Organocatalyzed Reactions Involving 3-Formylchromones and Acetylenedicarboxylates: Efficient Synthesis of Functionalized Benzophenones and Polysubstituted Xanthones

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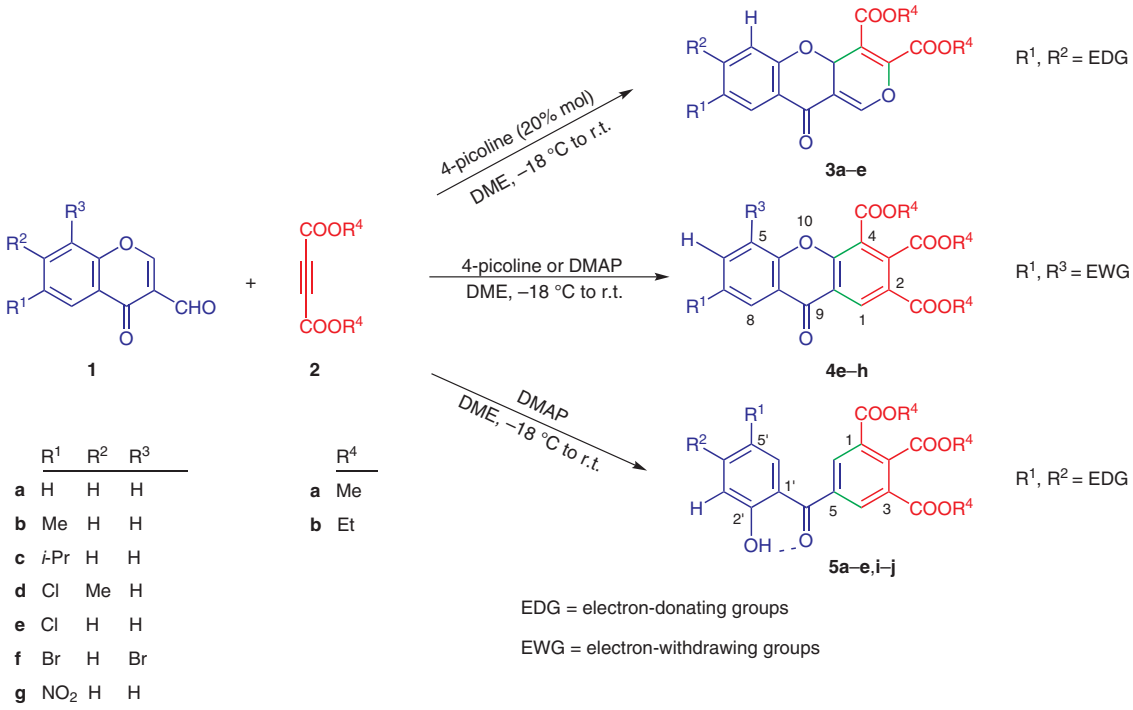
Abstract: Organocatalyzed reactions between chromones and acetylenedicarboxylates leading either to xanthone derivatives or to functionalized benzophenones are described. The outcome of the reactions was found to depend both on the nature of the chromone substituents and on the basicity of the organocatalyst.

Key words: DMAP, hetero-Diels–Alder reactions, Friedel–Crafts reactions, organocatalysis, xanthones, zwitterions

One of the rapidly growing areas of research in the field of organic synthesis is that of catalytic transformations utilizing small organic molecules called organocatalysts.[1] Although, for a long time, organocatalysis was not viewed as a viable alternative to the two main classes of established catalysts (transition-metal complexes and enzymes) a report, which appeared in 2000, completely changed this perception and highlighted the fascinating attributes of small organic molecules as catalysts.[2] Recently, the possibility of carbon–carbon bond formation by intermolecular trapping of 1,4-zwitterionic intermediates generated from pyridine, acting as an organocatalyst, and acetylenedicarboxylates with aldehydes, and also with carbonyl compounds more generally, was studied.[3] An analogous 4-dimethylaminopyridine (DMAP)-catalyzed reaction between dimethyl acetylenedicarboxylates (DMAD) and β-ketoesters has also been reported.[4]

In a continuation of the above mentioned literature reports, a hetero-Diels–Alder type reaction between formylchromones and acetylenedicarboxylates was studied,[5,6] whereupon, by using 4-picoline as organocatalyst, an efficient one-pot approach to a new class of pyrano[4,3-*c*]chromenes **3** was possible (Scheme 1). In the course of further studies on chromone organocatalytic reactions involving zwitterionic intermediates, in the present study



1

	R1	R2	R3
a	H	H	H
b	Me	H	H
c	*i*-Pr	H	H
d	Cl	Me	H
e	Cl	H	H
f	Br	H	Br
g	NO_2	H	H

2

	R4
a	Me
b	Et

Scheme 1 Reaction of substituted 3-formylchromones **1** with acetylenedicarboxylates **2** in the presence of 4-picoline or DMAP as organocatalysts

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we extended our investigation by introducing strong electron-withdrawing substituents into the chromone moiety, and found that, by using the same organocatalyst, 4-picoline, the reaction followed a completely different pathway leading to formation of xanthone derivatives **4** in good yields. The same xanthone derivatives **4** were also isolated when DMAP was used as organocatalyst. In contrast, the use of DMAP with chromones bearing electron-donating substituents led to formation of functionalized benzophenones **5** instead of either pyrano[4,3-*c*]chromenes **3** or xanthones **4**.

