Tetrahedron 69 (2013) 1694–1699

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Alternative simple and effective synthesis of (di)benzoxanthones and their functions toward fluorescent dyes

Eriko Azuma, Kouji Kuramochi, Kazunori Tsubaki *

Graduate School of Life and Environmental Sciences, Kyoto Prefectural University, Shimogamo, Sakyo-ku, Kyoto 606-8522, Japan

ARTICLE INFO

Article history:
Received 1 October 2012
Received in revised form 10 December 2012
Accepted 16 December 2012
Available online 21 December 2012

Keywords:
(Di)benzoxanthone
Xanthone
Fluorescence
Intramolecular dehydration

ABSTRACT

(Di)benzoxanthones possessing additional benzene units on one or both sides of xanthone were prepared via dehydration of the corresponding dihydroxybenzophenone, where a catalytic amount of K_2CO_3 dramatically increased the yields. Chemical transformations of the versatile carbonyl groups of (di)benzoxanthones could derive fluorescent materials.

1. Introduction

Xanthone skeletons, which commonly occur in natural products,[1] exhibit various pharmacological activities (e.g., anti-cancer and anti-bacterial properties)[2] and in the medicinal chemistry field, are frequently valued as effective pharmacophores.[3] Additionally, xanthone skeletons frequently display fluorescent responses, which have facilitated the development of fluorescent dyes derived from xanthone as a key fragment.[4] Consequently, much effort has been devoted to effectively synthesize xanthones. Larock et al. have constructed various xanthones though arynes and C–H activation.[5] Recently, xanthones have been constructed under mild conditions using palladium-catalyzed oxidative double C–H carbonylation of biarylethers.[6] Although many synthetic routes have been reported, cyclization from the benzophenone possessing the proper functional groups on the scaffolding 2,2′-positions remains the most common.

Xanthone synthetic routes are classified roughly into two groups according to the functional groups on the 2,2′-positions: (1) cyclization from 2-hydroxy-2′-halogen or alkoxy benzophenones under basic conditions though *ipso*-substitution[7] and (2) dehydrative cyclization from 2,2′-dihydroxybenzophenones under (mainly) harsh conditions. The latter route is further divided according to the reaction conditions. Dehydrative cyclization has been reported to occur under neutral conditions at high temperature in water using a sealed tube[8] or SiO_2 as a dehydration reagent,[9] as well as under acidic conditions using a catalytic amount of H_2SO_4[10] or melting pyridinium hydrochloride.[4d,8b] Additionally, there are a few cases where dehydrative cyclization occurs under basic conditions using ethanolic KOH or a large excess of sodium acetate.[11]

On the other hand, our research focuses on colorimetric molecular recognition based on phenolphthalein with two crown loops. To date, we have successfully visualized features of guest molecules, such as chirality, shape, and size.[12] In particular, our work has targeted spermidine and spermine, which are biogenic polyamines, to develop a practical method to determine the spermidine level in living cells.[13] We aim to change our molecular recognition system from a color-response type to a fluorescent-response type. We recently reported the exhaustive syntheses of naphthofluoresceins possessing additional benzene units on one or both sides of fluorescein, and revealed that some naphthofluoresceins exhibit fluorescent emissions in the near infrared region (>700 nm) with large Stokes shifts and humble quantum yields.[14]

To improve the quantum yields of the derivatives, we selected (di)benzoxanthone skeletons as key intermediates due to the versatility of the carbonyl groups of (di)benzoxanthones. These carbonyl groups can be converted into other functional groups through Wittig reactions, organometallic reagents, etc. to afford a variety of fluorescent molecules within a few reaction steps.[4]

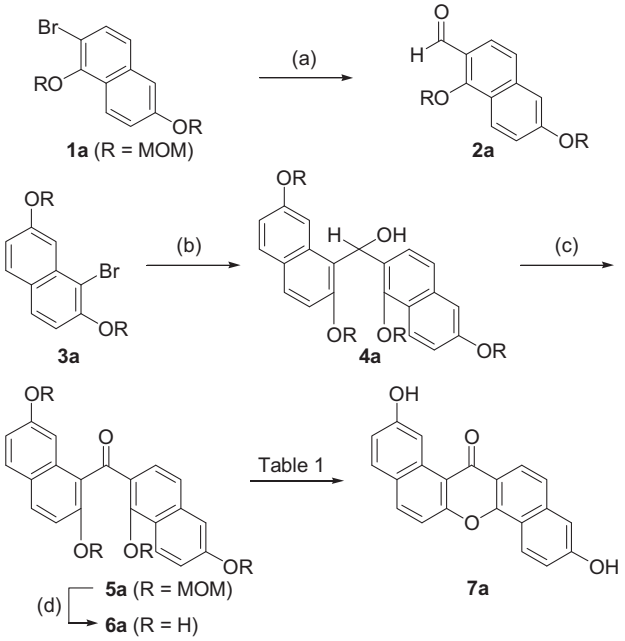
Herein, we describe the exhaustive syntheses of nine (di)benzoxanthones from their corresponding 2,2′-dihydroxybenzophenones in the presence of a catalytic amount of K_2CO_3, as well as their optical properties.

* Corresponding author. E-mail address: tsubaki@kpu.ac.jp (K. Tsubaki).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.12.035

2. Results and discussion

Scheme 1 shows the synthesis of dibenzoxanthone **7a**. Bromonaphthalene **1a**[14] was lithiated by *n*-BuLi and trapped with DMF to afford aldehyde **2a** in 81% yield. The corresponding coupling partner **3a** was treated with *n*-BuLi and allowed to react with aldehyde **2a** to give **4a** in 93% yield. Dibenzylic alcohol **4a** was oxidized by MnO_2 in 72% yield. HCl in dioxane was then used to remove the four MOM groups in compound **5a**, producing cyclization precursor **6a** in 96% yield. The other precursors were synthesized by the same procedure in moderate to good total yields (see Supplementary data). Table 1 shows the results of different reaction conditions on the intramolecular dehydration from precursor **6a** to dibenzoxanthone **7a**.



Scheme 1. Synthetic route for dibenzoxanthone **7a**. (a) *n*-BuLi, DMF, 81% yield; (b) *n*-BuLi, **2a**, 93% yield; (c) MnO_2, 72% yield; (d) HCl in dioxane, 96% yield.

