Polysubstituted 5-Functionalized 2-Pyrone Derivatives: Facile Synthesis via Tandem Nucleophilic Addition/Lactonization Reaction of 1,2-Allenyl Esters

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Abstract: Polysubstituted 5-functionalized 2-pyrone derivatives were synthesized via the K_2CO_3-catalyzed reaction of 1,2-allenyl esters and α-substituted ketones with electron-withdrawing groups through a tandem nucleophilic addition/lactonization process.

Key words: 2-pyrone derivatives, allenyl esters, nucleophilic addition, lactonization

2-Pyrone derivatives[1] are valuable building blocks and have versatile applications in organic chemistry due to the presence of functional groups such as conjugated dienes,[2] which allow further transformations to complex molecules.[2,3] The 2-pyrone moiety is also present in a large number of biologically active compounds,[4] which exhibit a wide range of activity such as potent non-peptidic HIV protease inhibitory,[5] androgen-like,[6] antifungal,[7] antimicrobial[7a,8] and pheromonal[9] effects. Researchers have also found that simple changes in the substitution pattern on the 2-pyrone ring often lead to incredibly diverse biological activity.[10] As a result, considerable effort has been directed toward the development of new and efficient methodologies for the synthesis of 2-pyrone derivatives with different substitution patterns,[11] and any new general route to 2-pyrone derivatives is of interest and value.

Meanwhile, activated allenes, which are endued with attractive features by the presence of the unique cumulated diene structural unit and diversity of the functionalities, have attracted remarkable interest in the last few years.[12,13] Several methods for the synthesis of various complex compounds with synthetic and biological importance from allenes have been developed.[13] One advantage of these methods is that various substituents can be introduced in the expected products due to the substituent-loading capability of allenes.[12,13a–c] Recently, Ma reported an efficient synthesis of 3-functionalized 2-pyrones from 1,2-allenic ketones,[11q] and Kwon disclosed a one-step phosphine-catalyzed annulation between aldehydes and ethyl allenoate to form 6-substituted 2-pyrones.[11s] However, methods utilizing allenes for the synthesis of 2-pyrone derivatives still remain scarce.

In this paper, we wish to report a facile method using allenyl esters and α-substituted ketones with electron-withdrawing groups as starting materials to afford polysubstituted 5-functionalized and annulated 2-pyrone derivatives. To the best of our knowledge, there is a general lack of simple and efficient procedures to synthesize these coumponds.[11e,11t,11w]

At first we examined the reaction of ethyl 2-benzylbuta-2,3-dienoate (**1a**) and 3-oxo-3-phenylpropanenitrile (**2a**) at 80 °C in DMF using one equivalent of K_2CO_3 as promoter. The corresponding pyrone **3a** was obtained unambiguously in 34% yield (Table 1, entry 1). With this encouraging result, various reaction conditions including the solvent, temperature, and the amount of K_2CO_3 were tested to improve the yield of the expected product. The results are summarized in Table 1. Better results were obtained when the reaction was run in acetone at 40 °C for 60 hours (entry 8). When the reaction was carried out in EtOH or acetone under reflux, the corresponding product was also isolated, but in slightly lower yields (entries 5, 6 and entries 9, 10). Satisfying results were also obtained when the reaction condition was chosen at 40 °C in EtOH with 0.1 equivalent of K_2CO_3, but much longer time was needed to finish the reaction (entry 11). The amount of K_2CO_3 used seems to have little effect on this reaction (entries 5, 6, entries 7, 8 and entries 9, 10). Therefore, the condition chosen to carry out this reaction was in acetone with 0.1 equivalent of K_2CO_3 at 40 °C.

Table 2 shows the results of several examples in the reaction of substituted allenyl esters with 3-oxo-3-phenylpropanenitrile (**2a**) under the optimized conditions. Not only 1-substituted allenyl esters, but also 3-substituted substrates, worked well to give the desired pyrones.

Next, we carried out the reaction of substituted allenyl esters with ethyl acetoacetate (**2b**) under the same conditions. Typical results are summarized in Table 3. Here, what we found is that when using ethyl acetoacetate as a substrate, this tandem reaction proceeded somewhat sluggishly to give the desired products, but in moderate to good yields in most cases. The 1-substituted allenyl esters seem to be more favored and competitive for this reaction both in efficiency and yields in comparison to 3-substituted allenyl esters. With ethyl 2-methylbuta-2,3-dienoate as the substrate, the yield can reach 82% (Table 3, entry 3).

