dihydroxybenzophenone respectively.

In Chapter IV the chloromethylation of 2,2'- and 4,4'-dihydroxydiphenyl methane and 4,4'-dihydroxydiphenyl sulfone and their methyl ethers is described.

Chloromethylation of 2,2'-dihydroxydiphenyl methane did not give a pure product but its dimethyl ether on chloromethylation gave 5,5'-di(chloromethyl) derivative. This on oxidation gave 2,2'-dimethoxybenzophenone-5,5'-dicarboxylic acid identical with the acid obtained by the oxidation of the known 2,2'-dimethoxy-5,5'-di(chloromethyl) benzophenone.

4,4'-Dihydroxydiphenyl methane on chloromethylation did not give a pure product. Its dimethyl ether on chloromethylation at room temperature however gave the 3,3'-di (chloromethyl) derivative which on oxidation gave 4,4'-dimethoxybenzophenone-3,3'-dicarboxylic acid, also prepared by the oxidation of 3,3'-diacetyl-4,4'-dimethoxydiphenyl methane and previously prepared by Ishiwata and Takada [J.Pharm.Soc., Japan. 71, 1254 (1951); C.A.; 46, 6101 (1952)] from 3,3'-diformyl-4,4'-dimethoxydiphenyl methane.

The 3,3'-di(chloromethyl) derivative was converted into the diacetoxy, di(cyanomethyl), di(carboxymethyl) and diformyl derivatives.

3,3'-Diformyl-4,4'-dimethoxydiphenyl methane on condensation with hippuric acid in the presence of sodium acetate and acetic anhydride gave the diazlactone derivative. Attempt to synthesise the di(phenyl alanyl) derivative from it by refluxing with hydriodic acid and acetic anhydride in the presence of red phosphorus however did not succeed.

Chloromethylation of 4,4'-dihydroxydiphenyl sulfone and its dimethyl ether did not succeed.