GENERAL INTRODUCTION

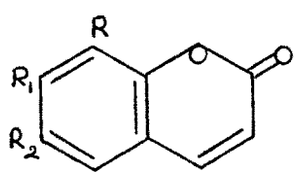
GENERAL INTRODUCTION

Oxygen heterocycles form an important group of organic compounds which occur widely in nature and some of them are substances of commercial and medicinal importance.

Among the important oxygen heterocycles are furan, α- and γ-pyrones and their derivatives such as benzofurans, coumarins, chromones, flavones, isoflavones and xanthones.

A number of naturally occurring oxygen heterocycles also have two or more similar or dissimilar oxygen heterocyclic rings. Furocoumarins, furochromones, furoflavones, coumarino-α-pyrones and coumarino-γ-pyrones are a few examples.

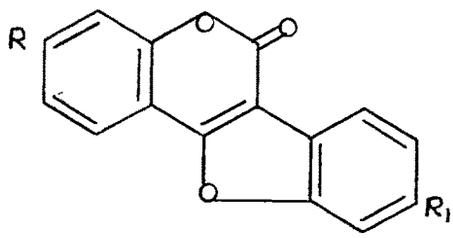
As the present work deals mainly with coumarins some aspects of the chemistry of coumarins are discussed here. Several coumarin derivatives are found to be widely distributed in the plant kingdom. Coumarin, Scopoletin, Aesculetin, Fraxetin, Daphnetin are a few of the simple coumarins found in nature.



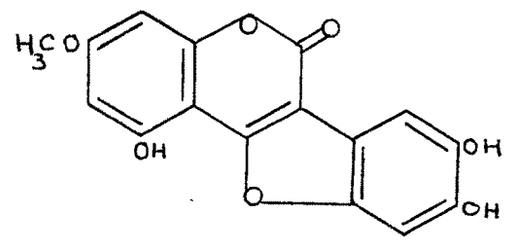
	R	R_1	R_2
Coumarin	H	H	H
Scopoletin	H	OH	OCH_3
Aesculetin	H	OH	OH
Fraxetin	OH	OH	OCH_3
Daphnetin	OH	OH	H

A wide variety of structural units are found to be associated with coumarin ring system. For example, among

those derived from 4-hydroxy-3-phenylcoumarins are coumestrol[1] (Ia), coumestan[2] (Ib) and wedelolactone[3] (II).



I



II

(a) R = R_1 = OH

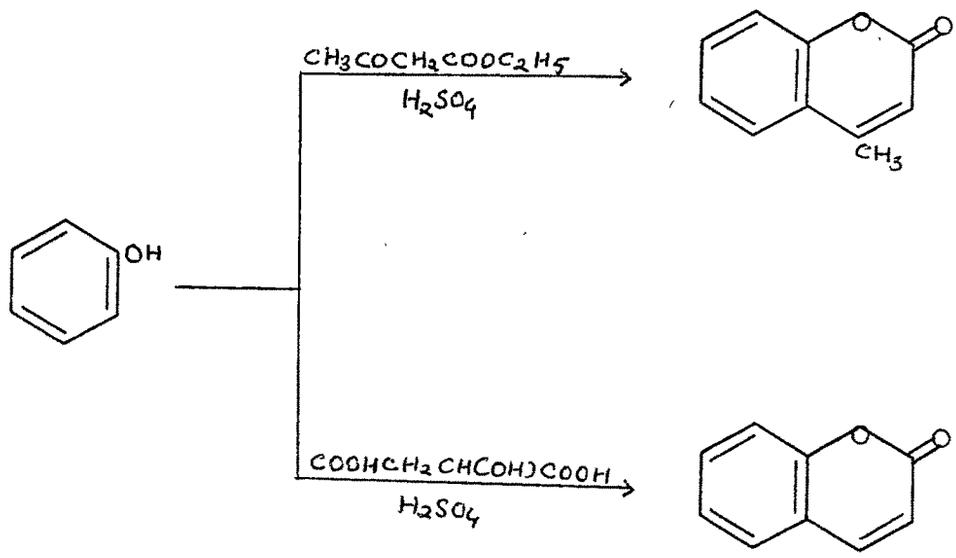
(b) R = R_1 = H

A group of interesting naturally occurring coumarin derivatives are the furocoumarins, which are discussed in Chapter III.

In recent years the interest in coumarin chemistry has increased considerably because of the discovery of their varied biochemical properties, analytical applications and their industrial and medicinal uses.

General methods for the synthesis of coumarins

The most important and extensively applied method for the synthesis of coumarins is Pechmann reaction[4]. It consists in the condensation of phenols with β-ketonic esters[5] or malic acid[6] to give a variety of coumarin derivatives, with or without the methyl group in the pyrone ring.