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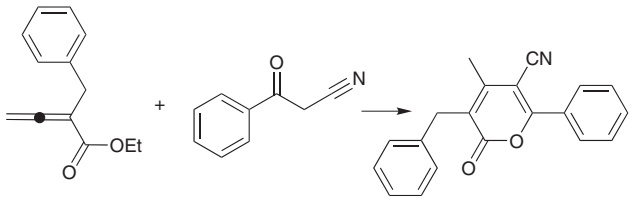
Table 1 Optimization of Conditions for the Synthesis of 2-Pyrone **3a** from Ethyl 2-Benzylbuta-2,3-dienoate (**1a**) and 3-Oxo-3-phenylpropanenitrile (**2a**)

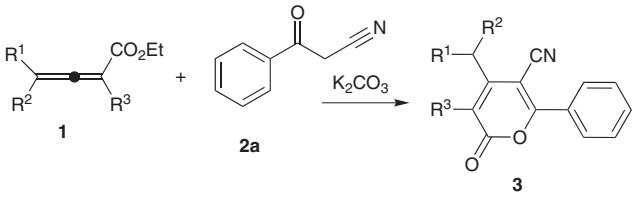


1a **2a** **3a**

Entry	K_2CO_3 (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[a]
1	1.0	DMF	80	18	34
2	0.5	DMF	60	24	42
3	1.0	MeCN	60	24	23
4	0.5	MeCN	80	20	19
5	0.5	acetone	reflux	28	60
6	0.1	acetone	reflux	28	55
7	1.0	acetone	40	60	69
8	0.1	acetone	40	60	71
9	1.0	EtOH	reflux	48	59
10	0.1	EtOH	reflux	48	61
11	0.1	EtOH	40	72	64
12	0.1	THF	reflux	24	12

[a] Isolated yields based on 3-oxo-3-phenylpropanenitrile.

Table 2 Synthesis of 2-Pyrones **3** from Substituted Allenyl Esters **1** and 3-Oxo-3-phenylpropanenitrile (**2a**)



1 **2a** **3**

Entry	R^1	R^2	R^3	Time (h)	Product	Yield (%)[a]
1	H	H	benzyl	48	**3a**	71
2	H	H	allyl	48	**3b**	69
3	H	H	Me	48	**3c**	68
4	Et	H	H	48	**3d**	65
5[b]	C_7H_{15}	H	H	60	**3e**	53

[a] Isolated yield based on **2a**.
[b] 1.2 Equiv of **2a** was added; isolated yield based on **1**.

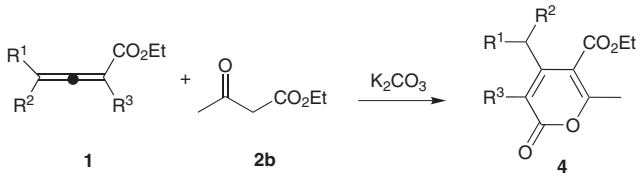
The present protocol can also be extended to 5,5-dimethylcyclohexane-1,3-dione (**2c**, R^4 = Me) or cyclohexane-1,3-dione (**2d**, R^4 = H) affording annulated 2-pyrone derivatives (Table 4). We found that the reactions proceeded smoothly to give the expected products in moderate yields in all the cases, and slightly lower yields were observed in the case of 3-substituted allenyl esters.

A plausible mechanism for the present reaction is proposed in Scheme 1. A conjugate addition of α-substituted ketone with an electron-withdrawing group to allenyl ester **1** at the β-position takes place in the presence of K_2CO_3 to afford the homoallylic ester **6**.[11r,14] Under the reaction conditions **6** may isomerize to form intermediate **7** through a C=C bond migration. Then, a subsequent intramolecular lactonization process occurs to give the desired 2-pyrone under the given condition (path a). On the other hand, the intermediate **6** may undergo a lactonization process to give **8** at first, followed by a C=C bond migration to form the 2-pyrone (path b).

However, when we carried out the reaction between ethyl 2-benzylbuta-2,3-dienoate and pentane-2,4-dione, we failed to get the expected pyrone, but compound **9** was isolated in 85% yield (Scheme 2). The spectral data unambiguously indicates the existence of intramolecular hydrogen bond in **9**.

