PART IV

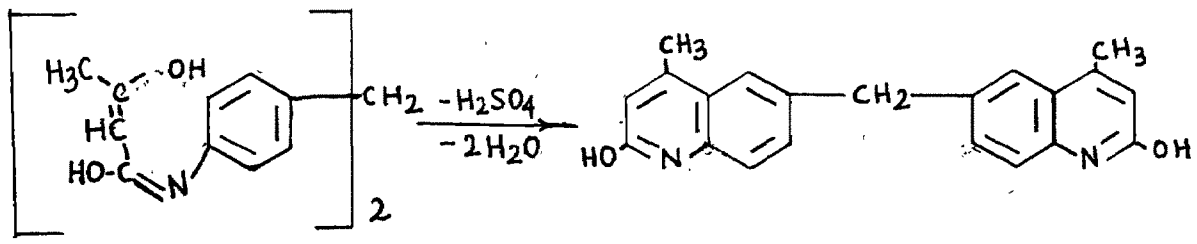
Synthesis of bis-hydroxyquinoline methanes by cyclisation of methylene bis-(acetoacet arylamides) using acetic anhydride and concentrated sulphuric acid as the cyclising agent.

PART IV

Theoretical

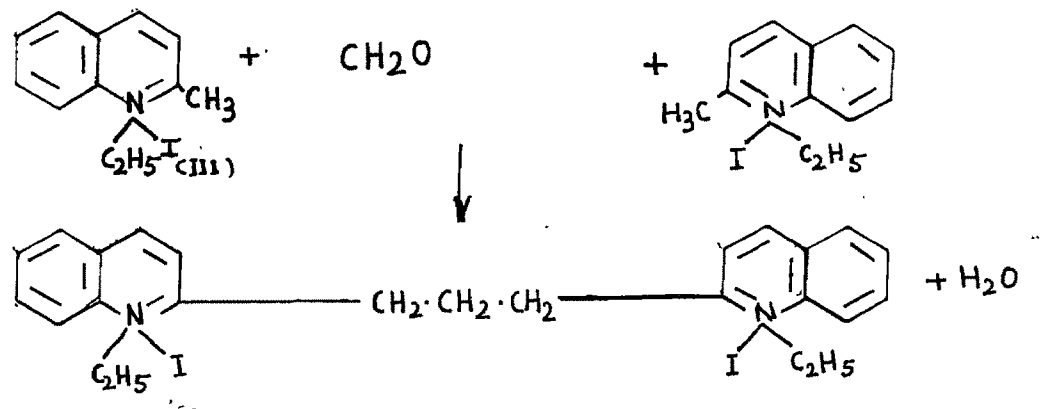
Kaslow and Reck (J. Amer. Chem. Soc., 1947, 69, 864) have stated, that very few diquinolylmethanes have been recorded in the literature. Schuller (loc.cit.) prepared 5,5'-methylene bis-8-hydroxyquinoline by treatment of 8-hydroxyquinoline with formaldehyde in concentrated sulphuric acid. Borsche and Kienitz (Ber., 1910, 43, 2334) obtained 6,6'-methylene bis-quinoline by a Skraup reaction on 4,4'-diaminodiphenyl methane, while Borsche and Meyer (loc.cit.) synthesised 6,6'-methylene bis-2-methylquinoline by the action of alcoholic alkali and acetone on 5,5'-diisatylmethane and decarboxylation of the 6,6'-methylene bis-2-methylcinchoninic acid which was obtained from this reaction. Monti and Verona (loc.cit.) have reported a preparation of methylene bis-6-hydroxyquinoline.

Further, Kaslow et al. reported on the synthesis of several 6,6'-methylene bis-lepidine derivatives from corresponding 6,6'-methylene bis-acetoacetanilides through the carbostyrils and chlorolepidine derivatives. 4,4'-methylene bis-acetoacetanilide was prepared from 4,4'-diaminodiphenylmethane in acetone with diketene. 6,6'-Methylene bis-4-methylcarbostyril (II) was obtained by cyclising 4,4'-methylene bis-acetoacetanilide (I) with concentrated sulphuric acid. This reaction is expressed as:



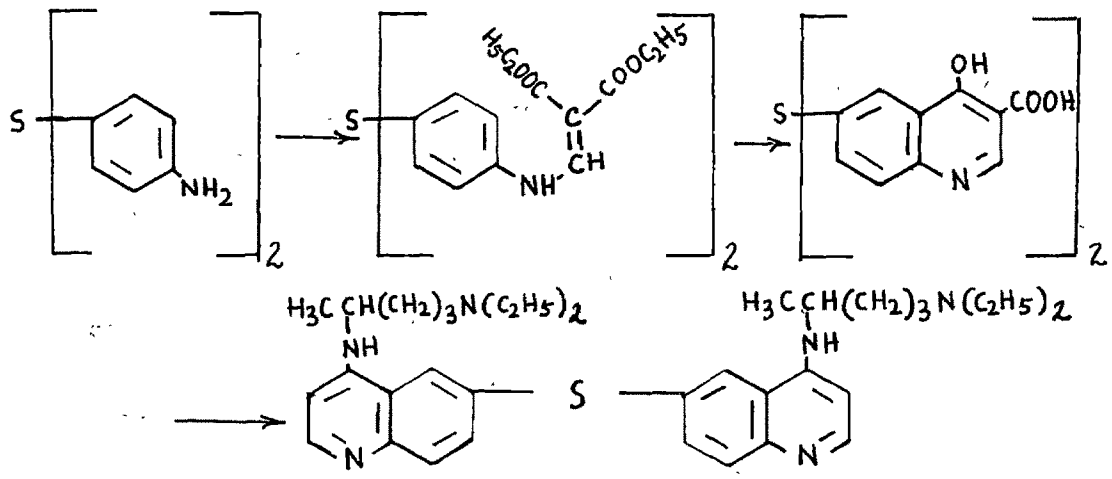
(I) (II)

All synthesis of carbocyanines involve condensation of two heterocycles, both of which contain **active** methyl groups ; with a 1-carbon-atom compound which supplies the third carbon atom in the trimethine bridge. Mills and Hamer (J. Chem. Soc., 1920, 117, 1550) condensed quinaldine ethiodide (III) with formaldehyde and obtained methylene diquinaldine. They concluded that the above reaction is a strict parallel to the condensation of acetoacetic ester and related compounds with formaldehyde, which gives methylene bis-acetoacetic ester and the compound diethiodide of methylenediquinaldine (IV) has actually been isolated as under:



