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A Facile Synthesis of 2-Benzoyl-3-methyl-6-phenyl-5-(substituted Styryl)-7H-furo [3,2-g] [1] Benzopyran-7-ones and Their Antifeedant Activity.

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A FACILE SYNTHESIS OF 2-BENZOYL-3-METHYL-6-PHENYL-5-(SUBSTITUTED STYRYL)-7H-FURO [3,2-g] [1] BENZOPYRAN-7-ONES AND THEIR ANTIFEEDANT ACTIVITY.

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Abstract : The synthesis, characterisation and antifeedant activity of some new furocoumarins prepared from 4,6-diacetyl resorcinol has been reported.

Several benzopyran derivatives are known to exhibit physiological properties[1-3] like antibacterial, anticoagulant, vasodilatory, diuretic and respiratory, stimulant activities. Furocoumarins are known to be effective in the treatment of leucoderma, due to high photosensitive activity of these compounds[4,5], certain natural furocoumarins such as psoralen, bergaptan possess dermal photosensitising activity and are used in the treatment of vtiligo, psoriasis and other dermal diseases[6]. Trioxasaten was found to exhibit photodynamic activity[7] and also remarkable antifeedant activity[8]. Literature survey revealed that the synthesis and antifeedant activity of the title compounds have not been reported so for. Therefore in the present investigation the synthesis of some new 2-benzoyl-3-methyl-6-phenyl-5-(substituted styryl)-7H-furo [3,2-g] [1] benzopyran-7-ones have been taken up with a view to study the effect of styryl substituted furocoumarin moiety on their antifeedant activity.

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The required starting materials, the cinnamoyl benzofurans (**3a-f**) were prepared by the condensation of 4,6-diacetyl resorcinol[9] (**1**) with ω-bromo acetophenone[10] (1:1) in the presence of acetone, anhydrous K_2CO_3 medium to yield 5-acetyl-2-benzoyl-6-hydroxy-3-methyl benzofuran[11] (**2**), which on condensation with aromatic aldehydes in the presence of 60% aq KOH and are characterised by comparision with authentic samples[12].

In the present investigation an alternative and more facile approach involving phase transfer catalysis method[13] has been explored by using tetrabutyl ammonium hydrogen sulphate ($TBAHSO_4$) as catalyst, benzene as solvent and K_2CO_3 as a base. The products obtained in these reactions were characterised as 2-benzoyl-3-methyl-6-phenyl-5-(substituted styryl)-7H-furo [3,2-g] [1] benzopyran-7-ones (**4 a-f**) on the basis of analytical and spectral data.

To authenticate the structures of (**4 a-f**) they were also synthesised unambiguously by adopting Baker-Venkatraman transformation method[14]. In this method the 2-benzoyl-5-cinnamoyl-6-hydroxy-3-methyl benzofurans (**3 a-f**) were refluxed with phenyl acetyl chloride in dry acetone-anhydrous K_2CO_3 medium for 8 hours. Workup of the reaction mixture yielded the corresponding 2-benzoyl-3-methyl-6-phenyl-5-(substituted styryl)-7H-furo [3,2-g] [1] benzopyran-7-ones (**4 a-f**). As a representative case the spectral identification of 2-benzoyl-3-methyl-6-phenyl-5-(p-chloro styryl)-7H-furo [3,2-g] [1] benzopyran-7-one (**4b**) mp 233°C, $C_{33}H_{21}O_4Cl$, M^+ 516 has been discussed.

The IR spectrum of **4b** showed a sharp peak at 1720 cm^{-1} which is characteristic of carbonyl group of the coumarin[15], another sharp peak observed at 1640 cm^{-1} was assigned to carbonyl group of benzoyl moiety. The UV spectrum of **4b** λ_{max}^{MeOH} 207nm (log ε 3.87), 225 (log ε 3.77), 274 (log ε 3.33). These absorption maxima are characteristic of coumarins reported in literature[16].

The ^{1}H-NMR spectrum (200 MHz, $CDCl_3$) of **4b** showed a multiplet between δ7.1-7.4 integrating for 12 protons for C_6 phenyl and styryl

group, another multiplet appeared at 7.5-7.8 integrating for 5 protons for benzoyl group. The spectrum also revealed two singlets at 8.1 and 6.8 integrating for one proton each assignable to H-4 and H-9 respectively. The spectrum exhibited one singlet at 2.6 integrating for 3 protons for C_3-methyl group.

The mass spectrum of **4b** showed molecular ion peak at m/z 516 (30%) which is consistant with its molecular formula $C_{33}H_{21}O_4Cl$. The other fragment ions at m/z 488 (10%) (M-CO), 405(40%) (M-C_6H_4Cl), 399(10%), 105(100%), 77(80%) were highly diagnostic[17]. On the basis of the above analytical and spectral data, compound **4b** has been characterised as 2-benzoyl-3-methyl-6-phenyl-5-(p-chloro styryl)-7H-furo [3,2-g] [1] benzopyran-7-one.

