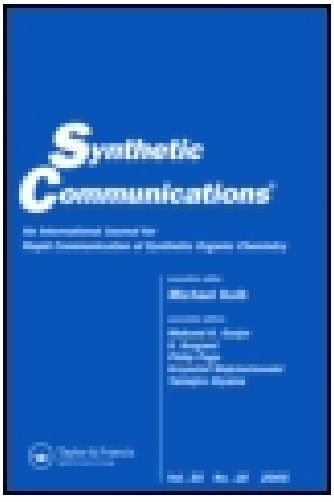

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Synthesis and Cytotoxicity of 9-Substituted Benzo[de]chromene-7,8-dione and 5-Benzyl-9-substituted Benzo[de]chromene-7,8-dione

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Synthesis and Cytotoxicity of 9-Substituted Benzo[*de*]chromene-7,8-dione and 5-Benzyl-9-substituted Benzo[*de*]chromene-7,8-dione

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Abstract: New Mansonone analogues of 9-substitued benzo[*de*]chromene-7,8-dione **5b–e** and 5-benzyl-9-substituted benzo[*de*]chromene-7,8-dione **6a–e** were prepared through a modified route. The first step involved a bulky base *t*-butylamine mediated regioselective deacetylation of 2-substituted-1,4-naphth-diyl diacetate, resulting in obtaining of monoacetate 4-acetate **2** in high yield. The mechanism of cyclization, debenzylation, and oxidation for the formation of **5a–e** and **6a–e** were discussed. The cytotoxicity of the prepared compounds **5** and **6** were comparable with naturally occurring Mansonone F.

Keywords: Antitumor, mansonone F, oxidation debenzyl rearrangement, selective hydrolization

INTRODUCTION

Mansonone compounds represent a series of naturally occurring *o*-quinones mainly isolated from the heartwood of *Mansonia altissima* and *Ulmus glabra*. This type of compound is classified as phytoalexin, which is produced and accumulated in plants in response to bacteria and fungi infections and is used to treat Dutch elm disease (DED). Mansonone F contained the oxaphenalene skeleton, which is a relatively novel structure and rarely exists in natural products (Fig. 1). This compound had shown comprehensive phamacological activities such as antibacterial and antitumor activity.[1–3] The limited source as well as the difficult synthesis of this compound prompted us to develop a facile synthetic route to prepare the Mansonone F analogues and to optimize their structure for enhancing bioactivity.[4–7]

A series of Mansonone F analogues bearing 9-substituted benzo[*de*]chromene-7,8-dione skeletons were prepared through a modified route. The first step involved a bulky base *t*-butylamine-mediated regioselective deacetylation of 2-substituted-1,4-naphth-diyl diacetate, resulting in obtaining monoacetate

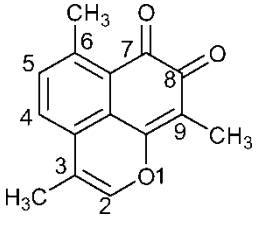


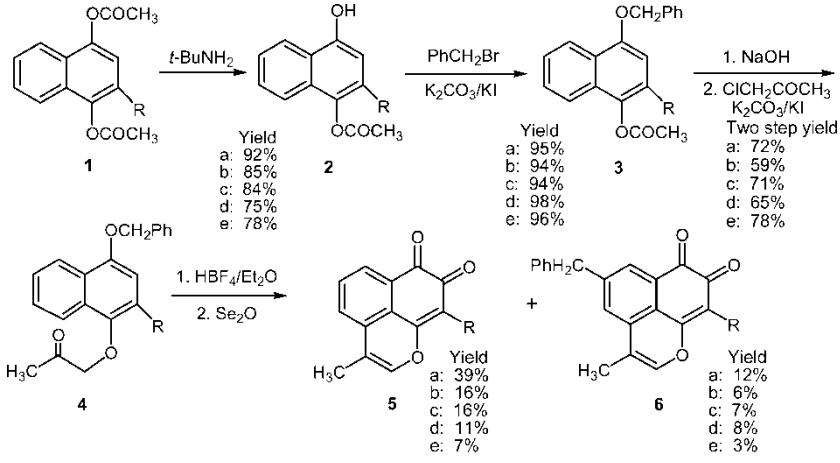
Figure 1. Mansonone F.

4-acetate **2** in high yield. The mechanism of cyclization, debenzylation, and oxidation for the formation of **5a**–**e** and **6a**–**e** were discussed. The cytotoxicity and the structure–activity relationship of the prepared compounds were studied.

RESULTS AND DISCUSSION

9-Substitued benzo[*de*]chromene-7,8-dione was synthesized as shown in Scheme 1. This route started from 2-substituted 1,4-naphenol diester **1**, which is easily commercially available. Alternatively, it could be conveniently prepared through a free radical alkylation.[8,9] Thus, in the presence of a bulky base *t*-$BuNH_2$, the deacetylation took place regioselectively and gave the corresponding monoacetate **2** in high yield (75–92%). Benzylation of the phenolic hydroxyl group produced compound **3** and subsequently removed the remaining acetyl group; treatment of the crude product with $ClCH_2COCH_3$ in the presence of K_2CO_3/KI gave compound **4** in high yield. After further electrophilc cyclization (in the presence of HBF_4), debenzylation and oxidation (with Se_2O) yielded the final products of **5a**–**e**. Accidentally, 5-benzyl substituted products **6a**–**e** were also obtained during the synthesis.

In the selective deacetylation step, we found that using potassium carbonate or ammonia as base failed to give satisfactory results, with both low regioselectivity and low yield.[5,10] A more bulky base *t*-butyl amine was chosen instead of potassium carbonate or ammonia as base to effectively regioselective deacetylate 2-substituted-1,4-naphth-diyl diacetate. To achieve better regioselectivity, the reaction was carried out at low temperature (5°C). With our



a R = CH_3; **b** R = C_2H_5; **c** R = $CH(CH_3)_2$; **d** R = $CH_2C_6H_5$; **e** R = $CH_2C_6H_4$-2-Cl

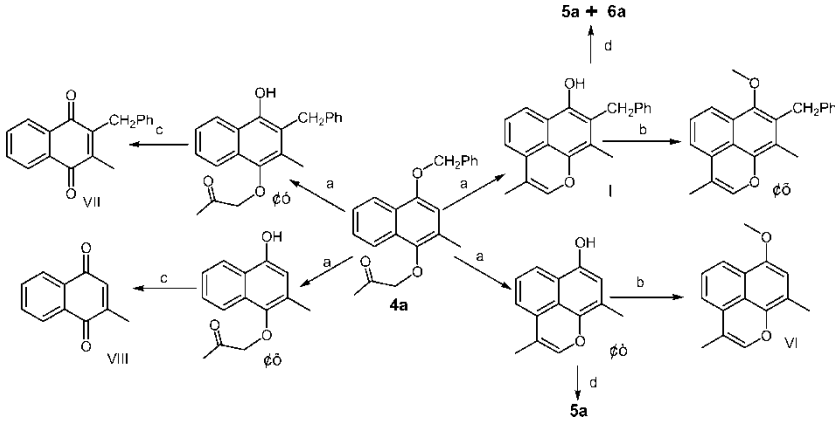
Scheme 1. Synthesis of Mansonone F analogues of **5a**–**e** and **6a**–**e**.

modification, the deacetylation demonstrated high regioselectivity, giving monoacetate **2** in much higher yields (75–92%). During the reaction, a small amount of diphenol compounds were produced, which could finally be oxidized to 2-methyl naphthoquinone and easily be washed off with CCl_4. Also the reaction time was significantly reduced from 4 days to about 5 h.[5]

The intermediates **3** and **4** were also obtained in high yields (overall yield of 55–75% for three steps from **2** to **4**). All of the crude intermediates produced in this way could be used in the next step reaction without special purification. The compound **4** was then treated with Lewis acid–mediated debenzylation, cyclization, and oxidation to produce target compounds **5a**–**e** and **6a**–**e** in 7–39% overall yield.

