STUDIES ON THE SYNTHESIS AND REACTIONS OF SOME HETEROCYCLIC COMPOUNDS

By

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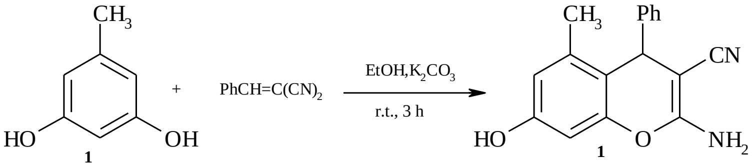
Part I

An approach to heterocyclic synthesis based on *2-Amino-5-hydroxy-4-phenyl-7-methyl-4H[1]benzopyran-3-carbonitrile*

The synthesis of the chromene **273** was achieved through the combination between orcinol monohydrate and benzylidenemalononitrile in absolute ethanol containing anhydrous potassium carbonate at room temperature (Scheme 1). The structure of compound **273** was confirmed based on spectroscopic and analytical data.



The cyano and amino substituents, in combination with chromene double bond, provide a rich opportunity for heterocyclic construction. In a first experiment, reaction between chromene **273** and formamide in refluxing dimethylformamide (DMF) furnished the aminopyrimidine **274** in 80% yield (Scheme 2). In contrast, a cyclocondensation of compound **273** with hot formic acid resulted in the formation of a separable mixture of the pyrimidinone **275** and the dihydrocoumarin **276**, in 52 and 38% yields respectively (Scheme 2). The reaction between the chromene **273** and acetic anhydride was conducted under both acidic and basic conditions. Thus, refluxing compound **273** in a mixture of acetic anhydride and phosphoric acid for several hours resulted in formation of the pyrimidine **277**, together with, once again, an enamine hydrolysis product, the dihydrocoumarin **278** (Scheme 2). In contrast, heating chromene **273** in a mixture of acetic anhydride and pyridine gave the oxazinone 2**79** (Scheme 2); the identities of all these compounds were deduced from spectroscopic data. A facile synthetic method for converting an oxazinone into the corresponding pyrimidinone is by reactions with amines. Thus, heating oxazinone 2**79** with hydrazine hydrate, formamide or hydroxylamine delivered around 60% isolated yields of the corresponding pyrimidinones 2**80a-c** (Scheme 2).

A number of other heterocyclic residues can be built onto the initial chromene **273**, by reason of the presence of the cyano enamine functional group combination. For example, condensation of the chromene **273** and cyclohexanone in the presence of the Lewis acid zinc chloride proceeded smoothly to give a 61% isolated yield of the pyridine derivative **281** (Scheme 2). Heating chromene **273** with malononitrile in refluxing DMF containing piperidine causes a reaction in a reverse sense, but one which produces a similar product, the 4-pyridinone **282**, in 75% isolated yield (Scheme 2).