Following the above method several substituted styryl furocoumarins (**4a-f**) were synthesised and their analytical and spectral data are given in table. This method is an one-step reaction, the conditions are mild, there was no significant substituent effect on the reaction, the yields are good to excellent and byproducts were not detected.

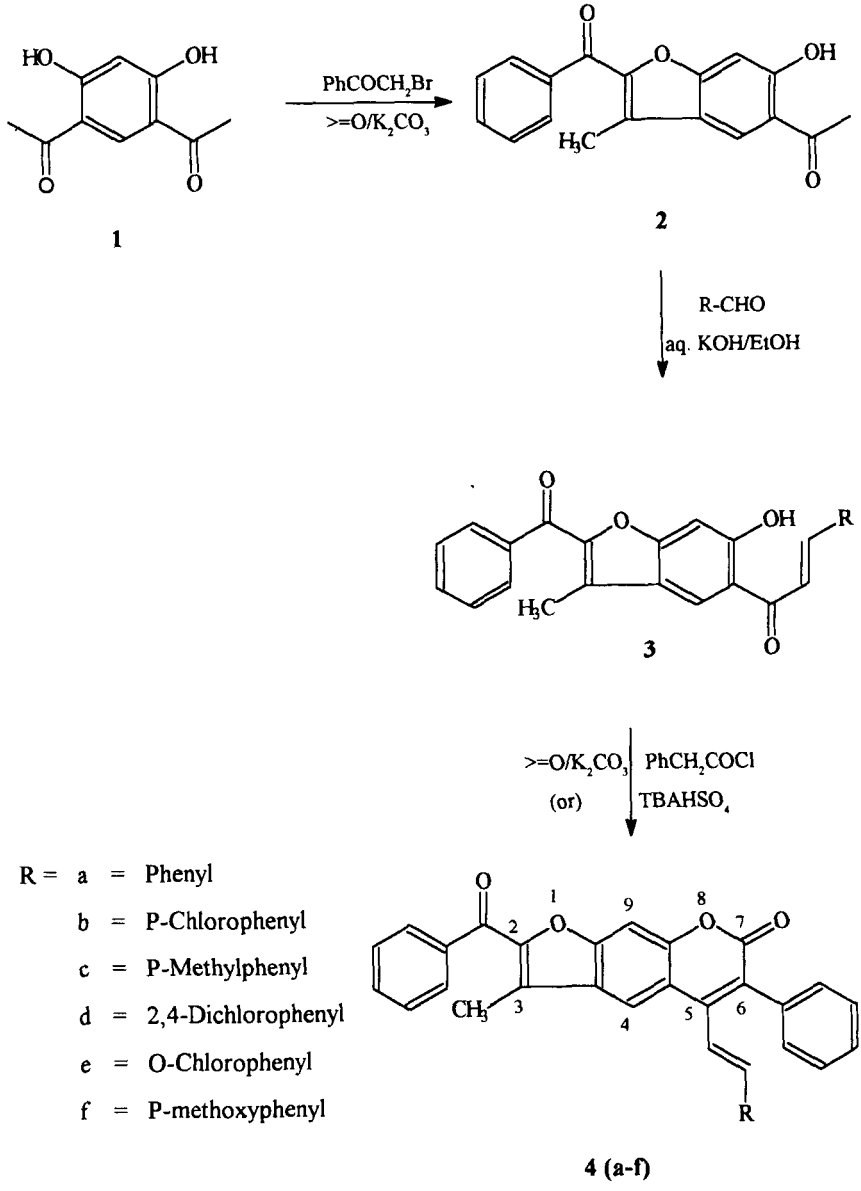
All the compounds **(4 a-f)** were tested for their antifeedant activity by the "Non-choice test method"[18] using 6 hrs prestarved fourth instar larvae of Spodoptera litura, and the results are shown in Table. Compounds **4a** and **4d** exhibited highest antifeedant activity.

Experimental

Cinnamoyl benzofurans (3 a-f) : General Procedure

A mixture of **1** and ω-bromo acetophenone (1:1 mole) refluxed in presence of acetone, anhydrous K_2CO_3 for 6hrs, after recovering excess acetone the contents poured over crushed ice. The solid separated was filtered washed with water and extracted with hot 5% NaOH solution. The crude product was obtained on neutralisation with dil Hcl. It was crystallised from MeOH afforded comp. **2**. A mixture of **2** (0.01 mole)

SCHEME



TABLE

Analytical and Spectral data of the title compounds (4 a-f)

