Synthesis and Reactions of Some New Allyl Furobenzopyranone Derivatives

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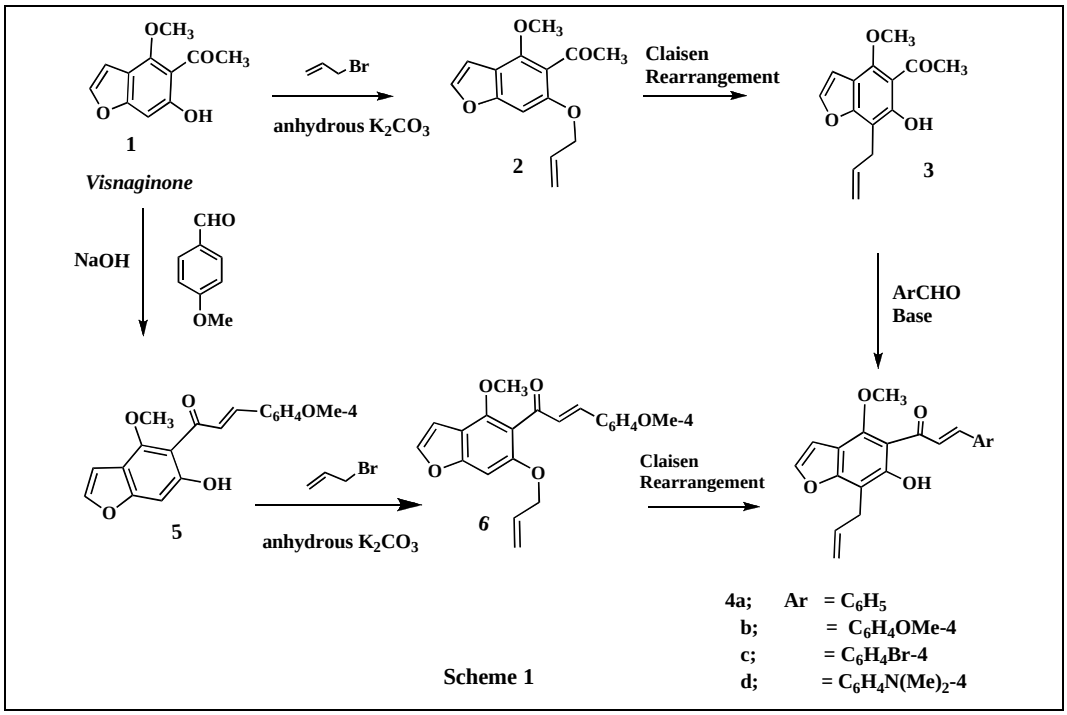

Scheme 1

Reaction of *visnaginone* **1** with allyl bromide gave *O*-allyl *visnaginone* **2** which underwent Claisen rearrangement to yield 7-allylbenzofuran derivative **3**. Reaction of **3** with different aromatic aldehydes gave the corresponding 5-cinnamoylbenzofuran derivatives **4a-d**. Condensation of the latter chalcones **4a,c,d** with hydrazine hydrate and phenylhydrazine provided, the corresponding pyrazoline derivatives **7a-f**. Claisen condensation of compound **3** with ethyl acetate and diethyl carbonate afforded Claisen adducts **8** and **12** which easily cyclized to **9** and **13**, which are endowed with interesting biological properties.

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INTRODUCTION

Benzopyranones and furobenzopyranones occupy a position of considerable significance as a result of their wide spread occurrence in plants and their potential as important pharmaceutical [1-7]. On the other hand, these compounds posses potent clinical application in the treatment of renal colic, anginal syndromes, whopping cough, peptic ulcer, lipid altering activity for example decreasing the atherogenic cholesterol fraction, elevating antiatherogenic HDL cholesterol fraction and antiatherosclerotic activity [8-10]. In view of these facts and in continuation of our research program in this field [11-17], we present here the synthesis of some allylfurobenzopyranones that are considered precursors [18] to synthesis of antitumor brnzopyranone acetic acid analogue compounds

RESULTS AND DISCUSSION

O-Allylation of 5-acetyl-6-hydroxy-4-methoxybenzofuran **(1)** "*visnaginone*" which was previously prepared from hydrolysis of the naturally occurring compound *visnagin* [19] afforded 5-acetyl-6-allyloxy-4-methoxybenzofuran **(2)**. Compound **2** was refluxed in *N,N*-diethylaniline and underwent Claisen rearrangement, to provide 5-acetyl-7-allyl-6-hydroxy-4-methoxybenzofuran **(3)** in quantitative yield (Scheme 1). The assigned structures of **2** and **3** were established on the basis of the analytical and spectral data. ^{1}H nmr of **2** showed in addition to the allyl protons, a singlet corresponding to H-7 at δ 6.75 which disappeared in Claisen adduct **3**, whereas the exchangeable OH appeared at δ 13.4 (Table 1 and 2).

Condensation of **3** with different aromatic aldehydes namely benzaldehyde, 4-methoxybenzaldehyde, 4-bromobenzaldehyde, and 4-*N,N*-dimethylaminobenzaldehyde gave the corresponding 5-cinnamoyl benzofuran derivatives **4a-d** (Scheme 1). Compound **4b** was chemically established by another method for its preparation as example of the latter compounds **4a-d**. Condensation of *visnaginone* **1** with *p*-anisaldehyde gave compound **5** as outlined in the literature [20] then, reaction of **5** directly with allyl bromide afforded 6-allyloxy-5-(4'-methoxycinnamoyl)-4-methoxybenzofuran **(6)**. The latter compound was thermally rearranged to result in compound **4b** and the observed melting point and polarity (TLC) is identical with that of the previously prepared compound (Scheme 1).

