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Regio and diastereoselective synthesis of functionalized 2,3-dihydrofuro[3,2-*c*]-coumarins via a one-pot three-component reaction

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ABSTRACT

An efficient and straightforward synthesis of furo[3,2-*c*]coumarins via the one-pot three-component condensation of aromatic aldehydes, 4-hydroxycoumarin and α-chloroketones in refluxing *n*-propanol is described. Pyridine or a mixture of AcOH and $AcONH_4$ was used as a basic catalyst.

1. Introduction

Multicomponent reactions (MCRs)[1] involving domino processes are increasingly emerging as a good way of rapidly and efficiently generating complex molecules with potential biological properties.[2] Our interest in these reactions to synthesize spiro or fused five- and six-membered bicyclic rings is well documented.[3] Recently,[4] we have successfully introduced the use of phenacyl chloride in new MCRs employing aromatic aldehydes as electrophiles and azol-5-ones as pronucleophiles with AcOH/$AcONH_4$ performing the dual function of catalyst and nitrogen atom provider.

Herein, we report the extension of this methodology, using 4-hydroxycoumarin **1** as a methylene active compound.[5] 4-Hydroxycoumarin is a recurring structural motif in many natural products of interest in medicinal chemistry.[6]

2. Results and discussion

Initially, we performed a preliminary experiment using our previously reported procedure.[4] In refluxing EtOH (Scheme 1, path i), the addition of **1** to benzaldehyde **2a** and phenacyl chloride **3** (1:2:1) in the presence of an excess of AcOH/$AcONH_4$ did not yield the expected spiro compound **6**, but gave instead an already known and synthetically uninteresting mixture of products including furocoumarin **7**,[3a] fused aziridine **8**[7] and bisderivative **9**.[8]

In contrast, when the reaction was performed in refluxing *n*-PrOH, the addition of **1** to arylaldehydes **2a**–**i** and **3** afforded dihydrofurocoumarins **10a**–**i** (Scheme 1, path ii) with complete regio and diastereoselectivity in fair to good yields (47–80%) (Table 1, method A).[10]

The exclusive formation of the unexpected derivatives **10** prompted our interest in developing a general route to access this valuable class of compounds.

First, it was noted that AcOH/$AcONH_4$ mixture acted only as a basic catalyst, unlike in our previous studies.[4] Therefore, our attention turned towards other catalysts to allow for a more efficient and selective reaction.

Using pyridine instead of the AcOH/$AcONH_4$ mixture this three-component condensation satisfactorily proceeded with a significant increase in the yield. Thus, 4-hydroxycoumarin **1** was tested with a large variety of aldehydes **2a**–**k** and α-chloroketones **3**, **4** and **5** (Scheme 1, path iii). The results are summarized in Table 1 (Method B).[11]

The structures of new compounds **10**–**12** were assigned on the basis of comprehensive spectroscopic analyses and, in the case of **10a**–**d**, confirmed by comparison with authentic samples.[12]

The proposed mechanism for this one-pot three-component tandem Knoevenagel cyclocondensation reaction is summarized in Scheme 2. The initial regiospecific formation of the non-isolated arylidene derivative **13** is followed by its irreversible capture by the in situ-generated dipole **14** to give **15**. This Michael adduct, in contrast with our earlier report,[8] irreversibly evolves to fused derivatives **10**–**12** by a regio- and stereocontrolled intramolecular five-membered ring O-cyclization. The expected trans-stereochemistry

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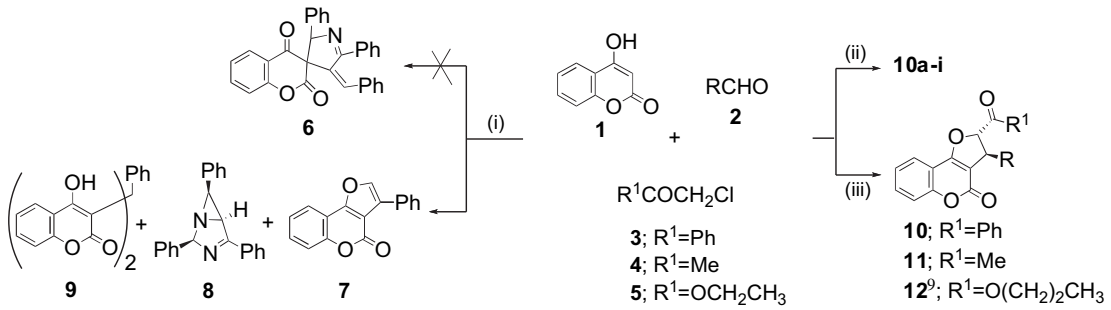