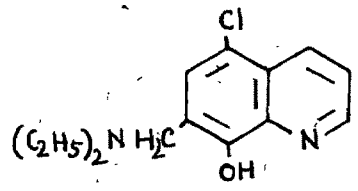
(IV)

Price, Leonard and Stacy (J. Amer. Chem. Soc., 1947, 69, 855) prepared 4-hydroxyquinolines with sulphur containing ~~substituents~~ using boiling diphenyl ether as the cyclising agent. For this they have applied the ethoxymethylmalonic ester synthesis to p-aminophenyl sulphide proceeded successfully to produce 6,6'-bis-[4-(4-diethylamino-1-methylbutylamino)-quinolyl] sulphide (V) as under:

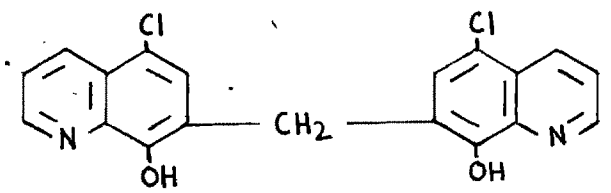


(V)

Edgerton et al. (loc.cit.) prepared some antiamebic agents which while preparing they obtained 5-chloro-7-diethylaminomethyl-8-quinolinol (Vi) and 7,7'-methylene bis-(5-chloro-8-quinolinol) VII, as an insoluble high melting by product.



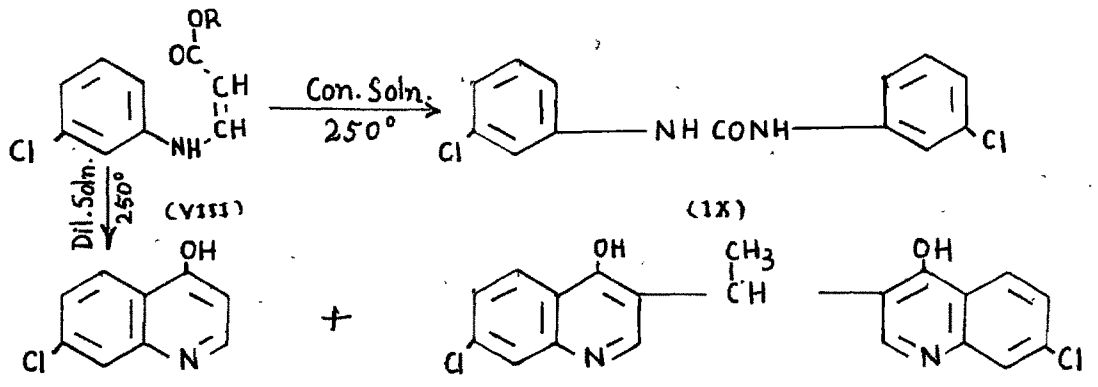
(VI)



(VII)

During the period of reflux, the insoluble 5,5'-methylenebis-(7-chloro-8-quinolinol) an isomer of VII gradually formed in appreciable amounts. It was found that methylene bis-compounds were inactive towards amebicidal activity.

Price, Leonard and Reitsema (J. Amer. Chem. Soc., 1946, 68, 1256) treated β-m-chloroanilinoacrylates (VIII) in concentrated diphenyl ether and obtained bis-(m-chlorophenyl) urea IX. But at high dilution there was obtained 7-chloro-4-hydroxyquinoline (X) along with 1,1-bis-(7-chloro-4-hydroxy-3-quinolyl)-ethane (XI), which could also be formed by condensation of 7-chloro-4-hydroxyquinoline with acetaldehyde.



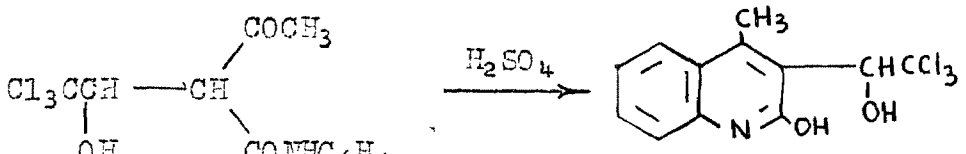
(VIII)

(IX)

(X)

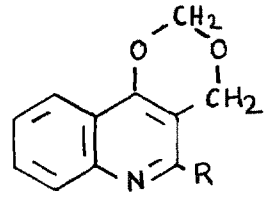
(XI)

Jean D'ecombe (Compt.rend., 1953, 237,336-7 ; Chem. Abst., 1954, 48, 10022) used sodium acetate as a catalyst in the condensation of aldehydes with compounds containing active hydrogen. Acetoacetanilide in aqueous alcohol with trichloroacetaldehyde in the presence of sodium acetate yielded trichlorohydroxymethylacetoacetanilide (XII), which, on cyclisation with sulphuric acid, gave 2-hydroxy-3-(1-hydroxy-2,2,2-trichloroethyl)-4-methyl-quinoline (XIII).



(XII) (XIII)

Lydia Monti, Valeria Cirelli and Berenice Romano (Gazz. chim. ital ; 1936, 66, 42-8) carried out the reaction of formaldehyde on γ-hydroxyquinolines in the presence of sulphuric acid giving the cyclic methylenic ethers of the general structure (XIV) as under (R=CH_3 or C_6H_5):



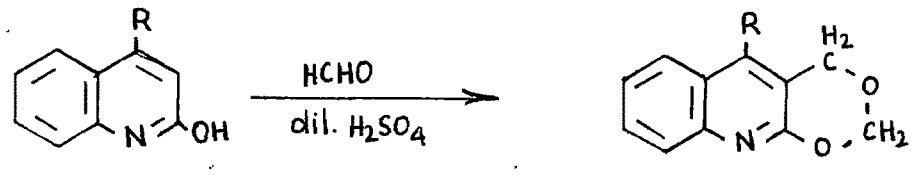
(XIV)

This reaction is analogous to the reactions with 6-hydroxyquinoline and p-nitrophenol or p-nitrocresols. The identity in behaviour of 6-hydroxyquinoline and γ-hydroxyquinoline is attributable to the positions of the OH with respect to the N-atoms in the two compounds. In 6-hydroxyquinoline the OH may be regarded as in the p-position to the N, as in p-nitrophenol, the OH and NO_2 are in p-position, whereas in γ-hydroxyquinoline, the OH is in the p-position to the N in the same ring. The relatively greater activity of γ-hydroxyquinolines is explainable by the Bonino theory of constitution of aromatic nuclei, i.e. the presence of OH and N in the p-position to each other disturbs the system of negative atoms and increases the activity of the β-H-atom. In α-hydroxy-γ-alkylquinolines, the OH in the o-position forms an active system which makes the former react with formaldehyde as do γ-hydroxy-α-alkylquinolines.

