SUMMARY

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Naphthalene and its derivatives are of considerable importance because of their applications and because the naphthalene derivatives occur in nature, especially in the form of naphthoquinone derivatives. Extensive work has been done on the monohydroxy naphthalenes and various heterocyclic compounds have been synthesised from naphthols. The studies on dihydroxy naphthalenes are comparatively meagre. Some work has been carried out on different dihydroxy naphthalenes to establish the bond structure. Investigations on the electrophilic substitution in dihydroxy naphthalenes has been going on in our laboratories. The present investigation deals with the synthesis of oxygen heterocyclic compounds from them and the synthesis of bichromonyls, bicoumarinyls, bibenzofuranyls and biflavonyl derivatives from 4,4'-dihydroxy diphenyl ether.

Chapter I deals with the synthesis of various α-and γ-pyrone derivatives from dihydroxy naphthalenes or their appropriate derivatives by the application of various reactions such as Pechmann, Perkin, Knoevenagel and Kostanecki-Robinson acylation. 2,7-Dihydroxy naphthalene on Pechmann condensation with malic acid in the presence of conc. sulphuric acid afforded 7-hydroxy naphtho (2,1:6',5') α-pyrone. This product was also obtained by Perkin acetylation of the known 2,7-dihydroxy-1-naphthaldehyde followed by hydrolysis with conc. sulphuric acid and by Knoevenagel condensation of 2,7-dihydroxy-1-naphthaldehyde with diethyl malonate in the

presence of piperidine and the hydrolysis and decarboxylation of ethyl-7-hydroxy naphtho(2,1:6,5')α-pyrone-3'-carboxylate, formed.

2,7-Dihydroxy naphthalene on Pechmann condensation with ethyl acetoacetate in alcohol in the presence of hydrogen chloride gas gave 7-hydroxy-4'-methyl naphtho(2,1:6,5')α-pyrone previously obtained by Buu Hoi et al. However, when the condensation was carried out in the presence of 80 % sulphuric acid, 7-hydroxy-4'-methyl naphtho(2,3:6,5')α-pyrone was obtained. The structures of these isomers were assigned on the basis of the NMR data. The α-pyrones were characterised by their conversion to the corresponding acrylic acid derivatives. The acrylic acid derivative obtained from 7-hydroxy-4'-methyl naphtho(2,3:6,5')α-pyrone was further oxidised to 2,7-dihydroxy-3-naphthoic acid proving the linear structure of this isomer. The mixed m.p. of the two isomers was depressed by over 40^{0}. The methoxy derivatives of the two isomers were also prepared and their m.ps. were found to be different.

When the condensation was carried out with excess of ethyl acetoacetate in the presence of conc.sulphuric acid a product insoluble in alkali was obtained. It analysed for a di-α-pyrone, but the definite structure could not be assigned as it was found insoluble in most of the solvents. and therefore the NMR could not be taken.

7-Hydroxy-4'-methyl naphtho(2,3:6,5')α-pyrone was formylated with hexamine in acetic acid. 7-Hydroxy-8-formyl-4'-methyl naphtho(2,3:6,5')α-pyrone structure has been assigned to this product on the basis of the NMR data. The synthesis

of 4'-methyl naphtho(2,3:6',5' and 7,8:6",5")di-α-pyrone has been achieved by the Knoevenagel condensation of 7-hydroxy-8-formyl-4'-methyl naphtho(2,3:6',5')α-pyrone with diethyl malonate and hydrolysis followed by the decarboxylation of the product obtained.

1,4-Dihydroxy naphthalene on condensation with ethyl acetoacetate in the presence of sulphuric acid afforded 4-hydroxy-4'-methyl naphtho(1,2:6',5')α-pyrone. 1,4-Diacetoxy naphthalene on Fries migration gave 1,4-dihydroxy-2-acetyl naphthalene which on condensation with diethyl carbonate in the presence of pulverised sodium yielded 4,4'-dihydroxy naphtho(1,2:6',5')α-pyrone.

The γ-pyrone derivatives were prepared from dihydroxy naphthalenes by condensation with ethyl acetoacetate in boiling diphenyl ether.

1,4-Dihydroxy naphthalene gave a product to which the 4-hydroxy-2'-methyl naphtho(1,2:6',5')γ-pyrone structure has been assigned as it was different from the corresponding α-pyrone and on alkaline hydrolysis gave 1,4-dihydroxy-2-acetyl naphthalene.

Similarly 1,5-dihydroxy naphthalene when condensed with ethyl acetoacetate in boiling diphenyl ether gave a product to which the 5-hydroxy-2'-methyl naphtho(1,2:6',5') γ-pyrone structure has been assigned as it was found to be different from 5-hydroxy-4'-methyl naphtho(1,2:6',5')α-pyrone on comparison.

