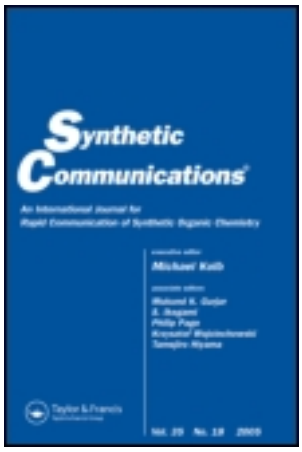

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A FACILE SYNTHESIS OF 2-BENZOYL-3-METHYL-6-SUBSTITUTED ARYL-5H-FURO [3,2-g] [1] BENZOPYRAN-5-ONES

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A FACILE SYNTHESIS OF 2-BENZOYL-3-METHYL-6-SUBSTITUTED ARYL-5*H*-FURO [3,2-g] [1] BENZOPYRAN-5-ONES

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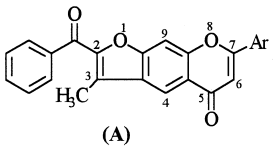
ABSTRACT

The synthesis and characterisation of some new furo-isoflavones prepared from 4, 6-diacetylresorcinol is reported.

In continuation of our interest in exploring synthetic heterocyclic compounds as potential antifeedants, we have synthesised a number of furocoumarins,[1] distyryl benzodifurans,[2] angular benzodifurans,[3] styryl benzodifurans,[4] 1,5-benzothiazepines,[5] pyrazolines,[6] 1,5-benzodiazepines,[7] benzothiazoles[8] and tested for their antifeedant activity.



(A)

Recently from our laboratory, we have synthesised several furoflavones (A) i.e., 2-benzoyl-3-methyl-7-substituted aryl-5*H*-furo[3,2-g][1]

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benzopyran-5-ones[9] and tested for their antifeedant activity. Among them 2-benzoyl-3-methyl-7-phenyl-*5H*-furo[3,2-g][1]benzopyran-5-one exhibited highest antifeedant activity against *Spodoptera litura* F. which destroys commercial crops like castor, cabbage, grapes etc. All the furoflavones tested earlier for their antifeedant activity contained aryl group at C-7 position. To understand the effect of aryl group at C-6 position on antifeedant activity, it was thought worthwhile to take up the synthesis of some new furoisoflavones i.e., 2-benzoyl-3-methyl-6-substituted aryl-*5H*-furo[3,2-g][1] benzopyran-5-ones (**6a–h**) possessing aryl group at C-6 position. Thus the synthesis of some new furoisoflavones was undertaken in the present investigation, with a view to test their antifeedant activity. Till now nobody has reported the synthesis of title compounds.

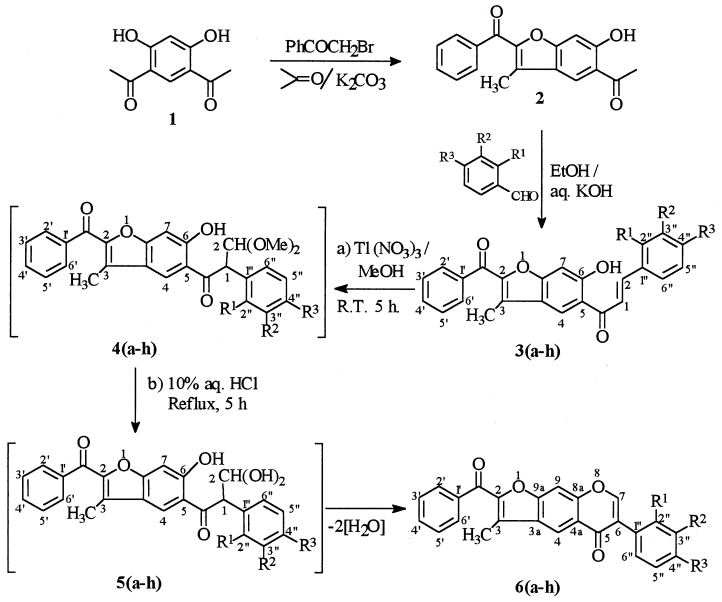
The required precursors, 2-benzoyl-5-substituted cinnamoyl-6-hydroxy-3-methyl benzofurans (**3a–h**) were prepared by the condensation of 4,6-diacetylresorcinol[10] (**1**) with ω-bromoacetophenone[11] (1:1) in acetone in the presence of anhydrous K_2CO_3 to yield 5-acetyl-2-benzoyl-6-hydroxy-3-methyl benzofuran[12] (**2**), followed by condensation of **2** with aromatic aldehydes in the presence of 60% aq. KOH. Compounds **3(a–h)** were characterised by comparison with authentic samples.[1]

