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Review

Cycloaddition reactions of 1-benzopyran-4-ones

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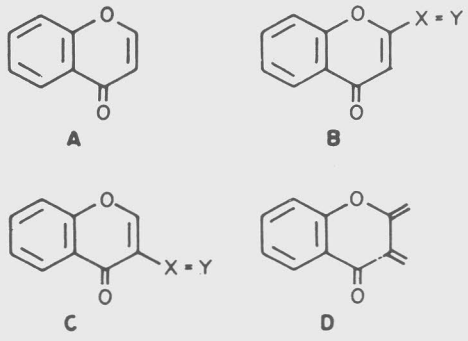
I. Introduction

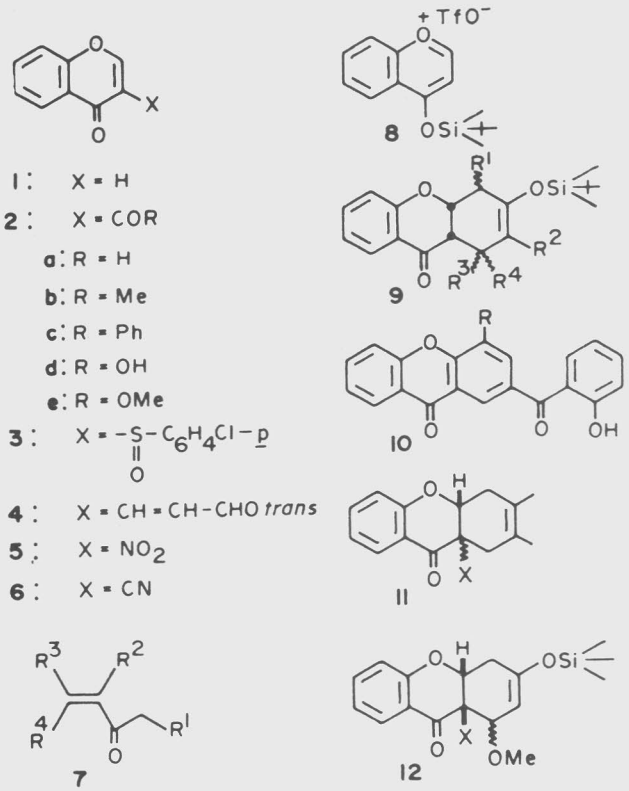
1-Benzopyran-4-one (trivial name : Chromone, **A**) is the benzannulated γ-pyrone and like γ-pyrone it is non-aromatic. It can be regarded as an α-aryloxy-β-aroylethene and its olefinic bond is amenable to three types of cycloaddition reactions; it can (i) act as a 2π component in [4π + 2π] cycloaddition, (ii) add to 1,3-dipoles giving [3+2] cycloadducts and (iii) undergo [2+2] cycloaddition with alkenes under suitable conditions. Furthermore, the substituted chromone systems **B** and **C**, where X as well as Y is either carbon or nitrogen, can (i) function as a 4π component in a normal or hetero Diels-Alder reaction and (ii) undergo photoirradiated [3+2] cycloaddition with olefins. The aforesaid cycloaddition reactions of the chromone systems **A-C** and [4+2] cycloaddition of the chromone system having *o*-quinodimethane structure **D** covering the literature upto June 1996 have been comprehended in the present review. Some interesting transformations of the initially formed cycloadducts have also been highlighted. Michael initiated heteroannulation of the systems **A-C** and electrocyclisation of the systems **B-D** having further conjugation are not included in this review. A review describing some



cycloaddition reactions of 3-formylchromone only covering the literature upto 1994 and that too very briefly has recently appeared[1].

II. [4+2]Cycloaddition

II. 1. Chromone as a 2π component. The enone moiety of the parent chromone **1** does not function as a dienophile. The formation of the *cis*-adduct **9** from chromone **1** and the α,β-unsaturated ketone **7** [R^1 = H, Me, Et; R^2 = H; R^3 = H, Me, Ph; R^2-R^3 = $(CH_2)_4$; R^4 = H, Me] in the presence of *t*-butyldimethylsilyl triflate and 2,6-lutidine is not regarded as a proper [4+2] cycloaddition reaction. Here the reaction is initiated by the attack of 2-silyloxybuta-1,3-diene, derived from **7** and silyl triflate, at 2-position of 4-*t*-butyl-dimethylsilyloxy-1-benzopyrrilium triflate **8**[2]. The presence of an electron-withdrawing substituent at C-3 is expected to enhance the dienophilicity of the pyran 2,3-olefinic bond of chromone. Based on this assumption, Ghosh *et al.*[3] rationalised the formation of 2-(2-hydroxybenzoyl)xanthone **10** (R



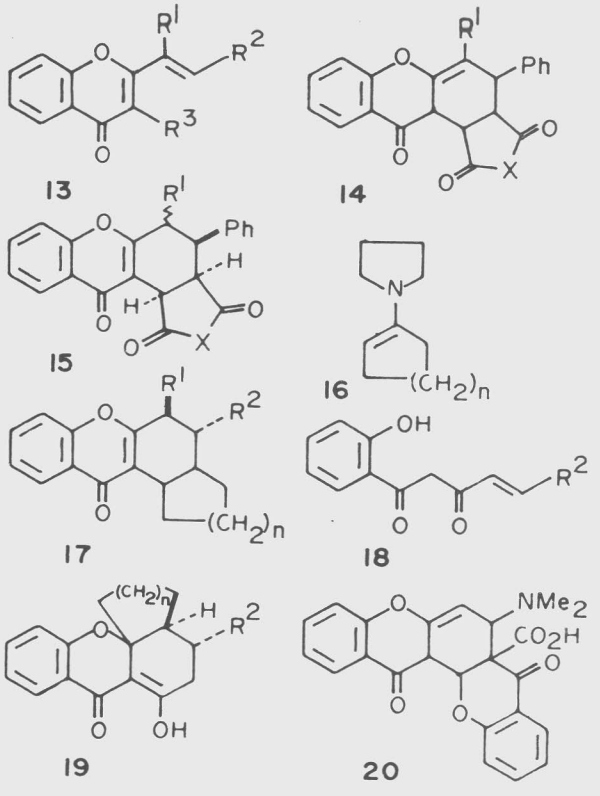
Born in 1943, Chandra Kanta Ghosh got from the University of Calcutta his M.Sc., Ph.D. and D.Sc. degrees in Chemistry in 1965, 1970 and 1996, respectively. A faculty member of the Department of Biochemistry, Calcutta University since 1969, Dr Ghosh is at present a Professor in his Department. He did his post-doctoral research in the Department of Organic Chemistry, Karlsruhe University, Germany (1973-74) and in the Biology Division of Oak Ridge National Laboratory, USA (1979-90). His research interest lies mainly in the chemistry of 1-benzopyran-4-one having an electron withdrawing group at its 3-position. He has so far published forty papers and four review articles in this field.

Miss Chandreyi Ghosh was born in 1970. She graduated with Honours in Chemistry from Presidency College, Calcutta in 1992 and got her M.Sc. degree from IIT, Kanpur in 1994. She is at present a Junior Research Fellow in the Department of Biochemistry, Calcutta University and has so far co-authored two publications concerning cycloaddition reactions of the 1-benzopyran-4-one system.