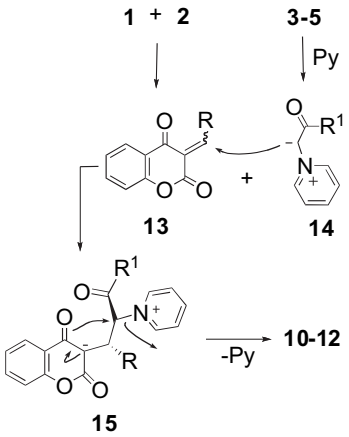
Scheme 1. Reagents and conditions: (i) **2a** and **3** in AcOH/$AcONH_4$, EtOH, 4 Å molecular sieves, reflux, 2 h; (ii) **2a**–**i** and **3** in AcOH/$AcONH_4$, *n*-PrOH, 4 Å molecular sieves, reflux, 3 h; (iii) **2a**–**k** and **3**–**5** in Pyridine, *n*-PrOH, 4 Å molecular sieves, reflux, 2–6 h.

Table 1
Synthesis of 2,3-dihydrofuro[3,2-*c*]coumarins

R	**10**		**11**	**12**
	(R^1=Ph) yield[a] %		(R^1=Me) yield[a] %	(R^1=OC_3H_7) yield[a] %
	Method A[b]	Method B[c]	Method B[c]	Method B[c]
a C_6H_5	80	95	85	80
b 4-MeC_6H_4	78	98	85	85
c 4-$MeOC_6H_4$	77	96		
d 4-ClC_6H_4	74	95		
e 3-MeC_6H_4	51	95	75	70
f 3-$MeOC_6H_4$	47	96		
g 2-MeC_6H_4	69	96	70	65
h 2-$MeOC_6H_4$	71	94		
i 2-ClC_6H_4	66	93		
j $C6H_5CH_2$		67		
k CH_3CH_2		64		

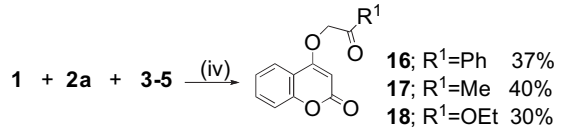
[a] Yield of pure isolated product.
[b] AcOH/$AcONH_4$, *n*-PrOH, 4 Å molecular sieves, reflux, 3 h.
[c] Pyridine, *n*-PrOH, 4 Å molecular sieves, reflux, 2–6 h.

of the reaction final step was proved from NOE NMR studies (no interactions between H_2 and H_3) and by analysis of vicinal coupling constants of the two-methine hydrogens. Our results demonstrate that the reaction conditions are critical for the successful and exclusive formation of dihydrofurocoumarin derivatives in a diastereoselective fashion. Indeed, using method B all the electrophilic halides **3**–**5** are converted to ylide **14** removing possible competitive reactions.



Scheme 2. Proposed mechanism of 2,3-dihydrofuro[3,2-c]coumarin formation.

For example, with DBU the reaction of **1**, **2a** and α-chloroketones **3**, **4** or **5** stopped (Scheme 3, path iv) at the exclusive formation of the *O*-alkyl derivatives **16**, **17** or **18**, respectively.



Scheme 3. Reaction conditions: (iv) DBU, *n*-PrOH, 4 Å molecular sieves, reflux, 3 h.

These structures were assigned on the basis of analytical and spectroscopic data and were confirmed by a gHMBCAD experiment on **16**. Surprisingly, these *O*-alkyl derivatives remain practically unaltered either in the presence of an aromatic aldehyde or under the influence of an acid or a base.