2,7-Dihydroxy naphthalene gave a product to which the 7-hydroxy-2'-methyl naphtho(2,1:6',5') γ-pyrone structure has been assigned as it

~~and~~ was different from both the angular and the linear α-pyrone isomers described before.

2,7-Dihydroxy-1,6-diacetyl naphthalene on Kostanecki-Robinson benzoylation with benzoic anhydride and sodium benzoate gave 2',2"-dimethyl-3',3"-dibenzoyl naphtho (2,1:6',5' and 7,6:6",5")di-γpyrone. Debenzoylation of this compound did not succeed.

Chapter II deals with the synthesis of various γ-pyrone derivatives from the hydroxy naphtho α-and γ-pyrones.

7-Acetoxy naphtho(2,1:6',5')α-pyrone,prepared by Perkin acetylation of 2,7-dihydroxy-1-naphthaldehyde,when subjected to Fries migration afforded a product which was insoluble in most of the solvents. Its NMR therefore could not be taken. 7-Hydroxy-6-acetyl naphtho(2,1:6',5')α-pyrone structure was assigned to it on the basis of the NMR data of the acid derivative obtained from it by its condensation with ethyl bromoacetate and hydrolysis of the ester obtained.

7-Hydroxy-6-acetyl naphtho(2,1:6',5')α-pyrone was converted into its benzoyloxy derivative which was subjected to Baker-Venkataraman rearrangement with powdered potassium hydroxide in pyridine. The β-diketone obtained was cyclised with conc.sulphuric acid to naphtho(2,1:6',5')α-pyrono-2"-phenyl(7,6:6",5")γ-pyrone.

7-Hydroxy-6-acetyl naphtho(2,1:6',5')α-pyrone when subjected to Kostanecki-Robinson benzoylation by heating it with benzoic anhydride and sodium benzoate gave naphtho -

(2,1:6',5')α-pyrone-2"-phenyl-3"-benzoyl(7,6:6",5")γ-pyrone. When the same o-hydroxy acetyl derivative was heated with acetic anhydride and sodium acetate it gave naphtho (2,1:6',5')α-pyrono-2"-methyl-3"acetyl(7,6:6",5")γ-pyrone.

7-Hydroxy-8-acetyl-4'methyl naphtho(2,3:6',5') α-pyrone was prepared by subjecting 7-acetoxy-4'methyl naphtho(2,3:6',5')α-pyrone to Fries mirgation. The structure was assigned on the basis of the NMR spectral data.

The synthesis of 4'methyl naphtho(2,3:6',5')α-pyrone 2"-phenyl(7,8:6",5")γ-pyrone was achieved by two different routes (i) by subjecting 7-benzoyloxy-8-acetyl-4'methyl naphtho(2,3:6',5')α-pyrone to Baker-Venkataraman rearrangement in pyridine with potassium hydroxide,when a cyclised product was obtained to which 4'methyl naphtho(2,3:6',5')α-pyrono-2"-phenyl(7,8:6",5")γ-pyrone structure was assigned (ii) by condensing 7-hydroxy-8-acetyl-4'methyl naphtho(2,3:6',5') α-pyrone with benzaldehyde in the presence of alcoholic potassium hydroxide and cyclization and dehydrogenation of 7-hydroxy-8-cinnamoyl-4'methyl naphtho(2,3:6',5')α-pyrone formed with selenium dioxide in iso-amyl alcohol. A similar condensation with anisaldehyde gave the 2"(p-methoxy phenyl) derivative.

7-Hydroxy-8-acetyl-4'methyl naphtho(2,3:6',5') α-pyrone on Kostanecki-Robinson benzoylation as usual gave 4'methyl naphtho(2,3:6',5')α-pyrono-2"-phenyl-3"-benzoyl (7,8:6",5")γ-pyrone. The debenzoylation of this flavone did not succeed. The same o-hydroxy acetyl ketone derivative on subjecting it to Kostanecki-Robinson acetylation afforded

4'-[illegible]naphtho(2,3:6',

4'-methyl naphtho(2,3:6',5')α-pyrono-2''-methyl-3''-acetyl (7,8:6'',5'')γ-pyrone.

Similarly 5-hydroxy-6-acetyl-4'-methyl naphtho (1,2:6',5')α-pyrone through benzoylation followed by Baker-Venkataraman transformation with pyridine and potassium hydroxide gave directly the cyclised product, 4'-methyl naphtho(1,2:6',5')α-pyrono-2''-phenyl(5,6:6'',5'')γ-pyrone. The same flavone derivative was obtained when 5-hydroxy-6-acetyl-4'-methyl naphtho(1,2:6',5')α-pyrone was condensed with benzaldehyde in the presence of alcoholic potassium hydroxide and the product obtained was cyclised and dehydrogenated by refluxing with selenium dioxide in iso-amyl alcohol.

