Tetrahedron 69 (2013) 5850–5858

Contents lists available at SciVerse ScienceDirect

Tetrahedron

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

Total syntheses of norartocarpin and artocarpin

Wen-Jing Zhang [a], Jing-Fang Wu [b], Peng-Fei Zhou [b], Yang Wang [b,*], Ai-Jun Hou [a,*]

[a] Department of Pharmacognosy, School of Pharmacy, Fudan University, Shanghai 201203, China
[b] Department of Medicinal Chemistry, School of Pharmacy, Fudan University, Shanghai 201203, China

ARTICLE INFO

Article history:
Received 3 March 2013
Received in revised form 25 April 2013
Accepted 10 May 2013
Available online 16 May 2013

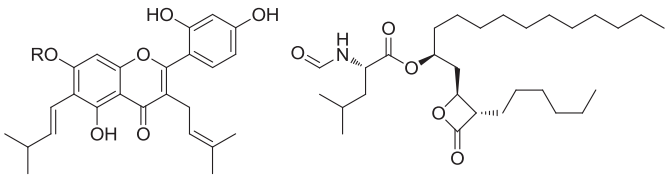
Keywords:
Norartocarpin
Artocarpin
Isoprenylated flavonoids
Total syntheses
Demethylation

ABSTRACT

The total syntheses of norartocarpin and artocarpin, two biologically interesting natural flavonoids with two regioisomeric isoprenyl side chains, were achieved for the first time via a linear reaction sequence of 9 and 12 steps with the overall yields of 14% and 3.5%, respectively, starting from commercially available 1,3,5-trimethoxybenzene.

1. Introduction

Norartocarpin (**1**) and artocarpin (**2**) are natural isoprenylated flavonoids isolated from the genus *Artocarpus* (Fig. 1),[1] which were reported to possess a variety of interesting biological activities including inhibitory effects on melanin biosynthesis and 5α-reductase, antibacterial activity, and cytotoxicity.[2] Recently, **1** was found to inhibit the activity of pancreatic lipase (PL) by our group[1a] with an IC_{50} value close to that of orlistat, a clinical PL inhibitor used as an anti-obesity drug.



Norartocarpin (**1**): R = H
Artocarpin (**2**): R = CH_3

Orlistat

Fig. 1. Structures of norartocarpin (**1**), artocarpin (**2**), and orlistat.

On the other hand, natural resources of **1** and **2** are limited due to the low contents in *Artocarpus* plants, which negatively influenced their further bioactivity evaluation. Therefore, chemical syntheses of **1** and **2** will be an important alternative approach for addressing the problem of their availability. As the continuation of our study on the chemistry and biology of isoprenylated flavonoids,[1a,3] we herein report the first total syntheses of **1** and **2** via a linear reaction sequence of 9 and 12 steps with the overall yields of 14% and 3.5%, respectively, starting from commercially available 1,3,5-trimethoxybenzene.

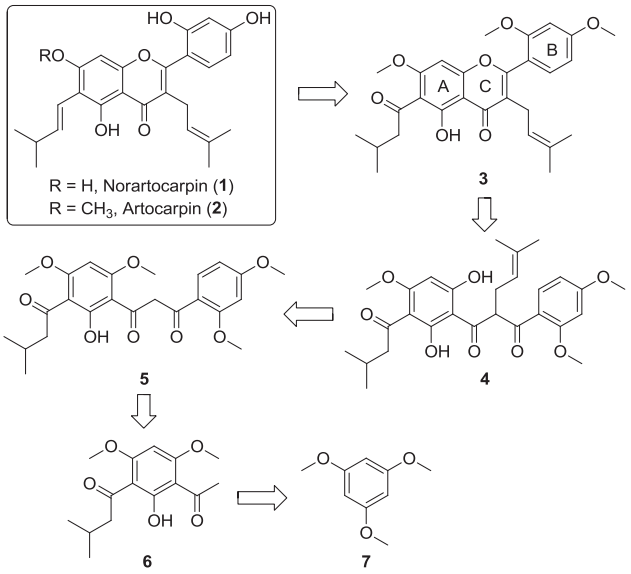
2. Results and discussion

Retrosynthetic analysis is shown in Scheme 1. These two flavones carry two different isoprenyl side chains, and our key synthetic strategy involves the introduction of isopentanoyl group into ring A and isoprenyl group into ring C of the flavone scaffold, respectively. The former relies on Friedel–Crafts acylation of 1,3,5-trimethoxybenzene (**7**) and the latter could be achieved by the enolate acylation[4] of 2-hydroxyl acetophenone **6** followed by alkylation with 1-bromo-3-methyl-2-butene at the α-position of two carbonyl groups of β-diketo **5** and the subsequent cyclization to obtain the key intermediate **3** with flavone scaffold. The key intermediate **3** could be converted into the target molecules **1** and **2** via the reduction of benzylic carbonyl group, dehydration and selective demethylation, respectively.

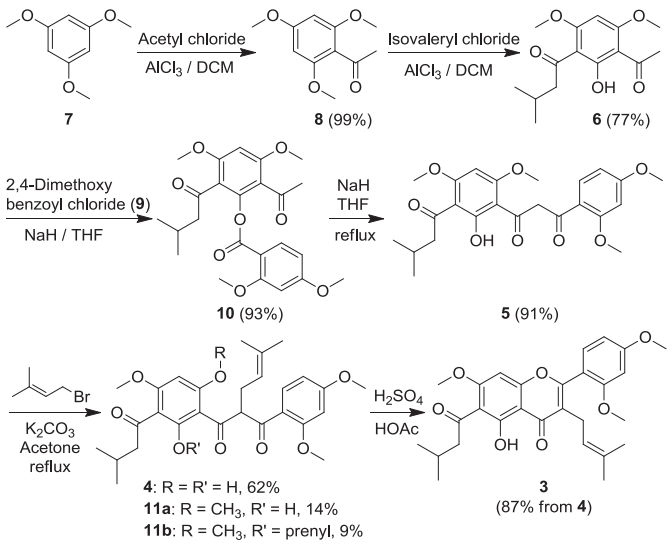
As shown in Scheme 2, the synthesis of key intermediate **3** is quite straightforward. Although the structure of **6** seems simple, its synthesis still remains unreported in the literature. Starting from 1,3,5-trimethoxybenzene (**7**), twice sequential Friedel–Crafts acylation of **7** in dichloromethane in the presence of $AlCl_3$ using acetyl chloride and 3-methylbutanoyl chloride as the acylated reagents,

* Corresponding authors. E-mail addresses: wangyang@shmu.edu.cn, ywang.spfdu@gmail.com (Y. Wang), ajhou@shmu.edu.cn (A.-J. Hou).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.05.024



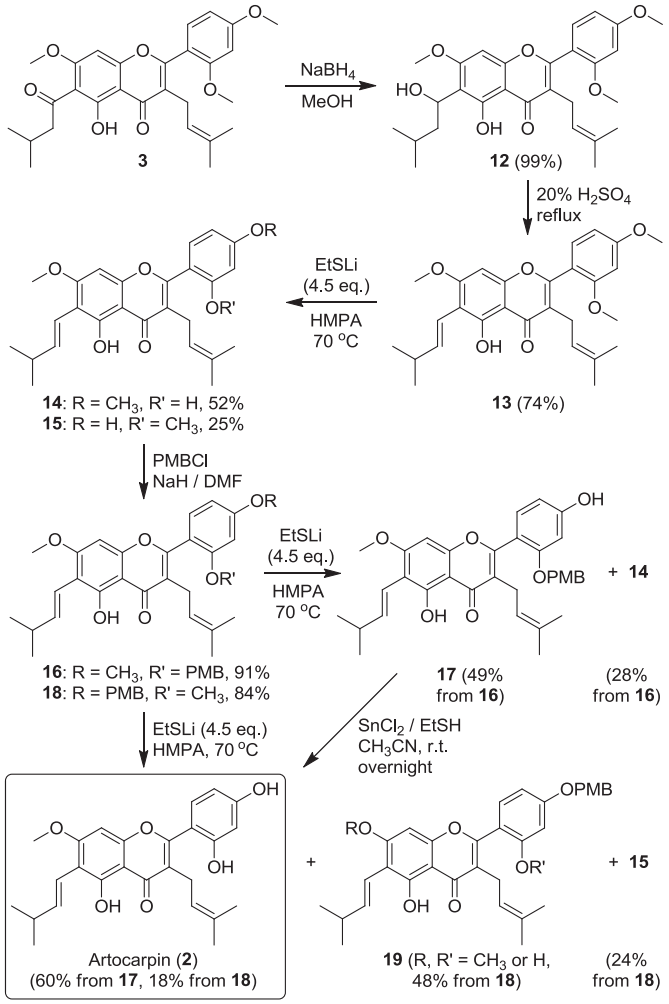
Scheme 1. Retrosynthetic analysis of norartocapin (**1**) and artocarpin (**2**).



Scheme 2. Synthesis of key intermediate **3**.

respectively, afforded the intermediate **6** in good yields (75% for two steps). In the course of Friedel–Crafts acylation, the desired demethylation simultaneously occurred, which may be attributed to the effect of two carbonyl groups at *ortho* positions. On the other hand, if the two F–C reactions were performed in a reversed sequence, 2,4,6-trimethoxyacetylbenzene (**8**) rather than expected target molecule **6** was obtained as the major product, i.e., the isopentanoyl group was cleaved via reverse F–C reaction during the second step. 2,4-Dimethoxybenzoyl chloride (**9**) was readily prepared by reacting the corresponding carboxylic acid with $SOCl_2$ at room temperature. With precursors **6** and **9** in hand, the esterification and Baker–Venkataraman rearrangement were carried out in a stepwise approach under the condition of NaH/THF to give β-diketo **5** in excellent yields (93% and 91%), rather than in one-pot manner to afford **5** in a poor yield. The alkylation of **5** with prenyl bromide in the presence of K_2CO_3 in refluxing acetone provided the prenylated and simultaneously demethylated intermediate **4** as the major product (62% yield), and on the other hand the expected monoprenylated product **11a** and diprenylated product **11b** as the minor (14% and 9% yields, respectively). The demethylation position in product **4** was confirmed by comprehensive spectroscopic methods, especially HMBC to be luckily at 6-position of ring A to give the correct demethylated product for the next step of cyclization. It was found that prolonging the reaction time was beneficial to the formation of the desired product **4** but the formation of **11a**–**b** seemed to be unavoidable. The following regioselective cyclization of **4** in the presence of H_2SO_4/AcOH generated the flavone intermediate **3** in 87% yield (overall yield of 35% from **7**).

