Choline hydroxide as an efficient catalyst for the diastereoselective synthesis of *trans*-2,3-dihydrofuro[3,2-*c*]coumarins in an aqueous medium

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A one-pot, three-component condensation of 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide with 4-hydroxycoumarin and an aromatic aldehyde in the presence of catalytic amounts of choline hydroxide in refluxing water gave *trans*-2-(4-chlorobenzoyl)-3-(aryl)-2,3-dihydro-4H-furo[3,2-c]chromen-4-ones in excellent yields and with short reaction times.

Keywords: furocoumarins, choline hydroxide, isoquinoline, green chemistry, diastereoselectivity, aryl aldehydes, 4-chlorophenacyl bromide, 4-hydroxycoumarin

Compounds containing the furocoumarin ring system are known to possess pharmacological properties such as anticancer,[1] antifungal,[2] antibacterial,[3] vasorelaxant,[4] antimicrobial[5] and photobiological[6] activities. The literature contains reports of the synthesis of furocoumarins in the presence of aldehydes and 4-hydroxycoumarin (2 equiv.) in poly(ethyleneglycol) (PEG) and a mixture of I_2 and $K_2S_2O_8$,[7] from the reactions of aromatic aldehydes, 4-hydroxycoumarin and α-chloroketones and a mixture of AcOH and $AcONH_4$,[8] from the sequential multicomponent reactions of 4-hydroxycoumarin, aromatic aldehydes and *in situ* generated cyanomethylpyridinium and phenacylpyridinium/(2-ethoxy-2-oxoethyl)pyridinium ylides in the presence of the ionic liquid [BMIm]OH,[9] from the reaction of pyridine, aromatic aldehyde, dimedone or 4-hydroxycoumarin and phenacyl bromide or *p*-nitrobenzyl bromide with Et_3N,[10] from aldehydes, a cyclic 1,3-diketone, 2-bromo-1-phenylethanone and *N*-methylimidazolium,[11] from the alkoxylation of 4-oxohydrocoumarins, alkenes and $Pd(CF_3COO)_2$,[12] from the reaction of 4-hydroxycoumarin derivatives with (*E*)-3-aryl/hetero-aryl-2-nitroprop-2-enols and 4-dimethylaminopyridine (DMAP),[13] and from the reactions of aryl aldehydes, a cyclic 1,3-diketone, 2-bromo-1-phenylethanone or 4-nitrobenzyl bromide and pyridine in the presence of 10 mol% sodium hydroxide in refluxing aqueous solution.[14] Although many of the reported methods are effective, some of them suffer from disadvantages such as harsh reaction conditions, use of hazardous solvents, long reaction times, complex working and purification procedures, high catalyst loadings and moderate yields. Therefore, the development of a simple, mild and efficient method is still needed. In the present work, we used choline hydroxide as an efficient catalyst to overcome these limitations.

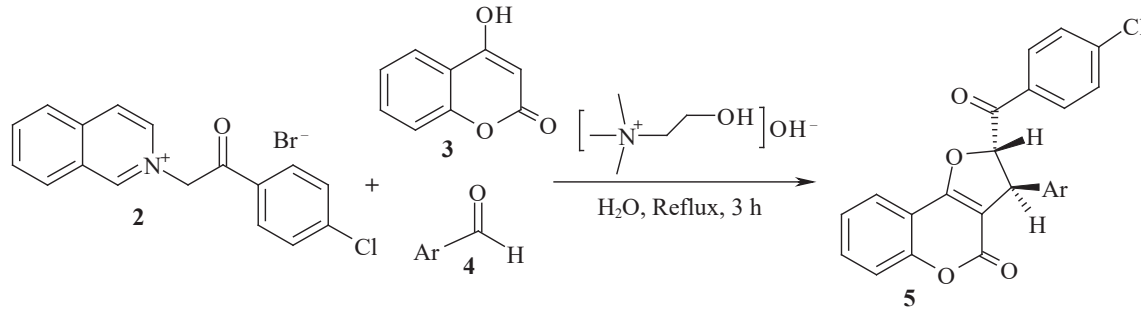
Recently, organic reactions in aqueous media have attracted a great deal of attention[15] as a result of increasing interest in the concepts of sustainability and green chemistry.[16] The latter synthesis used a procedure first described by Wang *et al.*[10] and by Khan *et al.*[14] in which a series of furocoumarins were synthesised *via* the pyridine-catalysed reaction of phenacyl bromides with a series of aromatic aldehydes and 4-hydroxycoumarin in the presence of catalytic amounts of NaOH or Et_3N. In this study, we have used the procedures of Wang *et al.*[10] and of Khan *et al.*[14] to synthesise another class of furocoumarins *via* a three-component condensation reaction of 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide **2** with 4-hydroxycoumarin **3** and an aromatic aldehyde **4** in the presence of catalytic amounts of choline hydroxide (Scheme 1).

