Tetrahedron 66 (2010) 1289–1293

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Convenient synthesis of fused pyrano[3,2-*h*]- and furo[3,2-*h*]benzo[*f*]coumarins from naphthalene-2,3-diol☆

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ARTICLE INFO

Article history:
Received 1 September 2009
Received in revised form
4 November 2009
Accepted 4 December 2009
Available online 18 December 2009

Keywords:
Pyranocoumarins
Furocoumarins
N-Methylformamide
Boron trifluoride
N,*N*-Dimethylformamide

ABSTRACT

The treatment of 8-propargyloxy-benzo[*f*]coumarin with boron trifluoride diethyl etherate in *N*,*N*-dimethylformamide under reflux or MW irradiation resulted in pyrano[3,2-*h*]benzo[*f*]coumarin, while the furo[3,2-*h*]benzo[*f*]coumarin is received from the treatment with *N*-methylformamide under MW irradiation.

1. Introduction

Coumarin derivatives are an interesting class of heterocyclic system, since the coumarin ring is an essential core moiety for a variety of natural and synthetic biologically active compounds.[1–3] In particular, fused coumarins and among them furocoumarins are important as photochemotherapeutic[4–9] agents and exhibit antitumorial,[10] antioxidant[3] and *anti*-inflammatory[3] activities. Pyranocoumarins are used also as photoactive drugs for skin disorders[11] and possess antifungal,[12] insecticidal,[12] anticancer,[12] *anti*-HIV,[6,13] *anti*-inflammatory,[3,14] antioxidant,[3,14] and antibacterial[15] activities.

The synthesis of furocoumarins[5,7,8,16–25] or pyranocoumarins[5,16,17,24–28] has been achieved mainly by formation of furan or pyran ring starting from hydroxycoumarins and using the Claisen[16,29] rearrangement of the intermediate propargyloxy- or allyloxycoumarins. The tandem Claisen rearrangement-cyclization reaction of 3- or 7-propargyloxycoumarins resulted in the formation of fused furo[2,3-*c*]- or [2,3-*h*]coumarins under pyrolysis at 150 °C without solvent[18] or by heating of *N*,*N*-dimethylformamide (DMF) solution[19] at 80–90 °C (when bulky substituents are present in the propargyloxy moiety). Furocoumarins were received also by the heating of the mixture of propargyloxycoumarin with NaOAc[21] at 190 °C or of *N*,*N*-dimethylaniline (*N*,*N*-DMA)[22] solution at 130 °C or by refluxing of pyridine solution[22] or by microwave irradiation[25] of *N*-methylformamide (NMF) solution (no substituents in the propargyloxy moiety). When the same reactions were performed under reflux in *N*,*N*-DMA[24] or *N*,*N*-diethylaniline (*N*,*N*-DEA)[19,24,25,26] or by heating in chlorobenzene[27] solution at 100 °C or in xylene or toluene solution[28] at 110 °C or by microwave irradiation[25] in NMF solution (with bulky substituents in propargyloxy moiety), the fused pyrano[2,3-*c*]- or [2,3-*h*]- or [3,2-*g*]-coumarins were received. Dihydrofurocoumarins were obtained also by tandem Claisen rearrangement-cyclization reaction of allyloxycoumarins with $BF_3 \cdot Et_2O$ and NMF[23] under microwave irradiation or by a step by step procedure[24] including Claisen rearrangement and subsequent cyclization by H_2SO_4. The dihydrofurocoumarins were oxidized with DDQ to furocoumarins.[24]

As we can see in the above procedures, $BF_3 \cdot Et_2O$ is not yet in use in the Claisen rearrangement of the propargyloxycoumarins. In the course of our interest on the synthesis[3,14,30–34] of fused coumarin derivatives and the study of their biological activity[3,14,33,34] we wish to report here the application of $BF_3 \cdot Et_2O$ on the synthesis of title compounds from 8-propargyloxy-benzo[*f*]coumarins. The reactions studied and the products received are depicted in Schemes 1 and 2.

☆ Preliminary communications presented at 11th Belgian Organic Synthesis Symposium, July 13–18, 2008, Ghent, Belgium, Abstrs., p. 229 and at 2nd International Symposium on Organic Chemistry, December 13–16, 2008, Sofia, Bulgaria, Abstrs., p. 80.

