NOVEL ANGULAR FURANOCOUMARINS: SYNTHESIS OF 8-AROYL-9-STYRYL FUROBENZOPYRAN-2-ONES

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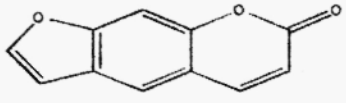
Abstract:

Novel angular furanocoumarin derivatives viz., 8-aroyl-9-styryl furopyran 2-ones (**9 a-j**) have been synthesized smoothly from 7-hydroxy α –pyrano chalcones (**7 a-d**) and phenacyl bromides. The required intermediates, pyrano chalcones, were prepared from 8-acetyl-7-hydroxy-4-methyl coumarins and substituted benzaldehydes. The structures of the title compounds (**9 a-j**) were established from evidences like IR, NMR and mass spectral data

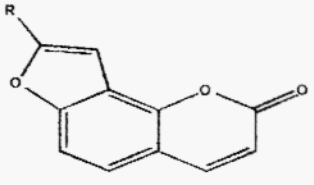
Introduction:

Furanocoumarins are natural products showing a wide range of biological properties. Many are potent photosensitizers of human skin, with valuable applications in medicine for treatment of skin

Figure 1



1 Psoralen



2 Angelicin H
3 Oroselone $CH_2=C(CH_3)$-
4 Oroselol $(CH_3)_2(OH)C$-

diseases

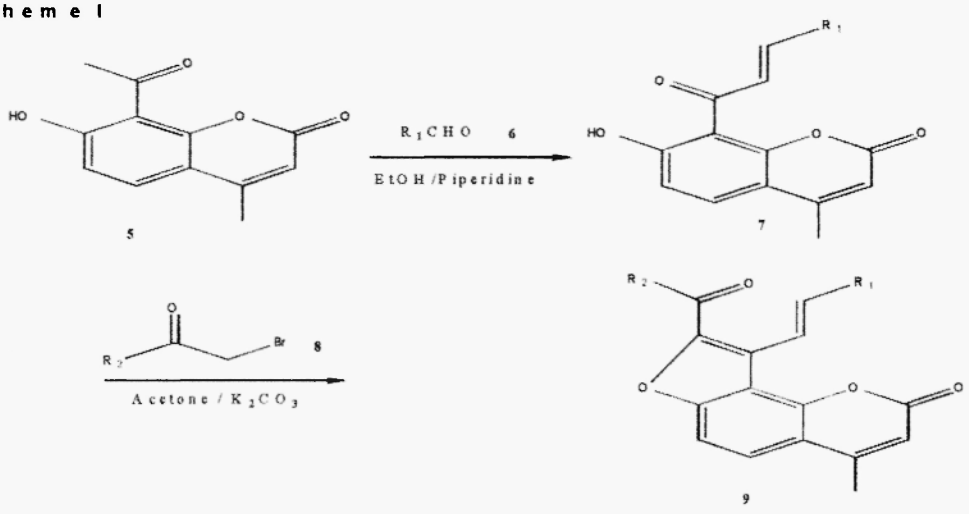
e.g., psoriasis and vitiligo[1,2,3] . They are also known to be phototoxic to insects, fungi, viruses and bacteria[4-7] . Furanocoumarins like Psoralin (**1**) have a linearly fused ring structure whereas Angellicin (**2**), Oroselone (**3**) and Oroselol (**4**) have an angular structure [Fig 1]. This structural difference has important consequences in their ability to interchelate between base pairs of nucleic acids and crosslink them by [2+2] photocycloaddition with pyrimidine base[8,9] which leads to mutagenicity and carcinogenicity [10]. Angelicin, because of its angular geometry can not crosslink DNA [11] . A similar effect was achieved by blocking the photoreactive α-pyrone double bond with appropriate substituents[12].

Synthesis of angular furanocoumarins has been previously achieved by Claisen rearrangement of 7-allyloxycoumarin[13] benzannulation reaction of carbene complexes with acetylenes [14] and coupling of an acetylenic reagent with an *o*-iodohydroxycoumarin[15]. In this paper we describe a simple and efficient general method of synthesis of 8, 9 substituted furanocoumarins.

