One-pot Synthesis of Angular Furocoumarins: a Simple Protocol Involving Unprecedented Intramolecular Aldol Condensation

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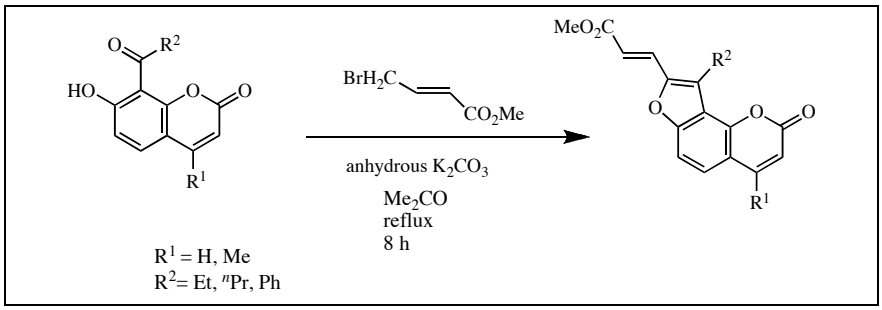

Refluxing of hydroxycoumarinyl ketones with methyl γ-bromocrotonate in dry acetone in presence of anhydrous K_2CO_3 afforded substituted angelicins (angular furanocoumarins) in satisfactory yields through intramolecular Aldol condensation followed by β-elimination.

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INTRODUCTION

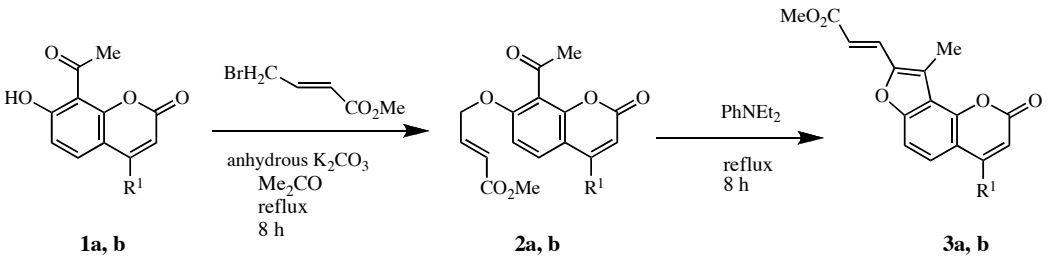
Coumarins are copiously encountered in nature and have been unequivocally characterized from natural sources [1]. Angelicin turns out to be the parent representative of much smaller and less available class of furanocoumarins detected in limited number of plant species of closely related genera [2]. These compounds exhibit a wide range of biological activities recording clinical applications as photoactive drugs in the treatment of skin diseases like psoriasis, vitiligo [3,4,5] and also in photochemotherapy of skin [6]. They are phototoxic to insects, fungi along with a number of viruses and bacteria [7-10].

Synthesis of angelicins has been achieved by various elaborate methods [11-14]. The most common is the allylation of 7-hydroxycoumarin followed by thermal Claisen rearrangement and consequent cyclisation of the allylhydroxycoumarin to produce 8-methylangelicin [15,16]. In our continuous endeavor to develop different synthetic methodologies for achieving coumarins [17,18] pericyclic reactions involving sigmatropic shift have been carried out in the form of thermal Claisen rearrangement on different coumarinyl ketones bearing mainly allyloxy moiety. Inspired by highly encouraging observations in the said studies a new synthon was envisaged having electron-withdrawing group attached to the allyl system and the results of the studies are reported herewith.

RESULTS AND DISCUSSION

The base molecule intended for the proposed study of the Claisen rearrangement was judiciously selected as 7-γ-crotonyloxy-8-coumarinyl ketone. In our maiden attempt to prepare the target molecules hydroxycoumarinyl methyl ketones **1a,b** were subjected to *O*-crotonylation by administering methyl γ-bromocrotonate in presence of anhydrous K_2CO_3 in refluxing acetone. The respective crotonylated compounds **2a,b** formed did not, however, follow the expected symmetry allowed [3,3]sigmatropic shift on refluxing in *N,N*-diethylaniline but led to generation of different angular furanocoumarins (*viz.* angelicin derivatives) **3a,b** in moderate yield as apparently unusual products (Scheme-1). Again, further experimentations led to the observation that refluxing of

Scheme 1



1a, b **2a, b** **3a, b**

the ketoalkyl and ketoarylcoumarins **1c-h** and methyl γ-bromocrotonate in acetone in presence of K_2CO_3 did not follow the similar itinerary to tamely afford the respective *O*-alkylated coumarins but did produce the angular furocoumarins **3c-h** (Scheme-2) straightaway. Thus the one-pot synthesis of angular furocoumarin derivatives could be simply achieved in satisfactory yield.