Kostanecki-Robinson benzoylation and acetylation of 5-hydroxy-6-acetyl-4'-methyl naphtho(1,2:6',5')α-pyrone yielded 4'-methyl naphtho(1,2:6',5')α-pyrono-2''-phenyl-3''-benzoyl(5,6:6'',5'')γ-pyrone and 4'-methyl naphtho(1,2:6',5') α-pyrono-2''-methyl-3''-acetyl(5,6:6'',5'')γ-pyrone.

5-Hydroxy-6-acetyl-2'-methyl naphtho(1,2:6',5') γ-pyrone prepared from 5-acetoxy-2'-methyl naphtho(1,2:6',5') γ-pyrone through Fries migration gave 2'-methyl-2''-phenyl naphtho(1,2:6',5' and 5,6:6'',5'')di-γ-pyrone on benzoylation and Baker-Venkataraman transformation with solid potassium hydroxide in pyridine of the benzoyl derivative and Cyclisation of the β-diketone derivative with conc.sulphuric acid.

Kostanecki-Robinson acetylation of 5-hydroxy-6-acetyl-2'-methyl naphtho(1,2:6',5')γ-pyrone gave 2',2''-dimethyl

3''-acetyl naphtho(1,2:6',5' and 5,6:6'',5'')di-γ-pyrone.

Chapter III deals with the synthesis of various furonaphtho-α-and γ-pyrones from the appropriate derivatives of hydroxy naphtho-α-and γ-pyrones.

7-Hydroxy-6-acetyl naphtho(2,1:6',5')α-pyrone was condensed with ethyl bromoacetate in the presence of anhydrous potassium carbonate in dry acetone. The rresulting ester was hydrolysed to 7-carboxymethoxy-6-acetylnaphtho (2,1:6',5')α-pyrone. Through simultaneous cyclisation and decarboxylation by refluxing it with acetic anhydride and sodium acetate gave 3''-methyl naphtho(2,1:6',5')α-pyrono (7,6:5'',4'')furan.

7-Hydroxy naphtho(2,1:6',5')α-pyrone was converted into its allyloxy derivative by condensing it with allyl bromide, which on Claisen rearrangement gave 7-hydroxy-8-allyl naphtho(2,1:6',5')α-pyrone. The structure was assigned on the basis of the NMR data. This o-hydroxy allyl derivative was triturated with conc.sulphuric acid when 2''-methyl naphtho(2,1:6',5')α-pyrono(7,8:5'',4'')2'',3''-dihydrofuran was obtained which on dehydrogenation with palladised charcoal in diphenyl ether gave 2''-methyl naphtho(2,1:6',5')α-pyrono (7,8:5'',4'')furan.

Synthesis of 3'',4'-dimethyl naphtho(2,3:6',5') α-pyrono(7,8:5'',4'')furan was achieved by the condensation of 7-hydroxy-8-acetyl-4'-methyl naphtho(2,3:6',5')α-pyrone with ethyl bromoacetate, hydrolysis of the ester obtained with sodium hydroxide and heating the corresponding acid

obtained with sodium acetate and acetic anhydride.

7-Allyloxy-4'methyl naphtho(2,3:6',5')α-pyrone was subjected to Claisen rearrangement in dimethyl aniline. 7-Hydroxy-8-allyl-4'-methyl naphtho(2,3:6',5')α-pyrone structure was assigned on the basis of NMR data to the product obtained. This was acetylated and brominated and the dibromo derivative was subjected to the action of alcoholic potassium hydroxide when the desired 2'',4'-dimethyl naphtho(2,3:6',5')α-pyrono(7,8:5'',4'')furan was obtained.

Synthesis of 4'-methyl naphtho(2,3:6',5')α-pyrono (7,8:5'',4'')furan was achieved by two different routes. By condensing 7-hydroxy-8-formyl-4'-methyl naphtho(2,3:6',5') α-pyrone with ethyl bromoacetate and subsequent hydrolysis and cyclisation of the 7-carbethoxymethoxy-8-formyl-4'-methyl naphtho(2,3:6',5')α-pyrone derivative formed.The same o-hydroxy formyl derivative was condensed with ethyl bromo-malonate in the presence of anhydrous potassium carbonate in dry methyl ethyl ketone which yielded the cyclised product 4'-methyl-2''-carbethoxy naphtho(2,3:6',5')α-pyrono(7,8:5'',4'') furan. This on hydrolysis with a mixture of acetic acid and hydrochloric acid gave the corresponding acid which on decarboxylation with copper bronze in quinoline gave the above furan.

7-Hydroxy-6-acetyl-4'methyl naphtho(2,1:6',5') α-pyrone was prepared as usual from 7-hydroxy-4'methyl naphtho(2,1:6',5')α-pyrone. This structure was assigned on the basis of the NMR data. It was condensed with ethyl

bromoacetate. and the ester obtained through usual reactions was converted into 3'',4'-dimethyl naphtho(2,1:6',5')α-pyrono (7,6:5'',4'')furan.