Results and Discussion:

The title compounds, 8-aroyl-9-styryl furopyran 2-ones (**9 a-j**), were prepared according to

Scheme I



Scheme 1 from 8-acetyl-4-methyl-7-hydroxy coumarins (**7 a-d**), which were prepared using a literature procedure[16]. **5** were first converted in to α-pyrano chalcones (**7**) by condensing with different aromatic

Table 1: Structure of various furocoumarins synthesized

Compound	R_1	R_2	Mp °C	Yield (%)
9a	4'OMe-C_6H_4	C_6H_5	183	85
9b	4'OMe-C_6H_4	4C_6H_5-C_6H_4	228	83
9c	4'OMe-C_6H_4	4,6-diOMe C_6H_3	>260	84
9d	4'OMe-C_6H_4	4 $CH_3SO_2C_6H_4$	245	84
9e	3' OMe-4'OMe-C_6H_3	C_6H_5	202	75
9f	3' OMe-4'OMe-C_6H_3	4C_6H_5-C_6H_4	210	70
9g	3' OMe-4'OMe-C_6H_3	4 $CH_3SO_2C_6H_4$	208	72
9h	3' OMe-4'OH C_6H_3	4 $CH_3SO_2C_6H_4$	189	60
9i	3'$NO_2C_6H_4$	C_6H_5	240	73
9j	3'$NO_2C_6H_4$	4 $CH_3SO_2C_6H_4$	>260	75

aldehydes in the presence of piperidine in ethanol[17]. These α-pyranochalcones were then reacted with different phenacyl bromides (**8**) in the presence of potassium carbonate in acetone to give 8-aroyl-9-styryl furanopyran2-ones (9 a-j) in good yields. The structures of these compounds (Table 1) have been confirmed from IR, H1NMR and Mass spectral data. Stretching for benzoyl carbonyl at 1640 cm^{-1} and styryl double bonds were observed at 1480 cm^{-1} along with furan ring stretching in **9**.

In the proton NMR spectrum characteristic chemical shift values and coupling constants for trans double bonds, two doublets at δ 7.8 and δ 8.2 with coupling constant of 12 Hertz were observed which are assignable to styryl double bonds at C-9 position. Other chemical shift values observed at δ 7.0 – 7.4 and 7.6- 7.8 are assignable to AB doublets of C-6 and C-5 protons and δ 6.1-6.3 peak is due to C-3 proton of coumarin nucleus. In the mass spectra (FAB) of all the compounds characteristic molecular ion peaks were observed.

Experimental:

Proton NMR spectra were recorded on a varian gemini 200 MHZ spectrometer in $CDCl_3$. Proton chemical shift values are reported in δ (PPM) down field from TMS which is an internal standard and J values are in Hz . IR spectra were obtained as KBr pellets. Purity of the compounds was checked by TLC and spots were visualized under U.V light.

8-acetyl-7-hydroxy-4-methyl-2H-1-benzopyran-2-one(5): This was prepared by fries migration of acetyl group of 7-acetyloxy coumarin which was prepared by acetylation of 7-hydroxy coummarin which inturn was prepared from resorcinol and ethyl acetoacetate by following literature method[16].

1-(2H-Benzopyran-2-one-8-yl)-3-aryl-2-propenones (7 a-d): A mixture of 8-acetyl-4-methyl-7-hydroxy-2H-1-benzopyran-2-one (1.5g, 0.00688 M) and aromatic aldehyde (6 a-d, 0.00825M) in 20ml of ethanol in the presence of piperidine (0.206ml) was refluxed on a steam bath for 4hourssss. After completion of the reaction (TLC monitoring), half of the ethanol removed under reduced pressure and cooled to RT the solid separated was filtered, washed with cold ethanol and recrystallized from alcohol to obtain pure compounds(7 a-d), physical and spectroscopic data of the compounds were respondent to known data[17].