3. Conclusions

In summary, we have successfully prepared a series of functionalized angularly-fused dihydrofurocoumarins by an efficient multicomponent domino process. This protocol offers several advantages including high diastereoselectivity, high product yields and simple work up procedures. Further examples of the applicability of our synthetic procedures towards cyclic 1,3-dicarbonyl compounds will be reported in future publications.

4. Experimental section

4.1. General method

Melting points were determined on a Kofler melting apparatus. IR spectra were recorded in Nujol with a Nicolet Impact 410D spectrometer. ^1H and ^{13}C NMR spectra were obtained on a Bruker AMX R300. The chemical shifts (δ) and coupling constants (J) are expressed in parts per million and hertz, respectively. Microanalyses were carried out on a Carlo Erba EA 1102. Merck Kieselgel $60F_{254}$ plates were used for TLC. All solvents and reagents were obtained from commercial sources and purified before use if necessary.

4.2. General procedure for the synthesis of compounds 10, 11, 12

Method A: To a stirred solution of 4-hydroxycoumarin **1** (0.5 g, 3.1 mmol) in *n*-PrOH (20 mL) containing 4 Å molecular sieves and a mixture of AcOH (10 mL) and $AcONH_4$ (1.55 g, 20 mmol) aldehyde **2** (6.2 mmol) and phenacyl chloride **3** (0.48 g, 3.1 mmol) were added. The mixture was heated at reflux for 3 h. After cooling, the reaction mixture was filtered to remove molecular sieves and evaporated. The resulting residue was washed with cool H_2O (20 mL) and the aqueous suspension was then extracted with $CHCl_3$ (3×30 mL). The combined organic layers were washed with H_2O (20 mL), dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was crystallized from Et_2O/acetone (9:1). Further recrystallization from MeOH led to **10a**–**i** as white solids.

Method B: As Method A, but using pyridine (0.47 g, 6 mml) instead of AcOH/$AcONH_4$ mixture, derivatives **10a**–**k** were isolated. The use of **4** (0.28 g, 3.1 mmol) or **5** (0.38 g, 3.1 mmol) in place of **3** provided **11** or **12** as white solids.

*4.2.1. Compound **10a**.* Mp 192–194 °C. (lit.[10] 193 °C).

*4.2.2. Compound **10b**.* Mp 194–196 °C. (lit.[10] 192 °C).

*4.2.3. Compound **10c**.* Mp 177–179 °C. (lit.[10] 180 °C).

*4.2.4. Compound **10d**.* Mp 168–170 °C. (lit.[10] 170–172 °C).

*4.2.5. Compound **10e**.* Mp 153–155 °C. IR (Nujol): 1718, 1689 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (3H, s, Me); 4.74 (1H, d, CH, *J* 4.9 Hz); 6.15 (1H, d, CH, *J* 4.9 Hz); 7.07–7.91 (13H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.4; 49.2; 92.6; 105.3; 112.1; 116.8; 116.9; 123.1; 124.0; 124.6; 128.0; 128.1; 128.8; 128.9; 129.0; 129.1; 132.8; 133.0; 134.3; 138.9; 139.4; 155.3; 159.2; 166.2; 192.0. Anal. Calcd for $C_{25}H_{18}O_4$: C, 78.52; H, 4.74. Found: C, 78.50; H, 4.55.

*4.2.6. Compound **10f**.* Mp 151–152 °C. IR (Nujol): 1718, 1686 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.80 (3H, s, Me); 4.77 (1H, d, CH, *J* 4.9 Hz); 6.17 (1H, d, CH, *J* 4.9 Hz); 6.82–7.93 (13H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.2; 55.2; 92.4; 105.0; 112.0; 113.2; 113.4; 116.8; 116.9; 119.7; 123.1; 140.1; 128.9; 129.0; 129.1; 130.2; 132.8; 133.0; 134.3; 141.0; 155.3; 159.2; 160.1; 166.3; 192.0. Anal. Calcd for $C_{25}H_{18}O_5$: C, 75.37; H, 4.55. Found: C, 75.45; H, 4.45.