To a solution of α, β-unsaturated ketones (cinnamoyl benzofurans (**3a–h, 1** mmol) in analytical grade methanol (200 ml), thallium(III) nitrate (2 mmol) was added in small portions and stirred at room temperature for 5 h. They were monitored by TLC. At the end of the reaction in each case the methanol solution containing the acetal[15] (**4a–h**) was treated with 10% aq. hydrochloric acid and the mixture was refluxed on a steam bath for 5 h. Work-up of the reaction yielded crude product which was crystallised from methanol as yellow crystals (**6a–h**). As a representative case the spectral identification of 2-benzoyl-3-methyl-6-(3,4-dimethoxy phenyl)-*5H*-furo [3,2-g] [1] benzopyran-5-one (**6g**) is discussed.

The **IR** spectrum of compound **6g** exhibited broad absorption band at 1649 cm^{-1} suggesting the presence of a carbonyl group characteristic of simple isoflavones.[13] The spectrum also exhibits another broad absorption band due to benzoyl carbonyl group at 1702 cm^{-1}. The UV spectrum of the compound **6g** in methanol exhibited absorption maxima at 297 nm (log ε 4.75) and 368 nm (log ε 4.92) which are characteristic of simple isoflavones.[13]

The ^{1}H-NMR spectrum of **6g** strongly suggests 2-benzoyl-3-methyl-6-(3,4-dimethoxyphenyl)-*5H*-furo[3,2-g][1]benzopyran-5-one structure. The spectrum showed a singlet integrating for one proton in the downfield at δ 8.47. This signal was assigned to the proton at C-7 position and it was the characteristic proton of furoisoflavone skeleton formed after 1,2-aryl shift and simultaneous condensation[15] of the 2-benzoyl-5-(3,4-dimethoxycinnamoyl)-3-methyl-6-hydroxy benzofuran (**3g**) in thallium(III)

nitrate-methanol mediated reaction. The spectrum also revealed the presence of one sharp singlet at δ 7.09 integrating for one proton which was attributed to H-9. The spectrum contained two double doublets in the aromatic region. The first one which appeared at δ 7.38 (J = 9.8, 2 Hz) integrating for one proton was assigned to H-6″. Another double doublet which appeared at δ 8.34 (J = 9.8, 2 Hz) integrating for two protons was attributed to H-2′,6′. One sharp doublet observed at δ 6.97 (J = 9.8 Hz) integrating for one proton was assigned to H-5″. The spectrum also exhibits two multiplets, the first one appeared between δ 7.52–7.70 for three protons was assigned to H-3′,4′,5′. The second multiplet appeared at δ 8.08 integrating for two protons was attributed to H-4, 2″. The aliphatic region of the spectrum contained three singlets at δ 2.78, 3.98 and 4.12 integrating for three protons, each was attributed to C-3 (CH_3), C-3″ (OCH_3), C-4″ (OCH_3) respectively.



	a	b	c	d	e	f	g	h
R^1	H	H	H	H	H	Cl	H	H
R^2	H	H	H	H	H	H	OCH_3	O–CH_2–O
R^3	H	CH_3	OCH_3	Cl	F	H	OCH_3	

Scheme.

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The mass spectrum of the compound **6g** exhibited the molecular ion peak at m/z 440 (88%), consistent with its molecular formula $C_{27}H_{20}O_6$. In the mass spectrum of furoisoflavone, the observed isoflavone ring fragmentation is in agreement with those reported for simple isoflavones.[14] The prominent ion fragments observed at m/z 439 (M-H, 19%), 425 (6%), 278 (8%), 162 (7%), 129 (10%), 105 (26%) and 77 (27%) are highly diagnostic and supports furoisoflavone structure. The ^{13}C-NMR spectrum of **6g** exhibited 24 signals corresponding to 27 carbons. The characteristic signals at δ 184.30 (carbonyl carbon of C-2 benzoyl group), 180.15 (C-5 carbonyl carbon), 56.76 (C-3″, OCH_3), (C-4″, OCH_3) and 9.87 (C-3, CH_3) confirmed its structure. On the basis of above analytical and spectral data the compound **6g** has been characterised as 2-benzoyl-3-methyl-6-(3,4-dimethoxyphenyl)-5*H*-furo[3,2-g][1]benzopyran-5-one.

