Reliable transformation of substituted 2-aminobenzophenones into methoxy substituted 9H-xanthene-9-ones and/or fluoren-9-ones

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Abstract: An easy conversion of substituted 2-aminobenzophenones to some novel 9H-xanthene-9-ones and/or fluoren-9-ones is reported. Potassium chromate oxidation of 2-nitrobiphenyl methanol afforded 2-nitrobenzophenone derivatives that were reduced to give the substituted 2-aminobenzophenones. Cyclization of substituted 2-aminobenzophenones with *n*-amylnitrite and potassium iodide by stirring at r.t for 12 h delivered methoxy substituted 9H-xanthene-9-ones in 73–96% yields. Reaction of aminobenzophenone with *n*-amylnitrite leads to a mixture of 9H-xanthene-9-ones and fluoren-9-ones. Optimization of the reaction time and the reagents on the synthesis of 9H-xanthene-9-ones and fluoren-9-ones is presented as well. The synthesized structures have been elucidated unambiguously by ($^{1}H/^{13}C$ NMR), Heteronuclear Single Quantum Spectroscopy (HSQC) and Heteronuclear Multiple-Bond Spectroscopy (HMBC) spectra.

Keywords: 9H-xanthene-9-ones, C-C bond formation, Pschorr cyclization, Fluorenes and Diazonium salts.

تحويل فعال لمشتقات ٢-أمينوبنزوفينون المستبدلة إلى مشتقات جديدة من ميثوكسي الفلورينون والأكسانسينون

الملخص: يتضمن البحث تحويل سريع وبسيط لمركبات ٢-أمينو بنزوفينون الي مشتقات جديدة من الفلورينون والأكسانسينون بنسبة تتراوح بين٧٣–٩٦٪ مستخدما أميل نيتريت ويوديد البوتاسيوم عند درجة حرارة الغرفة لمدة ١٢ ساعة. الدرجة المثلي لظروف التفاعل تم تحديدها بدقة. بالإضافة الي ذلك تم الحصول علي نواتج بكميات مرتفعة مع إثبات المركبات المحضرة من خلال أطياف الأشعة تحت الحمراء، الرنين النووي المغناطيسي للبروتون و الكربون والتحاليل الدقيقة والتجارب الطيفية بين البروتون وذرات الكربون.

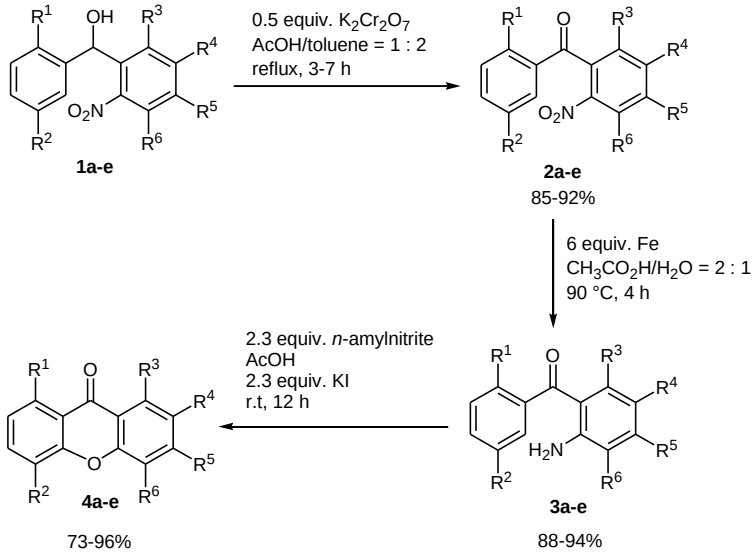
1.Introduction

9H-Xanthene-9-ones are one of the biggest classes of compounds in chemistry of natural products. Some of naturally occurring 9H-xanthene-9-ones have been isolated from natural sources of higher plants [1]. The 9H-xanthene-9-one ring constitutes the core structure of a wide variety of naturally occurring oxygen-containing and manmade heterocycles that show extraordinary anti-inflammatory and anti-cancer activity [2]. 9H-xanthene-9-ones are mainly found as secondary metabolites in higher plants and microorganisms [3]. Over the last decades xanthenes have been extensively studied not only because they participate in several biological functions but also as a consequence of their notable antimalarial [4, 5], anti-inflammatory [6], antifungal [7], antitumor activities [8] and even as outstanding antioxidant agents [9]. There are various known methods for the synthesis of 9H-xanthene-9-ones [10]. Also, fluoren-9-ones and their related compounds are among the most prominent synthetic derivatives that have therapeutic applications [11–16]. In addition, fluoren-9-ones play a significant role in building of several of natural products [17, 18]. Tilorone analogs with fluoren-9-one skeleton was screened as potential anticancer agents [19]. Recently, fluoren-9-one alkyl amine exhibited potential broad spectrum antimicrobial activities [20]. Fluorenes and their derivatives were synthesized via various procedures [21–23]. In the area of Cu(I)-catalyzed reactions naphthalenes or 4*H*-chromenes were built within Cu(I)-catalyzed domino reactions [24]. An intramolecular Cu(I)-catalyzed cyclization of substituted 2-iodobenzophenones for formation of substituted fluoren-9-ones was presented by Haggam [25]. Recently, Haggam et al reported microwave promoted syntheses of some novel benzisoxazoles and fluoren-9-ones [26].