In conclusion, we have provided here a facile and moderate-yielding method for the preparation of polysubstituted 5-functionalized 2-pyrone derivatives starting from 1,2-

Table 3 Synthesis of 2-Pyrones **4** from Substituted Allenyl Esters and Ethyl Acetoacetate (**2b**)



1 **2b** **4**

Entry	R^1	R^2	R^3	Time (h)	Product	Yield (%)[a]
1	H	H	allyl	64	**4a**	78
2	H	H	benzyl	64	**4b**	80
3	H	H	Me	64	**4c**	82
4	H	H	H	72	**4d**	65
5	H	Me_3	H	72	**4e**	66
6	*n*-Bu	H	H	72	**4f**	61
7[b]	*n*-Bu	H	H	72	**4f**	60
8[b]	Ph	H	Me	98	**4g**	69

[a] Isolated yields based on **2b**.
[b] Reaction conditions: a solution of **2b** (1.2 equiv), **1** and K_2CO_3 (0.1 equiv) acetone was heated to reflux with stirring.

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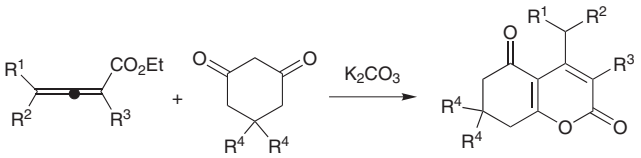
Table 4 Synthesis of 2-Pyrones **5** from Substituted Allenyl Esters **1** with 5,5-Dimethylcyclohexane-1,3-dione (**2c**, R^4 = Me) or Cyclohexane-1,3-dione (**2d**, R^4 = H)



1 **2c/2d** **5**

Entry	R^1	R^2	R^3	R^4	Time (h)	Product	Yield (%)[a]
1	H	H	H	Me	20	**5a**	61
2	H	H	allyl	Me	20	**5b**	65
3	H	H	allyl	H	20	**5c**	63
4	H	H	benzyl	Me	20	**5d**	65
5	Et	H	H	Me	24	**5e**	59
6	Et	H	H	H	24	**5f**	52
7	phenyl	H	H	Me	24	**5g**	48
8[b]	phenyl	H	H	H	24	**5h**	52
9[b]	α-naphthyl	H	H	Me	36	**5i**	51
10[b]	C_7H_{15}	H	H	Me	36	**5j**	49

[a] Isolated yields based on **2c** or **2d**.
[b] Reaction conditions: a solution of **1**, and **2c** or **2d** (1.2 equiv) with K_2CO_3 (0.1 equiv) in acetone was heated to reflux with stirring; isolated yields based on **1**.

allenyl esters. A mechanism for this one-pot tandem nucleophilic addition–lactonization reaction was also proposed. Further study of the reaction and application of this strategy towards the synthesis of biologically active 2-pyrones are in progress in our laboratory and will be reported in the future.

Melting points were determined on a hot-stage apparatus and are uncorrected. All NMR spectra were measured in $CDCl_3$ and recorded on Bruker Avance-400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometer with TMS as the internal standard. Chemical shifts are expressed in δ (ppm) and *J* values are given in Hz. IR spectra were run on a Bruker vector 22 spectrometer. EI mass spectra were determined with a HP5989B mass spectrometer. High-resolution mass spectra were carried out on a Waters Micromass GCT instrument. All reagents were CP or AR grade and were used as received without further purification. Petroleum ether (PE) refers to the fraction with boiling range of 60–90 °C. 1,2-Allenyl esters were prepared according to the known method by treatment of the acid chlorides with ethyl 2-(triphenylphoranylidene)propionate.[15]

3-Benzyl-4-methyl-2-oxo-6-phenyl-2*H*-pyran-5-carbonitrile (3a); Typical Procedure

A solution of ethyl 2-benzylbuta-2,3-dienoate (**1a**; 121 mg, 0.6 mmol), 3-oxo-3-phenylpropanenitrile (**2a**; 73 mg, 0.5 mmol), and K_2CO_3 (7 mg, 0.1 equiv) in acetone (0.8 mL) was heated to 40 °C with stirring. After the reaction was complete (monitored by TLC, eluent: 6:1 PE–EtOAc), the solvent was evaporated and the crude product was purified by chromatography on silica gel (6:1 PE–EtOAc) to afford **3a**; yield: 107 mg (71%); mp 152–153 °C.