= H) from 3-formyl-2-methylchromone and either of the chromones **2a** and **2d** by a mechanism involving a Diels-Alder reaction where the latter function as dienophiles. Later on, this type of several condensations between 3-acyl-2-methylchromone and 3-acylchromone leading to substituted xanthones has been explained with the help of a Michael Initiated Ring Closure (MIRC) followed by elimination reactions [4,5]. A convincing evidence for dienophilicity of 3-substituted chromones **2a, d, e** has emerged from a British laboratory[6]. 2,3-Dimethyl-1,3-butadiene undergoes cycloaddition to the chromones **2a, d, e** only in the presence of a catalytic amount of titanium tetrachloride, the resultant *cis*-adduct **11** (X = *β*-CHO) deformylating to an isomeric mixture of **11** (X = H) and **11** (X = *β*-CO_2H) giving a complex mixture and **11** (X = *β*-CO_2Me; being sufficiently stable), respectively. Cycloaddition of the chromones **2a, 2e** and **3** with electron rich Danishefsky's diene gives the corresponding cycloadduct **12** (isomeric mixture) without the assistance of any Lewis acid. The adduct **12** [X = -S(O)C_6H_4-Cl-*p*] is prone to undergo aromatisation to 3-hydroxyxanthone via *syn*-elimination of *p*-chlorobenzene-sulphenic acid and 1,4-elimination of methanol[6].

II. 2. 2-Vinylchromone (system B) as a 4π component. The wrong structure **14** previously assigned without any spectroscopic data [7] to the cycloadduct obtained from *E*-2-styrylchromone **13** ($R^1 = R^3 = H$; R^2 = Ph) and maleic anhydride or *N*-phenylmaleimide has been rectified as the 1,2,3,4-tetrahydroxanthone **15** (R^1 = H; X = O or NPh)[8]. The cycloaddition of *E*-2-(1-methylstyryl) chromone **13** (R^1 = Me; R^2 = Ph; R^3 = H) with the aforesaid dienophiles also gives the xanthones **15** (R^1 = Me; X = O, NPh)[8]. Here the Diels-Alder cycloaddition (*endo*-addition) reactions are clearly followed by 1,3-hydrogen shift from C-9a to C-4 and presumably the driving force for this shift is the formation of the resonance stabilised chromone system. In the light of this report[8], the structures of the type **14** assigned to the cycloadducts of maleic anhydride or *N*-phenylmaleimide with several substituted 2-styrylchromones[9-13] seem to be erroneous and warrant further scrutiny.

The reaction between 2 -vinylchromones **13** (R^1 = Me, Ph, R^2 = Ph, R^3 = H; $R^1 = R^3$ =H, R^2 = Me,

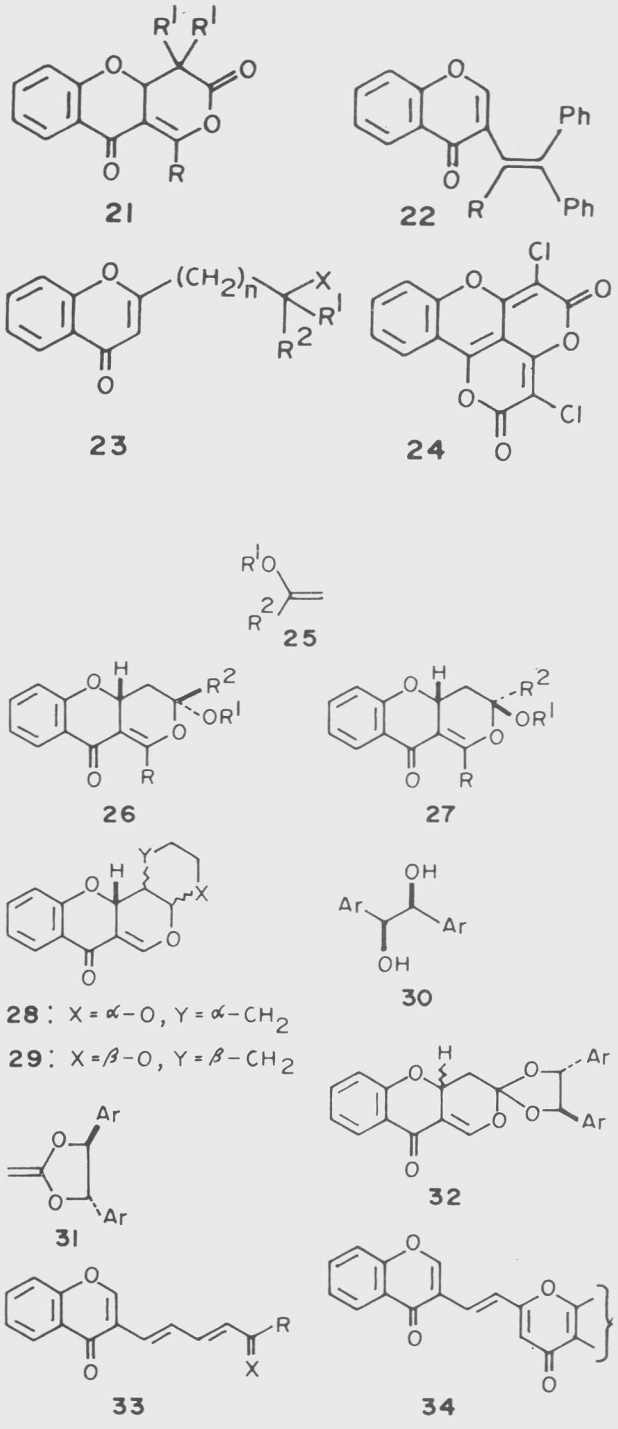


2-furfuryl) and 1-pyrrolidinylcyclopentene **16** (n=1) gives the substituted 2,3,3a,4-tetrahydrocyclopenta [*a*]xanthene- **11**(5*H*)-ones **17**; the stereochemistry of the products indicates that the initial step in the reaction is an *exo*-addition Diels-Alder reaction with inverse electron demand leading to the *cis*-fused C/D ring intermediate that rearranges to the chromone system and eliminates pyrrolidine molecule. The aforesaid cyclopentene derivative gives with **13** (R^1 = H; R^2 = Ph; R^3 = Me) a Michael adduct instead of any cycloadduct[14]. It is relevant to mention here that pentenedione **18** (R^2 = Ph or 2-furfuryl) reacts with the enamine **16** (n = 1 or 2) giving the cycloalkano [*d*]xanthone **19** which on base treatment slowly rearranges to **17** (R^1 = H; R^2 = Ph or 2-furfuryl). The compound **19** arises by an initial Michael addition of **16** to the *α,β*-unsaturated ketone **18** followed by double cyclisation[15]. So the ultimate formation of **17** from **16** and **18** through cyclisation of the latter to the vinylchromone **13** ($R^1 = R^3$ = H; R^2 = Ph or 2-furfuryl) followed by its [4+2] cycloaddition with **16** and subsequent elimination of pyrrolidine is ruled out. The enaminoketone **13** ($R^1 = R^3$ = H; R^2 =NMe_2) and the acid **2d** when refluxed together in

dimethylformamide affords the xanthone **10** (R = H) presumably through elimination of dimethylamine and decarboxylative pyran ring opening of the initially formed [4+2]cycloadduct 20[16].

