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Synthesis of fused chromene-1,4-naphthoquinones via ring-closing metathesis and Knoevenagel-electrocyclization under acid catalysis and microwave irradiation

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ABSTRACT

Two complementary methodologies involving olefin ring-closing metathesis and Knoevenagel-electrocyclization were utilized for the synthesis of α-xyloidones and fused chromene-1,4-naphthoquinones **5f**–**n** and **6**. The latter methodology was performed under acid catalysis or microwave irradiation allowing the synthesis of α-xyloidones **5f**–**j** in moderate to good yield, which could not be obtained via the Knoevenagel-electrocyclization method. On the other hand, the lawsone bis-alkylation (*C* and *O*) then RCM olefin enabled the preparation of simple xyloidone **5m**–**n** and the oxepin-1,4-naphthoquinones **6**.

1. Introduction

The 2*H*-chromene moiety is often found in natural products that exhibit biological activity.[1,2] The biological properties of this class include apoptotic,[3,4] anti-HIV,[5,6] estrogen receptor modulating,[7] antibacterial,[8] tripanocidal,[9] and leischmanicidal[10] activities. An important family are compounds containing chromenes coupled with *ortho*- and *para*-quinones, and these have been isolated from many types of plants, fungi, and insects.[11] For example, 3,4-dihydro-α-lapachone (**1**), and its isomer 3,4-dihydro-β-lapachone (**2**) are the most important members of this class of chromenes. Generally, these pyranonaphthoquinones are obtained in small quantities from plant extracts along with lapachol (**3**) (Fig. 1).[12] They are primarily isolated from the Central and South American lapacho tree (*Tabebuia avellanedae*) as 1,2- and 1,4-naphthoquinone moieties but can also be obtained from the stems of *Catalpa ovate*.[13] The xyloidones present different types of biological activity such as antibiotic activity against gram-negative bacteria of the genus Brucella,[14] strong antibacterial activity against multidrug resistant strains of *Staphylococcus aureus*[15] and antimycotic activity against fungal pathogens of plants.[13]

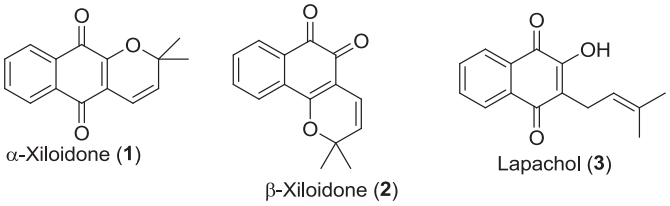

Fig. 1. Natural 1,4- and 1,2-naphthoquinones.

The wide range of important biological activities of these molecules has stimulated further research into the synthesis of natural and synthetic benzochromenes coupled with *ortho*- and *para*-quinone derivatives. Indeed, several synthetic approaches have been reported for the preparation of these compounds. One of the first reported syntheses of α-xyloidone (**1**) was described by Dudley and Chiang, and they performed an oxidative 6π-electrocyclization of isolapachol with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene to obtain a mixture of **1** and **2**.[16] Later, Ferreira and co-workers[17] reported the Knoevenagel condensations of