Following the above method several furoisoflavones (**6a–h**) were synthesised and their analytical and spectral data are given in table. This method is one step reaction, the conditions are mild, there was no significant substituent effect on the reaction, the yields are good to excellent and by-products were not detected.

EXPERIMENTAL

Melting points were taken in open capillary tubes in sulfuric acid-bath and are uncorrected. FT-IR spectra were obtained on Perkin-Elmer 1605 spectrophotometer. UV spectra were obtained on a Hitachi U-3410 spectrometer. ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50.3 MHz) spectra were taken

Table. Analytical and Spectral Data of Title Compounds (**6a–h**)

				IR KBr cm^{-1}			
Compd.	M^+	m.p (°C)	Yield (%)	C=O str	Benzoyl C=O str	UV(MeOH) nm (log ε)	
6a	380	192	61	1640	1676	282 (4.68)	341 (4.86)
6b	394	168	68	1642	1670	298 (4.53)	347 (4.78)
6c	410	186	65	1646	1690	290 (4.70)	352 (4.94)
6d	414	173	63	1648	1690	294 (4.60)	356 (4.80)
6e	398	169	69	1642	1685	290 (4.58)	358 (4.79)
6f	414	176	76	1645	1688	296 (4.65)	360 (4.80)
6g	440	198	78	1649	1702	297 (4.75)	368 (4.92)
6h	424	162	72	1648	1686	294 (4.80)	364 (4.96)

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in $CDCl_3$ on Varian Gemini 200 MHz spectrometer with TMS as internal standard (chemical shifts in δ, ppm). **EI** mass spectra were obtained on V.G. Micromass 70–70H instrument. Column chromatography was carried out using silica gel (200 mesh).

Synthesis of 2-Benzoyl-5-substituted Cinnamoyl-6-hydroxy-3-methyl Benzofurans (3a–h): General Procedure

An equimolar mixture of **1** (1.94 g) and ω-bromoacetophenone (1.99 g) was refluxed in acetone (50 ml) in the presence of anhydrous K_2CO_3 (5 g) for 6 hr. After distillation of the acetone in vaccum, the contents were poured over crushed ice. The solid separated was filtered, washed with water and extracted with hot 5% NaOH (3 × 40 ml) solution. The crude product was obtained on neutralisation with 5% dil. HCl. It was crystallised from methanol to afford the compound **2**. A mixture of **2** (0.01 mole) and the appropriate aldehyde (0.01 mole) in ethanol (40 ml) and aq. KOH (60%, 20 ml) was stirred at room temperature for 24 h. The product in each case obtained on dilution and neutralisation with dil. HCl was subjected to column chromatography over silica gel (18 cm × 3 cm, 200 mesh). Benzene-chloroform (6:4, 3 × 40 ml) eluates on concentration afforded yellow coloured crystalline compounds (**3a–h**).

Synthesis of 2-Benzoyl-3-methyl-6-substituted Aryl-5*H*-furo[3,2-g][1]benzopyran-5-ones (6a–h): General Procedure

A mixture of 2-benzoyl-5-substituted cinnamoyl-6-hydroxy-3-methyl benzofurans (**3a–h**, 1 mmol) in analytical grade methanol (200 ml) and thallium(III) nitrate (4.44 g, 2 mmol) was stirred at room temperature for 5 h. The reaction in each case was monitored by TLC. At the end of the reaction period, the methanol solution containing the acetal[15] was treated with 10% aq. HCl (15 ml) and the mixture was refluxed on steam bath for 5 h. Removal of the solvent under reduced pressure yielded yellow coloured solids which were crystallised from methanol as yellow crystals (**6a–h**).

5a: ^{1}**H-NMR** (200 MHz, $CDCl_3$): δ 2.6 (3H, s, CH_3-3), 7.0 (1H, s, H-9), 7.3–7.8 (8H, m, aromatic protons), 8.1 (1H, s, H-4), 8.3 (2H, dd, J = 9.2, 2 Hz, H-2′, 6′), 8.5 (1 H, s, H-7); Anal. calcd. for $C_{25}H_{16}O_4$: C, 78.94; H, 4.21; found: C, 78.90; H, 4.22%.