It is likely that the hydroxycoumarinyl ketones undergo the usual alkylation to afford initially the respective crotonyloxycoumarinyl ketones. The above simplified syntheses of angelicins may then be logically rationalized through an intramolecular base catalyzed Aldol condensation between the ketofunctionality and allyl methylene unit of the transiently formed crotonyloxy-coumarinyl ketones followed by a β-elimination observing E1cB mechanism of the intermediate aldol condensed product. Further *O*-crotonylation of hydroxy-coumarinyl ketones **1c-h** was ultimately achieved in very good yield simply by carrying out the crotonyl-ation reaction at room temperature in acetone using methyl γ-bromocrotonate in presence of K_2CO_3 by keeping for 12 h (Scheme-2). All these crotonyloxy-coumarins **2c-h** thus prepared did obediently afford the respective angelicins **3c-h** on refluxing in acetone in presence of anhydrous K_2CO_3 (Table-1). Hence it may be stated that the course of reaction in boiling acetone turned out to be perfectly in order through inter-mediacy of **2c-h** as delineated earlier.

It is, however, quite surprising that the *O*-crotonylated coumarinyl ketones failed to record any sort of sigmatropic rearrangements in various refluxing solvents *viz*. chlorobenzene, *N,N*-diethylaniline and diphenyl ether. In all such experimentations the parent crotonyloxy coumarinyl ketones could be recovered quantitatively.

The structure of all the angelicin derivatives synthesized were unequivocally established on the basis of extensive applications of ^1H, ^{13}C, 2D NMR and mass spectral evidences. In ^1H spectra of all the angelicin derivatives the one-proton signal required for 7-hydroxy functionality at ~ δ 14 and the *O*-allylic two-proton doublet expected at ~ δ 4.8

Scheme-2

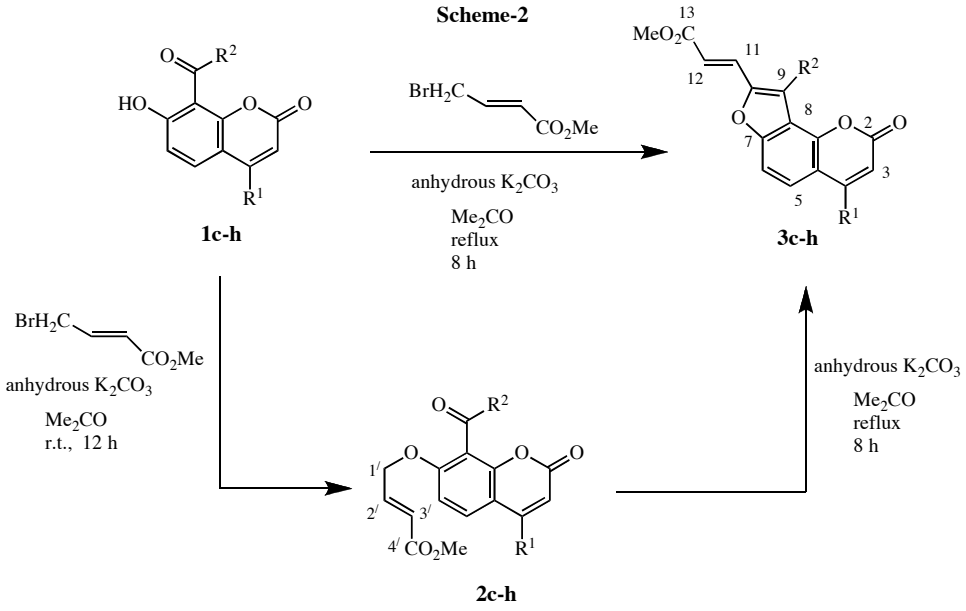


Table-1

Synthesis of Angular Furanocoumarins and Crotonyloxycoumarins

Entry	Substituents for compounds representing **1, 2, 3**			Angular furocoumarin (**3**)		Crotonyloxy ether (**2**)	
		R^1	R^2	Yield %	mp (°C)	Yield %	mp (°C)
1	**a**	H	—	40	232	65	165
2	**b**	Me	—	41	286	70	181
3	**c**	H	Et	74	175	68	125
4	**d**	Me	Et	73	228	72	138
5	**e**	H	^{n}Pr	80	192	69	118
6	**f**	Me	^{n}Pr	82	204	79	110
7	**g**	H	Ph	64	240	64	180
8	**h**	Me	Ph	62	247	71	185

were conspicuously absent. Moreover the display of proton signals for 3-H, 4-H/Me, 5-H, 6-H did reveal that sigmatropic shifts to 6-C or 3-C do not take place. It is highly pertinent to mention that the ^{13}C NMR spectral analyses discerned that the signal of C-8 carbonyl group at ~ δ 200 was routinely absent in the product which confirmed the ring closure involving the keto functionality of C-8.

In conclusion it may be stated that the different angelicin derivatives have been achieved in one-pot synthesis following a very simple protocol. Moreover in this procedure an intramolecular Aldol condensation did take place through vinylogous enolate intermediate without employing any exotic types of bases. Occurrence of the aldol condensation under such a mild basic condition not only highlights the eco-friendly conditions but also emphasizes the very simplicity of this protocol. Synthesis of such angular furanocoumarin derivatives involving unusual intramolecular Aldol condensation instead of simple thermal Claisen rearrangement by incorporation of electron withdrawing group on allyl

