APPENDIX

SYNTHESIS OF SOME BIQUINOLYS
Synthesis of some Biquinolyls

Having synthesised the oxygen heterocyclics such as biflavonyls from the biphenyl derivatives, it was thought of interest to synthesise nitrogen heterocyclics such as biquinolyl derivatives of known orientation from the diaminobiphenyls described in chapter V.

Huisgen reported the synthesis of 6,6-dichloro-5,5'-biquinolyl by boiling 5-iodo-6-chloroquinoline with copper bronze in nitrobenzene. Similarly Mehta and Mehta reported the synthesis of 2,2-dimethoxy-4,4'-dimethyl-3,3'-biquinolyl from 3-bromo-2-methoxy-4-methylquinoline by heating with copper bronze in diphenyl ether.

Several symmetrical and unsymmetrical biquinolyls have been synthesised from the aminobiphenyls by Skraup synthesis.

Thus Skraup reaction applied to benzidine gives 6,6'-biquinolyl and o-tolidine gives 8,8'-dimethyl-6,6'-biquinolyl. When crotonaldehyde is substituted for glycerine in the Skraup synthesis with benzidine 2,2'-dimethyl-6,6'-biquinolyl is obtained. Fischer obtained 6,6'-biquinolyl when 2,4-diaminobiphenyl was subjected to the above reaction. Several derivatives of 8,8'-biquinolyl have been prepared by the Skraup reaction on appropriate derivatives of 2,2'-diaminobiphenyl. These include 8,8'-diketone-5,5'-dimethyl-, 8,5,5'-dicarboxy-, 7,7'-dimethyl- and
5,5',7,7'-tetramethyl-8,8'-biqulrolyl.

Similarly 2,3'-diaminophenyl on Sraup reaction gave 5,8'- and 7,8'-biqulrolyl while 3,3'-diaminobiphenyl gave 7,7'- and 5,7'-biqulrolyl.

Gopalchari and Dhar obtained 8,8'-dimethoxy-5,5'-biqulrolyl from 3,3'-diamino-4,4'-dimethoxybiphenyl. Sivaramakrishnan and Suntharikar obtained 8,8'-dimethoxy-6,6'-biqulrolyl from o-dianisidine. Case and Buck reported the preparation of 6,7'-biqulrolyl from 3,3'-diaminobiphenyl.

Biquulrolys have also been synthesised by other methods.

Sivaramakrishnan and Suntharikar reported the synthesis of 4,4'-dihydroxy-2,2'-dimethyl-8,8'-dimethoxy-6,6'-biqulrolyl from o-dianisidine by condensation with acetoacetic ester in methyl alcohol and subsequent cyclisation of the ethyl-3,3'-dimethoxybiphenyl 4,4'-bis(3-aminoprotonate) thus obtained in diphenyl ether. They also synthesised 7,7'-dichloro-2,2'-dimethyl-6,6'-biqulrolyl from m-dichlorobenzidine by the same method.

By refluxing a mixture of benzidine in con. hydrochloric acid with a solution of paraldehyde in acetone saturated with dry hydrogen chloride at low temperature, Ardasheve and Malina prepared 2,2',4,4'-tetramethyl-6,6'-biqulrolyl. By the same method they also synthesised 2,2',4,4'-tetramethyl-8,8'-dimethoxy- and 2,2',4,4',8,8'-hexamethyl-6,6'-biqulrolyl from 3,3'-dimethoxy-4,4'-diaminobiphenyl and toolidine respectively.
2,2-Biquinolyls can be synthesised by heating a mixture of an appropriate quinoline derivative with palladium on carbon at high temperatures. Rapoport et al. prepared 8,8'-dimethyl- and 6,6'-dimethoxy-2,2'-biquinolyl by this method.

Catalytic reduction of a bromoquinoline can give rise to a biquinolyl. Thus 7,7'- and 5,5'-biquinolyl have been prepared by the catalytic reduction of 7- and 5-bromoquinolines respectively.

Apart from the methods already described, other approaches to the synthesis of biquinolyls are possible by starting with a suitable biphenyl derivatives and by applying the methods used for the synthesis of quinoline derivatives.

The present work deals with the synthesis of tetramethoxy-5,5',6,6'- and 7,7'-biquinolyl from diamino-biphenyl derivatives by the Skraup synthesis.