2.Results and discussion

Starting with substituted aryl bromides and substituted nitrobenzaldehyde we succeeded to synthesize some novel 9H-xanthene-9-ones and fluoren-9-one derivatives. For this issue, the substituted secondary alcohols **1a-e** were prepared in good yields [13, 27] by reaction of the substituted lithiated bromobenzenes with the substituted nitrobenzaldehyde [28]. Upon oxidation of the compounds **1a-e** via Fieser and Williamson procedure [29] the aromatic ketones **2a-e** were obtained in high yields. The substituted 2-aminobenzophenones **3a-e** were prepared by the reduction of the nitro group of the substituted 2-nitrobenzophenones according to the method of Stephenson et al [30] (Scheme 1). It was noted that an amazing transformation of the substituted 2-aminobenzophenones **3a-e** into 9H-xanthene-9-ones derivatives **4a-e** instead of the substituted 2-iodobenzophenones [25] on reaction with *n*-amylnitrite and

potassium iodide in acetic acid under stirring at r.t for 12 h [31]. After purification by flash chromatography the methoxy substituted 9H-xanthene-9-ones **4a-e** were isolated in 73–96% yields.

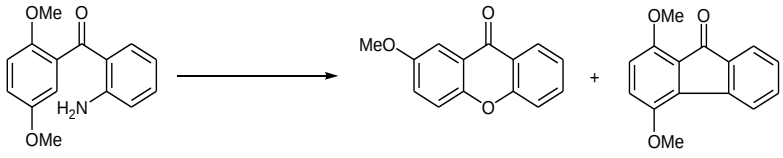


4	R^1	R^2	R^3	R^4	R^5	R^6	Yield (%)
a	OMe	H	H	H	H	H	85
b	OMe	OMe	H	H	H	H	96
c	OMe	H	H	OMe	OMe	H	82
d	OMe	OMe	H	OMe	OMe	H	78
e	OMe	OMe	OMe	H	H	OMe	73

Scheme 1. Synthesis of methoxy substituted 9H-xanthene-9-ones **4a-e** in 73–96% yields.

Initially, (2-aminophenyl)(2',5'-dimethoxyphenyl)methanone (**3b**) [32] was reacted with 2.3 equiv. *n*-amylnitrite and 2.3 equiv. potassium iodide in acetic acid under different reaction times as shown in (Table 1). Upon stirring the reaction for 1–3 h we obtained the 1,4-dimethoxyfluoren-9-one (**5**) [25, 28] in 23–40% yields while 2-methoxy-9H-xanthene-9-one (**4b**) was not observed at all (Table 1, entries 1–3). By increasing the reaction time for 4–10 h, a mixture of both fluoren-9-one **5** and 9H-xanthene-9-one **4b** was obtained with different yields. Also, it was observed that the yield of **4b** increased with increasing the time of reaction while that of dimethoxyfluoren-9-one **5** decreased (Table 1, entries 4–8). When the reaction was running for 12–14 h (Table 1, entries 9–11), the highest yield (96%) of methoxy-9H-xanthene-9-one **4b**.was obtained. Moreover, fluoren-9-one **5** was not formed. At this extent, we optimized the reaction condition to prepare methoxy substituted xanthene-9H-one derivatives (Table 1). By using other reaction conditions such as 1.0 equiv. sodiumnitrite in

AcOH/HCl (2:1) as solvent it was possible to synthesize methoxyfluoren-9-one **5** only and prevent 9H-xanthene-9-one **4b** formation as in (Table 1). We observed a gradual increasing in the yield of the product **5**. If the reaction was performed for 8–13 h via 1.0 equiv. sodiumnitrite, methoxyfluoren-9-one **5** was isolated with yields in the range 32–42% (Table 1, entries 12–15). Our results demonstrated that a new and simple transformation of the substituted 2-aminobenzophenones into 9H-xanthene-9-one and/or methoxyfluoren-9-one derivatives in good yields.