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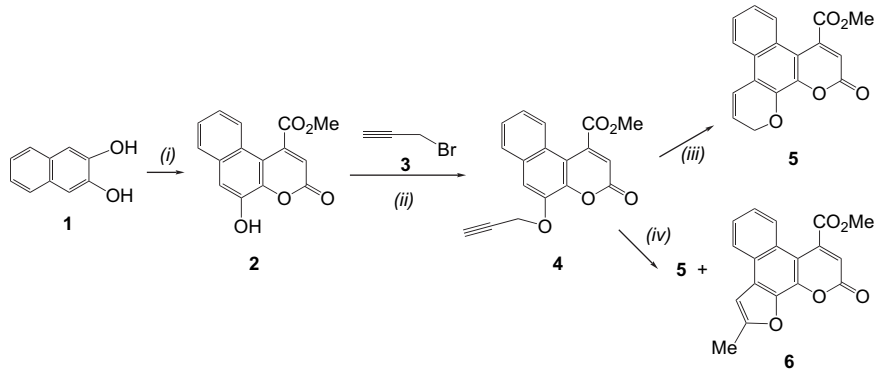
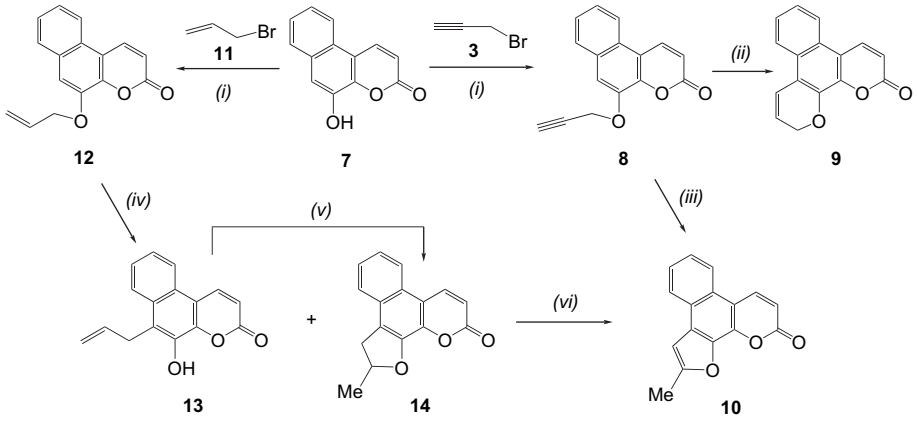
doi:10.1016/j.tet.2009.12.016



Scheme 1. Reagents and conditions: (i) Ph_3P, DMAD, DCM, 0 °C (15 min) then reflux (2 h). (ii) K_2CO_3, acetone (dry), reflux, 4 h. (iii) BF_3/Et_2O, DMF, reflux, 24 h or BF_3/Et_2O, DMF, MW (180 °C, 10 min) or *N*,*N*-DEA, reflux, 20 h. (iv) BF_3/Et_2O, NMF, MW (180 °C, 10 min).



Scheme 2. Reagents and conditions: (i) K_2CO_3, acetone (dry), reflux, 24 h. (ii) BF_3/Et_2O, DMF, reflux, 48 h or BF_3/Et_2O, DMF, MW (180 °C, 10 min). (iii) NMF, MW (180 °C, 10 min). (iv) BF_3/Et_2O, NMF, MW (200 °C, 20 min). (v) conc. H_2SO_4, 90 °C, 20 min. (vi) DDQ, toluene (dry), reflux, 24 h.

2. Results and discussion

By the treatment of a dichloromethane (DCM) solution of naphthalene-2,3-diol (**1**) in the presence of Ph_3P with a solution of dimethylacetylenedicarboxylate (DMAD)[31] in DCM at 0 °C for 15 min and reflux for 2 h we received after the separation of the reaction mixture by column chromatography the methyl 5-hydroxy-3-oxo-3*H*-benzo[*f*]chromen-1-carboxylate (**2**) in 52% yield (Scheme 1). We prepared the propargyloxycoumarin[26] derivative **4** (73%) by refluxing of a mixture of compound **2**, propargylbromide (**3**) and K_2CO_3 in dry acetone. Table 1 contains the efforts for the tandem Claisen rearrangement-cyclization of propargyloxy derivative **4**. The use of $BF_3\cdot Et_2O$ in DMF under MW irradiation gave the best results for the formation of pyran derivative **5** (90% yield), in comparison to the heating under reflux with the same solvent or with *N*,*N*-DEA. When we irradiated in $BF_3\cdot Et_2O$ in NMF the furan derivative **6** increased from 8%–22%, while the pyranocoumarin **5** received in 66% yield. The irradiation in NMF without the $BF_3\cdot Et_2O$ resulted to a complicated mixture without any –COOMe group in ^{1}H NMR, while in DMF the starting material remained unchanged.