With key intermediate **3** in hand, we subsequently proceeded to its reduction with $NaBH_4$ and dehydration of reduced product. As shown in Scheme 3, the reduction product **12** could be obtained in almost quantitative yield. The following dehydration of **12** was carried out in 20% H_2SO_4 to give **13** in 74% isolated yield.



Scheme 3. Synthesis of artocarpin (**2**) by demethylation with EtSLi/HMPA.

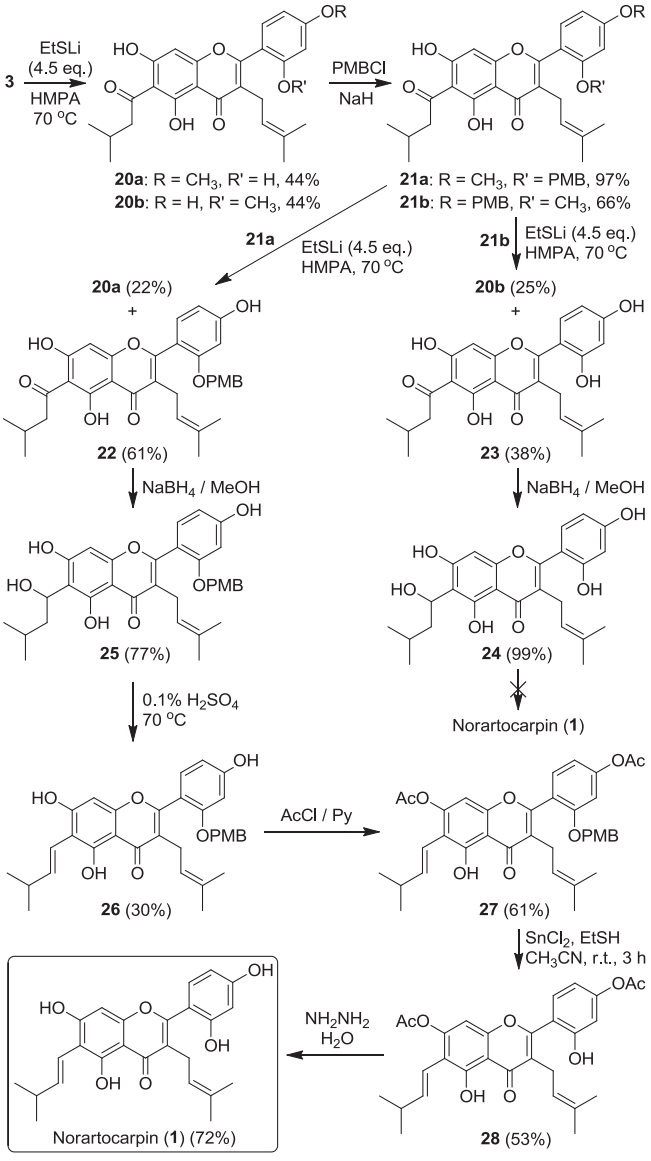
At this point, the final step of the synthesis was focused on the demethylation of **13**. Attempts to treat with BBr_3, $AlCl_3$, 48% HBr (aq) or pyridinium hydrohalides to give the target molecules were unsuccessful and in all cases they were proceeded with decomposed or recovered starting material. However, monodemethylated products **14** and **15** were obtained as a mixture (**14**/**15**=2:1) in 77% yield under the conditions of EtSLi (4.5 equiv)/HMPA,[5] which encouraged us to carry this synthetic route through to the end. Prolonging the reaction time, raising temperature and increasing the amount of EtSLi to 30 equiv did not result in the

formation of any di-demethylated artocarpin (**2**) or tri-demethylated norartocarpin (**1**). We then switched to further protect **14** and **15** with *p*-methoxybenzyl chloride (PMBCl) and subsequently treat with EtSLi/HMPA. Protection of **14** with PMBCl (91% yield) and then demethylation of its PMB derivative **16** with EtSLi (4.5 equiv)/HMPA at 70 °C did not give any **1** or **2**, but yielded debenzylation product **14** (28%) and demethylation product **17** (49%) as the major products. Removal of PMB from **17** in the presence of $SnCl_2$/EtSH provided the target molecule artocarpin (**2**) in 60% yield. Alternatively, protection of **15** with PMBCl and then demethylation of **18** with EtSLi/HMPA also afforded **2** in 18% yield, and at the same time, debenzylation product **15** and demethylation product **19** were isolated in 24% and 48% yields, respectively. Since the R_f values of **19** and **15** were almost the same in TLC analysis, the complete separation of **19** and **15** was not realized. Further raising temperature (100 °C) or prolonging the reaction time, the reaction became more complex and the yield of artocarpin (**2**) was not obviously improved. The obtained analytical data of **2** were identical to those of artocarpin reported previously.[3a]

With the extreme difficulties mentioned above in the demethylation of key intermediate **13** to afford the target molecule norartocarpin (**1**), we had to take a roundabout way by doing demethylation first and then reduction of ketone and dehydration of alcohol to realize its total synthesis. As shown in Scheme 4, the reaction of key intermediate **3** with EtSLi/HMPA afforded di-demethylation products **20a** and **20b** in 88% yield with a 1:1 ratio. These isomers exhibited quite different behaviors in the following steps. Both **20a** and **20b** were protected with PMBCl to give **21a** and **21b** in 97% and 66% yields, respectively, which were then subjected to the second demethylation with EtSLi/HMPA at 70 °C. The reaction of **21a** afforded demethylation product **22** in 61% yield with the co-production of debenzylation product **20a** in 22% yield, while **21b** provided debenzylation product **20b** and the complete demethylation and debenzylation product **23** in 25% and 38% yields, respectively. With compound **23** in hand, it was then subjected to the reduction with $NaBH_4$ and acidic dehydration. Unfortunately, the dehydration of **24** did not give any product **1** under various acidic conditions (including PTS, 0.1%, 1%, 10% H_2SO_4 or 7% HCl) despite the high yield of reduction of **23** to **24**.

We subsequently tried to take **22** as the key intermediate for reduction and dehydration reactions. As outlined in Scheme 4, **22** was then reduced by $NaBH_4$ to give **25** in 77% yield. The dehydration of **25** in the presence of 0.1% H_2SO_4 at 70 °C produced **26** in 30% yield. Direct cleaving PMB group of **26** to **1** could not be achieved by using $SnCl_2$/EtSH.[6] Obviously, the target norartocarpin was unstable under acidic condition, but it can make a detour by the protection of OH groups of **26** with AcCl in the presence of pyridine, which resulted in the formation of **27** in 61% yield. Removal of PMB and Ac groups from **27** in the presence of $SnCl_2$/EtSH and NH_2NH_2–H_2O, respectively, provided **28** and target molecule (**1**) in 53% and 72% yields. The analytical data of **1** were compared to previous report[2a] and the structure is identical to norartocarpin.

So far, the syntheses of norartocarpin (**1**) and artocarpin (**2**) were accomplished by demethylation of key intermediates **3** and **13** with EtSLi/HMPA, respectively, but the total synthetic routes are tediously long and inefficient. Attention was next directed toward seeking for more effective demethylated reagents, then Me_3SiI/quinoline/$CHCl_3$[7] and 1-trimethylsilylquinolinium iodide (TMSI-quinoline)[8] were investigated, respectively. There was no target products observed when treated **13** either with TMSI or its mixture with quinoline in $CHCl_3$ though mono-demethylated products **14** and **15** were indeed afforded in low yields with most of starting material remained. Most exciting of all, TMSI-quinoline, which was prepared according to a modified procedure,[8] proved to be most effective to give target product **1**. After the optimization of reaction conditions, treatment of **13** (30 mg) with TMSI-quinoline adduct



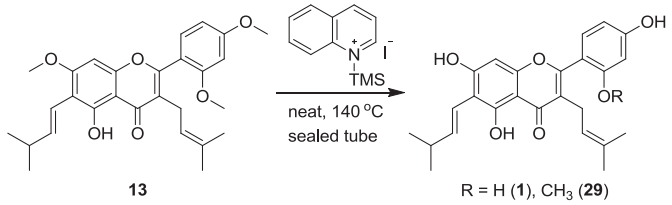
Scheme 4. Synthesis of norartocarpin (**1**) by demethylation with EtSLi/HMPA.

(24 equiv) resulted in removal of the protective ether methyl groups to provide **1** and **29** in 55% and 32% yields, respectively, by heating the reactant mixture in a sealed reaction vessel to 140 °C for 6 h (Table 1, entry 1). The structure of **29** was confirmed by comprehensive spectroscopic methods, especially HMBC and NOESY. Scaling up the amount of starting material **13** (1 g) and prolonging the reaction time to 12 h, **1** and **29** were obtained in 45% and 17% yields with the byproducts **14** and **15** in 1% and 2% yields, respectively (entry 2).

3. Conclusion

In summary, the efficient total syntheses of natural isoprenylated flavonoids norartocarpin and artocarpin have been accomplished via a linear reaction sequence of 9 and 12 steps with the overall yields of 14% and 3.5%, respectively, starting from commercially available 1,3,5-trimethoxybenzene. The synthetic route was greatly optimized by using TMSI-quinoline instead of EtSLi/HMPA as demethylation reagents and provided a simple and practical approach for the preparation of flavonoids with two regioisomeric isoprenyl side chains. The success of the present

Table 1
Demethylation of **13** with TMSI-quinoline



Entry	Compound **13**	*t* (h)	Yield of isolated product (%)			
			1	**29**	**14**	**15**
1	30 mg	6	55	32	/	/
2	1 g	12	45	17	1	2

concise synthesis will definitely stimulate future efforts on the preparation of norartocarpin and its diverse analogues for bioactivity evaluation as pancreatic lipase inhibitors in vitro and in vivo.

4. Experimental section

4.1. General

Starting materials and reagents were obtained from commercial suppliers and were used without purification unless otherwise stated. Melting points were measured in open capillary tubes using hot stage apparatus and were uncorrected. Reactions were monitored by analytical thin-layer chromatography (TLC) on 0.2 mm silica gel plates, and visualization of the developed chromatogram was enabled by UV absorbance or by using an ethanolic phosphomolybdic acid dip. Flash chromatography was performed using silica gel (300–400 mesh) with the indicated solvent system. ^{1}H NMR spectra were recorded at 400 MHz using TMS as an internal standard and ^{13}C NMR spectra were measured at 100 MHz with complete proton decoupling. All chemical shifts are reported in parts per million on the δ scale relative to an internal standard of TMS (^{1}H) or the signals of the solvent (^{13}C). Infrared (IR) spectra were recorded neat on KBr tablets with frequencies expressed in cm^{-1}. High-resolution mass spectra (HRMS) were recorded using either electron impact (EI) or electrospray ionization (ESI) techniques.