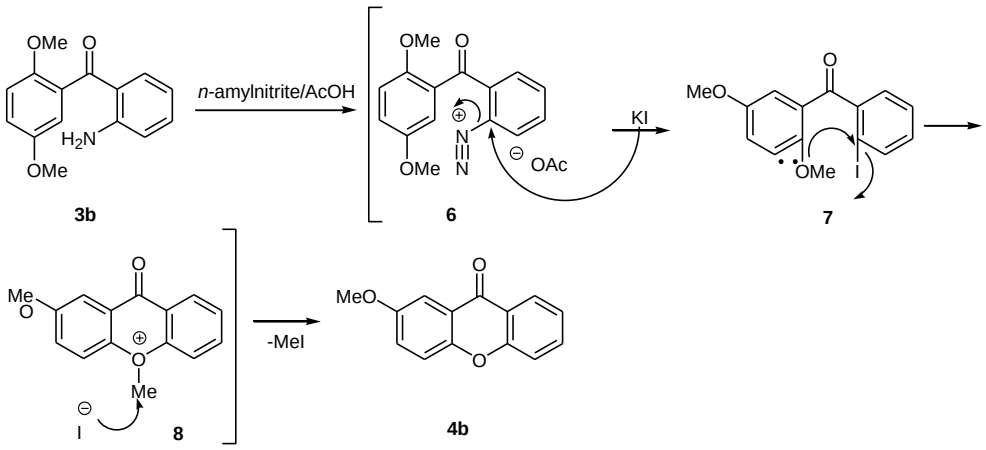
3b **4b** **5**

Entry	Reagents	Solvents	Temp. (0° C)	Time (h)	[%] **4b**	[%] **5**
1	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	1 h	0	23
2	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	2 h	0	35
3	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	3 h	0	40
4	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	4 h	24	48
5	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	5 h	27	53
6	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	6 h	52	22
7	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	8 h	63	24
8	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	10 h	71	28
9	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	12 h	96	0
10	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	13 h	96	0
11	2.3 equiv. *n*-amylnitrite/2.3 equiv. KI	AcOH	0° C → r.t	14 h	96	0
12	1 equiv. $NaNO_2$	AcOH/HCl (2:1)	0° C → r.t	8 h	0	32
13	1 equiv. $NaNO_2$	AcOH/HCl (2:1)	0° C → r.t	10 h	0	35
14	1 equiv. $NaNO_2$	AcOH/HCl (2:1)	0° C → r.t	12 h	0	42
15	1 equiv. $NaNO_2$	AcOH/HCl (2:1)	0° C → r.t	13 h	0	42

Table 1: The influence of the reaction time and the reagents on building of methoxy substituted 9H-xanthene-9-one **4b** and dimethoxy substituted fluoren-9-one **5**

Regarding the suggested mechanism for the cyclization of the disubstituted 2-aminobenzophenones **3b** in order to build 9H-xanthene-9-one **4b** it is assumed that formation of the diazonium acetate intermediate **6**. Attacking the iodide on the electrophilic carbon of **6** with evolving N_2-molecule resulted in establishment of the iodo derivative **7**. Subsequently, the intermediate **7** underwent an intramolecular cyclization via methoxy group yielding

oxonium intermediate **8** that lost methyl iodide to deliver 2-methoxy-9H-xanthene-9-one (**4b**) as in (Scheme 2).



Scheme 2. Proposed mechanism of 2-methoxy-9H-xanthene-9-one (**4b**) formation

As an example, the structure of compound **4b** was elucidated by the analysis of its (^{1}H/^{13}C NMR), Heteronuclear Multiple-Bond Spectroscopy (HMBC) and the Heteronuclear Single Quantum Spectroscopy (HSQC) spectra. In ^{13}C NMR spectrum there is two characteristic signals at δ = 56.2 and 177.4 ppm for methoxy and carbonyl groups, respectively (Figure 1).