Compound No.		Molecular formula	M^+	MP °C	Yield (%) >=0/K_2CO_3	Yield (%) PTC	υIR (KBr) C=0 str cm^{-1}	UV(MeOH) λmax nm (logε)	Antifeedant activity (%)
4	a	$C_{33}H_{22}O_4$	482	167	69	84	1722	262(3.30)	97.60
	b	$C_{33}H_{21}O_4Cl$	516	233	65	87	1720	225(3.77)	90.14
	c	$C_{34}H_{24}O_4$	496	180	71	91	1705	274(3.51)	90.44
	d	$C_{33}H_{20}O_4Cl_2$	550	240	63	87	1700	228(3.99)	97.66
	e	$C_{33}H_{21}O_4Cl$	516	246	58	89	1710	261(3.15)	82.98
	f	$C_{34}H_{24}O_5$	512	178	66	90	1710	268(3.48)	89.00

All the compounds gave satisfactory elemental analysis.

and appropriate aldehyde (0.01 mole) in ethanol (40 ml) and aq KOH (60%, 20ml) was kept at room temperature for 24 hrs. The product obtained on dilution and acidification with dil HCl was subjected to column chromatography over silicagel (200 mesh) Benzene : Chloroform (6:4 v/v) eluates on concentration afforded comp. **3**.

Synthesis of 2-benzoyl-3-methyl-6-phenyl-5-(substituted styryl)-7H-furo [3,2-g] [1] benzopyran-7-ones:

a) By Phase Transfer Catalysis Method: General Procedure:

To a stirred solution of substituted cinnamoyl benzofurans (**3 a-f**) (0.01 mole) and phenyl acetyl chloride (0.02 moles) in dichloromethane, 30% of aq K_2CO_3 (100ml) and tetrabutyl ammonium hydrogen sulphate ($TBAHSO_4$) 150mg was added dropwise with stirring during a period of 15 mts. Stirring was continued for 4-5 hrs at room temperature The organic layer was separated and washed with water (4x100ml) and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure and solid was subjected to column chromatography over silicagel (acme, 200 mesh), Chloroform : Ethyl acetate (8:2 v/v) eluates on concentration afforded compound **4**, which was further crystallised from methanol.

b) Baker-Venkatraman transformation method: General Procedure:

To a solution of substituted cinnamoyl benzofurans (**3a-f**) (0.01 mole) and phenyl acetyl chloride (0.02 moles) in dry acetone (200 ml) and anhydrous K_2CO_3 (5.0 gm) was added and the mixture was refluxed for 8hrs on steam bath. At the end of the reaction the acetone solution was filtered and potassium carbonate residue was washed with acetone, the combined acetone solution was distilled under reduced pressure. The crude product was washed with cold water, dried and it was subjected to column chromatography over silicagel (aceme, 200 mesh) Chloroform : Ethyl acetate (1:1 v/v) eluates on concentration afforded comp. **4**, which was further crystallised from methanol.

NMR data of the title compounds (4a-f):

4a : (200MHz, $CDCl_3$) δ7.2-7.4 (12H, m, aromatic protons of C_6 phenyl and styryl group) 7.5-7.6 (5H, m, benzoyl protons), 2.6 (3H, s, C_3-CH_3), 8.1 (1H, s, C_4-H), 6.8 (1H, s, C_9-H).

4b : (200MHz, $CDCl_3$) δ7.1-7.4 (11H, m, aromatic protons of C_6 phenyl and styryl group), 7.5-7.8 (5H, m, benzoyl protons), 2.6 (3H, s, C_3-CH_3), 8.1 (1H, s, C_4-H), 6.8 (1H, s, C_9-H).

4c : (200 MHz, $CDCl_3$) δ7.1-7.4 (11H, m, aromatic protons of C_6 phenyl and styryl group), 7.45-7.58 (5H, m, benzoyl protons), 2.65 (3H, s, C_3-CH_3), 2.32(3H, s, Ar-CH_3), 8.12 (1H, s, C_4-H), 6.78 (1H, s, C_9-H).

4d : (200 MHz, $CDCl_3$) δ7.15-7.6 (15H, m, aromatic protons), 2.72 (3H, s, C_3-CH_3), 8.2 (1H, s, C_4-H), 6.75 (1H, s, C_9-H).

4e : (200 MHz, $CDCl_3$) δ7.2-7.5 (11H, m, aromatic protons of C_6 phenyl and styryl group), 7.52-7.70 (5H, m, benzoyl protons), 2.7 (3H, s, C_3-CH_3), 8.3 (1H, s, C_4-H), 6.82 (1H, s, C_9-H).

4f : (200 MHz, $CDCl_3$) δ7.22-7.6 (11H, m, aromatic protons of C_6 phenyl and styryl group), 7.62-7.78 (5H, m, benzoyl protons), 2.7 (3H, s, C_3-CH_3), 3.82 (3H, s, Ar-OCH_3), 8.3 (1H, s, C_4-H) 6.84 (1H, s, C_9-H).

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