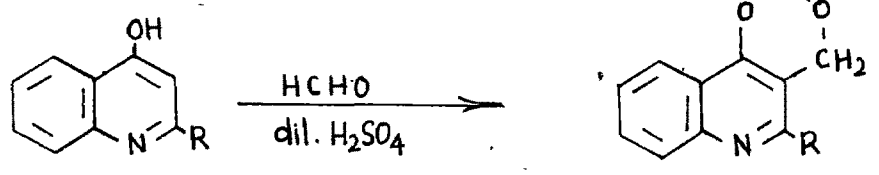
The γ-hydroxyquinolines were prepared by Lydia Kaufl et al. (loc.cit.) based on the method of Limpach (loc.cit.) Thus, they prepared cyclic methylene ether of 2-methyl-γ-hydroxy-3-quinoline alcohol ; and cyclic methylene ether of 2,8-dimethyl-, and 2,6-dimethyl-, -4-hydroxy-3-quinoline alcohols. Methylenequinoline alcohols are insoluble in aqueous alkalies but soluble in concentrated sulphuric acid and they do not give acetyl derivatives with acetic anhydride.

In the Borsche-Berkout modification of the Lederer-Manasse reaction, both 2- and 4-hydroxyquinolines give cyclic ethers (Ewing and Steck, J. Amer.Chem.Soc., 1946,68,

2181 ; Monti and Cirelli, Gazz. chim. ital., 1936, 66, 42).



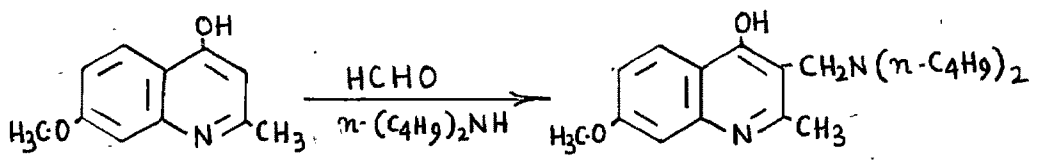
(XV)



(XVI)

(Where R = $-CH_3$ or $-C_6H_5$).

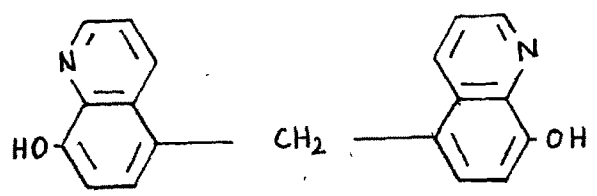
Price and Jackson (J. Amer. Chem. Soc., 1946,68, 1282) carried out the Mannich reaction of 4-hydroxyquinoline with formaldehyde and n-dibutylamine, giving 3-n-dibutylaminomethyl derivative (XVII) as under:



(XVII)

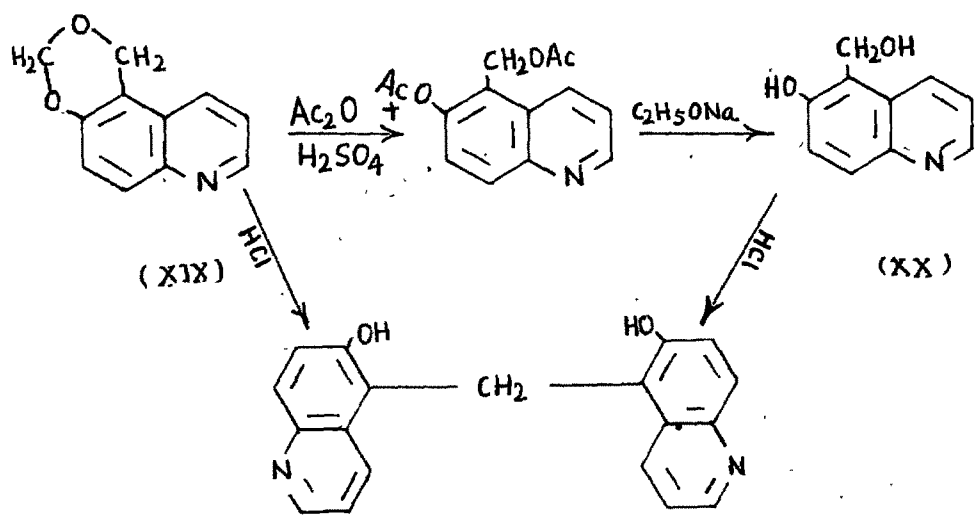
The Lederer-Manasse reaction with (6-or 8-) hydroxyquinoline, formaldehyde and alkali gives carbinols or methylenebis-diquinolyl derivatives (Manasse, Ber., 1894, 27, 2409 ; Cohn, J.prakt. Chem., 1911,[2], 83 498 ; Monti and Verona, loc.cit.). When sulphuric acid is used as the condensing agent, the products are generally diquinolylmethanes (Schuller, loc.cit.).

The typical reaction with 8-hydroxyquinoline, formaldehyde and sulphuric acid gave 5,5'-methylenebis-(8-hydroxyquinoline) (XVIII)



(XVIII)

Kaslow and Raymond (J. Amer. Chem. Soc., 1948, 70, 3912) obtained 6-hydroxy-5-quinolinemethanol (XX) by careful cleavage of dioxino[5,4-f] quinoline (XIX). The carbinol and dioxino compounds can be transformed by hydrochloric acid to 5,5'-methylenebis-(6-hydroxyquinoline) (XXI).