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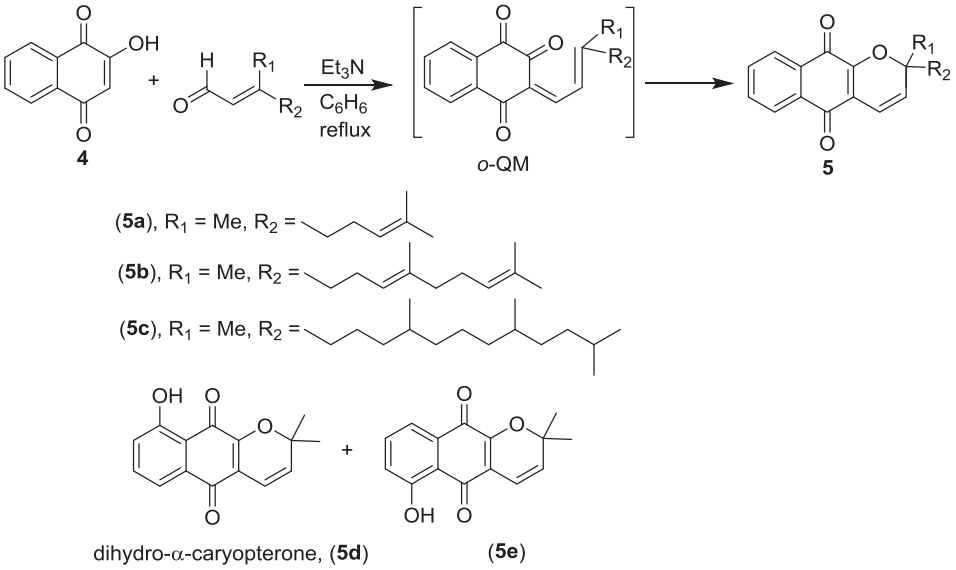
lawsone (**4**) under basic conditions with α,β-unsaturated aldehydes to generate an *ortho*-quinone methide (*o*-QM), which yielded α-xyloidone analogues **5a**–**c** in 33% yield after 6π-electrocyclization. The same synthetic route and conditions were used by Oliveira and co-workers for the preparation of the naturally occurring dihydro-α-caryopterone (**5d**) and its isomer 6-hydroxy-dehydro-α-lapachone (**5e**, Scheme 1).[18]

Initially, the reactions were performed using conventional heating under reflux; a mixture of lawsone (**4**) and aldehyde in a solution of EtOH/H_2O was refluxed for 6–24 h to give chromenes **5f**–**j**. However, good results were only obtained in entry 1 (Table 1). In the other examples tested, it was observed by TLC that the desired



Scheme 1. Synthesis of xyloidones **5a**–**e** from lawsone (**4**) via *o*-QM.

Lee and co-workers reinvestigated the electrocyclization reaction of **4** for R_1=R_2=Me under basic and Lewis acid catalysis. The best result was achieved with ethylenediamine diacetate 10 mol % in refluxing benzene (80%).[19,20] The same group used this methodology for the synthesis of (±)-rhinacanthin, an important new therapeutic target for the treatment of cancer.[21] Muller and co-workers also used this methodology for preparing α-xyloidone analogues in modest to good yield using β-alanine as the base.[22] Snieckus[23] and co-workers used phenylboronic acid and glacial acetic acid as the catalysts for the reaction with R_1=R_2=H to obtain a product with the chromene moiety fused with the 1,4-naphthoquinone system in 50% yield after 1 h in refluxing toluene.

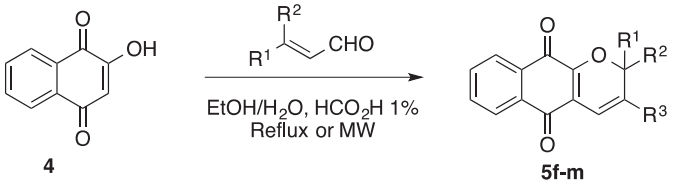
Since the lapachones are important minor components from plants and they have important bioactive profile it is important to produce them in large scale. Therefore, it is still necessary to develop new robust methods or improve existing methods for the synthesis of these substances. As part of our ongoing research concerning the synthesis of bioactive naphthoquinones,[24] we report a simple and inexpensive improvement and a new approach to the synthesis of fused chromene-1,4-naphthoquinones (**5f**–**n**) from lawsone (**4**) and α,β-unsaturated aldehydes using acid catalysis or microwave irradiation.[24]

2. Results and discussion

As previously mentioned, chromenes are substances of great importance in chemistry, but there are few methods to synthesize these compounds. When developing a new methodology to access this class of compounds, some guiding principles were considered: use of an inexpensive catalyst and green solvents. Thus, we utilized formic acid for the Knoevenagel condensation between lawsone (**4**) and α,β-unsaturated aldehydes to generate the *ortho*-quinone methide (*o*-QMs) intermediates; this was followed by 6π-electrocyclization to yield the α-xyloidone analogues.