Treatment of the recently[34] prepared by us 5-hydroxy-3*H*-benzo[*f*]chromen-3-one (**7**) with the bromide **3** and K_2CO_3 in boiling dry acetone resulted in propargyloxycoumarin[26] derivative **8** in 82% yield (Scheme 2). MW irradiation (Table 1) of the solution of compound **8** in $BF_3\cdot Et_2O$ and DMF resulted in the pyranocoumarin **9** (92% yield) and to the furan derivative **10** (4%). We succeeded to isolate the furan derivative **10** in 80% yield, when we followed an analogous procedure,[25] by heating compound **8** in NMF solution under MW irradiation. The starting compound **8** remained unchanged under MW irradiation (180 °C, 10 min) in *N*,*N*-DEA.

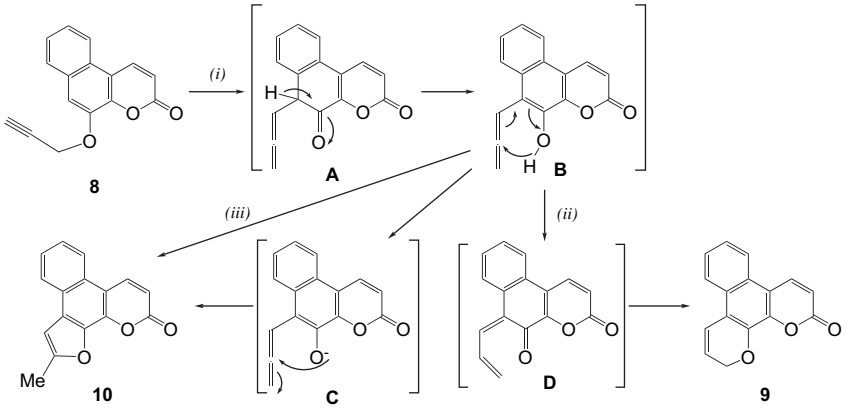
Table 1
Tandem Claisen rearrangement-cyclization of propargyloxycoumarin derivatives **4** or **8** to **5**, **6** or **9**, **10**

Solvent	Reflux, h	MW, 180 °C, min	From **4**		From **8**	
			5 (yield %)	**6** (yield %)	**9** (yield %)	**10** (yield %)
$BF_3\cdot Et_2O$/DMF	24	—	78	—	57[a]	—
$BF_3\cdot Et_2O$/DMF	—	10	90	8	92	4
$BF_3\cdot Et_2O$/NMF	—	10	66	22	—	—
NMF	—	10	[b]	[b]	—	80
N,*N*-DEA	20	—	35	—	—	—
N,*N*-DEA	—	10	—	—	[c]	[c]
DMF	—	5	[c]	[c]	—	—

[a] Reflux for 48 h.
[b] Complicated mixture at 100 °C.
[c] Unreacted starting material.

We prepared also the furan derivative **10** by another way. The mixture of compound **7**, allylbromide (**11**) and K_2CO_3 was heated under reflux in dry acetone and led to the allyloxycoumarin[26] derivative **12** in 84% yield. Treatment of the latter with $BF_3\cdot Et_2O$ in NMF under MW irradiation (200 °C, 20 min) gave the *o*-hydroxyallyl derivative **13** (82% yield) and the dihydrofuran derivative **14** (16% yield). When the compound **12** was irradiated at 180 °C for 10 min only the Claisen rearrangement product **13** was isolated (98%). Treatment of compound **13** with drops of concentrated H_2SO_4 resulted in the derivative **14** (72%). We received the furan derivative **10** (80% yield) by the oxidation of compound **14** with DDQ.[24]

A former mechanistic scheme proposed earlier[35] for the Claisen rearrangement of aryl propargyl ethers apparently could be applied, as depicted in Scheme 3. From the [3,3]-rearrangement of the propargyloxycoumarin derivative **8** the allenyl intermediate **A** was formed and aromatized through tautomerization to the hydroxyallenyl derivative **B**. A [1,5-*H*]-shift in **B** led to **D**, which was then cyclized to the pyran derivative **9**. In the presence of NMF, which has larger a dielectric constant[36] than DMF, there is a greater dissociation in intermediate **B** leading to oxyanion (**C**), which with internal nucleophilic attack in the central allenic carbon resulted in the furan derivative **10**. The formation of furan derivative **10** could be explained also by the nucleophilic attack of phenol oxygen lone pair of **B** to the central allenic carbon (III), which is promoted by the H-bonding activation from protic NMF solvent to chromene carbonyl.