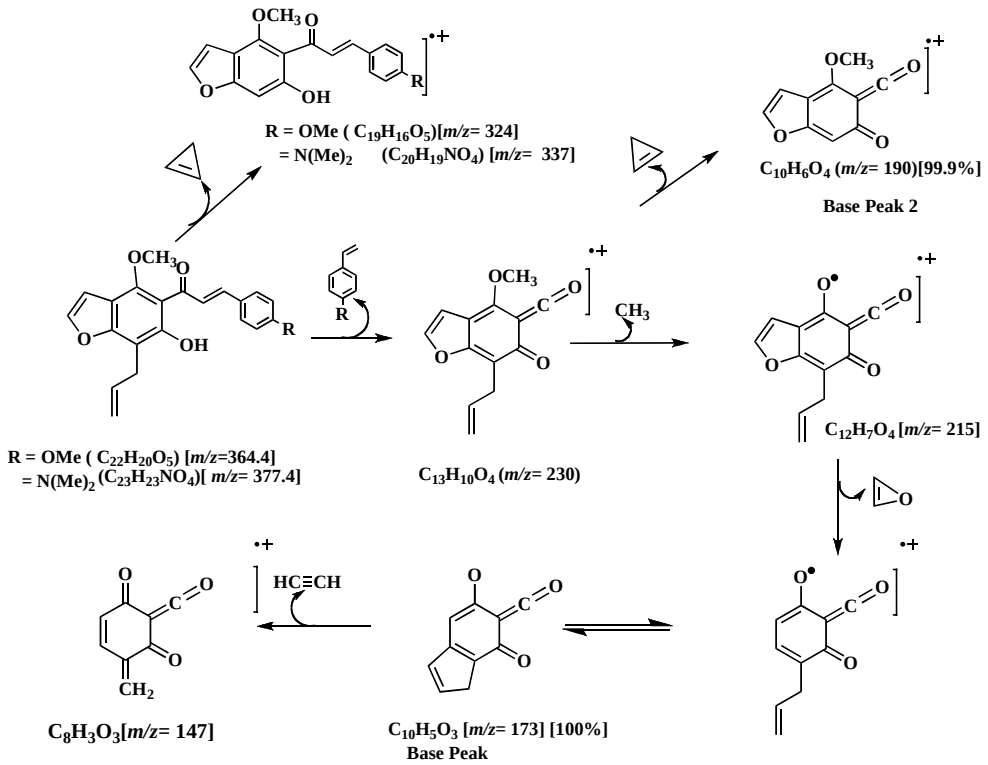
The ^{1}H nmr spectra of **4a-d** did not show acetyl protons signal, which would appeared at δ 2.73, while the two olefinic protons appeared as doublets in the aromatic region (Table 2). The electron impact mass spectra of both **4b** and **4d** showed the assigned molecular weights M^+ at *m/z* 364 and 377 respectively as well as a characteristic peaks at 324, 337 from extrusion of the cyclopropene nucleus in both of them. The major peaks M_1 at *m/z* (230), M_2 at *m/z* (215), M_3 at *m/z* (190) [Base peak 2] M_4 at *m/z* (173) [Base peak 1], and M_5 at *m/z* (147) were appeared in both of them, as outlined in the fragmentation pattern (Scheme 2).

Aziz *et al* [21], reported that the arylcrylobenzofuran dervatives reacted with hydrazine hydrate to give two isomeric pyrazoline derivatives *via* 1,2-addition or 1,4-addition according to the reaction conditions. In the present study, the cinnamoylbenzofuran derivatives **4a,c,d** were allowed to react with hydrazine hydrate or phenylhydrazine, in ethanol or glacial acetic acid to give the corresponding pyrazoline derivatives **7a-f** only. The formation of **7a-f** takes place as outlined in the literature [22,23], *via* 1,2-addition of hydrazine derivatives to the carbonyl group of the chalcone followed by dehydration, to give the corresponding hydrazones which are directly converted to the corresponding pyrazolines.

The analytical and spectral results of **7a-f** are in accordance with the suggested structures, ^{1}H nmr of compound **7a,e** revealed disappearance of the characteristic allyl protons, instead, a doublet methyl at δ 0.98, multiplet CH_2 at δ 1.67 and triplet CH_2 at δ 2.86 were observed, due to the reduction of the allyl group double bond under the reaction conditions, to provide the corresponding propyl derivative.

Claisen condensation of **3** with ethyl acetate afforded, the expected Claisen adduct 5-acetoacetyl-7-allyl-4,6-dihydroxybenzofuran **(8)** which was refluxed directly in glacial acetic acid in the presence of a catalytic amount of concentrated hydrochloric acid to give 9-allyl-4-hydroxy-7-methylfuro[3,2-*g*]chromen-5(5*H*)-one **(9)**. In addition to the analytical and spectral data the structure of **9** was confirmed through its preparation by the reported method [24], *via* initial fusion of *visnagin* in aniline hydrochloride