The structure of prepared compounds **5a**–**e** and **6a**–**e** were determined with fast atom bombardment-mass spectrometry (FAB-MS) and ^{1}H NMR analysis. The FAB-MS showed that the $[M + 1]^+$ peak of compounds **6** is 91 (m/z) more than the corresponding compounds **5**, and the ^{1}H NMR showed extra proton signals at δ 7.15–7.18 (2H, d), 7.23–7.24 (1H, t), 7.30–7.32 (2H, t), and 4.04–4.07 (2H, s), respectively. All these results indicated the presence of a benzyl group in compounds **6**. Comparing with compounds **5**, the aromatic proton signal in the 5-position at δ 7.58–7.65 (1H, t) disappeared, and the aromatic protons in 4- and 6-positions gave very simple signals. For example, the signals at δ 7.57 (dd, 1H, $J = 7.0$, 2.5 Hz), 8.05 (dd, 1H, $J = 7.0$, 2.5 Hz) in **5a** shifted to δ 7.34 (d, 1H, $J = 2.0$ Hz), 7.90 (d, 1H, $J = 2.0$ Hz) in **6a**. The ^{1}H-^{1}H correlated spectroscopy (COSY) spectra showed no correlation between H-4 and H-5 and no correlation between H-6 and H-5. Furthermore, the benzyl proton signal (PhC$\underline{\mathbf{H}}_2$) showed long-range correlations with C-4 and C-6, and 4,6-position protons also showed long-range correlations with the carbon of Ph$\underline{\mathbf{C}}\mathrm{H}_2$ in the heteronuclear multiple-bond correlation (HMBC) experiment. All of the observations strongly indicated that the benzyl group was located in the 5-position of the ring system.

There were four major products in the reaction of cyclization and debenzylation. The structure of these products were assigned as **I**, **II**, **III**, and **IV** (Scheme 2). Compounds **I** and **II** were difficult to purify because of their extraordinary phenolic hydroxyl group instability toward oxygen, but their structures could be determined by indirect ways. When compound **I** was methylated by $(CH_3)_2SO_4/K_2CO_3$/acetone, only one product **V** appeared. Based on the structure of **V**, we could confirm the structure of compound **I**. Structure of **II** was also proved the same way. Oxidation of **III** and **IV** by SeO_2 or air gave corresponding *p*-quinone **VII** and *p*-quinone **VIII** respectively. Based on the ^{1}H NMR spectra of **III**, **IV**, **VII**, and **VIII**, combined with the oxidation mechanisms of phenoloid, it was easy to confirm the structures of **III**, **IV**, **VII**, and **VIII**. Clearly formation of compound **I** and **III** was involved in a electrophilic substitution of benzyl cation generated and attracted to the nucleophilic *ortho*-position of phenol during the Lewis acid–mediated debenzylation of **4**.[11–13]



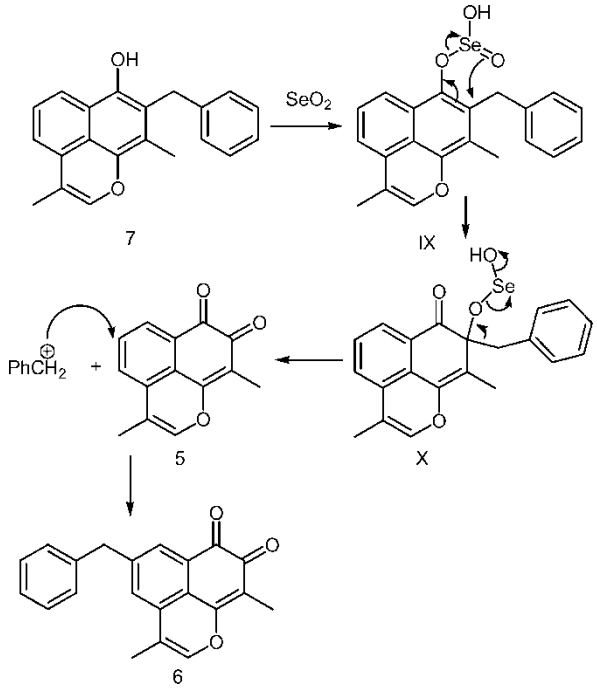
Scheme 2. Products of cyclization, debenzylation, and oxidation reactions of compound **4a**. Reagents and conditions: a, HBF_4/ether, 5°C, 5 min; b, $(CH_3)_2SO_4$/acetone/K_2CO_3, rt, 2 h; c, SeO_2 or air, rt; d, SeO_2, rt.

It was interesting that two products **5a** (39%) and **6a** (12%) were obtained when compound **I** was oxidized by SeO_2. The possible mechanism is proposed as shown in Scheme 3. It is reasonable that the phenol group of compound **I** could form the intermediate **IX** of organoselenium acid ester with SeO_2.[14,15] The intermediate **IX** was easy to transfer to the intermediate **X** by a [2,3]sigmatropic rearrangement.[14,15] Because the benzyl group was a very good leaving group, the benzyl cation was generated simultaneously when the oxygen–selenium bond of **X** split to form *o*-quinone **5a**. The benzyl cation then electrophilicly attacked the nucleophilic 5-position of **5a** by withdrawing the electron effect of 7,8-dione to give corresponding compound **6a**.

The series of analogues of 9-substitued benzo[*de*]chromene-7,8-dione **5b**–**e** and 5-benzyl-9-substitued benzo[*de*]chromene-7,8-dione **6b**–**e** were prepared through a similar way.

When HBF_4 was replaced by PPA (polyphosphoric acid) or TFA (trifluoroacetic acid), the reactions failed to give satisfactory cyclization products, and instead compound **III** and **IV** were formed as the major products. It was clear that PPA and TFA were strong acids and good reagents for debenzylation,[16] but their capability to catalyze the cyclization was insufficient in this reaction.

The in vitro cytotoxicity of Mansonone F (isolated from *Helicteres angustifolia Linn*), benzo[*de*]chromene-7,8-dione (prepared according to literature[4]), 9-substituted benzo[*de*]chromene-7,8-dione compounds **5a**–**e**, and 5-benzyl-9-substitued benzo[*de*]chromene-7,8-dione **6a, 6d, 6e** was evaluated. The growth inhibition effect was assayed using the methyl thiazolyl tetrazolium (MTT) method.[17] The concentration of tested compounds for 50% inhibition (IC_{50}) on human nasopharyngeal carcinoma cell line (CNE2), the human lung adenocarcinoma cell line (GLC-82), and



Scheme 3. Mechanism of oxidation of compound **4a** by selenium dioxide.

