Synthesis of chromones and 4-hydroxyquinolines based on uncatalyzed condensations of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene with 2-alkoxy- and 2-nitrobenzoyl chlorides and related reactions†

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The reaction of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene with 2-methoxybenzoyl chlorides afforded 3,5-diketoesters which were transformed, by treatment with boron tribromide, into functionalized 2-hydroxychroman-4-ones or chromones. The reaction of 1-methoxy-1,3-bis-(trimethylsilyloxy)-1,3-butadiene with 2-nitrobenzoyl chlorides and subsequent reduction of the nitro group afforded functionalized 4-hydroxyquinolines. Their tautomeric equilibrium was studied by NMR spectroscopy and by computational methods.

Introduction

Poly(β-oxo)esters occur in various pharmacologically relevant natural products (polyketides) and represent useful synthetic building blocks.[1] Harris and coworkers and others studied the synthesis of condensation of 1,3-dicarbonyl dianions[2] with carboxylic acid derivatives.[3–5] In most cases esters have been used. Their replacement by *N*-acyl-2-methylaziridines[6] and Weinreb amides proved to be advantageous in several cases.[7] However, several functionalized derivatives fail to give the desired condensation products, especially when simple carboxylic esters are used. For example, the reaction of 1,3-dicarbonyl dianions with nitro-substituted benzoates results in reduction of the nitro group and decomposition. The reaction of dianions with α,β-unsaturated esters results in a 1,4- rather than 1,2-addition. 1,3-Dicarbonyl dianions are not only strong nucleophiles, but also strong bases and reducing agents. Therefore, several side-reactions, such as proton transfer, eliminations, O-acylations, SET-processes, over-addition, and decomposition, are possible for dianions (in contrast to reactions of simple enolate monoanions).

1,3-Bis(silyloxy)-1,3-butadienes can be regarded as electroneutral equivalents of 1,3-dicarbonyl dianions and their synthetic application allows circumvention of the problems mentioned above for the use of free dianions.[8] Reactions of 1,3-bis(silyloxy)-1,3-butadienes and related compounds with carboxylic acid derivatives have been studied. Chan and coworkers reported the synthesis of functionalized phenols by formal [5 + 1] cyclization of 1-methoxy-1,3,5-tris(trimethylsilyloxy)-1,3,5-hexatriene with acid chlorides.[9] We have recently reported the synthesis of resorcins by cyclization of 1,3-bis(silyloxy)-1,3-butadienes with 3,3-dimethoxypentanoyl chloride.[10] 3(2*H*)-Furanones have been prepared based on the condensation of 1,3-bis(silyloxy)-1,3-butadienes with chloroacetyl chloride.[11] Recently, we have reported the synthesis of 3,5-dioxoesters by condensation of 1,3-bis(silyloxy)-1,3-butadienes with acid chlorides.[12,13] This work includes reactions of aromatic, aliphatic, and α,β-unsaturated acid chlorides. In addition, 3,5-dioxopimelic acid diesters, stable 1,3,5,7-tetracarbonyl derivatives, have been prepared by reaction of 1,3-bis(silyloxy)-1,3-butadienes with methyl malonyl chloride.[14] Herein, we report, for the first time, the synthesis of functionalized 2-hydroxychroman-4-ones, chromones, and 4-hydroxyquinolines by reaction of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene with 2-alkoxy- and 2-nitrobenzoyl chlorides.

Results and discussion

Reactions of 2-alkoxybenzoyl chlorides

The condensation of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene (**1**) with 2-alkoxybenzoyl chlorides **2a–e** afforded the 5-(2-alkoxyphenyl)-3,5-dioxoesters **3a–e** which mainly or exclusively exist in the form of their enol tautomers (Table 1). The dashed line indicates that there is a fast equilibrium between two enolic forms. Similar to acetylacetone, only one set of signals is observed by NMR. The best yields were obtained, in analogy to our previous studies,[12a,13,14] when the condensations were carried out in the *absence* of any Lewis acid. The formation of **3a–e** presumably proceeds by attack of the terminal carbon atom of **1** onto the acid chloride. This step might be catalyzed by a catalytic amount of HCl formed by hydrolysis of the acid chloride. The reaction works equally well using commercially available (new bottle) or freshly distilled **2a**. However, the yields significantly dropped when the acid chloride was too old.

Treatment of **3a** and **3c** with BBr_3 and subsequent addition of water afforded the chromones **5a** and **5c** in good yields, respectively. The reaction of BBr_3 with **3b**, containing two ethoxy substituents, was unsuccessful (no conversion). This might be explained by interaction of the additional ethoxy group with the Lewis acid. The reaction of BBr_3 with **3d** and **3e** afforded the

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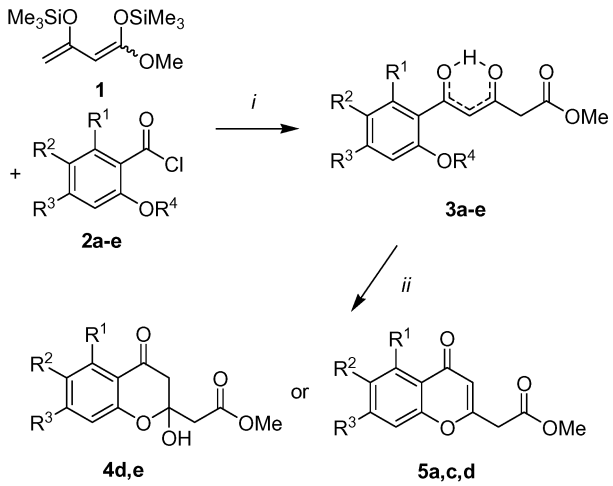
Table 1 Synthesis of **4d**,**e** and **5a**,**c**,**f**



Conditions: *i*: CH_2Cl_2, −78 → 20 °C, 2) $NaHCO_3$, H_2O; *ii*: 1) CH_2Cl_2, 0 °C, BBr_3 (4.0 equiv.); 2) H_2O

3–5	R^1	R^2	R^3	R^4	Keto/Enol	% (**3**)[a]	% (**4**)[a]	% (**5**)[a]
a	H	H	H	Me	14 : 86	45	0	76
b	H	OEt	H	Et	0 : 100	55	0	0
c	H	Cl	H	Me	0 : 100	84	0	73
d	H	H	Cl	Me	0 : 100	85	37[b]	37[b]
e	$-C_4H_4-$		H	Et	0 : 100	36	53	0

[a] Yields of isolated products; **3a**: keto/enol = 14 : 86, **3b–e**: keto/enol = 0 : 100. [b] **4d**/**5d** = 2 : 1.

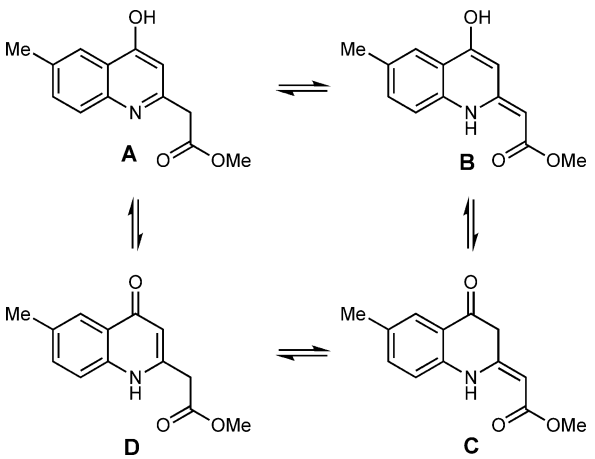
2-hydroxychroman-4-ones **4d** and **4e**, respectively. All attempts to transform **4d**,**e** into the corresponding chromones **5d**,**e** by acid-mediated elimination of water failed (decomposition). The reason for the influence of the substituents on the type of product remains unclear at present. It was shown that the surprising results are reproducible.