4.2. 2,4,6-Trimethoxyacetylbenzene (8)

A solution of **7** (2.0 g, 11.8 mmol) in CH_2Cl_2 was cooled down to 0 °C for 10 min, and then added $AlCl_3$ (1.9 g, 14.2 mmol) and acetyl chloride (1.26 mL, 1.4 g, 17.7 mmol). After stirring 2 h, the reaction mixture was cooled and quenched by adding a solution of 10% NaOH (aq) (40 mL), and extracted by CH_2Cl_2 (3×30 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was subjected to column chromatography (Silica gel, hexane/EA 5:1) to provide **8** (2.5 g, 99%) as a white solid: mp 103–106 °C (lit.[9] 101–103 °C). IR (neat): ν 3373, 2977, 1692, 1602, 1415, 1210, 1130, 818 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.09 (s, 2H, Ar–H), 3.81 (s, 3H, OCH_3), 3.78 (s, 6H, 2× OCH_3), 2.47 (s, 3H, CH_3CO–).

4.3. 1-(3-Acetyl-2-hydroxy-4,6-dimethoxyphenyl)-3-methyl-1-butanone (6)

A solution of **8** (0.884 g, 4.2 mmol) in CH_2Cl_2 was cooled down to 0 °C, and then added $AlCl_3$ (1.21 g, 8.41 mmol) and isovaleryl chloride (0.56 mL, 0.55 g, 4.63 mmol). The mixture was then heated to reflux for 24 h. The reaction mixture was cooled and quenched by adding a solution of 10% NaOH (aq) (20 mL), and extracted by CH_2Cl_2 (3×20 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was subjected to column chromatography (Silica gel, hexane/EA 3:1) to provide **6** (0.947 g, 77%) as a white solid: mp 60–62 °C. IR (neat): ν 2956, 1703, 1615, 1596, 1410, 1274, 1214, 1167, 1132, 800 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 14.15 (s, 1H, Ar–OH), 5.94 (s, 1H, Ar–H), 3.93, 3.89 (each s, 6H, 2× OCH_3), 2.72 (d, J=7.0 Hz, 2H, $-CH_2CO$–), 2.59 (s, 3H, CH_3CO–), 2.18–2.24 (m, 1H, $-CHMe_2$), 0.96 (d, J=7.0 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.1, 202.8, 163.7, 163.5, 162.9, 110.9, 107.4, 85.9, 55.7, 53.7, 33.0, 24.9, 22.7. ESI-MS: $[M+H]^+$ 281.1; HRMS (ESI) calcd for $C_{15}H_{21}O_5$ $[M+H]^+$ 281.1383, found 281.1383.

4.4. 2-Acetyl-3,5-dimethoxy-6-(3-methylbutanoyl)phenyl-2,4-dimethoxybenzoate (10)

To a cooled (ice bath) solution of **6** (0.238 g, 0.81 mmol) in THF (10 mL), NaH (60%, 65 mg, 1.62 mmol) was added. After stirring at 0 °C for 15 min, the mixture was added 2,4-dimethoxybenzoyl chloride [prepared from (0.222 g, 1.22 mmol) of 2,4-dimethoxy benzoic acid with 5 mL $SOCl_2$], and refluxed for 30 min. After the acylation was complete, the reaction was cooled to room temperature, poured into ice water (40 mL), and extracted with EtOAc (3×40 mL). The organic phase was washed with brine, dried over $MgSO_4$ and evaporated, and the residue was chromatographed over silica gel. Elution with hexanes/ethyl acetate (2:1) gave **10** (0.333 g, 93%) as a white powder: mp 99–100 °C. IR (neat): ν 3544, 2954, 1741, 1710, 1571, 1603, 1464, 1359, 1213, 1089, 1020, 833 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J=8.8 Hz, 1H, Ar–H), 6.50 (dd, J=8.8, 2.0 Hz, 1H, Ar–H), 6.45 (d, J=2.0 Hz, 1H, Ar–H), 6.37 (s, 1H, Ar–H), 3.91, 3.88 (each s, 9H, 3× OCH_3), 3.85 (s, 6H, 2× OCH_3), 2.65 (d, J=6.8 Hz, 2H, $-CH_2CO$–), 2.46 (s, 3H, CH_3CO–), 2.12–2.19 (m, 1H, $-CHMe_2$), 0.86 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.8, 199.5, 165.0, 162.8, 162.1, 159.2, 159.0, 146.1, 134.7, 118.6, 118.1, 110.7, 104.8, 98.9, 92.6, 56.0, 55.9, 55.6, 55.5, 53.3, 31.8, 24.2, 22.5. EIMS m/z (%): 444 (M^+, 2), 223 (1), 166 (11), 165 (100), 164 (10), 71 (5), 57 (10); HRMS (EI) calcd for $C_{24}H_{28}O_8$ (M^+) 444.1784, found 444.1778.

4.5. 1-(2,4-Dimethoxyphenyl)-3-(2-hydroxy-4,6-dimethoxy-3-(3-methylbutanoyl)phenyl)propane-1,3-dione (5)

To a cooled (ice bath) solution of **10** (0.275 g, 0.62 mmol) in THF (10 mL), NaH (60%, 37 mg, 0.93 mmol) was added. After stirring at 0 °C for 10 min, the mixture was heated to reflux, for 90 min and the Baker–Venkataraman rearrangement was over with the solution changed from colorless to dark yellow. The reaction was cooled to room temperature, poured into ice water (50 mL), and extracted with EtOAc (3×40 mL). The organic phase was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed over silica gel. Elution with hexane/ethyl acetate (2:1) gave **5** (0.232 g, 91%) as a yellow powder: mp 162–164 °C. IR (neat): ν 2924, 1710, 1597, 1572, 1459, 1211, 1311, 807 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 16.34 (s, 1H, enolic-OH), 14.13 (s, 1H, Ar–OH), 13.85 (s, 1H, Ar–OH), 7.97 (d, J=8.8 Hz, 1H, Ar–H), 7.92 (d, J=8.8 Hz, 1H, Ar–H), 7.01 (s, 1H, enolic-H), 6.58 (dd, J=8.8, 2.4 Hz, 1H, Ar–H), 6.56 (dd, J=8.8, 2.4 Hz, 1H, Ar–H), 6.47 (d, J=2.4 Hz, 1H, Ar–H), 6.45 (d, J=2.4 Hz, 1H, Ar–H), 5.98 (s, 1H, Ar–H), 5.88 (s, 1H, Ar–H), 4.51 (s, 2H, $-COCH_2CO$–), 3.93 (s, 6H, 2× OCH_3), 3.86–3.90 (m, 12H, 4× OCH_3), 3.80 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 2.81 (d, J=7.0 Hz, 2H, $-CH_2CO$–), 2.69 (d, J=7.0 Hz, 2H, $-CH_2CO$–), 2.20–2.23 (m, 2H, 2× CH), 0.97 (d, J=6.4 Hz, 6H, 2× CH_3), 0.95 (d, J=6.4 Hz, 6H, 2× CH_3). From the ^{1}H NMR data of compound **5**, it is obvious that the tautomerism occurred between its keto and enol

forms with about 1:1 ratio. ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.2, 203.6, 199.9, 193.2, 188.8, 178.7, 165.0, 163.8, 163.6, 163.3, 163.1, 163.0, 162.8, 161.0, 160.4, 132.9, 131.9, 120.0, 116.8, 112.1, 108.2, 106.2, 105.5, 105.1, 103.9, 98.8, 98.2, 86.3, 86.0, 60.0, 55.9, 55.7, 55.6, 55.5, 55.4, 53.7, 53.6, 29.7, 25.1, 24.8, 22.8, 22.7. EIMS *m*/*z* (%): 444 (M^+, 4), 426 (2), 413 (59), 265 (18), 247 (6), 207 (27), 181 (13), 165 (100); HRMS (EI) calcd for $C_{24}H_{28}O_8$ (M^+) 444.1784, found 444.1790.

4.6. 1-(2,6-Dihydroxy-4-methoxy-3-(3-methylbutanoyl)phenyl)-3-(2,4-dimethoxyphenyl)-2-(3-methylbut-2-en-1-yl)propane-1,3-dione (4), 1-(2,4-dimethoxyphenyl)-3-(2-hydroxy-4,6-dimethoxy-3-(3-methylbutanoyl)phenyl)-2-(3-methylbut-2-en-1-yl)propane-1,3-dione (11a) and 1-(4,6-dimethoxy-2-((3-methyl-2-butenyl)oxy)-3-(3-methylbutanoyl)phenyl)-3-(2,4-dimethoxyphenyl)-2-(3-methyl-2-butenyl)propane-1,3-dione (11b)