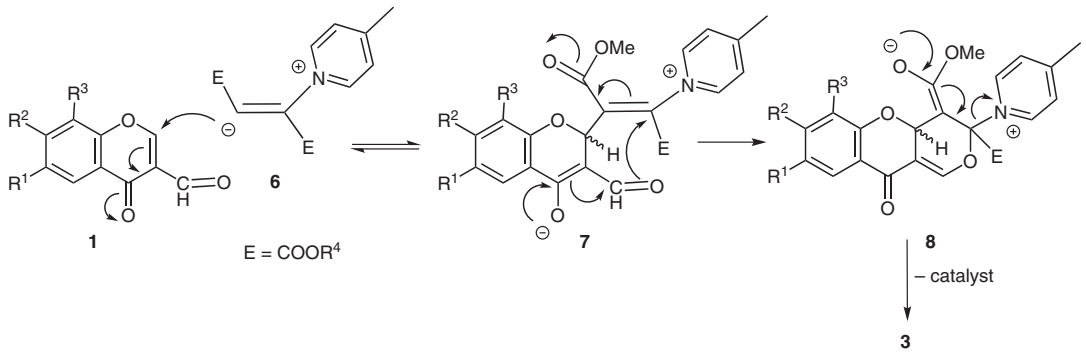
Functionalized benzophenones are of considerable interest as pharmacologically relevant natural products and natural product analogues, and they represent versatile synthetic building blocks.[7] Since classical synthesis through Friedel–Crafts acylation frequently leads to unsatisfactory results,[8] benzophenone syntheses rely on the reaction of organometallic reagents with aldehydes and subsequent oxidation.[9] More recently, some functionalized benzophenones were also prepared by domino 'Michael–retro-Michael–aldol' reactions.[10] On the other hand, xanthones are a class of natural products that have been shown to possess a wide range of pharmacological properties,[11] and it has been shown that electron-withdrawing substituents enhance the antimycobacterial activity of these compounds.[12]

Against this literature background, in the present study we wish to report our results in detail. Initially, as a continuation of our previous study,[6] the 6,8-dibromochromone **1f** (1.0 mmol) was allowed to react with DMAD (**2a**; 1.2 mmol) in 1,2-dimethoxyethane (DME; 10 mL) at –18 °C by using 4-picoline (1.0 mmol) as catalyst (Scheme 1). The reaction mixture was allowed to warm to room temperature and then stirred further for 12 hours, whereupon xanthone **4f** was isolated as the only reaction product in 64% yield. When less catalyst (0.2 mmol) was used, the reaction proceeded analogously, although much longer reaction times (7 days) were required to complete the reaction. By increasing the molar ratio of DMAD (2.2 mmol) the product yield was decreased and the reaction became turbid due to formation of substantial amounts of polymeric material. The reaction of 6-nitrochromone (**1g**) with acetylenedicarboxylates **2a** and **2b** proceeded in the same manner and resulted in the formation of the corresponding xanthones **4g** and **4h** (Table 1, entries 2 and 3). The reaction was then investigated by changing the catalyst to DMAP, whereupon chromones **1f** and **1g** reacted analogously to furnish the same xanthones **4f–h**, respectively, as summarized in Table 1 (entries 4–6). In contrast, when 6-chlorochromone (**1e**) was used, the xanthone derivative **4e** (9% yield) was formed as the minor product together with a second product that was isolated and identified as the benzophenone tricarboxylate **5e** (56% yield; Table 1, entry 11).

Table 1 Effect of the Substituents and Organocatalyst on the Reaction of 3-Formylchromones **1** and Acetylenedicarboxylates **2**

Entry	R^1	R^2	R^3	R^4	Catalyst	Product (%)
1	Br	H	Br	Me	4-picoline	**4f** (64)
2	NO_2	H	H	Me	4-picoline	**4g** (59)
3	NO_2	H	H	Et	4-picoline	**4h** (61)
4	Br	H	Br	Me	DMAP	**4f** (58)
5	NO_2	H	H	Me	DMAP	**4g** (53)
6	NO_2	H	H	Et	DMAP	**4h** (55)
7	H	H	H	Me	DMAP	**5a** (62)
8	Me	H	H	Me	DMAP	**5b** (61)
9	*i*-Pr	H	H	Me	DMAP	**5c** (59)
10	Cl	Me	H	Me	DMAP	**5d** (63)
11	Cl	H	H	Me	DMAP	**4e** (9) **5e** (56)
12	H	H	H	Et	DMAP	**5i** (63)
13	Me	H	H	Et	DMAP	**5j** (57)