Reactions of 2-nitrobenzoyl chlorides

The reaction of **1** with 2-nitrobenzoyl chlorides **6a–g** afforded the condensation products **7a–g** (Table 2). The hydrogenation (H_2, Pd/C 10 mol%, MeOH) of **7a**,**b**, and **7d–g** afforded the quinolines **8a**,**b**, and **8d–g**, respectively. The formation of **8c** from **7c** could be detected, however, the pure product could not be isolated, due to problems related to the chromatographic purification. The formation of products **8** can be explained by reduction of the nitro to an amino group and subsequent cyclization by attack of the amino onto the carbonyl group and extrusion of water.

Several tautomeric structures are possible for products **8a–g** (Scheme 1). Tautomers **A** and **D** contain a 4-hydroxyquinoline and a 4-quinolone structure, respectively. Tautomers **B** and **C** contain an exocyclic double bond. Only the *Z*-configured geometric isomers are considered because they contain an intramolecular hydrogen bond N–H ··· O and are expected to be more stable than the corresponding *E*-configured isomers.

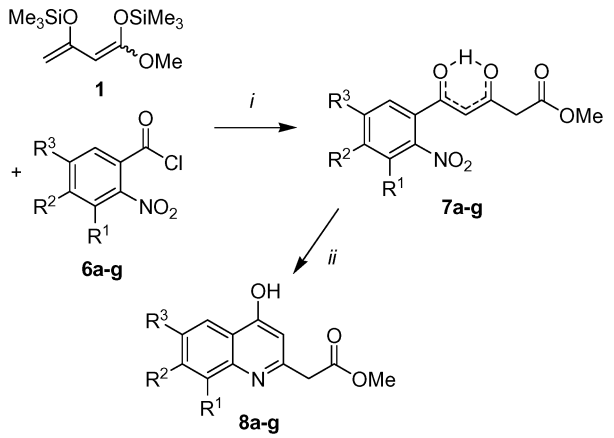
The tautomerism was studied by NMR spectroscopy and by computational methods. The NMR studies are hampered by the low solubility of products **8** in most organic solvents and in water. Derivative **8f** showed the best, albeit still poor, solubility of all



Scheme 1 Selected tautomeric structures of **8f**.

derivatives and was thus chosen for the NMR experiments. Due to solubility reasons, all experiments had to be carried out in DMSO. Therefore, low temperature experiments could not be carried out. Most signals are strongly temperature- and concentration-dependent. They are broad because of the intra- or intermolecular chemical exchange among the tautomers. Even in DMSO, no well-resolved or at least reasonably sharp signals were found for the "active" protons (OH or NH). Several ^{13}C NMR signals, which suffered broadening as well, sharpened a little bit upon warming of the solution to 50 °C. Despite these problems, it was possible to carry out shift correlation experiments which allowed to assign the signals of most of the atomic positions.

Table 2 Synthesis of 4-hydroxyquinolines **8a–g**



Conditions: *i*: 1) CH_2Cl_2, -78 → 20 °C; 2) $NaHCO_3$, H_2O; *ii*: Pd/C (10 mol-%), H_2, MeOH, 20 °C

7,**8**	R^1	R^2	R^3	% (**7**)[a]	% (**8**)[a]
a	H	H	H	60	67
b	H	Cl	H	62	69
c	OMe	H	H	94	0
d	Me	H	H	68	86
e	H	H	Cl	58	37
f	H	H	Me	63	86
g	H	H	F	58	68

[a] Yields of isolated products; **7a–g**: keto/enol = 0 : 100.

The presence of CH_2 protons next to the ester group shows that tautomers A or D are predominantly present. However, the resonance of quinoline carbon atom C-4 (attached to the oxygen) could not be located, due to extreme broadening (coalescence). Therefore, it remains unclear whether tautomer **A** or **D** is present. The broadening of the signals suggests that there is a fast equilibrium (on the NMR time scale). Only very small signals were observed which are tentatively assigned to tautomer **B** (with some uncertainty). In a ^{1}H NOESY experiment, a chemical exchange between the CH_2 protons of **A**/**D** and water was detected. The facile exchange might be explained by the presence of a small amount of enamine tautomers **B** or **C**. The complex exchange behaviour of compound **8f** became obvious from exchanging the acidic protons by D_2O addition. Not only the broad resonance at high frequency, but also the ^{1}H and ^{13}C signals assigned to the CH_2 group disappeared. This facile exchange might be again explained by the participation of a small amount of tautomer **B** or **C**. It is worth to be noted that the signals of carbon atom C-3 remained unaffected. This observation rules out a significant participation of tautomer **C**.

To further clarify this problem we have carried out computations[15] at the B3LYP/6–311+G** and MP2/6–311+G** levels of theory for getting the energetic order of the tautomeric structures **A–D**. At first we have optimized **A–D** at the B3LYP/6–311+G** level and they are found to energy minimums by frequency calculations. For comparison we have carried out MP2/6–311+G** single-point energy calculations on the B3LYP/6–311+G** geometries. As given in Table 3, isomer **D** is most stable at B3LYP/6–311+G**, while **A–C** are higher in energy. At MP2/6–311+G**, isomers **D** and **A** are most stable and in close energy, while **B** and **C** are higher in energy.

Table 3 Computed relative energies (ΔH/kcal mol^{-1})

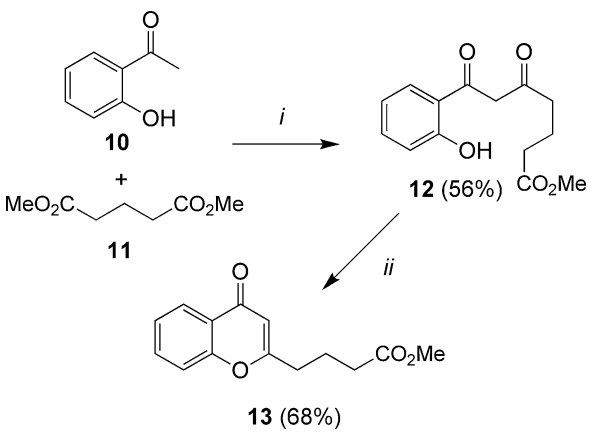
Method	**A**	**B**	**C**	**D**
B3LYP[a,b]	4.89 (4.28)	3.11 (3.55)	4.17 (3.77)	0.00 (0.00)
MP2[c]	0.46	6.91	6.71	0.00
B3LYP-IPCM/DMSO[d]	5.08	5.43	5.21	0.00
MP2-IPCM/DMSO[e]	–0.61	8.31	8.21	0.00

[a] At B3LYP/6–311+G** (full optimization). [b] The Gibbs free energies (corrected at 298 K) in parenthesis. [c] Single-point energy at B3LYP/6–311+G**//B3LYP/6–311+G**. [d] Single-point energy with DMSO as solvent at B3LYP/6–311+G**-IPCM//B3LYP/6–311+G**. [e] Single-point energy with DMSO as solvent at MP/6–311+G**-IPCM/B3LYP/6–311+G**.

Since all NMR data have been detected in DMSO, we have calculated the relative energies by using DMSO as solvent and an isodensity surface polarized continuum model (IPCM). At B3LYP-IPCM, **D** is most stable in DMSO, followed by **A**. At MP2-IPCM, **A** becomes most stable, closely followed by **D**, while **B** and **C** are higher in energy (Table 3).