Table 1. IC_{50} of Mansonone F and synthetic Mansonone analogous against human cancer cell line

		Human cancer cell and IC_{50} (μM)		
Compound	R	CNE2	Glc-82	A549
10-Hydroxycamptothecin[a]	—	1.04	0.23	3.71
Mansonone F	—	27.34	15.53	15.94
Benzo[*de*]chromene-7,8-dione	H	5.23	4.76	8.58
5a	$-CH_3$	14.90	21.75	17.15
5b	$-CH_2CH_3$	7.20	7.87	14.40
5c	$-CH(CH_3)_2$	14.11	23.04	16.99
5d	$-CH_2Ph$	12.40	10.02	7.51
5e	$-CH_2Ph$-2-Cl	10.72	24.55	25.27
6a	$-CH_3$	12.61	13.98	15.78
6d	$-CH_2Ph$	22.10	24.63	—
6e	$-CH_2Ph$-2-Cl	27.54	29.74	—

[a]10-Hydroxycamptothecin was used as control.

human lung adenocarcinoma cell line (A549) were determined, and the results are summarized in Table 1.

From these assay data, the cytotoxicity of prepared compounds **5** and **6** was similar to that of natural product Mansonone F, indicating that the split 6-methyl or introduction of 5-benzyl and 9-substituted group would not significantly effect the cytotoxicity.

CONCLUSION

In conclusion, we described a method for the synthesis of 6-demethyl-Mansonone analogues of **5a**–**e** and **6a**–**e**. A novel regioselective deacetylation of 2-substituted-1,4-naphthdiyl diacetate was developed, resulting in obtaining the monoacetate in high yield. The mechanisms of formation of **5a**–**e** and **6a**–**e** involving cyclization, debenzylation, and oxidation were discussed. The cytotoxicity of the prepared compounds **5** and **6** were comparable with naturally occurring Mansonone F. The results would provide us some useful information for future structural modification.

EXPERIMENTAL

Melting points were measured on a WRR melting-point apparatus (Shanghai Physical Optical Equipment Manufacturer) or SGW X-4 melting-point apparatus with microscope (Shanghai Physical Optical Equipment Manufacturer), and the thermometer was uncorrected. ^{1}H NMR and ^{13}C NMR were recorded on a Varian Inova 500NB or Mercury-Plus 300 NMR instrument with TMS as internal reference. Mass spectra were recorded on a VG ZAB-HS and Finnigan TSQ Quantum instrument. IR spectra were recorded on Bruker Equinox 55 Fourier transform spectrometer. Elemental analyses were performed by Elementar Vario EL instrument. Silica H (60) was purchased from Qingdao Marine Chemical Manufacturer.

Procedure for the Synthesis of Compound 2

1-Hydroxy-3-methylnaphthalen-4-yl Acetate (**2a**)

Vitamin K_4 (7.8 g, 30 mmol) was dissolved in 120 mL of methanol with stirring, and nitrogen was applied to maintain an inert atmosphere. To this solution was added 2.2 g (30 mmol) *t*-butyl amine and the solution was stirred for 30 min at room temperature. The solution was cooled to 5°C and stirred at this temperature for 5 h, and 3 mL of acetic acid was added to quench the reaction. The reaction mixture was concentrated in vacuo, and ice water was added to the solution to give deep brown oil, which was rapidly solidified. The solid was collected through filtration and redissolved

in 100 mL of chloroform. The organic phase was washed with water (30 mL × 2) and dried with anhydrous sodium sulfate. Removal of the solvent gave brown ropey gum, which could be easily solidified. Washing the solid with CCl_4 gave 6.0 g of **2** as yellow solid, yield 92%. The compound was pure enough for the next step of the reaction. For analytical purposes, the compound could be purified by crystallization from methanol: mp 124.5–125.8°C (lit.[18] mp 124–125°C). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm) 2.08 (3H, s), 2.45 (3H, s), 6.13 (1H, s), 6.25 (1H, b), 7.30 (1H, t, $J = 7$ Hz), 7.42 (1H, t, $J = 7$ Hz), 7.57 (1H, d, $J = 8$ Hz), 7.88 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ) 16.7, 21.1, 111.3, 120.4, 122.5, 124.2, 124.8, 126.7, 127.2, 127.6, 137.5, 149.7, 171.2. IR ν_{max} (KBr)/cm^{-1}: 3350, 3069, 2924, 1718, 1600, 1580, 1520, 1478, 1449, 1368, 1246, 1159, 1079. FAB-MS m/z 217 $[M + 1]^+$. Anal. calcd. for $C_{13}H_{12}O_3$: C, 72.21%; H, 5.59%. Found: C, 72.05%; H, 5.52%.

1-Hydroxy-3-ethylnaphthalen-4-yl Acetate (**2b**)

The compound was prepared from 2-ethyl-1,4-naphthoquinone according to the procedure for **2a**. Yield 85%. White solid, mp 138.5–139.6°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm) 1.18 (3H, t, $J = 8$ Hz), 2.48 (3H, s), 2.53 (2H, q, $J = 8$ Hz), 5.61 (1H, b), 6.46 (1H, s), 7.40 (1H, t, $J = 7$ Hz), 7.46 (1H, t, $J = 7$ Hz), 7.61 (1H, d, $J = 8$ Hz), 7.97 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 14.1, 20.7, 23.4, 109.3, 120.3, 122, 123.7, 124.5, 126.8, 127.3, 132, 136.6, 149.5, 170.8. IR ν_{max} (KBr)/cm^{-1}: 3428, 3065, 2967, 2929, 1727, 1600, 1579, 1517, 1449, 1402, 1369, 1231, 1155, 859, 763, 742. ESI-MS m/z 229 $[M - 1]^-$. Anal. calcd. for $C_{14}H_{14}O_3$: C, 73.03%; H, 6.13%. Found: C, 73.25%; H, 6.05%.

1-Hydroxy-3-isopropylnaphthalen-4-yl Acetate (**2c**)

The compound was prepared from 2-isopropyl-1,4-naphthoquinone according to the procedure for **2a**. Yield 84%. White solid, mp 92.1–94.3°C. ^{1}H NMR (300 MHz, CDCl3, δ, ppm) 1.21 (6H, d, $J = 7$ Hz), 2.52 (3H, s), 3.12 (1H, q, $J = 7$), 6.08 (1H, b), 6.65 (1H, s), 7.39 (1H, t, $J = 8$ Hz), 7.49 (1H, t, $J = 8$ Hz), 7.64 (1H, d, $J = 8$ Hz), 8.05 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 20.7, 22.8, 22.9, 27.5, 106.3, 120.7, 121.9, 123.6, 124.7, 126.8, 127.4, 135.9, 136.3, 149.8, 170.6. IR ν_{max} (KBr)/cm^{-1}: 3454, 3059, 2963, 1732, 1600, 1580, 1517, 1457, 1399, 1370, 1231, 1065, 771, 741. ESI-MS m/z 243 $[M - 1]^-$. Anal. calcd. for $C_{15}H_{16}O_3$: C, 73.75%; H, 6.60%. Found: C, 73.46%; H, 6.59%.