To a solution of **5** (67 mg, 0.15 mmol) in acetone (10 mL), K_2CO_3 (42 mg, 0.30 mmol) was added. After stirring for 30 min, the suspension was added 1-bromo-3-methyl-2-butene (24 mg, 0.16 mmol), and then refluxed for 24 h. After the alkylation was over, the reaction was worked up by cooling to room temperature, quenching with water (10 mL), removing acetone, and extraction with EtOAc (3×10 mL). The organic phase was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was chromatographed over silica gel. Elution with hexane/acetone (5:1) gave **4** (46 mg, 62%), **11a** (11 mg, 14%), and **11b** (8 mg, 9%) as light yellow oils. Compound **4**: IR (neat): ν 2955, 1635, 1602, 1445, 1288, 1208, 1154, 1032, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.39 (s, 1H, Ar−OH), 7.25 (d, *J*=8.2 Hz, 1H, Ar−H), 6.55−6.60 (m, 2H, Ar−H), 6.34 (s, 1H, Ar−H), 5.07 (br t, *J*=6.6 Hz, 1H, −CH_2CH═), 3.85 (br s, 1H, −COCHCO−), 3.88, 3.83, 3.79 (each s, 9H, 3× OCH_3), 3.03 (br d, *J*=6.6 Hz, 2H, −CH_2CH═), 2.74 (d, *J*=7.0 Hz, 2H, −$COCH_2$−), 2.22−2.26 (m, 1H, −$CHMe_2$), 1.61, 1.41 (each br s, 6H, 2× CH_3), 0.97 (d, *J*=6.6 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 182.3, 162.7, 161.9, 159.0, 158.4, 158.3, 132.2, 131.3, 121.9, 121.1, 114.4, 105.2, 104.6, 98.7, 89.7, 56.0, 55.5, 53.7, 25.6, 24.9, 24.1, 22.6, 17.5. ESI-MS: $[M-H_2O+H]^+$ 481.1, HRMS (ESI) calcd for $C_{28}H_{34}O_8$ $[M+Na]^+$ 521.2145, found 521.2150. Compound **11a**: IR (neat): ν 2955, 1701, 1658, 1593, 1463, 1407, 1252, 1209, 1157, 1124, 834, 802 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 14.00 (s, 1H, Ar−OH), 7.90 (d, *J*=8.8 Hz, 1H, Ar−H), 6.54 (dd, *J*=8.8, 2.2 Hz, 1H, Ar−H), 6.42 (d, *J*=2.2 Hz, 1H, Ar−H), 5.85 (s, 1H, Ar−H), 5.42 (t, *J*=6.4 Hz, 1H, −COCHCO−), 5.10 (t, *J*=7.0 Hz, 1H, −CH_2*C*H═), 3.85, 3.84, 3.75, 3.63 (each s, 12H, 4× OCH_3), 2.69 (d, *J*=6.8 Hz, 2H, −$COCH_2$−), 2.52−2.66 (m, 2H, −*C*H_2CH═), 2.15−2.26 (m, 1H, −$CHMe_2$), 1.63, 1.60 (each s, 6H, 2× CH_3), 0.95, 0.94 (s, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.9, 201.3, 195.0, 164.6, 163.8, 162.8, 162.5, 160.3, 133.6, 132.6, 122.4, 119.8, 106.4, 105.3, 98.1, 85.7, 65.1, 55.7, 55.5, 55.3, 55.2, 53.7, 27.1, 25.8, 24.8, 22.7, 17.7. ESI-MS: $[M+H]^+$ 513.2; HRMS (ESI) calcd for $C_{29}H_{36}O_8Na$ $[M+Na]^+$ 535.2302, found 535.2292. Compound **11b**: IR (neat): ν 2957, 1704, 1593, 1460, 1209, 1108, 831 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J*=8.7 Hz, 1H, Ar−H), 6.42 (dd, *J*=8.7, 2.3 Hz, 1H, Ar−H), 6.35 (d, *J*=2.3 Hz, 1H, Ar−H), 6.05 (s, 1H, Ar−H), 5.37 (t, *J*=6.8 Hz, 1H, −COCHCO−), 5.24−5.32 (m, 1H, −CH_2*C*H═), 5.11−5.15 (m, 1H, −CH_2*C*H═), 4.29 (d, *J*=7.1 Hz, 2H, −O*C*H_2CH═), 3.82, 3.77, 3.76, 3.63 (each s, 12H, 4× OCH_3), 2.63−2.73 (m, 2H, −*C*H_2CH═), 2.52 (d, *J*=6.4 Hz, 2H, −$COCH_2$−), 2.14−2.17 (m, 1H, −$CHMe_2$), 1.70, 1.63 (each s, 6H, 2× CH_3), 1.61, 1.59 (each s, 6H, 2× CH_3), 0.93, 0.92 (each s, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.3, 197.4, 195.6, 163.7, 159.8, 158.3, 158.1, 154.8, 137.5, 132.5, 121.5, 121.4, 119.5, 118.8, 117.5, 104.4, 97.7, 90.3, 73.8, 65.4, 55.2, 55.1, 55.0, 53.5, 27.3, 25.4, 25.4, 23.8, 22.2, 17.7, 17.4. ESI-MS: $[M+Na]^+$ 603.2; HRMS (ESI) calcd for $C_{34}H_{44}O_8Na$ $[M+Na]^+$ 603.29284, found 603.2939.

4.7. 2-(2,4-Dimethoxyphenyl)-5-hydroxy-7-methoxy-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (3)

A solution of **4** (0.522 g, 1.05 mmol) in acetic acid (10 mL) was added conc. H_2SO_4 (0.02 mL) and stirred at room temperature for 30 min. The resulting mixture was added H_2O (25 mL) and extracted with CH_2Cl_2 (3×20 mL). The organic phase was washed with brine, dried over $MgSO_4$, and the solvent was removed in vacuo, and the residue was subjected to column chromatography (silica gel, hexane/acetone 5:1) to afford **3** (0.371 g, 74%) as a light yellow oil. IR (neat): ν 2956, 1709, 1615, 1450, 1352, 1280, 1206, 1158, 1031, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.39 (s, 1H, Ar−OH), 7.24 (d, *J*=8.0 Hz, 1H, Ar−H), 6.58 (dd, *J*=8.0, 2.0 Hz, 1H, Ar−H), 6.55 (d, *J*=2.0 Hz, 1H, Ar−H), 6.34 (s, 1H, Ar−H), 5.07 (br t, *J*=6.8 Hz, 1H, 3-CH_2CH═), 3.88, 3.83, 3.79 (each s, 9H, 3× OCH_3), 3.03 (br d, *J*=6.8 Hz, 2H, 3-CH_2CH═), 2.73 (d, *J*=6.8 Hz, 2H, −$COCH_2$−), 2.19−2.29 (m, 1H, −$CHMe_2$), 1.61, 1.41 (each br s, 6H, 2× CH_3), 0.97 (d, *J*=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 202.9, 182.4, 162.8, 161.9, 161.0, 159.1, 158.5, 158.4, 132.2, 131.3, 122.0, 121.2, 114.5, 114.4, 105.2, 104.6, 98.7, 89.7, 56.1, 55.6, 53.8, 25.7, 24.9, 24.2, 22.7, 17.6. EIMS *m*/*z* (%): 480 (M^+, 82), 449 (84), 437 (80), 423 (100), 251 (40), 193 (72), 175 (48), 75 (63). HRMS (EI) calcd for $C_{28}H_{32}O_7$ (M^+) 480.2148, found 480.2149.

4.8. 2-(2,4-Dimethoxyphenyl)-5-hydroxy-6-(1-hydroxy-3-methylbutyl)-7-methoxy-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (12)

To a solution of **3** (2.60 g, 5.42 mmol) in MeOH (30 mL), $NaBH_4$ (0.82 g, 21.66 mmol) was added. After stirring for 0.5 h, the reaction was quenched with water (40 mL), and extracted with EtOAc (3×50 mL). The organic phase was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was chromatographed over silica gel. Elution with hexanes/acetone (2:1) gave **12** (2.59 g, 99%) as a light yellow oil. IR (neat): ν 3558, 2955, 2865, 1713, 1616, 1585, 1449, 1352, 1206, 1147, 1030, 833 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.55 (s, 1H, Ar−OH), 7.23 (d, *J*=8.2 Hz, 1H, Ar−H), 6.51−6.58 (m, 2H, Ar−H), 6.35 (s, 1H, Ar−H), 5.17−5.23 (m, 1H, 6-CH(OH)−), 5.08 (br t, *J*=7.0 Hz, 1H, 3-CH_2CH═), 3.87, 3.85, 3.78 (each s, 9H, 3× OCH_3), 3.02 (br d, *J*=7.0 Hz, 2H, 3-CH_2CH═), 1.86−1.93 (m, 1H, −$CHMe_2$), 1.63−1.76 (m, 2H, −CH_2CHMe_2), 1.61, 1.41 (each br s, 6H, 2× CH_3), 0.97 (d, *J*=6.3 Hz, 3H, CH_3), 0.93 (d, *J*=6.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 162.8, 162.2, 161.0, 158.6, 158.3, 157.0, 132.0, 131.3, 121.5, 121.4, 114.6, 105.3, 104.7, 98.7, 89.7, 65.7, 55.9, 55.6, 55.5, 46.2, 25.7, 25.1, 24.2, 23.2, 22.4, 17.6. ESI-MS: $[M-H]^-$ 481.1; HRMS (ESI) calcd for $C_{28}H_{33}O_7$ $[M-H]^-$ 481.2231, found 481.2246.

4.9. (*E*)-2-(2,4-Dimethoxyphenyl)-5-hydroxy-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (13)

A mixture of **12** (2.712 g, 5.62 mmol) in 20% H_2SO_4 (50 mL) was heated to reflux for 3 h. The resulting mixture was cooled to room temperature, and extracted with EtOAc (3×40 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/acetone 5:1) to obtain **13** (1.93 g, 74%) as a light yellow solid, mp 160−161 °C (lit.[10] 152 °C). IR (neat): ν 3606, 2919, 1714, 1628, 1589, 1434, 1357, 1210, 1134, 938, 792, 761 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.71 (s, 1H, Ar−OH), 7.26 (d, *J*=8.4 Hz, 1H, Ar−H), 6.72 (dd, *J*=16.0, 6.8 Hz, 1H, 6-CH═CH−), 6.55−6.61 (m, 3H, Ar−H, 6-CH═CH−), 6.35 (s, 1H, Ar−H), 5.11 (br t, *J*=6.8 Hz, 1H, 3-CH_2CH═), 3.88 (s, 6H, 2× OCH_3), 3.79 (s, 3H, OCH_3), 3.04 (br d, *J*=6.8 Hz, 3-CH_2CH═), 2.45−2.53 (m,

1H, −$CHMe_2$), 1.57, 1.40 (each br s, 6H, 2× CH_3), 1.13 (d, *J*=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.4, 162.6, 162.6, 160.4, 159.0, 158.3, 156.4, 142.2, 131.9, 131.4, 121.6, 121.4, 115.8, 114.8, 109.3, 105.3, 104.6, 98.7, 89.3, 55.9, 55.6, 33.1, 25.7, 24.2, 22.7, 17.6. ESI-MS: $[M+H]^+$ 465.2; HRMS (ESI) calcd for $C_{28}H_{33}O_6$ $[M+H]^+$ 465.2271, found 465.2261.