Table 1
Dehydration from **6a** to **7a**

Entry	Solvent	Additive (equiv)	Temp (°C)	Time (h)	Yield of **7a** (%)
1[8]	H_2O	—	150[a]	9	0.3[b]
2[9]	—	SiO_2	40	21	No reaction
3[10,14]	$MeSO_3H$	—	50	3.5	Decomposed
4[11b,c]	EtOH	KOH (1.0)	Reflux	9	Mixture
5[11e]	CH_3CN	K_2CO_3 (3.0)	Reflux	9	Mixture
6[4d,8b]	Py·HCl[c]	—	150	9	61
7[11d]	H_2O	AcONa (10)	Reflux	9	21
8	H_2O	K_2CO_3 (0.1)	Reflux	9	62
9	H_2O	K_2CO_3 (0.1)	150[a]	9	99
10	H_2O	Li_2CO_3 (0.1)	150[a]	9	93
11	H_2O	Na_2CO_3 (0.1)	150[a]	9	99
12	H_2O	Rb_2CO_3 (0.1)	150[a]	9	96
13	H_2O	Cs_2CO_3 (0.1)	150[a]	9	96
14	H_2O	$(^nBu)_4NOH$ (0.1)	150[a]	9	85

[a] Sealed tube condition.
[b] Yield of **7a** calculated based on the integral intensity of ^1H NMR.
[c] Pyridinium hydrochloride.

Dehydration in a sealed tube with neutral water and high temperature (150 °C),[8] which are the standard conditions to form the xanthone skeleton, did not proceed, and only a small amount of desired **7a** was detected by NMR (estimated in ca. 0.3% yield, entry 1). Similarly, the reaction did not occur using SiO_2 treatments (entry 2),[9] and cyclization under acidic conditions was not fruitful because several fragmental products, such as 2,7-dihydroxynaphthalene (8% yield) and 1,6-dihydroxy-naphthalene-2-carboxylic acid (17% yield) were obtained instead of desired compound **7a**, (entry 3).[10,14] These data indicate that in the case of compound **6a**, a retro Friedel–Crafts reaction predominantly occurs instead of the desired cyclization under acidic conditions. It is interesting to note that in the case of cyclization of compound **6d**, which is a structural isomer of **6a**, these reactions proceed smoothly under identical conditions to give corresponding dibenzoxanthone **7d** in quantitative yield. In entries 4[11b,c] and 5,[11e] which are from the literature, cyclization under basic conditions in an organic solvent was applied to give an inseparable and complicated compound mixture. In contrast, reactions under basic conditions in water[11d] or molten pyridinium hydrochloride[4d,8b] produced desired **7a** in moderate yields (entries 6 and 7). Because a promising result was obtained in the presence of K_2CO_3 (0.1 equiv) in water (entry 8), we modified the reaction conditions. Thus, the reaction was performed at 150 °C using a sealed tube, which increased the yield of **7a** to 99% (entry 9). Almost no influences of the counter cations (including quaternary ammonium cation) were observed (entries 9–14). Based on these observations, we estimate the conditions in entry 9 (0.1 equiv of K_2CO_3, water, 150 °C) are the most appropriate. It is especially noteworthy that the product was easily isolated from the reaction mixture; filtration isolated cyclized dibenzoxanthone **7a** from an acidified aqueous solution in an extremely pure form without chromatographic purification.

With the optimal reaction conditions in hand, we then studied the generality of substrates for the reaction using other dihydroxybenzophenones **6b–i** (Fig. 1). Intramolecular dehydration

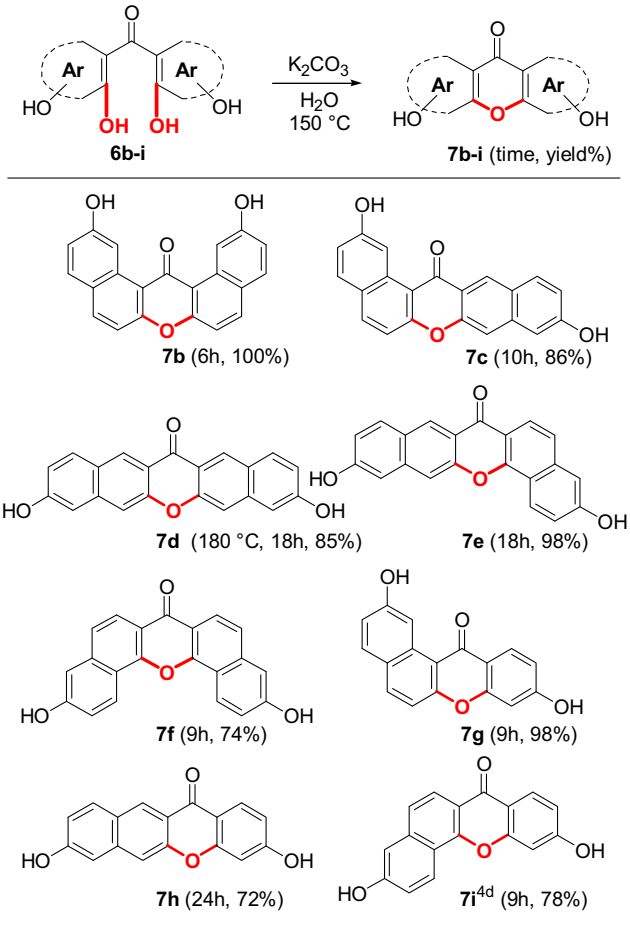


Fig. 1. Syntheses of (di)benzoxanthones **7b–i**.

occurred smoothly and afforded (di)benzoxanthones **7b**–**i** in good to excellent yields after filtration.

With respect to cyclization under basic conditions, we propose the following reaction mechanism (Fig. 2). K_2CO_3 acts as a weak base to generate a monoanion of 2,2′-dihydroxybenzophenone, which forms a pseudo-eight-membered ring via an intramolecular hydrogen bond. Then nucleophilic cyclization occurs through this conformation in a 6-*exo*-*trig* fashion. Finally, the hydroxy anion leaves, which re-aromatizes the ring and leads to a xanthone. The HOMO and LUMO of the eight-membered monoanion (DFT/B3LYP/6-31+G (d, p)) may support the plausible mechanism (see Supplementary data).[15]

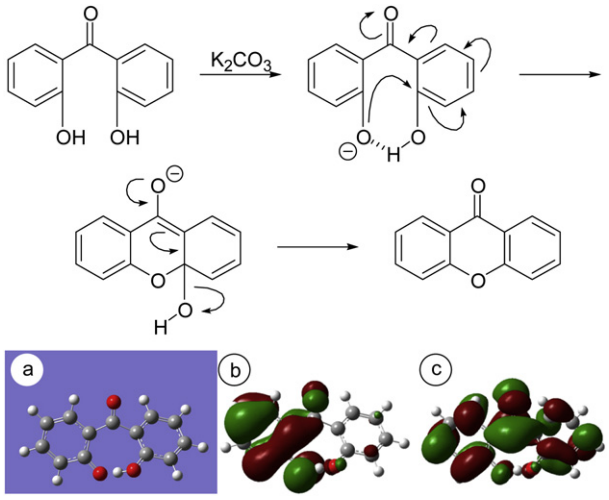


Fig. 2. Plausible mechanism for base catalyzed cyclization. (a) Optimized structure of the monoanionic benzophenone with (b) HOMO and (c) LUMO obtained by DFT calculations at the B3LYP/6-31+G (d, p) level.