**Synthesis of 6,6',8,8'-tetramethoxy-5,5'-biquinolyl**

A mixture of 2,2',4,4'-tetramethoxy-5,5'-diamino-biphenyl (I), anhydrous glycerol, nitrobenzene, ferrous sulphate and conc. sulphuric acid was heated in an oil bath at 130-40° for 2 hours. The reaction mixture was diluted with water and made alkaline when a product was obtained to which 6,6',8,8'-tetramethoxy-5,5'-biquinolyl(I2) structure has been assigned as the cyclisation can take place only in one position.
A mixture of 2,2',5,5'-tetramethoxy-4,4'-diaminobiphenyl (III), anhydrous glycerol, conc. sulphuric acid, nitrobenzene and ferrous sulphate was heated for 2 hours in an oil bath at 130-40°. The reaction mixture was diluted with water and made alkaline when a product was obtained to which 5,5',8,8'-tetramethoxy-6,6'-biquinolyl (IV) structure has been assigned as the cyclisation can take place only in one position.

\[ \text{Synthesis of } 5,5',8,8'-\text{tetramethoxy-6,6'-biquinolyl} \]
Synthesis of 6,6',8,8'-tetramethoxy-7,7'-biquinonyl

2,2',6,6'-Tetramethoxy-3,3'-diaminobiphenyl

(V) was mixed with anhydrous glycerol, ferrous sulphate, nitrobenzene and conc. sulphuric acid and the reaction mixture was heated in an oil bath at 130-40° for 2 hours. The reaction mixture on working up as before gave a product to which 6,6',8,8'-tetramethoxy-7,7'-biquinonyl (VI) is assigned as there is only one possibility for the formation of the quinoline rings.

![Structure of V and VI]
EXPERIMENTAL

6,6',8,8'-Tetramethoxy-5,5'-biquimyl

2,2',4,4'-Tetramethoxy-5,5'-diaminobiphenyl (1 g.) was mixed with anhydrous glycerol (4 g.), ferrous sulphate (0.5 g.), nitrobenzene (2 ml.) and conc. sulphuric acid (2 ml.) and the reaction mixture was heated in an oil bath at 130-40° for 2 hours. The reaction mixture was cooled, diluted with water and nitrobenzene was steam distilled. The residue was filtered and the filtrate was treated with alkali when a product was obtained which crystallised from benzene-petroleum ether in pale yellow cubes, m.p. 268°. Yield 80%.

Analysis: Found: C, 70.1%; H, 5.7%; N, 7.9%.
C_{22}H_{20}O_{4}N_{2} requires: C, 70.2%; H, 5.3%; N, 7.4%.

5,5',8,8'-Tetramethoxy-6,6'-biquimyl

2,2',5,5'-Tetramethoxy-4,4'-diaminobiphenyl (1 g.) was mixed with anhydrous glycerol (4 g.), ferrous sulphate (0.5 g.) and nitrobenzene (2 ml.). Conc. sulphuric acid (2 ml.) was added slowly and the reaction mixture heated in an oil bath at 130-40° for 2 hours. It was cooled, diluted with water and nitrobenzene was steam distilled. The residue was filtered and the filtrate on treating with alkali gave a product which crystallised from petroleum ether. M.P. 155°. Yield 75%.
Analysis Found: C, 68.8%; H, 4.9%; N, 7.1%.

C_{22}H_{20}O_4N_2 requires: C, 70.2%; H, 5.3%; N, 7.4%.

6,6',8,8'-Tetramethoxy-7,7'-biquinolyl

A mixture of 2,2',6,6'-tetramethoxy-3,3'-diaminobiphenyl (1 g.), anhydrous glycerol (4 g.), ferrous sulphate (0.5 g.), nitrobenzene (2 ml.) and conc. sulphuric acid (2 ml.) was heated in an oil bath at 130°-40° for 2 hours. The reaction mixture on working up as before gave a product which crystallised from benzene in colourless cubes, m.p. 214°. Yield 78%.

Analysis Found: C, 70.4%; H, 5.6%; N, 7.8%.

C_{22}H_{20}O_4N_2 requires: C, 70.2%; H, 5.3%; N, 7.4%.
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