II. 3. 3-Substituted chromone system C as a 4π component: II. 3.1. 3-Acylchromone. 3-Acylchromone having the exocyclic carbonyl double bond in conjugation with the pyran 2,3-olefinic bond can function as a heterodiene in inverse electron demand Diels-Alder reaction. Thus, 3-formyl (or benzoyl) chromone **2a** or **2c** gives with diphenylketen a mixture of the pyranobenzopyran derivative **21** (R = H or Ph; R^1 = Ph) and 3-(2,2-diphenylvinyl) chromone **22** (R = H or Ph), the latter arising from the former by thermal rearrangement with the extrusion of carbon dioxide[17]. Treatment with a base also converts **21** (R = H or Ph; R^1 =Ph) into **22** (R = H or Ph)[17]. Mild alkali hydrolysis of **21** (R = H; R^1 = Ph) to the acid **23** (n = O; R^1 = R^2 = Ph; X = CO_2H)[17] has been rationalised[18]. 3-Formylchromone **2a** also undergoes [4+2] cycloaddition with dichloroketen, generated *in situ* from dichloroacetyl chloride and triethylamine; the initially formed cycloadduct **21** (R = H; R^1 = Cl) being a reactive heterodiene captures a second molecule of dichloroketen and the resultant adduct eliminates two molecules of hydrogen chloride under base catalysis to form **24**[19].

Cycloaddition of 3-acylchromones **2a-d** with several enol ethers like **25** (R^1 = alkyl; R^2 = H, Me, OMe) has been extensively studied[20-25]. Alkoxyethene reacts with 3-formylchromone at room temperature but with 3-acetyl - and 3-benzoyl-chromones it reacts only at high temperature[20] whereas chromone-3-carboxylic acid **2d** with its 4π system being stabilised in the *S-cis* conformation by intramolecular hydrogen bonding between the carboxylic hydrogen and the pyrone carbonyl group functions as a highly reactive heterodiene[24]. Ghosh *et al.*[21] could isolate only the *endo*-adduct **26** (R = R^2 =H; R^1 = Et) by refluxing **2a** in excess ethyl vinyl ether. The *endo*-adduct exclusively obtained from 3-formyl-6-methylchromone and 2-methoxypropene at room temperature isomerises to the proper chromone system in contact with various rhodium catalysts



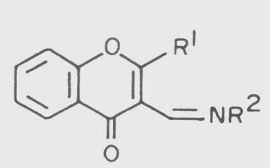
and can be converted into the corresponding *exo*-isomer by treatment with triphenylcarbenium perchlorate followed by selective reduction of the resultant pyrrilium salt with sodium borohydride in methanol[22]. Wallace *et al.*[20,23-25] obtained by treating the chromones **2a-d** with several enol ethers **25** an isomeric mixture of the cycloadducts

26 and **27**, the *endo*-addition always predominating over *exo*-addition. 3-Formylchromone **2a** gives with dihydropyran an isomeric mixture of the fused benzopyranones **28** and **29** in which the geometry of enol ether is retained[20]. An electron donor substituent in 6- or 7-position of **2a** retards the reaction and slightly increases the *endo*-selectivity while an electron withdrawing group has the reverse effect. The reaction of **2a** with *t*-butoxyethene is almost non-selective[20].

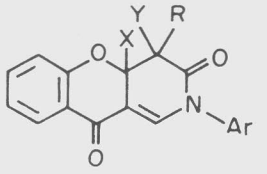
5-Substituted 3-formylchromone is more reactive than its unsubstituted analogue towards enol ethers[25]. Although the *endo*-cycloadducts are kinetically favoured, the *exo*-isomers are thermodynamically more stable due to anomeric effect. Each of the isomers **26** and **27** (R = R^2 = H; R^1 = Et) gives the same mixture of **27** and **26** (6.5 : 1) on treatment with trifluoroacetic acid in dichloromethane at 20°C for several hours. Under similar conditions, the 1-methyl system **26** (R = Me; R^1 = Et; R^2 = H) undergoes fragmentation to 3-acetylchromone (**2b**) to the extent of 33% while the cycloadducts **26** (R = Me; R^1 = *n*-Bu; R^2 =H) and **26** (R = Ph; R^1 = Et; R^2 = H) almost exclusively undergo a nett retro-cycloaddition to **2b** and **2c**, respectively. Diastereoselective heterocycloaddition of the C_2-symmetric keten acetal **31**, generated from the diol **30**, to 3-formylchromone yields the adduct **32** (diastereoisomeric mixture), *re*-addition mode predominating over *si*-addition[23]. The extent of *re*-addition over *si*-addition depends on the nature of Ar group in the acetal **31**. For example, when Ar = phenyl and 2-methylphenyl, the isomers **32** with β-hydrogen at 4a-position are formed in 40 and 90% diastereoisomeric excess, respectively. Acid catalysed methanolysis of **32** induces transesterification and retro-Claisen deformylation, generating the ester **23** (n = 1; R^1R^2 = O; X = OMe) and the diol **30**. The above sequence of reactions using (-) (*S,S*)- **30** (Ar = 2-methylphenyl) as the auxilary diol yields the aforesaid ester **23** of *S*-configuration (~85% ee) and releases the diol **30** of more than 98% optical purity; hence it can be regarded as a nett asymmetric conjugate addition of recyclable acetic ester enolate equivalent to an activated enone[23].

The adduct **26** (R =R^2 = H; R^1 = Et) rearranges to the aldehyde **4** on treatment with aqueous acid[21] or sodium methoxide[25], gives the diketone **33** (X = O) with enolisable ketone MeCOR (R = Me, Ph, C_6H_4-OMe-2) under acidic conditions[26] and 3-salicyloylpyridine and the corresponding *N*-oxide with ammonium acetate and hydroxylamine, respectively[27]. The compound **33** (R = Me; X = O) gives with hydroxylamine hydrochloride an isomeric mixture of the oxime **33** (R = Me; X = NOH) which on heating under reflux in nitrobenzene undergoes electrocyclisation and subsequent oxidation to the oxime of 4-acetylxanthone. The diketone **33** (R = C_6H_4OMe-2; X = O) on demethylation with boron tribromide in dichloromethane followed by treatment with iodine in dimethylsulphoxide affords the chromone **34**[26]. The cycloadducts derived from the acid **2d** and alkenes **25** undergo decarboxylation on treatment with alkanols or water. For example, **26** (R =OH; R^1 = Et; R^2 = H) gives the mixed acetal **23** (n = 1; R^1 = OMe; R^2 = OEt; X = H) as a pair of diastereoisomers with methanol and the unstable aldehyde **23** (n = 1; R^1R^2 =O; X = H) with water. The cycloadduct **26** (R = OH; R^1 = Me; R^2 = OMe), derived from **2d** and 1,1-dimethoxyethene is extremely labile and gets transformed into the ester **23** (n = 1; R^1R^2 = O; X = OMe) even on attempted chromatography over silica gel[24,25].