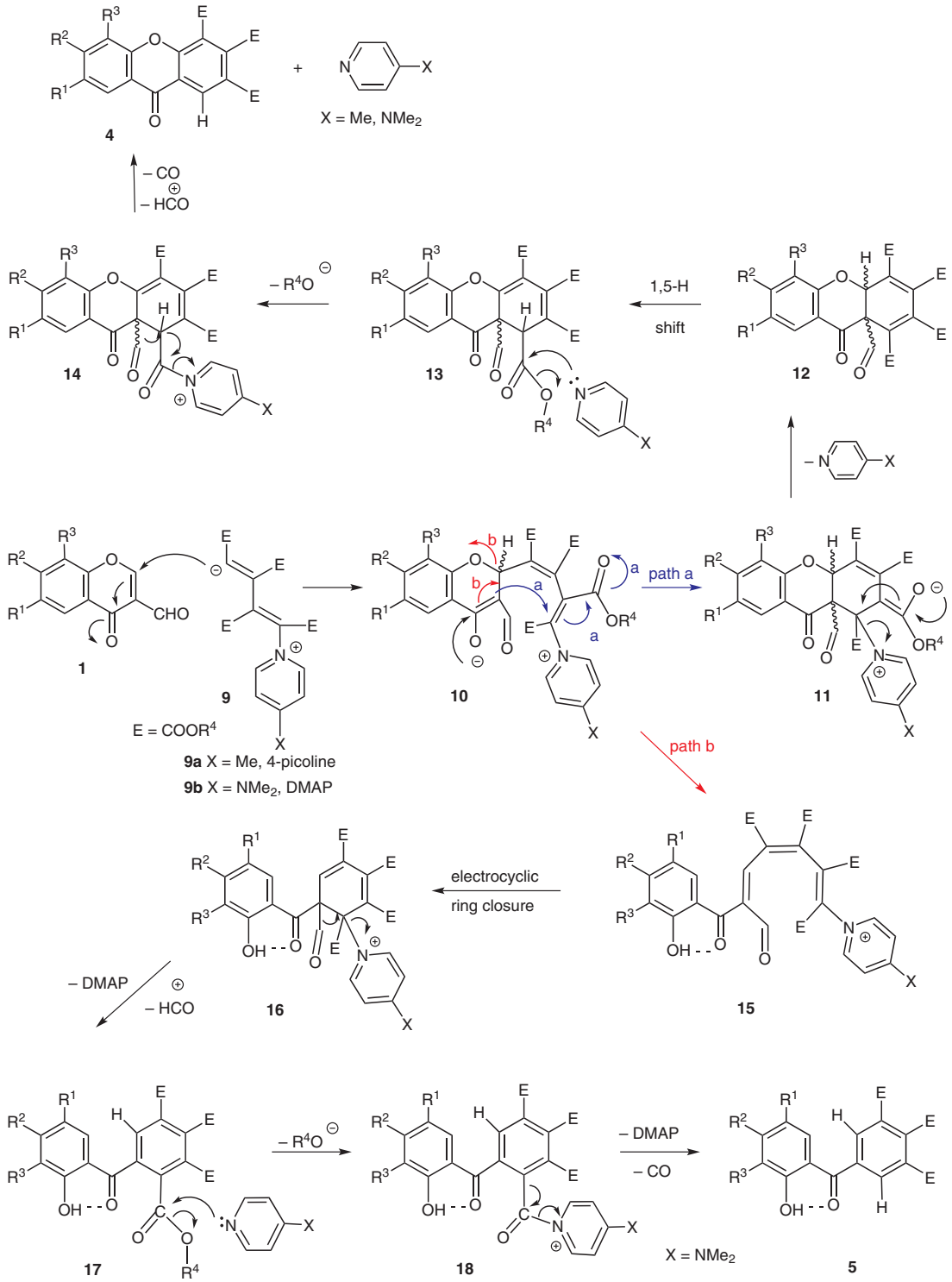
Functionalized benzophenones **5** were also formed in good yield (Table 1, entries 7–10, 12 and 13) with all chromones bearing electron-donating substituents in the chromone moiety. It is noteworthy that, as was previously reported,[6] the use of 4-picoline with all 'electron-rich' chromones resulted in the hetero-Diels–Alder cycloaddition products **3**. As a result, product formation proved to be greatly affected not only by the organocatalyst but also by the nature of the chromone substituents. However,



Scheme 2 Plausible mechanism for the reaction of substituted 3-formylchromones **1** with zwitterions **6**, formed from reaction of acetylenedicarboxylates **2** with 4-picoline, to afford compounds **3**

when the reaction with 'electron-rich' chromones was repeated with slow, dropwise addition of DMAD over two hours, small amounts of pyranochromenes **3** (approximately 5%) were also detected.