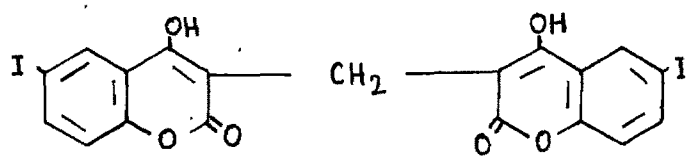
(XXI)

E. Noelting (Chimie et industrie, 1922, 8, 758 ; Chem. Abst., 1923, 17, 473) found that 8-hydroxyquinolines which are colourless, dissolve to yellow solution in alkali and are fixed by metallic mordants, giving yellow with aluminium and grey with ferric. When two moles of 8-hydroxyquinoline in hot alcohol with 1 mole of formaldehyde in the presence of hydrochloric acid gave bis(8-hydroxyquinolyl)methane, which dyes mordants much more intensely than 8-hydroxyquinoline.

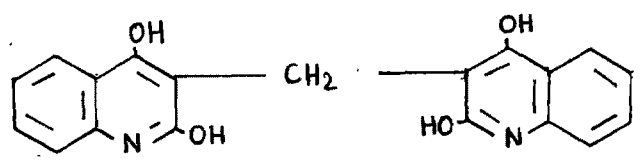
When 4-hydroxy-6-iodocoumarin condensed with formaldehyde gave 3,3'-methylenebis-(4-hydroxy-6-iodo-coumarin) (XXII) (Piscopo et al. Gazz.chim.ital., 1958, 88, 101 ; Chem. Abst., 1959, 53, 2216). Further Mentzer et al. (Bull soc.chim., 1945, 12, 430 ; Chem. Abst., 1947 , 41, 424) observed that the two hydroxy groups are essential for the antivitamin K activity of 3,3'-methylene bis-(4-hydroxycoumarin), and methylation or esterification of both groups destroys the physiological activity. Bis(4-hydroxy-3-coumarinyl) acetic acid -(Pelentan-) has been prepared by Fucik, Prochazka and Cechova,(Bull soc.chim. France 1949, 99-103.) on condensation of 4-hydroxycoumarin with a solution of glyoxilic acid. Hais (Chem. Listy., 1951,45, 76-81), used a paper chromatography for the detection and identification of pelentan and dicoumarol and some of their degradation products in blood and urine.

In order to prepare anticoagulant substances 4-hydroxycarbostyrils and formaldehyde (Fucik, Prochazka, Hach and Strof ; United Pharm. Works, Prague, Czech ;

Chem. Listy, 1951, 45,, 23), on condensation, gave 3,3'-methylenebis-(4-hydrocycarbostyril) (XXIII) as under:

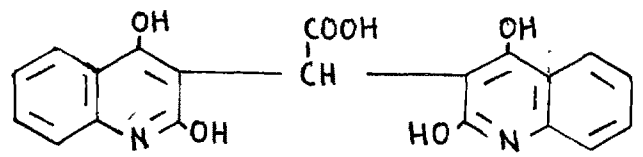


(XXII)

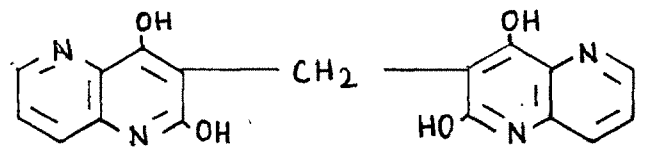


(XXIII)

Further, these authors condensed 2,4-dihydroxy-quinoline and glyoxilic acid and obtained 3,3'-bis-(4-hydroxy-3-carbostyril) acetic acid (XXIV) whereas 2,4-dihydroxynaphthyridine with glyoxilic acid yielded 3,3'-methylenebis-(2,4-dihydroxynaphthyridine) (XXV).

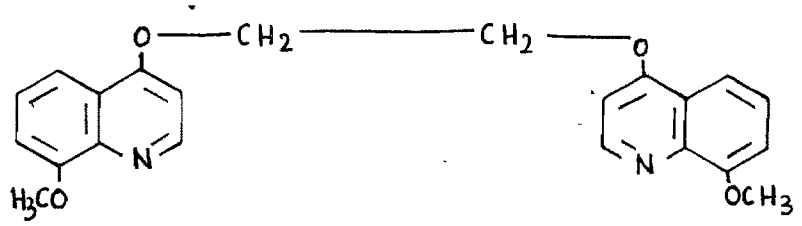


(XXIV)



(XXV)

Rastogi, Khanna and Dhar (J. Sci. industr. Res., 1956, 15C, 177) prepared 1,2-bis-(8-methoxy-4-qiinolyl oxy) ethane (XXVI) from 4-chloro-8-methoxyquinoline and the di-sodium salts of ethylene glycol.



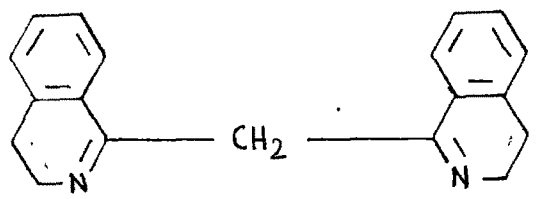
(XXVI)

Max Boetius et al. (German, 13870, 1957 ; Chem. Absts., 1959, 53, 11415) treated 1-substituted carbostyrils with carbonyl compounds at raised temperatures or with unsaturated ketones to give 3,3'-methylenebis-(4-hydroxycarbostyril). For example 3,3'-methylenebis-(1-methyl-4-hydroxycarbostyril) and 3,3'-propylidenebis-(1-phenyl-4-hydroxycarbostyril) have been prepared from 1-methyl (or 1-phenyl)-4-hydroxycarbostyril with 35 % formaldehyde (or propionaldehyde) respectively.

Rice et al. (U.S.2,803,627, 1957 ; Chem. Abst., 1958, 52, 2091), from 4-carbethoxy-6-hydroxyquinoline with formaldehyde and appropriate secondary amines synthesised compounds of low toxicity ; characterised by physiological activity, as antihistamine, bronchial dilators, medicaments of respiratory disorders and arthritis. Goldyrev (Zhur. Obshchei Khim., 1957, 27, 2837) prepared 2,2'-4,4'-8,8'-hexamethyl-6,6'-biquinolylmethane and the methylated biquinolines were converted to dyes. The introduction of a methylene bridge between the quinolyl groups reduces colour depth and substantivity.