Table-2

Elemental Analysis and Spectral Data of Synthesized Compounds

Compound	Elemental analysis Found	Calculated	UV, IR, ^1H, ^{13}C NMR and Mass spectral data
2a	C, 63.46; H, 4.67	C, 63.47; H, 4.68.	IR: 3097, 2951, 1744, 1721, 1698, 1621, 1578 cm^{-1}. δ_H: 2.65 (s, 3H, 8-COMe), 3.77 (sharp s, 3H, 3'-CO_2Me), 4.83 (broad dd, 2H, J = 3.8 Hz, 2Hz, 1'-H), 6.14 (broad d, 1H, J = 15.8 Hz, 3'-H), 6.30 (d, 1H, J = 9.5 Hz, 3-H), 6.83 (d, 1H, J = 8.7 Hz, 6-H), 7.06 (dt, 1H, J = 15.8 Hz, 3.8 Hz, 2'-H), 7.46 (d, 1H, J = 8.6 Hz, 5-H), 7.65 (d, 1H, J = 9.5 Hz, 4-H).
2b	C, 64.57; H, 5.06	C, 64.55; H, 5.09.	IR: 2972, 1728, 1710, 1609, 1569, 1495, 1431, 1388, 1366 cm^{-1}. δ_H: 2.38 (sharp s, 3H, 4-C*H*$_3$), 2.60 (s, 3H, 8-COMe), 3.73 (sharp s, 3H, 3'-CO_2Me), 4.70 (broad dd, 2H, J = 3.8 Hz, 2.1 Hz, 1'-H), 6.10 (dt, 1H, J = 15.0 Hz, 1.8 Hz, 3'-H), 6.13 (broad s, 1H, 3-H), 6.82 (d, 1H, J = 9.0 Hz, 6-H), 7.01 (dt, 1H, J = 15.0 Hz, 2.1 Hz, 2'-H), 7.55 (d, 1H, J = 9.0 Hz, 5-H). δ_C: 18.66 (1°, 4-CH_3), 32.41 (1°, 8-CO*C*H$_3$), 51.61 (1°, 3'-CO_2*C*H$_3$), 67.48 (2°, C-1'), 108.68 (3°, C-6), 113.01 (3°, C-3), 114.69 (4°, C-4a), 120.27 (4°, C-8), 122.59 (3°, C-3'), 126.3 (3°, C-5), 140.75 (3°, C-2'), 150.92 (4°, C-4), 151.68 (4°, C-8a), 156.78 (4°, C-2), 159.41 (4°, C-7), 165.94 (4°, C-4'), 198.27 (4°, 8-*C*OCH$_3$).
2c	C, 64.54; H, 5.11	C, 64.55; H, 5.09.	IR: 3121, 2950, 1722, 1687, 1609, 1575, 1491, 1441, 1405 cm^{-1}. δ_H: 1.18 (t, 3H, J = 7.2 Hz, 8-COCH$_2$C*H*$_3$), 2.84 (q, 2H, J = 7.2 Hz, 8-COC*H*$_2$CH$_3$), 3.69 (sharp s, 3H, 3'-CO_2Me), 4.74 (broad dd, 2H, J = 3.8 Hz, 2.0 Hz, 1'-H), 6.04 (dt, 1H, J = 15.0 Hz, 1.8 Hz, 3'-H), 6.22 (d, 1H, J = 9.6 Hz, 3-H), 6.75 (d, 1H, J = 8.7 Hz, 6-H), 6.96 (dt, 1H, J = 15.7 Hz, 3.8 Hz, 2'-H), 7.37 (d, 1H, J = 8.7 Hz, 5-H), 7.57 (d, 1H, J = 9.6 Hz, 4-H)
2d	C, 65.43; H, 5.52	C, 65.45; H, 5.49.	IR: 2952, 1730, 1714, 1666, 1608, 1560 cm^{-1}. δ_H: 1.24 (t, 3H, J = 7.2 Hz, 8-COCH$_2$C*H*$_3$), 2.41 (sharp s, 3H, 4-CH_3), 2.89 (q, 2H, J = 7.5 Hz, 8-COC*H*$_2$CH$_3$), 3.75 (sharp s, 3H, 3'-CO_2Me), 4.80 (broad dd, 2H, J = 3.8 Hz, 2.1 Hz, 1'-H), 6.10 (dt, 1H, J = 16.0 Hz, 2.1 Hz, 3'-H), 6.16 (broad s, 1H, 3-H), 6.82 (d, 1H, J = 9.0 Hz, 6-H), 7.02 (dt, 1H, J = 15.0 Hz, 2.1 Hz, 2'-H), 7.55 (d, 1H, J = 9.0 Hz, 5-H). δ_C: 7.54 (1°, 8-COCH$_2$*C*H$_3$), 18.49 (1°, 4-CH_3), 38.20 (2°, 8-CO*C*H$_2$CH$_3$), 51.65 (1°, 3'-CO_2*C*H$_3$), 67.63 (2°, C-1'), 108.68 (3°, C-6), 113.09 (3°, C-3), 114.73 (4°, C-4a), 120.29 (4°, C-8), 122.53 (3°, C-3'), 126.14 (3°, C-5), 140.83 (3°, C-2'), 150.94 (4°, C-4), 151.70 (4°, C-8a), 156.84 (4°, C-2), 159.50 (4°, C-7), 165.99 (4°, C-4'), 201.73 (4°, 8-*C*OCH$_2$CH$_3$).
2e	C, 65.47; H, 5.47	C, 65.45; H, 5.49.	IR: 3088, 2971, 1723, 1700, 1606, 1570, 1495, 1428, 1386 cm^{-1}. δ_H: 0.98 (t, 3H, J = 7.5 Hz, 8-COCH$_2$CH$_2$C*H*$_3$), 1.75 (sextet, 2H, J = 7.5 Hz, 8-COCH$_2$C*H*$_2$CH$_3$), 2.84 (t, 2H, J = 7.5 Hz, 8-COC*H*$_2$CH$_2$CH$_3$), 3.75 (sharp s, 3H, 3'-CO_2Me), 4.78 (broad dd, 2H, J = 3.8 Hz, 2.1 Hz, 1'-H), 6.09 (dt, 1H, J = 16.0 Hz, 2.1 Hz, 3'-H), 6.24 (d, 1H, J = 9.0 Hz, 3-H), 6.80 (d, 1H, J = 9.0 Hz, 6-H), 7.00 (dt, 1H, J = 15.0 Hz, 2.1 Hz, 2'-H), 7.43 (d, 1H, J = 9.0 Hz, 5-H), 7.62 (d, 1H, J = 9.0 Hz, 4-H). δ_C: 13.58 (1°, 8-COCH$_2$CH$_2$*C*H$_3$), 14.70 (3°, C-2'), 16.92 (2°, 8-COCH$_2$*C*H$_2$CH$_3$), 46.87 (2°, 8-CO*C*H$_2$CH$_2$CH$_3$), 51.74 (1°, 3'-CO_2*C*H$_3$), 67.67 (2°, C-1'), 108.98 (3°, C-6), 113.54 (4°, C-4a), 114.34 (3°, C-3), 120.26 (4°, C-8), 122.55 (3°, C-3'), 129.41 (3°, C-5), 142.76 (3°, C-4), 151.39 (4°, C-8a), 156.99 (4°, C-2), 159.37 (4°, C-7), 165.92 (4°, C-4'), 201.01 (4°, 8-*C*OCH$_2$CH$_2$CH$_3$).
2f	C, 66.30; H, 5.84	C, 66.27; H, 5.85.	IR: 3091, 2931, 1736, 1712, 1666, 1605, 1574, 1424, 1302 cm^{-1}. δ_H: 0.99 (t, 3H, J = 7.5 Hz, 8-COCH$_2$CH$_2$C*H*$_3$), 1.76 (sextet, 2H, J = 7.5 Hz, 8-COCH$_2$C*H*$_2$CH$_3$), 2.38 (sharp s, 3H, 4-CH_3), 2.84 (t, 2H, J = 7.5 Hz, 8-COC*H*$_2$CH$_2$CH$_3$), 3.74 (sharp s, 3H, 3'-CO_2Me), 4.78 (broad dd, 2H, J = 3.8 Hz, 1.8 Hz, 1'-H), 6.09 (broad d, 1H, J = 15.0 Hz, 3'-H), 6.14 (s, 1H, 3-H), 6.81 (d, 1H, J = 9.0 Hz, 6-H), 7.01 (broad d, 1H, J = 15.0 Hz, 2'-H), 7.54 (d, 1H, J = 9.0 Hz, 5-H). δ_C: 13.63 (1°, 8-COCH$_2$CH$_2$*C*H$_3$), 16.96 (2°, 8-COCH$_2$*C*H$_2$CH$_3$), 18.52 (1°, 4-CH_3), 46.93 (2°, 8-CO*C*H$_2$CH$_2$CH$_3$), 51.64 (1°, 3'-CO_2*C*H$_3$), 67.63 (2°, C-1'), 108.66 (3°, C-6), 113.13 (3°, C-3), 114.70 (4°, C-4a), 120.37 (4°, C-8), 122.56 (4°, C-3'), 126.11 (3°, C-5), 140.61 (3°, C-2'), 150.94 (4°, C-4), 151.69 (4°, C-8a), 156.63 (4°, C-2), 159.48 (4°, C-7), 165.91 (4°, C-4'), 201.24 (4°, 8-*C*OCH$_2$CH$_2$CH$_3$).