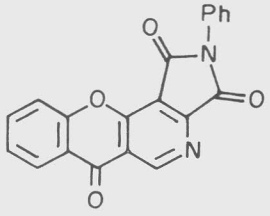
II. 3.2. Anils and hydrazones of 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde. [4+2] Cycloaddition of the Schiff bases **35** of 3-formylchromone with highly reactive dienophiles like ketens is successful. Thus, dichloroketen or chloro (phenyl)keten with **35** (Ar = C_6H_4R-*p*; R = Me, OMe, Cl) gives the adduct **39** that readily gets dehydrohalogenated under base catalysis to the pyranopyridine **40** (R = Cl or Ph)[28]. The hydrazone **36** when refluxed with *N*-phenylmaleimide (NPMI) in toluene produces the *endo*-adduct **41** whereas the anil **35** (Ar = C_6H_4Me-*p*) fails to react under similar conditions[29]. Palladised charcoal converts **41** into **42**. The hydrazone **37** behaves differently from its homologue **36** towards NPMI in giving the tetrahydroxanthone **43** together with a little amount of 3-cyano-2-methylchromone. Here the unsaturated hydrazone **37** participates through its enehydrazine tautomer **45**, a representative of the general structure **D**, in the normal Diels-Alder reaction with NPMI giving the *endo*-adduct **43**. With NPMI the anil **38**, like the analogous



35: $R^1 = H, R^2 = Ar$
36: $R^1 = H, R^2 = NMe_2$
37: $R^1 = Me, R^2 = NMe_2$
38: $R^1 = Me, R^2 = Ar$



39: X = H, Y = Cl
40: XY = bond



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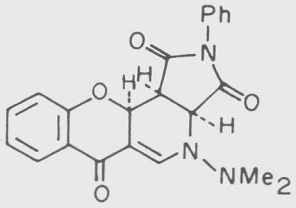

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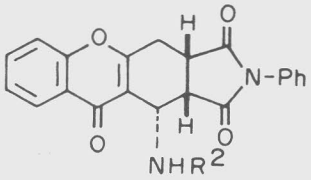
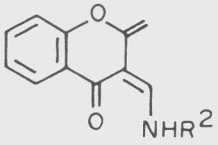
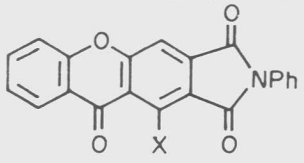




43: $R^2 = NMe_2$: **45**
44: $R^2 = C_6H_4Me\text{-}p$: **46**

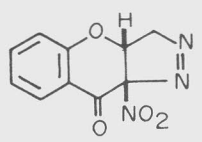


47: X = H
48: $NHC_6H_4Me\text{-}p$

hydrazone **37**, gives through its imine tautomer **46** the *endo*-adduct **44**. Palladised charcoal converts the tetrahydroxanthones **43** and **44** into xanthones **47** and **48**, respectively[29].

III. [3+2] Cycloaddition

III. 1. Reactions with diazoalkanes. Among the 1,3-dipoles, diazoalkanes have been mostly subjected to reaction with various chromone derivatives. Diazomethane and other active members of the diazoalkane series undergo *cis*-addition to an alkene; the resultant 1-pyrazoline adducts are generally unstable and undergo various transformations depending on the nature of the



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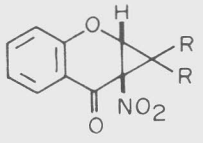

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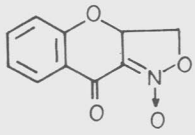

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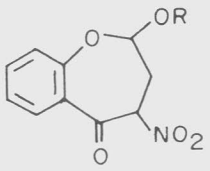

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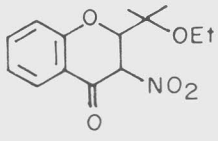
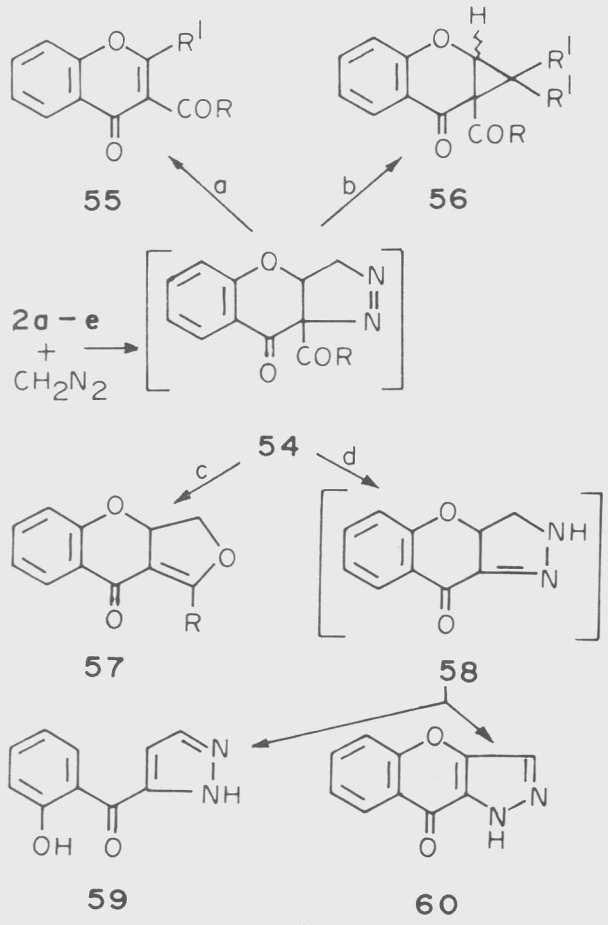


53

groups linked to the pyrazoline nucleus. The parent chromone has not been reacted with any member of the diazoalkane series.

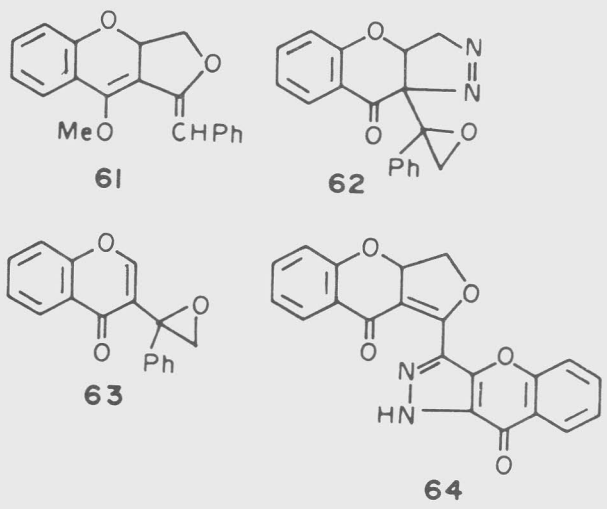
III. 1.1. Reaction of 3-substituted chromones. 3-Nitrochromone **5** with diazomethane gives via the unstable pyrazoline **49** the cyclopropabenzopyran **50** (R =H) admixed with a little of isoxazoline oxide **51**, the latter probably arising from **49** by elimination of nitrogen through an electrocyclic mechanism[30]. 2-Diazopropane similarly gives the cyclopropane **50** (R = Me) as the major product. The cyclopropane **50** (R =H) is very susceptible to nucleophiles; it reacts smoothly at ambient temperature with ROH (R =H or alkyl) giving the 1-benzoxepin 52. The cyclopropane ring in **50** (R =Me) is much stable; as for example, only refluxing ethanol opens it and that too in a different sense to give the chromanone derivative **53**[30].