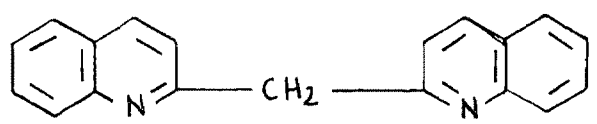
Ghosh et al. (loc.cit.) prepared 1,1'-methylene-bis-(3,4-dihydroisoquinoline) (XXVII) from malondi-β-phenylamide by Bischler-Napieralski cyclisation in presence

of phosphorus pentoxide and its bis-structure was confirmed by the study of ultraviolet absorption spectra (c.f.part V).



(XXVII)

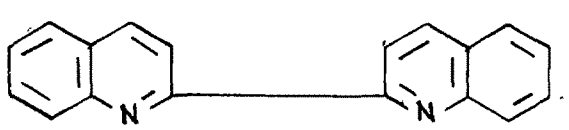
Medizin et al. (Ber., 1921, 54, 786) obtained 2,2'-diquinolylmethane (XXVIII) from 2-chloroquinoline and 2-methylquinoline at 180-200°C. Thus:



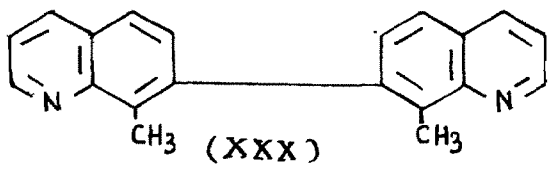
(XXVIII)

Over and above the diquinolylmethanes a number of biquinolines are also available. Biquinolines are generally obtained either by application of standard quinoline synthesis to bifunctional molecules, by pyrolysis of various qinoline derivatives, or by application of the Ullmann's synthesis. Thus, Nieuwenhuis, Wibaut and Willink (Rec. trav.chim., 1935, 54, 804) obtained 2,2'-biquinoline(XXIX), when quinoline was heated in a sealed tube at 325°C with nickel or alumina or by condensing o-aminobenzaldehyde with 2-acetylquinoline (Smirnoff, Helv. Chim. Acta., 1904,4,802).

Weidel (Monatsh., 1887, 8, 120) prepared 2,6'-biquinoline from aniline and quinoline hydrochloride which were heated at 180° with platinised asbestos in the presence of oxygen. Reich and Serpek (Helv. Chim. Acta., 1920, 3, 138) reported that 3,3'-biquinoline formed when quinoline was heated with calcium hydride at 220°C. Ueda (J. Pharm. Soc., Japan, 1937, 57, 180) obtained 2,2'-and 5,5'-biquinolines by the application of Ullmann's reaction on catalytic reduction of 2-bromo and 5-bromoquinoline respectively. Ruttan (Trans. Roy. Soc. Canada, 1892, III, 35 ; Chem. Zentr., 1893, 64, II, 52) obtained 8,8'-dimethyl-6,6'-biquinoline (XXX) by skraup reaction applied to o-toluidine.



(XXIX)

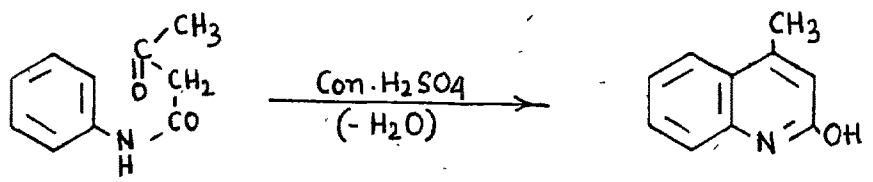


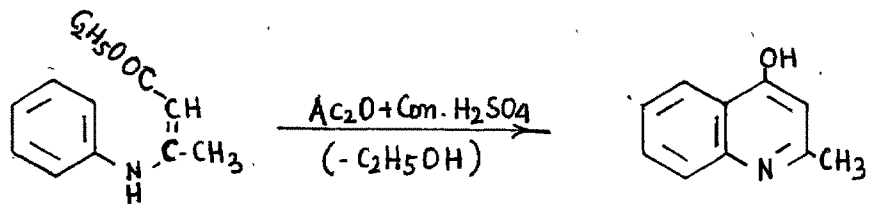
(XXX)

Ward and Waring (J. Amer. Chem. Soc., 1932, 54, 1697) obtained 5,5',7,7'-tetramethyl-8,8'-biquinoline by coupling two molecules of 5-nitro-4-iodo-1,3-dimethyl-benzene with copper powder, and the resulting dinitro-tetramethyldiphenyl was reduced and converted by a Skraup synthesis.

Acetoacet arylamides have been cyclised, using concentrated sulphuric acid, giving 2-hydroxy-4-methyl-quinoline derivatives by the method of Knorr (loc.cit.) as

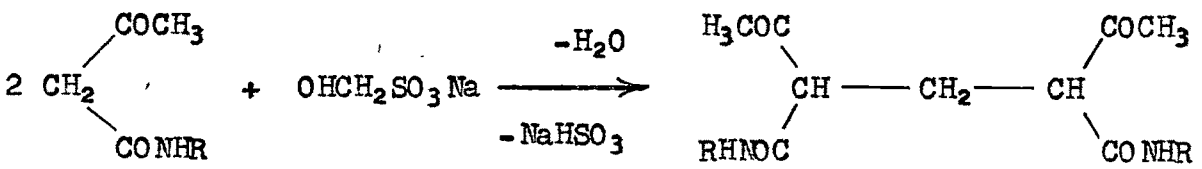
modified by Ewins and King (loc.cit.). Conrad and Limpach (loc.cit.) obtained 4-hydroxy-2-methylquinolines on thermal cyclisation of several ethyl β-arylamino α-β-unsaturated esters (crotonates) obtained from ethylacetoacetate and primary arylamines. Bangdiwala and Desai (loc.cit.) on cyclisation of a number of crotonates and acrylates, obtained 4-hydroxy-2-methylquinolines, using a mixture of acetic anhydride and concentrated sulphuric acid as the cyclising agent in the ratio of 1 : 1 by volume. They have observed that the presence of acetic anhydride prevents the tendency of decomposition of the intermediate product undergoing cyclisation. These reactions of the amides and the crotonates giving hydroxyquinolines respectively are expressed as :