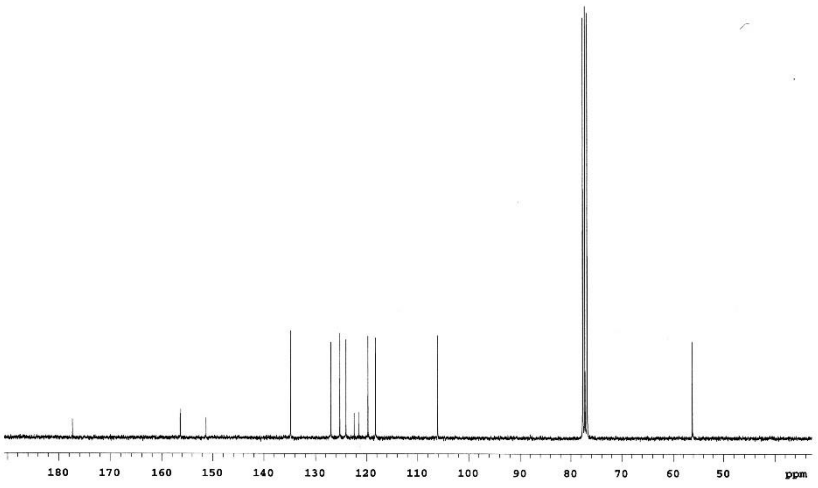


Figure 1. ^{13}C NMR spectrum of compound **4b**

The ^{1}H NMR and the HSQC spectrum of **4b** is shown in (Figure 2). The HSQC spectrum could be used to identify the carbon positions that are directly connected to hydrogen atoms. The HSQC spectrum of **4b** revealed the carbons C-1, C-3 and C-4 at δ = 125.2, 106.1 and 127.0 ppm, respectively. The carbons C-5, C-6, C-7 and C-8 appeared at δ = 124.0, 118.2, 119.7 and 123.2 ppm, respectively.

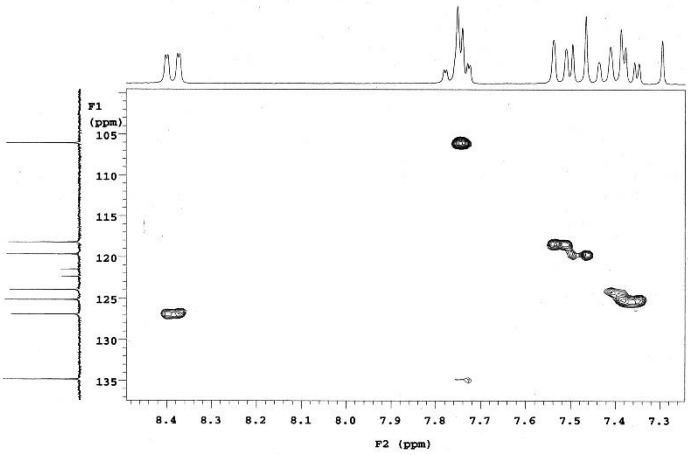
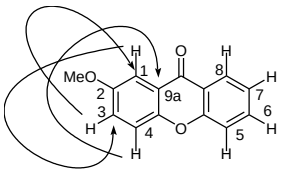


Figure 2. Section of the HSQC spectrum of **4b**.

Generally, the HMBC spectrum is used to determine the correlation between the carbons and the hydrogen atoms. From the ^{13}C NMR and HMBC spectra of compound **4b** (Figure 3), there are three strong $^{3}J_{CH}$-correlations between 4-H and C-9a at δ = 134.9 ppm. In addition to, the proton 3-H showed strong $^{3}J_{CH}$-correlations with C-1 at δ = 125.2 ppm while the proton 1-H exhibited $^{3}J_{CH}$-correlation with C-3 at δ = 106.1 ppm. This means that, both 1-H and 3-H protons are attached with the same benzene ring., (Figure 3).