1-Hydroxy-3-phenylnaphthalen-4-yl Acetate (**2d**)

The compound was prepared from 2-phenylpropyl-1,4-naphthoquinone according to the procedure for **2a**. Yield 75%. White solid, mp

127.5–128.9°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm) 2.37 (3H, s), 3.81 (2H, s), 5.87 (1H, b), 6.24 (1H, s), 7.07 (2H, d, $J = 7$ Hz), 7.13 (1H, t, $J = 7$ Hz), 7.19 (2H, t, $J = 7$ Hz), 7.33 (1H, t, $J = 8$ Hz), 7.44 (1H, t, $J = 8$ Hz), 7.60 (1H, d, $J = 8$ Hz), 7.96 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 21.1, 36.6, 110.4, 121, 122.5, 124.4, 125.2, 126.5, 127.3, 127.8, 128.7, 129.2, 129.6, 137.5, 139.8, 150, 170.7. IR ν_{max} (KBr)/cm^{-1}: 3409, 3026, 2922, 1726, 1606, 1495, 1456, 1370, 1234, 1171, 1074, 935, 874, 757, 734, 705. ESI-MS m/z 291 $[M - 1]^-$. Anal. calcd. for $C_{19}H_{16}O_3$: C, 78.06%; H, 5.52%. Found: C, 78.06%; H, 5.82%.

1-Hydroxy-3-(2-chlorophenyl)naphthalen-4-yl Acetate (**2e**)

The compound was prepared from 2-(2-chlorophenyl)-1,4-naphthoquinone according to the procedure for **2a**. Yield 78%, white solid, mp 136.2–137.9°C. ^{1}H NMR (300 MHz, CDCl3, δ, ppm) 2.45 (3H, s), 4.04 (2H, s), 5.55 (1H, b), 6.37 (1H, s), 7.06 (2H, d, $J = 7$ Hz), 7.13 (1H, t, $J = 7$ Hz), 7.16 (1H, t, $J = 7$ Hz), 7.38 (1H, d, $J = 7$ Hz), 7.44 (1H, t, $J = 8$ Hz), 7.52 (1H, t, $J = 8$ Hz), 7.66 (1H, d, $J = 8$ Hz), 8.06 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 21.1, 33.8, 110.2, 121, 122.5, 124.5, 125.3, 127, 127.3, 127.8, 128, 128.2, 129.5, 131.1, 134.2, 137.4, 137.8, 150, 170.8 . IR ν_{max} (KBr)/cm^{-1}: 3449, 1719, 1600, 1580, 1518, 1471, 1439, 1397, 1371, 1236, 1154, 1073, 857, 759. ESI-MS m/z 325 $[M - 1]^-$. Anal. calcd. for $C_{19}H_{15}ClO_3$: C, 69.84%; H, 4.63%. Found: C, 69.81%; H, 4.90%.

Procedure for the Synthesis of Compound 3

1-(Benzyloxy)-3-methylnaphthalen-4-yl Acetate (**3a**)

To a solution of 4.32 g (20 mmol) **2a** in 100 mL of acetone was added 3.76 g (22 mmol) benzyl bromine and 11 g (80 mmol) of grinded anhydrous potassium carbonate. Nitrogen was applied to maintain an inert atmosphere. The reaction mixture was stirred for 5 h at room temperature and was concentrated in vacuo. The solid was separated by filtration and was thoroughly washed with acetone. The filtrate was concentrated to give a yellow brown solid. Washing with hexane gave a yellow solid (5.81 g, 95% yield). The compound was pure enough for the next step of the reaction. For analytical purposes, the compound could be recrystallized in methanol: mp 103.8–104.9°C. (lit.[19] mp 105–107°C). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm) 2.30 (3H, s), 2.46 (3H, s), 5.21 (2H, s), 6.72 (1H, s), 7.34 (1H, tt, $J = 7$, 1.5 Hz), 7.38–7.52 (6H, m), 7.66 (1H, d, $J = 8$ Hz), 8.27 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 17.3, 21.0, 70.7, 107.9, 120.7, 122.8, 125.2, 125.4, 126.4, 127.4, 127.7, 128.0, 128.2, 128.8, 137.2, 138.1, 152.5, 169.6. IR ν_{max} (KBr)/cm^{-1}: 3034, 2923, 2873, 1761, 1635, 1600, 1584, 1505, 1455, 1360, 1199, 1156, 1110, 1085, 773, 749, 698. FAB-MS m/z

306 [M^+]. Anal. calcd. for $C_{20}H_{18}O_3$: C, 78.41%; H, 5.92%. Found: C, 78.63%; H, 5.96%.

1-(Benzyloxy)-3-ethylnaphthalen-4-yl Acetate (**3b**)

The compound was prepared from **2b** according to the procedure for **3a**. Yield 94%. White solid, mp 85.8–86.8°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.24 (3H, t, $J = 8$ Hz), 2.45 (3H, s), 2.64 (2H, q, $J = 8$ Hz), 5.22 (2H, s), 6.76 (1H, s), 7.34 (1H, tt, $J = 7$, 1.5 Hz), 7.41 (2H, tt, $J = 7$, 1.5 Hz), 7.42 (1H, td, $J = 8$, 1.5 Hz), 7.49 (1H, td, $J = 8$, 1.5 Hz), 7.52 (2H, d, $J = 7$ Hz), 7.65 (1H, dd, $J = 8$, 1.5 Hz), 8.29 (1H, dd, $J = 8$, 1.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 14.4, 20.6, 23.9, 70.2, 105.9, 120.5, 122.3, 124.7, 125, 126.9, 127.3(2c), 127.6, 127.8, 128.4(2c), 131.7, 136.8, 137, 152.4, 169.5. IR ν_{max} (KBr)/cm^{-1}: 3034, 2969, 2934, 1759, 1599, 1506, 1458, 1369, 1207, 1159, 771, 752, 698. ESI-MS m/z 343 $[M + Na]^+$. Anal. calcd. for $C_{21}H_{20}O_3$: C, 78.73%; H, 6.29%; Found: C, 78.99%; H, 6.46%.

1-(Benzyloxy)-3-isopropylnaphthalen-4-yl Acetate (**3c**)

The compound was prepared from **2c** according to the procedure for **3a**. Yield 94%. White solid, mp 89.2–89.5°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.26 (6H, d), 2.47 (3H, s), 3.17 (1H, d, $J = 7$ Hz), 5.24 (2H, s), 6.81 (1H, s), 7.35 (1H, tt, $J = 7$, 1.5 Hz), 7.42 (2H, tt, $J = 7$, 1.5 Hz), 7.43 (1H, td, $J = 8$, 1.5 Hz), 7.50 (1H, td, $J = 8$, 1.5 Hz), 7.53 (2H, d, $J = 7$ Hz), 7.65 (1H, dd, $J = 8$, 1.5 Hz), 8.29 (1H, dd, $J = 8$, 1.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 20.7, 23, 23, 27.8, 70.3, 102.9, 120.7, 122.3, 124.9, 124.9, 127, 127.4, 127.6, 127.8, 128.4, 136, 136.1, 136.9, 152.7, 169.6. IR ν_{max} (KBr)/cm^{-1}: 3068, 2960, 2871, 1762, 1599, 1507, 1464, 1365, 1199, 1156, 1075, 770, 740, 694. ESI-MS m/z 357 $[M + Na]^+$. Anal. calcd. for $C_{22}H_{22}O_3$: C, 79.02%; H, 6.63%. Found: C, 79.30%; H, 6.78%.