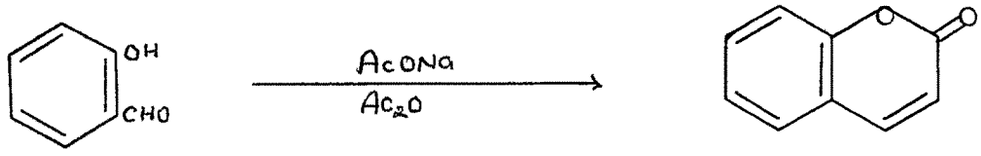
A variety of condensing agents are used in the Pechmann reaction such as sulphuric acid, phosphoric acid, phosphorus oxychloride, zinc chloride, stannic chloride, sodium ethoxide, boric anhydride, hydrogen fluoride[7], boron trifluoride etherate[8] and polyphosphoric acid[9]. The course of this reaction depends on all the three factors, viz. the nature of the β-ketonic ester, nature of the phenol and the nature of the condensing agent. The earlier work on this reaction has been reviewed by Sethna and Phadke[10].

An interesting observation was made by Mentzer[11,12,13] and his coworkers that the β-ketonic esters condense with phenols to give chromones on prolonged heating between 200-250° without using any condensing agent. Later, Desai et al.[14]

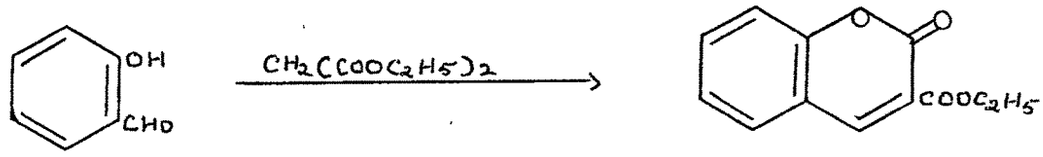
found that the same condensation takes place in 20 min. to 2 1/2 hr., if the phenol and the β-ketonic ester are heated in a high boiling solvent such as diphenyl ether, phenetol, nitrobenzene or acetylene tetrachloride.

Among the other convenient methods generally used for the coumarin synthesis are Perkin reaction[15] and Knovenagal reaction[16].

In Perkin reaction, a coumarin is formed when an o-hydroxy aldehyde is heated with an acid anhydride and its sodium salt at 175-80° for 5-6 hr.



A method developed by Knovenagal is the condensation of an o-hydroxy aldehyde with esters containing a reactive methylene group such as diethyl malonate, ethyl acetoacetate and ethyl cyanoacetate in the presence of pyridine, piperidine and other organic bases.



Besides these general methods there are others which have been developed for the synthesis of specific types of coumarins such as 4-hydroxycoumarins and these have been reviewed[17,18].

Extensive work has been done on the application of various reactions to simple and substituted coumarins with a view to study the pattern of substitution or to synthesise substituted coumarin derivatives of potential biological, industrial or further synthetical importance.

As the present work involves the application of some substitution reactions to coumarins some of the previous work is reviewed here.

Halogenation :

(a) Chlorination : Coumarin on chlorination gives 3-chlorocoumarin. Dey et al.[19] obtained two products from 7-methylcoumarin-4-acetic acid viz. 7-methylcoumarin-4-chloroacetic acid and the decarboxylated product 7-methyl-4-chloromethylcoumarin. Seshadri and coworkers[20] chlorinated 7-hydroxy-4-methylcoumarin, its methyl ether and its acetoxy derivative and obtained the corresponding 3-chloro derivative. Lindemann[21] had earlier given the 8-chloro structure to the chlorination product of 7-hydroxy-4-methylcoumarin. 4-Hydroxycoumarin gives the 3-chloro derivative[22].

(b) Bromination : The bromination of coumarins has been very extensively studied. The first bromine atom usually enters the 3-position. The second one enters the 6- or the

8-position. Where there is a reactive methylene group as in the case of coumarin-4-acetic acid one of these hydrogens may be replaced by bromine and coumarin-4-bromoacetic acid may be obtained.[23]

Peters and Simonis[24] obtained 3-bromo-, 3,6-dibromo-, and 3,6,8-tribromo derivatives from 4-methylcoumarin. 4,7-Dimethylcoumarin gave the 3-bromo derivative[25]. Seshadri and coworkers[26] obtained the 3,6-dibromo derivative from 4,7-dimethylcoumarin. 4,5,7-Trimethylcoumarin brominated in the 3-position[27]. Dey and Radhabai[28] obtained 7-methylcoumarin-4-bromoacetic acid along with 7-methyl-4-bromomethylcoumarin in the bromination of 7-methylcoumarin-4-acetic acid.

Several hydroxycoumarins have been brominated. Dalvi and Sethna[29] brominated 7-hydroxy-4-methylcoumarin, its 6-carboxy- and 6-carbmethoxy derivatives and their methyl ethers and found that in all cases the first bromine atom enters the 3-position. 7-Hydroxy-4-methylcoumarin on further bromination gave a mixture of the 3,6- and 6,8-dibromo derivatives but the acid and the ester gave the 3,8-dibromo derivative.

