urea present. But after the trimer stage rate of further reactions may be considerably reduced due to less reactivity of the methylol and primary amino groups of methylenureas. The mechanism of urea-formaldehyde reaction is discussed.

The reaction of acetamide and benzamide with formaldehyde were found to be slower than that of urea with formaldehyde. Introduction of a methyl group to one of the amino groups (methylurea) increased its reactivity whereas introduction of a phenyl group (phenylureas) reduced the reactivity. The effect of substituents on the reaction rate are explained on the basis of the electron donating and electron withdrawing property of the respective groups.

S. a.c. 2. RAMABHADRAN, P.—Synthesis and reactions of Flavazoles—1984—Dr. P. Madhavan Pillai

1-Phenylflavazole (1-phenyl-1H-pyrazole)[3, 4-b] quinoxaline is known to be prepared by the treatment of quinoxaline-2-carboxaldehyde phenylethyldrazine with phenylhydrazine. However, when stored or oxidised phenylhydrazine was used for this cyclisation, an unusual phenylation reaction was found to take place producing significant quantities of 1, 3-diphenylflavazole. This phenylation reaction was established as taking place by a free radical mechanism involving phenyl radicals formed from oxidised phenylhydrazine. Benzoyl peroxide which also produces phenyl radicals gave 1,3-diphenylflavazole under the same reaction conditions, thus providing additional evidence for the free radical mechanism. By using oxidised substituted phenylhydrazines, a number of new flavazoles such as 1-p-tolyl-3-phenyl, 1-(p-chlorophenyl)-3-phenyl, 1-(p-bromophenyl)-3-phenyl and 1-phenyl-3-p-tolyl-flavazoles were also prepared and characterised. The structures of these compounds were confirmed by their spectral data.

1-Phenylflavazoles with different substituents at position 3 such as the amino, chloro, hydroxy, chloromethyl, trichloromethyl, carboxamido, N-pyridyl and N-pyridylmethyl groups were also prepared for the first time. 3-Amino-1-phenylflavazole was prepared by two methods, i.e., the reaction of 3-chloro-1-phenylflavazole with amino and also by a Hofmann reaction of 1-phenylflavazolo-3-carboxamide. Other interconversions of the 3-amino, 3-hydroxy, and 3-chloro-1-phenylflavazoles were also investigated.

On the new reactions of flavazoles studied, the oxidation, reduction, bromination and hydrolysis reactions are worth mentioning. Thus the oxidation of 1-phenylflavazole produced 1-phenylpyrazole [3,4-b]pyrazine-5,6-dicarboxylic acid which was also characterised as its dimethyl ester. The flavazole ring was not easily reduced either with lithium aluminium hydride or with sodium borohydride. When 1-phenylflavazole was heated under reflux with sodium borohydride in isoprophenyl alcohol, the heterocyclic ring was broken and 1-anilinoquinoxaline-3-carboxamide was produced showing that the sodium borohydride acted only as a base rather than as a reducing agent under the reaction conditions. Also treatment of 1-phenylflavazole with hot aqueous sodium hydroxide again ruptured the heterocyclic ring system and produced 2-anilinoquinoxaline-3-carboxylic acid. This carboxylic acid underwent decarboxylation easily when heated giving the known 2-anilinoquinoxaline. The treatment of both 1-phenylflavazole and 1,3-diphenylflavazole with bromine in acetic acid led to clean bromination at the para position of the 1-phenyl group, thus producing 1-(bromophenyl)flavazole and 1-(p-bromophenyl)-3-phenylflavazole respectively in excellent yields.

The cyclisation reaction of phenylhydrazones was shown to take place even at very low temperatures. Also the lower yield when these compounds were crystallised from an atmosphere containing a polar solvent.

An analysis of the mass spectra of 11 flavazoles. Also the flavazoles have one of the characteristic of the uv spectra.

S. a.c.3. ANNAM CHAKKO, P.—Study of Strychine Derivatives—1967—Dr.

Strychnine, the major alkaloid present in the seeds of Strychnos toxifera, a tropical American tree. It is a potent convulsant and is used in the treatment of Parkinson's disease. Strychnine is a complex mixture of alkaloids, with strychnine being the most important pharmacologically. It is used as a diagnostic tool for the detection of cerebral hemorrhage.

A number of derivatives of strychnine with nitro, amino, acetoxy, bromo and other moieties have been synthesised and their pharmacological properties have been studied. Some of these compounds have been found to be more potent than strychnine itself. The use of these compounds in the treatment of convulsions has been investigated.

There have been reports of the use of these compounds in the treatment of Parkinson's disease. However, further research is needed to determine the safety and efficacy of these compounds in the treatment of this disease. Some of these compounds have also been found to be useful in the treatment of rheumatoid arthritis. The use of these compounds in the treatment of this disease is currently being investigated.