7-Hydroxy-4'methyl naphtho(2,1:6',5')α-pyrone by allylation with allyl bromide followed by Claisen rearrangement in dimethyl aniline gave 7-hydroxy-8-allyl-4'-methyl naphtho(2,1:6',5')α-pyrone. The structure was assigned on the basis of the NMR data. This was cyclised by triturating with conc.sulphuric acid to 2'',4'-dimethyl naphtho(2,1:6',5')α-pyrono(7,8:5'',4'') 2'',3''-dihydro furan. Attempt to dehydrogenate this with palladised charcoal did not succeed.

The synthesis of 2'',4'-dimethyl naphtho(1,2:6',5') α-pyrono(5,6:5'',4'')furan was also achieved from 5-allyloxy-4'-methyl naphtho(1,2:6',5')α-pyrone through similar reactions.

5-Hydroxy-6-acetyl-2'methyl naphtho(1,2:6',5') γ-pyrone was condensed with ethyl bromoacetate as usual and the ester obtained was hydrolysed and the acid cyclised with acetic anhydride and sodium acetate to 2',3''-dimethyl naphtho (1,2:6',5')γ-pyrono(5,6:5'',4'')furan.

Attempt to synthesise 2',2''-dimethyl naphtho (1,2:6',5')γ-pyrono(5,6:5'',4'')furan from 5-hydroxy-2'methyl naphtho(1,2:6',5')γ-pyrone, through the intermediate 5-hydroxy-6-allyl-2'methyl naphtho(1,2:6',5')γ-pyrone did not succeed.

Chapter IV deals with the synthesis of some oxygen heterocycles from 4,4'-dihydroxy diphenyl ether.

The synthesis of bi(2-methyl-6-chromonyl)ether was achieved by the Claisen condensation of 3,3'-diacetyl-4,4'-

dihydroxy diphenyl ether, prepared by the Fries migration of 4,4'-diacetoxy diphenyl ether, with ethyl acetate in the presence of pulverised sodium. The product underwent simultaneous condensation and cyclisation giving bi(2-methyl-6-chromonyl)ether.

3,3'-Diacetyl-4,4'-dihydroxy diphenyl ether on Kostanecki-Robinson acetylation by heating with acetic anhydride and sodium acetate gave bi(2-methyl-3-acetyl-6-chromonyl)ether. The deacetylation of this with alcoholic potassium hydroxide did not succeed.

4,4'-Dihydroxy diphenyl ether on reaction with acrylonitrile in the presence of cupric oxide gave 4,4'-di(ω-cyanoethoxy)diphenyl ether which on hydrolysis with conc.hydrochloric acid gave the corresponding acid. This was cyclised in the presence of polyphosphoric acid to bi(6-chromanonyl)ether which on dehydrogenation with palladised charcoal in diphenyl ether gave bi(6-chromonyl)ether.

Attempt to condense 4,4'-dihydroxy diphenyl ether with (i)malic acid in the presence of conc.sulphuric acid (ii) with ethyl acetoacetate in the presence of several condensing agents did not succeed. The original dihydroxy diphenyl ether was recovered. The condensation of 4,4'-dihydroxy diphenyl ether with ethyl acetoacetate in boiling diphenyl ether also did not succeed.

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

The synthesis of bi(3-methyl-5-benzofuranyl)ether was achieved through the condensation of 3,3'-diacetyl-4,4'-dihydroxy diphenyl ether with ethyl bromoacetate, the hydrolysis of the ester to corresponding acid and its cyclisation as usual.

Bi(6-flavonyl)ether was synthesised from 3,3'-diacetyl-4,4'-dihydroxy diphenyl ether through the Baker-Venkataraman rearrangement of its benzoyloxy derivative with solid potassium hydroxide and pyridine and the cyclisation of the β-diketone obtained. with conc. sulphuric acid.

With a view to synthesise unsubstituted dibenzo furanyl ether and bicoumarinyl ether from 4,4'-dihydroxy diphenyl ether, formylation of the same by the Gatterman method and by heating with hexamine and acetic acid was attempted but it did not succeed.

4,4'-Dimethoxy diphenyl ether when subjected to chloromethylation in acetic acid with paraformaldehyde and zinc chloride gave an oily product from which the 3,3'-di (chloromethyl) derivative could be obtained in very poor yield therefore its reaction with hexamine in acetic acid to get the diformyl derivative could not be studied.

Mannich reaction on 4,4'-dihydroxy diphenyl ether with dimethyl amine and paraformaldehyde gave 3,3'-dimethyl-aminomethyl-4,4'-dihydroxy diphenyl ether but the yield was poor therefore no further work could be done.