Table 2 summarizes the optical properties of the (di)benzoxanthones **7a**–**i** (λ_{max} and ε of the absorbance, emission wavelengths, quantum yields (Φ), and Stokes shifts). The maximum absorption wavelengths for (di)benzoxanthones **7a**–**i** were distributed within a narrow area between 352 nm (**7g**) and 380 nm (**7d**). However, these compounds can be roughly divided into four groups based on the maximum emission wavelength (λ_{em}): (1) compounds **7f** and **7i**[4d] (400 nm<λ_{em}<440 nm), (2) compounds **7a**, **b**, and **7g** (440 nm<λ_{em}<480 nm), (3) compounds **7c**, **7e**, and **7h** (480 nm<λ_{em}<520 nm), and (4) compound **7d** (520 nm<λ_{em}<560 nm). The properties of this series of (di) benzoxanthones **7a**–**i** are suitable for multi-color system applications with a single wavelength excitation in the chemical biology field. For example, the combination of compounds **7f**, **7a**, **7e**, and **7d**, whose maximum emission wavelengths are in ca. 40 nm increments, is expected for multi-color fluorescence sensing (Fig. 3).

Table 2
Optical properties of compounds **7a**–**i** in methanol[a]

Compound	$\lambda_{Abs\ max}$ (nm)	ε ($\lambda_{Abs\ max}$)	λ_{em} (nm)	Φ (%)[b]	Stokes shift (nm)
7a	367	16,000	475	4	105
7b	356	18,000	478	0.4	98
7c	374	22,000	507	2	133
7d	380	15,000	528	7	154
7e	358	21,000	494	46	134
7f	368	11,000	420	18	58
7g	352	15,000	480	5	122
7h	353	21,000	493	48	138
7i[4d]	357	10,000	413	28	53

[a] UV and FL spectra of compounds **7a**–**i**, see Supplementary data.
[b] Fluorescence quantum yields of **7a**–**i** (Φ) determined using a solution of quinine sulfate in 1 N H_2SO_4 as a reference standard (Φ=0.546).

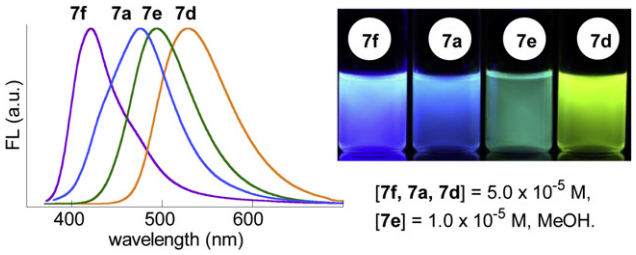
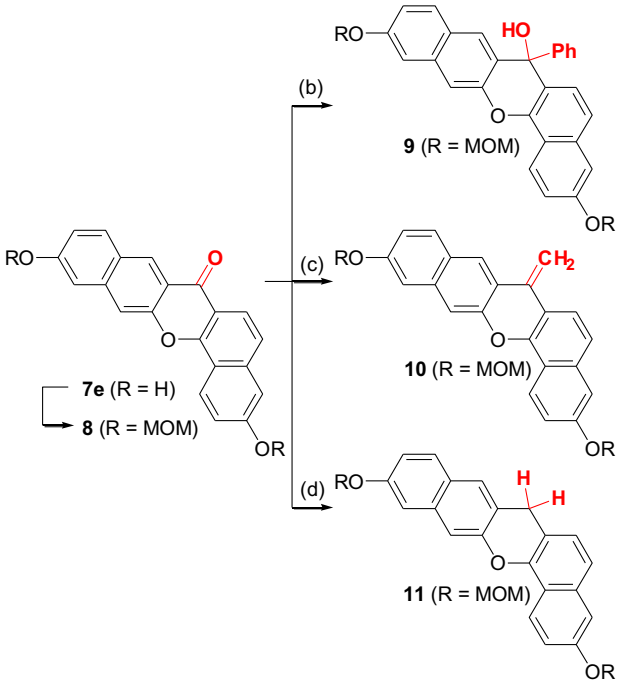


Fig. 3. FL spectra of **7a**, **7d**, **7e**, and **7f** in methanol and picture of FL under UV light (365 nm).

The quantum yields (Φ) dramatically decreased for compounds **7a**, **7b**, **7c**, and **7g**, which all possess at least one benzene ring fused on the same side of the central carbonyl group. On the other hand, compounds **7e** and **7h** displayed emissions near 490 nm with large quantum yields (Φ). The same tendencies have been observed in a series of naphthofluoresceins in a previous study.[14]

Finally, the diversity of products obtained from MOM-protected dibenzoxanthone **8**, which was prepared from **7e** in 90% yield, was demonstrated (Scheme 2). Phenyllithium easily reacted with **7e** at −78 °C in dry THF to give triarylalcohol **9** in 98%. The Wittig reaction using methyltriphenylphosphonium bromide and *n*-BuLi afforded *exo* methylene compound **10** in 47% yield. Additionally, the carbonyl group on **7e** was removed easily, giving **11** in 65% yield.[8b] These products could be further converted into more useful compounds for fluorescent dyes.



Scheme 2. Transformation from dibenzoxanthone **8**. (a) NaH, MOMCl, 90% yield; (b) PhLi, −78 °C, 98% yield; (c) Ph_3PMeBr, *n*-BuLi, 47% yield; (d) BH_3–THF, 65% yield.

3. Conclusions

We successfully constructed (di)benzoxanthones via dehydration of the corresponding dihydroxybenzophenones. We synthesized all types of (di)benzoxanthones **7a**–**i**, and indicated the possibility that a combination of compounds is expected for multi-color fluorescence sensing (e.g., **7a**, **7d**, **7e**, and **7f**). Merits of this reaction include simplicity, usefulness, and good atom economy.

Moreover, this reaction is environmentally benign because the solvent is water and column purification is not employed. Currently we are synthesizing various derivatives through (di)benzoxanthones as the key intermediates for new fluorescent materials.

4. Experimental

4.1. Compound 2a

A solution of *n*-BuLi (1.62 M *n*-hexane solution; 0.68 ml, 1.11 mmol) was added dropwise to a solution of **1a**[14] (330 mg, 1.01 mmol) in dry THF (5 ml) under N_2 atmosphere at −78 °C. After 1 h stirring, dry DMF (109 μl) was added dropwise to the solution. The resultant solution was stirred at −78 °C for 1 h, and then allowed to warm to room temperature. The reaction mixture was poured into the mixed solvent of ethyl acetate and 0.1 M aq HCl. The organic layer was separated and washed successively with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to dryness. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc=8/1) to afford **2a** (225.3 mg, 81% yield) as a pale yellow powder. Mp 53.5–54.0 °C; IR (KBr) 2881, 1676, 1626, 1471, 1240, 1157, 1009, 904 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 10.46 (s, 1H, Ar−C*H*O), 8.16 (d, *J*=8.9 Hz, 1H), 7.84 (d, *J*=8.9 Hz, 1H), 7.56 (d, *J*=8.9 Hz, 1H), 7.41 (d, *J*=2.4 Hz, 1H), 7.30 (dd, *J*=8.9, 2.4 Hz, 1H), 5.33 (s, 2H, $-CH_2OCH_3$), 5.27 (s, 2H, $-CH_2OCH_3$), 3.66 (s, 3H, $-CH_2OCH_3$), 3.53 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (68 MHz, $CDCl_3$) δ 189.7, 159.4, 157.7, 139.6, 125.3, 124.1, 123.9, 123.4, 123.4, 119.5, 110.2, 101.9, 94.2, 58.2, 56.3; MS (EI^+) *m*/*z* (rel int.) 276 (M^+, 63), 230 (100), 201 (21), 115 (27), 102 (18), 75 (8); HRMS (EI^+) calcd for $C_{15}H_{16}O_5$ (M^+): 276.0998. Found: 276.0997. Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.22; H, 5.87.