Mechanistically, the reaction may be rationalized as involving initial attack of the zwitterion **6**, generated from 4-picoline and acetylenedicarboxylate, on the C2 chromone carbon of **1** to give the intermediate **7**, which, after ring closure to form **8**, yields compound **3** by regeneration of the catalyst (R^1, R^2 = electron-donating; Scheme 2). However, when R^1 and R^3 are electron-withdrawing, the ring closure to **3** becomes difficult because the negative charge on the formyl oxygen is substantially reduced. In this case, zwitterion **6** preferentially reacts with a second molecule of acetylenic ester **2** to yield zwitterion **9** which, again, most probably, attacks the C2 chromone carbon to furnish intermediate **10**. Depending



Scheme 3 Plausible mechanism for the reaction of substituted 3-formylchromones **1** with zwitterions **9** to afford compounds **4** or **5**

on the nature of the chromone substituents, intermediate **10** can follow two different reaction paths, as shown in Scheme 3. When R^1 and R^2 are electron-withdrawing, it is likely that intermediate **10** reacts further by Path a; thus, after ring closure to **11** and elimination of the catalyst, intermediate **12** is generated, which, by 1,5-H shift, gives **13**. By attack of the catalyst on the ester carbon[13] at the 1-position of **13**, finally the xanthone derivatives **4** are obtained. However, when R^1 and R^2 are electron-donating and the organocatalyst is DMAP, Path b is followed leading to intermediate **15** through pyran ring opening. Subsequent electrocyclic ring closure to **16** generates the functionalized benzophenone derivatives **5**, as depicted in Scheme 3.

The assigned molecular structures of all new compounds **4** and **5** are based on rigorous spectroscopic analysis, including IR, NMR (^{1}H, ^{13}C, DEPT, COSY, NOESY, HETCOR and COLOC), MS and elemental analysis data.

Regarding the structure of the xanthones **4**, as a representative example the assignment of **4h** is described. In the ^{1}H NMR spectrum, the presence and position of the three chromone aromatic protons was unequivocally identified from their splitting pattern and COLOC correlations (Figure 1). The presence of one more aromatic proton resonating at δ = 8.99 ppm with its carbon at δ = 131.3 ppm and of only three ester ethyl groups were also identified. This proton gave characteristic COLOC correlations with one of the three ester carbonyl carbons at δ = 163.9 ppm, with the chromone carbonyl carbon at δ = 174.1 ppm (the corresponding carbonyl carbon in **1g** resonates at δ = 174.5 ppm) and also with the quaternary carbons at δ = 154.5 (C4a) and 140.4 ppm (C3); thus, the whole molecular carbon connectivity was assigned (Figure 1).

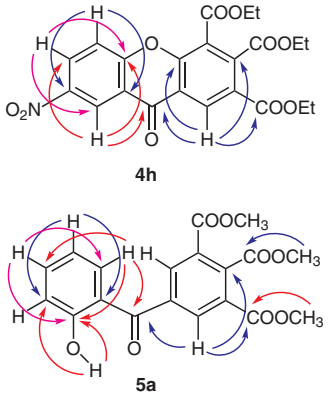


Figure 1 Diagnostic COLOC correlations between protons and carbons (via $^2J_{C-H}$ and $^3J_{C-H}$) in compounds **4h** and **5a**

Regarding the structure of the polysubstituted benzophenones, the assignment of **5a** is described. The assignment of the four aromatic protons of the hydroxybenzoyl moiety was clear from the splitting patterns, with protons resonating as a doublet at δ = 7.12 ppm, as a doublet of doublets at δ = 7.58 ppm, as a doublet of doublets at δ = 6.93 ppm and as a doublet at δ = 7.44 ppm, and their carbons resonating at δ = 118.9, 137.3, 119.3 and 132.9 ppm, respectively. Moreover, a hydroxyl proton appears in the ^{1}H NMR spectrum as a singlet at δ = 11.74 ppm that correlates with the quaternary carbons at δ = 118.5 (C3′) and 163.4 ppm (C2′). In addition, the proton at δ = 7.44 ppm shows COLOC correlations with the carbonyl carbon at δ = 198.7 ppm, and also with C2′ and C4′. In addition to the hydroxybenzoyl moiety, the presence of a symmetrically substituted aromatic ring was established as follows. A two-proton singlet appears at δ = 8.50 ppm with its carbon at δ = 134.3 ppm (C4 and C6) showing COLOC correlations with the hydroxybenzoyl carbonyl carbon at δ = 198.7 ppm, the two identical ester carbonyl carbons at δ = 164.3 ppm and also to C2 (δ = 139.3 ppm) bearing the third carbomethoxy group.

In conclusion, a new and efficient protocol for the organocatalytic one-pot synthesis of the otherwise almost inaccessible, functionalized benzophenones and polysubstituted xanthones has been described; their formation depends on the chromone substitution pattern and on the basicity of the catalyst. The isolated products could possess valuable biological activities. The experimental simplicity and metal-free conditions of the synthesis are especially noteworthy.