IR (KBr): 2222, 1726, 1623, 1545, 1447, 1352, 1095 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–8.01 (m, 2 H), 7.54–7.58 (m, 3 H), 7.23–7.31 (m, 5 H), 3.96 (s, 2 H), 2.44 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 160.2, 148.7, 137.6, 132.6, 129.8, 128.9, 128.7, 128.4, 128.3, 126.8, 123.4, 115.6, 93.9, 32.7, 18.4.

MS: *m*/*z* (%) = 301 (M^+, 100), 273 (87), 258 (69).

3-Allyl-4-methyl-2-oxo-6-phenyl-2*H*-pyran-5-carbonitrile (3b)

Mp 94–96 °C.

IR (KBr): 2222, 1723, 1624, 1549, 1446, 1350, 1079 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–8.01 (m, 2 H), 7.51–7.58 (m, 3 H), 5.81–5.88 (m, 1 H), 5.10–5.14 (m, 2 H), 3.35 (d, *J* = 6 Hz, 2 H), 2.39 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 159.6, 148.6, 137.6, 132.5, 132.4, 129.6, 128.8, 128.2, 121.8, 116.6, 115.5, 93.8, 31.1, 17.7.

MS: *m*/*z* (%) = 251 (M^+, 80), 223 (86), 77 (100).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{13}NO_2$: 251.0946; found: 251.0950.

3,4-Dimethyl-2-oxo-6-phenyl-2*H*-pyran-5-carbonitrile (3c)

Mp 158–160 °C.

IR (KBr): 2228, 1731, 1650, 1541, 1112 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–8.01 (m, 2 H), 7.51–7.58 (m, 3 H), 2.40 (s, 3 H), 2.17 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.2, 160.3, 147.4, 132.4, 129.8, 128.9, 128.2, 120.5, 115.8, 93.8, 18.2, 13.0.

MS: *m*/*z* (%) = 225 (M^+, 47), 197 (100), 105 (53).

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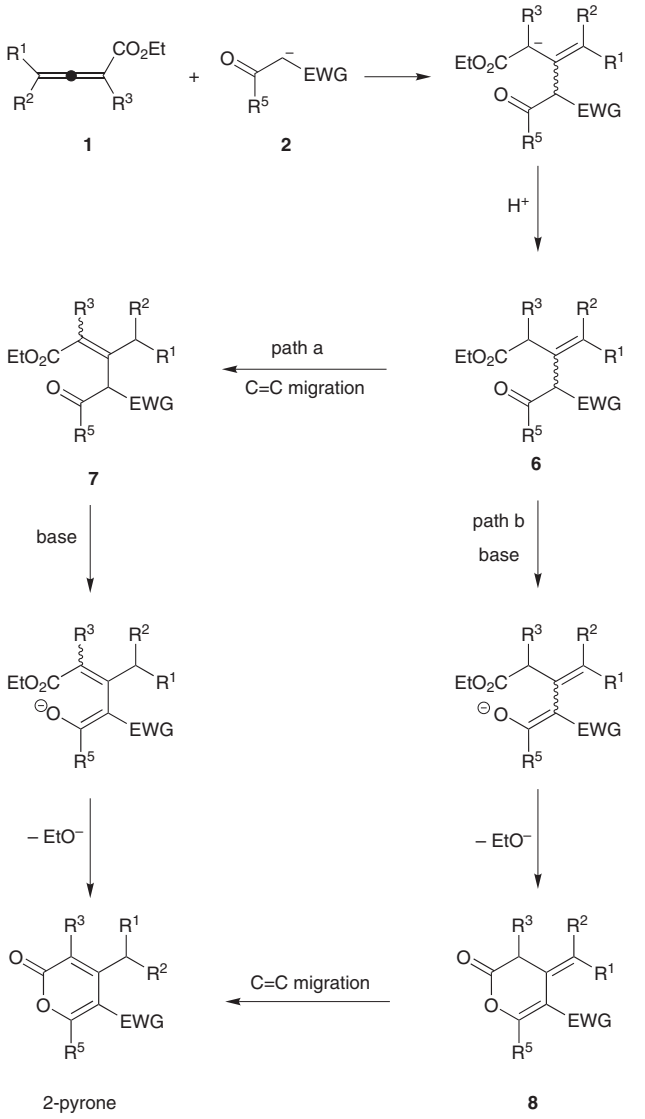
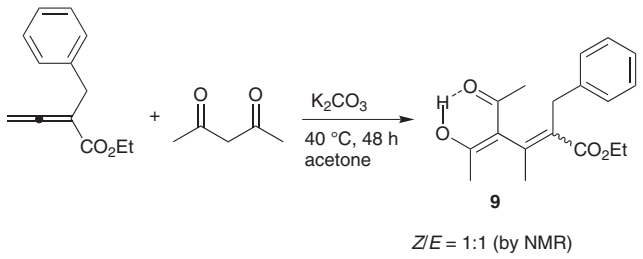