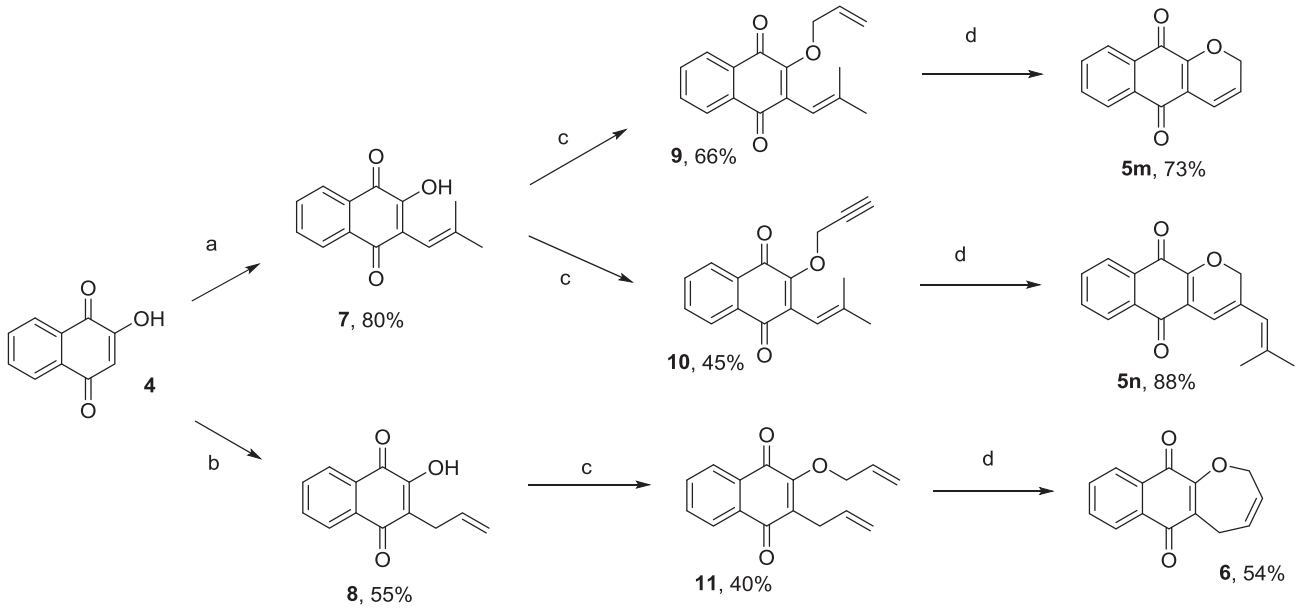
product was formed but seems to degrade during the additional time necessary for theses reactions. The reactions with cinnamaldehyde and acrolein were unsuccessful, and the starting materials were recovered (entries 7 and 8). Reaction conditions with a better heat distribution were necessary and could be achieved with the use of a microwave irradiation. To avoid degradation, the reactions were performed at 80 °C, which increased the reaction times for several reactions but resulted in good yields. Despite the fact that the use of a microwave reactor increased the yields of the reactions in most cases, this method was not very efficient for the reactions with furfural, cinnamaldehyde and acrolein (entries 6–8).

Table 1
Synthesis of xyloidones by Knoevenagel-electrocyclization.



Entry	Product	Reflux	MW
1	**5f**, R^1=R^2=Me, R^3=H	65% (24 h)	73% (1.5 h, 80 °C)
2	**5g**, R^1=Me; R^2=CH_2–prenyl, R_3=H	8% (72 h)	70% (5.5 h, 80 °C)
3	**5h**, R^1=R^2=H, R^3=Me	26% (6 h)	70% (1.2 h, 80 °C)
4	**5i**, R^1=Me, R^2=R_3=H	14% (24 h)	54% (1 h, 80 °C)
5	**5j**, R^1=R^3=H, R^2=Pr	6% (7 h)	46% (1.5 h, 80 °C)
6	**5k**, R^1=R^3=H, R^2=furyl	Decompose	Decompose
7	**5l**, R^1=R^3=H, R^2=phenyl	Reagent recovered	Reagent recovered
8	**5m**, R^1=R^2=R^3=H	Reagent recovered	Reagent recovered

Given the difficulty of synthesizing other xyloidone derivatives, including product **5m**, we attempted another synthetic method involving the *O*- and *C*-alkylation of lawsone (**4**) followed by cyclization using ring-closing metathesis (RCM), Scheme 2 (entries 9–11).