Results and discussion

Treatment of isoquinoline with 4-chlorophenacyl bromide **1** in acetonitrile after 20 min yielded the 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide **2** in nearly quantitative yields (Scheme 2).

A one-pot, three-component reaction of 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide **2** with 4-hydroxycoumarin **3** and an aromatic aldehyde **4** in the presence of catalytic amounts of choline hydroxide in refluxing water provided the corresponding products **5** in excellent yields (Scheme 3).

The structures of compounds **5a**–**l** were deduced from their IR and ^{1}H and ^{13}C NMR spectra. The mass spectra of compounds **5a**–**l** were fairly similar and displayed molecular ion peaks. In the ^{1}H NMR spectra the two protons at the 2,3-positions of the dihydrofuran ring displayed two doublets at 5.52 and 5.10 ppm with a *vicinal* coupling constant $J = 4.4$ Hz. It has been documented that in *cis*-2,3-dihydrofurans the *vicinal* coupling constant of the two methine protons is $J = 7$–10 Hz, while in the *trans*-2,3-dihydrofuran the *vicinal* coupling constant is $J = 2.8$–6 Hz. Thus we concluded that the more thermodynamically stable *trans* isomers of the 2,3-dihydrofuran derivatives were formed.[14]



Scheme 1

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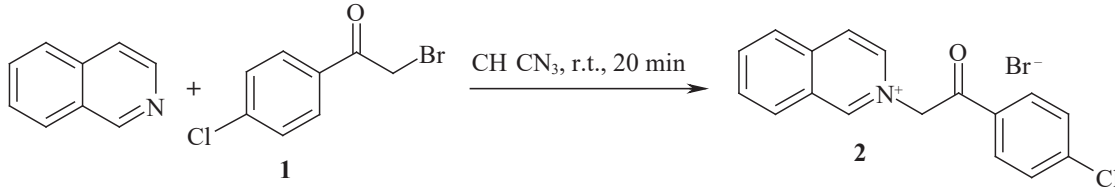
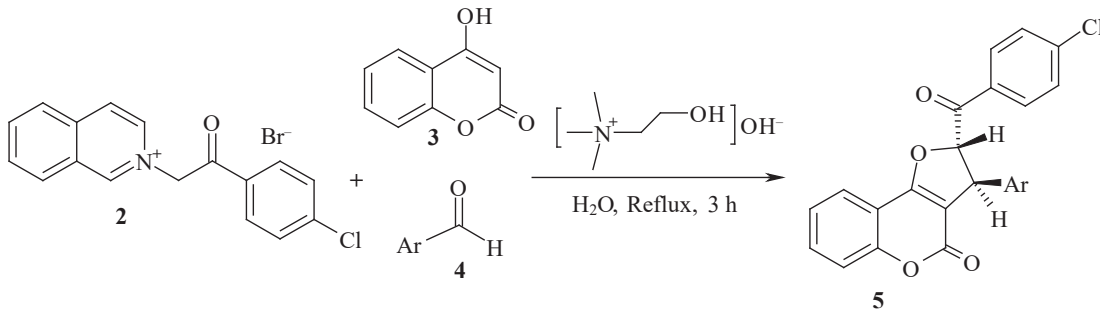