Scheme 1



Scheme 2

2-Oxo-6-phenyl-4-propyl-2*H*-pyran-5-carbonitrile (3d)
Mp 88–90 °C.

IR (KBr): 2222, 1742, 1626, 1541, 1446, 1104 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00–8.03 (m, 2 H), 7.52–7.63 (m, 3 H), 6.18 (s, 1 H), 2.65 (t, *J* = 7.6 Hz, 2 H), 1.71–1.80 (m, 2 H), 1.07 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 158.8, 158.1, 132.9, 129.7, 128.9, 128.5, 115.0, 110.8, 92.7, 36.1, 21.3, 13.6.

MS: *m*/*z* (%) = 239 (M^+, 47), 211 (45), 183 (100).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}NO_2$: 239.0946; found: 239.0949.

4-Octyl-2-oxo-6-phenyl-2*H*-pyran-5-carbonitrile (3e)
Mp 59–61 °C.

IR (KBr): 2224, 1741, 1626, 1543, 1446, 1092 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.01–8.03 (m, 2 H), 7.53–7.61 (m, 3 H), 6.18 (s, 1 H), 2.66 (t, *J* = 8.0 Hz, 2 H), 1.66–1.74 (m, 2 H), 1.27–1.46 (m, 10 H), 0.89 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 158.8, 158.4, 132.8, 129.8, 128.9, 128.5, 115.0, 110.1, 92.8, 34.3, 31.7, 29.2, 29.1, 28.0, 22.6, 14.0.

MS: *m*/*z* (%) = 309 (M^+, 11), 211 (100).

Ethyl 3-Allyl-4,6-dimethyl-2-oxo-2*H*-pyran-5-carboxylate (4a)
Oil.

IR (neat): 2981, 1718, 1638, 1560, 1442 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.77–5.87 (m, 1 H), 5.06–5.07 (m, 1 H), 5.03–5.04 (m, 1 H), 4.36 (q, *J* = 7.2 Hz, 2 H), 3.28 (d, *J* = 6.0 Hz, 2 H), 2.33 (s, 3 H), 2.15 (s, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 161.5, 159.7, 148.4, 133.2, 120.7, 125.7, 114.2, 61.5, 30.6, 18.7, 16.8, 13.9.

MS: *m*/*z* (%) = 236 (M^+, 40), 208 (34), 43 (100).

Ethyl 3-Benzyl-4,6-dimethyl-2-oxo-2*H*-pyran-5-carboxylate (4b)
Oil.

IR (neat): 3061, 2981, 1715, 1637, 1559, 1451 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.16–7.28 (m, 5 H), 4.32 (q, *J* = 7.2 Hz, 2 H), 3.90 (s, 2 H), 2.32 (s, 3 H), 2.16 (s, 3 H), 1.34 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 161.9, 159.8, 148.6, 138.3, 128.3, 128.0, 126.1, 122.0, 114.2, 61.5, 32.0, 18.7, 17.3, 13.9.

MS: *m*/*z* (%) = 286 (M^+, 97), 258 (49), 43 (100).

Ethyl 3,4,6-Trimethyl-2-oxo-2*H*-pyran-5-carboxylate (4c)
Oil.

IR (neat): 2983, 1717, 1635, 1567, 1446 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.28 (q, *J* = 7.2 Hz, 2 H), 2.25 (s, 3 H), 2.07 (s, 3 H), 1.99 (s, 3 H), 1.31 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1, 162.1, 158.9, 147.2, 119.1, 114.2, 61.5, 18.6, 17.3, 14.0, 12.4.