4b

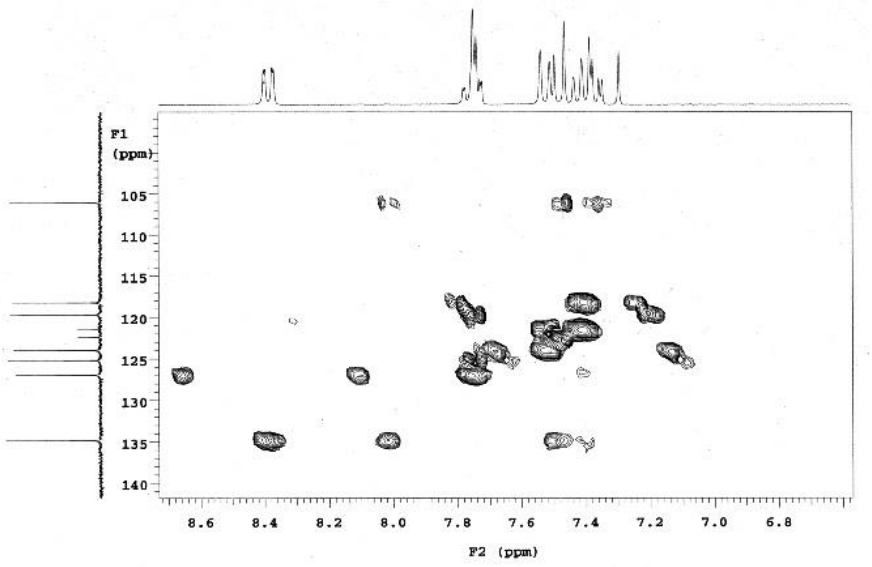
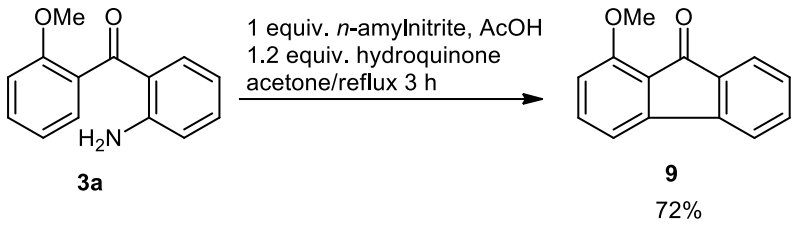


Figure 3. Section of the HMBC spectrum of **4b**

The methoxy 2-aminobenzophenone **3a** was changeded into the corresponding methoxyfluoren-9-one **9** [25, 33] in 72% yield according to the general reaction mechanism of the Gomberg-Bachmann reaction [34] and the Pschorr cyclization [35] (Scheme 3).



Scheme 3. Synthesis of methoxyfluoren-9-one **9**

3. Conclusion

This research involves an effective transformation substituted 2-aminobenzophenones via *n*-amylnitrite and potassium iodide to some new 9H-xanthene-9-ones and/or fluoren-9-ones. The prepared compounds have been established unambiguously by ($^{1}H/^{13}C$ NMR) and the correlation experiments.

4. Experimental

All melting points were measured on a Büchi melting point apparatus B-545 and are uncorrected. IR spectra were recorded on a Perkin–Elmer Spectrum One (FT-IR-Spectrometer). UV/VIS spectra were measured with a Varian Cary 50. ^{1}H and ^{13}C NMR spectra were recorded at 300 (75) MHz on a Varian^{Inova} Spectrometer with $CDCl_3$ as solvent and TMS as internal standard. The ^{1}H and ^{13}C chemical shifts were referenced to residual solvent signals at δH/C 7.26/77.00 ($CDCl_3$). HSQC-, HMBC- and COSY-spectra were recorded on a Varian^{Inova} at 300 MHz. Coupling constants *J* [Hz] were directly taken from the spectra and are averaged. Low-resolution electron impact mass spectra (MS) and exact mass electron impact mass spectra (HRMS) were recorded on a Finnigan MAT 90 spectrometer operating at an ionization potential of 70 eV. Elemental analyses were carried out at Institute of Organic and Biomolecular Chemistry, Gottingen University, Germany. Temperatures are reported as inner temperatures. Solvents used in extraction and purification were distilled prior to use. Thin-layer chromatography (TLC) was performed on Alugram SIL G/UV 254 (Macherey and Nagel). Compounds were visualized with UV light (λ = 254 nm) and/or by immersion in an ethanolic

vanillin solution followed by heating. Products were purified by flash chromatography on silica gel 60 M, 230–400 mesh (Macherey & Nagel).

General synthetic method of methoxy substituted 9H-xanthene-9-one derivatives 4a-e and 1,4-dimethoxyfluoren-9-one (5)

The substituted 2-aminobenzophenones **3a-e** (1.94 mmol) were stirred in glacial acetic cid (20 mL). *n*-Amyl nitrite (10.7 mmol) was added drop by drop to the previous solution 0 °C and the resulting reaction mixture was stirred for 1 h. A solution of potassium iodide 10.7 mmol) in water (10 mL) was added within 5 min and the reaction mixture was stirred further for 12 h at r.t. The reaction mixture was poured into crushed ice (100 mL), neutralized with 10% NaOH solution (30 mL) and extracted with dichloromethane (5 × 20 mL). The combined organic phases were washed with water (3 × 30 mL) and brine (1 × 30 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude products were purified by flash chromatography.