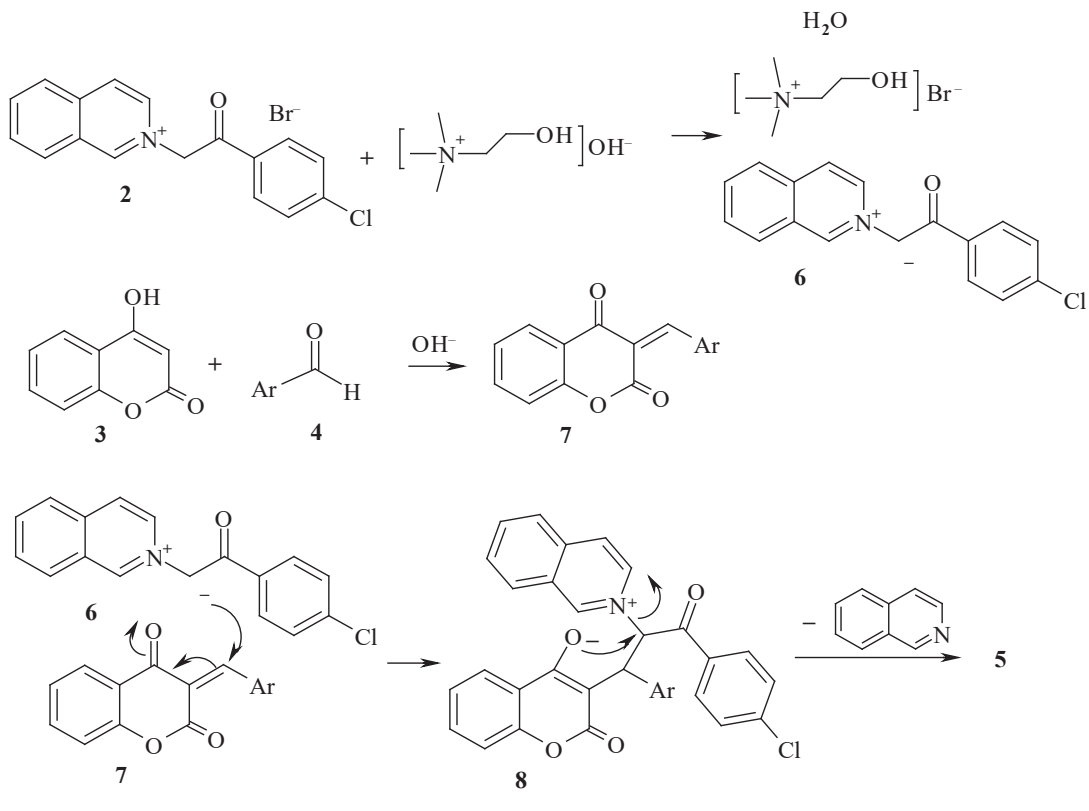
Scheme 2



5	Ar	% Yield*	m.p./°C
a	C_6H_5	92	201–203
b	2-O_2N C_6H_4	93	185–187
c	4-O_2N C_6H_4	94	181–183
d	2-Cl C_6H_4	90	233–235
e	4-ClC_6H_4	91	249–251
f	2-FC_6H_4	94	219–221
g	4-CH_3O C_6H_4	90	177–179
h	4-F C_6H_4	95	226–228
i	4-Cl-3-O_2N C_6H_3	92	235–237
j	4-NC C_6H_4	90	194–196
k	4-CH_3 C_6H_4	90	195–197
l	4-Br C_6H_4	91	189–191

*Yields refer to the pure isolated products

Scheme 3



Scheme 4

A proposed mechanism for this reaction is shown in Scheme 4. The formation of the product can be explained as follows. The 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide **2** undergoes deprotonation in the presence of aqueous choline hydroxide to give the reactive isoquinolinium ylide **6** at room temperature. The 4-hydroxycoumarin **3** reacts with aromatic aldehyde **4** in the presence of choline hydroxide to give the Knoevenagel product **7**. The latter reacts instantly with the isoquinolinium ylide **6** to form the zwitterionic intermediate **8**. The intermediate **8** undergoes cyclisation with the elimination of isoquinoline to give the desired product **5**.

In summary, here we report a simple and efficient one-pot synthesis of *trans*-2,3-dihydrofuro[3,2-*c*]coumarins *via* a three-component reaction between 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide with 4-hydroxycoumarin and an aromatic aldehyde in the presence of catalytic amounts of choline hydroxide. The advantages of this method are simple, readily available, starting materials, short reaction times, easy and clean work-up and excellent yields of products.

Experimental

Melting points were determined with an Electrothermal 9100 apparatus. Elemental analyses were performed using a Heraeus CHN-O-Rapid Analyzer. Mass spectra were recorded on a Finnigan-MAT 8430 mass spectrometer operating at an ionisation potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 Avance spectrometer in $CDCl_3$ solution using tetramethylsilane (TMS) as internal standard. 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide **2** was prepared by the literature method.[17] All other chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification.