4.2. Compound 4a

A solution of *n*-BuLi (1.59 M *n*-hexane solution; 1.42 ml, 2.26 mmol) was added dropwise to a solution of **3a**[14] (677.4 mg, 2.07 mmol) in dry THF (15 ml) under N_2 atmosphere at −78 °C. After 1 h stirring, a solution of **2a** (520 mg, 1.88 mmol) in THF (5 ml) was added dropwise to the solution at −78 °C. The resultant solution was allowed to warm to room temperature with stirring for 5 h. The reaction mixture was poured into the mixed solvent of ethyl acetate and 0.1 M aq HCl. The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to dryness. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc=4/1) to afford **4a** (915.3 mg, 93% yield) as pale yellow oil. IR (film) 3500, 1626, 1514, 1236, 1151, 999, 831 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.09 (d, *J*=8.9 Hz, 1H), 7.86 (d, *J*=2.4 Hz, 1H), 7.73 (d, *J*=8.9 Hz, 1H), 7.70 (d, *J*=8.9 Hz, 1H), 7.36–7.30 (m, 4H), 7.23 (dd, *J*=8.9, 2.4 Hz, 1H), 7.15 (d, *J*=7.3 Hz, 1H, Ar_2CHOH), 7.10 (dd, *J*=8.9, 2.4 Hz, 1H), 5.32–5.24 (m, 6H, $-CH_2OCH_3$), 5.19 (ABq, $\Delta\nu$=25.7 Hz, J_{AB}=6.5 Hz, 2H, $-CH_2OCH_3$), 4.82 (d, *J*=7.3 Hz, 1H, Ar_2CHOH), 3.74 (s, 3H, $-CH_2OCH_3$), 3.50 (s, 3H, $-CH_2OCH_3$), 3.46 (s, 3H, $-CH_2OCH_3$), 3.40 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (68 MHz, $CDCl_3$) δ 155.2, 155.1, 152.9, 151.3, 135.6, 133.4, 130.7, 129.7, 129.3, 126.4, 126.0, 124.3, 124.0, 123.4, 122.8, 118.8, 116.8, 113.9, 109.8, 107.6, 100.8, 95.1, 94.3, 94.3, 67.3, 57.8, 56.5, 56.1, 56.0; MS (EI^+) *m*/*z* (rel int.) 524 (M^+, 5), 476 (5), 401 (100), 357 (40), 313 (19), 216 (42), 169 (15), 115 (29), 69 (25); HRMS (EI^+) calcd for $C_{29}H_{32}O_9$ (M^+): 524.2046. Found: 524.2048. Anal. Calcd for $C_{29}H_{32}O_9$: C, 66.40; H, 6.15. Found: C, 66.56; H, 6.01.

4.3. Compound 5a

To a solution of **4a** (890 mg, 1.70 mmol) in CH_2Cl_2 (50 ml), manganese dioxide (8.9 g) was added. The suspension was stirred at room temperature for 12 h. The solid materials were filtered through Celite, and the filtrate was concentrated under reduced pressure to dryness. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc=5/1) to afford **5a** (636.3 mg, 72% yield) as a yellow oil. IR (film) 2956, 1664, 1622, 1512, 1240, 1151, 995, 829 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J*=8.8 Hz, 1H), 7.84 (d, *J*=8.8 Hz, 1H), 7.76 (d, *J*=8.8 Hz, 1H), 7.52 (d, *J*=8.8 Hz, 1H), 7.40 (d, *J*=8.8 Hz, 1H), 7.34 (d, *J*=2.4 Hz, 1H), 7.31 (d, *J*=8.8 Hz, 1H), 7.29 (d, *J*=2.4 Hz, 1H), 7.27 (dd, *J*=8.8, 2.4 Hz, 1H), 7.15 (dd, *J*=8.8, 2.4 Hz, 1H), 5.31 (s, 2H, $-CH_2OCH_3$), 5.14 (s, 2H, $-CH_2OCH_3$), 5.12 (s, 2H, $-CH_2OCH_3$), 5.04 (s, 2H, $-CH_2OCH_3$), 3.52 (s, 3H, $-CH_2OCH_3$), 3.46 (s, 3H, $-CH_2OCH_3$), 3.37 (s, 3H, $-CH_2OCH_3$), 3.22 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (68 MHz, $CDCl_3$) δ 196.2, 157.2, 156.2, 155.5, 152.7, 138.3, 132.8, 131.0, 129.6, 127.9, 126.5, 125.7, 125.4, 124.7, 124.5, 122.5, 119.3, 117.3, 113.4, 109.3, 106.9, 102.0, 94.6, 94.4, 94.2, 57.7, 56.3, 56.2, 56.1; MS (EI^+) *m*/*z* (rel int.) 522 (M^+, 6), 461 (9), 445 (26), 429 (97), 385 (43), 341 (26), 292 (26), 216 (100), 186 (21), 71 (7); HRMS (EI^+) calcd for $C_{29}H_{30}O_9$ (M^+): 522.1890. Found: 522.1887. Anal. Calcd for $C_{29}H_{30}O_9$: C, 66.66; H, 5.79. Found: C, 66.54; H, 5.70.