Borsche[30] assigned the 5,7-dibromo structure to the bromination product from 6-hydroxy-4-methylcoumarin. 3-Hydroxycoumarin has been found to give the 4-bromo derivative[31] and 8-hydroxycoumarin and its methyl ether gave the 5-bromo derivative[32].

The bromination of 5-hydroxy-4-methyl- and 5-hydroxy-4,7-dimethylcoumarin and their methyl ethers has

been studied under different conditions[33]. The first bromine atom was found to enter the 8-position. On further bromination both the coumarin derivatives gave the 6,8-dibromo- and the 3,6,8-tribromo derivatives.

Lele and Sethna[34] in their study of bromination of dihydroxycoumarin derivatives found that in the bromination of 4,7-dihydroxycoumarin the 3-bromo derivative was obtained and thus the 8-bromo structure earlier assigned by Bauer and Schoder[35] was incorrect. They brominated 7,8-dihydroxy--4-methylcoumarin and its methyl ether and obtained the 3-bromo derivatives. On further bromination they obtained a dibromo derivative which they found was the 3,6- and not the 3,4-dibromo derivative as reported by Sakai and Kato[36].

Some work has been carried out using N-bromosuccinimide as the brominating agent and interesting results have been obtained. Molho and Mentzer[37] obtained 3-bromomethylcoumarin and 7-methoxy-3-bromo-4-methylcoumarin by the action of N-bromosuccinimide on 3-methylcoumarin and 7-methoxy-4-methylcoumarin respectively. 7-Methoxy-3-ethyl--4-methylcoumarin gave a mixture of 7-methoxy-3-(1-bromoethyl)--4-methylcoumarin in good yield and 7-methoxy-6-bromo-3-ethyl-4-methylcoumarin in poor yield. Lecocq and Buu-Hoi[38] studied the action of N-bromosuccinimide on methylcoumarins and found that it reacts only with methyl groups in the benzene ring and not with methyl groups in the heterocyclic ring. Thus 6-methyl-, 4,6-dimethyl- and 4,7-dimethylcoumarin gave 6-bromomethyl-, 4-methyl-6-bromomethyl- and 4-methyl-

-7-bromomethylcoumarin respectively. Lecocq[39] obtained 3-bromo-4-methylcoumarin from 4-methylcoumarin on reaction with N-bromosuccinimide. Molho and Mentzer[40] observed halogen migration in certain brominations. Thus bromination of 3-ethyl- and 3-propyl-4-methyl-7-methoxycoumarin with N-bromosuccinimide gave 3-ethyl-6-bromo- and 3-propyl-6-bromo-4-methyl-7-methoxycoumarin, the 3-(α-bromo-alkyl) compound being the intermediate. Bromination of 7-hydroxy--4-methyl-8-acetyl and 5-hydroxy-4-methyl-6-acetylcoumarin with cupric bromide in dioxane has been found to provide the ω -bromoacyl derivative[41].

(c) Iodination : The iodination of various coumarins with different iodinating agents such as iodine monochloride, iodine and iodic acid, iodine and ammonia has been studied by Sethna and his coworkers[42,43]. 7-Hydroxy-4-methylcoumarin gave first the 8-iodo derivatige and then with more of the iodinating agent the 3,8-diiodo and the 3,6,8-triiodo derivatives. Its methyl ether, however, gave first the 3-iodo and then 3,6-diiodo derivative with more of the iodinating agent. 5-Hydroxy-4-methylcoumarin and its methyl ether gave first the 8-iodo derivative. Further iodination led to the 6,8-diiodo derivative in the case of 5-hydroxy-4-methylcoumarin. The authors have converted some of these iodo coumarins into the cyanocoumarins by Rosenmund reaction i.e. by heating with cuprous cyanide.

Nitration :

Several studies on the nitration of coumarins have been made. Morgan[44] reported the formation of 6-nitrocoumarin in the nitration of coumarin. Dey and Krishnamurthy[45] found that in the nitration of coumarin, both the 6- and 8-isomers were formed. Clayton[46] observed that further nitration of 6-nitrocoumarin and 8-nitrocoumarin yielded first the 3,6-dinitro and the 3,8-dinitrocoumarin respectively and then the 3,6,8-trinitrocoumarin. Clayton[47] also studied the nitration of 7-methyl-, 6,7-dimethyl- and 4,6,8-trimethylcoumarin and obtained various nitro derivatives. The ease of nitration was found to increase with the introduction of alkyl groups.

Several hydroxycoumarins have also been nitrated. 5-Hydroxy-4-methylcoumarin gave the 8-nitro and the 6,8-dinitro derivatives while 5-hydroxy-6-carboxy-4-methylcoumarin and its esters gave the 8-nitro derivative[48]. 7-Hydroxy-4-methylcoumarin and its methyl ether gave the 6-nitro and the 3,6,8-trinitro derivatives[49].

