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# SYNTHESIS OF FUSED HETEROCYCLICS

A THESIS SUBMITTED  
TO  
THE UNIVERSITY OF MYSORE  
FOR  
THE DEGREE OF DOCTOR OF PHILOSOPHY

88

By  
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1957

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## SYNOPSIS

The thesis consists of two parts. Investigations on quinolinoquinolines are embodied in the first part, and investigations on 4(3)quinazolones are embodied in the second part. Preceding the two parts, there is a brief general introduction on heterocyclics.

### PART I

In the first introductory chapter all the known quinolinoquinolines have been briefly reviewed.

In the second chapter the synthesis of 6,7-dimethoxy-4'oxo-1',4'dihydro-quinolino(2,3:2',3')quinoline -- starting from vanillin and through 6-nitro-veratraldehyde, diethyl (6-nitroveratrylidene)-malonate, ethyl 6,7-dimethoxy-2-hydroxyquinoline-3-carboxylate, and ethyl 6,7-dimethoxy-2-anilino-3-carboxylate -- which was undertaken with a view to clearing up some structural uncertainties present in the work of Arnold Reissert on the quinolino(2,3:2',3')quinoline system, is described. This has helped in suggesting correct structures for some of the quinolino(2,3:2',3')-quinolines isolated by Reissert.

By modifying Kefford's method, a more-elegant procedure for the synthesis of 6,7-dimethoxy carbostyryl has been arrived at.

## P A R T II

In the first chapter, which is introductory in nature, general methods of preparation and the importance of quinazolones are described.

In the second chapter the synthesis of five new  $\beta$ -phenylethyl-quinazolones has been described. They were synthesised with a view to building quinazolino-isoquinolinium salts, possibly having <sup>Curariform</sup> carcinogenic activity. Attempts at synthesising quinazolino-isoquinolinium salts were, however, unsuccessful.

An attempt at synthesising isoquinolino(2,3:3',2')quinazolinone-4', has resulted in the synthesis of 2-methyl-3-benzyl-quinazolone-4 and 2-formyl-3-benzyl-quinazolone-4, the former showing properties at variance with the reported ones. The results have been discussed.

Some Mannich-condensation products of 2-methyl-quinazolone-4 have been described, and their structures discussed.

An interesting phenomenon of debenzylation and demethylation has been observed in the hydrochlorides of 2-methyl-3-benzyl-quinazolone-4 and 2,3-dimethyl-quinazolone-4 respectively. By studying the behaviour of the hydrochlorides of three more substituted quinazolones, debenzylation and demethylation have been attributed to water of crystallisation present in the hydrochlorides of the quinazolones.

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DECLARATION

I hereby declare that the entire work, except microanalyses, embodied in this thesis has been carried out by me. Wherever reference to observations of other investigators has been made, it has been duly acknowledged.

*S. Somasekhara*

(S. Somasekhara)

Signature of the Candidate



CERTIFICATE

I hereby certify that the work embodied in this thesis or any part of it has not been submitted by the candidate for any degree or diploma of any Institution previously.

*D. K. Banerjee*

(D. K. Banerjee)  
Signature of the Guide



## GENERAL INTRODUCTION TO HETEROCYCLICS

Heterocyclic compounds, which constitute an interesting part of organic chemistry, are, as the name itself suggests, compounds containing hetero atoms (atoms of elements other than carbon and hydrogen) in the ring. Various types of heterocyclics are therefore possible, the more important of them being the oxygen-, the sulphur-, and the nitrogen heterocyclics.

Only the nitrogen heterocyclics will be dealt with in this thesis. The simplest nitrogen heterocyclic is azacyclopropane (aziridine)<sup>1</sup>. Next to it in size comes azacyclobutadiene (azete)<sup>2</sup>, which is only known in its hydrogenated form. The aforementioned heterocyclics, having three or four atoms in the ring, are all strained systems, formed with difficulty and opened with ease, and generally display high reactivity. The five- and six-membered heterocyclics, whose typical representatives are pyrrole and pyridine respectively, are stable and occur widely in nature.