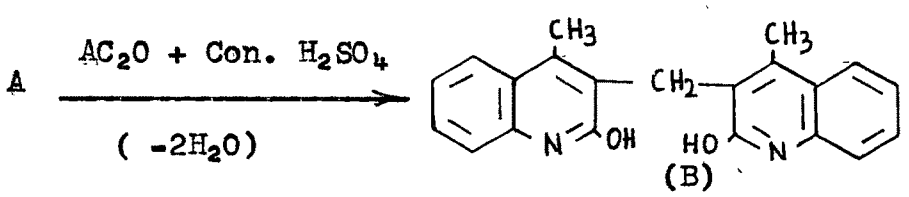
In the present investigation, using a mixture of acetic anhydride and concentrated sulphuric acid as the cyclising agent, 3,3'-methylenebis-(2-hydroxy-4-methyl-quinoline) derivatives (B) have been synthesised, on cyclisation of the corresponding methylene bis-(acetoacet

arylamides) (A), which are formed by the interaction of acetoacet arylamides (2 mols) with sodium hydroxy methane sulphonate (1 mole) as described in Part III. Ewins and King (loc.cit.) used concentrated sulphuric acid as the cyclising agent ; but here a mixture of acetic anhydride and concentrated sulphuric acid in the ratio of (1 : 1) by volume was found to be efficient to bring about cyclisation of the compounds of the types A to types B. It has also been observed that the intermediate products, undergoing cyclisation due to the presence of acetic anhydride, have been prevented from charring due to decomposition as the final products are found to be cleaner with better yields than those obtained with concentrated sulphuric acid alone. These reactions are expressed as under:



(A)

(Where, R is phenyl, tolyl, xylyl and naphthyl radicals.)



(B)

Here, the reactive methylene hydrogen atoms, situated between the two carbonyl groups, present in the molecules of the type of compound (A), are enolised and

cyclised under the influence of the attacking cyclising agent, giving the corresponding bis-quinolinemethane derivatives (B).

(A) Methylene bis-(acetoacet arylamides)

Two moles of acetoacet arylamide and one mole of sodium hydroxy methane sulphonate were refluxed in 90 % methanol for three hours. The crude product was obtained on dilution with water, which was filtered and crystallised from acetic acid.

(B) 3,3'-Methylenebis-(4-methylcarbostyrils)

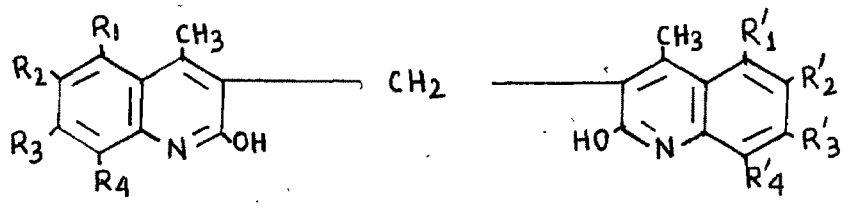
To a mixture of methylene bis-(acetoacet arylamide) (0.01 M) and acetic anhydride (3.0 ml.), concentrated sulphuric acid (3 ml.) was gradually added. The reaction mixture was kept at room temperature for about an hour, when considerable heat was developed. It was then heated on a water-bath for about 5-10 minutes. The mixture, on pouring in excess of water, gave brownish mass. The filtered mass after charcoaling was crystallised from acetic acid. In the same way other members of the methylene bis-(4-methyl carbostyrils) have been prepared. (Mehta and Patel, Currt. Sci., 1960, 29, 95).

The following methylene bis-(acetoacet arylamides) have, accordingly, been prepared :

Methylenebis-(acetoacetanilide) ; Methylene bis-(acetoacet-p-toluidide) ; Methylene bis-(acetoacet-o-toluidide) Methylene bis-(acetoacet-m-chloroanilide) ; Methylene bis-(acetoacet-1:2:4-xylidide) ; Methylene bis-(acetoacet-1:3:4-xylidide) ; Methylene bis-(acetoacet-

α-naphthylamide) and Methylene bis-(acetoacet-β-naphthylamide).

The following 3,3'-methylene bis-(2-hydroxy-4-methylquinolines) have, further, been synthesised on cyclisation of the corresponding methylene bis-(acetoacet-arylamides). Thus,



(VII)

(1) 2,2'-Dihydroxy-4,4'-dimethyl-3,3'-diquinolylmethane
(VII, $R_1=R_1'=R_2=R_2'=R_3=R_3'=R_4=R_4'=H$)

(2) 2,2'-Dihydroxy-4,4',6,6'-tetramethyl-3,3'-diquinolylmethane
(VII, $R_1=R_1'=R_3=R_3'=R_4=R_4'=H$; $R_2=R_2'=CH_3$)

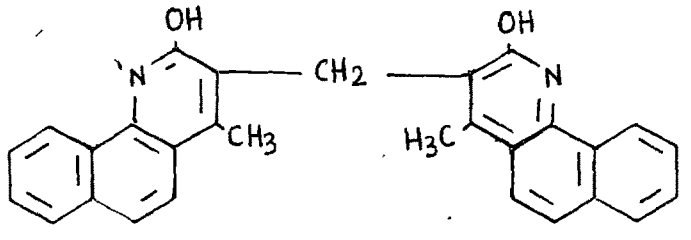
(3) 2,2'-Dihydroxy-4,4',8,8'-tetramethyl-3,3'-diquinolylmethane
(VII, $R_1=R_1'=R_2=R_2'=R_3=R_3'=H$; $R_4=R_4'=CH_3$)

(4) 2,2'-Dihydroxy-4,4'-dimethyl-7,7'-dichloro-3,3'-diquinolylmethane
(VII, $R_1=R_1'=R_2=R_2'=R_4=R_4'=H$; $R_3=R_3'=Cl$)

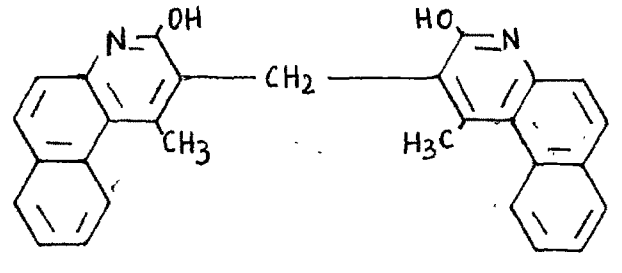
(5) 2,2'-Dihydroxy-4,4',6,6',8,8'-hexamethyl-3,3'-diquinolylmethane
(VII, $R_1=R_1'=R_3=R_3'=H$; $R_2=R_2'=R_4=R_4'=CH_3$)