General procedure

To a magnetically stirred solution of 2-[2-(4-chlorophenyl)-2-oxoethyl]isoquinolinium bromide (1 mmol), 4-hydroxycoumarin (1 mmol) and aryl aldehyde (1 mmol) in H_2O (10 mL) was added choline hydroxide (0.0121 g, 0.1 mmol) in H_2O (4 mL). The mixture was then refluxed for 3 h. The solid product was filtered off and recrystallised from ethanol to yield the pure product.

*trans-2-(4-Chlorobenzoyl)-3-phenyl-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5a**): White powder, m.p. 201–203 °C; IR (KBr) ν_{max}/cm^{-1}: 2921, 2850, 1718, 1644, 1448, 1405, 1036, 756, 578; Anal. calcd for $C_{24}H_{15}ClO_4$: C, 71.56; H, 3.75; found: C, 71.43; H, 3.61%; MS (*m/z*, %): 402 (5); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.84 (1H, d, *J* = 5.2 Hz, H-3), 6.14 (1H, d, *J* = 5.2 Hz, H-2), 7.22 (2H, t, *J* = 7.6 Hz, Ar-H), 7.33 (1H, t, *J* = 6.8 Hz, Ar-H), 7.37 (1H, t, *J* = 7.6 Hz, Ar-H), 7.38 (2H, d, *J* = 6.8, Ar-H), 7.42 (2H, t, *J* = 6.8 Hz, Ar-H), 7.55 (1H, m, Ar-H), 7.85 (2H, d, *J* = 7.4 Hz, Ar-H), 7.84 (2H, d, *J* = 7.4 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 49.2, 92.5, 105.3, 112.1, 117.3, 123.1, 124.2, 126.6, 127.9, 128.3, 129.4, 130.5, 131.5, 133.1, 139.4, 141.1, 155.4, 159.2, 166.2, 191.1 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(2-nitrophenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5b**): White powder, m.p. 185–187 °C; IR (KBr) ν_{max}/cm^{-1}: 2923, 2842, 1729, 1644, 1510, 1410, 1023, 745, 570; Anal. calcd for $C_{24}H_{14}ClNO_6$: C, 64.37; H, 3.15; N, 3.13; found: C, 64.26; H, 3.30; N, 3.22%; MS (*m/z*, %): 447 (3); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.20 (1H, d, *J* = 5.2 Hz, H-3), 6.08 (1H, d, *J* = 5.2 Hz, H-2), 7.30 (2H, m, Ar-H), 7.33 (1H, t, *J* = 8.2 Hz, Ar-H), 7.42 (1H, d, *J* = 8 Hz, Ar-H), 7.49 (1H, m, Ar-H), 7.58 (1H, d, *J* = 7.4 Hz, Ar-H), 7.66 (2H, d, *J* = 8 Hz, Ar-H), 7.85 (1H, t, *J* = 7.4 Hz, Ar-H), 7.91 (2H, d, *J* = 8 Hz, Ar-H) 8.20 (1H, d, *J* = 7.6 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 45.2, 91.3, 104.8, 112.2, 116.4, 117.3, 123.4, 124.2, 124.8, 126.5, 126.8, 129.3, 129.7, 130.6, 131.8, 133.1, 141.2, 155.3, 159.2, 161.7, 166.2, 191.1 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-nitrophenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5c**): White powder, m.p. 181–183 °C; IR (KBr) ν_{max}/cm^{-1}: 2931, 2856, 1727, 1640, 1523, 1411, 747, 575; Anal. calcd for $C_{24}H_{14}ClNO_6$: C, 64.37; H, 3.15; N, 3.13; found: C, 64.23; H, 3.24; N, 3.25%; MS (*m/z*, %): 447 (6); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.08 (1H, d, *J* = 5.2 Hz, H-3), 6.09 (1H, d, *J* = 5.2 Hz, H-2), 7.36 (2H, m, Ar-H), 7.38 (1H, t, *J* = 8.2 Hz, Ar-H), 7.44 (1H, d, *J* = 8 Hz, Ar-H), 7.55 (2H, d, *J* = 7.4 Hz, Ar-H), 7.80 (2H, d, *J* = 7.4 Hz, Ar-H), 7.95 (2H, d, *J* = 8 Hz, Ar-H), 8.18 (2H, d, *J* = 7.6 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 48.0, 92.0, 104.3, 111.7, 117.2, 123.1, 124.4, 125.3, 128.8, 129.4, 130.6, 131.6, 133.5, 141.4, 146.5, 147.7, 155.4, 159.0, 166.4, 190.4 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(2-chlorophenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5d**): White powder, m.p. 233–235 °C; IR (KBr) ν_{max}/cm^{-1}: 2924, 2843, 1723, 1644, 1450, 1402, 1026, 754, 575; Anal. calcd for $C_{24}H_{14}Cl_2O_4$: C, 65.92; H, 3.23; found: C, 65.77; H, 3.35%; MS (*m/z*, %): 436 (7); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34 (1H, d, *J* = 5.2 Hz, H-3), 6.07 (1H, d, *J* = 5.2 Hz, H-2), 7.16–7.30 (3H, m, Ar-H), 7.34 (1H, d, *J* = 7.4 Hz, Ar-H), 7.41 (1H, d, *J* = 7.4 Hz, Ar-H), 7.49 (1H, t, *J* = 8.2 Hz, Ar-H), 7.56 (1H, d, *J* = 7.2 Hz, Ar-H), 7.65 (1H, d, *J* = 8.2 