*4.2.7. Compound **10g**.* Mp 201–202 °C. IR (Nujol): 1724, 1704 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.31 (3H, s, Me); 5.10 (1H, d, CH, *J* 5.0 Hz); 6.18 (1H, d, CH, *J* 5.0 Hz); 7.18–7.90 (13H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.6; 44.7; 93.0; 93.2; 106.2; 112.1; 116.8; 116.9; 122.9; 123.0; 123.9; 126.8; 126.9; 127.8; 129.0; 130.7; 132.6; 133.2; 134.3; 136.2; 138.2; 155.2; 159.2; 165.8; 192.0. Anal. Calcd for $C_{25}H_{18}O_4$: C, 78.52; H, 4.74. Found: C, 78.30; H, 4.70.

*4.2.8. Compound **10h**.* Mp 150–152 °C. IR (Nujol): 1716, 1690 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.10 (3H, s, Me); 4.81 (1H, d, CH, *J* 5.0 Hz); 6.11 (1H, d, CH, *J* 5.0 Hz); 7.12–7.94 (13H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 44.0; 55.0; 90.7; 90.9; 103.6; 110.8; 112.2; 116.9; 120.8; 120.9; 122.8; 123.0; 123.8; 128.0; 128.6; 128.7; 128.9; 132.5; 134.0; 136.0; 138.0; 155.2; 156.8; 165.0; 192.0. Anal. Calcd for $C_{25}H_{18}O_5$: C, 75.37; H, 4.55. Found: C, 75.35; H, 4.75.

*4.2.9. Compound **10i**.* Mp 170–173 °C. IR (Nujol): 1726, 1702 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.47 (1H, d, CH, *J* 5.0 Hz); 6.15 (1H, d, CH, *J* 5.0 Hz); 7.23–7.98 (13H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.6; 90.9; 104.1; 112.0; 117.0; 123.0; 124.1; 125.1; 127.6; 128.5; 128.6; 128.9; 129.1; 129.3; 130.2; 131.3; 133.0; 133.5; 134.3; 136.7; 155.3; 159.2; 166.7; 191.3. Anal. Calcd for $C_{24}H_{15}ClO_4$: C, 71.56; H, 3.75; Cl, 8.80. Found: C, 71.60; H, 3.70; Cl, 8.82.

*4.2.10. Compound **10j**.* Mp 182–184 °C. IR (Nujol): 1720, 1689 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.84 (1H, dd, CH_aH_bPh, *J* 13.9, 10.3 Hz); 3.55 (1H, dd, CH_aH_bPh, *J* 13.9, 3.8 Hz); 3.90 (1H, ddd, CH, *J* 13.9, 3.8, 3.4 Hz); 6.02 (1H, d, CH, *J* 3.4 Hz); 7.21–7.77 (14H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.1; 45.8; 87.4; 87.6; 104.6; 112.1; 116.8; 122.9; 124.0; 127.0; 128.4; 128.6; 128.9; 129.0; 129.5; 129.6; 132.6; 132.7; 133.7; 137.4; 155.0; 158.9; 159.9; 166.7; 192.6. Anal. Calcd for $C_{25}H_{18}O_4$: C, 78.52; H, 4.74. Found: C 78.55; H 4.70.

*4.2.11. Compound **10k**.* Mp 124–126 °C. IR (Nujol): 1718, 1704 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.02 (3H, t, Me, *J* 7.4 Hz); 1.96 (1H, sex, CH_aH_bMe, *J* 13.8, 7.4, 3.8 Hz); 2.06 (1H, sex, CH_aH_bMe, *J* 13.8, 7.4, 3.8 Hz); 3.83 (1H, ddd, CH, *J* 6.8, 4.8, 3.8 Hz); 5.92 (1H, d, CH, *J* 4.8 Hz); 7.28–8.02 (9H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.1; 24.8; 44.5; 104.3; 112.1; 116.8; 116.9; 122.8; 122.9; 124.0; 124.1; 128.8; 128.9; 132.5; 133.7; 134.1; 155.0; 159.9; 166.1; 193.3. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 75.00; H, 5.05.