Scheme 3. (i) [3,3]-rearrangement. (ii) [1,5-*H*] sigmatropic shift. (iii) nucleophilic attack of phenol oxygen lone pair of **B** to the central allenic carbon.

In conclusion, we demonstrated methodologies using $BF_3 \cdot Et_2O$ and DMF or NMF for the *regio*selective synthesis of fused pyrano- or furocoumarins in good yields.

3. Experimental

3.1. General

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were obtained with a Perkin–Elmer 1310 spectrophotometer as Nujol mulls. NMR spectra were recorded on a Bruker AM 300 (300 MHz and 75 MHz for ^1H and ^{13}C, respectively) using $CDCl_3$ as solvent and TMS as an internal standard. *J* values are reported in hertz. Mass spectra were determined on a LCMS-2010 eV Instrument (Shimadzu) under Electrospray Ionization (ESI) conditions. Microanalyses were performed on a Perkin–Elmer 2400-II Element analyzer. Silica gel N^0 60, Merck A.G. was used for column chromatography. The MW experiments were performed in a Biotage (Initiator 2.0) scientific MW oven.

*3.1.1. 5-Hydroxy-3-oxo-3H-benzo[f]chromen-1-carboxylate (**2**).* A solution of Ph_3P (2.624 g, 10 mmol) in DCM (30 mL) was dissolved in a solution of naphthalene-2,3-diol (**1**) (1.602 g, 10 mmol) in DCM (100 mL); then a solution of DMAD (1.42 g, 1.24 mL, 10 mmol) in DCM (20 mL) was added dropwise over 15 min at 0 °C, and the orange solution was heated under reflux for 2 h. Evaporation of the solvent and separation by column chromatography (hexane/ethyl acetate 5:2) afforded **2** as yellow needles (1.404 g, 52%), mp 204–205 °C (DCM); IR(Nujol) ν (cm^{-1}): 3406, 3090, 1736, 1705, 1631, 1557; ^1H NMR ($CDCl_3$, 300 MHz) δ: 4.08 (s, 3H), 6.32 (s, 1H), 6.61 (s, 1H), 7.44–7.55 (m, 2H), 7.59 (s, 1H), 7.69 (d, *J*=9.1 Hz, 1H), 7.80 (d, *J*=9.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 53.6, 104.9, 114.7, 115.1, 116.0, 121.6, 122.9, 125.8, 126.6, 128.2, 142.3, 147.1, 150.4, 160.7, 167.4; MS (ESI) 293 $[M+Na]^+$. Anal. Calcd for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73. Found: C, 66.59; H, 3.66.

*3.1.2. Procedure for the synthesis of methyl 3-oxo-5-(prop-2-yn-1-yloxy)-3H-benzo[f]chromen-1-carboxylate (**4**).* To a solution of compound **2** (0.405 g, 1.5 mmol) in dry acetone (10 mL) propargylbromide (**3**) (0.178 g, 0.13 mL, 1.5 mmol) and anhydrous K_2CO_3 (0.228 g, 1.165 mmol) were added and the mixture was refluxed for 4 h to give, after filtration and crystallization of the hot filtrate, the propargyloxy derivative **4** as yellow crystals (0.337 g, 73%), mp 182–184 °C (acetone); IR (Nujol) ν (cm^{-1}): 3250, 3080, 2130, 1722, 1707, 1620, 1550; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.60 (t, *J*=1.9 Hz, 1H), 4.06 (s, 3H), 4.98 (d, *J*=1.9 Hz, 2H), 6.63 (s, 1H), 7.46–7.57 (m, 2H), 7.59 (s, 1H), 7.70 (d, *J*=8.1 Hz, 1H), 7.85 (d, *J*=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 53.5, 56.8, 87.4, 109.8, 111.9, 114.1, 116.0, 122.9, 123.0, 126.0, 126.5, 128.3, 130.6, 144.1, 145.9, 158.6, 160.9, 165.5; MS (ESI) 331 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{12}O_5$: C, 70.13; H, 3.92. Found: C, 69.92; H, 3.84.