Scheme 2. Synthetic xyloidone derivatives obtained using ring-closing metathesis.

For this purpose, the alkylation of the C-3 position of lawsone (**4**) was initially considered. Thus, the synthesis of the intermediate 3-allyl-lawsone (**8**) was performed using the methodology of Kongkathip and co-workers,[25] in which a mixture of lawsone (**4**) and allyl bromide was irradiated in a microwave vessel at 150 °C using *N*,*N*-dimethylformamide (DMF) as the solvent and potassium carbonate as the base. In this reaction, the [3,3]-sigmatropic rearrangement of the initial *O*-alkylation product provided 3-allyl-lawsone in 55% yield (Scheme 2). In contrast, the preparation of the intermediate nor-lapachol (**7**) involved an adaptation of the method described by Glazunov and research group,[26] which is a more modern and practical synthesis than that developed by Fieser[27] from lapachol. This methodology involves a Mannich reaction of lawsone (**4**) methylamine and isobutyraldehyde followed by elimination with *p*-toluenesulfonic acid in toluene under reflux using a Dean–Stark trap. Thus, it was possible to isolate nor-lapachol as yellow crystals in 80% yield (Scheme 2). Subsequently, we performed the *O*-alkylation using classical methods with an alkyl bromide in dry acetone and potassium carbonate. The reactions with allyl and propargyl bromides generated the *O*-alkylation products in yields ranging from 40 to 66% (Scheme 2).

Finally, the bis-alkylated derivatives were heated in refluxing dichloromethane in the presence of Grubbs' catalyst (second generation), thus forming xyloidone derivatives **5m** and **5n** in good yields and oxepin **6** (Scheme 2). Notably, this method enabled the synthesis and isolation of α-xyloidone (**5m**), which had been unsuccessful using the Knoevenagel condensation reaction described above.

3. Conclusion

The two methodologies explored for the synthesis of fused chromene-1,4-naphthoquinones resulted in the successful synthesis of several α- and β-xyloidones. The acid catalysis or microwave irradiation methods used to promote the Knoevenagel-electrocyclization reaction between lawsone and the α,β-unsaturated aldehydes were complementary, and several α and β-xyloidones were obtained in moderate to good yields. The second methodology involving the *O*- and *C*-alkylation of lawsone followed by cyclization using ring closing metathesis (RCM) with Grubbs' catalyst led to the formation of α-xyloidone derivatives and one oxepin in good yield. This latter method allowed the synthesis and isolation of α-xyloidone, which could not be obtained via the Knoevenagel-electrocyclization method.

4. Experimental

4.1. General methods

The reagents were purchased from Aldrich or Acros Chemical Co. Column chromatography was performed on silica gel 60 (Merck 70-230 mesh). Yields refer to purified compounds obtained by chromatography and confirmed by spectroscopic data. Analytical grade solvents were used. Melting points were obtained using a Fischer Jones melting point device and are uncorrected. The reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm E. Merck silica gel plates (60F-254) using UV light for visualization. Infrared spectra were recorded on a Perkin–Elmer FTIR Spectrum One spectrophotometer, calibrated relative to the 1601.8 cm^{-1} absorbance of polystyrene. NMR spectra were recorded on a Varian Unity Plus VXR (300 MHz) in $CDCl_3$. The chemical shift data are reported in units of δ parts per million (ppm) downfield from tetramethylsilane or the solvent, which was used as an internal standard; coupling constants (*J*) are reported in Hertz and refer to the apparent peak multiplicities.