4.10. (*E*)-5-Hydroxy-2-(2-hydroxy-4-methoxyphenyl)-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (14)and (*E*)-5-hydroxy-2-(4-hydroxy-2-methoxyphenyl)-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (15)

A solution of EtSH (1.1 mL, 14.82 mmol) in HMPA (10.0 mL) was cooled down to 0 °C for 10 min, and then added *n*-BuLi (2.5 M, 5.9 mL, 14.82 mmol) under N_2 atmosphere at that temperature and stirred for 30 min. Subsequently, compound **3** (1.153 g, 3.29 mmol) was introduced to the fresh solution of EtSLi in HMPA, and the resulting solution was warmed to 70 °C under N_2 atmosphere. After stirring at 70 °C for 2 h, the reaction mixture was cooled to room temperature and quenched with a saturated solution of NH_4Cl (7 mL), and extracted with ethyl acetate (3×10 mL). The organic phase was washed with saturated aqueous LiCl (20 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/acetone 5:1) to provide **14** (0.583 g, 52%) and **15** (0.371 g, 25%) as light yellow powders. Compound **14**: mp 161–162 °C. IR (neat): ν 3240, 1708, 1624, 1432, 1352, 1205, 1147, 968, 807 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 13.95, 8.94 (each s, 2H, 2× Ar−OH), 7.32 (d, *J*=8.4 Hz, 1H, Ar−H), 6.74 (dd, *J*=16.0, 6.8 Hz, 1H, 6-CH=CH−), 6.59–6.65 (m, 3H, 2× Ar−H, 6-CH=CH), 6.56 (s, 1H, Ar−H), 5.13 (br t, *J*=7.2 Hz, 1H, 3-CH_2CH=), 3.97, 3.85 (each s, 6H, 2× OCH_3), 3.13 (br d, *J*=7.2 Hz, 2H, 3-CH_2CH=), 2.43–2.48 (m, 1H, −$CHMe_2$), 1.58, 1.44 (each br s, 6H, 2× CH_3), 1.10 (d, *J*=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): 182.4, 163.0, 162.8, 161.2, 158.9, 156.6, 156.3, 141.4, 131.4, 131.4, 121.6, 121.2, 116.1, 113.0, 109.0, 105.6, 104.7, 101.7, 89.6, 55.7, 54.9, 33.1, 24.9, 23.7, 22.2, 16.8. ESI-MS: $[M-H]^-$ 449.2; HRMS (ESI) calcd mass for $C_{27}H_{31}O_6$ $[M+H]^+$ 451.2115, found 451.2102. Compound **15**: mp 195–196 °C. IR (neat): ν 3248, 2958, 1614, 1586, 1478, 1449, 1349, 1302, 1203, 1163, 835, 812 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 13.96, 9.04 (each s, 1H, Ar−OH), 7.26 (d, *J*=8.0 Hz, 1H, Ar−H), 6.74 (dd, *J*=16.4, 6.8 Hz, 1H, 6-CH=CH−), 6.67 (d, *J*=2.0 Hz, 1H, Ar−H), 6.59–6.63 (m, 2H, Ar−H, 6-CH=CH−), 6.54 (s, 1H, Ar−H), 5.09 (br t, *J*=7.2 Hz, 1H, 3-CH_2CH=), 3.97, 3.82 (each s, 6H, 2× OCH_3), 3.05 (br d, *J*=7.2 Hz, 2H, 3-CH_2CH=), 2.42–2.47 (m, 1H, −$CHMe_2$), 1.59, 1.41 (each br s, 6H, 2× CH_3), 1.10 (d, *J*=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 182.3, 163.0, 161.5, 161.0, 159.0, 158.7, 156.5, 141.4, 131.3, 131.2, 121.6, 121.0, 116.1, 113.3, 109.0, 107.2, 104.7, 99.2, 89.6, 55.7, 55.1, 33.1, 24.9, 23.7, 22.3, 16.7. ESI-MS: $[M-H]^-$ 449.2; HRMS (ESI) calcd for $C_{27}H_{31}O_6$ $[M+H]^+$ 451.2115, found 451.2098.

4.11. (*E*)-5-Hydroxy-7-methoxy-2-(4-methoxy-2-((4-methoxy benzyl)oxy)phenyl)-6-(3-methylbut-1-en-1-yl)-3-(3-methyl but-2-en-1-yl)-4*H*-chromen-4-one (16)

A solution of **14** (0.106 g, 0.24 mmol) in DMF (5 mL) was cooled down to 0 °C, NaH (19 mg, 0.47 mmol) was added. After stirring for 10 min, PMBCl (48 μL, 0.35 mmol) was added. The mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was cooled to room temperature and poured into ice water (30 mL), and extracted with EtOAc (3×30 mL). The organic phase was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was chromatographed over silica gel. Elution with hexanes/acetone (5:1) gave **16** (0.122 g, 91%) as a yellow oil. IR (neat): ν 3002, 2957, 1613, 1584, 1448, 1248, 1203, 1165, 1037, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.72 (s, 1H, Ar−OH), 7.25 (d, *J*=8.4 Hz, 1H, Ar−H), 7.20 (d, *J*=8.4 Hz, 2H, Ar−H), 6.80 (d, *J*=8.4 Hz, 2H, Ar−H), 6.72 (dd, *J*=16.0, 7.2 Hz, 1H, 6-CH=CH−), 6.56–6.62 (m, 3H, Ar−H, 6-CH=CH−), 6.30 (s, 1H, Ar−H), 5.09 (br t, *J*=6.8 Hz, 1H, 3-CH_2CH=), 5.01 (s, 2H, $ArCH_2O$−), 3.88, 3.84, 3.76 (each s, 9H, 3× OCH_3), 3.05 (br d, *J*=6.8 Hz, 2H, 3-CH_2CH=), 2.44–2.53 (m, 1H, −$CHMe_2$), 1.59, 1.40 (each br s, 6H, 2× CH_3), 1.12 (d, *J*=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.1, 162.3, 162.1, 160.2, 158.9, 158.6, 157.1, 156.0, 141.8, 131.7, 131.1, 128.2, 127.9, 121.2, 120.9, 115.4, 115.0, 113.5, 108.8, 104.9, 104.7, 100.1, 88.9, 69.9, 55.5, 55.2, 54.9, 32.8, 25.3, 24.0, 22.4, 17.3. ESI-MS: $[M+H]^+$ 571.2; HRMS (ESI) calcd mass for $C_{35}H_{39}O_7$ $[M+H]^+$ 571.2671, found 571.2690.

4.12. (*E*)-5-Hydroxy-2-(4-hydroxy-2-((4-methoxybenzyl)oxy) phenyl)-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (17)

Compound **17** was prepared as a light yellow oil in 49% yield according to the previous procedures. IR (neat): ν 3584, 2955, 1612, 1512, 1449, 1246, 1172, 1031, 815 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 13.69 (s, 1H, Ar−OH), 7.18–7.20 (m, 3H, Ar−H), 6.80 (d, *J*=8.8 Hz, 2H, Ar−H), 6.71 (dd, *J*=16.0, 6.8 Hz, 1H, 6-CH=CH−), 6.49–6.58 (m, 3H, Ar−H, 6-CH=CH−), 6.32 (s, 1H, Ar−H), 5.07 (br t, *J*=6.8 Hz, 1H, 3-CH_2CH=), 4.99 (s, 2H, $ArCH_2O$−), 3.87, 3.77 (each s, 6H, 2× OCH_3), 3.05 (br d, *J*=6.8 Hz, 2H, 3-CH_2CH=), 2.45–2.50 (m, 1H, −$CHMe_2$), 1.58, 1.40 (each br s, 6H, 2× CH_3), 1.11 (d, *J*=6.3 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.5, 162.7, 161.0, 159.4, 159.2, 158.7, 157.6, 156.3, 142.3, 132.7, 132.1, 131.5, 128.7, 128.5, 128.2, 121.4, 121.2, 115.7, 113.9, 113.8, 109.2, 107.6, 105.2, 101.0, 89.3, 70.1, 55.2, 33.1, 25.6, 24.3, 22.7, 17.6. ESI-MS: $[M-H]^-$ 555.2; HRMS (ESI) calcd mass for $C_{34}H_{35}O_7$ $[M-H]^-$ 555.2368, found 555.2388.

4.13. (*E*)-5-Hydroxy-7-methoxy-2-(2-methoxy-4-((4-methoxy benzyl)oxy)phenyl)-6-(3-methylbut-1-en-1-yl)-3-(3-methyl but-2-en-1-yl)-4*H*-chromen-4-one (18)

Compound **18** was prepared as a yellow oil in 84% yield according to the previous procedure. IR (neat): ν 2958, 1612, 1584, 1448, 1352, 1202, 1163, 1032, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.71 (s, 1H, Ar−OH), 7.38 (d, *J*=8.8 Hz, 2H, Ar−H), 7.23 (d, *J*=8.4 Hz, 1H, Ar−H), 6.94 (d, *J*=8.8 Hz, 2H, Ar−H), 6.72 (dd, *J*=16.4, 7.2 Hz, 1H, 6-CH=CH−), 6.63 (dd, *J*=8.4, 2.4 Hz, 1H, Ar−H), 6.56–6.61 (m, 2H, Ar−H, 6-CH=CH−), 6.33 (s, 1H, Ar−H), 5.09 (br t, *J*=6.8 Hz, 1H, 3-CH2CH=), 5.00 (s, 2H, $ArCH_2O$−), 3.86, 3.82, 3.76 (each s, 9H, 3× OCH_3), 3.03 (br d, *J*=6.8 Hz, 2H, 3-CH_2CH=), 2.44–2.52 (m, 1H, −$CHMe_2$), 1.60, 1.38 (each br s, 6H, 2× CH_3), 1.12 (d, *J*=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.4, 162.7, 161.8, 160.4, 159.7, 159.0, 158.3, 156.4, 142.2, 131.9, 131.3, 129.3, 128.4, 121.6, 121.4, 115.8, 115.0, 114.1, 109.4, 105.5, 105.3, 99.6, 89.3, 70.1, 55.9, 55.6, 55.3, 33.1, 25.7, 24.2, 22.7, 17.6. ESI-MS: $[M+H]^+$ 571.2; HRMS (ESI) calcd for $C_{35}H_{39}O_7$ $[M+H]^+$ 571.2690, found 571.2689.