MS: *m*/*z* (%) = 210 (M^+, 37), 182 (57), 43 (100).

Ethyl 4,6-Dimethyl-2-oxo-2*H*-pyran-5-carboxylate (4d)
Oil.

IR (neat): 2983, 1722, 1631, 1551, 1443 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.03 (s, 1 H), 4.35 (q, *J* = 7.2 Hz, 2 H), 2.40 (s, 3 H), 2.23 (s, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 164.6, 160.6, 154.3, 113.1, 111.9, 61.6, 21.2, 19.5, 14.1.

MS: *m*/*z* (%) = 196 (M^+, 43), 168 (60), 43 (100).

Ethyl 4-Ethyl-6-methyl-2-oxo-2*H*-pyran-5-carboxylate (4e)
Oil.

IR (neat): 2979, 1724, 1632, 1550, 1461 cm^{-1}.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.04 (s, 1 H), 4.35 (q, *J* = 7.2 Hz, 2 H), 2.57 (q, *J* = 7.4 Hz, 2 H), 2.37 (s, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H), 1.16 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 163.5, 161.1, 159.3, 113.0, 109.9, 61.7, 26.6, 19.2, 14.0, 12.4.

MS: *m*/*z* (%) = 210 (M^+, 18), 182 (28), 43 (100).

Ethyl 6-Methyl-2-oxo-4-pentyl-2*H*-pyran-5-carboxylate (4f)
Oil.

IR (neat): 2931, 1723, 1631, 1550, 1462 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.01 (s, 1 H), 4.34 (q, *J* = 7.2 Hz, 2 H), 2.52 (t, *J* = 7.6 Hz, 2 H), 2.37 (s, 3 H), 1.48–1.52 (m, 2 H), 1.37 (t, *J* = 7.2 Hz, 3 H), 1.27–1.35 (m, 4 H), 0.89 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 163.7, 161.0, 158.3, 113.1, 110.8, 61.7, 33.6, 31.3, 28.1, 22.3, 19.3, 14.1, 13.8.

MS: *m*/*z* (%) = 252 (M^+, 112), 168 (61), 43 (100).

Ethyl 4-Benzyl-3,6-dimethyl-2-oxo-2*H*-pyran-5-carboxylate (4g)
Oil.

IR (neat): 3061, 2983, 1715, 1634, 1563, 1452 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.29 (m, 2 H), 7.20–7.22 (m, 1 H), 7.05–7.07 (m, 2 H), 4.05 (q, *J* = 7.2 Hz, 2 H), 3.99 (s, 2 H), 2.29 (s, 3 H), 2.13 (s, 3 H), 1.08 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 162.4, 159.3, 150.0, 136.5, 128.5, 128.3, 126.6, 120.5, 113.8, 61.4, 35.5, 18.7, 13.6, 12.7.

MS: *m*/*z* (%) = 286 (M^+, 25), 258 (8), 212 (100).

4,7,7-Trimethyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5a)
Mp 108–110 °C.

IR (KBr): 2970, 1721, 1662, 1617, 1398 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (s, 1 H), 2.73 (s, 2 H), 2.48 (s, 3 H), 2.42 (s, 2 H), 1.13 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 173.2, 159.8, 156.0, 113.8, 112.9, 52.5, 42.6, 31.7, 28.1, 22.5.

MS: *m*/*z* (%) = 206 (M^+, 28), 178 (43), 122 (100).

3-Allyl-4,7,7-trimethyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5b)
Oil.

IR (neat): 2961, 1730, 1680, 1617, 1553, 1423, 1377, 1278, 1018 cm^{-1}.

^{1}H NMR: δ = 5.78–5.86 (m, 1 H), 5.06–5.08 (m, 1 H), 5.03–5.04 (m, 1 H), 3.30 (d, *J* = 6.0 Hz, 2 H), 2.73 (s, 2 H), 2.46 (s, 3 H), 2.43 (s, 2 H), 1.13 (s, 6 H).

^{13}C NMR: δ = 195.8, 170.3, 160.7, 150.5, 133.3, 121.6, 115.9, 114.0, 52.8, 42.4, 31.6, 30.4, 28.0, 17.4, 17.3.

