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

1-Phenylflavazole (1-pheni-1-H-pyrazolo[3, 4-b] quinoxaline) is known to be prepared by the treatment of quinoxaline-2-carboxaldehyde phenylhydrazone 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-diphenyl-flavazole 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-pyrrolidyl and N-pyrrolidylmethyl 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 ammonia 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-phenylpyrazolo [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-phenyl-flavazole was heated under reflux with sodium borohydride in isopropyl alcohol, the heterocylic ring was broken and 2-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-phenyl-flavazole with hot aqueous sodium hydroxide again ruptured the heterocyclic ring system and produced 2-anilino-quinoxaline-3-carboxylic acid. This carboxylic acid underwent decarboxylation easily when heated giving the known 2-anilino-quinoxaline. 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 several quinoxaline-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.