*3.1.3. Procedures for the synthesis of methyl 2-oxo-2,11-dihydrobenzo[f]pyran[3,2-h]chromen-4-carboxylate (**5**).* (a) To a solution of compound **4** (93 mg, 0.3 mmol) in DMF (2.5 mL), $BF_3 \cdot Et_2O$ (0.21 mL, 1.7 mmol) was added and the mixture was refluxed for 24 h. After cooling the mixture was poured in H_2O (50 mL) and the precipitate was washed with H_2O, dried in the air and recrystallized to give compound **5** as yellow crystals (72 mg, 78%), mp 132–134 °C (ethyl acetate); IR (Nujol) ν (cm^{-1}): 3090, 1732, 1714, 1652, 1548; ^1H NMR ($CDCl_3$, 300 MHz) δ: 4.05 (s, 3H), 5.04 (dd, J_1=3.9 Hz, J_2=1.8 Hz, 2H), 6.16 (dt, J_1=10.0 Hz, J_2=3.9 Hz, 1H), 6.58 (s, 1H), 7.17 (dt, J_1=10.0 Hz, J_2=1.8 Hz, 1H), 7.47–7.58 (m, 2H), 7.70 (d, *J*=8.2 Hz, 1H), 8.02 (d, *J*=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 53.2, 62.0, 114.9, 115.5, 119.8, 122.6, 124.1, 125.5, 126.2, 131.7, 133.1, 134.0, 134.3, 141.9, 145.3, 150.1, 160.0, 169.5; MS (ESI) 309 $[M+H]^+$, 331 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{12}O_5$: C, 70.13; H, 3.92. Found: C, 70.13; H, 3.74.

(b) To a solution of **4** (50 mg, 0.16 mmol) in DMF (1.5 mL), $BF_3 \cdot Et_2O$ (0.11 mL, 0.89 mmol) was added and the mixture irradiated at 180 °C for 10 min. After cooling the mixture was poured in H_2O and extracted by Et_2O. The ether layer dried ($MgSO_4$), concentrated and separated by column chromatography (silica gel, hexane/ethyl acetate (3:1)) to give the furan derivative **6** (4 mg, 8%) followed by compound **5** (45 mg, 90%).

*3.1.4. Procedure for the synthesis of methyl 2-methyl-10-oxo-10H-benzo[f]furo[3,2-h]chromen-8-carboxylate (**6**).* $BF_3 \cdot Et_2O$ (0.14 mL, 1.14 mmol) was added to a solution of compound **4** (62 mg, 0.2 mmol) in NMF (1 mL) and irradiated at 180 °C for 10 min. After cooling, H_2O was added and the resulting mixture was extracted with DCM. The organic layer was washed with H_2O, dried ($MgSO_4$), concentrated and separated by column chromatography [silica gel, hexane/ethyl acetate (3/1)] to give compound **6** as deep yellow crystals (14 mg, 22% yield); mp 196–198 °C (DCM-hexane); IR (Nujol) ν (cm^{-1}): 3030, 1722, 1708, 1630, 1545; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.64 (s, 3H), 4.06 (s, 3H), 6.50 (s, 1H), 6.94 (s, 1H), 7.51–7.62 (m, 2H), 7.80 (d, J=8.2 Hz, 1H), 8.10 (d, J=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.1, 53.5, 102.9, 112.2, 112.8, 114.1, 122.0, 123.0, 123.6, 124.1, 124.6, 125.3, 126.1, 126.3, 146.6, 158.4, 159.6, 167.9; MS (ESI) 331 $[M+Na]^+$, 347 $[M+K]^+$. Anal. Calcd for $C_{18}H_{12}O_5$: C, 70.13; H, 3.92. Found: C, 70.30; H, 4.16. From the next fractions eluted the starting material **4** (7 mg, 12%) and the pyran derivative **5** (41 mg, 66%).