4.14. (*E*)-2-(2,4-Dihydroxyphenyl)-5-hydroxy-7-methoxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (2)

Artocarpin (**2**) was prepared as a yellow powder in 18% yield according to the previous procedures, mp 164–165 °C (lit.[11] 174–175 °C). IR (neat): ν 3296, 2959, 1644, 1609, 1478, 1450, 1354, 1206, 1147, 978, 811 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 13.97 (s, 1H, Ar−OH), 8.82 (br s, 2H, 2× Ar−OH), 7.22 (d, *J*=8.4 Hz, 1H, Ar−H), 6.73 (dd, *J*=16.4, 6.8 Hz, 1H, 6-CH=CH−), 6.61 (br d, *J*=16.4 Hz, 1H, 6-CH=CH−), 6.58 (d, *J*=2.4 Hz, 1H, Ar−H), 6.56 (s, 1H, Ar−H), 6.54 (dd, *J*=8.4, 2.4 Hz, 1H, Ar−H), 5.14 (br t,

J=7.2 Hz, 1H, 3-CH_2CH=), 3.98 (s, 3H, OCH_3), 3.14 (br d, J=6.8 Hz, 2H, 3-CH_2CH=), 2.43–2.48 (m, 1H, −$CHMe_2$), 1.58, 1.45 (each br s, 6H, 2× CH_3), 1.10 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 182.4, 163.0, 161.6, 160.6, 159.0, 156.5, 156.3, 141.3, 131.4, 131.3, 121.6, 121.1, 116.1, 112.0, 108.9, 107.2, 104.7, 103.0, 89.6, 55.7, 33.1, 24.9, 23.8, 22.2, 16.8. ESI-MS: $[M-H]^-$ 435.2; HRMS (ESI) calcd for $C_{26}H_{27}O_6$ $[M-H]^-$ 435.1813, found 435.1803.

4.15. 5,7-Dihydroxy-2-(2-hydroxy-4-methoxyphenyl)-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (20a) and 5,7-dihydroxy-2-(4-hydroxy-2-methoxyphenyl)-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (20b)

Compounds **20a** and **20b** were prepared according to the previous procedure in 88% yield with a 1:1 ratio. **20a**: a yellow oil. IR (neat): ν 3401, 2959, 1624, 1584, 1456, 1377, 1172, 1035, 823 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6): δ 15.97, 14.15, 9.03 (each s, 3H, 3× Ar−OH), 7.33 (d, J=9.0 Hz, 1H, Ar−H), 6.62–6.64 (m, 2H, Ar−H), 6.27 (s, 1H, Ar−H), 5.11 (br t, J=7.0 Hz, 1H, 3-CH_2CH=), 3.84 (s, 3H, OCH_3), 3.12 (br d, J=7.0 Hz, 2H, 3-CH_2CH=), 3.08 (d, J=6.7 Hz, 2H, 6-$COCH_2$−), 2.24–2.31 (m, 1H, −$CHMe_2$), 1.58, 1.44 (each br s, 6H, 2× CH_3), 1.01 (d, J=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 206.6, 182.8, 169.3, 167.5, 163.0, 161.9, 160.7, 156.3, 131.9, 131.4, 121.1, 121.0, 112.4, 106.0, 105.7, 103.1, 101.7, 94.2, 54.9, 52.8, 24.9, 24.6, 23.7, 22.1, 16.8. ESI-MS: $[M-H]^-$ 451.1; HRMS (ESI) calcd for $C_{26}H_{29}O_7$ $[M+H]^+$ 453.1907, found 453.1895. **20b**: a yellow oil. IR (neat): ν 3408, 2959, 1636, 1584, 1457, 1382, 1307, 1177, 960, 887, 822 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6): δ 15.96, 14.15, 9.08 (each s, 3H, 3× Ar−OH), 7.28 (d, J=8.0 Hz, 1H, Ar−H), 6.65 (d, J=2.0 Hz, 1H, Ar−H), 6.60 (dd, J=8.0, 2.0 Hz, 1H, Ar−H), 6.24 (s, 1H, Ar−H), 5.09 (br t, J=7.2 Hz, 1H, 3-CH_2CH=), 3.82 (s, 3H, OCH_3), 3.08 (d, J=6.8 Hz, 2H, 6-$COCH_2$−), 3.04 (br d, J=7.2 Hz, 2H, 3-CH_2CH=), 2.28–2.33 (m, 1H, −$CHMe_2$), 1.59, 1.42 (each br s, 6H, 2× CH_3), 1.01 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 207.5, 183.6, 170.2, 168.4, 163.0, 162.1, 161.6, 159.7, 132.6, 132.3, 122.0, 121.7, 113.5, 108.2, 107.0, 103.9, 100.2, 95.1, 56.1, 53.7, 25.8, 25.5, 24.6, 23.0, 17.6; ESI-MS: $[M-H]^-$ 451.1; HRMS (ESI) calcd mass for $C_{26}H_{27}O_7$ $[M-H]^-$ 451.1762, found 451.1773.

4.16. 5,7-Dihydroxy-2-(4-methoxy-2-((4-methoxybenzyl)oxy)phenyl)-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (21a) and 5,7-dihydroxy-2-(2-methoxy-4-((4-methoxybenzyl)oxy)phenyl)-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (21b)

Compounds **21a** and **21b** were prepared according to the previous procedure. **21a**: a yellow oil, 97% yield. IR (neat): ν 3462, 2958, 1632, 1582, 1457, 1380, 1172, 1037, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 15.64, 14.23 (each s, 2H, 2× Ar−OH), 7.21–7.24 (m, 3H, Ar−H), 6.84 (d, J=8.8 Hz, 2H, Ar−H), 6.61 (d, J=2.0 Hz, 1H, Ar−H), 6.57 (dd, J=8.4, 2.0 Hz, 1H, Ar−H), 6.24 (s, 1H, Ar−H), 5.05 (br t, J=6.8 Hz, 1H, 3-CH_2CH=), 5.01 (s, 2H, $ArCH_2O$−), 3.84, 3.77 (each s, 6H, 2× OCH_3), 3.05 (d, J=6.8 Hz, 4H, 2× CH_2), 2.26–2.32 (m, 1H, −$CHMe_2$), 1.61, 1.43 (each br s, 6H, 2× CH_3), 1.00 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.0, 182.9, 169.4, 167.6, 162.8, 161.3, 160.7, 159.4, 157.6, 132.6, 131.5, 128.8, 128.2, 121.1, 114.6, 114.0, 106.3, 105.1, 103.4, 100.4, 94.5, 70.4, 55.6, 55.2, 53.2, 25.7, 25.0, 24.3, 22.8, 17.7. ESI-MS: $[M-H]^-$ 571.2; HRMS (ESI) calcd for $C_{34}H_{37}O_8$ $[M+H]^+$ 573.2483, found 573.2470. **21b**: a yellow oil, 66% yield. IR (neat): ν 3435, 3388, 1636, 1582, 1446, 1383, 1280, 1174, 1040, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 15.65, 14.21 (each s, 2H, 2× Ar−OH), 7.37 (d, J=8.4 Hz, 2H, Ar−H), 7.23 (d, J=8.4 Hz, 1H, Ar−H), 6.94 (d, J=8.4 Hz, 2H, Ar−H), 6.64 (dd, J=8.4, 2.4 Hz, 1H, Ar−H), 6.61 (d, J=2.4 Hz, 1H, Ar−H), 6.25 (s, 1H, Ar−H), 5.07–5.09 (m, 1H, 3-CH_2CH=), 5.07 (s, 2H, $ArCH_2O$−), 3.83, 3.78 (each s, 6H, 2× OCH_3), 3.06 (d, J=6.4 Hz, 2H, −$COCH_2$−), 3.03 (br d, J=6.8 Hz, 2H, 3-CH_2CH=), 2.26–2.33 (m, 1H, −$CHMe_2$), 1.62, 1.42 (each br s, 6H, 2× CH_3), 1.00 (d, J=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9, 182.7, 169.2, 167.4, 161.9, 160.9, 160.6, 159.5, 158.2, 132.4, 131.2, 129.2, 128.1, 121.1, 120.8, 114.0, 106.1, 105.2, 103.3, 99.5, 94.5, 70.0, 55.5, 55.2, 53.1, 25.6, 24.9, 24.0, 22.6, 17.5. ESI-MS: $[M+H]^+$ 573.1; HRMS (ESI) calcd mass for $C_{34}H_{37}O_8$ $[M+H]^+$ 573.2483, found 573.2471.

4.17. 5,7-Dihydroxy-2-(4-hydroxy-2-((4-methoxybenzyl)oxy)phenyl)-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (22)

According to the previous procedure, compounds **22** and **20a** were obtained in 61% and 22% yields, respectively. **22**: a light yellow oil. IR (neat): ν 3368, 2925, 1632, 1582, 1454, 1379, 1172, 1012, 822 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 15.62, 14.24 (each s, 2H, 2× Ar−OH), 7.24 (d, J=8.4 Hz, 2H, Ar−H), 7.18 (d, J=8.0 Hz, 1H, Ar−H), 6.84 (d, J=8.4 Hz, 2H, Ar−H), 6.57 (d, J=2.4 Hz, 1H, Ar−H), 6.49 (dd, J=8.0, 2.4 Hz, 1H, Ar−H), 6.25 (s, 1H, Ar−H), 5.07 (br t, J=6.8 Hz, 1H, 3-CH_2CH−), 5.00 (s, 2H, $ArCH_2O$−), 3.78 (s, 3H, OCH_3), 3.05 (d, J=6.8 Hz, 4H, 2× CH_2), 2.28–2.31 (m, 1H, −$CHMe_2$), 1.56, 1.44 (each br s, 6H, 2× CH_3), 1.00 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.2, 182.9, 169.3, 167.6, 161.5, 160.7, 159.4, 159.3, 157.9, 132.7, 131.6, 128.8, 128.1, 121.2, 121.0, 114.2, 114.0, 107.6, 106.3, 103.5, 101.0, 94.6, 70.3, 55.3, 53.2, 25.7, 25.0, 24.3, 22.8, 17.6. ESI-MS: $[M-H]^-$ 557.2; HRMS (ESI) calcd for $C_{33}H_{34}O_8Na$ $[M+Na]^+$ 581.2146, found 581.2135.

4.18. 2-(2,4-Dihydroxyphenyl)-5,7-dihydroxy-3-(3-methylbut-2-en-1-yl)-6-(3-methylbutanoyl)-4*H*-chromen-4-one (23)

Compound **23** was prepared as a yellow powder in 38% yield according to the previous procedure, mp 183–185 °C. IR (neat): ν 3292, 1623, 1581, 1452, 1367, 1173, 820 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6): δ 16.02, 14.14 (each s, 2H, 2× Ar−OH), 8.91, 8.86 (each br s, 2H, 2× Ar−OH), 7.23 (d, J=8.4 Hz, 1H, Ar−H), 6.57 (d, J=2.0 Hz, 1H, Ar−H), 6.53 (dd, J=8.4, 2.0 Hz, 1H, Ar−H), 6.28 (s, 1H, Ar−H), 5.12 (br t, J=6.8 Hz, 1H, 3-CH_2CH=), 3.13 (br d, J=6.8 Hz, 2H, 3-CH_2CH=), 3.08 (d, J=6.4 Hz, 2H, 6-$COCH_2$−), 2.26–2.33 (m, 1H, −$CHMe_2$), 1.58, 1.44 (each br s, 6H, 2× CH_3), 1.00 (d, J=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 207.4, 183.7, 170.2, 168.4, 163.1, 161.7, 161.6, 157.3, 132.7, 132.3, 130.4, 122.0, 121.6, 114.2, 112.1, 108.2, 103.8, 95.0, 53.6, 25.8, 25.4, 24.6, 23.0, 17.6. ESI-MS $[M-H]^-$: 437.1; HRMS (ESI) calcd mass for $C_{25}H_{25}O_7$ $[M-H]^-$ 437.1606, found 437.1623.