*4.2.12. Compound **11a**.* Mp 127–128 °C. IR (Nujol): 1734, 1692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.37 (1H, s, CO*Me*); 4.76 (1H, d, CH, *J* 5.2 Hz); 5.23 (1H, d, CH, *J* 5.2 Hz); 7.26–7.85 (9H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.1; 48.7; 95.6; 104.8; 111.8; 117.0; 122.8; 124.1; 127.1; 127.2; 127.8; 129.0; 129.1; 132.9; 139.5; 155.2; 159.0; 165.8; 203.3. Anal. Calcd for $C_{19}H_{14}O_4$: C, 74.50; H, 4.61. Found: C, 74.52; H, 4.62.

*4.2.13. Compound **11b**.* Mp 113–115 °C. IR (Nujol): 1735, 1695 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.29 (3H, s, CO*Me*); 2.32 (3H, s, Me); 4.69 (1H, d, CH, *J* 5.2 Hz); 5.20 (1H, d, CH, *J* 5.2 Hz); 7.03–7.82 (8H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9; 26.0; 48.4; 95.6; 104.8; 111.8; 116.9; 122.7; 124.0; 126.9; 127.0; 129.6; 129.7; 132.8; 136.5; 137.4; 155.1; 158.9; 165.7; 203.3. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H 5.03. Found: C, 75.01; H, 5.06.

*4.2.14. Compound **11e**.* Mp 104–106 °C. IR (Nujol): 1733, 1700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.29 (3H, s, CO*Me*); 2.32 (3H, s, Me); 4.69 (1H, d, CH, *J* 5.2 Hz); 5.20 (1H, d, CH, *J* 5.2 Hz); 7.03–7.82 (8H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1; 25.9; 48.4; 95.4; 104.6; 111.6; 116.7; 122.6; 123.9; 127.6; 128.4; 128.5; 128.7; 132.7; 138.5; 139.4; 154.9; 158.8; 165.6; 203.4. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 74.98; H, 5.05.

*4.2.15. Compound **11g**.* Mp 157–159 °C. IR (Nujol): 1734, 1699 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.36 (3H, s, CO*Me*); 2.54 (3H, s, Me); 5.02 (1H, d, CH, *J* 4.6 Hz); 5.20 (1H, d, CH, *J* 4.6 Hz); 7.01–7.85 (8H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.7; 26.1; 44.4; 95.9; 105.9; 111.9; 117.0; 122.6; 124.1; 126.4; 126.7; 127.5; 130.8; 132.8; 136.0; 137.9; 155.1; 158.8; 165.4; 203.2. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 75.02; H, 5.05.

*4.2.16. Compound **12a**.* Mp 101–102 °C. IR (Nujol): 1729, 1717 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (3H, t, CH_2Me, *J* 7.0 Hz); 1.70–1.73 (2H, m, CH_2Me); 4.25–4.27 (2H, m, OCH_2); 4.78 (d, CH, *J* 5.0 Hz); 5.28 (d, CH, *J* 5.0 Hz); 7.28–7.85 (9H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9; 21.6; 50.2; 62.1; 88.9; 104.4; 111.8; 116.8; 123.0; 124.0; 126.8; 126.9; 127.8; 128.8; 128.9; 132.8; 139.3; 155.1; 159.1; 166.4; 168.5. Anal. Calcd for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18. Found: C, 71.98; H, 5.20.

*4.2.17. Compound **12b**.* Mp 132–133 °C. IR (Nujol): 1730, 1718 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (3H, t, CH_2Me, *J* 7.2 Hz); 1.80–1.84 (2H, m, CH_2Me); 2.33 (3H, s, Me); 4.33–4.37 (2H, m, OCH_2); 4.74 (1H, d, CH, *J* 5.0 Hz); 5.25 (1H, d, CH, *J* 5.0 Hz); 7.17–7.85 (8H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1; 21.0; 21.2; 50.1; 62.2; 89.2; 104.7; 12.0; 116.9; 123.1; 124.1; 126.8; 126.9; 129.7; 129.8; 132.8; 136.5; 137.7; 155.2; 159.2; 166.4; 168.7. Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.52; H, 5.55.