4.4. Compound 6a

A solution of 4 M hydrogen chloride in 1,4-dioxane (17.9 ml) was added dropwise to a solution of **5a** (1.88 g, 3.60 mmol) in 1,4-dioxane (15 ml) and stirred for 10 h at room temperature. The solvent was evaporated in vacuo to afford crude **6a** as brown foam (1.20 g, 96% yield). Crude **6a** was directly used for the next step without further purification. IR (KBr) 3261, 1628, 1581, 1473, 1240, 831 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 8.36 (d, *J*=8.8 Hz, 1H), 7.75 (d, *J*=8.8 Hz, 1H), 7.67 (d, *J*=8.8 Hz, 1H), 7.10 (d, *J*=8.8 Hz, 1H), 7.03 (d, *J*=8.8 Hz, 1H), 6.99 (s, 1H), 6.98 (d, *J*=8.8 Hz, 1H), 6.91 (d, *J*=8.8 Hz, 1H), 6.88 (d, *J*=8.8 Hz, 1H), 6.73 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 204.8, 164.6, 161.1, 157.7, 153.5, 141.8, 134.7, 132.2, 130.9, 129.2, 127.4, 124.4, 120.0, 118.8, 118.6, 118.2, 116.7, 115.5, 114.4, 110.5, 106.3; MS (FAB^+) *m*/*z* (rel int.) 347 ($M+H^+$, 7), 241 (15), 185 (58), 149 (51), 93 (100), 75 (78), 57 (43), 45 (26); HRMS (FAB^+) calcd for $C_{21}H_{14}O_5$ (M^+): 346.0841. Found: 346.0841. Anal. Calcd for $C_{21}H_{14}O_5$: C, 72.83; H, 4.07. Found: C, 72.54; H, 4.10.

4.5. General procedure for the preparation of xanthones 7a–i

The preparation of **7a** is typical. A suspension of **6a** (50 mg, 0.144 mmol), K_2CO_3 (2.0 mg, 0.014 mmol) in water (8.0 ml) in a pressure tube was stirred for 9 h at 150 °C. To the reaction mixture, 1 M aq HCl was added and the insoluble matter was collected by filtration to afford **7a** (47.1.9 mg, 99% yield) as a pale gray powder.

*4.5.1. Compound **7a**.* Mp >300 °C; IR (KBr) 3136, 1635, 1597, 1577, 1442, 1219, 1159, 1022, 827 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 10.47 (s, 1H, ArO*H*), 10.24 (s, 1H, ArO*H*), 9.48 (d, *J*=2.4 Hz, 1H), 8.58 (d, *J*=8.8 Hz, 1H), 8.27 (d, *J*=8.8 Hz, 1H), 8.11 (d, *J*=8.8 Hz, 1H), 7.95 (d, *J*=8.8 Hz, 1H), 7.72 (d, *J*=8.8 Hz, 1H), 7.69 (d, *J*=8.8 Hz, 1H), 7.33 (dd, *J*=8.8, 2.4 Hz, 1H), 7.32 (d, *J*=2.4 Hz, 1H), 7.19 (dd, *J*=8.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 177.2, 159.1, 157.4, 151.9, 138.2, 136.4, 132.6, 130.6, 124.7, 124.6, 123.3, 121.6, 119.4, 117.8, 116.8, 116.8, 114.5, 113.4, 110.3, 109.5 (one peak overlapped); MS (FAB^+) *m*/*z* (rel int.) 329 ($M+H^+$, 36), 185 (54), 149 (45), 93 (100), 75 (73), 57 (43), 45 (29); HRMS (FAB^+) calcd for $C_{21}H_{13}O_4$ ($M+H^+$): 329.0814. Found: 329.0812. Anal. Calcd for $C_{21}H_{12}O_4 \cdot 1/4H_2O$: C, 75.78; H, 3.79. Found: C, 75.88; H, 3.67.

*4.5.2. Compound **7b**.* Yield 100%; pale gray powder; mp >300 °C; IR (KBr) 3325, 1633, 1591, 1533, 1444, 1257, 1242, 1217, 823 cm^{-1}; ^1H

NMR (270 MHz, DMSO-d_6) δ 10.21 (s, 2H, ArO*H*), 9.49 (s, 2H), 8.23 (d, *J*=8.6 Hz, 2H), 7.95 (d, *J*=8.6 Hz, 2H), 7.51 (d, *J*=8.6 Hz, 2H), 7.20 (d, *J*=8.6 Hz, 2H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 179.3, 158.7, 155.8, 136.0, 132.1, 130.4, 124.4, 117.4, 114.2, 113.6, 109.3; MS (EI$^+$) *m*/*z* (rel int.) 328 (M$^+$, 19), 256 (7), 232 (31), 193 (41), 178 (100), 177 (100), 135 (88), 97 (100), 91 (87); HRMS (EI$^+$) calcd for $C_{21}H_{12}O_4$ (M$^+$): 328.0736. Found: 328.0738. Anal. Calcd for $C_{21}H_{12}O_4 \cdot 1/4H_2O$: C, 75.78; H, 3.79. Found: C, 75.82; H, 3.75.

4.5.3. Compound ***7c***. Yield 86%; gray powder; mp >300 °C; IR (KBr) 3255, 1699, 1618, 1535, 1483, 1437, 1360, 1221, 1186, 849 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.38 (s, 1H, ArO*H*), 10.27 (s, 1H, ArO*H*), 9.40 (d, *J*=2.4 Hz, 1H), 8.79 (s, 1H), 8.23 (d, *J*=8.8 Hz, 1H), 8.12 (d, *J*=8.8 Hz, 1H), 7.91 (d, *J*=8.8 Hz, 1H), 7.90 (s, 1H), 7.44 (d, *J*=8.8 Hz, 1H), 7.24 (d, *J*=2.4 Hz, 1H), 7.16 (dd, *J*=8.8, 2.4 Hz, 1H), 7.15 (dd, *J*=8.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.2, 159.4, 158.5, 158.3, 151.4, 138.3, 137.3, 132.9, 131.9, 130.7, 127.5, 125.0, 124.3, 119.9, 119.8, 117.4, 114.5, 111.9, 110.7, 109.5, 107.4; MS (FAB$^+$) *m*/*z* (rel int.) 329 (M+H$^+$, 23), 241 (17), 185 (60), 149 (51), 117 (29), 93 (100), 75 (76), 57 (52), 45 (35); HRMS (FAB$^+$) calcd for $C_{21}H_{13}O_4$ (M+H$^+$): 329.0814. Found: 329.0811. Anal. Calcd for $C_{21}H_{12}O_4 \cdot 1/3H_2O$: C, 75.44; H, 3.82. Found: C, 75.84; H, 3.66.

4.5.4. Compound ***7d***. Yield 85%; pale gray powder; mp >300 °C; IR (KBr) 3269, 1624, 1610, 1469, 1356, 1180 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 2H, ArO*H*), 8.77 (s, 2H), 8.10 (d, *J*=8.8 Hz, 2H), 7.80 (s, 2H), 7.22 (d, *J*=2.4 Hz, 2H), 7.13 (dd, *J*=8.8, 2.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.8, 158.5, 152.5, 138.9, 131.8, 127.9, 124.1, 119.1, 117.8, 110.3, 107.2; MS (FAB$^+$) *m*/*z* (rel int.) 329 (M+H$^+$, 5), 241 (12), 207 (18), 185 (51), 149 (49), 115 (54), 93 (100), 75 (82), 57 (47); HRMS (FAB$^+$) calcd for $C_{21}H_{13}O_4$ (M+H$^+$): 329.0814. Found: 329.0821.