On the basis of the calculated energies and the NMR parameters, it is to conclude that isomers **A** and **D** are the most dominant resonance structures (rapid equilibrium). Tautomer **B** might be present in small quantity, and **C** can be ruled out.

The condensation of the dianion of 2-acetylphenol (**10**), with dimethyl pentane-1,5-dioate (**11**) afforded product **12** which is structurally related to **3a** (Scheme 2). The reaction of **12** with boron tribromide resulted, following the conditions of the transformation of **3a** into **5a**, in the formation of chromone **13** in 68% yield. In addition, a small amount of the starting material **12** (14%) was recovered.



Scheme 2 Synthesis of chromone **13**; *i*, (1) LDA (2.2 equiv.), THF, 0 °C, 1 h; (2) **10**, −78 °C, 30 min; (3) **11** (1.0 equiv.), 78 → 10 °C, 12 h, HCl (10%); *ii*, BBr_3 (8.0 equiv.), CH_2Cl_2, 0 °C.

Conclusions

In conclusion, we reported the reaction of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene with 2-methoxybenzoyl chlorides to give 3,5-diketoesters which were transformed, by treatment

with boron tribromide, into functionalized 2-hydroxychroman-4-ones or chromones. The reaction of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene with 2-nitrobenzoyl chlorides and subsequent hydrogenation afforded functionalized 4-hydroxyquinolines. The tautomeric equilibrium of these molecules was studied by NMR spectroscopy and by computational methods.

Experimental section

General Comments

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C NMR spectra the deuterated solvents indicated were used. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O) or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

General procedure for the synthesis of 3,5-dioxoalkanoates 3a–e and 7a–g

To a CH_2Cl_2 solution of **1** (2.0 equiv.) was slowly added the acid chloride (1.0 equiv.) at −78 °C. The reaction mixture was slowly warmed to 20 °C during 6 h and the solution was stirred at 20 °C for a further 6–8 h. To the solution was added a saturated aqueous solution of $NaHCO_3$ (20 mL). The organic and the aqueous layer were separated and the latter was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, *n*-heptane/EtOAc = 2 : 1) to give the respective products.

Methyl 3,5-dioxo-5-(2-methoxyphenyl)pentanoate (3a). Starting with **2a** (0.980 g, 5.8 mmol) and **1** (3.00 g, 11.5 mmol), dissolved in CH_2Cl_2 (10 mL), **3a** was isolated as a yellow oil (0.650 g, 45%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 14 : 86): keto: δ = 3.62 (s, 2H, CH_2), 3.74 (s, 3H, OCH_3), 3.91 (s, 3H, $ArOCH_3$), 4.21 (s, 2H, CH_2), 6.99 (d, ^{3}J = 8.4 Hz, 1H, Ar), 7.03 (ddd, ^{3}J = 7.3 Hz, ^{3}J = 8.8 Hz, ^{4}J = 1.0 Hz, 1H, Ar), 7.52 (ddd, ^{3}J = 8.8 Hz, ^{3}J = 7.3 Hz, ^{4}J = 1.0 Hz, 1H, Ar), 7.86 (dd, ^{3}J = 7.8 Hz, ^{4}J = 1.8 Hz, 1H, Ar); enol: 3.49 (s, 2H, CH_2), 3.77 (s, 3H, OCH_3), 3.92 (s, 3H, $ArOCH_3$), 6.59 (s, 1H, CH), 6.98 (d, ^{3}J = 8.4 Hz, 1H, Ar), 7.04 (ddd, ^{3}J = 7.3 Hz, ^{3}J = 8.8 Hz, ^{4}J = 1.0 Hz, 1H, Ar), 7.47 (ddd, ^{3}J = 8.8 Hz, ^{3}J = 7.3 Hz, ^{4}J = 1.0 Hz, 1H, Ar), 7.91 (dd, ^{3}J = 7.8 Hz, ^{4}J = 1.8 Hz, 1H, Ar), 15.82 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): enol: δ = 46.3 (CH_2), 52.8 (OCH_3), 55.9 (OCH_3), 102.1 (CH), 111.9, 121.1 (CHAr), 123.4 (CAr), 131.2, 133.8 (CHAr), 159.0 (CAr), 168.5, 180.8, 190.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3463 (w), 3078 (w), 2952 (m), 2842 (m), 2362 (w), 1744 (s), 1606 (s), 1491 (s), 1457 (s), 1437 (s), 1328 (m), 1250 (s), 1164 (m), 1074 (m), 1020 (m), 955 (w), 856 (w), 797 (w), 764 (m). MS (EI, 70 eV): *m/z* (%) = 250 (M^+, 13), 219 (24), 177 (14), 135 (100), 77 (12). HRMS (EI, 70 eV): calcd. for $C_{13}H_{14}O_5$ (M^+) 250.0836, found 250.0828.

Methyl 3,5-dioxo-5-(2,5-diethoxyphenyl)pentanoate (3b). Starting with **2b** (1.200 g, 5.3 mmol) dissolved in CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **3b** was isolated as a yellow solid (0.890 g, 55%); mp 37–38 °C. ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 1.39 (t, ^{3}J = 6.97 Hz, 3H, OCH_2CH_3), 1.45 (t, ^{3}J = 6.98 Hz, 3H, OCH_2CH_3), 3.47 (s, 2H, CH_2), 3.99 (s, 3H, CH_3), 4.02 (q, ^{3}J = 6.98 Hz, 2H, OCH_2CH_3), 4.06 (q, ^{3}J = 6.97 Hz, 2H, OCH_2CH_3), 6.76 (s, 1H, CH), 6.88 (d, ^{3}J = 9.03 Hz, 1H, Ar), 6.99 (dd, ^{3}J = 9.00 Hz, ^{4}J = 3.18 Hz, 1H, Ar), 7.47 (d, ^{4}J = 3.15 Hz, 1H, Ar), 15.82 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.2 (CH_3), 46.4 (CH_2), 52.7 (CH_3), 64.4, 65.3 (CH_2), 102.1 (CH), 114.6, 114.9, 120.8 (Ar), 123.8, 152.9, 153.1 (C), 168.4, 180.3, 190.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3452 (w), 3151 (w),3094 (w), 2981 (m), 2936 (m), 2885 (m), 1741 (s), 1575 (s, br), 1503 (s), 1474 (s), 1438 (m), 1396 (s), 1250 (s), 1218 (s), 1148 (m), 1112 (s), 1049 (s), 1012 (m), 967 (w), 926 (m), 888 (w), 857 (w), 814 (m), 801 (m), 776 (w), 751 (m). MS (EI, 70 eV) *m/z* = 308 (M^+, 5.9), 293 (18.2), 250 (21.3), 193 (100), 165 (28.5), 137 (19.5), 109 (11.6), 69 (10.2). Anal. calcd. for $C_{16}H_{20}O_6$ (308.33): C, 62.33; H, 6.54. Found: C, 62.16; H, 6.48.