5b: ^{1}**H-NMR** (200 MHz, $CDCl_3$): δ 2.5 (3H, s, CH_3-3), 2.8 (3H, s, CH_3-Ar), 7.1 (1H, s, H-9), 7.3–7.4 (2H, m, H-3″, 5″), 7.6–7.7 (3 H, m, H-3′,4′,5′), 8.0 (2H, m, H-2″, 6″), 8.2 (1H, s, H-4), 8.3 (2H, dd, J = 8.8,

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2 Hz, H-2′,6′), 8.4 (1H, s, H-7); Anal. calcd. for $C_{26}H_{18}O_4$: C, 79.18; H, 4.56; found: C, 79.15; H, 4.55%.

5c: **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 2.5 (3H, s, CH_3-3), 3.8 (3H, s, Ar-OCH_3), 7.1 (1H, s, H-9), 7.4–7.4 (2H, m, H-3″,5″), 7.6–7.7 (3H, m, H-3′, 4′,5′), 8.0 (2H, m, H-2″,6″), 8.1 (1H, s, H-4), 8.3 (2H, dd, J = 9.2, 2 Hz, H-2′,6′), 8.5 (1H, s, H-7); Anal. calcd. for $C_{26}H_{18}O_5$: C, 76.09; H, 4.39; found: C, 76.05; H, 4.37%.

5d: **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 2.5 (3H, s, CH_3-3), 7.1 (1H, s, H-9), 7.3–7.4 (2H, m, H-3″,5″), 7.6–7.7 (3 H, m, H-3′,4′,5′), 8.0 (2H, m, H-2″,6″), 8.2 (1H, s, H-4), 8.3 (2H, dd, J = 8.6, 2 Hz, H-2′,6′), 8.4 (1H, s, H-7); Anal. calcd. for $C_{25}H_{15}O_4Cl$: C, 72.46; H, 3.62; found: C, 72.48; H, 3.60%.

5e: **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 2.6 (3H, s, CH_3-3), 7.1 (1H, s, H-9), 7.3–7.4 (2 H, m, H-3″,5″), 7.6–7.7 (3H, m, H-3′,4′,5′), 8.0 (2H, m, H-2″,6″), 8.2 (1H, s, H-4), 8.3 (2H, dd, J = 8.8, 2 Hz, H-2′, 6′), 8.4 (1H, s, H-7); Anal. calcd. for $C_{25}H_{15}O_4F$: C, 75.37; H, 3.76; found: C, 75.35; H, 3.77%.

5f: **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 2.6 (3H, s, CH_3-3), 7.1 (1H, s, H-9), 7.4–7.8 (7H, m, aromatic protons), 8.0 (1H, s, H-4), 8.3 (2H, dd, J = 8.8, 2 Hz, H-2′,6′), 8.5 (1H, s, H-7); Anal. calcd. for $C_{25}H_{15}O_4Cl$: C, 72.46; H, 3.62; found: C, 72.42; H, 3.60%.

5g: **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 2.7 (3H, s, CH_3-3), 3.9 (3H, s, OCH_3-3″), 4.1 (3H, s, OCH_3-4″), 6.9 (1H, d, J = 9.8 Hz, H-5″), 7.0 (1H, s, H-9), 7.3 (1H, dd, J = 9.8, 2 Hz, H-6″), 7.5–7.7 (3H, m, H-3′,4′,5′), 8.0 (2H, m, H-4,2″), 8.3 (2H, dd, J = 9, 2 Hz, H-2′,6′), 8.4 (1H, s, H-7); ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ 9.87 C-3 (CH_3), 56.76 (C-3″ OCH_3 and C-4″-OCH_3), 99.52 (C-9), 107.46 (C-6), 111.02, 112.98, 119.80 (C-4a), 122.08 127.28 (C-3a), 127.86 (C-4), 128.80, 129.54, 129.90, 131.96, 136.40, 141.40 (C-2), 143.66, 149.92, 150.86, 155.68 (C-8a), 162.46 (C-9a), 165.68 (C-7), 180.15 (C-5) and 184.30 (carbonyl carbon C-2 benzoyl group); Anal. calcd. for $C_{27}H_{20}O_6$: C, 73.63; H, 4.56; found: C, 73.60; H, 4.52%.

5h: **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 2.7 (3H, s, CH_3-3), 6.1 (2H, s, O-CH_2-O), 6.9 (1H, d, J = 9.5 Hz, H-5″), 7.1 (1H, s, H-9), 7.3–7.7 (4H, m, aromatic protons), 8.0 (2H, m, H-4,2″), 8.3 (2H, dd, J = 9.2, 2 Hz, H-2′,6′), 8.5 (1H, s, H-7); Anal. calcd. for $C_{26}H_{16}O_6$: C, 73.58; H, 3.77; found: C, 73.55; H, 3.75%.

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