*4.2.18. Compound **12e**.* Mp 100–101 °C. IR (Nujol): 1755, 1719 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (3H, t, CH_2Me, *J* 7.1 Hz); 1.75–1.79 (2H, m, CH_2Me); 2.33 (3H, s, Me); 4.32–4.36 (2H, m, OCH_2); 4.73 (1H, d, CH, *J* 4.6 Hz); 5.27 (1H, d, CH, *J* 4.6 Hz); 7.07–7.85 (8H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1; 21.4; 21.6; 50.3; 62.2; 89.2; 104.7; 112.0; 117.0; 123.1; 124.1; 124.2; 127.7; 128.8; 129.0; 132.9; 138.8; 139.4; 155.3; 159.2; 166.4; 168.7. Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.53; H, 5.56.

4.2.19. Compound ***12g***. Mp 137–138 °C. IR (Nujol): 1752, 1720 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (3H, t, CH_2*Me*, *J* 7.0 Hz); 1.72–1.76 (2H, m, *CH*$_2$Me); 2.23 (3H, s, Me); 4.20–4.24 (2H, m, OCH_2); 5.00 (1H, d, CH, *J* 4.4 Hz); 5.23 (1H, d, CH, *J* 4.4 Hz); 6.99–7.85 (8H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1; 19.7; 21.2; 46.2; 62.2; 89.2; 104.8; 114.0; 117.0; 123.0; 124.1; 126.2; 126.8; 127.8; 130.9; 132.8; 138.8; 139.4; 155.3; 159.2; 166.4; 168.7. Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.52; H, 5.54.

4.3. General procedure for the synthesis of compounds 16, 17, 18

To a stirred solution of 4-hydroxycoumarin **1** (0.5 g, 3.1 mmol) in *n*-PrOH (20 mL), containing 4 Å molecular sieves and an excess of DBU (0.56 g, 3.7 mmol), benzaldehyde **2a** (0.66 g, 6.2 mmol) and α-chloroketones **3**, **4** or **5** (3.1 mmol) were added. The resulting mixture was heated at reflux for 3 h. After cooling, the reaction products **16**, **17** and **18**, respectively, were collected for filtration. Recrystallization from MeOH led to colourless needles. Benzaldehyde **2a** was recovered unaltered.

4.3.1. Compound ***16***. Mp 190–192 °C. IR (Nujol): 1701, 1713 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.48 (2H, s, OCH_2), 5.59 (1H, s, CH), 7.26–7.99 (9H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 70.4; 91.3; 115.0; 116.7; 123.8; 124.0; 127.8; 127.9; 129.0; 129.1; 132.6; 134.0; 134.4; 153.3; 162.4; 164.9; 184.4. Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.75; H, 4.30.

4.3.2. Compound ***17***. Mp 173–175 °C. IR (Nujol): 1699, 1710 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.36 (3H, s, CO*Me*), 4.75 (2H, s, OCH_2), 5.55 (1H, s, CH), 7.29–7.93 (4H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.5; 72.5; 91.2; 115.0; 116.7; 123.0; 124.0; 132.7; 153.2; 162.2; 164.4; 200.8. Anal. Calcd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 66.25; H, 4.49.

4.3.3. Compound ***18***. Mp 86–88 °C. IR (Nujol): 1712, 1745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.95 (3H, t, CH_2*Me*, *J* 7.45 Hz), 1.70–1.74 (2H, m, *CH*$_2$Me, *J* 7.45, 6.85 Hz), 4.20 (2H, t, *CH*$_2$CH$_2$Me, *J* 6.85 Hz), 4.77 (2H, s, OCH_2), 5.57 (1H, s, CH), 7.26–7.92 (4H, m, $CH_{arom.}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.1; 21.7; 65.2; 67.4; 91.0; 115.1; 116.7; 123.2; 123.9; 132.7; 153.2; 162.3; 164.6; 166.4. Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.10; H, 5.33.

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.10.023.

References and notes

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9. Performing the reaction with **5** (R^1=OCH_2CH_3) in *n*-PrOH, an unavoidable transesterification led to exclusive formation of **12** (R^1=$OCH_2CH_2CH_3$).
10. Under these conditions, no reaction occurred with aliphatic aldehydes **2j**, **k** or with aliphatic α-halogen ketones **4** and **5**.
11. Our one-pot procedure is more convenient with respect to Ref.12 in terms of yield and reaction time.
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