4.5.5. Compound ***7e***. Yield 98%; gray powder; mp >300 °C; IR (KBr) 3398, 3107, 1647, 1622, 1597, 1481, 1390, 1365, 1259, 1173, 850 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.53 (s, 1H, ArO*H*), 10.42 (s, 1H, ArO*H*), 8.77 (s, 1H), 8.56 (d, *J*=8.8 Hz, 1H), 8.13 (d, *J*=8.8 Hz, 1H), 8.07 (s, 1H), 8.02 (d, *J*=8.8 Hz, 1H), 7.64 (d, *J*=8.8 Hz, 1H), 7.33 (dd, *J*=8.8, 2.4 Hz, 1H), 7.30 (d, *J*=2.4 Hz, 1H), 7.27 (d, *J*=2.4 Hz, 1H), 7.17 (dd, *J*=8.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.1, 159.4, 158.5, 154.0, 152.2, 138.9, 138.5, 132.0, 127.3, 125.0, 125.0, 122.4, 121.7, 119.9, 119.4, 118.8, 117.1, 114.1, 111.5, 110.4, 107.5; MS (EI$^+$) *m*/*z* (rel int.) 328 (M$^+$,14), 313 (29), 247 (20), 231 (50), 149 (100), 83 (37); HRMS (EI$^+$) calcd for $C_{21}H_{12}O_4$ (M$^+$): 328.0736. Found: 328.0738.

4.5.6. Compound ***7f***. Yield 74%; yellow powder; mp >300 °C; IR (KBr) 3114, 1618, 1473, 1248, 858, 777, 733 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 10.60 (s, 2H, ArO*H*), 8.84 (d, *J*=8.6 Hz, 2H), 8.06 (d, *J*=8.6 Hz, 2H), 7.74 (d, *J*=8.6 Hz, 2H), 7.41 (dd, *J*=8.6, 2.2 Hz, 2H), 7.37 (d, *J*=2.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.0, 159.3, 153.0, 138.4, 124.9, 123.5, 121.3, 119.7, 117.3, 115.6, 110.3; MS (FAB$^+$) *m*/*z* (rel int.) 329 (M+H$^+$, 4), 279 (7), 241 (11), 207 (22), 185 (50), 149 (51), 115 (75), 93 (100), 75 (86), 57 (50); HRMS (FAB$^+$) calcd for $C_{21}H_{13}O_4$ (M+H$^+$): 329.0814. Found: 329.0814.

4.5.7. Compound ***7g***. Yield 98%; yellow powder; 280 °C (decomp.); IR (KBr) 3398, 1618, 1473, 1396, 1238, 1194, 781 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (br s, 1H, ArO*H*), 10.19 (s, 1H, ArO*H*), 9.41 (d, *J*=2.4 Hz, 1H), 8.18 (d, *J*=8.8 Hz, 1H), 8.11 (d, *J*=8.8 Hz, 1H), 7.90 (d, *J*=8.8 Hz, 1H), 7.42 (d, *J*=8.8 Hz, 1H), 7.14 (dd, *J*=8.8, 2.4 Hz, 1H), 6.94 (dd, *J*=8.8, 2.4 Hz, 1H), 6.91 (d, *J*=2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.9, 163.3, 159.1, 157.9, 156.2, 136.5, 132.7, 130.6, 128.1, 124.5, 117.6, 115.9, 114.5, 114.4, 112.6, 109.4, 101.8; MS (FAB$^+$) *m*/*z* (rel int.) 279 (M+H$^+$, 21), 241 (16), 185 (56), 149 (53), 117 (30), 93 (100), 75 (83), 57 (48); HRMS (FAB$^+$) calcd for $C_{17}H_{11}O_4$ (M+H$^+$): 279.0657. Found: 279.0661.

4.5.8. Compound ***7h***. Yield 72%; gray powder; mp >300 °C; IR (KBr) 3423, 3170, 1606, 1489, 1267, 1163, 850 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.96 (s, 1H, ArO*H*), 10.35 (s, 1H, ArO*H*), 8.69 (s, 1H), 8.08 (d, *J*=8.8 Hz, 1H), 8.04 (d, *J*=8.8 Hz, 1H), 7.80 (s, 1H), 7.20 (d, *J*=2.4 Hz, 1H), 7.12 (dd, *J*=8.8, 2.4 Hz, 1H), 6.86 (dd, *J*=8.8, 2.4 Hz, 1H), 6.83 (d, *J*=2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.5, 164.4, 158.4, 158.2, 152.6, 138.6, 131.9, 128.5, 127.6, 124.6, 119.6, 118.5, 113.7, 113.6, 111.0, 107.4, 102.3; MS (FAB$^+$) *m*/*z* (rel int.) 279 (M+H$^+$, 22), 185 (50), 149 (29), 93 (100), 75 (59), 57 (40); HRMS (FAB$^+$) calcd for $C_{17}H_{11}O_4$ (M+H$^+$): 279.0657. Found: 279.0658. Anal. Calcd for $C_{17}H_{10}O_4 \cdot 1/3H_2O$: C, 71.83; H, 3.78. Found: C, 72.03; H, 3.57.

4.5.9. Compound ***7i***. Yield 78%; yellow powder; mp >300 °C; IR (KBr) 3375, 1630, 1616, 1570, 1394, 1254, 1194, 845 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.94 (s, 1H, ArO*H*), 10.44 (s, 1H, ArO*H*), 8.52 (d, *J*=8.8 Hz, 1H), 8.06 (d, *J*=8.8 Hz, 1H), 7.98 (d, *J*=8.8 Hz, 1H), 7.65 (d, *J*=8.8 Hz, 1H), 7.30 (dd, *J*=8.8, 2.4 Hz, 1H), 7.29 (d, *J*=2.4 Hz, 1H), 7.09 (d, *J*=2.4 Hz, 1H), 6.95 (dd, *J*=8.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.6, 163.6, 159.1, 157.3, 153.5, 138.4, 127.8, 124.8, 122.8, 121.5, 119.4, 117.1, 114.9, 114.7, 114.6, 110.2, 102.7; MS (FAB$^+$) *m*/*z* (rel int.) 279 (M+H$^+$, 17), 241 (15), 185 (56), 149 (50), 117 (27), 93 (100), 75 (81), 57 (46); HRMS (FAB$^+$) calcd for $C_{17}H_{11}O_4$ (M+H$^+$): 279.0657. Found: 279.0659. Anal. Calcd for $C_{17}H_{10}O_4 \cdot 2/3H_2O$: C, 70.34; H, 3.94. Found: C, 70.60; H, 3.78.