Methyl 3,5-dioxo-5-(2-methoxy-5-chlorophenyl)pentanoate (3c). Starting with **2c** (1.100 g, 5.4 mmol) dissolved in CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **3c** was isolated as an orange solid (1.280 g, 84%); mp 64–66 °C. ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 3.48 (s, 2H, CH_2), 3.75 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 6.57 (s, 1H, CH), 6.89 (d, ^{3}J = 8.91 Hz, 1H, Ar), 7.37 (dd, ^{3}J = 8.88 Hz, ^{4}J = 2.73 Hz, 1H, Ar), 7.85 (d, ^{4}J = 2.73 Hz, 1H, Ar), 15.69 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.2 (CH_2), 52.7, 56.3 (CH_3), 102.2 (CH), 113.3 (Ar), 124.5, 126.3 (C), 130.1, 133.1 (Ar), 157.4 (C), 168.3, 178.9, 190.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3452 (m), 3148 (m), 3092 (m), 3033 (w), 2977 (w), 2957 (m), 2848 (m), 1735 (s), 1694 (w), 1609 (s), 1564 (s), 1492 (s), 1457 (s), 1438 (s), 1413 (m), 1327 (s), 1273 (s), 1251 (s), 1209 (s), 1172 (s), 1128 (s), 1113 (s), 1072 (s), 1020 (s), 1004 (m), 967 (m), 934 (w), 911 (m), 883 (m), 826 (s), 810 (s), 770 (m). MS (EI, 70 eV): *m/z* (%) = 284 (M^+, 7.8), 253 (28.3), 211 (12.4), 171 (29.7), 169 (100), 126 (9.6), 111 (8.3), 69 (11.0). Anal. calcd. for $C_{13}H_{13}ClO_5$ (284.69): C, 54.84; H, 4.60. Found: C, 54.73; H, 4.73.

Methyl 3,5-dioxo-5-(2-methoxy-4-chlorophenyl)pentanoate (3d). Starting with **2d** (1.180 g, 5.7 mmol) dissolved in CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **3d** was isolated as an orange solid (1.380 g, 85%); mp 37–38 °C. ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 3.47 (s, 2H, CH_2), 3.74 (s, 3H, CH_3), 3.91 (s, 3H, CH_3), 6.56 (s, 1H, CH), 6.96 (d, ^{4}J = 1.98 Hz, 1H, Ar), 7.02 (dd, ^{3}J = 8.46 Hz, ^{4}J = 1.98 Hz, 1H, Ar), 7.87 (d, ^{3}J = 8.46 Hz, 1H, Ar), 15.79 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.3 (CH_2), 52.7, 56.3 (CH_3), 102.0 (CH), 112.6, 121.4 (Ar), 121.9 (C), 131.7 (Ar), 139.5, 159.4 (C), 168.4, 179.5, 190.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3443 (w), 3149 (w), 3098 (w), 2980 (w), 2854 (w), 1728 (s), 1597 (s), 1571 (s), 1485 (s), 1472 (m), 1436 (s), 1414 (m), 1397 (m), 1344 (s), 1288 (m), 1243 (s), 1219 (s), 1176 (s), 1153 (m), 1135 (m), 1110 (m), 1068 (m), 1020 (s), 997 (m), 960 (m), 906 (w), 887 (s), 845 (w), 833 (s), 803 (s), 764 (m). MS (CI, isobutane): *m/z* (%) = 285 ($[M+H]^+$, 100). Anal. calcd. for $C_{13}H_{13}ClO_5$ (284.69): C, 54.84; H, 4.60. Found: C, 54.48; H, 4.27.

Methyl 3,5-dioxo-5-(3-ethoxynaphth-2-yl)pentanoate (3e). Starting with **2e** (1.340 g, 5.7 mmol) dissolved in CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **3e** was isolated as a yellow solid (0.640 g, 36%); mp 46–48 °C. ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 1.42 (t, ^{3}J = 6.99 Hz, 3H, OCH_2CH_3), 3.47 (s, 2H, CH_2), 3.77 (s, 3H, CH_3), 4.20 (q, ^{3}J = 6.97 Hz, 2H,

OCH_2CH_3), 5.99 (s, 1H, CH), 7.21–7.96 (m, 6H, Ar), 15.44 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.3 (CH_3), 45.4 (CH_2), 52.8 (CH_3), 65.8 (CH_2), 105.2 (CH), 114.9 (Ar), 120.5 (C), 124.5, 127.9, 128.4 (Ar), 129.1, 131.8 (C), 132.4 (Ar), 154.4 (C), 168.3, 186.4, 187.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3397 (w), 2982 (m), 2952 (w), 2894 (w), 1745 (s), 1623 (s), 1596 (s), 1511 (s), 1465 (m), 1435 (s), 1375 (m), 1338 (m), 1277 (s), 1249 (s), 1150 (s), 1114 (m), 1091 (m), 1063 (s), 1025 (m), 966 (w), 861 (w), 809 (m), 751 (m). MS (EI, 70 eV) m/z = 314 (M^+, 39.2), 282 (10.3), 269 (42.8), 241 (11.7), 213 (20.3), 199 (100), 171 (89.2), 149 (10.8), 142 (17.8), 127 (13.2), 115 (33.8), 69 (9.3). HRMS (EI, 70 eV): calcd. for $C_{18}H_{18}O_5$ (M^+) 314.1149, found 314.1148.

Methyl 3,5-dioxo-5-(2-nitrophenyl)pentanoate (7a). Starting with **6a** (1.070 g, 5.8 mmol), CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **7a** was isolated as a brownish oil (0.910 g, 60%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 3.46 (s, 2H, CH_2), 3.77 (s, 3H, CH_3), 5.96 (s, 1H, CH), 7.57–7.71 (m, 3H, Ar), 7.93–7.96 (m, 1H, Ar), 14.91 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.2 (CH_2), 52.6 (CH_3), 100.5 (CH), 124.5, 129.3 (Ar), 131.1 (C), 131.5 (Ar), 132.0 (C), 133.0 (Ar), 167.6, 185.4, 185.5 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2954 (w), 2361 (w), 1739 (m), 1595 (m, br), 1572 (m), 1526 (s), 1436 (m), 1407 (w), 1346 (s), 1307 (m), 1243 (m, br), 1146 (m), 1060 (m), 1012 (m), 951 (w, br), 854 (m), 784 (m), 756 (m). MS (EI, 70 eV) m/z = 264 (M^+, 4.6), 205 (3.6), 177 (16.3), 159 (3.2), 150 (100), 135 (13.8), 134 (14.5), 119 (8.6), 104 (18.1), 78 (11.2), 76 (24.7), 69 (13.4). Anal. calcd. for $C_{12}H_{11}NO_6$ (265.22): C, 54.34; H, 4.18; N, 5.28. Found: C, 54.43; H, 4.11; N, 5.28.

Methyl 3,5-dioxo-5-(4-chloro-2-nitrophenyl)pentanoate (7b). Starting with **6b** (1.270 g, 5.8 mmol), CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **7b** was isolated as an orange oil (1.070 g, 62%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 3.46 (s, 2H, CH_2), 3.77 (s, 3H, CH_3), 5.94 (s, 1H, CH), 7.54 (d, ^3J = 8.10 Hz, 1H, Ar), 7.65 (dd, ^3J = 8.25 Hz, ^4J = 1.74 Hz, 1H, Ar), 7.91 (d, ^4J = 1.60 Hz, 1H, Ar), 14.82 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.2 (CH_2), 52.7 (CH_3), 100.3 (CH), 124.8 (Ar), 130.1 (C), 130.5, 133.0 (Ar), 137.6, 148.4 (C), 167.5, 184.4, 185.6 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3090 (w, br), 2955 (w), 1738 (m), 1598 (m, br), 1534 (s), 1436 (m), 1348 (s), 1260 (s, br), 1153 (s), 1115 (m), 1094 (m), 1065 (m), 1010 (m), 937 (w, br), 890 (s), 840 (m), 799 (m), 766 (m). HRMS (ESI): calcd. for $C_{12}H_{10}ClNO_6$ ([M+1]$^+$) 300.02694, found 300.02663. Anal. calcd. for $C_{12}H_{10}ClNO_6$ (299.66): C, 48.10; H, 3.36; Cl, 11.83; N, 4.67. Found: C, 48.33; H, 3.86; Cl, 11.37; N, 4.37.