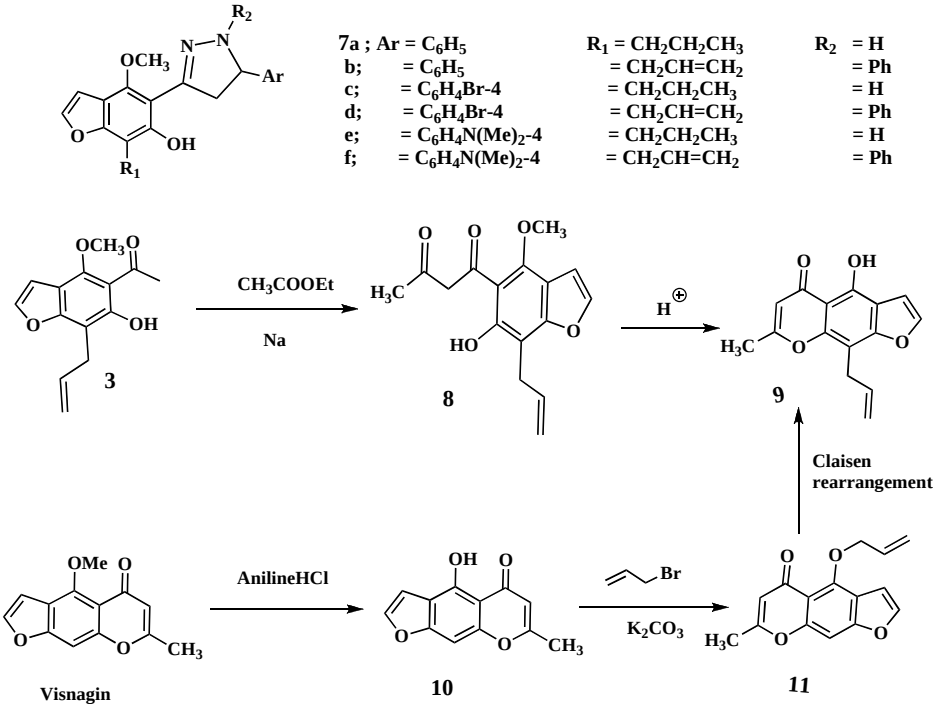
Scheme 2



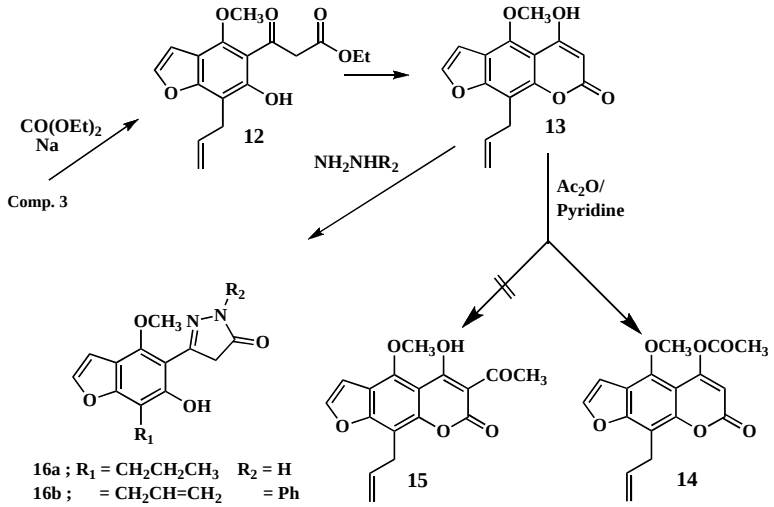
to give *demethyl visnagin* **10** [25]. Thereafter, treatment of **10** with allyl bromide yielded the corresponding 4-allyloxy furochromone **11** in quantitative yield. Refluxing of **11** with *N,N*-diethylaniline underwent Claisen rearrangement according the method described above to form the same compound **9**. Melting points and TLC with an authentic sample were completely identical (Scheme 3)]. The ^{1}H nmr spectra of **9** revealed disappearance the singlet OCH_3 at δ 4.20, whereas two singlets at δ 6.09 and δ 13.45 ppm corresponding to H-6 and OH respectively.

Furocoumarin/ultraviolet therapy, known as photopheresis, has recently become an effective treatment of cutaneous T cell lymphoma, Sezary syndrome and related diseases. The photochemotherapeutic effects of furocoumarins such as psoralen and bergapten are based on intercalation of the molecules between the pyrimidine bases of the microorganism's DNA [26]. The intercalation is then followed by the UV light activated cycloaddition reactions of furocoumarin with the pyrimidine bases. These [2+2] photocycloaddition reactions result in a cross-linking of DNA and prevent a microorganism's reproduction [27]. We present here the synthesis of some medicinal interesting psoralen and bergapten analogues with hope to have biological interest.

Scheme 3



Scheme 4



In a similar manner, Claisen condensation of **3** with diethyl carbonate afforded directly the target 9-allyl-5-hydroxy-4-methoxypsoralen (**13**) without isolation of **12** [28,29]. The analytical and spectral data are in excellent agreement with the assigned structure (Scheme 4).

Earlier acetylation of 5-hydroxy bergapten have been reported to give 3-acetyl-4-hydroxy-5-acetoxypsoralen [29]. In the present study acetylation of **13** with acetic anhydride in pyridine, the expected 6-acetyl bergapten derivative **15** not obtained insteaed, 5-acetoxy derivative