Table-2 (Continued)

Compound	Elemental analysis		UV, IR, ^{1}H, ^{13}C NMR and Mass spectral data
2g	C, 69.27; H, 4.43	C, 69.23; H, 4.43.	IR: 2952, 1735, 1717, 1686, 1599, 1509, 1495, 1437 cm^{-1}. δ_H: 3.68 (sharp s, 3H, 3'-CO_2Me), 4.72 (broad dd, 2H, J = 3.8 Hz, 2Hz, 1'-H), 5.74 (dt, 1H, J = 16.0 Hz, 2.1 Hz, 3'-H), 6.25 (d, 1H, J = 9.0 Hz, 3-H), 6.85 (dt, 1H, J = 16.0 Hz, 3.8 Hz, 2'-H), 6.87 (d, 1H, J = 9.0 Hz, 6-H), 7.43 (t, 2H, J = 7.0 Hz, 3"-H and 5"-H), 7.53 (d, 1H, J = 9.0 Hz, 5-H), 7.60 (broad t, 1H, J = 7.0 Hz, 4"-H) 7.66 (d, 1H, J = 9.0 Hz, 4-H), 7.84 (broad d, 2H, J = 7.2 Hz, 2"-H and 6"-H).
2h	C, 69.81; H, 4.82	C, 69.83; H, 4.79.	IR: 294**7**, 1723, 1675, 1613, 1568 cm^{-1}. δ_H: 2.42 (sharp s, 3H, 4-CH_3), 3.68 (sharp s, 3H, 3'-CO_2Me), 4.74 (broad dd, 2H, J = 3.8 Hz, 2.1 Hz, 1'-H), 5.76 (dt, 1H, J = 15.0 Hz, 2.1 Hz, 3'-H), 6.14 (s, 1H, 3-H), 6.85 (broad d, 1H, J = 15.0 Hz, 2'-H), 6.89 (d, 1H, J = 9.0 Hz, 6-H), 7.45 (t, 2H, J = 7.5 Hz, 3"-H and 5"-H), 7.56 (broad t, 1H, J = 7.0 Hz, 4"-H), 7.66 (d, 1H, J = 9.0 Hz, 5-H), 7.84 (broad d, 2H, J = 7.2 Hz, 2"-H and 6"-H). δ_C: 51.50 (1°, 3'-CO_2*C*H_3), 67.59 (2°, C-1'), 108.98 (3°, C-6), 113.74 (4°, C-4a), 114.62 (3°, C-3), 118.11 (4°,C-8), 122.35 (4°, C-3'), 128.70 (3°, 4"-C), 129.39 (3°, C-5), 129.72 (3°, 2"-C and 6"-C), 133.84 (3°, 3"-C and 5"-C), 137.16 (4°, Ph-C), 140.51 (3°, C-2'), 142.58 (3°, C-4), 158.87 (4°, C-2), 159.32 (4°, C-7), 152.33 (4°, C-8a), 165.92 (4°, C-4'), 191.36 (4°, 8-*C*OPh).
3a	C, 67.62; H, 4.27	C, 67.60; H, 4.25.	IR: 3094, 2953, 1736, 1637, 1610, 1578, 1477, 1458, 1397 cm^{-1}. δ_H: 2.62 (s, 3H, 9-CH_3), 3.82 (s, 3H, 12-CO_2Me), 6.36 (d, 1H, J = 9.0 Hz, 3-H), 6.51 (d, 1H, J = 15.0 Hz, 12-H), 7.32 (d, 1H, J = 9.0 Hz, 6-H), 7.39 (d, 1H, J = 9.0 Hz, 5-H), 7.60 (d, 1H, J = 15.0 Hz, 11-H) 7.76 (d, 1H, J = 9.0 Hz, 4-H). δ_C: 9.93 (1°, 9-CH_3), 51.71 (1°, 12-CO_2*C*H_3), 108.42 (3°, C-6), 113.01 (4°, C-4a), 114.22 (3°, C-3), 118.38 (3°, C-12), 118.48 (4°, C-8), 119.90 (4°, C-9), 125.82 (3°, C-5), 128.43 (3°, C-11), 144.39 (3°, C-4), 149.38 (4°, C-8a), 150.04 (4°, C-10), 157.04 (4°, C-2), 160.00 (4°, C-7), 166.95 (4°, C-13). *m/z* 284 (100, M^+), 269 (2.7, M^+-CH_3), 253 (47.2, M^+-OCH_3), 225 (30, M^+-$\dot{C}OOCH_3$), 197 (11.8, M^+-$\dot{C}OOCH_3$-CO), 141 (10.9), 115 (11.8).
3b	C, 68.41; H, 4.74	C, 68.45; H, 4.73.	IR: 3090, 2953, 1739, 1637, 1600, 1576, 1439, 1397 cm^{-1}. δ_H: 2.49 (s, 3H, 4-CH_3), 2.66 (s, 3H, 9-CH_3), 3.84 (s, 3H, 12-CO_2Me), 6.27 (s, 1H, 3-H), 6.64 (d, 1H, J = 15.0 Hz, 12-H), 7.36 (d, 1H, J = 9.0 Hz, 6-H), 7.56 (d, 1H, J = 9.0 Hz, 5-H), 7.64 (d, 1H, J = 15.0 Hz, 11-H). *m/z* 298 (100, M^+), 267 (34.5, M^+-OCH_3), 239 (24.5, M^+-$\dot{C}OOCH_3$), 211 (9.1, M^+-CO-$\dot{C}OOCH_3$).