Heterocyclics containing two heteroatoms (both nitrogen) are equally widespread in nature, the important representatives of the monocyclic system being pyrazole, iminazole, pyridazine, pyrimidine,

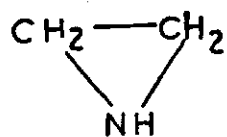
and pyrazine, and of the bicyclic system being (nitrogen not in the bridge) benzopyrazole, benzimidazole, benzopyridazines, benzopyrimidine (quinazoline), benzopyrazines and pyridopyridines<sup>3</sup>.

Various interesting heterocyclic systems emerge when two nitrogen atoms are distributed over three six-membered rings in a condensed system (nitrogen not in the bridge). They are: naphthopyridazines, naphthopyrimidine, naphthopyrazine, pyridoquinolines, phenanthrolines, dibenzpyrazine and diazaphenalenones.

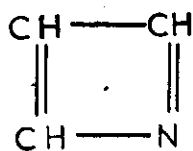
Quinolonoquinolines, naphthyl-naphthyridines, naphthobenzopyrazine, diazabenzophenalenones, diazachrysenes, diazapyrenes, diazanaphthacenes, benzophenanthrolines, and pyridophenanthridines are the heterocyclic systems that result when two nitrogen atoms are distributed over four six-membered rings in a condensed system (nitrogen, again, not in the bridge).

Investigations on the quinolonoquinoline systems constitute part I and investigations on quinazolones (benzopyrimidones) constitute part II of this thesis.

Chart 1



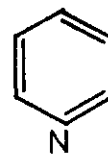
Aziridine



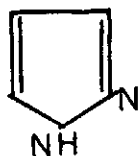
Azete



Pyrrole



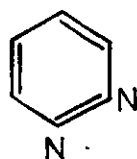
Pyridine



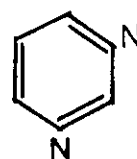
Pyrazole



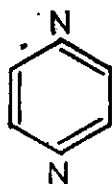
Imidazole



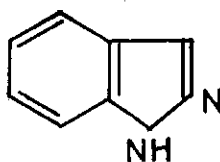
Pyridazine



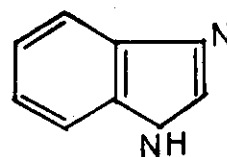
Pyrimidine



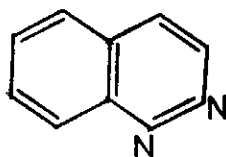
Pyrazine



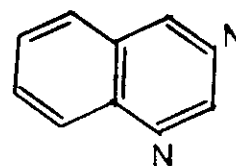
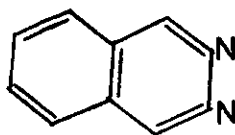
Benzopyrazole



