Expedient One-Pot Synthesis of γ-Hydroxybutenolides Starting from Baylis-Hillman Adducts: Lactonization, Isomerization, and Aerobic Oxidation of α-Methylene-γ-hydroxyester

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We developed an efficient three-step synthetic protocol of γ-hydroxybutenolides starting from the Baylis-Hillman adducts: (i) bromination, (ii) Barbier reaction and (iii) one-pot K_2CO_3-mediated synthesis of γ-hydroxybutenolides. In addition, we showed the synthetic applicability of butenolides including self-dimerization, conjugate addition reaction, and alkylations.

Key Words: Baylis-Hillman adducts, γ-Hydroxybutenolides, Hydroxylation, Lactones

Introduction

5-Hydroxyfuran-2(5*H*)-ones (γ-hydroxybutenolides) are an important class of compounds because they often occur in natural products and exhibit a broad range of biological activities.[1-3] These compounds are considered as antimutagen, bactericides, antitumor agents, allergy inhibitors, phospholipase A2 inhibitors, etc.[1] Relevant examples include dysidiolide, manoalide, petrosaspongiolides and cacospongionolides (Figure 1).[1] γ-Hydroxybutenolides are also useful as synthetic intermediates in the preparation of physiologically active compounds. Because of the importance in chemical as well as pharmaceutical research much attention has been focused on the efficient and diverse synthesis of this class of compounds.[1-3]

The most prevalent way to γ-hydroxybutenolide is the photooxidation of the furan moiety under basic conditions.[1a-e,3] γ-Hydroxybutenolides can also be synthesized from the corresponding butenolides by the aerobic oxidation of butenolide-containing sugar[2e] or 4-halobutenolides.[2a]

Results and Discussion

Based on the reported results,[2a,2e] we imagined that α-methylene-γ-butyrolactone such as **4a** can be transformed into γ-hydroxybutenolide **7a** *via* the sequential migration of double bond and concomitant aerobic oxidation process (Scheme 1). α-Methylene-γ-butyrolactones[4] can be synthesized by lactonization (*p*-TsOH) of the corresponding α-methylene-γ-hydroxyester **3a** which can be prepared from the Baylis-Hillman adduct[4-6] *via* the two-step bromination and indium-mediated Barbier reaction protocol.[4]

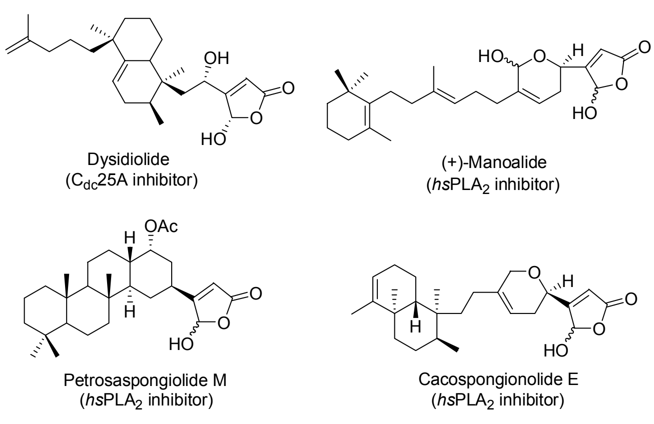
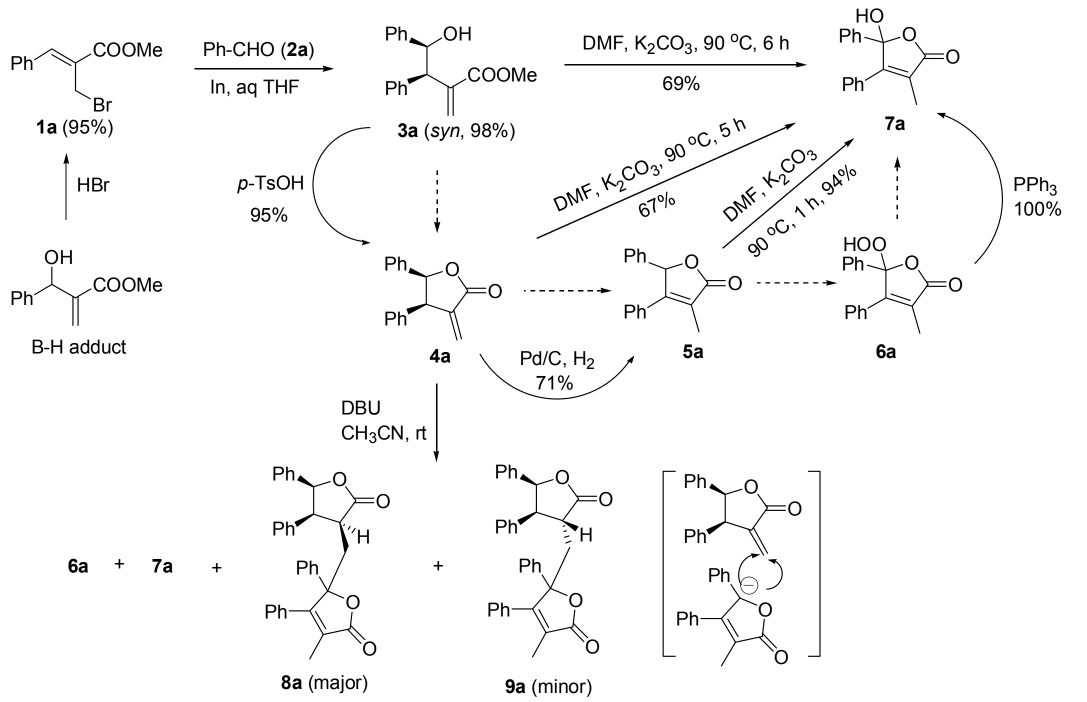


Figure 1. Natural γ-hydroxybutenolides.