Melting points were measured with a Kofler hot-stage apparatus and are uncorrected. Petroleum ether (PE) refers to the fraction boiling between 60–80 °C. Column chromatography was carried out using Merck silica gel. TLC was performed using precoated silica gel glass plates (0.25 mm) containing fluorescent indicator UV_{254} purchased from Macherey–Nagel (PE–EtOAc, 3:1). NMR spectra were recorded at r.t. with Bruker AM 300 or AVANCE 300 spectrometers operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C, respectively, using $CDCl_3$ as solvent. Chemical shifts (ppm) are expressed in δ values relative to TMS as internal standard for ^{1}H and relative to TMS (δ = 0.00 ppm) or to $CDCl_3$ (δ = 77.05 ppm) for ^{13}C NMR spectra. Coupling constants (^nJ) are reported in Hz. Second order ^{1}H NMR spectra were analyzed by simulation.[14] IR spectra were recorded with a Perkin–Elmer 1600 series FTIR spectrometer and are reported in wavenumbers (cm^{-1}). LC-MS (ESI, 1.65 eV) spectra were recorded with an LCMS-2010 EV system (Shimadzu). Elemental analyses were performed with a Perkin–Elmer 2400-II CHN analyzer.

Reaction of Substituted 3-Formylchromones 1 with Acetylenedicarboxylates 2 Catalyzed by 4-Picoline or DMAP; Typical Procedure

DMAD (**2a**; 0.170 g, 1.2 mmol) was added to a stirred solution of 3-formylchromone (**1a**; 0.174 g, 1 mmol) and DMAP (0.025 g, 1.0 mmol) in dimethoxyethane (10 mL) at –18 °C. The system was allowed to come to r.t. (~25 °C) and then stirred for 12 h. Distillation of the solvent in vacuo was followed by column chromatography on silica gel (PE–EtOAc, 5:1→3:1) to give either 9-oxo-9*H*-xanthene-2,3,4-tricarboxylates (**4e–h**) or 2-hydroxybenzoylbenzene-1,2,3-tricarboxylates (**5a–e**, **5i** and **5j**).

In all cases some unreacted chromone was also isolated. The yields were calculated on the basis of acetylene dicarboxylate. In the case of chromones **1f** and **1g** the reaction also proceeded analogously with 4-picoline leading to formation of xanthones **4**.

Trimethyl 5-(2-Hydroxybenzoyl)benzene-1,2,3-tricarboxylate (5a)

Yield: 0.139 g (62%); yellow crystals; mp 141–143 °C.

IR (KBr): 1752 (C=O), 1735 (C=O), 1696 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.95 (s, 6 H, 1-$COOCH_3$, 3-$COOCH_3$), 4.05 (s, 3 H, 2-$COOCH_3$), 6.93 (ddd, *J* = 8.1, 7.2, 1.0 Hz, 1 H, H-5′), 7.11 (dd, *J* = 8.4, 1.0 Hz, 1 H, H-3′), 7.44 (dd, *J* = 8.1, 1.5 Hz, 1 H, H-6′), 7.58 (ddd, *J* = 8.4, 7.2, 1.5 Hz, 1 H, H-4′), 8.50 (s, 2 H, H-4, H-6), 11.73 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 53.1 (1-OCH_3, 2-OCH_3, 3-OCH_3), 118.5 (C1′), 118.9 (C3′), 119.3 (C5′), 129.0 (C5), 132.9 (C6′), 134.3 (C4, C6), 137.3 (C4′), 138.7 (C1, C3), 139.3 (C2), 163.4 (C2′), 164.3 (1-CO, 3-CO), 167.9 (2-CO), 198.7 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 427 (95) [M^+ + Na + MeOH], 395 (100) [M^+ + Na].

Anal. Calcd for $C_{19}H_{16}O_8$: C, 61.29; H, 4.33. Found: C, 61.16; H, 4.28.

Trimethyl 5-(2-Hydroxy-5-methylbenzoyl)benzene-1,2,3-tricarboxylate (5b)

Yield: 0.161 g (61%); yellow crystals; mp 127–129 °C.

IR (KBr): 1743 (C=O), 1738 (C=O), 1635 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.26 (s, 3 H, 5′-CH_3), 3.95 (s, 6 H, 1-$COOCH_3$, 3-$COOCH_3$), 4.05 (s, 3 H, 2-$COOCH_3$), 7.02 (d, *J* = 8.5 Hz, 1 H, H-3′), 7.17 (d, *J* = 2.1 Hz, 1 H, H-6′), 7.39 (dd, *J* = 8.5, 2.1 Hz, 1 H, H-4′), 8.48 (s, 2 H, H-4, H-6), 11.55 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 20.4 (5′-CH_3), 53.1 (1-OCH_3, 2-OCH_3, 3-OCH_3), 118.2 (C1′), 118.6 (C3′), 128.5 (C5′), 128.9 (C5), 132.5 (C6′), 134.2 (C4, C6), 138.5 (C4′), 138.9 (C1, C3), 139.0 (C2), 161.4 (C2′), 164.3 (1-CO, 3-CO), 168.0 (2-CO), 198.6 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 441 (95) [M^+ + Na + MeOH], 409 (100) [M^+ + Na].

Anal. Calcd for $C_{20}H_{18}O_8$: C, 62.17; H, 4.70. Found: C, 62.05; H, 4.78.