The pyran 2,3-olefinic bond of 3-acylchromones **2a** and **2b** is more active than its acyl carbonyl group towards diazoalkanes. Hence, the 1-pyrazoline intermediate **54**, obtained from **2a, b** with diazomethane in 1:1 stoichiometric ratio, can presumably (i) lead to the methylated product **55** (R^1 = Me) by a concerted electrocyclic elimination of nitrogen and migration of hydrogen (Scheme I, path a), (ii) collapse to the cyclopropane **56** (R^1 = H) (path b), (iii) produce the furopyran **57** by an



Scheme I

electrocyclic mechanism involving nitrogen extrusion and carbonyl oxygen participation (path c), and (iv) undergo base catalysed deacylation to **58** (path d) that can ultimately give the pyrazoles **59** and **60** by pyran ring opening and oxidation, respectively. Nohara *et al.*[31] cursorily reported the formation of 3-formyl-2-methylchromone **55** (R = H; R^1 = Me) in a poor yield by reacting **2a** with diazomethane whereas Dean and Johnson[32] observed the dual alkylation of 3-formyl-6-methylchromone by both diazomethane and diazopropane, the formyl group surviving only in the case of reaction with diazoethane. Ghosh *et al.*[33] have reported that both 3-formyl- and 3-acetylchromones with excess diazomethane give the products mostly in accordance with the pathways depicted in Scheme I. Thus, **2a** affords 3-acetyl-2-methylchromone **55** (R = R^1 = Me), furopyran **57**



(R = H) and pyrazole **60** whereas **2b** produces **55** (R = R^1 = Me), **57** (R = Me) and **60**.

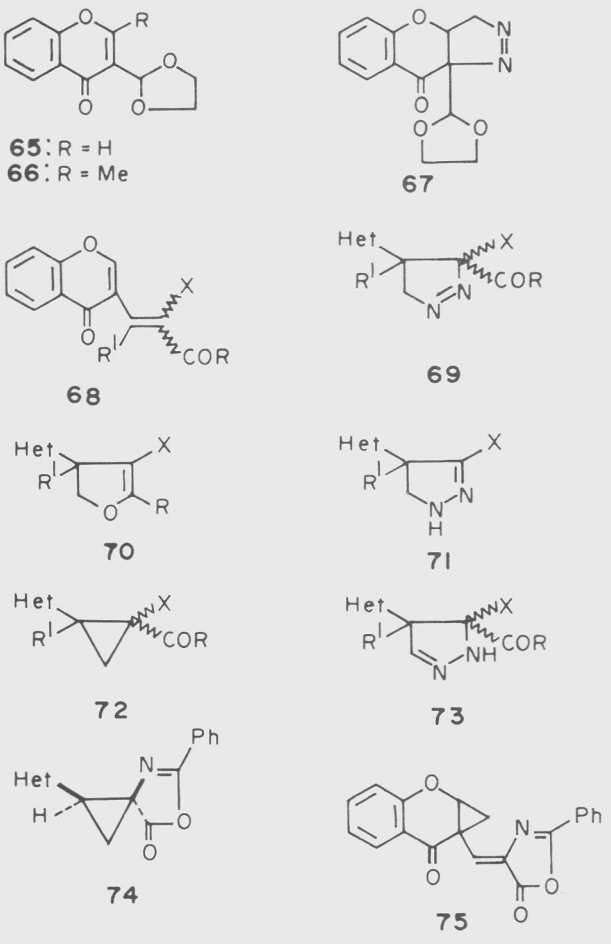
3-Benzoylchromone **2c** behaves towards diazomethane a bit differently from its analogues **2a** and **2b**; in addition to the usual alkylated product **55** (R = Ph; R^1 = Me) and pyrazole **60**,two other compounds **61** and **62** are produced. Formation of the latter two products has been rationalised as follows. The exocyclic carbonyl group of 3-benzoylchromone **2c** does little to activate its 2,3-olefinic bond, hence the former competes favourably with the latter; initial addition of diazomethane to the carbonyl group results in the ketone **55** (R = CH_2Ph; R^1 = H) and the oxirane **63** intermediates; the former with excess diazomethane affords the furan derivative **61** via **54** and **57** (R = CH_2Ph) whereas the latter captures a molecule of diazomethane to form the stable 1-pyrazoline **62**[33]. 3-Formylchromone **2a** with phenyldiazomethane gives mainly the xanthone **10** (R = Ph). Here the 2-benzylated chromone **55** (R = H; R^1 = CH_2Ph), as soon as it is formed from **2a** and phenyldiazomethane, undergoes condensation with the substrate **2a** giving the aforesaid xanthone[5].

The ester **2e** with diazomethane produces the corresponding 2-methylhomologue **55** (R = OMe; R^1 = Me) together with a little of the cyclopropane **56** (R = OMe; R^1 = H) whereas the acid **2d** gives under similar conditions the cyclopropane **56** (R = OMe; R^1 = H), furobenzopyran **57** (R = OMe) and the pyrazoles **59**, **60** and **64**[34]. Here, unlike the corresponding ester **54** (R = OMe), the 1-

pyrazoline-carboxylic acid intermediate **54** (R = OH), obtained from **2d** and diazomethane, assumes due to chelation a preferred conformation having its carboxylic carbonyl group suitably oriented so as to induce electrocyclic elimination of nitrogen as shown in Scheme I (path c), the resultant furan **57** (R = OH) being subsequently methylated by diazomethane. The pyrazoline **54** (R = OH) being a β-ketoacid gets decarboxylated and ultimately forms the pyrazoles **59** and **60** (path d). The pyrazole **60** behaves as an enehydrazine in undergoing 1,4-addition to α,β-unsaturated ketone functionality of **57** (R = OMe) with concomitant elimination of methanol to form the pyrazole **64**. The formation of the cyclopropane **56** (R = OMe; R^1 = H) and not the ester **55** (R =OMe; R^1 = H) from **2d** and diazomethane reveals that the pyrazoline **54** (R = OH), instead of getting esterified to **54** (R = OMe) and then following the path a, collapses to **56** (R = OH) (path b) which is subsequently esterified with diazomethane.

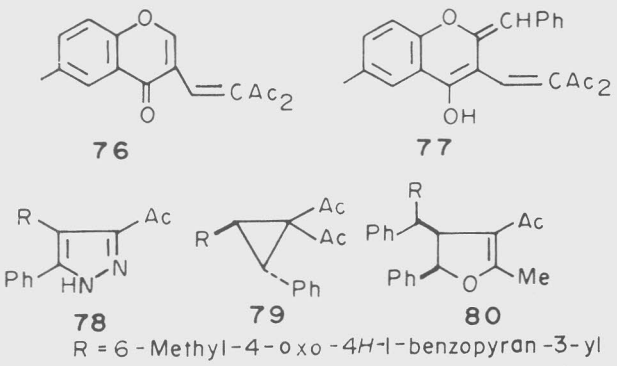
Reactions of several simple condensates of **2a** have also been studied in this laboratory. The 1-pyrazoline **67**, obtained from [3+2] cycloaddition of diazomethane to the acetal **65**, survives crystallisation from ethyl acetate. It gives exclusively the 2-methylated product **66** when heated under reflux in toluene, but gives a mixture of **66** and the pyrazole **59** when heated to its decompostion point. The pyrazole **59** also results from percolation of a solution of **67** in chloroform through a column of Brockman neutral alumina[35].