Pharmacological studies of the derivatives of strychnine have been carried out to determine their mechanism of action. These studies have shown that these compounds act at the level of the spinal cord to produce a direct effect on the central nervous system.
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of the methyloxy and primary amino groups of
of urea-formaldehyde reaction is discussed.
benzaldehyde and formaldehyde were found to
formaldehyde, introduction of a methyl group
ion increased its reactivity whereas introduction
red the reactivity. The effect of substituents
ed on the basis of the electron donating and
if the respective groups.

IAN. P.-Synthesis and reactions of
Machavan Pillai

1-pyrazol[3, 4-b] quinazoline is known to be
imipazine-2-carboxaldehyde phenylhydrazine with
in store or oxidised phenylhydrazine was used.
phenation reaction was found to take place
of 1, 3-diphenylflavazole. This phenylation reaction
be by a free radical mechanism involving phenyl
phenylhydrazine. Benzoyl peroxide which also
a 1,3-diphenyl-flavazole under the same reaction
mental evidence for the free radical mechanism.
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3-phenyl, 1-(p-chlorophenyl)-3-phenyl,
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heated under reflux with sodium borohydride in
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base rather than as a reducing agent under the
of 1-phenyl-flavazole with hot aqueous sodium
the heterocyclic ring system and produced
c acid. This carboxylic acid underwent
mer with the known 2-amino-quinazoline.
azole and 1, 3-diphenyllavazole with bromine in
ion at the para position of the 1-phenyl group,
flavazole and 1-(p-bromophenyl)-3-phenylflavazole
respectively in excellent yields.

The cyclisation reaction of several quinazoline-2-carboxaldehyde
phenylhydrazones was shown to take place by using a mild dehydrogenating
agent such as azobenzene. Also the same cyclisation took place although in a
lower yield when these compounds were heated at a temperature above their
melting points in an atmosphere containing oxygen.

An analysis of the mass spectra of several flavazoles showed similar fragmentation
patterns. Also the flavazoles have characteristic ultraviolet adsorptions as seen
from the correlation of the UV spectra of a number of flavazole derivatives.

S. a.c.3. ANNAM CHACKO, P.-Studies on the Synthesis and CNS Activity
of Strychnine Derivatives-1987-Dr. P. Machavan Pillai

Strychnine, the major alkaloid present in Strychnos nuxvomica seeds has been
reported to stimulate the entire central nervous system with preference for the
spinal cord. It is a powerful convulsant and because of this property, it is an
important pharmacological tool as it plays a unique role as an inhibitor of post
synaptic inhibitory impulses. It is useful to study inhibitory transmitter and receptor
types. However, because of its extreme toxicity, strychnine does not have any
therapeutic application in the Western system of medicine.

The present work was undertaken with a view to obtaining strychnine derivatives
having CNS stimulating properties but with sufficiently low toxicity so that they
may eventually find some application in medicine. As nuxvomica seeds, its
possible utilization in therapeutics will have considerable commercial significance.

A number of derivatives of strychnine were prepared. These included products
with nitro, amino, acetamido, bromo and sulphanamido groups introduced at the
2-position by electrophilic aromatic substitutions and subsequent chemical
conversions as required. Also reduction of the amide carboxy group at position
10 using lithium aluminium hydride provided strychnine. Treatment of strychnine
with benzaldehyde and substituted benzaldehydes yielded derivatives with
benzyldiene groups attached at 11-position. Similarly an oxime was obtained at
this position by reaction with amminitrile. Catalytic hydrogenation of strychnine in
the presence of palladium on carbon provided the known 21, 22-dihydrostrychnine
which on nitration gave another derivative having nitrogrooup at 2-position and
with the 21, 22 double bond saturated. The structures of all new compounds
were established with the help of spectral data and elemental analysis. Finally
a reaction of strychnine with chloroform in the presence of benzoyl peroxide
yielded a trichloromethyl derivative, but the exact position of this group has not
been determined. These reactions have thus yielded structural analogues of
strychnine with modifications at the aromatic ring and at position 10, 11 and 21, 22.

There have been reports that the N-oxides of alkaloids generally modify their
pharmacological properties and the N-oxide of strychnine (known as
genostrychnine) is less toxic and less convulsive than strychnine itself. However,
strychnine N-oxide is not being used as a therapeutic agent now probably
because of the threat of convulsions at higher doses. All the derivatives
of strychnine which were prepared as mentioned earlier were, therefore, converted
into their N-oxides by well established procedures. Brucine N-oxide was also
prepared from brucine for the same type of comparative studies.

Pharmacological studies were carried out on the derivatives of strychnine and