4.6. Compound 8

To a stirred solution of **7e** (260 mg, 0.79 mmol) in dry DMF (10 ml), NaH (60% dispersion in mineral oil, 76 mg, 1.90 mmol) was added portionwise at room temperature. After 30 min, MOMCl (132.3 μl, 1.74 mmol) was added to the solution and stirred for 6.5 h at room temperature. The reaction mixture was poured into the mixed solvent of ethyl acetate and 0.1 M aq HCl. The organic layer was separated and washed successively with water and brine. After dried over sodium sulfate, the solvent was evaporated in vacuo to give a residue. The residue was purified by column chromatography (SiO_2; *n*-hexane/ethyl acetate=4/1) to afford **8** (297.0 mg, 90% yield) as a pale yellow powder. Mp 175–176 °C; IR (KBr) 1655, 1626, 1504, 1469, 1423, 1358, 1080 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.63 (d, *J*=8.8 Hz, 1H), 8.26 (d, *J*=8.8 Hz, 1H), 8.01 (d, *J*=8.8 Hz, 1H), 7.94 (s, 1H), 7.61 (d, *J*=8.8 Hz, 1H), 7.48 (d, *J*=2.4 Hz, 1H), 7.46 (d, *J*=2.4 Hz, 1H), 7.41 (dd, *J*=8.8, 2.4 Hz, 1H), 7.25 (dd, *J*=8.8, 2.4 Hz, 1H), 5.37 (s, 2H, $-CH_2OCH_3$), 5.37 (s, 2H, $-CH_2OCH_3$), 3.57 (s, 3H, $-CH_2OCH_3$), 3.56 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 158.1, 157.3, 154.1, 152.4, 138.5, 137.8, 131.4, 127.5, 126.0, 124.8, 122.6, 122.3, 119.9, 119.5, 119.1, 118.9, 115.3, 112.4, 110.4, 107.8, 94.3, 94.2, 56.3 (one peak overlapped); MS (EI$^+$) *m*/*z* (rel int.) 416 (M$^+$, 100), 386 (7), 242 (7); HRMS (EI$^+$) calcd for $C_{25}H_{20}O_6$ (M$^+$): 416.1260. Found: 416.1266. Anal. Calcd for $C_{25}H_{20}O_6$: C, 72.11; H, 4.84. Found: C, 71.85; H, 4.97.

4.7. Compound 9

To a stirred solution of **8** (52.1 mg, 0.125 mmol) in dry THF (2 ml), phenyllithium (1.15 M in cyclohexane/diethylether, 163 μl, 0.188 mmol) was added dropwise at −78 °C and stirred for 2 h. The reaction mixture was poured into the mixed solvent of ethyl acetate and 0.1 M aq HCl. The organic layer was separated and washed successively with water and brine. After dried over sodium sulfate, the solvent was evaporated in vacuo to give a residue. The residue was purified by column chromatography (SiO_2; *n*-hexane/ethyl acetate=5/1) to afford **9** (60.6 mg, 98% yield) as a black oil. IR (film)

3444, 1637, 1608, 1412, 1352, 1252, 1149, 1078, 1001, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J=9.2 Hz, 1H), 7.88 (s, 1H), 7.68 (s, 1H), 7.65 (d, J=9.2 Hz, 1H), 7.47–7.45 (m, 2H), 7.40–7.34 (m, 5H), 7.28–7.25 (m, 2H), 7.17 (dd, J=7.2, 7.2 Hz, 1H), 7.07 (dd, J=9.2, 2.4 Hz, 1H), 5.31 (s, 2H, $-CH_2OCH_3$), 5.30 (s, 2H, $-CH_2OCH_3$), 3.53 (s, 3H, $-CH_2OCH_3$), 3.52 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 155.7, 148.4, 145.0, 135.2, 134.7, 129.7, 128.8, 128.0, 127.4, 126.6, 126.6, 126.1, 126.0, 123.8, 122.2, 119.4, 119.3, 118.7, 118.0, 111.0, 110.0, 108.3, 94.4, 94.3, 70.8, 56.1 (four peaks overlapped); MS (EI^+) m/z (rel int.) 494 (M^+, 0.5), 477 (100), 401 (35); HRMS (EI^+) calcd for $C_{31}H_{26}O_6$ (M^+): 494.1729. Found: 494.1715.

4.8. Compound 10

To a stirred solution of methyltriphenylphosphonium bromide (128.7 mg, 0.36 mmol) in dry toluene (6 ml), a solution of *n*-BuLi (1.57 M *n*-hexane solution; 236 μl, 0.37 mmol) was added dropwise at −78 °C. The resultant solution was allowed to warm to 0 °C with stirring for 50 min. A solution of **8** in dry toluene (4 ml) was added dropwise at −78 °C. The reaction mixture was stirred at room temperature for 2 h and at 40 °C for 2 h. The reaction mixture was poured into the mixed solvent of ethyl acetate and 0.1 M aq HCl. The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to dryness. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc=5/1) to afford **10** (14.1 mg, 47% yield) as a yellow oil. Compound **10** was gradually decomposed in a solution state. IR (film) 2927, 1631, 1506, 1392, 1252, 1149, 1076, 1003 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J=8.8 Hz, 1H), 8.21 (s, 1H), 7.79 (d, J=8.8 Hz, 1H), 7.77 (d, J=8.8 Hz, 1H), 7.61 (s, 1H), 7.48 (d, J=8.8 Hz, 1H), 7.39 (d, J=2.4 Hz, 1H), 7.32 (d, J=2.4 Hz, 1H), 7.31 (dd, J=8.8, 2.4 Hz, 1H), 7.14 (dd, J=8.8, 2.4 Hz, 1H), 5.75 (s, 1H, $=CH_2$), 5.62 (s, 1H, $=CH_2$), 5.33 (s, 2H, $-CH_2OCH_3$), 5.32 (s, 2H, $-CH_2OCH_3$), 3.55 (s, 3H, $-CH_2OCH_3$), 3.55 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 155.8, 149.4, 145.8, 135.5, 135.3, 132.8, 129.8, 126.6, 124.0, 122.8, 122.1, 122.0, 120.4, 120.1, 118.7, 118.3, 113.9, 111.8, 110.1, 108.4, 101.0, 94.4, 56.2 (two peaks overlapped); MS (EI^+) m/z (rel int.) 414 (M^+, 2), 279 (38), 167 (36), 149 (100); HRMS (EI^+) calcd for $C_{26}H_{22}O_5$ (M^+): 414.1467. Found: 414.1463.