Hz, Ar-H), 7.80 (2H, d, *J* = 8.0 Hz, Ar-H), 7.90 (2H, d, *J* = 8.0 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 46.1, 91.2, 104.6, 112.3, 116.5, 117.2, 123.5, 124.3, 124.6, 126.3, 126.7, 129.2, 129.6, 130.5, 131.7, 133.2, 141.8, 155.2, 159.3, 161.6, 166.3, 190.2 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-chlorophenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5e**): White powder, m.p. 249–251 °C; IR (KBr) ν_{max}/cm^{-1}: 2934, 2824, 1722, 1646, 1414, 1024, 758, 536; Anal. calcd for $C_{24}H_{14}Cl_2O_4$: C, 65.92; H, 3.23; found: C, 65.80; H, 3.32%; MS (*m/z*, %): 436 (10); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.88 (1H, d, *J* = 5.2 Hz, H-3), 6.08 (1H, d, *J* = 5.2 Hz, H-2), 7.28 (2H, t, *J* = 7.4 Hz, Ar-H), 7.29 (2H, d, *J* = 7.4 Hz, Ar-H), 7.36 (1H, t, *J* = 7.4 Hz, Ar-H), 7.38 (2H, d, *J* = 7.4 Hz, Ar-H), 7.52 (1H, d, *J* = 7.4 Hz, Ar-H), 7.83 (2H, d, *J* = 8 Hz, Ar-H), 7.90 (2H, d, *J* = 7.4 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 48.3, 92.5, 105.3, 112.0, 116.4, 117.1, 123.1, 124.2, 129.3, 129.4, 130.5, 131.6, 133.3, 133.7, 135.1, 141.2, 155.4, 159.1, 166.14, 190.8 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(2-fluorophenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5f**): Yellow powder, m.p. 219–221 °C; IR (KBr) ν_{max}/cm^{-1}: 2930, 2853, 1713, 1644, 1450, 1402, 1024, 755, 574; Anal. calcd for $C_{24}H_{14}ClFO_4$: C, 68.50; H, 3.35; found: C, 68.36; H, 3.22%; MS (*m/z*, %): 420 (4); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.19 (1H, d, *J* = 5.4 Hz, H-3), 6.16 (1H, d, *J* = 5.4 Hz, H-2), 7.17–7.31 (3H, m, Ar-H), 7.38 (1H, d, *J* = 7.4 Hz, Ar-H), 7.41 (1H, d, *J* = 7.4 Hz, Ar-H), 7.43 (1H, t, *J* = 8.2 Hz, Ar-H), 7.52 (1H, d, *J* = 7.2 Hz, Ar-H), 7.66 (1H, d, *J* = 8.2 Hz, Ar-H), 7.80 (2H, d, *J* = 8.0 Hz, Ar-H), 7.94 (2H, d, *J* = 8.0 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 43.1, 91.0, 103.7, 112.0, 116.3, 117.1, 123.1, 124.2, 124.9, 126.0, 126.1, 129.4, 129.6, 130.5, 131.7, 133.0, 141.1, 155.4, 159.5, 166.4, 166.4, 192.4 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-methoxyphenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5g**): White powder, m.p. 177–179 °C; IR (KBr) ν_{max}/cm^{-1}: 1728, 1692, 1642, 1617, 1512, 1418, 1258, 1210, 1235, 1176, 1080, 1022, 935; Anal. calcd for $C_{25}H_{17}ClO_5$: C, 69.37; H, 3.96; found: C, 69.20; H, 3.85%; MS (*m/z*, %): 432 (8); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (3H, s, OMe), 5.33 (1H, d, *J* = 5.2 Hz, H-3), 6.09 (1H, d, *J* = 5.2 Hz, H-2), 7.25 (2H, d, *J* = 8.4 Hz, Ar-H), 7.29 (2H, d, *J* = 8.4 Hz, Ar-H), 7.33 (1H, t, *J* = 7.6 Hz, Ar-H), 7.40 (1H, d, *J* = 8.4 Hz, Ar-H), 7.49 (2H, t, *J* = 8.0 Hz, Ar-H), 7.56–7.65 (2H, m, Ar-H), 7.82 (1H, d, *J* = 7.6, 1.6 Hz, Ar-H), 7.90 (2H, d, *J* = 8.8 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 46.2, 55.7, 91.3, 104.8, 112.4, 116.8, 117.3, 123.6, 124.3, 124.5, 126.2, 126.6, 130.1, 131.8, 133.2, 141.6, 155.3, 159.4, 166.4, 190.3 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-fluorophenyl)-2,3-dihydro-4*H-*furo[3,2-*c*]chromen-4-one* (**5h**): Yellow powder, m.p. 226–228 °C; IR (KBr) ν_{max}/cm^{-1}: 2924, 2836, 1724, 1646, 1412, 1024, 754, 534; Anal. calcd for $C_{24}H_{14}ClFO_4$: C, 68.50; H, 3.35; found: C, 68.38; H, 3.19%; MS (*m/z*, %): 420 (5); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.88 (1H, d, *J* = 5.2 Hz, H-3), 6.09 (1H, d, *J* =5.2 Hz, H-2), 7.29 (2H, t, *J* = 8.4 Hz, Ar-H), 7.32 (2H, d, *J* = 8.4 Hz, Ar-H), 7.43 (1H, t, *J* = 8.4 Hz, Ar-H), 7.53 (2H, d, *J* = 8.4 Hz, Ar-H), 7.66 (1H, d, *J* = 8.4 Hz, Ar-H), 7.88 (2H, d, *J* = 8.4 Hz, Ar-H), 7.90 (2H, d, *J* = 8 Hz, Ar-H) ppm; ^{13}C NMR (100.6