4.2. General experimental procedures

*4.2.1. General procedure for preparing **5f–k** under conventional heating.* To a round-bottom flask equipped with a magnetic stirring

bar, lawsone (**4**, 1 equiv), and 100 mL of a 1:1 ethanol/water mixture (v/v), the aldehyde (1 equiv) and formic acid (1.5 equiv) were added and mixed. The reaction mixture was heated at reflux for 1 h with stirring. After total consumption of the starting material (verified by TLC), the reaction mixture was cooled to room temperature and concentrated under reduced pressure. Then, the resulting residue was added to water, and this mixture was extracted with ethyl acetate. The combined organic extracts were washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel and a gradient of hexane/EtOAc as the eluent. The products were obtained in yields ranging from 6 to 65%. Microwave irradiation experiments were performed on a model monowave 300 from Anton Paar using the 10 mL pressure vial for closed vessel reactions, under the indicated power automatically to reach and maintain the set temperature, specified in each case, with ruby thermometer temperature for temperature control and medium stirring speed using cylindrical stir bars (10×6 mm).

*4.2.2. General procedure for preparing **5f**–**k** under microwave heating.* A 10 mL microwave tube was loaded with **4** (11.5 mmol), the corresponding aldehyde (11.5 mmol), formic acid (17.3 mmol), and 5 mL of a 1:1 ethanol/water mixture (v/v), and the resulting mixture was irradiated from 1 to 5.5 h. The internal temperature reached 80 °C. The solvent was evaporated under reduced pressure, and the crude mixture was extracted with ethyl acetate (30 mL). The organic layer was washed with water (3×20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residual solid product was purified by column chromatography using silica gel and a gradient of hexane/EtOAc as the eluent. The products were obtained in yields ranging from 10 to 73%.

*4.2.3. Spectroscopic data for products **5f**–**m** and **6***

*4.2.3.1. 2,2-Dimethyl-2H-benzo[g]chromene-5,10-dione (α-xyloidone, **5f**).* Yield (reflux/MW) 65/73%, Orange solid. Mp 145–146 °C; IR (KBr, cm^{-1}): ν 2974, 2923, 1675, 1644, 1333, 1274, 1190, 1132, 967, 717; ^{1}H NMR (DMSO-d_6, 300 MHz): 8.08–8.11 (2H, m), 7.67–7.71 (2H, m), 6.65 (1H, d, J=10.0 Hz), 5.72 (1H, d, J=10.0 Hz), 1.66 (6H, s) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz): 28.3, 80.4, 115.5, 117.8, 126.2, 130.8, 131.5, 131.6, 133.1, 133.9, 152.4, 179.8, 181.8 ppm.

*4.2.3.2. 2-Methyl-2-(4-methylpent-3-en-1-yl)-2H-benzo[g]chromene-5,10-dione (**5g**).* Yield (reflux/MW) 8/70%. Orange solid. Mp 96–98 °C; IR (KBr, cm^{-1}): ν 3340, 2970, 2926, 1675, 1651, 1337, 1272, 966, 720; ^{1}H NMR (DMSO-d_6, 300 MHz): 8.07–8.10 (2H, m), 7.67–7.71 (2H, m), 6.70 (1H, d, J=10.0 Hz), 5.67 (1H, d, J=10.0 Hz), 5.05–5.10 (1H, m), 1.90–2.00 (2H, m), 1.65–1.70 (2H, m), 1.62 (3H, s), 1.54 (3H, s), 1.51 (3H, s) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz): 17.6, 22.6, 25.5, 27.5, 41.5, 83.0, 115.9, 117.4, 123.3, 126.1, 129.7, 131.4, 132.2, 133.1, 133.8, 152.7, 179.6, 181.7 ppm.

*4.2.3.3. 3-Methyl-2H-benzo[g]chromene-5,10-dione (**5h**).* Yield (reflux/MW) 26/70%. Red solid. Mp 189–191 °C; IR (KBr, cm^{-1}): ν 2924, 1675, 1649, 1593, 1375, 1337, 1208, 720; ^{1}H NMR (DMSO-d_6, 300 MHz): 8.01–8.04 (2H, m), 7.63–7.67 (2H, m) 6.40 (1H, dd, J=1.6, 1.6 Hz), 4.89 (1H, dd, J=1.6, 1.3 Hz), 1.82 (3H, dd, J=1.3, 1.3 Hz) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz): 19.2, 70.4, 112.1, 119.5, 126.0, 126.1, 131.2, 131.3, 133.1, 133.2, 133.8, 151.3, 179.2, 181.8 ppm.