3c	C, 68.46; H, 4.69	C, 68.45; H, 4.73.	IR: 2953, 1720, 1698, 1611, 1570, 1492, 1434, 1408 cm^{-1}. δ_H: 1.40 (t, 3H, J = 7.2 Hz, 9-CH_2CH_3), 3.08 (q, 2H, J = 7.5 Hz, 9-CH_2CH_3), 3.85 (s, 3H, 12-CO_2Me), 6.41 (d, 1H, J = 9.5 Hz, 3-H), 6.58 (d, 1H, J = 15.0 Hz, 12-H), 7.38 (d, 1H, J = 8.5 Hz, 6-H), 7.44 (d, 1H, J = 8.5 Hz, 5-H), 7.66 (d, 1H, J = 15.0 Hz, 11-H), 7.81 (d, 1H, J = 9.0 Hz, 4-H). δ_C: 15.59 (1°, 9-CH_2CH_3), 17.97 (2°, 9-CH_2CH_3), 51.71 (1°, 12-CO_2*C*H_3), 108.08 (3°, C-6), 112.77 (4°, C-4a), 114.12 (3°, C-3), 118.18 (3°, C-12), 123.04 (4°, C-8), 125.97 (3°, C-5), 126.48 (4°, C-9), 128.47 (3°, C-11), 144.25 (4°, C-10), 144.35 (3°, C-4), 148.70 (4°, C-8a), 157.15 (4°, C-2), 160.30 (4°, C-7), 167.14 (4°, C-13). *m/z* 298 (100, M^+), 283 (10.9, M^+-CH_3), 267 (23.6, M^+-OCH_3), 251 (7.27, M^+-OCH_3-$\dot{C}H_3$-H), 238 (54.5, M^+-OCH_3-$\dot{C}_2H_5$), 223 (37.2, M^+- $\dot{C}OOCH_3$- $\dot{C}H_3$-H), 210 (20.5, M^+- $\dot{C}OOCH_3$- $\dot{C}_2H_5$), 195 (10, M^+-CO-$\dot{C}OOCH_3$- $\dot{C}H_3$-H), 181 (34.1, M^+- CO-$\dot{C}OOCH_3$- $\dot{C}_2H_5$-H), 152 (23.6, M^+-coumarin), 139 (29.1), 128 (25.5), 115 (14.1,), 91 (22.3, +$\dot{C}H_2$Ph), 69 (20.9), 55 (20).
3d	C, 69.21; H, 5.19	C, 69.23; H, 5.16.	IR: 3047, 2976, 1734, 1654, 1607, 1570, 1458, 1438, 1391 cm^{-1}. UV: 383.5 (4.36), 315 (4.24), 269 (4.23). δ_H: 1.38 (t, 3H, J = 7.2 Hz, 9-CH_2CH_3), 2.49 (s, 3H, 4-CH_3), 3.07 (q, 2H, J = 7.0 Hz, 9-CH_2CH_3), 3.83 (s, 3H, 12-CO_2Me), 6.27 (s, 1H, 3-H), 6.55 (d, 1H, J = 15.0 Hz, 12-H), 7.37 (d, 1H, J = 9.0 Hz, 6-H), 7.57 (d, 1H, J = 9.0 Hz, 5-H), 7.64 (d, 1H, J = 15.0 Hz, 11-H). δ_C: 15.59 (1°, 9-CH_2CH_3), 17.95 (2°, 9-CH_2CH_3), 19.42 (1°, 4-CH_3), 51.82 (1°, 12-CO_2*C*H_3), 108.07 (3°, C-6), 112.79 (3°, C-3), 114.72 (4°, C-4a), 117.55 (4°, C-8), 117.99 (3°, C-12), 122.61 (3°, C-5), 126.68 (4°, C-9), 128.41 (3°, C-11), 148.55 (4°, C-8a), 148.91 (4°, C-4), 153.27 (4°, C-10), 156.97 (4°, C-2), 160.19 (4°, C-7), 167.08 (4°, C-13). $[M+H]^+$ at *m/z* 313.1, $[M+Na]^+$ at *m/z* 335.1
3e	C, 69.26; H, 5.14	C, 69.23; H, 5.16.	IR: 3070, 2962, 1735, 1654, 1617, 1577, 1483, 1434, 1403 cm^{-1}. UV: 324 (4.20), 221 (4.27). δ_H: 1.00 (t, 3H, J = 7.5 Hz, 9-$CH_2CH_2CH_3$), 1.80 (sextet, 2H, J = 7.5 Hz, 9-$CH_2CH_2CH_3$), 2.99 (t, 2H, J = 7.5 Hz, 9-$CH_2CH_2CH_3$), 3.83 (s, 3H, 12-CO_2Me), 6.37 (d, 1H, J = 9.0 Hz, 3-H), 6.54 (d, 1H, J = 15.0 Hz, 12-H), 7.33 (d, 1H, J = 9.0 Hz, 6-H), 7.40 (d, 1H, J = 9.0 Hz, 5-H), 7.60 (d, 1H, J = 15.0 Hz, 11-H), 7.76 (d, 1H, J = 9.0 Hz, 4-H). δ_C: 13.56 (1°, 9-$CH_2CH_2CH_3$), 23.86 (2°, 9-$CH_2CH_2CH_3$), 26.25 (2°, 9-$CH_2CH_2CH_3$), 51.73 (1°, 13-CO_2*C*H_3), 108.45 (3°, C-6), 113.83 (4°, C-4a), 114.22 (3°, C-3), 118.04 (3°, C-12), 118.45 (4°, C-8), 124.72 (4°, C-9), 125.84 (3°, C-5), 128.57 (3°, C-11), 144.07 (3°, C-4), 149.49 (4°, C-8a), 149.74 (4°, C-10), 157.21 (4°, C-2), 159.87 (4°, C-7), 166.99 (4°, C-13). $[M-H]^+$ at *m/z* 311.1 $[M+NH_4]^+$ at *m/z* 329.3