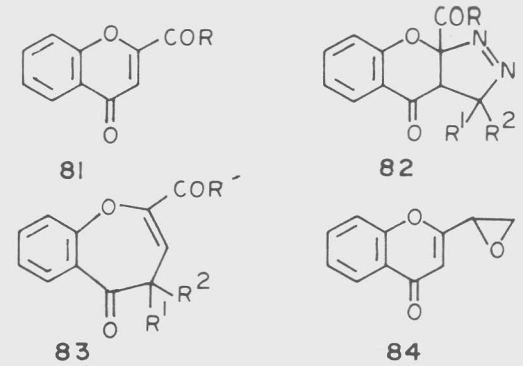
Diazomethane adds to the exocyclic alkenic bond of **68** (R = Me, X = COMe, COPh, CO_2Et; R = OEt, X = CO_2Et; R = OEt, X = CN; R^1 = H) leaving the pyran 2,3-double bond intact and the resultant 1-pyrazoline intermediate **69** (R^1 = H) gives the product(s) in accordance with pathways similar to the analogous ones as depicted in Scheme I. Thus, 1,1-diacylethylene **68** (R = Me; R^1 = H; X = COMe, COPh) gives a mixture of dihydrofuran **70** and 2-pyrazoline **71**[36], and the acrylic ester **68** (R = Me; R^1 = H; X = CO_2Et) gives only **70** (R, R^1 and X as before)[37]. The α-ethoxycarbonylacrylic ester **68** (R = OEt; R^1 = H; X = CO_2Et) is methylated to **68** (R = OEt; R^1 = Me; X = CO_2Et) that does not react further with diazomethane whereas the corresponding α-cyano-

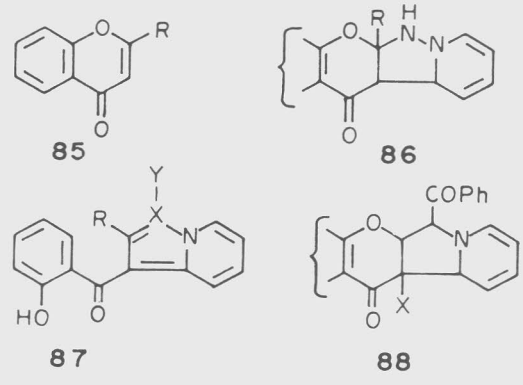


β-methyl-acrylic ester **68** (R = OEt; R^1 = Me; X = CN) reacts further with diazomethane furnishing via 1-pyrazoline **69** the dihydrofuran **70**, a stereoisomeric mixture of the cyclopropane **72** and the pyrazoline **73**, the dihydrofuran **70** thermally isomerising to **72** (R, R^1 and X as before) through a reversed alkoxycarbonylcyclopropane $\rightarrow$5-alkoxy-2,3-dihydrofuran transformation[37]. 4-Oxo-4*H*-1-benzopyran-3-ylethylenazalactone, derived from **2a** and hippuric acid, is cyclopropanated by diazomethane to **74** and **75**[36].

Phenyldiazomethane also undergoes 1,3-dipolar cycloaddition to the exocyclic alkenic bond of the chromone derivative **76**, the resultant 1-pyrazoline intermediate in the presence of excess phenyldiazomethane giving ultimately a mixture of the benzopyran **77**, pyrazole **78**, *trans*-cyclopropane **79**, and *cis*-dihydrofuran **80**[38].

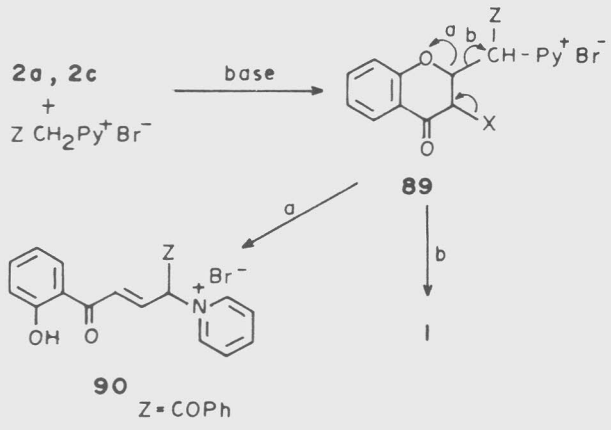






III. 1.2. Reaction of 2-substituted chromones. A diazoalkane homologates the formyl group of 2-formylchromone **81** (R = H) as well as adds to the chromone nucleus, the resultant fused 1-pyrazoline intermediate generally undergoing ring enlargement by carbonyl group migration[32]. Diazomethane with 2-formylchromone is reported to give a mixture of 2-acetylchromone **81** (R = Me) and the oxiran **84**, isolation of chromone nuclear reaction products not being attempted. Diazoethane gives the oxepin **83** (R = Et; R^1 = H; R^2 = Me) in addition to the ketone **81** (R = Et). 2-Diazopropane converts 2-formylchromone into the oxepin **83** via **82** (R = $CHMe_2$; R^1 = R^2 = Me). 2-Propanoylchromone **81** (R = Et) is exclusively methylated by diazomethane at its 3-position[32]. The 2,3-alkenic bond of 2-ethoxycarbonyl-chromone **81** (R = OEt) is less reactive towards diazomethane and diazoethane; it, however, undergoes [3+2] cycloaddition with highly reactive 2-diazopropane to give *via* **82** the benzoxepin **83** (R = OEt; R^1 = R^2 = Me) as the major product[32]. The cyano group of 2-cyano-6-methylchromone reacts with diazomethane in preference to chromone 2,3-double bond to form a triazole which after prototropy undergoes methylation with diazomethane, the structure of the product as 1,2,3 or 1,2,4-triazole being not ascertained[32].