9H-Xanthene-9-one (4a) [٣٦]

The crude product of was purified by flash chromatography (SiO_2; CH_2Cl_2/cyclohexane = 1:1) to give compound **4a** in (0.33 g, 85%) yield as white crystals. R_f (SiO_2; CH_2Cl_2/cyclohexane = 1:1) 0.26; Mp. 171–172 °C; IR (ATR): 3056 cm^{-1}(CH arom.), 1663 cm^{-1} (C=O), 1138, 1121, 1109 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDC1_3$): δ = 8.35 (d, 2H, ^3J = 7.8 Hz), 7.73 (t, 2H, ^3J = 7.8 Hz), 7.50 (t, 2H, ^3J = 7.8 Hz), 7.38 (d, 2H, ^4J = 7.8 Hz); ^{13}C NMR (300 MHz, $CDC1_3$): δ = 118.1 (C-3, C-6), 122.0 (C-2, C-7), 124.1 (C-4, C-5), 126.9 (C-1, C-8), 135.0 (C-8a, C-9a), 156.3 (C-4a, C-10a), 176.1 (C=O); HRMS (EI, 70 eV): $[M+H]^+$ $C_{13}H_9O_2$ found 197.09. calcd. 197.06.

2-Methoxy-9H-xanthene-9-one (4b)

The crude product was purified by flash chromatography (SiO_2; CH_2Cl_2/cyclohexane = 2:1) to give compound **4b** in (0.45 g, 96%) yield as white crystals. R_f (CH_2Cl_2) 0.38; Mp. 129–130 °C; IR (ATR): 3058 cm^{-1} (CH arom.), 2922, 2853 cm^{-1} (CH aliph.), 1658 cm^{-1} (C=O), 1487, 1464 cm^{-1} (CH_3), 1143, 1126, 1109 cm^{-1} (C-O); λ_{max} (MeCN) (log ε) 361 nm (3.46), 301 nm (3.34), 249 nm (4.16), 236 nm (4.20) nm; ^{1}H NMR (300 MHz, $CDC1_3$): δ = 8.39 (d, 1H, $^3J_{HH}$ = 7.8 Hz, 4-H), 7.80 (d, 1H, $^3J_{HH}$ = 7.8 Hz, 3-H), 7.51–7.39 (m, 5-H, 6-H, 7-H and 8-H), 7.32 (s, 1H, 1-H), 3.96 (s, 3H, 2-OCH_3); ^{13}C NMR (300 MHz, $CDC1_3$): δ = 56.2 (2-OMe), 106.1 (C-3), 118.2 (C-6), 119.7 (C-7), 121.5 (C-8a), 123.2 (C-8), 124.0 (C-5), 125.2 (C-1), 127.0 (C-4), 134.9 (C-9a), 151.2 (C-2), 156.3 (C-10a), 156.4 (C-4a), 177.4 (C=O); *m/z* (EI, 70 eV) 244

(100, M^+), 226 (100), 225 (M^+-H, 80), 211 (M^+-Me, 69), 211 (M^+-CH_2O, 42), 183 (11), 155 (52), 127 (24), 28 (21%); HRMS (EI, 70 eV): (M^+) $C_{14}H_{10}O_3$ found 226.06. calcd. 226.06.

2,3-Dimethoxy-9H-xanthene-9-one (4c)

The crude product of was purified by flash chromatography (SiO_2; CH_2Cl_2/cyclohexane = 1:2) to give compound **4c** in (0.41 g, 82%) yield as white crystals. R_f (SiO_2; CH_2Cl_2/cyclohexane = 1:2) 0.31; Mp. 151–152 °C; IR (ATR): 3035 cm^{-1} (CH arom.), 2928, 2837 cm^{-1} (CH aliph.), 1668 cm^{-1} (C=O), 1481, 1464 cm^{-1} (CH_3), 1138, 1121, 1109 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDC1_3$): δ = 7.53 (s, 1H, 4-H), 7.48–7.30 (m, 5-H, 6-H, 7-H and 8-H), 6.32 (s, 1H, 1-H), 3.97 (s, 3H, 3-OCH_3), 3.96 (s, 3H, 2-OCH_3); ^{13}C NMR (300 MHz, $CDC1_3$): δ = 56.4 (2-OMe), 56.5 (3-OMe), 103.6 (C-1), 106.7 (C-6), 109.0 (C-4), 121.7 (C-8a), 123.6 (C-7), 127.2 (C-8), 136.8 (C-5), 155.7 (C-2), 155.8 (C-3), 156.4 (C-4a), 156.6 (C-10a), 175.0 (C=O); HRMS (EI, 70 eV): (M^+) $C_{15}H_{12}O_4$ found 256.25. calcd. 256.25. Anal. calcd. for $C_{15}H_{12}O_4$ (256.25): 70.31; H, 4.72. Found: C, 70.23; H, 4.65.