8-aroyl-9-styrylfurobenzopyran-2-ones (9 a-j): A mixture of 1-(2H-Benzopyran-2-one-8-yl)-3-aryl-2-propenones(1M), phenacyl bromides (8 a-d, 1.2M) have taken in acetone(20ml) in the presence of K_2CO_3 (1.5M) refluxed in steam bath . After completion of the reaction by TLC monitoring (nearly one hour). Concentrated the reaction mixture upto 90% then total reaction mixture poured into the ice water and precipitate was filtered and recrystallized from ethanol and THF.

9 Spectral data of furobenzopyran-2-one derivatives:

9a: 2.4 (s, CH_3), 3.7 (s, OCH_3), 6.3 (s,H-3), 8.1&7.8 (d,2H,vinyl double bond), 6.8 (d,2H,vinyl benzene 3^1,5^1) 7.4,7.6&7.9 (m,d,d,9H,aroyl,vinyl benzene2^1,6^1,H-5,11-6).

9b: 2.5 (s,CH_3,), 3.8 (s,OCH_3), 6.38 (s,H-3), 6.9 (d,2H,vinyl; benzene3^1,5^1), 8.2&7.9 (d,2H for vinyl db), 8.1,7.6 to 7.8& 7.4 (m,13H,aroyl,vinyl benzene 2^1,6^1,H-5,H-6).

9c: 2.5 (s,CH_3), 2.7,2.8 & 2.9 (s,9H,OCH_3), 6.38 (S,H-3), 6.3 (s,H,aroyl3^1), 7.49&6.9 (d,2H,vinyl benzene3^1,5^1), 7.2,7.7&8.1 (m,6H,db,aroyl&5,6hydrogen).

9d: 2.56 (s,CH_3,), 3 (s,3,Sulfonyl), 3.9 (s,OCH_3), 6.3 (s,3-H), 6.9 (d,2H,Vinyl benzene3^1,5^1), 7.6 (d,2H,vinyl benzene2^1,6^1), 7.4,7.8 (d,2H,5,6), 8.2,7.9 (d,2H,db), 8.1(m,aroyl).

9e: 2.56 (s,CH_3), 3.9&4 (s,6H,OCH_3), 6.3 (s,H-3), 6.85 (d.H-6), 7.3 to 8.2 (m,11H,styryl,aroyl,H-5).

9f: 2.56 (s,CH_3), 4&3.9 (s,6H,OCH_3), 6.3 (s,H-3), 6.89 (d,H-6), 7.7(d,H-5), 7.7(d,2H,aroyl3 ^{1},5 ^{1}), 8.1(d.2H,aroyl2 ^{1},6 ^{1}), 7.8&8.1 (d,vinyldb), 7.5(m,3H), 7.7(m,5H).

9g: 2.5 (s, CH_3), 3.9&4(s,6H,O CH_3), 3.1 (S,3Hsulfonyl), 6.38 (s,H-3), 6.9 (d,H-6), 7.79 (d,H-5), 7.45 (d,H,vinyl benzene5 ^{1}), 8&8.19(d,2H,db), 8.1 (m,4H,aroyl), 7.3 (m,2H,vinylbenzene2 ^{1},5 ^{1}).

9h: 2.5 (s CH_3,), 3.1 (s,3H,sulfonyl), 4 (s,3H,O CH_3), 5.8 (S,phenolic OH), 6.3 (S,H-3), 6.9 (d,H-6), 7.9 (d,H-5), 7.2 to 8.3 (m,9H,aroyl,styryl gp).

9i: 2.5 (s, CH_3), 6.3 (s,H-3), 8.4 (s,H,vinylbenzene2 ^{1}), 7.2 to8.2 (m,10H,aroyl,styryl gp).

9j: 2.5 (s, CH_3), 3.1 (s,3H,Sulfonyl), 6.3 (s,H-3), 8.4 (s,H,vinyl benzene2 ^{1}), 7.2 to 8.2 (m,9H,aroyl&styryl gp).

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