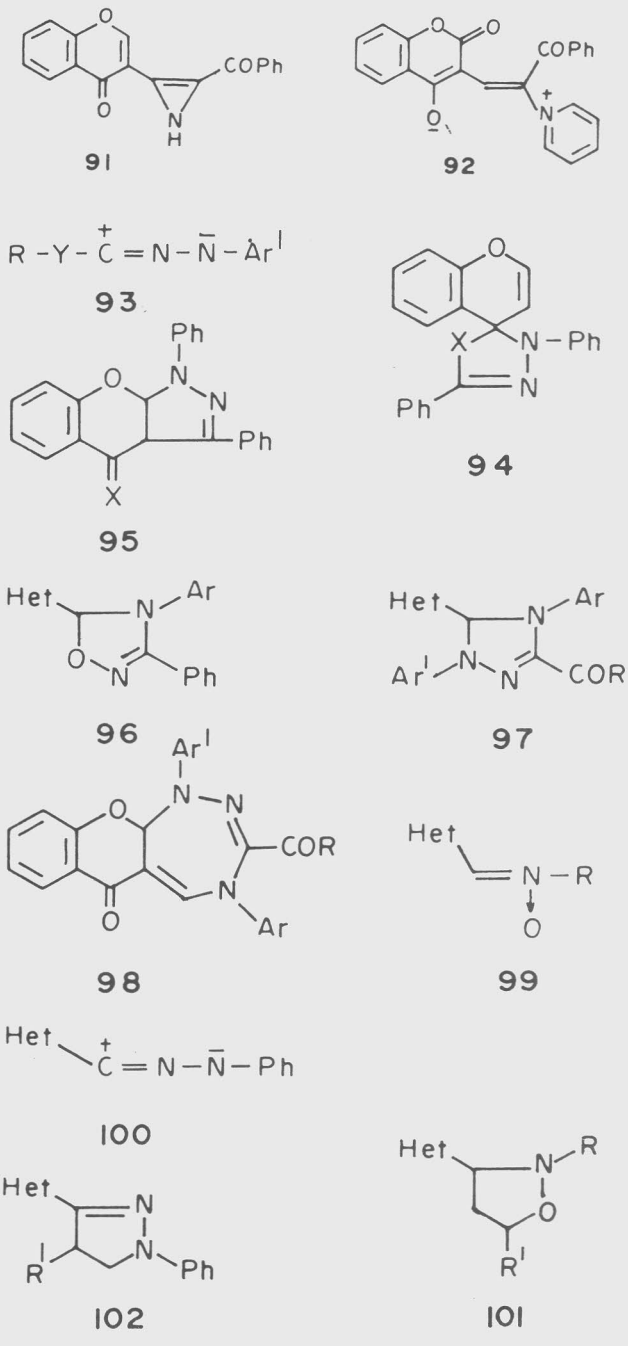
III. 2. Reactions with pyridinium ylids. [3+2] Cycloadduct **86** of the chromone **85** (R = H, Me, Ph) and *N*-aminopyridinium ylid spontaneously aromatises to the pyrazolo [1,5-*a*]pyridine **81** (R as before; X = N; Y = electron pair) by pyran ring opening and dehydrogenation[39]. *N*-Pyridinium phenacylide similarly reacts with the parent chromone **1** giving the indolizine **87** (R = H; X = C; Y = COPh) *via* the cycloadduct **88** (X = H)[39]. The aldehyde **2a** as well as the acid **2d** when refluxed with *N*-phenacylpyridinium bromide in 1:1 stoichiometric proportion in dry acetone in the presence of anhydrous potassium carbonate affords a mixture of chromone **1**, indolizine **87** (R = H; X = C; Y = COPh) and the pyridinium salt **90**, the latter on heating under reflux in dimethylformamide giving a mixture of the former two compounds[40]. Had the pyridinium phenacylide ($Z\overline{C}H$-Py^+), generated by base treatment of *N*-phenacylpyridinium bromide, undergone a concerted cycloaddition to the 2,3-olefinic bond of **2a** (or **2d**), the indolizine **87** (R = H; X = C; Y =COPh) would have been exclusively formed by base-catalysed deformylative (or decarboxylative) pyran ring opening of the initially formed cycloadduct **88** (X = CHO or CO_2H) and subsequent dehydrogenation. The other two products **1** and **90** emerge from the Michael addition of phenacylide to **2a** (or **2c**) (Scheme II); the resultant Michael adduct **89** (X = CHO or CO_2H) gives **90** by deformylative (or decarboxylative) opening of the pyran ring (path a) and chromone **1** by elimination of the nucleofugal phenacylide (path b). It should be mentioned here that neither the nitrile **6** nor the corresponding ester **55** (R = OEt; R^1 = H) gives with *N*-pyridinium



Scheme II

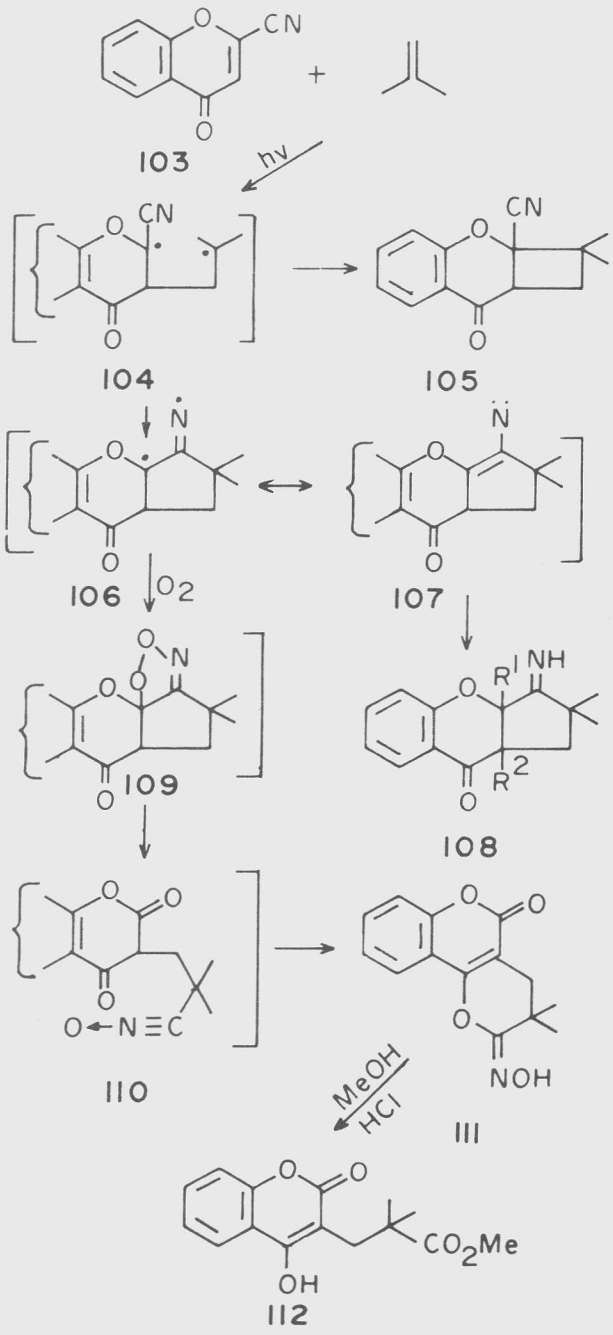
phenacylide any [3+2] cycloadduct or any product arising therefrom. 1,2-Addition of the phenacylide to the nitrile functionality of **6** followed by cyclisation and isomerisation gives the 2-azirine **91** which due to extended π- conjugation is more stable than the corresponding 1-azirine[40]. Base-catalysed Michael addition of *N*-phenacylpyridinium bromide to the ester **55** (R = OEt; R^1 = H) is accompanied by pyran ring opening, recyclisation and hydrogen bromide elimination giving the zwitterion **92** as the final product[40].

III. 3. Reactions with other 1,3-dipoles. Diphenylnitrilimine **93** (R = Ar′=Ph; Y = bond) reacts with chromone **1** giving the adduct **94** (X = O) in exclusion of the [3+2] cycloadduct **95** (X = O)[41]. This is in contrast to the formation of **95** (Y = S) from 1-benzopyran-4-thione and diphenyl-nitrilimine but in conformity with the reaction between the above thione and benzonitrile oxide[42]. Benzonitrile oxide adds across the azomethine function of **35** leaving its pyrone olefinic bond intact so as to form the 1,2,4-oxadiazolidine **96**[43] whereas the nitrilimine **93** [R = Me, OEt; Y = CO; Ar^1 = C_6H_4-Me (or Br)-*p*] undergoes both [3+2]- and [4+3]-cycloadditions with **35** to give the 1,2,4-triazoline **97** and benzopyranotriazepin **98**, respectively[44]. The nitrile oxide **99** (R = Me, Ph) and the nitrilimine **100** containing chromone moiety do not undergo electrocyclisation but undergo cycloaddition with the appropriate alkene CH_2=CHR^1 (R^1 = CH_2Br, COMe, CN, Ph, CO_2Me) giving the isoxazolidine **101**[44] and the pyrazoline **102**[43], respectively.