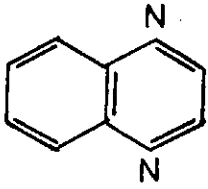
Benzoimidazole



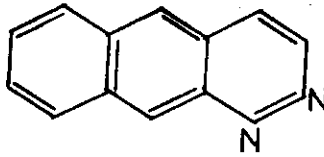
Benzopyridazines



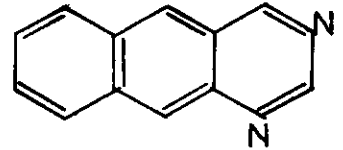
Quinazoline



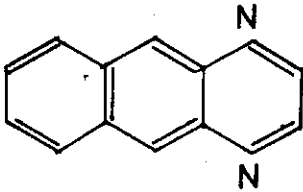
Benzopyrazine



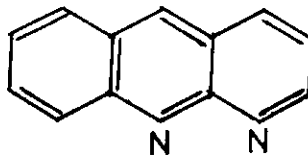
Naphthopyridazine †



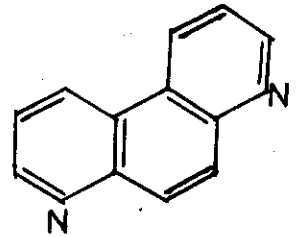
Naphthopyrimidine



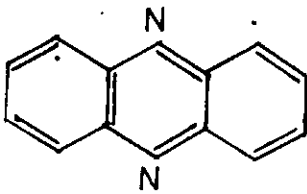
Naphthopyrazine



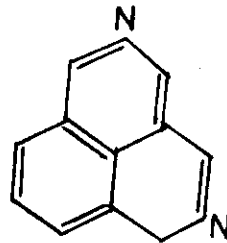
Pyridoquinoline †



Phenanthroline †

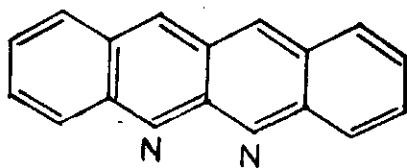


Dibenzopyrazine

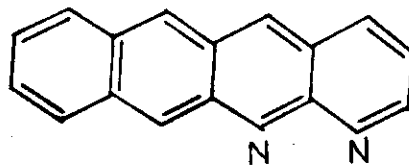


Diazaphenalene †

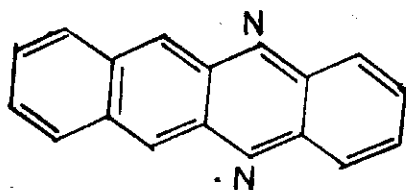
† The other structural isomers of naphthopyridazine, pyridoquinoline, phenanthroline, and diazaphenalene are not shown.



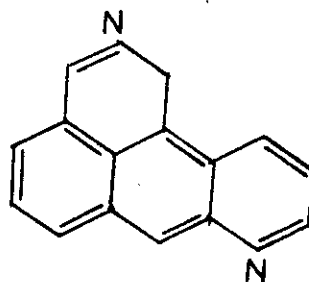
Quinolinoquinoline †



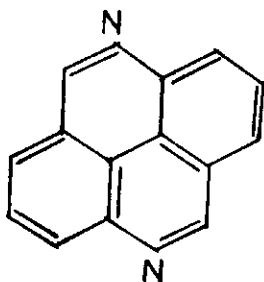
Naphthyl-naphthyridine †



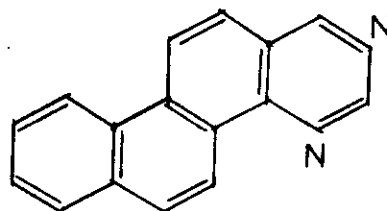
Naphthobenzopyrazine



Diazabenzophenylene †

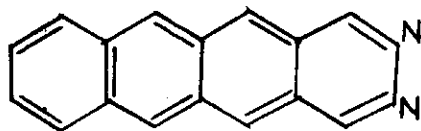


Diazapyrene †

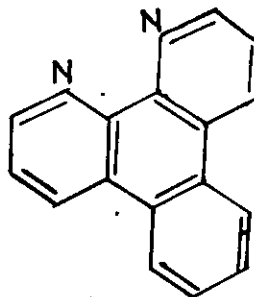


Diazachrysene †

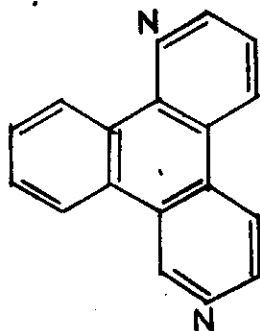
† The other structural isomers of quinolinoquinoline, naphthyl-naphthyridine, diazabenzophenylene, diazapyrene, and diazachrysene are not shown.



Diazanaphthacene ‡



Benzophenanthroline ‡



Pyridophenanthridine ‡

‡ The other structural isomers of diazanaphthacene, benzophenanthroline, and pyridophenanthridine are not shown.