2,3,7-Trimethoxy-9H-xanthene-9-one (4d)

The crude product of was purified by flash chromatography (SiO_2; CH_2Cl_2/cyclohexane = 1:3) to give compound **4d** in (0.43 g, 78%) yield as white crystals. R_f (SiO_2; CH_2Cl_2/cyclohexane = 1:3) 0.23; Mp. 143–144 °C; IR (ATR): 3053 cm^{-1} (CH arom.), 2927, 2833 cm^{-1} (CH aliph.), 1661 cm^{-1} (C=O), 1483, 1460 cm^{-1} (CH_3), 1140, 1124, 1109 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDC1_3$): δ = 7.40 (s, 1H, 8-H), 7.32–7.28 (m, 2H, 5-H and 6-H), 7.05 (s, 1H, 4-H), 6.92 (s, 1H, 1-H), 3.97 (s, 3H, 3-OCH_3), 3.96 (s, 3H, 2-OCH_3), 3.95 (s, 3H, 7-OCH_3); ^{13}C NMR (300 MHz, $CDC1_3$): δ = 56.4 (7-OMe), 56.6 (2-OMe), 56.7 (3-OMe), 103.6 (C-1), 106.2 (C-6), 108.4 (C-4), 121.6 (C-8a), 127.4 (C-8), 135.1 (C-5), 151.2 (C-9a), 155.8 (C-2), 155.9 (C-3),156.3 (C-7), 156.5 (C-10a), 156.8 (C-4a), 176.8 (C=O); HRMS (EI, 70 eV): (M^+) $C_{16}H_{14}O_5$ found 286.08 calcd. 286.08; Anal. calcd. for $C_{16}H_{14}O_5$ (286.0823): 67.13; H, 4.93. Found: C, 67.01; H, 4.85.

1,4,7-Trimethoxy-9H-xanthene-9-one (4e)

The crude product was purified by flash chromatography (SiO_2; CH_2Cl_2/cyclohexane = 1:3) to give compound **4e** in (0.41 g, 73%) yield as white crystals. R_f (SiO_2; CH_2Cl_2/cyclohexane = 1:3) 0.29; Mp. 137–138 °C; IR (ATR): 3065 cm^{-1} (CH arom.), 2925, 2843 cm^{-1} (CH aliph.), 1669 cm^{-1} (C=O), 1489, 1462 cm^{-1} (CH_3), 1147, 1122, 1108 cm^{-1} (C-O); ^{1}H NMR (300 MHz, $CDC1_3$): δ = 7.43 (s, 1H, 8-H), 7.30–7.27 (m, 2H, 5-H and 6-H), 7.15 (d, 1H, $^3J_{HH}$ = 7.6 Hz, 3-H), 6.92 (d, 1H, $^3J_{HH}$ = 7.6 Hz, 2-H), 3.98 (s, 3H, 4-OCH_3), 3.97 (s, 3H, 1-OCH_3), 3.96 (s, 3H,

7-OCH_3); ^{13}C NMR (300 MHz, $CDC1_3$): δ = 56.3 (7-OMe), 56.5 (1-OMe), 56.6 (4-OMe), 106.2 (C-6), 116.1 (C-2), 121.4 (C-8a), 124.4 (C-3), 127.2 (C-8), 135.5 (C-5), 151.1 (C-9a), 156.2 (C-7), 156.5 (C-10a), 156.7 (C-4a), 157.2 (C-1), 157.3 (C-4), 177.6 (C=O); HRMS (EI, 70 eV): (M^+) $C_{16}H_{14}O_5$ found 286.08. calcd. 286.08; Anal. calcd. for $C_{16}H_{14}O_5$ (286.0823): 67.13; H, 4.93. Found: C, 67.08; H, 4.78.

1,4-Dimethoxyfluoren-9-one (5) [25, 28]