4.19. 2-(2,4-Dihydroxyphenyl)-5,7-dihydroxy-6-(1-hydroxy-3-methylbutyl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (24)

Compound **24** was prepared as a yellow oil in 99% yield according to the previous procedure. IR (neat): ν 3236, 1705, 1621, 1433, 1363, 1228, 1152, 978, 845, 811 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6): δ 13.59 (s, 1H, Ar−OH), 10.26 (br s, 1H, Ar−OH), 8.81 (br s, 2H, 2× Ar−OH), 6.93 (d, J=7.2 Hz, 1H, Ar−H), 6.52 (d, J=2.0 Hz, 1H, Ar−H), 6.48 (dd, J=7.2, 2.0 Hz, 1H, Ar−H), 6.32 (s, 1H, Ar−H), 5.39–5.41 (m, 1H, 6-CH(OH)−), 5.07 (br t, J=6.8 Hz, 1H, 3-CH_2CH=), 3.05 (br d, 2H, 3-CH_2CH=), 1.73–1.89 (m, 2H, −CH_2CHMe_2), 1.48–1.50 (m, 1H, −$CHMe_2$), 1.52, 1.38 (each br s, 6H, 2× CH_3), 0.93 (d, J=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 183.2, 164.2, 162.4, 161.4, 158.4, 157.8, 157.2, 132.1, 130.4, 122.5, 121.4, 114.1, 112.8, 112.3, 107.9, 103.7, 94.9, 67.6, 46.5, 25.7, 25.2, 24.5, 23.7, 22.0, 17.5. ESI-MS: $[M-H]^-$ 439.2; HRMS (ESI) calcd mass for $C_{25}H_{27}O_7$ $[M-H]^-$ 439.1762, found 439.1760.

4.20. 5,7-Dihydroxy-2-(4-hydroxy-2-((4-methoxybenzyl)oxy) phenyl)-6-(1-hydroxy-3-methylbutyl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (25)

Compound **25** was prepared as a white powder in 77% yield according to the previous procedure, mp 81–83 °C. IR (neat): ν 3239, 2956, 1616, 1459, 1360, 1247, 1169, 1030, 821 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 13.60 (s, 1H, Ar–OH), 10.32, 9.00 (each br s, 2H, 2× Ar–OH), 7.32 (d, J=8.4 Hz, 2H, Ar–H), 7.26 (d, J=8.0 Hz, 1H, Ar–H), 6.87 (d, J=8.4 Hz, 2H, Ar–H), 6.75 (d, J=2.0 Hz, 1H, Ar–H), 6.61 (dd, J=8.0, 2.0 Hz, 1H, Ar–H), 6.30 (s, 1H, Ar–H), 5.44–5.48 (m, 1H, 6-CH(OH)–), 5.07–5.09 (m, 1H, 3-CH_2CH=), 5.09 (s, 2H, $ArCH_2O$–), 3.77 (s, 3H, OCH_3), 3.08 (br d, J=7.0 Hz, 2H, 3-CH_2CH=), 1.80–1.91 (m, 2H, –CH_2CHMe_2), 1.52–1.55 (m, 1H, –$CHMe_2$), 1.57, 1.42 (each br s, 6H, 2× CH_3), 1.00 (d, J=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 182.3, 163.4, 161.7, 160.8, 159.5, 157.8, 157.6, 156.9, 131.4, 131.2, 128.9, 128.8, 121.8, 120.5, 113.9, 113.7, 113.7, 111.6, 107.5, 103.6, 100.9, 94.1, 69.8, 66.8, 54.6, 45.7, 24.9, 24.4, 23.8, 22.9, 21.2, 16.8. ESI-MS: $[M-H]^-$ 559.2; HRMS (ESI) calcd for $C_{33}H_{35}O_8$ $[M-H]^-$ 559.2337, found 559.2362.

4.21. (*E*)-5,7-Dihydroxy-2-(4-hydroxy-2-((4-methoxybenzyl) oxy)phenyl)-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (26)

A mixture of **25** (71 mg, 0.13 mmol) and 0.1% H_2SO_4 (20 mL) was warmed to 70 °C. After stirring for 2 h, the reaction mixture was cooled and extracted with EtOAc (3×20 mL). The organic phase was wash with brine, dried over $MgSO_4$, and evaporated, and the residue was chromatographed over silica gel. Elution with petroleum ether/acetone (2:1) gave **26** (20 mg, 30%) as a yellow solid, mp 70–74 °C. IR (neat): ν 3375, 1613, 1458, 1362, 1301, 1247, 1172, 1008, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.54 (s, 1H, Ar–OH), 7.21 (d, J=8.6 Hz, 2H, Ar–H), 7.17 (d, J=8.0 Hz, 1H, Ar–H), 6.82 (d, J=8.6 Hz, 2H, Ar–H), 6.56 (d, J=2.0 Hz, 1H, Ar–H), 6.49 (dd, J=8.0, 2.0 Hz, 1H, Ar–H), 6.42 (br d, J=16.8 Hz, 1H, 6-CH=CH–), 6.34 (s, 1H, Ar–H), 6.17 (dd, 1H, J=16.8, 6.6 Hz, 6-CH=CH–), 5.08 (br t, J=6.6 Hz, 1H, 3-CH_2CH=), 5.00 (s, 2H, $ArCH_2O$–), 3.78 (s, 3H, OCH_3), 3.04 (br d, J=6.6 Hz, 2H, 3-CH_2CH=), 2.54–2.57 (m, 1H, –$CHMe_2$), 1.58, 1.39 (each s, 6H, 2× CH_3), 1.14 (d, J=6.7 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 161.4, 159.3, 159.1, 159.0, 157.7, 156.4, 143.3, 132.2, 131.6, 128.6, 128.4, 121.5, 121.0, 116.8, 114.7, 114.0, 108.5, 107.7, 104.9, 101.1, 93.4, 70.2, 55.3, 32.5, 31.0, 25.6, 22.5, 17.6. ESI-MS: $[M+H]^+$ 543.2; HRMS (ESI) calcd for $C_{33}H_{35}O_7$ $[M+H]^+$ 543.2377, found 543.2364.

4.22. (*E*)-2-(4-Acetoxy-2-((4-methoxybenzyl)oxy)phenyl)-5-hydroxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-7-acetoxy-4*H*-chromen-4-one (27)

To a solution of **26** (28 mg, 0.052 mmol) in pyridine (3 mL) was added acetyl chloride (20 μL) dropwise at room temperature, and followed by stirring for 1 h. The resulting reaction mixture was quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/acetone 3:1) to obtain the product **27** (20 mg, 61%) as a viscous oil. IR (neat): ν 2960, 1770, 1616, 1446, 1198, 1153, 1017, 823 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.65 (s, 1H, Ar–OH), 7.32 (d, J=8.4 Hz, 1H, Ar–H), 7.19 (d, J=8.4 Hz, 2H, Ar–H), 6.86 (d, J=2.0 Hz, 1H, Ar–H), 6.80–6.84 (m, 3H, Ar–H), 6.56 (s, 1H, Ar–H), 6.46 (dd, J=16.0, 6.8 Hz, 1H, 6-CH=CH–), 6.29 (dd, J=16.0, 1.2 Hz, 1H, 6-CH=CH–), 5.00–5.04 (m, 1H, 3-CH_2CH=), 5.00 (s, 2H, $ArCH_2O$–), 3.78 (s, 3H, OCH_3), 3.04 (br d, J=6.4 Hz, 2H, 3-CH_2CH=), 2.43–2.52 (m, 1H, –$CHMe_2$), 2.33, 2.32 (each s, 6H, 2× $COCH_3$), 1.57, 1.38 (each br s, 6H, 2× CH_3), 1.10 (d, J=6.4 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 168.9, 168.3, 160.7, 159.7, 159.5, 157.1, 154.8, 153.3, 153.1, 143.6, 132.5, 131.1, 128.7, 127.8, 121.9, 121.0, 119.8, 115.6, 114.3, 114.1, 113.8, 108.5, 107.1, 101.2, 70.6, 55.2, 32.7, 25.5, 24.0, 22.5, 21.2, 21.0, 17.5. ESI-MS: $[M+H]^+$ 627.2; HRMS (ESI) calcd for $C_{37}H_{39}O_9$ $[M+H]^+$ 627.2588, found 627.2574.

4.23. (*E*)-2-(4-Acetoxy-2-hydroxyphenyl)-5-hydroxy-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-7-acetoxy-4*H*-chromen-4-one (28)

A mixture of compound **27** and $SnCl_2$ (20 mg, 0.032 mmol) in acetonitrile (3 mL) was added EtSH (15 μL) at room temperature under N_2 atmosphere, and monitored by TLC. After 3 h, the solvent was removed and the residue was subjected to column chromatography (silica gel, hexane/acetone 2:1) to give the product **28** as a light yellow solid (6 mg, 53%) with the recovery of **27** (6 mg, 30%). Further prolonging the reaction time, the reaction became more complex. **28**: mp 77–80 °C, IR (neat): ν 2960, 2926, 1771, 1618, 1446, 1368, 1199, 1147, 1017, 978, 899 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.54 (s, 1H, Ar–OH), 7.31 (d, J=8.8 Hz, 1H, Ar–H), 6.78–6.80 (m, 2H, Ar–H), 6.60 (s, 1H, Ar–H), 6.48 (dd, J=16.0, 7.2 Hz, 1H, 6-CH=CH–), 6.28 (dd, J=16.0, 1.2 Hz, 1H, 6-CH=CH–), 5.09 (br t, J=6.8 Hz, 1H, 3-CH_2CH=), 3.13 (br d, J=6.8 Hz, 2H, 3-CH_2CH=), 2.45–2.50 (m, 1H, –$CHMe_2$), 2.32 (s, 6H, 2× $COCH_3$), 1.63, 1.44 (each br s, 6H, 2× CH_3), 1.10 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.7, 168.9, 168.4, 159.6, 159.3, 154.5, 154.4, 153.3, 153.2, 143.9, 133.6, 131.0, 122.2, 120.3, 117.2, 115.3, 114.7, 114.1, 110.4, 108.2, 101.2, 32.7, 25.6, 24.1, 22.4, 21.2, 21.0, 17.6. ESI-MS: $[M+H]^+$ 507.1; HRMS (ESI) calcd for $C_{29}H_{31}O_8$ $[M+H]^+$ 507.2013, found 507.2016.