*4.2.3.4. 2-Methyl-2H-benzo[g]chromene-5,10-dione (**5i**).* Yield (reflux/MW) 14/54%. Orange solid. Mp 82–86 °C; IR (KBr, cm^{-1}): ν 2974, 2924, 1674, 1647, 1632, 1336, 1303, 1259, 1199, 967, 719; ^{1}H NMR (DMSO-d_6, 300 MHz): 8.04–8.06 (2H, m), 7.65–7.70 (2H, m), 6.66–6.68 (1H, m), 5.77–5.79 (1H, m), 5.24–5.28 (1H, m), 1.52–1.53 (3H, m) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz): 21.6, 74.2, 116.6, 118.4, 126.1, 126.2, 127.1, 131.3, 131.4, 133.2, 134.0, 152.7, 179.6, 181.7 ppm.

*4.2.3.5. 2-Propyl-2H-benzo[g]chromene-5,10-dione (**5j**).* Yield (reflux/MW) 6/46%. Orange solid. Mp 67–69 °C; IR (KBr, cm^{-1}): ν 2955, 2869, 1672, 1650, 1570, 1254, 1202, 969, 720; ^{1}H NMR (DMSO-d_6, 300 MHz): 8.06–8.07 (2H, m), 7.65–7.71 (2H, m), 6.687–6.70 (1H, m), 5.78–5.81 (1H, m), 5.14–5.17 (1H, m), 1.72–1.90 (2H, m), 1.44–1.58 (2H, m), 0.94–0.97 (3H, m) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz): 13.8, 17.4, 37.7, 77.7, 116.9, 118.6, 126.1, 126.2, 131.5, 133.2, 134.0, 153.0, 179.6, 181.7 ppm.

*4.2.3.6. 2-Hydroxy-3-(2-methylprop-1-en-1-yl)naphthalene-1,4-dione (**7**).* To a solution of lawsone (**4**) (5 g, 28.7 mmol) in dry toluene (300 mL) was added methylamine hydrochloride (2.3 g, 34 mmol), isobutyraldehyde (10.5 mL, 143.6 mmol) and *p*-toluenesulfonic acid (6.47 g, 34 mmol). The reaction mixture was then refluxed in a system equipped with a Dean–Stark trap for 5 h. The reaction mixture was then concentrated in vacuo, and the crude solid was recrystallized from hexane (80%). Yellow solid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.68 (3H, d, J=0.9 Hz), 1.99 (3H, d, J=0.9 Hz), 6.01 (1H, sept, 0.9 Hz), 7.52 (1H, s), 7.69 (1H, dt, J=1.8, 7.5 Hz), 7.76 (1H, dt, J=1.8, 7.5 Hz), 8.10 (1H, dd, J=1.8, 8.0 Hz), 8.13 (1H, dd, J=1.8, 8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): 21.6, 26.4, 113.5, 120.8, 125.9, 126.8, 129.4, 132.7, 132.8, 134.8, 143.4, 151.0, 181.4, 184.6.

*4.2.3.7. 2-Allyl-3-hydroxy-1,4-naphthoquinone (**8**).* A solution of lawsone (**4**) (1.74 g, 10 mmol) in dimethylformamide (5 mL) was added to potassium carbonate (1.4 g, 10 mmol) with stirring for 15 min at room temperature. Allyl bromide (3.0 g, 25 mmol) was added dropwise at the same temperature. After the reaction mixture was irradiated in a microwave for 10 min at 150 °C in a sealed vessel, the reaction mixture was cooled to room temperature and filtered, and dichloromethane (30 mL) was added. The reaction mixture was then washed with water (5×25 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash column silica gel chromatography eluting with a hexane/EtOAc gradient to afford the product **8** (55%). Yellow solid; mp: 110–111 °C. IR (KBr, cm^{-1}): ν 3356, 1660, 1644, 1589, 1372, 1350, 1272, 1230, 729; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.29–3.31 (2H, m), 4.93–5.05 (2H, m), 5.80–5.88 (1H, m), 7.30 (1H, s), 7.60–7.72 (1H, m), 7.60–7.72 (1H, m), 8.00–8.07 (1H, m), 8.00–8.07 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): 27.3, 116.6, 121.7, 126.0, 126.7, 129.3, 132.7, 132.8, 133.6, 134.8, 153.0, 181.3, 184.0.