MS: *m*/*z* (%) = 246 (M^+, 47), 231 (17), 218 (36), 162 (100).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{18}O_3$: 246.1256; found: 246.1253.

3-Allyl-4-methyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5c)
Oil.

IR (neat): 2956, 17328, 1679, 1615, 1551, 1426, 1380, 1168, 1064 cm^{-1}.

^{1}H NMR: δ = 5.77–5.86 (m, 1 H), 5.06–5.07 (m, 1 H), 5.02–5.04 (m, 1 H), 3.30 (d, *J* = 6.0 Hz, 2 H), 2.86 (t, *J* = 6.4 Hz, 2 H), 2.56 (t, *J* = 6.4 Hz, 2 H), 2.46 (s, 3 H), 2.06–2.13 (m, 2 H).

^{13}C NMR: δ = 196.0, 171.8, 160.5, 151.0, 133.4, 122.0, 116.0, 115.2, 38.9, 30.5, 29.0, 19.8, 17.7.

MS: *m*/*z* (%) = 218 (M^+, 69), 203 (25), 190 (75), 91 (100).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{14}O_3$: 218.0943; found: 218.0947.

3-Benzyl-4,7,7-trimethyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5d)
Mp 125–126 °C.

IR (KBr): 2961, 1710, 1673, 1614, 1546, 1377, 1024 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17–7.28 (m, 5 H), 3.92 (s, 2 H), 2.72 (s, 2 H), 2.51 (s, 3 H), 2.41 (s, 2 H), 1.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.9, 170.5, 161.2, 150.8, 138.5, 128.5, 128.2, 126.3, 123.1, 114.2, 52.9, 42.5, 32.0, 31.6, 28.1, 18.1.

MS: *m*/*z* (%) = 296 (M^+, 100), 281 (7), 268 (56).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}O_3$: 296.1412; found: 296.1413.

7,7-Dimethyl-4-propyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5e)
Mp 57–59 °C.

IR (neat): 2961, 2873, 1754, 1681, 1616, 1543, 1400, 1370, 1279, 1041 cm^{-1}.

^{1}H NMR: δ = 6.00 (s, 1 H), 2.85 (t, *J* = 7.6 Hz, 2 H), 2.74 (s, 2 H), 2.42 (s, 2 H), 1.48–1.57 (m, 2 H), 1.13 (s, 6 H), 0.99 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR: δ = 195.2, 173.5, 160.0, 159.8, 113.3, 111.8, 52.7, 42.8, 36.2, 31.6, 28.0, 22.2, 13.8.

MS: *m*/*z* (%) = 234 (M^+, 32), 206 (40), 191 (100), 178 (55).

4-Propyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5f)
Mp 54–56 °C.

IR (neat): 2963, 2874, 1755, 1680, 1613, 1541, 1399, 1299 cm^{-1}.

^{1}H NMR: δ = 6.00 (s, 1 H), 2.83–2.90 (m, 4 H), 2.56 (t, *J* = 6.8 Hz, 2 H), 2.08–2.14 (m, 2 H), 1.49–1.58 (m, 2 H), 1.00 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR: δ = 195.2, 174.9, 160.1, 159.7, 114.2, 112.0, 38.7, 36.4, 29.2, 22.1, 19.6, 13.8.

MS: *m*/*z* (%) = 206 (M^+, 27), 178 (35), 163 (100).

4-Benzyl-7,7-dimethyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5g)
Mp 78–80 °C.

IR (KBr): 2956, 1734, 1676, 1613, 1543, 1409 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.33 (m, 3 H), 7.14–7.16 (m, 2 H), 5.78 (s, 1 H), 4.26 (s, 2 H), 2.73 (s, 2 H), 2.41 (s, 2 H), 1.12 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 173.4, 159.9, 158.3, 136.8, 129.4, 128.7, 126.8, 113.2, 113.0, 52.5, 42.7, 39.8, 31.7, 28.0.

MS: *m*/*z* (%) = 282 (M^+, 69), 254 (100), 198 (54).

4-Benzyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5h)
Mp 60–61 °C.

IR (KBr): 2956, 1745, 1677, 1616, 1542, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.33 (m, 3 H), 7.15–7.17 (m, 2 H), 5.79 (s, 1 H), 4.26 (s, 2 H), 2.87 (t, *J* = 6.4 Hz, 2 H), 2.55 (t, *J* = 6.8 Hz, 2 H), 2.06–2.13 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 174.8, 159.6, 158.5, 136.8, 129.4, 128.7, 126.8, 114.1, 113.2, 40.0, 38.6, 29.1, 19.6.