Methyl 3,5-dioxo-5-(3-methoxy-2-nitrophenyl)pentanoate (7c). The reaction was carried out following the procedure as given for the synthesis of **5a**. Starting with **6c** (1.240 g, 5.8 mmol), CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **7c** was isolated as an orange solid (1.600 g, 94%); mp 87 °C. ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 3.45 (s, 2H, CH_2), 3.75 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 6.11 (s, 1H, CH), 6.96–7.48 (m, 3H, Ar), 15.04 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.5 (CH_2), 52.7, 56.7 (CH_3), 99.4 (CH), 116.3, 120.2 (Ar), 129.1 (C), 131.3 (Ar), 139.4, 151.2 (C), 167.6, 182.4, 187.0 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3005 (w), 2955 (w), 2906 (w), 1734 (m), 1601 (m, br), 1575 (s), 15.35 (s), 1461 (s, br), 1373 (s), 1281 (s, br), 1207 (s), 1144 (s), 1044 (s), 1006 (m), 946 (m), 909 (m), 894 (w), 852 (s), 819 (w), 808 (w), 789 (s), 757 (m, br). HRMS (ESI): calcd. for $NaC_{13}H_{13}NO_7$ ([M+Na]$^+$) 318.05842, found 318.05826. Anal. calcd. for $C_{13}H_{13}NO_7$ (295.24): C, 52.88; H, 4.44; N, 4.74. Found: C, 52.70; H, 4.61; N, 4.35.

Methyl 3,5-dioxo-5-(3-methyl-2-nitrophenyl)pentanoate (7d). The reaction was carried out following the procedure as given for the synthesis of **5a**. Starting with **6d** (1.150 g, 5.8 mmol), CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **7d** was isolated as a yellow oil (1.100 g, 68%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 2.37 (s, 3H, CH_3), 3.46 (s, 2H, CH_2), 3.77 (s, 3H, CH_3), 6.09 (s, 1H, CH), 7.45–7.54 (m, 3H, Ar), 15.11 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4 (CH_3), 44.5 (CH_2), 52.6 (CH_3), 99.4 (CH), 126.8 (Ar), 128.9 (C), 130.2 (Ar), 131.2 (C), 134.8 (Ar), 167.6, 183.4, 186.6 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2955 (w), 1739 (m), 1669 (w), 1600 (m, br), 1530 (s), 1463 (m, br), 1366 (m), 1262 (s, br), 1197 (m), 1154 (m), 1073 (w), 1014 (m), 948 (w), 921 (w), 852 (m), 828 (w), 785 (s). HRMS (ESI): calcd. for $NaC_{13}H_{13}NO_6$ ([M+Na]$^+$) 302.06351, found 302.06317. Anal. calcd. for $C_{13}H_{13}NO_6$ (279.25): C, 55.91; H, 4.69; N, 5.02. Found: C, 56.00; H, 4.67; N, 5.03.

Methyl 3,5-dioxo-5-(5-chloro-2-nitrophenyl)pentanoate (7e). Starting with **6e** (1.270 g, 5.8 mmol), CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **7e** was isolated as an orange oil (1.000 g, 58%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 3.47 (s, 2H, CH_2), 3.76 (s, 3H, CH_3), 5.94 (s, 1H, CH), 7.54–7.60 (m, 2H, Ar), 7.93 (d, ^3J = 8.40 Hz, 1H, Ar), 14.29 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.9 (CH_2), 52.7 (CH_3), 100.6 (CH), 126.0, 129.3, 131.4 (Ar), 133.7, 139.6, 145.8 (C), 167.6, 184.8, 185.3 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3102 (w), 2955 (w), 1740 (m), 1609 (m, br), 1566 (m), 1528 (s), 1437 (m), 1342 (s), 1300 (m), 1242 (m, br), 1149 (m), 1103 (m), 1060 (w), 1011 (w), 907 (s), 839 (m), 727 (s). MS (EI, 70 eV) m/z = 298 (M^+, 1.0), 268 (9.1), 255 (10.2), 253 (34.7), 226 (10.3), 184 (100), 170 (21.8), 138 (17.1), 126 (17.9), 110 (23.2), 101 (55.7), 76 (32.4), 69 (28.2). HRMS (ESI): calcd. for $NaC_{12}H_{10}ClNO_6$ ([M+Na]$^+$) 322.00889, found 322.00825.

Methyl 3,5-dioxo-5-(5-methyl-2-nitrophenyl)pentanoate (7f). Starting with **6f** (1.150 g, 5.8 mmol), CH_2Cl_2 (10 mL) and **1** (3.000 g, 11.5 mmol), **7f** was isolated as a yellow oil (1.01 g, 63%). ^{1}H NMR (300 MHz, $CDCl_3$, keto/enol = 0 : 100): δ = 2.47 (s, 3H, CH_3), 3.44 (s, 2H, CH_2), 3.77 (s, 3H, CH_3), 5.30 (s, 1H, CH), 7.34–7.40 (m, 2H, Ar), 7.86–7.89 (m, 1H, Ar), 14.84 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4 (CH_3), 44.1 (CH_2), 52.6 (CH_3), 100.6 (CH), 124.5 (C), 124.6, 129.8, 131.7 (Ar), 144.7, 145.4 (C), 167.8, 184.7, 186.8 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3107 (w), 3067 (w), 2955 (w), 2852 (w), 1741 (m), 1587 (m), 1519 (s), 1436 (m), 1403 (w), 1342 (s), 1313 (m), 1250 (m), 1190 (m), 1154 (m), 1117 (m), 1056 (m), 1012 (m), 895 (w), 834 (s), 757 (m), 735 (s). MS (EI, 70 eV) m/z = 278 (M^+, 3.3), 191 (3.2), 164 (100), 148 (4.7), 118 (5.6), 89 (7.1), 77 (4.3). Anal. calcd. for $C_{13}H_{13}NO_6$ (279.25): C, 55.91; H, 4.69; N, 5.02. Found: C, 55.57; H, 4.46; N, 5.49.

(4-Oxo-4*H*-chromen-2-yl)acetic acid methyl ester (5a). To a CH_2Cl_2 solution (8 mL) of **3a** (0.200 g, 0.8 mmol) was dropwise added BBr_3 (0.800 g, 3.2 mmol) at 0 °C. The reaction mixture was slowly warmed to 20 °C and was stirred for 6–8 h at this temperature. The reaction was quenched by adding 30 mL of water. The organic layer was separated and washed with water. The aqueous layer was repeatedly extracted with CH_2Cl_2. The combined organic layers were dried (sodium sulfate), filtered, and dried *in vacuo*. The residue was purified by column chromatography (silica,

n-heptane/EtOAc = 2 : 1) to give **5a** as a colourless solid (0.130 g, 76%); mp 96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 6.30 (s, 1H, CH), 7.37–7.46 (m, ^3J = 8.1 Hz, 2H, Ar), 7.66 (ddd, ^3J = 6.9 Hz, ^3J = 8.0 Hz, ^4J = 1.7 Hz, 1H, Ar), 8.18 (dd, ^3J = 8.0 Hz, ^4J = 1.4 Hz, 1H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.4 (CH_2), 53.0 (OCH_3), 112.7 (CH), 118.3 (CHAr), 123.9 (CAr), 125.6, 126.0, 134.1 (CHAr), 156.8 (CAr), 161.4, 168.1, 178.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3450 (m), 3064 (w), 3006 (w), 2955 (m), 2932 (m), 1985 (w), 1951 (w), 1731 (s), 1644 (s), 1609 (s), 1572 (m), 1475 (m), 1465 (m), 1438 (m), 1416 (m), 1397 (s), 1344 (s), 1307 (m), 1251 (m), 1204 (s), 1165 (s), 1122 (m), 1024 (w), 995 (m), 969 (m), 953 (m), 907 (m), 871 (m), 848 (m), 785 (m), 758 (s), 740 (m). MS (CI, isobutane): *m*/*z* (%) = 219 ([M+isobutane]$^+$, 13). HRMS (CI): calcd. for $C_{12}H_{11}O_4$ ([M+1]$^+$) 219.0652, found 219.0649. Anal. calcd. for $C_{12}H_{10}O_4$ (218.12): C, 66.08; H, 4.62. Found C, 66.11; H, 4.60.