4.24. (*E*)-2-(2,4-Dihydroxyphenyl)-5,7-dihydroxy-6-(3-methyl but-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (1)

Compound **28** (10 mg, 0.02 mmol) was dissolved in THF (1 mL), and followed by deacetylation with NH_2NH_2–H_2O (6 μL, 0.11 mmol) at room temperature. The mixture was stirred for 1 h, and the resulting solution was diluted with CH_2Cl_2 (10 mL) and filtered by silica gel. The organic solvent was concentrated in vacuo, and the residue was purified by flash column chromatography (silica gel, hexane/acetone 3:2) to achieve **1** (6 mg, 72%) as an orange solid: mp 163–164 °C (lit[2a] 158–159 °C). IR (neat): ν 3468, 3415, 1711, 1616, 1435, 1364, 1230, 978, 818 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 14.08 (s, 1H, Ar–OH), 9.80 (br s, 1H, Ar–OH), 8.80 (br s, 2H, 2Ar–OH), 7.20 (d, J=8.4 Hz, 1H, Ar–H), 6.78 (dd, J=16.4, 7.2 Hz, 1H, 6-CH=CH–), 6.65 (dd, J=16.4, 1.0 Hz, 1H, 6-CH=CH–), 6.57 (d, J=2.0 Hz, 1H, Ar–H), 6.52 (dd, J=8.4, 2.0 Hz, 1H, Ar–H), 6.43 (s, 1H, Ar–H), 5.13 (br t, J=7.2 Hz, 1H, 3-CH_2CH=), 3.13 (br d, J=7.2 Hz, 2H, 3-CH_2CH=), 2.42–2.50 (m, 1H, –$CHMe_2$), 1.58, 1.44 (each br s, 6H, 2× CH_3), 1.11 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 182.4, 161.3, 161.3, 160.6, 159.9, 156.3, 156.1, 140.9, 131.4, 131.2, 121.8, 120.7, 116.4, 112.1, 108.3, 107.2, 104.1, 103.0, 92.9, 33.0, 24.9, 23.7, 22.2, 16.7. ESI-MS: $[M-H]^-$ 421.1; HRMS (ESI) calcd for $C_{25}H_{27}O_6$ $[M+H]^+$ 423.1802, found 423.1817.

4.25. Demethylation of compound 13 with 1-trimethylsilyl quinolinium iodide. (*E*)-5,7-Dihydroxy-2-(4-hydroxy-2-methoxyphenyl)-6-(3-methylbut-1-en-1-yl)-3-(3-methylbut-2-en-1-yl)-4*H*-chromen-4-one (29)

Hexane, quinoline, and iodotrimethylsilane were freshly distilled before use. In a glove box, a solution of iodotrimethylsilane (1.25 mL, 9.18 mmol, 1.0 equiv) in hexane (5 mL) was slowly added to a solution of quinoline (2.18 mL, 18.38 mmol, 2.0 equiv) in hexane (12.5 mL) with vigorous stirring, and a yellow precipitate formed

immediately. The solid was filtered and washed with hexane (5 mL×3) to afford 1-trimethylsilylquinolinium iodide, which was stored in a glove box.

In a glove box, compound **13** (30 mg, 0.0646 mmol, 1.0 equiv) and freshly prepared 1-trimethylsilylquinolinium iodide (510 mg, 1.55 mmol, 24.0 equiv) were added to a sealed tube equipped with a magnetic stir bar. The reaction vessel was sealed and heated to 140 °C for 6 h. Then the dark red mixture was cooled to room temperature and 1 N HCl (aq) was slowly added. The reaction mixture was extracted with EtOAc (10 mL×4). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by thin-layer chromatography (silica gel, hexane/acetone 2:1) to achieve **1** (15 mg, 55%) and **29** (9 mg, 32%). **29**: a light yellow powder, mp 90–91 °C. IR (neat): ν 3327, 2960, 1698, 1617, 1458, 1303, 1165, 1033, 979, 817, 738 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ 14.06 (s, 1H, Ar–OH), 7.23 (d, J=8.4 Hz, Ar–H), 6.77 (dd, 1H, J=16.4, 7.2 Hz, 1H, 6-CH=CH–), 6.64 (dd, J=16.4, 1.0 Hz, 1H, 6-CH=CH–), 6.64 (d, J=2.0 Hz, 1H, Ar–H), 6.58 (dd, J=8.0, 2.0 Hz, 1H, Ar–H), 6.40 (s, 1H, Ar–H), 5.08 (br t, J=6.8 Hz, 1H, 3-CH_2CH=), 3.80 (s, 3H, –OCH_3), 3.02 (br d, J=6.8 Hz, 2H, 3-CH_2CH=), 2.45 (m, 1H, –$CHMe_2$), 1.57, 1.39 (each br s, 6H, 2× CH_3), 1.09 (d, J=6.8 Hz, 6H, 2× CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ 183.1, 162.2, 162.1, 161.8, 160.7, 159.5, 156.9, 141.9, 132.2, 132.0, 122.6, 121.5, 117.3, 114.2, 109.2, 108.1, 105.0, 100.1, 93.8,60.0, 33.9, 25.8, 24.6, 23.1, 17.6. ESI-MS: $[M+H]^+$ 437.1; HRMS (ESI) calcd for $C_{26}H_{29}O_6$ $[M+H]^+$ 437.1959, found 437.1942.

Acknowledgements

Financial support from the National Natural Science Foundation of China (No. 81222045, 21072035, 21172044), the program for New Century Excellent Talents in University (No. NCET-09-0313), and the Science and Technology Commission of Shanghai Municipality (09dZ1976100) are gratefully acknowledged. We thank Dr. Xin Li for valuable discussions and help.

Supplementary data

These data include ^1H, ^{13}C NMR, and HMBC data for the most important compounds described in this article. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.05.024.

References and notes

1. (a) Zhao, T.; Yan, G. R.; Pan, S. L.; Wang, H. Y.; Hou, A. J. *Chem. Biodiversity* **2009**, *6*, 2209–2216; (b) Arung, E. T.; Shimizu, K.; Kondo, R. *Chem. Biodiversity* **2007**, *4*, 2166–2171; (c) Han, A. R.; Kang, Y. J.; Windono, T.; Lee, S. K.; Seo, E. K. *J. Nat. Prod.* **2006**, *69*, 719–721; (d) Venkataraman, K. *Phytochemistry* **1972**, *11*, 1571–1586; (e) Likhitwitayawuid, K.; Chaiwiriya, S.; Sritularak, B.; Lipipun, V. *Chem. Biodiversity* **2006**, *3*, 1138–1143; (f) Lin, C.-N.; Lu, C.-M.; Huang, P.-L. *Phytochemistry* **1995**, *39*, 1447–1451.
2. (a) Arung, E. T.; Shimizu, K.; Kondo, R. *Planta Med.* **2006**, *72*, 847–850; (b) Sato, S. F.; Tsuchiya, H.; Fujii, T.; Iinuma, M.; Tosa, H.; Ohkawa, Y. *J. Ethnopharmacol.* **1996**, *54*, 171–176; (c) Arung, E. T.; Yoshikawa, K.; Shimizu, K.; Kondo, R. *Fitoterapia* **2010**, *81*, 120–123; (d) Nagahata, T. PCT Int. Appl. WO 2008020490 A1, 2008; *Chem. Abstr. 148*, 268932.
3. (a) Wang, Y. H.; Hou, A. J.; Chen, L.; Chen, D. F.; Sun, H. D.; Zhao, Q. S.; Bastow, K. F.; Nakanish, Y.; Wang, X. H.; Lee, K. H. *J. Nat. Prod.* **2004**, *67*, 757–761; (b) Zou, Y. S.; Hou, A. J.; Zhu, G. F. *Chem. Biodiversity* **2005**, *2*, 131–138; (c) Hu, X.; Wu, J. W.; Zhang, X. D.; Zhao, Q. S.; Huang, J. M.; Wang, H. Y.; Hou, A. J. *J. Nat. Prod.* **2011**, *74*, 816–824; (d) Hu, X.; Ji, J.; Wang, M.; Wu, J. W.; Zhao, Q. S.; Wang, H. Y.; Hou, A. J. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4441–4446; (e) Yu, M. H.; Zhao, T.; Yan, G. R.; Yang, H. X.; Wang, H. Y.; Hou, A. J. *Chem. Biodiversity* **2012**, *9*, 394–402; (f) Zhang, L. B.; Ji, J.; Lei, C.; Wang, H. Y.; Zhao, Q. S.; Hou, A. J. *J. Nat. Prod.* **2012**, *75*, 699–706.
4. (a) Gissaub, M. A.; Tarafdar, S. A. *Indian J. Chem., Sect. B* **1998**, *37*, 540–543; (b) Rajendra Prasad, K. J.; Periasamy, P. A.; Vijayalakshmi, C. S. *J. Nat. Prod.* **1993**, *56*, 208–214.
5. Tseng, T. H.; Chuang, S. K.; Hu, C. C.; Chang, C. F.; Huang, Y. C.; Lin, C. W.; Lee, Y. J. *Tetrahedron* **2010**, *66*, 1335–1340.
6. Bouzide, A.; Sauve, G. *Synlett* **1997**, 1153–1154.
7. Jung, M. E.; Lyster, M. A. *Organic Syntheses*; 1988; Collect. Vol. No. 6353 1979, Vol. 59, 35.
8. (a) Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 5767–5769; (b) O'Malley, S. J.; Tan, K. L.; Watzke, A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 13496–13497; (c) Minamikawa, J.; Brossi, A. *Tetrahedron Lett.* **1978**, *34*, 3085–3086.
9. Masao, T. *Heterocycles* **2007**, *71*, 1589–1600.
10. Dave. *J. Sci. Ind. Res., Sect. B* **1961**, *20*, 112–119.
11. Dave; Venkataraman. *J. Sci. Ind. Res., Sect. B* **1956**, *15*, 183–187.