Trimethyl 5-(2-Hydroxy-5-isopropylbenzoyl)benzene-1,2,3-tricarboxylate (5c)

Yield: 0.147 g (59%); yellow crystals; mp 61–63 °C.

IR (KBr): 1752 (C=O), 1735 (C=O), 1696 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.19 [d, *J* = 8.5 Hz, 6 H, 5′-$CH(CH_3)_2$], 2.84 [sept, *J* = 8.5 Hz, 1 H, 5′-$CH(CH_3)_2$], 3.97 (s, 6 H, 1-OCH_3, 3-OCH_3), 4.06 (s, 3 H, 2-OCH_3), 7.05 (d, *J* = 8.6 Hz, 1 H, H-3′), 7.29 (d, *J* = 2.5 Hz, 1 H, H-6′), 7.46 (dd, *J* = 8.6, 2.5 Hz, 1 H, H-4′), 8.56 (s, 2 H, H-4, H-6), 11.53 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 20.4 [5′-$CH(CH_3)_2$], 33.1 [5′-$CH(CH_3)_2$], 52.9 (1-OCH_3, 3-OCH_3), 53.0 (2-OCH_3), 118.2 (C1′), 118.6 (C3′), 128.5 (C5′), 128.9 (C5), 132.5 (C6′), 134.2 (C4, C6), 138.0 (C1, C3), 139.0 (C4′), 139.0 (C2), 161.5 (C2′), 164.2 (1-CO, 3-CO), 167.8 (2-CO), 198.2 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 437 (100) [M^+ + Na].

Anal. Calcd for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.88; H, 5.46.

Trimethyl 5-(2-Hydroxy-4-methyl-5-chlorobenzoyl)benzene-1,2,3-tricarboxylate (5d)

Yield: 0.159 g (63%); yellow crystals; mp 156–158 °C.

IR (KBr): 1751 (C=O), 1736 (C=O), 1697 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.42 (s, 3 H, 4′-CH_3), 3.97 (s, 6 H, 1-OCH_3, 3-OCH_3), 4.05 (s, 3 H, 2-OCH_3), 7.00 (s, 1 H, H-3′), 7.36 (s, 1 H, H-6′), 8.47 (s, 2 H, H-4, H-6), 11.60 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 21.0 (4′-CH_3), 53.2 (1-OCH_3, 2-OCH_3, 3-OCH_3), 117.4 (C1′), 120.8 (C3′), 124.8 (C5′), 129.2 (C5), 132.1 (C6′), 134.1 (C4, C6), 138.3 (C1, C3), 147.0 (C4′), 139.4 (C2), 161.8 (C2′), 164.1 (1-CO, 3-CO), 168.0 (2-CO), 197.4 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 443/445 (100) [M^+ + Na].

Anal. Calcd for $C_{20}H_{17}ClO_8$: C, 57.09; H, 4.07. Found: C, 57.16; H, 4.20.

Trimethyl 7-Chloro-9-oxo-9*H*-xanthene-2,3,4-tricarboxylate (4e)

Yield: 0.022 g (9%); yellowish crystals; mp 167–169 °C.

IR (KBr): 1743 (C=O), 1728 (C=O), 1671 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.96 (s, 3 H, 2-OCH_3), 3.97 (s, 3 H, 4-OCH_3), 4.02 (s, 3 H, 3-OCH_3), 7.50 (d, *J* = 9.0 Hz, 1 H, H-5), 7.73 (dd, *J* = 9.0, 2.7 Hz, 1 H, H-6), 8.29 (d, *J* = 2.7 Hz, 1 H, H-8), 8.99 (s, 1 H, H-1).

^{13}C NMR ($CDCl_3$): δ = 53.1 (3-OCH_3), 53.4 (2-OCH_3, 4-OCH_3), 120.2 (C5), 121.8 (C4), 122.3 (C2), 123.0 (C8a), 124.8 (C9a), 126.2 (C8), 131.4 (C7), 131.9 (C1), 135.9 (C6), 139.9 (C3), 154.2 (C10a), 154.8 (C4a), 163.7 (4-CO), 164.4 (2-CO), 166.5 (3-CO), 174.3 (C9).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 443/445 (60) [M^+ + K], 319 (60), 274/276 (100).

Anal. Calcd for $C_{19}H_{13}ClO_8$: C, 56.38; H, 3.24. Found: C, 56.16; H, 3.28.

Trimethyl 5-(2-Hydroxy-5-chlorobenzoyl)benzene-1,2,3-tricarboxylate (5e)

Yield: 0.136 g (56%); yellow crystals; mp 183–185 °C.

IR (KBr): 1745 (C=O), 1739 (C=O), 1686 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.96 (s, 6 H, 1-OCH_3, 3-OCH_3), 4.05 (s, 3 H, 2-OCH_3), 7.03 (d, *J* = 9.0 Hz, 1 H, H-3′), 7.51 (dd, *J* = 9.0, 2.4 Hz, 1 H, H-4′), 7.65 (s, 2 H, H-4, H-6), 8.30 (d, *J* = 2.4 Hz, 1 H, H-6′), 11.58 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 53.0 (1-OCH_3, 3-OCH_3), 53.1 (2-OCH_3), 119.2 (C1′), 120.6 (C3′), 124.1 (C6′), 128.5 (C5′), 129.4 (C5), 134.1 (C4, C6), 137.2 (C4′), 138.1 (C1, C3), 139.5 (C2), 161.9 (C2′), 164.1 (1-CO, 3-CO), 167.6 (2-CO), 197.8 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 406/408 (100) [M^+].