Table-2 (Continued)

Compound	Elemental analysis		UV, IR, ^{1}H, ^{13}C NMR and Mass spectral data
3f	C, 69.89; H, 5.58	C, 69.93; H, 5.56.	IR: 3090, 2964, 1736, 1666, 1605, 1570, 1391 cm^{-1}. UV: 323 (4.33), 224.5 (4.25). δ_H: 1.01 (t, 3H, J = 7.5 Hz, 9-$CH_2CH_2CH_3$), 1.80 (sextet, 2H, J = 7.5 Hz, 9-$CH_2CH_2CH_3$), 2.49 (s, 3H, 4-CH_3), 3.02 (t, 2H, J = 7.5 Hz, 9-$CH_2CH_2CH_3$), 3.83 (s, 3H, 12-CO_2Me), 6.27 (s, 1H, 3-H), 6.55 (d, 1H, J = 15.0 Hz, 12-H), 7.37 (d, 1H, J = 9.0 Hz, 6-H), 7.56 (d, 1H, J = 9.0 Hz, 5-H), 7.62 (d, 1H, J = 15.0 Hz, 11-H). δ_C: 13.37 (1°, 9-$CH_2CH_2CH_3$), 19.51 (1°, 4-CH_3) 23.95 (2°, 9-$CH_2CH_2CH_3$), 26.32 (2°, 9-$CH_2CH_2CH_3$), 51.74 (1°, 12-CO_2CH_3), 108.07 (3°, C-6), 113.03 (3°, C-3), 114.92 (4°, C-4a), 118.20 (3°, C-12), 118.37 (4°, C-8), 122.56 (4°, C-5), 125.11 (4°, C-9), 128.71 (3°, C-11), 148.71 (4°, C-4), 149.48 (4°, C-8a), 154.01 (4°, C-10), 157.19 (4°, C-7), 157.80 (4°, C-2), 167.08 (4°, C-13). $[M+H]^+$ at *m/z* 327.2, $[M+Na]^+$ at *m/z* 349.2
3g	C, 72.81; H, 4.11	C, 72.83; H, 4.07.	IR: 2952, 1734, 1604, 1419 cm^{-1}. δ_H: 3.79 (s, 3H, 12-CO_2Me), 6.35 (d, 1H, J = 9.5 Hz, 3-H), 6.67 (d, 1H, J = 15.0 Hz, 12-H), 7.44 (d, 1H, J = 9.0 Hz, 6-H), 7.46 (t, 2H, J = 5.0 Hz, 3'-H and 5'-H), 7.47 (d, 1H, J = 15.0 Hz, 11-H), 7.50 (broad t, 1H, J = 5.1 Hz, 4'-H), 7.52 (broad d, 2H, J = 5.1 Hz, 2'-H and 6'-H), 7.59 (d, 1H, J = 9.0 Hz, 5-H), 7.76 (d, 1H, J = 9.5 Hz, 4-H) δ_C: 51.71 (1°, 12-CO_2CH_3), 108.54 (3°, C-6), 114.26 (4°, C-4a), 114.75 (3°, C-3), 118.3 (3°, C-12), 120.20 (3°, C-5), 125.15 (4°, C-8), 126.23 (4°, C-4), 126.23 (3°, 4'-C), 128.47 (3°, C-11), 128.92 (3°, 2'-C and 6'-C), 129.67 (4°, C-9), 129.78 (3°, 3'-C and 5'-C), 143.84 (4°, Ph-C), 149.77 (4°, C-8a), 153.32 (4°, C-10), 157.09 (4°, C-7), 159.44 (4°, C-2), 166.77 (4°, C-13). $[M+H]^+$ at *m/z* 347.2, $[M+Na]^+$ at *m/z* 369.3
3h	C, 73.31; H, 4.49	C, 73.33; H, 4.48.	IR: 2927, 1736, 1617, 1423, 1391 cm^{-1}. UV: 394 (4.46), 382 (4.46), 341 (4.46), 324 (4.46), 237 (4.39). δ_H: 2.65 (s, 3H, 4-CH_3), 3.81 (s, 3H, 12-CO_2Me), 6.25 (s, 1H, 3-H), 6.68 (d, 1H, J = 15.7 Hz, 12-H), 7.47 (d, 1H, J = 8.7 Hz, 6-H), 7.51 (t, 2H, J = 6.0 Hz, 3'-H and 5'-H), 7.52 (d, 1H, J = 15.8 Hz, 11-H), 7.60 (broad t, 1H, J = 6.2 Hz, 4'-H), 7.61 (broad d, 2H, J = 6.2 Hz, 2'-H and 6'-H), 7.64 (d, 1H, J = 8.7 Hz, 5-H). δ_C: 19.49 (1°, 4-CH_3), 51.85 (1°, 12-CO_2CH_3), 108.15 (3°, C-6), 113.30 (3°, C-3), 115.13 (4°, C-4a), 116.76 (4°, C-8), 119.74 (3°, C-12), 122.94 (3°, C-5), 128.33 (3°, C-11), 129.69 (4°, C-9), 129.75 (3°, 4'-C), 130.39 (3°, 2'-C and 6'-C), 130.52 (3°, 3'-C and 5'-C), 143.33 (4°, Ph-C) 148.90 (4°, C-4), 149.47 (4°, C-8a), 152.87 (4°, C-10), 156.78 (4°, C-7), 159.71 (4°, C-2), 166.88 (4°, C-13). $[M+H]^+$ at *m/z* 361.2, $[M+Na]^+$ at *m/z* 383.2

moiety encourages further study of such rearrangement and synthesis of more furano and pyranocoumarins by varying substituents at the 8- position and also on electron deficient allyloxy moiety of the coumarin derivatives.