4.2.4. General procedure of the O-alkylation. A solution of **7** or **8** (1 mmol) in dry acetone (5 mL) was added to potassium carbonate (1.5 mmol) and stirred for 15 min at room temperature. Allyl or propargyl bromide (1.5 mmol) was added dropwise at the same temperature. After the reaction mixture was stirred for 3 h, the reaction mixture was cooled to room temperature and filtered, and dichloromethane (30 mL) was added. The reaction mixture was then washed with water (5×25 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash column silica gel chromatography eluting with a hexane/EtOAc gradient to afford the product.

*4.2.4.1. 2-(Allyloxy)-3-(2-methylprop-1-enyl)naphthalene-1,4-dione (**9**).* Yield: 66%; yellow oil. IR (KBr, cm^{-1}): ν 3079, 2915, 1668, 1651, 1596, 1574, 1447, 1379, 1328, 1295, 1265, 1200, 795, 728; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.62–1.63 (3H, m), 1.97–1.98 (3H, m), 4.75–4.78 (2H, m), 5.20–5.25 (1H, m), 5.30–5.37 (1H, m), 5.91–6.04 (1H, m), 5.91–6.04 (1H, m), 7.66–7.72 (1H, m), 7.66–7.72 (1H, m), 8.03–8.08 (1H, m), 8.03–8.08 (1H, m); ^{13}C NMR ($CDCl_3$,

125 MHz): 21.4, 26.3, 73.4, 114.6, 118.2, 126.0, 126.2, 130.8, 131.4, 131.9, 133.1, 133.2, 133.6, 143.2, 155.3, 181.6, 185.3; HRESIMS *m/z* 269.1169 $[M+H]^+$ (Calcd for $C_{17}H_{17}O_3^+$: 269.1172).

*4.2.4.2. 2-(2-Methylprop-1-enyl)-3-(prop-2-ynyloxy)naphthalene-1,4-dione (**10**).* Yield: 45%; orange solid; mp: 80–81 °C. IR (KBr, cm^{-1}): *ν* 3261, 1663, 1649, 1594, 1562, 1332, 1310, 1264, 1199, 717; ^1H NMR ($CDCl_3$, 500 MHz): *δ* 1.58 (3H, s), 1.91–1.92 (3H, m), 1.96 (2H, d, *J*=2.4 Hz), 2.42 (1H, t, *J*=2.4), 5.95 (1H, m), 7.62–7.66 (1H, m), 7.62–7.66 (1H, m), 8.00–8.02 (1H, m), 8.00–8.02 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): 21.5, 26.4, 59.6, 76.2, 78.1, 114.2, 126.0, 126.3, 131.2, 131.9, 132.2, 133.2, 133.7, 143.8, 153.8, 181.4, 185.0; HRESIMS *m/z* 267.1015 $[M+H]^+$ (Calcd for $C_{17}H_{15}O_3^+$: 267.1016).

*4.2.4.3. 2-Allyl-3-(allyloxy)naphthalene-1,4-dione (**11**).* Yield: 40%; yellow oil. IR (KBr, cm^{-1}): *ν* 3077, 2924, 1671, 1655, 1607, 1595, 1578, 1458, 1423, 1337, 1303, 1264, 1231, 1196, 1043, 994; ^1H NMR ($CDCl_3$, 500 MHz): *δ* 3.30–3.32 (2H, m), 4.84–4.86 (2H, m), 4.97 (1H, dd, *J*=1.5, 9.8 Hz), 5.07 (1H, dd, *J*=1.5, 17.1 Hz), 5.20 (1H, dd, *J*=1.0, 10.3 Hz), 5.31 (1H, dd, *J*=1.5, 17.1 Hz), 5.76–5.84 (1H, m), 5.94–6.02 (1H, m), 7.60–7.65 (1H, m), 7.60–7.65 (1H, m), 7.96–8.01 (1H, m), 7.96–8.01 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): 27.9, 74.0, 116.4, 118.6, 126.0, 126.1, 131.3, 131.8, 133.1, 133.2, 133.4, 133.7, 134.1, 156.8, 181.5, 184.8.