MHz, $CDCl_3$): δ 48.3, 92.5, 105.1, 112.0, 116.4, 117.1, 123.1, 124.2, 129.3, 129.4, 130.5, 131.6, 133.1, 135.1, 141.2, 155.4, 159.5, 161.9, 166.4, 190.6 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-chloro-3-nitrophenyl)-2,3-dihydro-4*H-*furo[3,2-c]chromen-4-one* (**5i**): White powder, m.p. 235–237 °C; IR (KBr) ν_{max}/cm^{-1}: 2930, 2853, 1727, 1647, 1524, 1410, 747, 578; Anal. calcd for $C_{24}H_{13}Cl_2NO_6$: C, 59.77; H, 2.72; N, 2.90; found: C, 59.61; H, 2.85; N, 3.04%; MS (*m/z*, %): 481 (5); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.17 (1H, d, *J* = 5.6 Hz, H-3), 6.05 (1H, d, *J* = 5.6 Hz, H-2), 7.36 (2H, m, Ar-H), 7.44 (1H, t, *J* = 8.2 Hz, Ar-H), 7.54 (1H, d, *J* = 8.2 Hz, Ar-H), 7.58 (1H, m, Ar-H), 7.66 (1H, d, *J* = 7.4 Hz, Ar-H), 7.69 (2H, d, *J* = 8.2 Hz, Ar-H), 7.85 (1H, t, *J* = 7.4 Hz, Ar-H), 7.96 (2H, d, *J* = 8.2 Hz,) 7.98 (1H, d, *J* = 7.6 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 47.2, 91.9, 103.9, 111.6, 117.3, 123.6, 124.0, 126.9, 127.1, 127.5, 128.6, 129.5, 130.7, 131.3, 132.7, 133.6, 135.9, 141.5, 155.5, 159.5, 166.4, 190.3 ppm.