Table 1

Characterization Data of the Newly Prepared Compounds

Comp. No.	mp. (°C)	Colour	Yield (%)	M. Formula (M. Weight)	Calcd. / Found Analysis C	H	N
2	101-103	pale brown	95	$C_{14}H_{14}O_4$	68.28	5.73	-
				(246.26)	68.13	5.60	
3	82-84	yellowish grey	97	$C_{14}H_{14}O_4$	68.28	5.73	-
				(246.26)	68.09	5.59	
4a	85-86	pale orange	93	$C_{21}H_{18}O_4$	75.43	5.43	-
				(334.37)	75.25	5.61	
4b	110-112	pale brown	80	$C_{22}H_{20}O_5$	72.51	5.53	-
				(364.39)	73.37	5.39	
4c	115-116	Reddish brown	95	$C_{21}H_{17}$ Br O_4	61.03	4.15	-
				(413.26)	61.30	4.00	
4d	173-174	Reddish brown	90	$C_{23}H_{23}NO_4$	73.19	6.14	3.71
				(377.44)	73.01	6.20	3.61
6	110-113	yellowish brown	85	$C_{22}H_{20}O_5$	72.51	5.53	-
				(364.39)	72.71	5.80	
7a	101-102	Pale grey	80	$C_{21}H_{20}N_2O_3$	71.98	6.33	7.99
				(350.41)	72.22	6..14	7.86
7b	132-133	pale yellow	85	$C_{27}H_{24}N_2O_3$	76.39	5.70	6.60
				(424.49)	76.10	5.50	6.83
7c	157-159	colorless	80	$C_{21}H_{19}N_2O_3Br$	58.75	4.93	6.53
				(429.31)	58.90	4.79	6.32
7d	161-163	yellow	80	$C_{27}H_{23}N_2O_3Br$	64.42	4.61	5.56
				(503.39)	64.68	4.49	5.82
7e	107-108	yellow	95	$C_{23}H_{27}N_3O_3$	70.21	6.92	10.68
				(393.48)	70.44	6.78	10.80
7f	142-144	Pale yellow	75	$C_{29}H_{29}N_3O_3$	74.50	6.25	8.99
				(467.57)	74.37	6.42	8.81
9	165-167	Faint yellow	88	$C_{15}H_{12}O_4$	70.31	4.72	-
				(256.25)	70.16	4.79	
11	97-99	Pale brown	90	$C_{15}H_{12}O_4$	70.31	4.72	
				(256.25)	70.16	4.79	
13	163-165	Pale yellow	85	$C_{15}H_{12}O_5$	66.17	4.44	
				(272.25)	66.30	4.23	
14	187-189	Faint yellow	90	$C_{17}H_{14}O_6$	64.97	4.49	-
				(314.29)	65.13	4.50	
16a	240-242	pale yellow	78	$C_{15}H_{16}N_2O_4$	62.49	5.59	9.72
				(288.30)	62.69	4.74	9.67
16b	217-219	Reddish brown	75	$C_{21}H_{18}N_2O_4$	69.60	5.01	7.73
				(362.38)	69.68	5.22	7.49

Table 2

Spectral Data of the Newly Prepared Compounds

No	Spectral data
2	ir (Cm^{-1}) ν = 1650 (C=O) , 1580 (C=C) , 1575 (Ar) .
	^{1}H nmr ($CDCl_3$) δ: 2.45 (s, 3H, CH_3CO) , 4.07 (s, 3H, OCH_3) , 4.56 (d, 2H, 2H-1', J = 4.56 Hz), 5.28 (dd, 1H, 1H-3', J_{gem}= 2.3 Hz, J_{cis}=10.34 Hz), 5.40 (dd, 1H, 1H-3', J_{gem}= 2.3 Hz, J_{trans}=17.18 Hz), 6.01 (m, 1H, H-2') , 6.75 (s, 1H, H-7), 6.87 (d, 1H, H-3, J = 2.07 Hz) and 7.49 ppm (d, 1H, H-2, , J = 2.07 Hz) .
3	ir (Cm^{-1}) ν = 3670-3500 (br, OH) , 1627 (C=O), 1589 (C=C).
	^{1}H nmr ($CDCl_3$) δ: 2.73 (s, 3H, CH_3CO) , 3.60 (d, 2H, 2H-1', , J = 4.92 Hz), 4.20 (s, 3H, OCH_3) , 5.02 (dd, 1H, H-3', J_{gem}= 1.49 Hz, J_{cis}= 10.00 Hz) , 5.09 (dd, 1H, H-3', J_{gem}= 1.58 Hz, J_{trans}= 17.10 Hz) , 6.05 (m, 1H, H-2'), 6.90 (d, 1H, H-3, J = 2.32 Hz), 7.49 (d, 1H, H-2, J = 2.32 Hz) and 13.40 ppm (s, 1H, OH).
	^{13}C nmr ($CDCl_3$) δ: 27.66 (*CH*$_3$CO), 33.74 (C-1'), 60.58 (OCH_3), 77.10 (C-2') , 77.43 (C-3'), 77.75 (C-3) , 79.15 (C-3a), 105.82 (C-6) , 109.74 (C-5), 110.08 (C-7), 115.32 (C-4) , 135.79 (C-7a) , 143.81 (C-2), and 159.66 ppm (C=O).
	ms *m/z* (%) 247 $(M+1)^+$ (13) , 246 (M^+) (87), 231$(M-CH_3)^+$ (100), 216 (38), 185(14) , 128(14), 115(26), 91(36), 63 (35).