*3.1.5. 5-(Prop-2-yn-1-yloxy)-3H-benzo[f]chromen-3-one (**8**).* (According to 3.1.2. with reflux for 24 h). Yellow crystals (82% yield), mp 225–227 °C (acetone); IR (Nujol) ν (cm^{-1}): 3270, 3060, 2120, 1710, 1630, 1555; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.58 (t, J=2.7 Hz, 1H), 4.98 (d, J=2.7 Hz, 2H), 6.62 (d, J=10.0 Hz, 1H), 7.54 (s, 1H), 7.55–7.61 (m, 2H), 7.85 (d, J=9.1 Hz, 1H), 8.16 (d, J=9.1 Hz, 1H), 8.49 (d, J=10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 56.8, 69.2, 93.9, 105.6, 107.0, 112.9, 116.2, 121.2, 126.3, 126.5, 127.9, 138.1, 139.2, 141.1, 145.7, 159.0; MS (ESI) 273 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.96; H, 4.22.

*3.1.6. Benzo[f]pyran[3,2-h]chromen-2(11H)-one (**9**).* (a) [According to 3.1.3. (a) after reflux for 48 h]. After cooling and evaporation of the solvent the residue was subjected to repeated PTLC [silica gel, hexane/DCM (1:1), four elutions] to give from the faster moving band the pyran derivative **9** as yellow crystals (57%), mp 187–190 °C (dec) (DCM/hexane); IR(Nujol) ν (cm^{-1}): 3060, 1706, 1630, 1540; ^1H NMR ($CDCl_3$, 300 MHz) δ: 5.03 (d, J=5.5 Hz, 2H), 6.11–6.16 (m, 1H), 6.55 (d, J=10.0 Hz, 1H), 7.17 (d, J=10.0 Hz, 1H), 7.53–7.58 (m, 2H), 7.99 (d, J=9.1 Hz, 1H), 8.14 (d, J=9.1 Hz, 1H), 8.43 (d, J=10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 65.6, 112.9, 115.6, 120.3, 121.7, 122.2, 122.8, 123.6, 124.9, 125.5, 125.9, 126.2, 126.5, 138.9, 155.8, 160.0; MS (ESI) 251 $[M+H]^+$, 273 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.65; H, 4.21. From the next moving band eluted the starting compound **8** (24 mg, 40%).

(b) [According to 3.1.3. (b)]. The furan derivative **10** (4%) was received from column chromatography followed by the starting material **8** (4%) and the pyran derivative (92%).

*3.1.7. Procedure for the synthesis of 2-methyl-10H-benzo[f]furo[3,2-h]chromen-10-one (**10**).* A solution of derivative **8** (70 mg, 0.28 mmol) in NMF (1.5 mL) was irradiated at 180 °C for 10 min. After cooling, H_2O was added and the resulting mixture was extracted with DCM. The organic layer was washed with H_2O, dried ($MgSO_4$), evaporated and separated by column chromatography [silica gel, hexane/ethyl acetate (3:1)] to give the furan derivative **10** as light brown needles (56 mg, 80%), mp 255–257 °C (DCM-hexane); IR(KBr) ν (cm^{-1}): 3087, 1713, 1652, 1587; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.63 (s, 3H), 6.50 (d, J=10.0 Hz, 1H), 6.95 (s, 1H), 7.59–7.64 (m, 2H), 8.10 (d, J=8.2 Hz, 1H), 8.26 (d, J=8.2 Hz, 1H), 8.53 (d, J=10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.4, 102.8, 113.0, 118.4, 122.0, 122.2, 124.3, 126.0, 126.5, 130.1, 130.6, 139.9, 140.3, 155.4, 158.8, 159.9; MS (ESI) 273 $[M+Na]^+$, 289 $[M+K]^+$. Anal. Calcd for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 77.01; H, 3.94. The starting compound **8** (13 mg, 18%) followed.

*3.1.8. 5-Allyloxy-3H-benzo[f]chromen-3-one (**12**).* To a solution of hydroxy compound **7** (0.250 g, 1.18 mmol) in dry acetone (20 mL), K_2CO_3 (0.181 g, 1.3 mmol) and allylbromide (**11**) (0.157 g, 0.113 mL, 1.3 mmol) were added and the mixture was refluxed for 27 h. After filtering, the hot filtrate was crystallized to give compound **12** as light yellow crystals (0.249 g, 84%), mp 120–122 °C (acetone); IR (KBr) ν (cm^{-1}): 3080, 1706, 1571; ^1H NMR ($CDCl_3$, 300 MHz) δ: 4.80 (d, J=4.5 Hz, 2H), 5.38 (d, J=10.9 Hz, 1H), 5.54 (d, J=17.3 Hz, 1H), 6.10–6.23 (m, 1H), 6.61 (d, J=9.1 Hz, 1H), 7.35 (s, 1H), 7.50–7.58 (m, 2H), 7.78 (d, J=8.2 Hz, 1H), 8.14 (d, J=8.2 Hz, 1H), 8.47 (d, J=9.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 69.9, 108.4, 111.8, 113.9, 116.1, 118.5, 121.1, 125.9, 126.4, 127.6, 130.5, 132.4, 137.0, 139.2, 145.4, 160.2; MS (ESI) 275 $[M+Na]^+$, 291 $[M+K]^+$. Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.12; H, 4.54.