(6) 2,2'-Dihydroxy-4,4',6,6',7,7'-hexamethyl-3,3'-diquinolylmethane
(VII, $R_1=R_1'=R_4=R_4'=H$; $R_2=R_2'=R_3=R_3'=CH_3$)

(7) 2,2'-Dihydroxy-4,4'-dimethyl-3,3'-dibenzoquinolyl (7:8)- methane



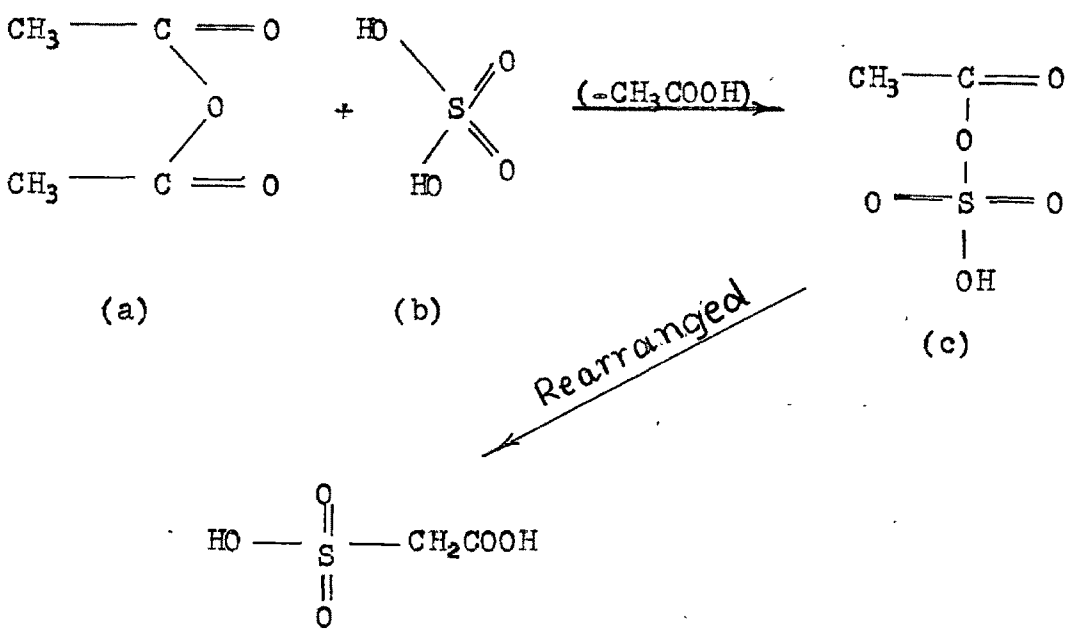
(8) 2,2'-Dihydroxy-4,4'-dimethyl-3,3'-dibenzoquinolyl (5:6)- methane



It may here be pointed out that 4-hydroxy-carbostyrils with formaldehyde gave 3,3'-methylene bis-(4-hydroxycarbostyrils), which are known anti coagulants ; but 3,3'-methylene bis-(4-methylcarbostyrils) have not so far been reported in the literature.

Russell and Cameron (J. Amer. Chem. Soc., 1938, 60, 1347) have suggested that when acetic anhydride (a) and sulphuric acid (b) are mixed, a mixed anhydride of the two (c) is formed, which is monobasic and exhibits ultra-acidic behaviour. This is a fast reaction. The mixed anhydride on standing undergoes rearrangement to sulphoacetic acid (d), which is also monobasic, but it does not exhibit ultra-acidic behaviour. This produces a slow decrease in the pH of the mixture. The formation of sulphoacetic acid

via the mixed anhydride has been formulated as follows:



(d)

In view of the fact that cyclisation takes place to some extent with a freshly prepared mixture of acetic anhydride and sulphuric acid together with the observation, that the extent of cyclisation is considerably improved, when sulphuric acid is added to a solution of the amide in acetic anhydride, it seems reasonable that the instantaneous formation of the mixed anhydride may be an important governing factor in such a ring closure.

It may, here, be pointed out that in the formation of bis-hydroxyquinoline derivatives from arylamides, both sulphuric acid as well as a mixture of acetic anhydride and sulphuric acid have been tried as the

condensing or the cyclising agents ; and it has been observed that the latter in the ratio of 1 : 1 by volume, has served as a superior cyclising agent than the former, as seen from better yields and cleaner products. The fact, observed in the present investigation, however, finds support in the process adopted by Bangdiwala and Desai (loc.cit.): It has also been noted that the use of sulphuric acid alone causes some charring due to the decomposition of products undergoing cyclisation ; whereas the presence of acetic anhydride in it may stabilize the formation of intermediate products and thus minimise, thus, the chances of decomposition, giving better yields.

E X P E R I M E N T A L

2,2'-Dihydroxy-4,4'-dimethyl-3,3'-diquinolylmethane

To a mixture of methylenebis-(aceto-acetanilide) (3.66 g. ; 0.01 M) and acetic anhydride (3 ml.), concentrated sulphuric acid (3 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about five minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling, was crystallised from acetic acid, m.p. 325°C(dec.).
Yield 1.9 g.

Analysis :

7.00 mg. of the substance gave 0.520 ml. of nitrogen at 30°C and 761 mm. pressure.

Found : N = 8.38 %.

$C_{21}H_{18}O_2N_2$ requires : N = 8.50 %.

2,2'-Dihydroxy-4,4',6,6'-tetramethyl-3,3'-diquinolylmethane

To a mixture of methylenebis-(acetoacet-p-toluidide) (3.94 g.) and acetic anhydride (5 ml.) concentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when the considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling was crystallised from acetic acid, m.p.295°C.

Yield 1.80 g.

Analysis :

6.56 mg. of the substance gave 0.466 ml. of nitrogen at 32°C and 759 mm. pressure.

Found : N = 7.94 %.

$C_{23}H_{22}O_2N_2$ requires : N = 7.82 %.

2,2'-Dihydroxy-4,4',8,8'-tetramethyl-3,3'-diquinolylmethane

To a mixture of methylene bis-(acetoacet-o-toluidide)(3.94 g.) and acetic anhydride (5 ml.), concentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water it gave a brownish white mass. The filtered mass, after charcoaling, was crystallised from acetic acid, m.p. 330°C (dec.). Yield 1.95 g.