III. 4. Photochemical addition. Unlike the unsubstituted and 2,3-alkyl substituted chromones (*vide* section IV. 2), 2-cyanochromone **103** when irradiated in the presence of an alkyl substituted ethylene under nitrogen atmosphere produces the [3+2]cycloadduct together with a minor amount of normal [2+2] cycloadduct. Raising the reaction temperature gives an increased yield of the former at the expense of the latter. Thus, 2-

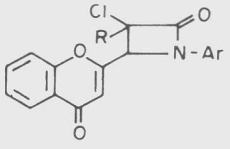
cyanochromone on irradiation with isobutene in methanol gives the cyclobutane **105** (12%) and the imine **108** (R^1R^2 = bond) (81%), the latter spontaneously hydrolysing to the corresponding ketone during work-up. The formation of the [3+2] cycloadduct involves the vinylnitrene intermediate **107** (Scheme III). 2-Cyano-3-methylchromone under similar conditions affords **108** (R^1 = OMe; R^2 = Me) as the major product[45]. However, a methanolic solution of **103** and isobutene on irradiation under oxygen bubbling produces the pyranocoumarin **111** (55%) with the yield of **105** (13%) being unchanged. Here the five-membered iminyl biradical **106**, a precursor of the [3+2] cycloadduct like **108**, is intercepted by the ground state triplet oxygen giving rise to the cyclic peroxide **109**. Subsequent ring cleavage of **109** forms the nitrile oxide **110** which by enolisation and internal addition gives **111** (Scheme III). This compound on acid treatment affords the coumarin **112**[46].



Scheme III

IV. [2+2] Cycloaddition

IV. 1. Chemical reaction. No report on chemical [2+2] cycloaddition with the chromone 2,3-double bond has appeared as yet. A keten adds across the azomethine double bond of 2-(aryliminomethyl)chromone **85** (R = CH = NAr). Thus, the aforesaid imine gives a 1:1 isomeric mixture of the azetidin-2-one **113** (R = H) with monochloroketen, and **113** (R = Cl) with dichloroketen[28]. The formation of the azetidine derivative **114** from the imine **35** and *N*-aroylalanine in the presence of chlorosulfonyl-methylene(dimethyl)-ammonium chloride does not involve any keten tautomer of the oxazolinone derived from the aroylalanine[47].



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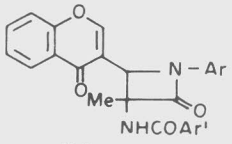

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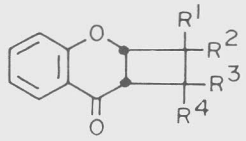
IV.2. Photochemical addition. Photoaddition reactions of chromone with different alkenes and alkynes leading to [2+2] cycloaducts have been extensively studied by Hanifin and Cohen[48]. As for example, chromone **1** on irradiation with 2,3-dimethylbut-2-ene, cyclopentene and 1,1-dimethoxyethylene gives respectively the cyclobutachromanone **115** (R^1-R^4 = Me), **115** (R^1 = R^3 = α-H; R^2R^4 = $CH_2CH_2CH_2$) and **115** (R^1 = R^2 = OMe; R^3 = R^4 = H) together with some minor products. Under similar conditions, **1** with 2-butyne gives the cyclobutenochromanone **115** (R^1R^3 = bond; R^2 = R^4 = Me). The mechanism of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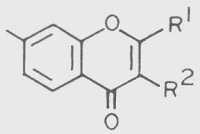
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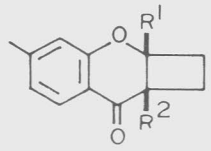
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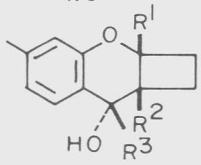
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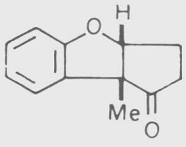
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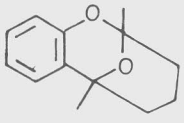
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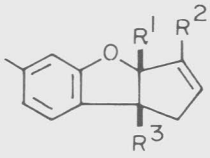
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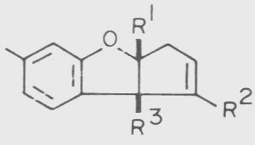
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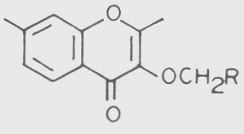
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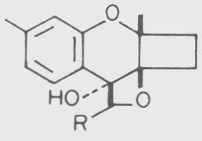
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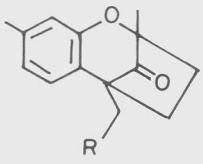
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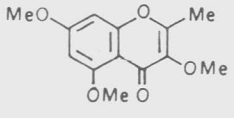
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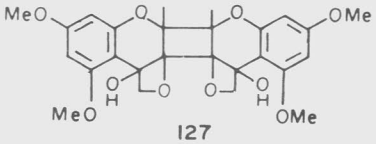
127

these additions involves an electrophilic attack by C-3 of the $n\rightarrow\pi^*$ chromone triplet on the extramolecular multiple bond, the resultant 1,4-diradical closing to the cyclobutane or cyclobutene. The minor products arise from initial hydrogen abstraction from the olefin by carbonyl oxygen of the excited chromone or by photoaddition of the second molecule of the olefin across the pyrone carbonyl group of **115**.

An Indian group[49-52] has shown that ethylene undergoes *cis*-[2+2]-cycloaddition to the 2,3-olefinic bond of 2,3-unsubstituted as well as substituted chromones like **116** under UV irradiation; the resultant cyclobutachromanone **117** on hydride reduction or Grignard addition gives the cyclobutachromanol with relative stereochemistry as shown in **118**. Rearrangement of **118** leads to the compounds with interesting structural frameworks as featured in several natural products. Thus, the [2+2]cycloadduct, derived from 3-methylchromone and ethylene, on hydride reduction, acid catalysed (*p*-toluenesulfonic acid in benzene) rearrangement and oxidation (dimethyl-sulphoxide) gives the tricyclic ketone **119** as the major product[49]. Boron trifluoride etherate in benzene rearranges the chromanol **118** ($R^1 = R^3$ =Me; R^2 =H) to the benzo-1,3-dioxane **120**[50] and furnishes with **118** (R^1-R^3 = Me) a mixture of the cycloalkenes **121** and **122**[51]. Rearrangement of **118** (R^1-R^3 = Me) with sulphuric acid in pet. ether at –78°C furnishes **121** almost exclusively whereas the same reaction in nitroethane at –78°C affords **122** exclusively[51]. Compound **121** (R^1-R^3 = Me) is an advanced precursor of the marine sesquiterpenes debromoaplysin and aplysin. The photoadduct **124**, obtained by photoaddition of 3-alkoxy-2,7-dimethylchromone **123** (R = H, Me) with ethylene, on lithium aluminium hydride reduction and boron trifluoride catalysed rearrangement affords the benzooxabicyclo[3.2.1]-octane **125**, the bridged ketone **125** (R = H) being a synthon for the marine sesquiterpenes filiformin and aplysin[52].

Unlike thiochromone[53], simple chromones are less susceptible to photodimerisation but 3,5,7-trimethoxy-2-methylchromone **126** is converted to a dimer of the probable structure **127**[54].

Acknowledgement

Financial assistance from CSIR, New Delhi is duly acknowledged.

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