The nitration of 8-hydroxycoumarin and its methyl ether gave the 7-nitro- and the 5-nitro derivative respectively,[50] and the 5,7-dinitro derivative[51]. 4-Hydroxycoumarin gave the 3-nitro and 3,6-dinitro derivatives[52]. The nitration of 6-hydroxy-4-methylcoumarin gave the 5-nitro and the 5,7-dinitro derivatives[53].

Sulphonation :

Kruger[54] studied the sulphonation of some methyl coumarins and assumed that the sulphonic acid group had entered the 6-position in each case. Coumarin on sulphonation with chloro sulphonic acid gave the 6-sulphonyl chloride derivative[55]. 4-Hydroxycoumarin on sulphonation with fuming sulphuric acid gave the 3-sulphonic acid[56]. Merchant and Shah[57] in an extensive study of the sulphonation with chloro-sulphonic acid of various 7-hydroxy-4-methylcoumarins with alkyl, bromo and carboxy groups in different positions found that the 6-sulphonic acid derivative was obtained where the 6-position was free. When it was occupied by another substituent the sulphonation took place in the 8-position. In the case of 6-nitrocoumarin, however, the sulphonic acid group entered the 3-position. With larger amounts of chloro-sulphonic acid they obtained the 3,6-disulphonic acid derivatives from coumarin and 7-methoxy-4-methylcoumarin. 7-Hydroxy-4-methylcoumarin and 7-hydroxy-3,4-dimethylcoumarin gave the 6,8-disulphonic acids. The former also gave the 3,6,8-trisulphonic acid. 5-Hydroxy-4-methylcoumarin gave the 8-sulphonic acid, the 3,6-disulphonic acid and the 3,6,8-tri-sulphonic acid derivatives.

Fries migration and Friedel-Crafts reaction : Limaye[58] carried out the Fries migration of various esters of 7-hydroxycoumarin and in all cases obtained the 8-acylcoumarins accompanied in some cases with traces of the 6-acyl isomers. The same 8-acyl

derivatives were also obtained in the Friedel-Crafts acylation of 7-hydroxycoumarin derivatives. These 8-acylcoumarins on hydrolysis with hot alkali gave 2-acyl resorcinols. Shah and Shah[59] studied the Fries migration of 5-acetoxy, 5-benzoyloxy, 5-propionoxy and 5-butyroxy-4-methylcoumarin and obtained the corresponding 6-acyl derivatives which were also obtained from the Friedel-Crafts acylation of 5-hydroxy-4-methyl-coumarin. Thakor[60] studied the Fries migration of 6-acetoxy and 6-benzoyloxycoumarin and obtained the corresponding 5-acyl derivatives which were also obtained in the Friedel-Crafts acetylation and benzoylation of 6-hydroxycoumarin.

Bhavsar and Desai[61] studied the Fries migration of 4-methylcoumarinyl-7-p-toluene sulphonate and obtained the 8- and the 6-p-toluene sulphonyl derivatives. The Fries-migration of 4,7-dimethyl-5-coumarinyl-p-toluene sulphonate yielded the 6-p-toluene sulphonyl derivative. The Fries migration of 4-methyl-7-coumarinylbenzene sulphonate yielded the 8-phenyl sulphonyl derivative but when the isomerisation was carried out in nitrobenzene the 6-isomer was also obtained along with the 8-isomer[62].

3-Acyl derivatives were obtained from 4-acyloxy-coumarins on Fries migration, which were also obtained by condensing 4-hydroxycoumarin with various organic acids in the presence of phosphoryl chloride[63]. The Fries rearrangement of 5,7-diacetoxy-3-chloro-4-methylcoumarin in the presence of boron trifluoride gave the 8-acetyl derivative and that of

5,7-diacetoxy-3-chloro-4,8-dimethylcoumarin in the presence of aluminium chloride gave the 6-acetyl derivative[64]. The Fries rearrangement of 3-acetoxycoumarin gave the 4-acetyl derivative which was also obtained on the Friedel-Crafts acetylation of 3-hydroxycoumarin[65].

The natural coumarin Geijerin which is 7-methoxy--6-isovalerylcoumarin was synthesised by Shah and coworkers[66] by the Fries migration of 7-isovaleroxycoumarin and subsequent methylation of the 6-isomer which was obtained in a very poor yield the main product being the 8-isomer.

Formylation : Sen and Chakravarti[67] prepared 6-formylcoumarin by heating coumarin with aqueous potassium hydroxide solution and chloroform. Spath and Pailer[68] obtained the 8-formyl derivative from 7-hydroxycoumarin by the Duff and Bills method. 6-Hydroxy- and 6-hydroxy-4-methylcoumarin gave the 5-formylcoumarin[69] and 5-hydroxy-4-methyl and 5-hydroxy-4,7-dimethylcoumarin with hexamethylene tetramine gave the 6,8-diformyl derivative and 7,8-dihydroxy-4-methylcoumarin gave the 6-formyl derivative[70]. Formylation of 5-hydroxy-4-methylcoumarin with N-methyl formanilide furnished the 6-formyl and the 8-formyl derivative[71]. Ziegler and Maier[72] formylated 4-hydroxycoumarin in chlorobenzene with N-methylformanilide in the presence of phosphorus oxychloride and obtained the 3-formyl derivative.