Anal. Calcd for $C_{19}H_{15}ClO_8$: C, 56.10; H, 3.72. Found: C, 55.96; H, 3.62.

Trimethyl 5,7-Dibromo-9-oxo-9*H*-xanthene-2,3,4-tricarboxylate (4f)

a) 4-Picoline as catalyst.

Yield: 0.203 g (64%); yellowish crystals; mp 211–213 °C.

IR (Nujol): 1753 (C=O), 1730 (C=O), 1665 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.97 (s, 3 H, 2-OCH_3),* 3.99 (s, 3 H, 4-OCH_3),* 4.07 (s, 3 H, 3-OCH_3), 8.15 (d, *J* = 2.5 Hz, 1 H, H-6), 8.41 (d, *J* = 2.5 Hz, 1 H, H-8), 9.00 (s, 1 H, H-1). *The assignments may be interchanged.

^{13}C NMR ($CDCl_3$): δ = 53.1 (OCH_3), 53.4 (OCH_3), 53.6 (OCH_3), 113.2 (C5), 118.5 (C8a), 121.4 (C7), 123.4 (C4), 123.5 (C2), 125.3 (C9a), 128.8 (C8), 131.9 (C1), 140.5 (C3), 141.4 (C6), 151.6 (C4a), 154.6 (C10a), 163.8 (4-CO), 164.3 (2-CO), 167.8 (3-CO), 173.8 (C9).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 581/583/585 (60) [M^+ + Na + MeOH], 565/567/569 (100) [M^+ + K], 549/551/553 (50) [M^+ + Na].

Anal. Calcd for $C_{19}H_{12}Br_2O_8$: C, 43.21; H, 2.29. Found: C, 43.11; H, 2.28.

b) DMAP as catalyst.

Yield: 0.184 g (58%).

Trimethyl 7-Nitro-9-oxo-9*H*-xanthene-2,3,4-tricarboxylate (4g)
a) 4-Picoline as catalyst.

Yield: 0.166 g (59%); yellow crystals; mp 181–183 °C.

IR (KBr): 1748 (C=O), 1740 (C=O), 1732 (C=O), 1688 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.98 (s, 6 H, 2-OCH_3, 4-OCH_3), 4.04 (s, 3 H, 3-OCH_3), 7.71 (d, *J* = 9.1 Hz, 1 H, H-5), 8.62 (dd, *J* = 9.1, 2.7 Hz, 1 H, H-6), 9.02 (d, *J* = 2.7 Hz, 1 H, H-8), 9.02 (s, 1 H, H-1).

^{13}C NMR ($CDCl_3$): δ = 53.2 (3-OCH_3), 53.5 (2-OCH_3, 4-OCH_3), 120.3 (C5), 121.5 (C4),* 121.7 (C2),* 123.2 (C8a), 123.5 (C8), 125.7 (C9a), 130.0 (C6), 131.9 (C1), 140.6 (C3), 144.8 (C7), 154.6 (C4a), 158.6 (C10a), 163.3 (4-CO), 164.2 (2-CO), 166.2 (3-CO), 174.0 (C9). *The assignments may be interchanged.

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 470 (40) [M^+ + MeOH + Na], 448 (15) [M^+ + H + MeOH], 416 (60) [M^+ + H], 386 (95), 371 (50), 328 (100).

Anal. Calcd for $C_{19}H_{13}NO_{10}$: C, 54.95; H, 3.16; N, 3.37. Found: C, 55.06; H, 3.28; N 3.46.

b) DMAP as catalyst.

Yield: 0.149 g (53%).

Triethyl 7-Nitro-9-oxo-9*H*-xanthene-2,3,4-tricarboxylate (4h)
a) 4-Picoline as catalyst.

Yield: 0.167 g (61%); yellowish crystals; mp 159–161 °C.

IR (Nujol): 1752 (C=O), 1735 (C=O), 1696 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.40 (t, *J* = 7.3 Hz, 3 H, 2-OCH_2CH_3), 1.44 (t, *J* = 7.3 Hz, 3 H, 4-OCH_2CH_3), 1.47 (t, *J* = 7.1 Hz, 3 H, 3-OCH_2CH_3), 4.43 (q, *J* = 7.1 Hz, 2 H, 3-OCH_2CH_3), 4.44 (q, *J* = 7.3 Hz, 2 H, 2-OCH_2CH_3), 4.52 (q, *J* = 7.3 Hz, 2 H, 4-OCH_2CH_3), 7.69 (d, *J* = 9.3 Hz, 1 H, H-5), 8.62 (dd, *J* = 9.3, 2.7 Hz, 1 H, H-6), 8.97 (s, 1 H, H-1), 9.19 (d, *J* = 2.7 Hz, 1 H, H-8).