(6-Chloro-4-oxo-4*H*-chromen-2-yl)acetic acid methyl ester (5c). The reaction was carried out following the procedure as given for the synthesis of **5a**. Starting with **3c** (0.230 g, 0.8 mmol), CH_2Cl_2 (8 mL), and BBr_3 (0.31 mL, 3.2 mmol), **5c** was isolated as a colorless solid (0.150 g, 73%); mp 90–93 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 2H, CH_2), 3.78 (s, 3H, CH_3), 6.31 (s, 1H, CH), 7.33 (d, ^3J = 8.94 Hz, 1H, Ar), 7.61 (dd, ^3J = 8.91 Hz, ^4J = 2.61 Hz, 1H, Ar), 8.15 (d, ^4J = 2.58 Hz, 1H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.3 (CH_2), 53.2 (CH_3), 112.7 (CH), 120.1 (Ar), 124.9 (C), 125.5 (Ar), 131.6 (C), 134.3 (Ar), 155.1, 161.7 (C), 168.0, 177.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3421 (s, br), 3123 (w), 3065 (m), 2999 (w), 2955 (w), 1747 (s), 1698 (w), 1654 (s), 1610 (s), 1572 (m), 1473 (m), 1450 (s), 1400 (m), 1380 (m), 1332 (m), 1268 (m), 1198 (s), 1177 (s), 1156 (s), 1137 (m), 1105 (m), 1070 (w), 1001 (m), 959 (m), 942 (w), 903 (w), 864 (m), 846 (m), 801 (m), 775 (w), 740 (m). MS (EI, 70 eV) *m*/*z* = 252 (M$^+$, 100), 208 (22.0), 165 (55.5), 126 (15.5), 102 (11.4). HRMS (EI, 70 eV): calcd. for $C_{12}H_9O_4Cl$ (M$^+$) 252.0184, found 252.0181.

(7-Chloro-2-hydroxy-4-oxo-4*H*-chroman-2-yl)acetic acid methyl ester (4d). The reaction was carried out following the procedure as given for the synthesis of **5a**. Starting with **2d** (0.230 g, 0.8 mmol), CH_2Cl_2 (8 mL) and BBr_3 (0.31 mL, 3.2 mmol), **8d** was isolated as a colorless solid (0.08 g, 37%); mp 72–74 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.77–3.07 (m, 4H, CH_2), 3.84 (s, 3H, CH_3), 5.94 (s, 1H, OH), 6.98–7.04 (m, 2H, Ar), 7.83 (d, ^3J = 8.34 Hz, 1H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.8, 47.5 (CH_2), 52.9 (CH_3), 101.0 (C), 118.9 (Ar), 119.7 (C), 122.9, 128.0 (Ar), 142.2, 158.5 (C), 176.9, 195.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3369 (s, br), 3005 (w), 2952 (w), 2922 (w), 1733 (s),1685 (s), 1647 (w), 1603 (w), 1569 (m), 1495 (w), 1475 (w), 1459 (w), 1425 (m), 1352 (m), 1318 (m), 1306 (m), 1288 (w), 1217 (s), 1179 (w), 1147 (m), 1118 (w), 1099 (m), 1079 (m), 1062 (w), 1003 (m), 950 (m), 923 (m), 901 (w), 866 (m), 831 (w), 822 (m), 779 (w), 742 (w), 725 (w). MS (EI, 70 eV) *m*/*z* = 270 (M$^+$, 13.5), 238 (8.4), 199 (38.4), 197 (98.0), 157 (38.2), 155 (100), 126 (13.4), 99 (11.1), 69 (17.5). HRMS (EI, 70 eV): calcd. for $C_{12}H_{11}O_5Cl$ (M$^+$) 270.0290, found 270.0288.

Methyl 2-(3-hydroxy-1-oxo-2,3-dihydro-1*H*-benzo[*f*]-chromen-3-yl)acetate (4e). The reaction was carried out following the procedure as given for the synthesis of **5a**. Starting with **2e** (0.250 g, 0.8 mmol), CH_2Cl_2 (8 mL) and BBr_3 (0.3 mL, 3.2 mmol), **4e** was isolated as a colorless solid (0.120 g, 53%); mp 120–122 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80–3.13 (m, 4H, CH_2), 3.84 (s, 3H, CH_3), 5.89 (s, 1H, OH), 7.07 (d, ^3J = 8.97 Hz, 1H, Ar), 7.40–7.96 (m, 4H, Ar), 9.28 (d, ^3J = 8.01 Hz, 1H, Ar). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.7, 49.0 (CH_2), 52.8 (CH_3), 100.5, 112.6 (C), 119.3, 125.3, 126.2, 128.6 (Ar), 129.7 (C), 130.0 (Ar), 131.4 (C), 137.8 (Ar), 160.1 (C), 171.9, 191.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3406 (m), 2956 (w), 1711 (s), 1674 (s), 1618 (m), 1597 (m), 1572 (w), 1513 (m), 1463 (m), 1440 (s), 1407 (m), 1370 (m), 1347 (m), 1282 (w), 1265 (w), 1232 (s), 1209 (s), 1178 (m), 1157 (s), 1123 (m), 1083 (w), 1027 (w), 1008 (s), 986 (w), 964 (w), 921 (w), 878 (m), 863 (w), 829 (s), 789 (w), 762 (m). MS (EI, 70 eV): *m*/*z* = 286 (M$^+$, 19.2), 268 (16.9), 254 (18.4), 213 (36.2), 181 (15.4), 171 (100), 142 (30.9), 114 (45.4), 89 (9.3), 77 (10.8), 69 (14.2). HRMS (EI, 70 eV): calcd. for $C_{16}H_{14}O_5$ (M$^+$) 286.0836, found 286.0830.

General procedure for the synthesis of quinolines 8a–g

A MeOH solution of **7a–g** and of Pd/C was stirred under a hydrogen atmosphere for 24 h at 20 °C. The catalyst was filtered off and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, EtOAc/heptanes).