1-(Benzyloxy)-3-phenylnaphthalen-4-yl Acetate (**3d**)

The compound was prepared from **2d** according to the procedure for **3a**. Yield 98%. White solid, mp 88.8–89.3°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.41 (3H, s), 4.00 (2H, s), 5.11 (2H, s), 6.63 (1H, s), 7.18 (2H, d, $J = 7$ Hz), 7.21 (1H, tt, $J = 7$, 1.5 Hz), 7.28 (2H, t, $J = 7$ Hz), 7.33 (1H, tt, $J = 7$, 1.5 Hz), 7.37 (2H, t, $J = 7$ Hz), 7.43 (2H, d, $J = 7$ Hz), 7.45 (1H, td, $J = 8$, 1 Hz), 7.51 (1H, td, $J = 8$, 1 Hz), 7.68 (1H, dd, $J = 8$, 1 Hz), 8.29 (1H, dd, $J = 8$, 1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 20.6, 36.6, 70.2, 106.9, 120.7, 122.4, 125.1, 125.3, 126.1, 127.1, 127.3, 127.6, 127.8, 128.4(4c), 128.8, 128.8(2c), 136.6, 137.7, 139.5, 152.3, 169.4. IR ν_{max} (KBr)/cm^{-1}: 3025, 2947, 1753, 1602, 1494, 1455, 1368, 1207, 1157, 1116, 1082, 897, 847, 770, 732, 698. ESI-MS m/z 405 $[M + Na]^+$. Anal. calcd. for $C_{26}H_{22}O_3$: C, 81.65%; H, 5.80%. Found: C, 81.88%; H, 5.89%.

1-(Benzyloxy)-3-(2-chlorophenyl)naphthalen-4-yl Acetate (**3e**)

This compound was prepared from **2e** according to the procedure for **3a**. Yield 96%. White solid, mp 116.4–117.5°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.40 (3H, s), 4.11 (2H, s), 5.10 (2H, s), 6.59 (1H, s), 7.06 (1H, dd, $J = 7$, 1.5 Hz), 7.12 (1H, td, $J = 7$, 1.5 Hz), 7.15 (1H, td, $J = 7$, 1.5 Hz), 7.33 (1H, tt, $J = 7$, 1.5 Hz), 7.35 (2H, tt, $J = 7$, 1.5 Hz), 7.37 (1H, td, $J = 8$, 1.5 Hz), 7.41 (2H, dd, $J = 7$, 1.5 Hz), 7.45 (1H, td, $J = 8$, 1.5 Hz), 7.51 (1H, td, $J = 8$, 1.5 Hz), 7.67 (1H, dd, $J = 8$, 1.5 Hz), 8.30 (1H, dd, $J = 8$, 1.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 20.6, 33.8, 70.2, 106.7, 120.7, 122.4, 125.2, 125.4, 126.7, 127.1, 127.2(2C), 127.5, 127.6, 127.7, 128.3(3C), 129.2, 130.7, 133.9, 136.5, 137.1, 137.9, 152.3, 169.3. IR ν_{max} (KBr)/ cm^{-1}: 3065, 3032, 2941, 1753, 1602, 1447, 1369, 1213, 1156, 1081, 920, 856, 760, 740, 698. ESI-MS m/z 439 $[M + Na]^+$. Anal. calcd. for $C_{26}H_{21}ClO_3$: C, 74.91%; H, 5.08%. Found: C, 74.92%; H, 5.22%.

Procedure for the Synthesis of Compound 4

1-(1-(Benzyloxy)-3-methylnaphthalen-4-yloxy)propan-2-one (**4a**)

Sodium hyposulphite (7 g, 40 mmol) and 3.2 g (80 mmol) of sodium hydroxide were added to a solution of 6.12 g (20 mmol) **3a** in 120 mL of methanol/water (2 : 1). The reaction mixture was refluxed for 1 h with stirring and was concentrated in vacuo. Ice water (100 mL) was added, and the pH value was adjusted to 4–5 with 5% hydrochloric acid. The thus-formed pink solid was collected through vacuum filtration and was re-dissolved in ether. The organic phase was washed with water (30 ml × 2) and was dried with anhydrous sodium sulfate. Removal of the solvent gave 4.85 g of brown solid, which was pure enough for the next step of the reaction without further purification.

To a solution of this solid (4.85 g, 18.4 mmol) in 100 mL of actone, 2.04 g (22 mmol) chloroacetone, 7.62 g (55 mmol) grinded anhydrous potassium carbonate, and 0.25 g potassium iodide were added. Nitrogen was applied to maintain an inert atmosphere, and the reaction mixture was stirred for 5 h at room temperature. The solvent was then removed in vacuo, and 100 mL of water was added. The mixture was extracted with ether (30 mL × 3), washed with water (30 mL × 2), and dried with anhydrous sodium sulfate. Removal of the solvent gave brown solid. Washing the solid with methanol gave 4.6 g (two steps, 72% yield) of **4a** as yellowish brown solid. The compound could be used directly in the next step without purification. For analytical purposes, the sample could be recrystallized from methanol: mp 102.6–104.9°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm) 2.39 (3H, s), 2.42 (3H, s), 4.49 (2H, s), 5.19 (2H, s), 6.67 (1H, s), 7.33 (1H, tt, $J = 7$, 1.5 Hz), 7.38–7.44 (3H, m), 7.47–7.52 (3H, m), 7.93 (1H, d, $J = 8$ Hz), 8.26 (1H,

d, $J = 7$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 16.6, 26.7, 70.2, 78.0, 107.9, 120.9, 122.5, 124.7, 125.3, 125.5, 126.8, 127.2, 127.8(2C), 128.2, 128.4(2C), 136.9, 144.9, 151.0, 204.8. IR ν_{max} (KBr)/cm^{-1}: 3056, 2917, 2873, 1740, 1632, 1598, 1493, 1460, 1398, 1376, 1354, 1266, 1233, 1091, 1064, 764, 708. FAB-MS m/z 320 [M^+, 10], 229 [M^+-$PhCH_2$, 20], 91 [$PhCH_2^+$, 100]. Anal. calcd. for $C_{21}H_{20}O_3$: C, 78.73%; H, 6.29%. Found: C, 78.76%; H, 6.32%.