^{13}C NMR ($CDCl_3$): δ = 13.9 (OCH_2CH_3), 14.2 (OCH_2CH_3), 14.2 (OCH_2CH_3), 62.4 (OCH_2CH_3), 62.7 (OCH_2CH_3), 62.8 (OCH_2CH_3), 120.2 (C5), 121.5 (C4),* 121.6 (C2),* 123.5 (C8), 123.6 (C8a), 126.3 (C9a), 129.9 (C6), 131.3 (C1), 140.4 (C3), 144.7 (C7), 154.4 (C4a), 158.6 (C10a), 163.0 (4-CO), 163.9 (2-CO), 165.6 (3-CO), 174.1 (C9). *The assignments may be interchanged.

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 457 (100) [M^+].

Anal. Calcd for $C_{22}H_{19}NO_{10}$: C, 57.77; H, 4.19; N, 3.06. Found: C, 57.86; H, 4.28; N 3.00.

b) DMAP as catalyst.

Yield: 0.151 g (55%).

Triethyl 5-(2-Hydroxybenzoyl)benzene-1,2,3-tricarboxylate (5i)
Yield: 0.177 g (63%); yellowish crystals; mp 84–86 °C.

IR (KBr): 1739 (C=O), 1696 (C=O), 1638 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.39 (t, *J* = 7.2 Hz, 6 H, 1-OCH_2CH_3, 3-OCH_2CH_3), 1.43 (t, *J* = 7.1 Hz, 3 H, 2-OCH_2CH_3), 4.40 (q, *J* = 7.2 Hz, 4 H, 1-OCH_2CH_3, 3-OCH_2CH_3), 4.50 (q, *J* = 7.1 Hz, 2 H, 2-OCH_2CH_3), 6.92 (ddd, *J* = 8.1, 7.3, 1.5 Hz, 1 H, H-5′), 7.12 (dd, *J* = 8.4, 0.8 Hz, 1 H, H-3′), 7.44 (dd, *J* = 8.1, 1.5 Hz, 1 H, H-6′), 7.57 (ddd, *J* = 8.4, 7.3, 1.5 Hz, 1 H, H-4′), 8.46 (s, 2 H, H-4, H-6), 11.78 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 13.9 (2-OCH_2CH_3), 14.1 (1-OCH_2CH_3, 3-OCH_2CH_3), 62.2 (2-OCH_2CH_3), 62.3 (1-OCH_2CH_3, 3-OCH_2CH_3), 118.6 (C1′), 118.9 (C3′), 119.3 (C5′), 129.6 (C5), 133.0 (C6′), 134.1 (C4, C6), 137.3 (C4′), 138.5 (C1, C3), 139.2 (C2), 163.5 (C2′), 164.0 (1-CO, 3-CO), 167.4 (2-CO), 198.9 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 469 (60) [M^+ + Na + MeOH], 437 (80) [M^+ + Na], 281 (100).

Anal. Calcd for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.66; H, 5.28.

Triethyl 5-(2-Hydroxy-5-methylbenzoyl)benzene-1,2,3-tricarboxylate (5j)
Yield: 0.165 g (57%); yellow crystals; mp 129–131 °C.

IR (KBr): 3434 (br, OH), 1747 (C=O), 1729 (C=O), 1712 (C=O), 1633 (C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.39 (t, *J* = 7.2 Hz, 6 H, 1-OCH_2CH_3, 3-OCH_2CH_3), 1.43 (t, *J* = 6.9 Hz, 3 H, 2-OCH_2CH_3), 2.26 (s, 3 H, 5′-CH_3), 4.41 (q, *J* = 7.2 Hz, 4 H, 1-OCH_2CH_3, 3-OCH_2CH_3), 4.51 (q, *J* = 6.9 Hz, 2 H, 2-OCH_2CH_3), 7.02 (d, *J* = 8.4 Hz, 1 H, H-3′), 7.19 (d, *J* = 2.1 Hz, 1 H, H-6′), 7.39 (dd, *J* = 8.4, 2.1 Hz, 1 H, H-4′), 8.45 (s, 2 H, H-4, H-6), 11.60 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 13.9 (2-OCH_2CH_3), 14.2 (1-OCH_2CH_3, 3-OCH_2CH_3), 20.4 (5′-CH_3), 62.2 (2-OCH_2CH_3), 62.3 (1-OCH_2CH_3, 3-OCH_2CH_3), 118.3 (C1′), 118.6 (C3′), 128.6 (C5′), 128.9 (C5), 132.6 (C6′), 134.0 (C4, C6), 138.7 (C1, C3), 138.5 (C4′), 139.1 (C2), 161.4 (C2′), 164.0 (1-CO, 3-CO), 167.5 (2-CO), 198.9 (5-CO).

LC-MS (ESI, 1.65 eV): *m*/*z* (%) = 483 (80) [M^+ + Na + MeOH], 451 (100) [M^+ + Na].

Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.32; H, 5.73.

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