EXPERIMENTAL

All melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr with Perkin-Elmer 883-IR, and RXI FT IR spectrophotometers. The UV spectra were measured in 95% ethanol using Hitachi U 2000 and Lamda 20 ELMER spectrophotometer. The elemental analyses were carried out in Perkin Elmer 240C elemental analyzer. The ^{1}H NMR and ^{13}C NMR spectra were recorded in Bruker AV300 supercon NMR spectrometer operating at 300.13 MHz for proton and 75.47 MHz for carbon using $CDCl_3$ as a solvent and TMS as an internal standard. Mass spectra were recorded on Finnigan Mat 1020 C, Shimadzu Model GEMS QP1000A, LC-MS MS Q-TOF-micro spectrometers and Q TRAP LC/MS/MS system operative at 70 eV. The column chromatographic separation and filtration were performed with silica gel (mesh size 60-120) prepared by Glaxo (India) Ltd and Merck (India) Ltd. Petroleum ether used had a boiling point 60-80 °C.

Synthesis of crotonyloxy ether 2a,b. 7-Hydroxy-8-acetyl-coumarin **1a** and 4-methyl-7-hydroxy-8-acetylcoumarins **1b** (2.5 mmol) dissolved in dry acetone (50 mL) was treated with methyl γ-bromocrotonate (0.3 mL, 2.5 mmol) and refluxed in the presence of anhydrous K_2CO_3 (0.5 g, 3.6 mmol) for 8 h. Acetone was distilled off and the residual content was treated with water and acidified with cold 4 *N* HCl (15 mL). The organic part of the mixture was extracted out with chloroform (2x50 mL) followed by successive washing of combined chloroform layer with saturated brine solution (15 mL), saturated sodium bicarbonate solution (2×15 mL) and finally with saturated brine solution (3×15 mL). The chloroform layer was dried over anhydrous sodium sulphate for 30 minutes. Filtration and solvent removal afforded crude solid mass, which crystallized from ethyl acetate as white needles, yield (65-75%).

Synthesis of crotonyloxy ether 2c-h. To a solution of 7-hydroxy-8-ketocoumarins and 4-methyl-7-hydroxy-8-keto-coumarins **1c-h** (2.5 mmol) in dry acetone (15 mL) were added methyl γ-bromocrotonate (0.3 mL, 2.5 mmol) and anhydrous K_2CO_3 (0.5 g, 3.6 mmol). The mixture was kept at room temperature for 12 h. Acetone was then removed by evaporation and the content was treated with water to dissolve K_2CO_3. The organic part of the mixture was extracted with chloroform (2x50 mL) and acidified with cold 4 *N* HCl (15 mL). The chloroform layer was subsequently washed respectively with saturated brine solution (20 mL), saturated sodium bicarbonate solution (20 mL) and brine solution (3×20 mL). Drying of the organic layer over anhydrous sodium sulphate for 30 minutes, and solvent removal afforded a solid

mass crystallizable from ethyl acetate as white flaky crystals yield (64-72%).

Synthesis of angular furanocoumarins 3a,b. Crotonyloxy ethers of 7-hydroxy-8-acetylcoumarin **3a** and 4-methyl-7-hydroxy-8-acetylcoumarin **3b** (2.5 mmol) dissolved in $PhNEt_2$ (20 mL) was refluxed for 8 h. Excess $PhNEt_2$ was distilled off and the residual content was treated with water and acidified with cold 2 *N* HCl (15 mL). The organic part of the mixture was extracted out with chloroform (2x50 mL) followed by successive washing of combined chloroform layer with saturated brine solution (15 mL), saturated sodium bicarbonate solution (2×15 mL) and finally with saturated brine solution (3×15 mL). The chloroform layer was dried over anhydrous sodium sulphate for 30 minutes. Filtration and solvent removal afforded crude oil, which was column chromatographed on silica gel. The angular furanocoumarins **2a,b** were obtained on elution with petroleum ether and ethyl acetate (4:1) and crystallized from ethyl acetate as white needles, yield (40-41%).

Synthesis of angular furanocoumarins 3c-h. 7-Hydroxy-8-ketocoumarins and 4-methyl-7-hydroxy-8-ketocoumarins **1c-h** (2.5 mmol) dissolved in dry acetone (50 mL) was treated with methyl γ-bromocrotonate (0.3 mL, 2.5 mmol) and refluxed in the presence of anhydrous K_2CO_3 (0.5 g, 3.6 mmol) for 8 h. Acetone was distilled off and the residual content was treated with water and acidified with cold 4 *N* HCl (15 mL). The organic part of the mixture was extracted out with chloroform (2x50 mL) followed by successive washing of combined chloroform layer with saturated brine solution (15 mL), saturated sodium bicarbonate solution (2×15 mL) and finally with saturated brine solution (3×15 mL). The chloroform layer was dried over anhydrous sodium sulphate for 30 minutes. Filtration and solvent removal afforded crude solid mass, which crystallized from ethyl acetate as white needles, yield (62-82%).

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