1-(1-(Benzyloxy)-3-ethylnaphthalen-4-yloxy)propan-2-one (**4b**)

The compound was prepared from **3b** according to the procedure for **4a**. Yield 59%. White solid, mp 77.6–78.3°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.29 (3H, t, $J = 7.5$ Hz), 2.40 (3H, s), 2.81 (2H, q, $J = 7.5$ Hz), 4.51 (2H, s), 5.22 (2H, s), 6.73 (1H, s), 7.36 (1H, tt, $J = 7$, 1.5), 7.42 (2H, t, $J = 7$ Hz), 7.44 (1H, td, $J = 8$, 1.5 Hz), 7.51 (1H, td, $J = 8$, 1.5 Hz), 7.53 (2H, d, $J = 7$ Hz), 7.95 (1H, d, $J = 8$ Hz), 8.29 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) δ 15.2, 23.2, 26.7, 70.3, 78.8, 106.4, 121, 122.4, 124.8, 125.4, 126.7, 127.3, 127.8, 128.2, 128.4, 131.8, 136.9, 144.3, 151.2, 204.8. IR ν_{max} (KBr)/cm^{-1}: 3068, 2970, 2874, 1725, 1595, 1502, 1461, 1375, 1265, 1234, 1161, 1097, 983, 838, 759, 700. ESI-MS m/z 357 $[M + Na]^+$. Anal. calcd. for $C_{22}H_{22}O_3$: C, 79.02%; H, 6.63%. Found: C, 78.83%; H, 6.71%.

1-(1-(Benzyloxy)-3-isopropylnaphthalen-4-yloxy)propan-2-one (**4c**)

The compound was prepared from **3c** according to the procedure for **4a**. Yield 71%. White solid, mp 111.0–111.9°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.27 (6H, d, $J = 7.5$ Hz), 2.39 (3H, s), 3.52 (1H, sept, $J = 7$ Hz), 4. 49 (2H, s), 5.23 (2H, s), 6.76 (1H, s), 7.35 (1H, t, $J = 7$ Hz), 7.40 (2H, t, $J = 7$ Hz), 7.42 (1H, t, $J = 8$ Hz), 7.50 (1H, t, $J = 8$ Hz), 7.52 (2H, d, $J = 7$ Hz), 7.93 (1H, d, $J = 8$ Hz), 8.28 (1H, d, $J = 8$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 23.6, 26.6, 26.7, 70.3, 79.1, 103.3, 121.2, 122.4, 124.8, 125.3, 126.7, 127.3, 127.8, 128.1, 128.4, 136.2, 136.9, 143.3, 151.5, 204.7. IR ν_{max} (KBr)/cm^{-1}: 3072, 2964, 2932, 2874, 1738, 1597, 1504, 1457, 1394, 1372, 1234, 1158, 1091, 980, 842, 765, 703. ESI-MS m/z 371 $[M + Na]^+$. Anal. calcd. for $C_{23}H_{24}O_3$: C, 79.28%; H, 6.94%. Found: C, 79.07%; H, 6.98%.

1-(1-(Benzyloxy)-3-phenylnaphthalen-4-yloxy)propan-2-one (**4d**)

The compound was prepared from **3d** according to the procedure for **4a**. Yield 65%. White solid, mp 83.1–84.6°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.25 (3H, s), 4.16 (2H, s), 4.37 (2H, s), 5.13 (2H, s), 6.64 (1H, s), 7.16–7.20 (3H, m), 7.26 (2H, tt, $J = 7$, 1 Hz), 7.33 (1H, tt, $J = 7$, 1 Hz), 7.38 (2H, tt, $J = 7$, 1 Hz), 7.44–7.47 (3H, m), 7.52 (1H, td, $J = 8$, 1 Hz), 7.95 (1H, dd, $J = 8$, 1 Hz), 8.31 (1H, dd, $J = 8$, 1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 26.5, 36.1, 70.2, 78.6, 107.6, 121.1, 122.5, 125.1, 125.7, 126, 126.8,

127.3(2C), 127.7, 128.2, 128.4(3C), 128.5, 128.6(2C), 136.7, 140.3, 145.1, 151, 204.3. IR ν_{max} (KBr)/cm^{-1}: 3063, 3032, 2917, 2874, 1724, 1596, 1496, 1455, 1359, 1232, 1155, 1093, 980, 847, 763, 706. ESI-MS m/z 419 $[M + Na]^+$. Anal. calcd. for $C_{27}H_{24}O_3$: C, 81.79%; H, 6.10%. Found: C, 82.05%; H, 6.16%.

1-(1-(Benzyloxy)-3-(2-chlorophenyl)naphthalen-4-yloxy) propan-2-one (**4e**)

The compound was prepared from **3e** according to the procedure for **4a**. Yield 78%. White solid, mp 99.7–100.3°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.31 (3H, s), 4.26 (2H, s), 4.45 (2H, s), 5.11 (2H, s), 6.57 (1H, s), 7.03 (1H, dd, $J = 7$, 2 Hz), 7.12 (1H, td, $J = 7$, 1.5 Hz), 7.17 (1H, td, $J = 7$, 2 Hz), 7.32 (1H, tt, $J = 7$, 1 Hz), 7.36 (2H, tt, $J = 7$, 1.5 Hz), 7.39 (1H, dd, $J = 7$, 1.5 Hz), 7.43 (2H, d, $J = 7$ Hz), 7.47 (1H, td, $J = 8$, 1 Hz), 7.54 (1H, td, $J = 8$, 1 Hz), 7.96 (1H, dd, $J = 8$, 1 Hz), 8.31 (1H, dd, $J = 8$, 1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm) 26.6, 33.5, 70.2, 78.5, 107.2, 121.2, 122.6, 125.2, 125.9, 126.8, 126.9, 127.2, 127.3(2C), 127.5, 127.7, 128.2, 128.4(2C), 129.3, 130.5, 134, 136.7, 137.8, 145.2, 151.1, 204.5. IR ν_{max} (KBr)/cm^{-1}: 3061, 2935, 2910, 2881, 1734, 1594, 1503, 1465, 1391, 1359, 1264, 1231, 1183, 1157, 1089, 980, 847, 755, 703. ESI-MS m/z 453 $[M + Na]^+$. Anal. calcd. for $C_{27}H_{23}ClO_3$: C, 75.25%; H, 5.38%. Found: C, 75.45%; H, 5.50%.