4.9. Compound 11

To a stirred solution of **8** (40 mg, 0.096 mmol) in dry THF (4 ml), a solution of borane–THF complex (1.1 M THF solution; 700 μl, 0.77 mmol) was added at 0 °C. The resultant solution was allowed to warm to room temperature for 5 h. The reaction mixture was poured into the mixed solvent of ethyl acetate and water. The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to dryness. The residue was purified by column chromatography (SiO_2; *n*-hexane/EtOAc=4/1) to afford **11** (25.2 mg, 65% yield) as a white powder. Mp 153.0–155.0 °C; IR (KBr) 1641, 1610, 1508, 1427, 1244, 1146, 1082, 1018, 876, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J=8.8 Hz, 1H), 7.68 (d, J=8.8 Hz, 1H), 7.63 (s, 1H), 7.53 (s, 1H), 7.43 (d, J=8.8 Hz, 1H), 7.38 (d, J=2.4 Hz, 1H), 7.34 (d, J=2.4 Hz, 1H), 7.29 (dd, J=8.8, 2.4 Hz, 1H), 7.25 (d, J=8.8 Hz, 1H), 7.11 (dd, J=8.8, 2.4 Hz, 1H), 5.31 (s, 2H, $-CH_2OCH_3$), 5.30 (s, 2H, $-CH_2OCH_3$), 4.30 (s, 2H, $ArCH_2Ar$), 3.54 (s, 3H, $-CH_2OCH_3$), 3.54 (s, 3H, $-CH_2OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 155.3, 150.8, 146.7, 134.6, 134.4, 128.8, 127.4, 127.3, 126.6, 123.1, 121.5, 120.2, 120.2, 118.7, 117.6, 112.7, 111.2, 109.9, 109.0, 94.6, 56.1, 28.1 (two peaks overlapped); MS (EI^+) m/z (rel int.) 462 (M^+, 100), 357 (12); HRMS (EI^+) calcd for $C_{25}H_{22}O_5$ (M^+): 402.1467. Found: 402.1470. Anal. Calcd for $C_{25}H_{22}O_5$: C, 74.61; H, 5.51. Found: C, 74.47; H, 5.50.

Acknowledgements

We appreciate the help received from Ms. Akiko Fujihashi (ICR, Kyoto University) and Ms. Mayumi Shikata (VL, Kyoto Institute of Technology) with the mass spectral analyses, and Ms. Toshiko Hirano (ICR, Kyoto University) with the elemental analyses. This study was partly supported by JSPS KAKENHI (No. 22390003), Kyoto Prefectural University Research Fund, A-STEP from JST (No. 231Z03077), and a Grant-in-Aid for JSPS Fellows to E.A.

Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2012.12.035.

References and notes

1. (a) Kupchan, S. M.; Streelman, D. R.; Sneden, A. T. *J. Nat. Prod.* **1980**, *43*, 296; (b) Gopalakrishnan, G.; Banumathi, B.; Suresh, G. *J. Nat. Prod.* **1997**, *60*, 519.
2. (a) Mehta, G.; Venkateswarlu, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 1200; (b) Suphavanich, K.; Maitarad, P.; Hannongbua, S.; Sudta, P.; Suksamrarn, S.; Tantirungrotechai, Y.; Limtrakul, J. *Monatsh. Chem.* **2009**, *140*, 273.
3. (a) Kolokythas, G.; Kostakis, I. K.; Pouli, N.; Marakos, P.; Skaltsounis, A.-L.; Pratsinis, H. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1443; (b) Liu, Y.; Zou, L.; Ma, L.; Chen, W.-H.; Wang, B.; Xu, Z.-L. *Bioorg. Med. Chem.* **2006**, *14*, 5683.
4. (a) Urano, Y.; Kamiya, M.; Kanda, K.; Ueno, T.; Hirose, K.; Nagano, T. *J. Am. Chem. Soc.* **2005**, *127*, 4888; (b) Yang, Y.; Lowry, M.; Schowalter, C. M.; Fakayode, S. O.; Escobedo, J. O.; Xu, X.; Zhang, H.; Jensen, T. J.; Fronczek, F. R.; Warner, I. M.; Strongin, R. M. *J. Am. Chem. Soc.* **2006**, *128*, 14081; (c) Yang, Y. J.; Lowry, M.; Xu, X. Y.; Escobedo, J. O.; Sibrian-Vazquez, M.; Wong, L.; Schowalter, C. M.; Jensen, T. J.; Fronczek, F. R.; Warner, I. M.; Strongin, R. M. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 8829; (d) Kim, S. H.; Gunther, J. R.; Katzenellenbogen, J. A. *Org. Lett.* **2008**, *10*, 4931; (e) Li, J.; Hu, M.; Yao, S. O. *Org. Lett.* **2009**, *11*, 3008.
5. (a) Zhao, J.; Larock, R. C. *Org. Lett.* **2005**, *7*, 4273; (b) Zhou, C.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3551; (c) Zhao, J.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 583; (d) Zhao, J.; Yue, D.; Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2007**, *129*, 5288.
6. Zhang, H.; Shi, R.; Gan, P.; Liu, C.; Ding, A.; Wang, Q.; Lei, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 5204.
7. Barbero, N.; SanMartin, R.; Domínguez, E. *Green Chem.* **2009**, *11*, 830.
8. (a) Davies, J. S. H.; Scheinmann, F.; Suschitzky, H. *J. Org. Chem.* **1958**, *23*, 307; (b) Shi, J.; Zhang, X.; Neckers, D. C. *J. Org. Chem.* **1992**, *57*, 4418; (c) Chen, C.-A.; Yeh, R.-H.; Lawrence, D. S. *J. Am. Chem. Soc.* **2002**, *124*, 3840.
9. (a) Gil, S.; Palanca, P.; Sanz, V.; Tortajada, A. *J. Nat. Prod.* **1990**, *53*, 1198; (b) Hamada, M.; Iikubo, K.; Ishikawa, Y.; Ikeda, A.; Umezawa, K.; Nishiyama, S. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3151.
10. (a) Mottram, L. F.; Maddox, L. E.; Schwab, M.; Beaufils, F.; Peterson, B. R. *Org. Lett.* **2007**, *9*, 3741; (b) Vandana, T.; Prasad, K. J. R. *Indian J. Chem., Sect. B* **2005**, *44*, 815.
11. (a) Bichan, D. J.; Yates, P. *Can. J. Chem.* **1975**, *53*, 2054; (b) Sundholm, E. G. *Tetrahedron* **1978**, *34*, 577; (c) Elix, J. A.; Jiang, H.; Portelli, V. J. *Aust. J. Chem.* **1990**, *43*, 1291; (d) Ojida, A.; Nonaka, H.; Miyahara, Y.; Tamaru, S.; Sada, K.; Hamachi, I. *Angew. Chem., Int. Ed.* **2006**, *45*, 5518; (e) Kogan, K.; Biali, S. E. *Org. Lett.* **2007**, *9*, 2393.
12. (a) Tsubaki, K. *J. Inclusion Phenom. Macrocycl. Chem.* **2008**, *61*, 217; (b) Fuji, K.; Tsubaki, K.; Tanaka, K.; Hayashi, N.; Otsubo, T.; Kinoshita, T. *J. Am. Chem. Soc.* **1999**, *121*, 3807.
13. Tanima, D.; Imamura, Y.; Kawabata, T.; Tsubaki, K. *Org. Biomol. Chem.* **2009**, *7*, 4689.
14. Azuma, E.; Nakamura, N.; Kuramochi, K.; Sasamori, T.; Tokitoh, N.; Sagami, I.; Tsubaki, K. *J. Org. Chem.* **2012**, *77*, 3492.
15. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision B.01*; Gaussian: Wallingford CT, 2010.