MS: *m*/*z* (%) = 254 (M^+, 76), 226 (100), 198 (21).

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7,7-Dimethyl-4-[(naphthalen-1-yl)methyl]-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5i)
Mp 136–137 °C.

IR (KBr): 2958, 1746, 1674, 1542, 1410 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.88 (m, 3 H), 7.41–7.49 (m, 3 H), 7.25–7.27 (m, 1 H), 5.45 (s, 1 H), 4.72 (s, 2 H), 2.76 (s, 2 H), 2.50 (s, 2 H), 1.66 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.8, 173.3, 159.9, 158.0, 133.9, 132.8, 131.8, 128.8, 128.0, 127.9, 126.3, 125.8, 125.5, 123.7, 113.2, 112.8, 52.6, 42.7, 37.2, 31.7, 28.1.

MS: *m*/*z* (%) = 332 (M^+, 90), 304 (100).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{20}O_3$: 332.1412; found: 332.1409.

7,7-Dimethyl-4-octyl-7,8-dihydro-2*H*-chromene-2,5(6*H*)-dione (5j)
Oil.

IR (neat): 2962, 1750, 1679, 1616, 1540 cm^{-1}.

^1H NMR: δ = 6.00 (s, 1 H), 2.86 (t, *J* = 8.0 Hz, 2 H), 2.73 (s, 2 H), 2.42 (s, 2 H), 1.44–1.51 (m, 2 H), 1.26–1.40 (m, 10 H), 1.13 (s, 6 H), 0.88 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR: δ = 195.2, 173.5, 160.2, 160.1, 113.3, 111.8, 52.7, 42.8, 34.4, 31.8, 31.6, 29.4, 29.3, 29.2, 29.00, 28.0, 22.6, 14.1.

MS: *m*/*z* (%) = 304 (M^+, 24), 276 (34), 191 (100).

Ethyl (2*E*,4*Z*)-4-Acetyl-2-benzyl-5-hydroxy-3-methylhexa-2,4-dienoate and Ethyl (2*Z*,4*Z*)-4-Acetyl-2-benzyl-5-hydroxy-3-methylhexa-2,4-dienoate [(*E*/*Z*)-9]
A solution of ethyl 2-benzylbuta-2,3-dienoate (**1a**; 121 mg, 0.6 mmol), pentane-2,4-dione (51 mg, 0.5 mmol) and K_2CO_3 (7 mg, 0.1 equiv) in acetone (0.8 mL) was heated to 40 °C with stirring. After the reaction was complete (48 h, monitored by TLC, eluent: 6:1 PE–EtOAc), the solvent was evaporated and the crude product was purified by chromatography on silica gel (6:1 PE–EtOAc) to afford **9**; yield: 128 mg (85%); oil.

IR (neat): 3355, 2981, 2921, 1714, 1603, 1495, 1416, 1266 cm^{-1}.

^1H NMR: δ = 16.46 (s, 0.5 H), 16.16 (s, 0.5 H), 7.20–7.29 (m, 4 H), 7.05–7.08 (m, 1 H), 4.18 (q, *J* = 7.6 Hz, 1 H), 4.02 (q, *J* = 7.6 Hz, 1 H), 3.80 (s, 1 H), 3.57 (s, 1 H), 2.12 (s, 1.5 H), 2.02 (s, 3 H), 2.01 (s, 1.5 H), 1.91 (s, 3 H), 1.20 (t, *J* = 6.8 Hz, 1.5 H), 1.09 (t, *J* = 6.8 Hz, 1.5 H).

^{13}C NMR: δ = 189.4, 188.9, 168.8, 168.7, 140.1, 138.7, 138.6, 137.7, 134.6, 133.7, 128.5, 128.4, 128.2, 126.3, 126.2, 115.2, 114.3, 60.6, 60.5, 36.9, 35.7, 23.1, 22.9, 22.8, 21.4, 14.0, 13.9.

MS: *m*/*z* (%) = 302 (M^+, 6), 211 (91), 43 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{22}O_4$: 302.1518; found: 302.1519.

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