Claisen rearrangement : 7-Allyloxy- and 7-allyloxy-4-methylcoumarin gave the 8-allyl derivative on Claisen rearrangement[73,74] and 5-allyloxy-4,7-dimethylcoumarin gave

the 6- or the 8-allyl derivative depending on the temperature of the reaction[75]. The Claisen migration of γ-dimethyl allyl ether of 5-hydroxy-, 6-hydroxy- and 8-hydroxycoumarin did not give the C-allyl derivatives. Only degradation to the correspodnding hydroxycoumarins and isoprene took place[76].

Elbs persulphate oxidation : A number of coumarin derivatives have been subjected to this reaction. 6-Hydroxy-coumarins are invariably obtained in this reaction if that position is free. If it is occupied, then the reaction usually does not take place. Bargellini and Monti[77] oxidised simple coumarin and its 7-methoxy derivative. 7,8-Dimethoxy-[78] and 8-methoxycoumarin[79] were also oxidised. Sethna and his coworkers[80,81] applied this reaction to 4-methyl-, 7-methoxy--4-methyl-, 5-methoxy-4-methyl-, 5-methoxy-4,7-dimethyl-, 5,7-dimethoxy-4-methyl- and 7,8-dimethoxy-4-methylcoumarin. In all the cases, the corresponding 6-hydroxycoumarin derivatives were obtained. Bhavsar and Desai[82] applied this reaction to several coumarins after protecting the hydroxy group by preparing its p-toluene sulphonyl derivative. They could prepare isomeric methoxy hydroxycoumarins by this method. Oliverio et al.[83] oxidised 5-hydroxy-6-acetyl-4--methylcoumarin and obtained 5,8-dihydroxy-6-acetyl-4-methyl-coumarin. This reaction has been very useful in the synthesis of natural and new coumarins.

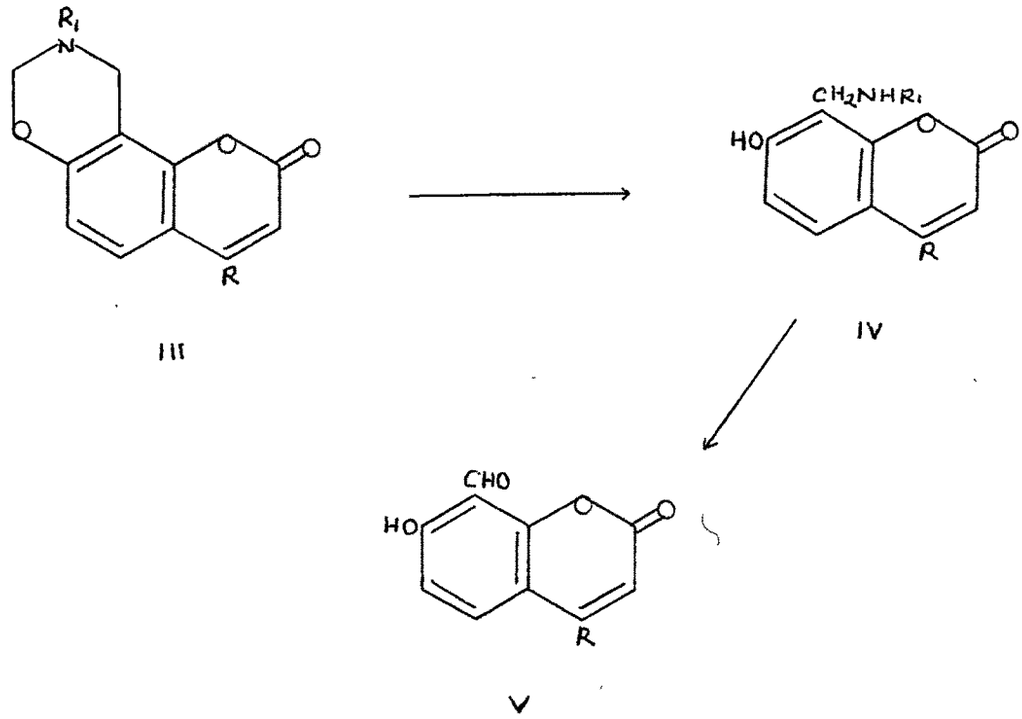
Chloromethylation : Sethna and coworkers[84,85] studied the chloromethylation of a number of coumarin derivatives.