Procedure for the Synthesis of Compounds 5 and 6

3,9-Dimethylbenzo[*de*]chromene-7,8-dione (**5a**) and 5-Benzyl-3, 9-dimethylbenzo[*de*]chromene-7,8-dione (**6a**)

Compound **4a** (4 g, 12.5 mmol) was dissolved in 40 mL of dichloromethane, and the mixture was cooled to 5°C. To this solution, 18 mL of ice-cooled tetrafluoroboric acid/ether solution (anhydrous, 58% HBF_4 in ether) were added under vigorous stirring. After 5 min, 50 mL of water were added and the organic layer was separated. The aqueous layer was extracted with dichloromethane (30 mL × 2). The organic layer was combined, washed with water (30 mL × 2), and dried with anhydrous sodium sulfate. The solution was concentrated, and the residue was redissolved in 80 mL of chloroform. Selenium dioxide (8.2 g, 75 mmol) was added, and the solution was stirred overnight at room temperature. The solid was removed, and the organic solution was concentrated to give 4.5 g of a purple solid. The crude product was purified by chromatography (chloroform/methanol 5 : 1) to give a purple-black solid as the final product **5a**[20] (1.10 g, 39% yield). Mp 205–207°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.97 (3H, s), 2.11 (3H, d, $J = 1.5$ Hz), 7.06 (1H, q, $J = 1.5$ Hz), 7.57 (1H, dd, $J = 7$, 2.5 Hz), 7.58 (1H, t, $J = 7$ Hz),

8.05 (1H, dd, $J = 7$, 2.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm) 8.1, 13.4, 112.6, 114.1, 127.0, 128.9, 129.5, 130.9, 131.2, 132.4, 141.5, 161.8, 178.3, 179.7. IR ν_{max} (KBr)/cm^{-1}: 3444, 2923, 1695, 1654, 1599, 1571, 1494, 1452, 1378, 1334, 1276, 1200, 1141, 758, 701. FAB-MS m/z 227 $[M + 1]^+$. Anal. calcd. for $C_{14}H_{10}O_3$: C, 74.33%; H, 4.46%. Found: C, 74.29%; H, 4.36%.

Compound **6a** was also isolated from the reaction mixture: purple-black solid, 0.45 g, yield 12%. Mp 145–147°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.94 (3H, s), 2.04 (3H, d, $J = 1$ Hz), 4.04 (2H, s), 7.02 (1H, q, $J = 1$ Hz), 7.18 (2H, dd, $J = 7$, 1.5 Hz), 7.24 (1H, tt, $J = 7$, 1.5 Hz), 7.31 (2H, td, $J = 7$, 1.5 Hz), 7.34 (1H, d, $J = 2$ Hz), 7.90 (1H, d, $J = 2$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$, δ, ppm) 7.5, 12.8, 41.9, 112.2, 113.1, 121.6, 126.9, 128.8(3C), 128.9(2C), 129.1, 131.2, 131.4, 138.8, 141.3, 146.2, 161.7, 178.1, 179.8. IR ν_{max} (KBr)/cm^{-1}: 2922, 1693, 1631, 1606, 1579, 1494, 1437, 1375, 1277, 1180, 846, 757, 710. FAB-MS m/z 317 $[M + 1]^+$. Anal. calcd. for $C_{21}H_{16}O_3$: C, 79.73%; H, 5.10%. Found: C, 79.91%; H, 5.08%.

9-Ethyl-3-methylbenzo[*de*]chromene-7.8-dione (**5b**) and
5-Benzyl-9-ethyl-3-methylbenzo[*de*]chromene-7,8-dione (**6b**)

Compound **5b** was prepared from **4b** according to the procedure for **5a**: yield 16%, purple-black solid. Mp 145–147°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.08 (3H, t, $J = 7$ Hz), 2.11 (3H, s), 2.51 (2H, q, $J = 7$ Hz), 7.06 (1H, s), 7.55 (1H, d, $J = 6$ Hz), 7.58 (1H, t, $J = 7$ Hz), 8.04 (1H, dd, $J = 6$, 2.5 Hz). IR ν_{max} (KBr)/cm^{-1}: 2971, 2931, 1693, 1626, 1597, 1574, 1457, 1365, 1334, 1278, 1196, 1169, 1140, 866, 785. FAB-MS m/z 241 $[M + 1]^+$. Anal. calcd. for $C_{15}H_{12}O_3$: C, 74.99%; H, 5.03%. Found: C, 75.21%; H, 4.85%.

Compound **6b** was also isolated from the reaction mixture: yield 6%, purple-black solid. Mp 106–110°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.05 (3H, t, $J = 7$ Hz), 2.05 (3H, s), 2.47 (2H, q, $J = 7$ Hz), 4.03 (2H, s), 7.03 (1H, s), 7.17 (2H, d, $J = 7$ Hz), 7.24 (1H, t, $J = 7$ Hz), 7.31 (2H, t, $J = 7$ Hz), 7.35 (1H, d, $J = 1$ Hz), 7.92 (1H, d, $J = 1$ Hz). IR ν_{max} (KBr) cm^{-1}: 3061, 3027, 2967, 1695, 1652, 1602, 1572, 1493, 1453, 1375, 1336, 1277, 1178, 1092, 765, 700. FAB-MS m/z 331 $[M + 1]^+$. Anal. calcd. for $C_{22}H_{18}O_3$: C, 79.98%; H, 5.49%. Found: C, 80.23%; H, 5.38%.

9-Isopropyl-3-methylbenzo[*de*]chromene-7,8-dione (**5c**) and
5-Benzyl-9-isopropyl-3-methylbenzo[*de*]-chromene-7,8-dione (**6c**)

Compound **5c** was prepared from **4c** according to the procedure for **5a**: yield 16%, purple-black solid. Mp 154–157°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.26 (6H, d, $J = 7.0$ Hz), 2.11 (3H, d, $J = 1.5$ Hz), 3.38 (1H, d,

$J = 7.0$ Hz), 7.06 (1H, q, $J = 1.5$ Hz), 7.57 (2H, m), 8.06 (1H, dd, $J = 6$, 2.5 Hz). IR ν_{max} (KBr) cm^{-1}: 3067, 2971, 2926, 1694, 1630, 1597, 1557, 1455, 1376, 1357, 1325, 1192, 1137, 885, 788, 753. FAB-MS m/z 255 $[M + 1]^+$. Anal. calcd. for $C_{16}H_{14}O_3$: C, 75.57%; H, 5.55%. Found: C, 75.49%; H, 5.34%.

Compound **6c** was also isolated from the crude product: yield 7%, purple-black solid. Mp 137–140°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.25 (6H, d, $J = 7$ Hz), 2.06 (3H, s), 3.36 (1H, sept, $J = 7$ Hz), 4.05 (2H, s), 7.04 (1H, s), 7.16 (2H, d, $J = 7$ Hz), 7.24 (1H, t, $J = 7$ Hz), 7.31 (2H, t, $J = 7$ Hz), 7.35 (1H, d, $J = 1.5$ Hz), 7.92 (1H, d, $J = 1.5$ Hz). IR ν_{max} (KBr) cm^{-1}: 3062, 3027, 2957, 1695, 1628, 1604, 1555, 1494, 1453, 1378, 1332, 1280, 1178, 1112, 1068, 754, 705. FAB-MS m/z 345 $[M + 1]^+$. Anal. calcd. for $C_{23}H_{20}O_3$: C, 80.21%; H, 5.85%. Found: C, 80.05%; H, 5.88%.