Table 2 (continued)

No	Spectral data
4a	ir (Cm^{-1}) ν = 3600 (OH), 1620 (C=O), 1580 (C=C). ^{1}H nmr ($CDCl_3$) δ: (d, 2H, 2H-1', J = 4.68 Hz), 4.09 (s, 3H, OCH_3), 5.02 (dd, 1H, 1H-3', J_{gem}= 1.83 Hz, J_{cis}= 10.15 Hz), 5.11 (dd, 1H, 1H-3', J_{gem}= 1.83 Hz, J_{trans}= 15.43 Hz), 6.07 (m, 1H, H-2'), 6.86 (d, 1H, H-3) , 7.38-7.91 (m, 8H, Ar-H, α-H, β-H, H-2), and 12.96 ppm (s, 1H, OH).
4b	ir (Cm^{-1}) ν = 3600-3470 (br,OH) , 1624 (C=O), 1603 (C=C), 1546 (Ar.). ^{1}H nmr ($CDCl_3$) δ: 3.62 (d, 2H, 2H-1', J = 4.88 Hz) , 3.86 (s, 3H, OCH_3), 4.09 (s, 3H, OCH_3), 5.04 (dd, 1H, 1H-3', J_{gem}= 1.80 Hz, J_{cis}= 10.17 Hz)), 5.12 (dd, 1H, 1H-3', J_{gem}= 1.80 Hz, J_{trans}= 17.13 Hz), 6.75 (m, 1H, H-2'), 6.80-7.87 (m, 8H, Ar -H and α,β-H),13.11 (s, 1H, OH). ms *m/z* (%) 365 $(m+1)^+$(13), 364 $(m)^+$ (58) , 324 (16) [M-(cyclopropene), 230 (75), 215 (39), 203 (20) , 201 (31), 190 (99.9)[M-(cyclopropene, 4-methoxy styryl)], 187(34), 173 (100) , 161 (30), 147 (39), 145 (49), 91 (76) and 78 ppm (86).
4c	ir (Cm^{-1}) ν = 3520(OH), 1650 (C=O), 1585 (C=C). ^{1}H nmr ($CDCl_3$) δ: 3.64 (d, 2H, 2H-1', J = 5.11 Hz), 4.11 (s, 3H, OCH_3), 5.00 (dd,1H, 1H-3', J_{gem}= 1.82 Hz, J_{cis}= 10.22 Hz), 5.16 (dd,1H, 1H-3', J_{gem}= 1.82 Hz, J_{trans}= 17.33 Hz), 6.08 (m, 1H, H-2'), 6.88 (d, 1H, H-3) , 7.38-7.91 (m, 9 H, Ar-H, α-H, β-H) and 13.09 ppm (s, 1H, OH).
4d	ir (Cm^{-1}) ν = 3650-3500 (br, OH), 1627 (C=O), 1526 (C=C). ^{1}H nmr ($CDCl_3$) δ: 3.05 (s, 6H , $N(CH_3)_2$) , 3.62 (d, 2H, 2H-1') 4.06 (s, 3H, OCH_3), 5.02 (dd, 1H, 1H-3', J_{gem}= 1.56 Hz, J_{cis}= 10.04 Hz), 5.10 (dd, 1H, 1H-3', J_{gem}= 1.58 Hz, J_{trans}= 17.08 Hz), 6.08 (m, 1H, H-2'), 6.70 (d, 2H, H-3",5" J = 8.8 Hz), 6.86 (d, 1H, H-3, J= 2.3 Hz), 7.49 (d, 1H, H-2, J= 2.3 Hz), 7.56 (d, 2H, H-2", 6", J= 8.4 Hz), 7.74 (d, 1H, H-β, J = 15.4 Hz) 7.90 (d, 1H, H-∝, J = 15.4 Hz) and 13.31 ppm (s, 1H, OH) ms *m/z* (%) 378 $(m+1)^+$ (2) , 377 (m^+) (8), 337 (23) [M-(cyclopropene), 230 (55), 215 (39), 190 (99.9)[M-(cyclopropene, 4-*N*,*N*-dimethyl styryl)].
6	ir (Cm^{-1}) ν = 1670 (C=O), 1600 (C=C), 1590 (Ar). ^{1}H nmr ($CDCl_3$) δ: 3.80 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 4.56 (d, 2H, 2H-1', J = 4.53 Hz), 5.31 (dd, 1H, 1H-3', J_{gem}= 2.12 Hz, J_{cis}= 10.30 Hz), 5.43 (dd, 1H, 1H-3', J_{gem}= 2.10 Hz, J_{trans}= 17.19 Hz), 6.08 (m, 1H, H-2',), 6.70 (s, 1H, H-7), 6.88 (d, 1H, H-3, J= 2.07 Hz), 7.11-7.39 (m, 4H, Ar-H) and 7.49 ppm (d,1H, H-2, J = 2.07 Hz).
7a	ir (Cm^{-1}) ν = 3500-3450 (br, OH, NH), 1580 (Ar). ^{1}H nmr ($CDCl_3$) δ: 1.01 (t, 3H, $CH_3CH_2CH_2$, J = 7.36 Hz), 1.70 (m, 2H, $CH_3CH_2CH_2$), 2.87 (t, 2H, $CH_3CH_2CH_2$, J = 7.45 Hz), 3.40 (dd, 1H, CH_2 of pyrazoline, J = 9.08 Hz, 8.98 Hz), 3.82 (dd, 1H, CH_2 of pyrazoline, J = 10.45 Hz), 3.96 (s, 3H, OCH_3), 4.82 (t, 1H, CH of pyrazoline, J = .9.65), 5.85 (s, br., 1H, NH), 6.80 (m, 1H, H-4 phenyl group), 7.29-7.46 (m, 6H, Ar.H), and 12.38 ppm (s, 1H, OH).
7b	ir (Cm^{-1}) ν = 3520 (OH), 1588(C=C), 1579 (Ar). ^{1}HNMR ($CDCl_3$) δ: 3.33 (d, 2H, 2H-1', J= 5.02 Hz), 3.45 (dd, 1H, CH_2 of pyrazoline, J = 9.05 Hz, 8.95 Hz), 4.07 (s, 3H, OCH_3) , 4.18 (dd, 1H, CH_2 of pyrazoline, J = 10.40 Hz), 4.89 (t, , 1H, CH of pyrazoline, J = 9.75), 5.03 (dd, 1H, H-3', J_{gem}= 1.59 Hz, J_{cis}=10.23 Hz) , 5.14 (dd,1H, H-3', J_{gem}= 1.67 Hz, J_{trans}= 16.87 Hz) , 6.12 (m, 1H, H-2'), 7.01 (d, 1H, H-3), 6.89-7.30 (m, 10H , Ar.-H), 7.49 (d, 1H, H-2), and 12.18 ppm (s, br, 1H, OH).