Coumarin, 4-methylcoumarin and 7,8-dimethoxy-4-methylcoumarin gave the 3-chloromethyl derivatives. 7-Methoxy-4-methylcoumarin gave under different conditions 6-chloromethyl-, 3,6-dichloromethyl-, 3,8-dichloromethyl- and 3,6,8-trichloromethyl derivatives. 5-Methoxy-4-methylcoumarin gave the 3,8-dichloromethyl derivative and 6-hydroxy-4-methylcoumarin gave the 5-chloromethyl derivative. The chloromethylation of some other substituted coumarins such as methyl-7-hydroxy-4-methyl- and methyl-5-hydroxy-4-methylcoumarin-6-carboxylate and 4'-methyl-1,2-naphtha-α-pyrone have also been studied. Further discussion is given in Chapter II of this thesis.

Mannich reaction : Robertson and Link[86] prepared a series of 3-substituted aminomethyl-4-hydroxycoumarins from 4-hydroxycoumarin by reacting it with paraformaldehyde and aminohydrochlorides. Gupta et al.[87] sysnthesised Mannich bases from 7-hydroxy- and 7-hydroxy-4-methylcoumarin and found them to be powerful nervous system and respiratory stimulants. Da Re et al.[88] found that of the 50 coumarin derivatives examined, 6-methoxy-5-dimethylaminomethylcoumarin was the most active in stimulating the central nervous system. They further found that the Mannich bases from coumarins were less active than those from the corresponding chromones and flavones.

5-Hydroxy-, 6-hydroxy- and 7-hydroxy-4-methylcoumarin were found to give the oxazino derivatives when

the primary amines were used[89]. 6-Hydroxy-, 7-hydroxy- and 8-hydroxycoumarins gave Mannich bases with secondary amines and oxazinocoumarins (III) with primary amines[90,91]. The oxazino derivatives were decomposed with dilute hydrochloric acid and the Mannich bases (IV) obtained. Mannich bases were converted into the corresponding formyl derivatives (V) by Sommelet reaction.



In addition to the reactions described above coumarins have been subjected to a number of other reactions such as coupling reaction[92,93,94,95], Meerwein reaction[96,97,98,99], Nuclear methylation[100], Diels-Alder reaction[101,102] and Michael reaction[103,104,105,106].

Further, a good deal of work has been done on the synthesis of coumarino-α-pyrones, coumarino-γ-pyrones and furocoumarins in which the α- and γ-pyrone or the furan ring has been built up on the benzenoid or the heterocyclic part of the coumarin ring system.

Present work

For the past several years extensive work has been going on in our laboratories on (i) the synthesis of various oxygen heterocycles from different types of phenolic compounds such as dihydroxy naphthalenes, anthrols, hydroxy derivatives of fluorene, acenaphthene, biphenyl, biphenyl methane, benzophenone and biphenyl sulphone and (ii) on the application of the various reactions discussed above to study the pattern of substitution in the oxygen heterocycles such as benzofurans, coumarins, chromones, flavones, isoflavones and xanthones.

The present work is a part of these studies and deals with the following :

Chapter I deals with the bromination of some alkyl coumarins with N-bromosuccinimide, establishment of the structures of the compounds formed and further synthetical work on the bromomethylcoumarins obtained.

Chapter II deals with the chloromethylation of several alkylcoumarins with and without a 4-methyl group

and some further reactions on the 3-chloromethylcoumarins obtained.

Chapter III deals with the synthesis of some furocoumarins, coumarino-α-pyrones and coumarino-γ-pyrones from some alkyl coumarins.

Appendix I deals with the attempts to synthesise 6,7- and 5,7-dimethylchromone from 3,4- and 3,5-xylenol through cyanoethylation.

REFERENCES

1. O.H.Emmerson and E.M.Bickoff., J.Amer.Chem.Soc., 80, 4381 (1958).
2. C.Deschampo-Vallet and C.Mentzer., Compt. rend., 251, 736 (1960) ; C.A., 55, 4492 (1961).
3. N.R.Krishnaswamy and T.R.Seshadri., J.Sci.Ind.Res. India, 16 B, 268 (1957).
4. H.Pechmann., Ber., 17, 929 (1884).
5. H.Pechmann and C.Duisberg., Ber., 16, 2119 (1883).
6. H.Pechmann., Ber., 17, 929 (1884).
7. O.Dann and G.Mylins., Ann., 587, 1 (1954).
8. L.G.Shah, G.D.Shah and R.C.Shah., J.Indian Chem.Soc., 32, 302 (1959).
9. J.Koo., Chem. and Ind., 445 (1955).
10. S.Sethna and R.Phadke., Organic Reactions. Vo. VII (Wiley) New York, 1-58 (1953).
11. C.Mentzer and D.Pillon., Compt. rend., 234, 444 (1952).
12. C.Mentzer and D.Pillon., Bull.Soc.Chem., 538 (1953).
13. C.Mentzer, D.Molho and P.Vercier., Compt. rend., 232, 1488 (1950).
14. K.B.Desai, K.N.Trivedi and S.Sethna., J.M.S.Univ. Baroda., IV, 1 (1955).
15. W.H.Perkin, J.Chem.Soc., 53 (1868); 388 (1877).
16. E.Knoevenggel., Ber., 31, 2585, 2596 (1898); 37, 4461 (1904).
17. S.Sethna and N.M.Shah., Chem.Rev., 36, 1 (1945).