9-Benzyl-3-methylbenzo[*de*]chromene-7,8-dione (**5d**) and
5,9-Dibenzyl-3-methylbenzo[*de*]chromene-7,8-dione (**6d**)

Compound **5d** was prepared from **4d** according to the procedure for **5a**: yield 11%, purple-black solid. Mp 136–139°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.11 (3H, d, $J = 1$ Hz), 3.85 (2H, s), 7.09 (1H, q, $J = 1.5$ Hz), 7.15 (1H, tt, $J = 7$, 1.5 Hz), 7.23 (2H, t, $J = 7$ Hz), 7.34 (2H, d, $J = 7$ Hz), 7.56 (1H, dd, $J = 7$, 1.5 Hz), 7.60 (1H, t, $J = 8$ Hz), 8.06 (1H, dd, $J = 7$, 1.5 Hz). IR ν_{max} (KBr)/cm^{-1}: 1694, 1631, 1598, 1565, 1492, 1473, 1453, 1363, 1333, 1275, 1208, 1139, 758, 703. FAB-MS m/z 303 $[M + 1]^+$. Anal. calcd. for $C_{20}H_{14}O_3$: C, 79.46%; H, 4.67%. Found: C, 79.69%; H, 4.55%.

Compound **6d** was also isolated from the crude product: yield 8%, purple-black solid. Mp 191–194°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.05 (3H, d, $J = 1.5$ Hz), 3.83 (2H, s), 4.05 (2H, s), 7.07 (1H, q, $J = 1$ Hz), 7.14 (1H, tt, $J = 6$, 1.5 Hz), 7.15 (2H, d, $J = 6$ Hz), 7.21 (2H, t, $J = 6$ Hz), 7.23 (1H, tt, $J = 6$, 1.5 Hz), 7.30 (2H, t, $J = 7$ Hz), 7.33 (2H, d, $J = 7$ Hz), 7.36 (1H, d, $J = 2$ Hz), 7.94 (1H, d, $J = 1.5$ Hz). IR ν_{max} (KBr)/cm^{-1}: 3026, 1697, 1629, 1605, 1574, 1493, 1452, 1362, 1335, 1278, 1242, 1169, 702. FAB-MS m/z 393 $[M + 1]^+$. Anal. calcd. for $C_{27}H_{20}O_3$: C, 82.63%; H, 5.14%. Found: C, 82.85%; H, 5.13%.

9-(2-Chlorobenzyl)-3-methylbenzo[*de*]chromene-7,8-dione (**5e**) and
5-Benzyl-9-(2-chlorobenzyl)-3-methylbenzo[*de*]chromene-7,8-dione (**6e**)

Compound **5e** was prepared from **4e** according to the procedure for **5a**: yield 7%, purple-black solid. Mp 197–199°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) δ 2.11 (3H, d, $J = 1$ Hz), 3.99 (2H, s), 7.05 (1H, q, $J = 1$ Hz), 7.10 (2H, m), 7.23 (1H, dd, $J = 6$, 3.5 Hz), 7.33 (1H, dd, $J = 6$, 3 Hz), 7.61 (1H, d, $J = 7$ Hz), 7.65 (1H, t, $J = 8$ Hz), 8.13 (1H, d, $J = 7$ Hz). IR ν_{max}

(KBr)/cm^{-1}: 1696, 1630, 1598, 1565, 1472, 1439, 1362, 1335, 1272, 1207, 1161, 1139, 942, 853, 764. FAB-MS m/z 337 $[M+1]^+$. Anal. calcd. for $C_{20}H_{13}ClO_3$: C, 71.33%; H, 3.89%. Found: C, 71.12%; H, 3.95%.

Compound **6e** was also isolated from the crude product: yield 3%, purple-black solid. Mp 192–195°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) δ 2.05 (3H, d, $J = 1$ Hz), 3.97 (2H, s), 4.07 (2H, s), 7.03 (1H, q, $J = 1$ Hz), 7.08 (1H, t, $J = 6$ Hz), 7.09 (1H, t, $J = 6$ Hz), 7.18 (2H, d, $J = 7$ Hz), 7.22 (1H, dd, $J = 6$, 3.5 Hz), 7.24 (1H, tt, $J = 7$, 1.5 Hz), 7.32 (3H, m), 7.39 (1H, s), 7.98 (1H, s). IR ν_{max} (KBr)/cm^{-1}: 1696, 1632, 1604, 1575, 1493, 1470, 1440, 1368, 1336, 1278, 1224, 1173, 753, 704. FAB-MS m/z 427 $[M+1]^+$. Anal. calcd. for $C_{27}H_{19}ClO_3$: C, 75.97%; H, 4.49%. Found: C, 75.78%; H, 4.61%.

1-Methylbenzo[*de*]chromene-7,8-dione

Produced as in the literature[4]: purple-black solid. Mp 235–237°C. ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 2.15 (3H, d, $J = 1.5$ Hz), 6.06 (1H, s), 7.06 (1H, q, $J = 1.5$ Hz), 7.66 (1H, d, $J = 8$ Hz), 7.72 (1H, t, $J = 8$ Hz), 8.16 (1H, d, $J = 8$ Hz). IR ν_{max} (KBr)/cm^{-1}: 3087, 1696, 1622, 1601, 1569, 1555, 1473, 1369, 1279, 1205, 1133, 845, 771. ESI-MS m/z 213 $[M+1]^+$. Anal. calcd. for $C_{13}H_8O_3$: C, 73.58%; H, 3.80%. Found: C, 73.81%; H, 3.75%.

8-Benzyl-7-methoxy-3,9-dimethylbenzo[*de*]chromene (**V**)

Compound **I** was prepared from **4a** and subjected to flash chromatography (silica, ethyl acetate–petroleum ether, 1 : 8) under N_2, after concentration of the appropriate fraction under vacuum at room temperature. A pale brown solid was obtained. Immediately, compound **II** (320 mg, 1.05 mmol), acetone (5 mL), dimethyl sulfate (400 mg, 3.15 mmol), and anhydrous potassium carbonate (870 mg, 6.30 mmol) were stirred under N_2 at room temperature for 2 h. Compound II disappeared, and a new bright green dot was observed by thin-layer chromatography (TLC) in UV365 ($R_F = 0.29$, petroleum ether). Acetone was concentrated in vacuo. Water was added and then extracted with $CHCl_3$, and the product was washed once with H_2O, dried (Na_2SO_4), filtered, and evaporated in vacuo to yield a crude residue. The residue was purified by flash chromatography (silica, petroleum ether) to afford compound **III** (285 mg, yield 86%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm) 1.85 (3H, d, $J = 1$ Hz), 2.06 (3H, s), 3.72 (3H, s), 4.22 (2H, s), 6.66 (1H, d, $J = 8$ Hz), 6.70 (1H, d, $J = 1$ Hz), 7.08–7.22 (5H, m), 7.26 (1H, t, $J = 8$ Hz), 7.56 (1H, d, $J = 8$ Hz). ESI-MS m/z 317 $[M+1]^+$.

7-Methoxy-3,9-dimethylbenzo[*de*]chromene (**VI**)

Compound **VI** was prepared from **4a** according to the procedure for Compound **V**: yield 82%, white solid.[20] ^{1}H NMR (500 MHz, $CDCl_3$, δ, ppm) 1.85 (3H, d, $J = 1$ Hz), 2.25 (3H, s), 3.92 (3H, s), 6.60 (1H, s), 6.68 (2H, m), 7.20 (1H, t, $J = 8.5$ Hz), 7.63 (1H, t, $J = 8.5$ Hz), 7.56 (1H, d, $J = 8$ Hz). ESI-MS m/z 227 $[M + 1]^+$.

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