Methyl 2-(4-hydroxyquinolin-2-yl)acetate (8a). Starting with **7a** (0.200 g, 0.8 mmol), MeOH (3 mL) and Pd/C (10 mol%), **8a** was isolated as a pale grey solid (0.110 g, 67%); mp 179 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.67 (s, 3H, CH_3), 3.90 (s, 2H, CH_2), 6.11 (s, 1H, CH), 7.43 (m, 1H, Ar), 7.76 (m, 1H, Ar), 7.87 (m, 1H, Ar), 8.10 (m, 1H, Ar), 11.85 (s, 1H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 37.2 (CH_2), 52.1 (CH_3), 108.7 (CH), 115.3, 124.3 (C), 124.7, 124.8, 131.9, 132.0 (Ar), 140.8 (CO), 145.7 (C), 169.0 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3100 (w), 3075 (w), 2988 (w), 2959 (w), 1733 (s), 1594 (m, br), 1547 (m, br), 1454 (m), 1430 (m), 1407 (m), 1342 (s), 1247 (m, br), 1212 (m, br), 1166 (s), 1150 (s), 985 (s, br), 899 (s), 829 (s), 779 (s), 751 (s). MS (EI, 70 eV) *m*/*z* = 217 (M$^+$, 34.0), 201 (100), 185 (14.2), 173 (11.7), 159 (43.7), 157 (17.8), 145 (14.6), 129 (46.1), 102 (18.4), 77 (13.7), 67 (19.1). HRMS (EI, 70 eV): calcd. for $C_{12}H_{11}NO_3$ (M$^+$) 217.0733, found 217.0739.

Methyl 2-(7-chloro-4-hydroxyquinolin-2-yl)acetate (8b). Starting with **7b** (0.230 g, 0.8 mmol), MeOH (3 mL) and Pd/C (10 mol%), **8b** was isolated as a pale grey solid (0.13 g, 69%); mp 204 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.67 (s, 3H, CH_3), 3.93 (s, 2H, CH_2), 6.20 (s, 1H, CH), 7.45 (d, ^3J = 8.61 Hz, 1H, Ar), 7.87 (s, 1H, Ar), 8.11 (d, ^3J = 8.64 Hz, 1H, Ar), 12.03 (s, 1H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 37.0 (CH_2), 52.1 (CH_3), 109.3 (CH), 114.4 (Ar), 123.0 (C), 124.1, 127.2 (Ar), 137.0 (CCl), 140.6 (CO), 146.8 (C), 168.7 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3097 (w), 3010 (w), 2956 (w), 2845 (w), 2113 (w, br), 1731 (s), 1594 (m, br), 1546 (m, br), 1437 (m), 1405 (m), 1340 (s), 1237 (m, br), 1142 (s), 976 (s), 903 (s), 843 (s), 821 (s), 755 (s). MS (EI, 70 eV) *m*/*z* = 251 (M$^+$, 28.7), 237 (16.9), 235 (47.3), 219 (13.1), 207 (15.4), 195 (25.5), 193 (76.9), 179 (18.9), 164 (46.1), 128 (16.9), 105 (10.6), 101 (13.6), 91 (11.5), 75 (15.9), 69 (38.9). HRMS (ESI): calcd. for $C_{12}H_{11}ClNO_3$ ([M+H]$^+$) 252.0422, found 252.0416.

Methyl 2-(4-hydroxy-8-methylquinolin-2-yl)acetate (8d). Starting with **7d** (0.210 g, 0.8 mmol), MeOH (3 mL) and Pd/C (10 mol%), **8d** was isolated as a pale green solid (0.150 g, 86%); mp 221 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.50 (s, 3H, CH_3), 3.67, 3.68 (s, 3H, CH_3), 3.87, 3.89 (s, 2H, CH_2), 6.03, 6.04 (s, 1H, CH), 7.23 (dd, ^3J = 7.62 Hz, ^3J = 7.59 Hz, 1H, Ar), 7.49

(m, 1H, Ar), 7.94, 8.02 (dd, ^3J = 7.60 Hz, ^4J = 1.56 Hz, 1H, Ar), 10.59, 11.58 (s, 1H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 17.6 (CH_3), 37.7, 38.4 (CH_2), 52.0 (CH_3), 110.3 (CH), 122.7, 122.8 (Ar), 124.9, 126.1 (C), 132.6 (Ar), 138.8, 146.0 (C), 169.1, 169.6, 177.1 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3253 (w), 3172 (w), 3114 (w), 3068 (w), 2988 (w), 2950 (w), 1732 (s), 1628 (w), 1610 (m), 1599 (m), 1563 (s), 1519 (m, br), 1421 (s), 1344 (s), 1310 (m), 1248 (m, br), 1200 (s), 1168 (s), 1072 (m), 1006 (m), 989 (m), 899 (m, br), 848 (m), 804 (s), 751 (s). MS (EI, 70 eV) m/z = 231 (M^+, 100), 199 (14.4), 171 (72.4), 143 (76.3), 115 (9.9). HRMS (EI, 70 eV): calcd. for $C_{13}H_{13}NO_3$ (M^+) 231.08899, found 231.08879.

Methyl 2-(6-chloro-4-hydroxyquinolin-2-yl)acetate (8e). Starting with **7e** (0.230 g, 0.8 mmol), MeOH (3 mL) and Pd/C (10 mol%), **8e** was isolated as a yellow solid (0.070 g, 37%); mp 218 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.61 (s, 3H, CH_3), 3.90 (s, 2H, CH_2), 6.22 (s, 1H, CH), 7.62–7.90 (m, 2H, Ar), 8.04 (s, 1H, Ar), 12.34 (s, 1H, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 37.0 (CH_2), 52.2 (CH_3), 109.1 (CH), 118.0, 123.6 (Ar), 125.5, 128.6 (C), 131.9 (Ar), 138.7 (CCl), 146.5, 168.8 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3096 (w), 3011 (w), 2953 (w), 2849 (w), 1737 (m), 1594 (m, br), 1564 (m), 1528 (m), 1436 (m), 1341 (s), 1299 (m), 1251 (m, br), 1199 (m), 1170 (m), 1102 (m), 1009 (m), 933 (m), 886 (m), 818 (s), 756 (s). HRMS (ESI): calcd. for $C_{12}H_{11}ClNO_3$ ([M+H]$^+$) 252.0422, found 252.0422.

Methyl 2-(4-hydroxy-6-methylquinolin-2-yl)acetate (8f). Starting with **7f** (0.210 g, 0.8 mmol), MeOH (3 mL) and Pd/C (10 mol%), **8f** was isolated as a yellow solid (0.150 g, 86%); mp 172 °C. ^{1}H NMR (300 MHz, 298 K, DMSO-d_6): δ = 2.44 (s, 3H, 6-CH_3), 3.64 (s, 3H, OCH_3), 3.89 (s, 2H, CH_2), 6.25 (s, 1H, 3-H), 7.57 (dd, ^3J= 3.6 Hz, ^4J= 1.7 Hz, 1H, 7-H), 7.85 (d, ^3J= 8.6 Hz, 1H, 8-H), 7.91 (br, 1H, 5-H), 11.6 (very broad, OH/NH). ^{13}C NMR (75 MHz, 298 K, DMSO-d_6): δ = 20.7 (6-CH_3), 37.2 (CH_2), 52.0 (OCH_3), 108.0 (C3), 115.9 (C8), 123.7 (C5), 124.2 (C4a), 133.2 (C7), 133.8 (C6), 138.5 (C8a), 145.0 (C2), 169.0 (CO). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2953 (w), 2921 (w), 2850 (w), 1731 (m), 1591 (m, br), 1561 (m, br), 1434 (m), 1336 (s), 1249 (s, br), 1168 (s, br), 1009 (s, br), 818 (s), 760 (s). HRMS (ESI): calcd. for $C_{13}H_{14}NO_3$ ([M+H]$^+$) 232.09682, found 232.09677.