18. S.Wawzonek, Heterocyclic Compounds, edited by Elderfield, (Wiley)New York, Vol. II. p. 181 (1951).

19. B.B.Dey and K.Radhabai., J.Indian Chem.Soc., 11, 635 (1934).

20. P.K.Grover, T.R.Seshadri and S.Varadarajan., J. Sci. Ind.Res. India., 11 B, 50 (1952).

21. H. Lindemann, Ann., 404, 53 (1914); C.A., 8, 1744 (1914).

22. C.Mentzer and P.Meunier., Compt. rend., 225, 1329 (1947).

23. B.B.Dey and K.Radhabai., J.Indian Chem. Soc., 11, 635 (1934).

24. F.Peters and H.Simonis., Ber., 41, 830 (1908).

25. K.Fries and G.Frickewirth., Ann., 362, 49 (1908); C.A., 2, 3067 (1908).

26. P.S.Rao, V.D.N.Sastri and T.R.Seshadri., Proc. Indian Acad.Sci., 9 A, 22 (1939).

27. L.A.Jordan and J.F.Thorpe., J.Chem.Soc., 107, 387 (1915).

28. B.B.Dey and K.Radhabai., J.Indian Chem. Soc., 11, 635 (1934).

29. V.J.Dalvi and S.Sethna., J.Indian Chem.Soc., 26, 359; 467 (1949).

30. W.Borsche., Ber., 40, 2731 (1907).

31. K.N.Trivedi and S.Sethna., J.Org.Chem., 25, 1817 (1960).

32. B.B.Dey and V.A.Kutti., Proc.Natl.Inst.Sci.India., 6, 641 (1940).

33. S.S.Lele, R.J.Parikh and S.Sethna., J.Indian Chem.Soc., 30, 610 (1953).

34. S.S.Lele and S.Sethna., J.Sci.Ind.Res.India., 14 B, 101 (1955).

35. K.G.Bauer and F.Schoder., Arch.Pharm., 259, 53 (1921); C.A., 15, 2856 (1921).

36. T.Sakai and C.Kato., J.Pharm.Soc., Japan., 55, 691 (1935); C.A., 29, 7311 (1935).

37. D.Molho and C.Mentzer., Compt. rend., 223, 1141 (1946); 228, 578 (1949); C.A., 41, 2709 (1947).

38. J.Lecocq and N.P.Buu-Hoi., Compt. rend., 224, 937 (1947); C.A., 41, 5121 (1947).

39. J.Lecocq., Ann. Chim., 3, 62 (1948); C.A., 42, 7281 (1948).

40. D.Molho and C.Mentzer., Compt. rend., 223, 1141 (1946); 228, 578 (1949); C.A., 41, 2709 (1947).

41. K.B.Doifode and M.G.Marathey., J.Org.Chem., 29, 2025 (1964).

42. S.S.Lele and S.Sethna., J.Org.Chem., 23, 1731 (1958).

43. S.S.Lele, M.G.Patel and S.Sethna., J.Indian Chem.Soc., 37, 775 (1960).

44. Morgan., J.Chem.Soc., 85, 1233 (1904).

45. B.B.Dey and P.Krishnamurthy., J.Indian Chem.Soc., 4, 197 (1927).

46. A.Clayton., J.Chem.Soc., 97, 1388 (1910).

47. A.Clayton., J.Chem.Soc., 97, 1388 (1910).

48. N.B.Parekh and R.C.Shah., J.Indian Chem.Soc., 19, 335 (1942).

49. A.R.Naik and G.V.Jadhav., J.Indian Chem.Soc., 25, 171 (1948); J.Univ.Bombay., 16, 46 (1948).

50. B.B.Dey and V.A.Kutti., Proc.Natl.Inst.Sci.India., 6, 641 (1940).

51. W.Borsche and P.H.Weinheimer., Ber., 85, 198 (1952).

52. C.F.Huebner and K.P.Link., J.Amer.Chem.Soc., 67, 99 (1945).

53. N.M.Shah and G.S.Mewada., Ber., 89, 2209 (1956).

54. M.Kruger., Ber., 56 B, 481 (1923).

55. M.V.Rubtsov and V.M.Fedosova., J.Gen.Chem., U.S.S.R., 14, 848 (1944); C.A., 40, 1804 (1946).

56. J.Lecocq and N.P.Buu-Hoi., Compt. rend., 224, 937 (1947); C.A., 41, 5121 (1947).

57. J.R.Merchant and R.C.Shah., J.Indian Chem.Soc., 34, 45 (1957); J.Org.Chem., 22, 884 (1957).

58. D.B.Limaye., Ber., 65, 375 (1932); 67, 12 (1934).

59. N.M.Shah and R.C.Shah., J.Chem.Soc., 228, 1424 (1938); 1250 (1939).

60. V.M.Thakor., Curr. Sci., India., 20, 234 (1951).