*3.1.9. 6-Allyl-5-hydroxy-3H-benzo[f]chromen-3-one (**13**) and 2-methyl-2,3-dihydro-10H-benzo[f]furo[3.2-h]chromen-10-one (**14**).* To a solution of compound **12** (88 mg, 0.35 mmol) in NMF (1 mL), $BF_3 \cdot Et_2O$ (0.25 mL, 2.03 mmol) was added and the mixture was irradiated at 200 °C for 20 min. After cooling, the mixture was poured in H_2O and extracted by DCM. The organic layer was washed with H_2O, dried ($MgSO_4$), concentrated and separated by column chromatography [silica gel, hexane/ethyl acetate (4:1)] to give compound **13** as yellow crystals (72 mg, 82%), mp 214–216 °C (dec) (DCM); IR (Nujol) ν (cm^{-1}): 3350, 3020, 1705, 1635; ^1H NMR ($CDCl_3$, 300 MHz) δ: 3.95 (d, J=5.9 Hz, 2H), 5.04 (d, J=16.5 Hz, 1H), 5.08 (d, J=10.1 Hz, 1H), 6.00–6.12 (m, 1H), 6.37 (br s, 1H), 6.57 (d, J=9.8 Hz, 1H), 7.51–7.61 (m, 2H), 8.02 (d, J=9.1 Hz, 1H), 8.17 (d, J=9.1 Hz, 1H), 8.52 (d, J=9.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 67.9, 112.1, 114.6, 116.1, 121.6, 123.6, 124.0, 124.4, 125.5, 126.4, 129.9, 135.0, 139.9, 140.0, 143.9, 159.8; MS (ESI) 275 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.02; H, 4.53. Compound **14** as yellow crystals (14 mg, 16%) was eluted next, mp 244–246 °C (DCM-hexane); IR(KBr) ν (cm^{-1}): 3060, 1704, 1595, 1567; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.63 (d, J=6.4 Hz, 3H), 3.21 (dd, J_1=16.4 Hz, J_2=8.2 Hz, 1H), 3.75 (dd, J_1=16.4 Hz, J_2=9.1 Hz, 1H), 5.24–5.37 (m, 1H), 6.54 (d, J=9.9 Hz, 1H), 7.51–7.61 (m, 2H), 7.65 (d, J=9.1 Hz, 1H), 8.18 (d, J=9.1 Hz, 1H), 8.39 (d, J=9.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 22.1, 36.7, 81.9, 113.6, 115.0, 122.1, 123.6, 125.0, 125.2, 126.4, 127.5, 139.3, 142.0, 145.2, 146.0, 159.7; MS (ESI) 275 $[M+Na]^+$, 291 $[M+K]^+$. Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.25; H, 4.64. From the next moving band the starting compound **12** (20 mg, 23%) was eluted.

*3.1.10. Cyclization of compound **13** to dihydrofuran derivative **14**.* The compound **13** (25 mg, 0.1 mmol) was treated with concentrated H_2SO_4 (three drops, 65 mg, 0.66 mmol) and heated at 90 °C for 20 min. After cooling, ice (4 g) was added and the mixture was extracted with DCM (4×5 mL). The organic layer was washed with water (2×3 mL) and dried over $MgSO_4$ to give after filtration and evaporation of the solvent compound **14** (19 mg, 72%).

*3.1.11. Oxidation of dihydrofuran derivative **14** to furan derivative **10**.* To a solution of compound **14** (25 mg, 0.1 mmol) in dry toluene (5 mL), 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (28 mg, 0.12 mmol) was added and the mixture was refluxed for 48 h. After filtration, evaporation of the solvent and crystallization of the residue from ethanol compound **10** (20 mg, 80%) was obtained.

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