7c	ir (Cm^{-1}) ν = 3510-3470 (br, OH, NH), 1590 (C=C), 1580 (Ar). ^{1}HNMR ($CDCl_3$) δ: 0.98 (t, 3H, $CH_3CH_2CH_2$, J = 7.33 Hz), 1.75 (m, 2H, $CH_3CH_2CH_2$), 2.83 (t, 2H, $CH_3CH_2CH_2$, J = 7.41 Hz), 3.35 (dd, 1H, CH_2 of pyrazoline, J = 9.18 Hz), 3.80 (dd, 1H, CH_2 of pyrazoline, J = 10.55 Hz, 10.73 Hz), 3.90 (s, 3H, OCH_3), 4.80 (t, 1H, CH of pyrazoline, J = .9.60), 5.80 (s, br., 1H, NH), 6.79-7.53 (m, 6H , Ar.-H), and 12.18 ppm (s, 1H, OH).
7d	ir (Cm^{-1}) ν = 3560 (OH), 15810 (C=C), 1577 (Ar). ^{1}H nmr ($CDCl_3$) δ: 3.42 (dd, 1H, CH_2 of pyrazoline, J = 9.28 Hz), 3.70 (d, 2H, 2H-1', , J= 4.81 Hz), 4.00 (s, 3H, OCH_3) , 4.20 (dd, 1H, CH_2 of pyrazoline, J = 10.44 Hz), 5.00-5.10 (m, 3H, CH of pyrazoline ,2x H-3'), 6.14 (m, 1H, H-2'), 6.80-7.50 (m, 11H, Ar.-H), and 12.04 ppm (s,1H, OH).
7e	ir (Cm^{-1}) ν = 3540-3500 (br, OH, NH), 1583 (Ar). ^{1}H nmr ($CDCl_3$) δ: 1.0 (t, 3H, $CH_3CH_2CH_2$, J = 7.38 Hz), 1.67 (m, 2H, $CH_3CH_2CH_2$), 2.86 (t, 2H, $CH_3CH_2CH_2$, J = 7.49 Hz), 2.94 (s, 6H, 2 x CH_3), 3.40 (dd, 1H, CH_2 of pyrazoline, J = 9.03 Hz, 8.88 Hz), 3.74 (dd, 1H, CH_2 of pyrazoline, J = 10.85 Hz), 3.97 (s, 3H, OCH_3), 4.74 (t, 1H, CH of pyrazoline, J = .9.15), 5.80 (s, br., 1H, NH), 6.71 (d, 2H, H-3",5", J = 8.6 Hz), 6.79 (d, 1H, H-3, J = 2.2 Hz), 7.25 (d, 2H, H-2", H-6", J = 8.6 Hz), 7.45 (d, 1H, H-2, J = 2.2 Hz) and 12.33 ppm (s, 1H, OH).
7f	ir (Cm^{-1}) ν = 3530 (OH), 1590 (C=C), 1588 (Ar). ^{1}H nmr ($CDCl_3$) δ: 2.85 (s, 6H, 2 x CH_3), 3.30 (d, 2H, 2H-1', J = 4.90 Hz), 3.40 (dd, 1H, CH_2 of pyrazoline, J = 9.00 Hz, 9.08 Hz), 3.99 (s, 3H, OCH_3) , 4.20 (dd, 1H, CH_2 of pyrazoline, J = 10.45 Hz), 5.00 (t, 1H, CH of pyrazoline, J = .9.65), 5.05 (dd, 1H, H-3', J_{gem}= 1.86 Hz, J_{cis}= 9.97 Hz) , 5.22 (dd, 1H, H-3', J_{gem}= 1.89 Hz, J_{trans}=17.18 Hz) , 6.00 (m, 1H, H-2'), 6.90 (d, 1H, H-3), 6.89-7.30 (m, 9H , Ar.-H), 7.80 (d, 1H, H-2) and 12.10 ppm (s,1H, OH).
9	ir (Cm^{-1}) ν = 3421 (br., OH), 3109 (CH), 1659 (C=O), 1600 (C=C), 1585 (Ar). ^{1}H nmr ($CDCl_3$) δ: 2.40 (s, 3H, CH_3) , 3.69 (d, 2H, 2H-1, J = 4.92 Hz), 5.00 (dd, 1H, H-3', J_{gem}= 1.54 Hz, J_{cis}= 9.89 Hz), 5.04 (dd, 1H, H-3', J_{gem}= 1.60 Hz, J_{trans}=17.23 Hz) , 5.98 (m, 1H, H-2'), 6.09 (s, 1H , H-6) , 6.97 (d, 1H, H-3, J = 2.4 Hz), 7.58 (d, 1H, H-2, J = 2.4 Hz) and 13.45 ppm (s,1H, OH).
11	ir (Cm^{-1}) ν = 3100 (CH), 1670 (C=O), 1605 (C=C, Ar). ^{1}H nmr ($CDCl_3$) δ: 2.33 (s, 3H, CH_3), 4.97 (d, 2H, 2H-1'', J = 4.76 Hz), 4.79 (dd, 1H, H-3' J_{gem}= 2.2 Hz, J_{cis}=10.36 Hz) , 5.47 (dd, 1H, H-3' J_{gem}=2.2 Hz, J_{trans}= 17.15 Hz) , 6.03 (s, 1H , H-6) , 6.18 (m, 1H, H-2'), 6.95 (d, 1H, H-3, J = 2.36 Hz) and 7.58 ppm (d, 1H, H-2, J = 2.36 Hz).
13	ir (Cm^{-1}) ν = 3317(br, sharp, OH), 1785 (lactone COO), 1643 (C=C), 1596 (Ar.). ^{1}H nmr ($CDCl_3$) δ: 3.61 (d, 2H, 2H-1', J= 5.03Hz), 4.32 (s, 3H, OCH_3), 5.02 (dd, 1H, 1H-3', J_{gem}= 1.44 Hz, J_{cis}= 9.90 Hz), 5.08 (dd, 1H, 1H-3', J_{gem}=1.46 Hz, J_{trans}= 16.65 Hz), 6.03 (m, 1H, H-2'), 6.87 (d, 1H, H-3, J = 2.46 Hz), 7.55 (d, 1H, H-2, J = 2.46 Hz), 11.5 (s, br., 1H, H-6) and 12.40 ppm (s, 1H, OH).