Analysis :

4.292 mg. of the substance gave 12.172 mg. of carbon dioxide and 2.424 mg. of water.

6.14 mg. of the same substance gave 0.426 ml. of nitrogen at 30°C and 761 mm. pressure.

Found : C = 77.39 % ; H = 6.31 % ; N = 7.83 %.

$C_{23}H_{22}O_2N_2$ requires : C = 77.07 % ; H = 6.19 % ; N = 7.82 %.

2,2'-Dihydroxy-4,4'-dimethyl-7,7'-dichloro-3,3'-diquinolylmethane

To a mixture of methylene bis-(acetoacet-m-

chloroanilide) (4.35 g.) and acetic anhydride (5 ml.), concentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling, was crystallised from acetic acid, m.p. 266°C. Yield 1.85 g.

Analysis :

5.98 mg. of the substance gave 0.367 ml. of nitrogen at 32°C and 761 mm. pressure.

Found : N = 7.12 %.

$C_{21}H_{16}O_2N_2Cl_2$ requires : N = 7.00 %.

2,2'-Dihydroxy-4,4',6,6',8,8'-hexamethyl-3,3'-diquinolylmethane

To a mixture of methylenebis-(acetoacet-1:2:4-xylidide) (4.22 g.) and acetic anhydride (5 ml.), concentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling was crystallised from acetic acid, m.p. 390°C.(dec.). Yield 2.0 g.

Analysis :

3.928 mg. of the substance gave 11.200 mg. of carbon dioxide and 2.302 mg. of water.

6.26 mg. of the same substance gave 0.397 ml. of nitrogen at 30°C and 760 mm. pressure.

Found : C = 77.81 % ; H = 6.55 % ; N = 7.14 %.

$C_{25}H_{26}O_2N_2$ requires : C = 77.69 % ; H = 6.78 % ; N = 7.25 %.

2,2'-Dihydroxy-4,4',6,6',7,7'-hexamethyl-3,3'-diquinolylmethane

To a mixture of methylenebis-(acetoacet-1:3:4-xylidide) (4.22 g.) and acetic anhydride (5 ml.), concentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling, was crystallised from acetic acid, m.p. 340°C(dec.). Yield 2.2 g.

Analysis :

6.18 mg. of the substance gave 0.371 ml. of nitrogen at 30°C and 761 mm. pressure.

Found : N = 6.78 %.

$C_{25}H_{26}O_2N_2$ requires : N = 7.25 %.

2,2'-Dihydroxy-4,4'-dimethyl-3,3'-dibenzoquinolyl (7:8) methane

To a mixture of methylenebis-(acetoacet-a-naphthylamide) (4.62 g.) and acetic anhydride (5 ml.),

concentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling, was crystallised from acetic acid, m.p. 391°C(dec.). Yield 2.1 g.

Analysis :

6.16 mg. of the substance gave 0.322 ml. of nitrogen at 28°C and 761 mm. pressure.

Found : N = 5.94 %.

$C_{29}H_{22}O_2N_2$ requires : N = 6.51 %.

2,2'-Dihydroxy-4,4'-dimethyl-3,3'-dibenzo-quinolyl (5:6) methane

To a mixture of methylenebis-(acetoacet-β-naphthylamide) (4.62 g.) and acetic anhydride (5 ml.), coencentrated sulphuric acid (5 ml.) was gradually added. The reaction mixture was kept at room temperature for about half an hour with a calcium chloride guard tube, when considerable heat was developed and was then heated on a steam-bath for about 5 minutes. On pouring into excess of ice-water, it gave a brownish white mass. The filtered mass, after charcoaling, was crystallised from acetic acid, m.p. above 400°C.(dec.). Yield 1.9 g.

Analysis :

6.64 mg. of the substance gave 0.392 ml. of nitrogen at 32°C and 761 mm. pressure.

Found : N = 6.61 %.

$C_{29}H_{22}O_2N_2$ requires : N = 6.51 %.

Table 5

Methylene bis-(hydroxyquinolines)

S.No.	Compound	Molecular formula	M.P. °C	Yield %	Nitrogen Found %	Nitrogen Reqd. %	Carbon Found %	Carbon Reqd. %	Hydrogen Found %	Hydrogen Reqd. %
1.	2,2'-Dihydroxy-4,4'-dimethyl-3,3'-diquinolylmethane	$C_{21}H_{18}O_2N_2$	325 (d)	52.0	8.38	8.50	-	-	-	-
2.	2,2'-Dihydroxy-4,4',6,6'-tetramethyl-3,3'-diquinolyl-methane	$C_{23}H_{22}O_2N_2$	295	45.6	7.94	7.82	-	-	-	-
3.	3,3'-Dihydroxy-4,4',8,8'-tetramethyl-3,3'-diquinolyl-methane	$C_{23}H_{22}O_2N_2$	330 (d)	49.5	7.83	7.82	77.39	77.07	6.31	6.19
4.	2,2'-Dihydroxy-4,4'-dimethyl-7,7'-dichloro-3,3'-diquinolylmethane	$C_{21}H_{16}O_2N_2Cl_2$	266	42.5	7.12	7.00	-	-	-	-
5.	2,2'-Dihydroxy-4,4',6,6',8,8'-hexamethyl-3,3'-diquinolylmethane	$C_{25}H_{26}O_2N_2$	390 (d)	47.4	7.14	7.25	77.81	77.69	6.55	6.78

Table 5 (Contd)

S. No.	Compound	Molecular formula	M.P. °C	Yield %	Nitrogen Found %	Nitrogen Reqd. %	Carbon Found %	Carbon Reqd. %	Hydrogen Found %	Hydrogen Reqd. %
6.	2,2'-Dihydroxy-4,4', 6,6', 7,7'-hexamethyl-3,3'-diquinolylmethane	$C_{25}H_{26}O_2N_2$	340 (d)	54.0	6.78	7.25	-	-	-	-
7.	2,2'-Dihydroxy-4,4'-dimethyl-3,3'-dibenzo-quinolyl(7:8)methane	$C_{29}H_{22}O_2N_2$	391 (d)	45.6	5.94	6.51	-	-	-	-
8.	2,2'-Dihydroxy-4,4'-dimethyl-3,3'-dibenzo-quinolyl(5:6)methane	$C_{29}H_{22}O_2N_2$	above 400 (d)	41.1	6.61	6.51	-	-	-	-