Methyl 2-(6-fluoro-4-hydroxyquinolin-2-yl)acetate (8g). Starting with **7g** (0.210 g, 0.8 mmol), MeOH (3 mL) and Pd/C (10 mol%), **8g** was isolated as a yellow solid (0.12 g, 68%); mp >310 °C. ^{1}H NMR (300 MHz, DMSO): δ = 3.63 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 6.23 (s, 1H, CH), 7.54–7.60 (m, 1H, Ar), 7.75 (dd, ^3J = 9.21 Hz, ^4J = 2.79 Hz, 1H, Ar), 7.95 (dd, ^3J = 9.27 Hz, ^3J = 9.27 Hz, 1H, Ar). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 37.1 (CH_2), 51.9 (CH_3), 108.0 (CH), 108.6 (d, ^2J = 22.7 Hz, Ar), 118.9 (d, ^3J = 8.5 Hz, Ar), 120.3 (d, ^2J = 26.4 Hz, Ar), 125.7 (d, ^3J = 8.4 Hz, C), 137.0 (C), 145.7 (CO), 158.4 (d, ^1J = 243.4 Hz, CF), 168.9 (CO).^{19}F NMR (282 MHz, DMSO-d_6): δ = –116.92 (CF). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3114 (w), 3081 (w), 2957 (w), 1733 (m), 1599 (m, br), 1561 (m), 1488 (m), 1467 (s), 1431 (s), 1339 (s), 1244 (s), 1202 (s), 1170 (s), 1004 (m), 939 (s), 923 (s), 880 (s), 825 (s), 764 (s). MS (EI, 70 eV) m/z = 235 (M^+, 76.3), 219 (100), 203 (35.2), 191 (30.7), 177 (71.1), 163 (28.9), 155 (26.7), 147 (93.5), 137 (47.4), 120 (33.6), 109 (27.9). HRMS (EI, 70 eV): calcd. for $C_{12}H_{10}FNO_3$ (M^+) 235.06392, found 235.06341.

7-(2′-Hydroxyphenyl)-5,7-dioxoheptanoic acid methyl ester (12). To a THF solution of LDA (44.0 mmol) was added **10** (2.72 g, 20.0 mmol) at –78 °C. After stirring for 1 h, **11** (3.20 g, 20.0 mmol) was dropwise added. The solution was allowed to slowly warm to 10 °C during 12 h. To the solution was added hydrochloric acid (20 mL, 10%) and the organic and the aqueous layer were separated. The latter was extracted with ether (5 × 40 mL). The combined organic layers were dried (sodium sulfate), filtered and the filtrate was concentrated in vacuo. The residue w purified by chromatography (silica gel, hexanes/EtOAc = 10 : 1 → 1 : 1) to give **12** (2.90 g, 56%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, enol): δ = 1.99–2.05 (m, 2 H, CH_2), 2.36 (m, 4 H, CH_2), 3.69 (s, 3 H, OCH_3), 6.18 (s, 1 H, Enol-CH), 6.85–7.01 (m, 2 H, Ar), 7.47 (m, 1 H, Ar), 7.65 (m, 1 H, Ar), 12.02 (s, 1 H, enol-OH), 14.97 (s, 1 H, Ar-OH). ^{13}C NMR (DEPT, $CDCl_3$, 75.5 MHz, enol): δ = 21.5 ($CH_2CH_2CH_2$), 33.0, 35.4 (CH_2), 51.6 (CH_3), 95.0 (enol-CH), 118.7, 119.0, 128.5 (ArCH), 130.7 (C), 135.8 (ArCH), 162.5, 173.3, 184.7, 195.6 (C). IR (neat, cm^{-1}): $\tilde{\nu}$ = 3422 (m), 2953 (m), 1736 (s), 1693 (s), 1610 (s), 1579 (s), 1488 (s), 1440 (s), 1367 (m), 1301 (s), 1213 (s), 1157 (s), 1114 (m), 1029 (m), 895 (m), 815 (w), 762 (m). UV-VIS (CH_3CN, nm): λ_{max} (log ε): 314 (3.83), 251 (3.94), 212 (4.37). MS (EI, 70 eV): m/z (%) = 264 (M^+, 21), 233 ([M–OCH_3]$^+$, 12), 163 ([M–$C_5H_9O_2$]$^+$, 98), 121 ([M–$C_7H_{11}O_3$]$^+$, 100), 101 (21). HRMS (FT-ICR): calcd. for $C_{14}H_{17}O_5$ ([M+1]$^+$): 265.10705; found: 265.10738.

4-(Chromon-2′-yl)butanoic acid methyl ester (13). To a CH_2Cl_2 solution (30 mL) of **12** (630 mg, 2.4 mmol) was slowly added BBr_3 (2.390 g, 10.0 mmol) at 0 °C. The temperature was allowed to slowly rise to 20 °C during 12 h with stirring. Hydrochloric acid (5%) was added and the organic and aqueous layers were separated. The latter was extracted with CH_2Cl_2 (4 × 10 mL). The combined organic layers were dried (sodium sulfate), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, hexanes/EtOAc = 5 : 1 → 1 : 3) to give **13** (398 mg, 68%) as a yellow solid and recovered starting material **12** (89 mg, 14%); mp 121 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (m, 2 H, $CH_2CH_2CH_2$), 2.45 (t, ^3J = 7.3 Hz, 2 H, CH_2C=CH), 2.70 (t, ^3J = 7.4 Hz, 2 H, CH_2COOCH_3), 3.69 (s, 3 H, OCH_3), 6.19 (s, 1 H, CH), 7.36 - 7.44 (m, 2 H, Ar), 7.65 (m, 1 H, Ar), 8.17 (d, 3J = 8.1 Hz, ^4J = 1.7 Hz, 1 H, Ar). ^{13}C NMR (DEPT, 75.5 MHz, $CDCl_3$): δ = 21.9 ($CH_2CH_2CH_2$), 32.8, 33.4 (CH_2), 51.6 (OCH_3), 110.1 (CH), 117.8 (ArCH), 123.6 (C), 124.9, 125.6, 133.5 (ArCH), 156.4, 168.3 (C), 173.0 (C=O, ester), 178.1 (C=O, ketone). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3446 (m), 2952 (m), 1738 (s), 1654 (s), 1609 (s), 1574 (m), 1464 (s), 1434 (m), 1386 (s), 1342 (s), 1251 (m), 1214 (s), 1204 (s), 1155 (m), 1119 (w), 963 (m), 840 (w), 784 (m), 759 (m). UV-VIS (CH_3CN, nm): λ_{max} (log ε): 302 (3.76), 292 (3.76), 260 (3.72), 251 (3.76), 227 (3.94). MS (EI, 70 eV): m/z (%) = 246 (M^+, 18), 215 (12), 187 (5), 173 (10), 160 (5), 121 (15), 92 (11), 55 (15). Anal. calcd. for $C_{14}H_{14}O_4$ (246): C 68.28 H 5.73. Found: C 67.95, H 5.72.

Computed energetic data. (a) B3LYP/6–311+G** (full optimization) total energies (au): **A** (–783.88149); **B** (–783.88433); **C** (–783.88264); **D** (–783.88929). (b) B3LYP/6–311+G** Gibbs energies (au, corrected at 298 K): **A** (–783.68893); **B** (–783.69008); **C** (–783.68974); **D** (–783.69575). (c) MP2/6–311+G**//B3LYP/6–311+G** total energies (au): **A** (–781.69276); **B** (–781.68249); **C** (–781.68281); **D** (–781.69350). (d) B3LYP-IPCM/6–311+G**//

B3LYP/6–311+G** total energies (au): **A** (–783.90064); **B** (–783.90008); **C** (–783.90043); **D** (–783.90874). (e) MP2-IPCM/6–311+G**//B3LYP/6–311+G** total energies (au): **A** (–781.71039); **B** (–781.69618); **C** (–781.69634); **D** (–781.70942).

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