Table 2 (continued)

No	Spectral data
14	ir (Cm^{-1}) ν = 1780 (lactone COO), 1715 (OCOMe), 1620 (C=C), 1600 (Ar). ^{1}H nmr ($CDCl_3$) δ: 2.38 (s, 3H, $COCH_3$) 3.79 (d, 2H, 2H-1', J = 6.36 Hz), 4.11(s, 3H, OCH_3), 5.03 (dd, 1H, 1H-3', ' J_{gem}= 2.20 Hz, J_{cis}= 10.06 Hz), 5.18 (dd, 1H, 1H-3', J_{gem}= 2.15 Hz, J_{trans}= 16.77 Hz), 6.02 (s, 1H, H-6) , 6.03 ((m, 1H, H-2'), 6.94 (d, 1H, H-3, J = 2.28 Hz) and 7.63 ppm (d, 1H, H-2, J = 2.28 Hz).
16a	ir (Cm^{-1}) ν = 3200 (OH), 2951 (NH), 1701(C=O), 1620(Ar.) ^{1}H nmr ($CDCl_3$) δ: 0.96 (t, 3H, $CH_3CH_2CH_2$, J = 7.53 Hz), 1.65 (m, 2H, $CH_3CH_2CH_2$), 2.84 (t, 2H, $CH_3CH_2CH_2$, J = 7.47 Hz), 3.85 (s, 2H, CH_2 of pyrazolone), 4.16 (s, 3H, OCH_3), 6.86 (d, 1H, H-3, J = 2.47 Hz), 7.48 (d, 1H, H-2, J = 2.47 Hz), 8.57 (s, br., NH) and 11.18 ppm (s, 1H, OH).
16b	ir (Cm^{-1}) ν = 3320 (OH), 1680 (C=O), 1620 (C=C) , 1570 (Ar.). ^{1}H nmr ($CDCl_3$) δ: 3.673 (d, 2H, 2H-1'), 4.07 (s, 3H, OCH_3) , 4.22 (s, 2H, CH_2 of pyrazolone), 5.01 (dd, 1H, H-3', J_{gem}= 2.11 Hz, J_{cis}= 9,85 Hz) , 5.19 (dd, 1H, H-3', ', J_{gem}=2.1 Hz, J_{trans}= 16.80 Hz) , 6.10 (m, 1H, H-2'), 6.88 (d, 1H, H-3, J = 2.49 Hz), 7.20-7.50 (m, 5H , Ar.-H), 8.00 (d, 1H, H-2, J = 2.48 Hz) and 14.20 ppm (s, br. , 1H, OH).

14 was obtained. The ^{1}H nmr of **14** showed the existence of the characteristic H-6 as a singlet at δ 6.02 and disappearance the singlet hydroxyl peak at δ 12.4 ppm.

Treatment of 9-allyl-5-hydroxy-4-methoxypsoralen **(13)** with hydrazine hydrate or phenylhydrazine [22,30] afforded the corresponding pyrazolinone **16a,b** (Scheme 4). Also, the ^{1}H nmr of **16a** showed presence of triplet methyl group at δ 0.96, multiplet methylene group at δ 1.65 and triplet methylene group at δ 2.84 suggesting that, hydrogenation of the allyl group to propyl under the reaction condition as previously described above especially in presence of hydrazine hydrate.

EXPERIMENTAL

All melting points were determined on an electrothermal Gallenkamp apparatus and are uncorrected. IR spectra were recorded.(KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR spectra were carried out in $CDCl_3$ solution on a Varian Mercurry V-300 MHz spectrometer and chemical shifts were expressed in δ units using TMS as internal reference, Mass spectra were recorded on a GC-MS-QP-1000EX mass spectrometer at 70 e.V.(Faculty of Science, Cairo university). Elemental analyses were carried out in the CHN Elementar Autoanalyzer unit, Faculty of Science, King Faisal University. Thin layer Chromatography Silica gel 60 F_{254}. Layer thickness 0.2 mm.