61. M.D.Bhavsar and R.D.Desai., J.Indian Chem.Soc., 31, 141 (1954).

62. A.A.Aleykutty and V.Baliah., J.Indian Chem.Soc., 32, 773 (1955).

63. J.K.Klosa., Arch. Pharm., 289, 71 (1956); C.A., 51, 491 (1957).

64. F.M.Dean, E.Evans and A.Robertson., J.Chem.Soc., 4565 (1954).

65. K.N.Trivedi and S.Sethna., J.Org.Chem., 25, 1817 (1960).

66. L.G.Shah, G.D.Shah and R.C.Shah., J.Sci.Ind.Res., 15 B, 580 (1956).

67. R.N.Sen and D.Chakravarti., J.Amer.Chem.Soc., 50, 2428 (1928).

68. E.Spath and M.Pailer., Ber., 68, 940 (1935).

69. V.D.N.Sastri, N.N.Narasimhachari, P.Rajagopalan, T.R.Seshadri and T.R.Thiruvengadam., Proc.Indian Acad.Sci., 37 A, 681 (1953).

70. R.M.Naik and V.M.Thakore., J.Org.Chem., 22, 1626 (1957).

71. R.M.Naik and V.M.Thakor., J.Org.Chem., 22, 1630 (1957).

72. E.Ziegler and H.Maier., Monatsch., 89, 787 (1958); C.A., 52, 17253 (1958).

73. W.Baker and O.M.Lothian., J.Org.Chem., 628 (1935).

74. B.Krishnaswamy and T.R.Seshadri., Proc.Indian Acad. Sci., 13 A, 43 (1941).

75. P.S.Rao and T.R.Seshadri., Proc. Indian Acad.Sci., 19 A, 5 (1944).

76. B.Chaudhury, S.K.Saha and A.Chatterjee., J.Indian Chem.Soc., 39, 783 (1962).

77. G.Bargellini and L.Monti., Gazz.Chim. Italy, 45, 1, 90 (1915); C.A., 9, 2239 (1915).

78. F.Wesseley and E.Demmer., Ber., 62, 120 (1929).

79. N.Mauthner., J.Prakt.Chem., 152, 23 (1939).

80. R.J.Parikh and S.Sethna., J.Indian Chem.Soc., 27, 369 (1950).

81. R.B.Desai and S.Sethna., J.Indian Chem.Soc., 28, 213 (1951).

82. M.D Bhavsar and R.D.Desai., Indian J.Pharm., 13, 200 (1951).

83. A.Oliverio, A.Schiavello and C.Sebastiani., Ricerca, Sci., 20, 1304 (1950); C.A., 45, 4584 (1951).

84. S.S.Lele, N.G.Sawant and S.Sethna., J.Indian Chem.Soc., 38, 975 (1961).

85. S.S.Lele, N.G.Sawant and S.Sethna., J.Org.Chem., 25, 1713 (1960).

86. D.N.Robertson and K.P.Link., J.Amer.Chem.Soc., 75, 1883 (1953).

87. V.N.Gupta, B.R.Sharma and R.B.Arora., J.Sci.Ind.Res. 20 B, 300 (1961).

88. P. Da Re, L.Bonola, I.Setnikar and M.J.Magistretti., Experientia., 18, 387 (1962); C.A., 57, 11811 (1962).

89. R.B.Desai., J.Org.Chem., 26, 5251 (1961).

90. M.G.Patel and S.Sethna., J.Indian Chem.Soc., 39, 595 (1962).

91. R.H.Mehta and S.Sethna., J.Indian Chem.Soc., 40, 384 (1963).

92. W.Borsche., Ber., 37, 346 (1904).

93. S.Rangaswamy and T.R.Seshadri., Proc.Indian Acad.Sci. 9 A, 526 (1939).

94. S.Rangaswamy and K.R.Rao., Proc.Indian Acad.Sci., 19 A, 14 (1944).

95. C.F.Huebner and K.P.Link., J.Amer.Chem.Soc., 67, 99 (1945).

96. H.Meerwein, E.Buchner and K.Van Emster., J.Prakt. Chem., 152, 237 (1939).

97. W.Freund., J.Chem.Soc., 1943 (1951).

98. Surinder Kumar., J.L.Bose and S.Siddiqui., J.Sci. Ind.Res.India., 11 B, 81 (1952).

99. P.L.Sawhney and T.R.Seshadri., J.Sci.Ind.Res., India., 13 B, 316 (1954).

100. V.N.Gupta and T.R.Seshadri., J.Sci.Ind.Res. India., 16 B, 257 (1957).

101. R.Adams, W.D.Mc Phee, R.B.Carlin and Z.W.Wicks., J.Amer.Chem.Soc., 65, 356 (1943).

102. A.Mustafa and M.Kamal., J.Amer.Chem.Soc., 77, 1828 (1955).

103. T.R.Seshadri., J.Chem.Soc., 166 (1928).