4.2.5. General procedure for the metathesis reaction. A solution of **9**–**11** (1 mmol) and second generation Grubbs catalyst (10% mol, 0.01 mmol) in degassed dry dichloromethane (5 mL) was heated at reflux under argon. After 30 min at reflux, the reaction mixture was cooled to room temperature, the solvent was evaporated, and the residue was purified by flash chromatography using a gradient of toluene/EtOAc as the eluent.

*4.2.5.1. 2H-Benzo[g]chromene-5,10-dione (**5m**).* Yield: 73%; red solid; mp: 162 °C. IR (KBr, cm^{-1}): *ν* 2921, 1671, 1647, 1587, 1334, 1299, 1253, 1196, 1114, 996, 940, 794, 714, 671; ^1H NMR ($CDCl_3$, 500 MHz): *δ* 5.03 (2H, dd, *J*=2.0, 3.5 Hz), 5.81 (1H, dt, *J*=3.5, 10.0 Hz), 6.66 (1H, dt, *J*=2.0, 10.0 Hz), 7.59–7.68 (1H, m), 7.59–7.68 (1H, m), 8.00–8.03 (1H, m), 8.00–8.03 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): 67.2, 117.6, 119.0, 122.2, 126.1, 126.0, 131.2, 131.1, 133.2, 133.9, 153.3, 179.2, 181.4; HRESIMS *m/z* 213.0538 $[M+H]^+$ (Calcd for $C_{13}H_9O_3^+$: 213.0546).

*4.2.5.2. 3-(2-Methylprop-1-enyl)-2H-benzo[g]chromene-5,10-dione (**5n**).* Yield: 88%; purple solid; mp: 153–154 °C. IR (KBr, cm^{-1}): *ν* 1666, 1648, 1608, 1591, 1560, 1351, 1340, 1215, 1195, 720; ^1H NMR ($CDCl_3$, 500 MHz): *δ* 1.83 (3H, s), 1.87 (3H, s), 4.98 (2H, s), 5.57 (1H, s), 6.47 (1H, s), 7.59–7.65 (1H, m), 7.59–7.65 (1H, m), 8.00–8.02 (1H, m), 8.00–8.02 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): 20.8, 27.6, 69.5, 113.5, 120.8, 121.3, 125.9, 126.1, 131.3, 131.4, 132.4, 133.1, 133.6, 142.1, 151.0, 178.8, 181.9; HRESIMS *m/z* 267.1012 $[M+H]^+$ (Calcd for $C_{17}H_{15}O_3^+$: 267.1016).

*4.2.5.3. Naphtho[2,3-b]oxepine-6,11(2H,5H)-dione (**6**).* Yield: 54%; yellow solid; mp: 125–126 °C. IR (KBr, cm^{-1}): *ν* 2922, 2852, 1675,1288, 1247, 1194, 1060, 1017, 723; ^1H NMR ($CDCl_3$, 500 MHz): *δ* 3.56 (2H, d, *J*=5.9 Hz), 4.84 (2H, d, *J*=5.9 Hz), 5.97–6.01 (1H, m), 6.13–6.17 (1H, m), 7.58–7.67 (1H, m), 7.58–7.67 (1H, m), 7.99–8.01 (1H, m), 7.99–8.01 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz): 22.7, 66.8, 124.4, 126.1, 126.2, 126.9, 130.6, 131.6, 133.0, 133.6, 133.8, 158.3, 180.6, 184.6; HRESIMS *m/z* 227.0711 $[M+H]^+$ (Calcd for $C_{14}H_{11}O_3^+$: 227.0703).

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