5-Acetyl-6-allyloxy-4-methoxybenzofuran (2). A mixture of *visnaginone* **1** [19] (2.1 g, 10 mmol), allyl bromide (1.45 g, 12 mmol) and anhydrous potassium carbonate (2 g) in acetone (50 ml) was refluxed for 2 hrs, then filtered while hot and the residue was washed repeatedly with small portions of hot acetone. Evaporating the combined filtrate gave a pale yellow residue, which was crystallized from ethanol to give compound **2** (Tables 1 and 2).

5-Acetyl-7-allyl-6-hydroxy-4-methoxybenzofuran (3). Compound **2** (2 g) was refluxed for 2 hrs with *N,N*-diethylaniline (20 ml), was allowed to stand at room temperature for 5 hrs. The reaction mixture was poured in a mixture of crushed ice (100 g) and conc. HCl (20 ml) with good stirring. The resulting precipitate was collected by filtration, washed with water, dried and recrystallized from ethanol to give compound **3** (Tables 1 and 2).

Condensation of 3 with aromatic aldehydes: Synthesis of chalcones 4a-d "General procedure". To a stirred solution of 5-acetyl benzofuran derivative **3** (2.46 g, 10 mmol) and sodium hydroxide (2.5 g) in ethanol (100 ml) was added dropwise, at 0-5°C during 30 min, a solution of the appropriate aldehyde (benzaldehyde, 4-methoxybenzaldehyde, 4-bromobenzaldehyde, and 4-*N,N*-dimethyl aminobenzaldehyde (11 mmol) in ethanol (10 ml). The stirring was continued overnight at room temperature, then diluted with cold water (100 ml) and neutralized with diluted hydrochloric acid. The precipitate was collected by filtration, washed with water, dried and crystallized from ethanol to give the corresponding chalcones **4a-d** (physical and spectral data in Tables 1 and 2).

N.B. Compound **4d** was also prepared through Claisen rearrangement of compound **6** according the procedure outlined above for the synthesis of compound **3**.

5-(4-Methoxycinnamoyl)-6-hydroxy-4-methoxybenzofuran (5). Compound **5** was prepared from *visnaginone* **1** by the same procedure outlined in the synthesis of compound **4a-d** (Melting point was identical with that published in the literature [20]).

6-Allyloxy-4-methoxy-5-(4'-methoxycinnamoyl)benzofuran (6). Compound **6** was prepared upon treatment of compound **5** with allyl bromide, according to the procedure previously described for the synthesis of compound **3** (Tables 1 and 2).

Reaction of cinnamoylbenzofuran derivatives 4a,c,d with hydrazine hydrate or phenyl hydrazine "synthesis of compounds 7a-f "General Procedure". A mixture of the appropriate chalcone **4a,c,d** (10 mmol) and hydrazine hydrate (3 ml) or phenylhydrazine (10 mmol) was refluxed in absolute ethanol (50 ml) for 5-8 hrs. The precipitate which was filtered, washed with ethanol, dried and crystallized from ethanol to give the corresponding pyrazolines **7a-f**.

Claisen condensation Synthesis of compounds 8 and 12. Compound **3** (4 g) was dissolved in the appropriate ester (ethyl acetate or diethyl carbonate) (20 ml) and was gradually added with stirring to a warm suspension of powdered sodium metal (2 g) [prepared under dry xylene] in dry ether (20 ml) was gradually added with shaking. A violent reaction took place which was slowed down, when necessary, by external cooling. The mixture was left overnight at a temperature 30-40°C and then digested with ethanol, treated with cold water and then extracted three times with ether. The alkaline solution was acidified with diluted hydrochloric acid and the crystalline precipitate was collected by filtration, washed with water,

dried and crystallized from ethanol to give the corresponding Claisen adducts **8** and **12**

N.B. The compound **8** was used directly in the synthesis of compound **9**, Also, the compound **12** was converted to **13** directly under the reaction condition (Tables 1 and 2).

9-Allyl-4-hydroxy-7-methylfuro[3,2-g]chromen-5(5H)-one (9) "Procedure A". A suspension of **8** (2 g) in glacial acetic acid and few drops of concentrated hydrochloric acid was refluxed with stirring for 2 hrs then, left overnight at room temperature. The product was suspended in water, collected by filtration, washed with $NaHCO_3$ solution (20%) followed by water, dried and crystallized from ethanol.

"Procedure B". Compound **9** was also prepared from the Claisen rearrangement of compound **11** by the same procedure as outlined above in synthesis of compound **3**. (Melting points, TLC, and spectral data were completely identical with an authentic sample).

4-Hydroxy-7-methylfuro[3,2-*g*]chromen-5(5*H*)-one (10). Compound **10** was prepared from *visnagin* **1** by the same procedure outlined in the literature [25]) (Melting point was completely identical with the published article).

4-Allyloxy-7-methylfuro[3,2-*g*]chromen-5(5*H*)-one (11). Upon treatment of compound **10** with allyl bromide, according to the procedure which was previously described for the synthesis of compound **3** (Tables 1 and 2).

5-Acetoxy-9-allyl-4-methoxyfuro[3,2-*g*]chromen-7(7*H*)-one (14). A mixture of compound **13** (1 g) in acetic anhydride (20 ml) and pyridine (1ml) was refluxed for 1 hr. The reaction was allowed to cool at room temperature and was poured into ice-cold water (20 ml). The precipitate was collected by filtration, washed with water, dried and crystallized from ethanol (Tables 1 and 2).

Reaction of furocoumarin 13 with hydrazine hydrate or phenyl hydrazine "Synthesis of pyrazolinone derivatives 16a,b". The compounds **16a,b** prepared upon treatment of **13** with hydrazine hydrate or phenyl hydrazine according to the procedure described above for the synthesis of compounds **7a-f** (Tables 1 and 2).

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