According to the general procedure the crude product of 1,4-dimethoxyfluoren-9-one (**5**) was purified by flash chromatography (SiO_2; cyclohexane/EtOAc = 3:1) to give compound **5** in ((0.25 g, 53%) yield as orange crystals. R_f (cyclohexane/EtOAc) 0.26; Mp. 170–171 °C; IR (ATR): 3012 cm^{-1} (CH arom.), 2930, 2839 cm^{-1} (CH aliph.), 1698 cm^{-1} (C=O), 1584, 1499 cm^{-1} (C=C arom.), 1453, 1437 cm^{-1} (CH_3), 1263, 1177 and 1055 cm^{-1} (C-O); λ_{max} (MeCN) (log ε) 433 nm (2.95), 373 nm (2.96), 250 nm (4.15), 244 nm (4.03); ^1H NMR (300 MHz, $CDC1_3$): δ = 7.83 (d, 1H, ^3J = 7.8 Hz , 5-H), 7.62 (d, 1H, ^3J = 7.2 Hz, 8-H), 7.42 (dd, 1H, ^3J = 8.4 Hz, ^4J = 1.2 Hz, 6 -H), 7.21 (dd, 1H, ^3J = 7.4 Hz, ^4J = 0.8 Hz , 7-H), 7.02 (d, 1H, ^3J = 9.0 Hz, 3-H), 6.78 (d, 1H, ^3J = 9.0 Hz, 2-H), 3.96 (s, 6H, 1-OCH_3, 4-OCH_3); ^{13}C NMR (300 MHz, $CDC1_3$): δ = 56.3 (1-OCH_3), 56.5 (4-OCH_3), 114.4 (C-2), 120.6 (C-3), 124.0 (C-8), 124.6 (C-5), 128.5 (C-7), 132.6 (C-9a), 134.2 (C-6), 134.4 (C-8a), 136.8 (C-4a), 142.8 (C-4b), 149.9 (C-1), 152.8 (C-4), 192.4 (C=O); *m/z* (EI, 70 eV) 240 (60, M^+), 211 (M^+-CHO) (85), 197 (37), 169 (30),139 (17%); HRMS (EI, 70 eV): (M^+) $C_{15}H_{12}O_3$ found 240.08. calcd. 240.07.

1-Methoxyfluoren-9-one (9) [33]

A solution of (2-aminophenyl)(2'-methoxyphenyl)methanone (**3a**) (18 mmol) in 30 mL glacial acetic acid was prepared. 5.4 mL *n*-amylnitrite (18 mmol) were added at 0 °C and the resulting reaction mixture was stirred for 1 h at room temperature. A solution of hydroquinone (21.6 mmol) in 40 mL acetone was added dropwise and the reaction mixture was stirred for 3 h at room temperature. Subsequently, the reaction mixture was poured into 400 mL water, neutralized with 80 mL 10 % sodium hydroxide solution and extracted with dichloromethane (4 × 100 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (2 × 50 mL) and dried over anhydrous magnesium sulfate. The crude product was purified by flash chromatography (SiO_2; cyclohexane/CH_2Cl_2 = 1:1) to give compound **9** in (2.70 g, 72%) yield as pale yellow crystals. R_f (cyclohexane/EtOAc.= 8:1) 0.33; Mp. 133–134 °C; IR (ATR): 3058 (CH arom.), 2947, 2838 cm^{-1} (CH aliph.), 1660 cm^{-1} (C=O), 1597, 1580, 1486 cm^{-1} (C=C arom.), 1449, 1435 cm^{-1} (CH_3), 1293, cm^{-1} (C-O); λ_{max} (MeCN) (log ε) 249 nm (3.89), 203 nm

(4.15); ^{1}H NMR (300 MHz, CDC1$_3$): δ = 7.85 (d, 1H, ^{3}J = 7.8 Hz, 8-H), 7.58 (dd, 1H, ^{3}J = 7.2 Hz, ^{3}J = 7.3 Hz, 3-H), 7.44–7.53 (m, 2H, 5-H, 6-H), 7.40 (dd, 1H, ^{3}J = 7.8 Hz, ^{4}J = 1.3 Hz, 7-H), 7.09 (t, 1H, ^{3}J = 7.8 Hz, 4-H), 7.03 (dd, 1H, ^{3}J = 8.5 Hz, ^{4}J = 1.3 Hz, 2-H), 3.76 (s, 3H, 1-OCH$_3$); ^{13}C NMR (300 MHz, CDC1$_3$): δ = 55.9 (1-OCH$_3$), 111.7 (C-4), 120.8 (C-2), 128.5 (C-5), 129.1 (C-9a), 129.8 (C-8a), 130.1 (C-7), 130.0 (C-8), 132.1 (C-3), 133.2 (C-4b), 138.1 (C-4a), 157.6 (C-1), 196.7 (C=O); *m/z* (EI, 70 eV) 212 (87, M^{2+}), 201 (M^{+}-CH_2=CH_2) 195 (66), 194 (33), 136 (15), 135 (M^{2+}-C_6H_5) (100), 105 (73), 77 (90%).

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4.2 Conflict of interest

This paper holds no confict of interest and is not funded through any source.

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