*trans-[2-(4-Chlorobenzoyl)-4-oxo-2,3-dihydro-4*H-*furo[3,2-c]chromen-3-yl]benzonitrile* (**5j**): White powder, m.p. 194–196 °C; IR (KBr) ν_{max}/cm^{-1}: 2935, 2854, 1725, 1645, 1527, 1410, 747, 575; Anal. calcd for $C_{25}H_{14}ClNO_4$: C, 70.18; H, 3.30; N, 3.27; found: C, 70.31; H, 3.19; N, 3.40%; MS (*m/z*, %): 427 (7); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.08 (1H, d, *J* = 5.4 Hz, H-3), 6.07 (1H, d, *J* = 5.4 Hz, H-2), 7.29 (2H, m, Ar-H), 7.38 (1H, t, *J* = 8.4 Hz, Ar-H), 7.44 (1H, d, *J* = 8.4 Hz, Ar-H), 7.47 (2H, d, *J* = 8.4 Hz, Ar-H), 7.69 (2H, d, *J* = 7.6 Hz, Ar-H), 7.81 (2H, d, *J* = 7.6 Hz, Ar-H), 7.93 (2H, d, *J* = 8.4 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 48.3, 92.0, 104.3, 112.2, 117.2, 118.4, 123.1, 124.4, 128.5, 129.5, 130.6, 131.6, 132.2, 133.1, 133.4, 141.4, 155.4, 159.0, 166.3, 190.4 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-methylphenyl)-2,3-dihydro-4*H-*furo[3,2-c]chromen-4-one* (**5k**): White powder, m.p. 195–197 °C; IR (KBr) ν_{max}/cm^{-1}: 2932, 2864, 1723, 1646, 1453, 1407, 1025, 753; Anal. calcd for $C_{25}H_{17}ClO_4$: C, 72.03; H, 4.11; found: C, 72.18; H, 4.00%; MS (*m/z*, %): 416 (12); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (3H, s, CH_3), 4.78 (1H, d, *J* = 5.4 Hz, H-3), 6.12 (1H, d, *J* = 5.4 Hz, H-2), 7.37 (2H, d, *J* = 7.2 Hz, Ar-H), 7.40 (2H, d, *J* = 7.2 Hz, Ar-H), 7.52 (2H, m, Ar-H), 7.63 (1H, t, *J* = 8.4 Hz, Ar-H), 7.65 (1H, d, *J* = 8.4 Hz, Ar-H), 7.85 (2H, d, *J* = 7.6 Hz, Ar-H), 7.89 (2H, d, *J* = 7.6 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 21.2, 49.0, 92.6, 105.4, 112.1, 117.1, 123.1, 124.2, 127.4, 129.4, 130.0, 130.4, 131.5, 132.9, 136.3, 138.1, 141.1, 155.4, 159.2, 166.1, 191.1 ppm.

*trans-2-(4-Chlorobenzoyl)-3-(4-bromophenyl)-2,3-dihydro-4*H-*furo[3,2-c]chromen-4-one* (**5l**): White powder, m.p. 189–191 °C; IR (KBr) ν_{max}/cm^{-1}: 2917, 2821, 1718, 1645, 1405, 1028, 755, 538; Anal. calcd for $C_{24}H_{14}BrClO_4$: C, 59.84; H, 2.93; found: C, 59.96; H, 3.08%; MS (*m/z*, %): 481 (4); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (1H, d, *J* = 5.4 Hz, H-3), 6.07 (1H, d, *J* = 5.4 Hz, H-2), 7.37 (2H, d, *J* = 7.4 Hz, Ar-H), 7.42 (2H, d, *J* = 8.2 Hz, Ar-H), 7.64 (1H, m, Ar-H), 7.66 (1H, d, *J* = 8 Hz, Ar-H), 7.88 (2H, d, *J* = 7.4 Hz, Ar-H), 7.88 (2H, d, *J* = 8.2 Hz, Ar-H), 8.03 (2H, d, *J* = 8.2 Hz, Ar-H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 49.1, 92.5, 105.3, 112.1, 117.1, 123.1, 124.3, 127.4, 12.5, 130.1, 130.5, 131.5, 132.9, 136.4, 138.2, 141.1, 155.5, 159.3, 166.1, 191.2 ppm.

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