Cinnamyl bromide **1a** was prepared by the reaction of Baylis-Hillman adduct and HBr as reported (95%).[4,5] Indium-mediated Barbier type reaction of **1a** and benzaldehyde (**2a**) produced *syn*-**3a** as the sole compound as reported in 98%.[4] Treatment of **3a** with *p*-toluenesulfonic acid (10 mol%) in CH_2Cl_2 furnished α-methylene-γ-butyrolactone **4a** in 95%.[4] Double bond migration was carried out under the influence of Pd/C under hydrogen balloon atmosphere in ethanol to produce butenolide **5a** in 71%.[7] Fully-reduced compound was not observed in this case (*vide infra*). As expected **5a** was converted into its 5-hydroxy derivative **7a** by aerobic oxidation process under the conditions of K_2CO_3 (30 mol%) in DMF in good yield (94%).[2a,2e,8] Initially we exposed the reaction mixture under air stream, however, the reaction showed almost same reactivity without bubbling of air. In some cases, especially under the influence of DBU instead of K_2CO_3, we observed the formation of a trace amount of hydroperoxide **6a**,[9] which was changed to **7a** by treatment with PPh_3 quantitatively (*vide infra*).

The reaction of **4a** under the same conditions (DMF, K_2CO_3, 90 °C) also produced **7a** in 67% yield, presumably *via* the simultaneous double bond isomerization and aerobic oxidation. More preferably, the reaction of α-methylene-γ-hydroxyester **3a** under the same conditions (DMF, K_2CO_3, 90 °C) gave **7a** in good yield (69%) also. Overall yields of compound **7a** were all similar: overall 63% yield for the three-step process (from **3a** *via* **4a** and **5a**); 64% for the two-step sequence (from **3a** *via* **4a**); 69% for direct synthesis from **3a**. Based on the simplicity and the yield of product **7a**, direct synthesis from **3a** was found as the best process. However, we observed some unknown compounds during the



DBU (0.3 equiv), CH_3CN, rt, 5 h: **6a** (1%), **7a** (5%), **8a** (62%), **9a** (12%)
DBU (1.2 equiv), CH_3CN, rt, 1 h: **6a** (14%), **7a** (13%), **8a** (43%), **9a** (8%)

Scheme 1. Optimization of conditions for the conversion of **3a** to **7a**.

synthesis of **7a** from **3a** or **4a**. In order to identify the side products we examined the reactions carefully. When we run the reaction of **4a** in the presence of DBU (30 mol%) in CH_3CN at room temperature, we observed the formation of compounds **6a** (1%), **7a** (5%) and diastereomeric dimers, **8a** (62%) and **9a** (12%).[10] With excess amounts of DBU (1.2 equiv) the ratio was changed to increase the amounts of **6a** (14%) and **7a** (13%). Hydroperoxide **6a** might be the plausible intermediate for the formation of **7a** as mentioned above. Dimeric compounds **8a** and **9a** were produced (51-74%) by conjugate addition of the anion of **4a** to the *exo*-methylene moiety of **4a**. The ratio of major and minor was 84:16 in both cases. The structures of compound **7a** and **8a** were assigned unequivocally by their X-ray crystal structures (Figures 2 and 3).[11,12]

Encouraged by the results, we prepared some analogous α-methylene-γ-hydroxyesters **3b-i** by following the same procedure of **3a**, and examined the one-pot synthesis of γ-hydroxybutenolides and the results are summarized in Table 1. We selected three Baylis-Hillman adducts which were derived from benzaldehyde (R_1 = Ph), 4-chlorobenzaldehyde (R_1 = 4-ClC_6H_4) and hexanal (R_1 = C_5H_{11}). In the next Barbier reaction, we examined six aldehydes, namely benzaldehyde (R_2 = Ph), 2-bromobenzaldehyde (R_2 = 2-BrC_6H_4), 4-chlorobenzaldehyde (R_2 = 4-ClC_6H_4), 4-methoxybenzaldehyde (R_2 = 4-$MeOC_6H_4$), 2-naphthylaldehyde (R_2 = 2-naphthyl) and hexanal (R_2 = C_5H_{11}). In all cases except entries 8 and 9, γ-hydroxybutenolides **7a-g** were prepared successfully in 53-69% yields. Aryl substituents R_1 and R_2 might facilitate both double-bond isomerization and aerobic oxidation process. When R_1 or R_2 is pentyl (entries 8 and 9), α-methylene-γ-butyrolactones **4h** and **4i** were isolated in high yields (94-95%) instead of desired γ-hydroxybutenolides **7h** and **7i**.

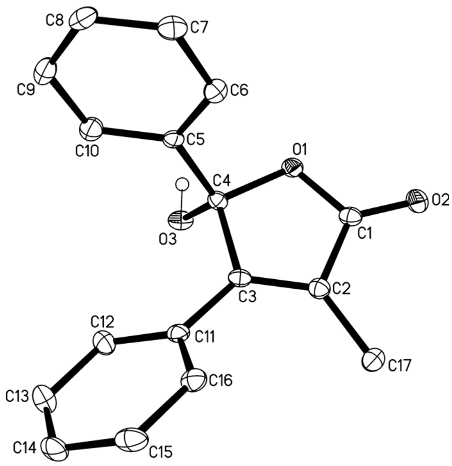


Figure 2. ORTEP drawing of compound **7a**.

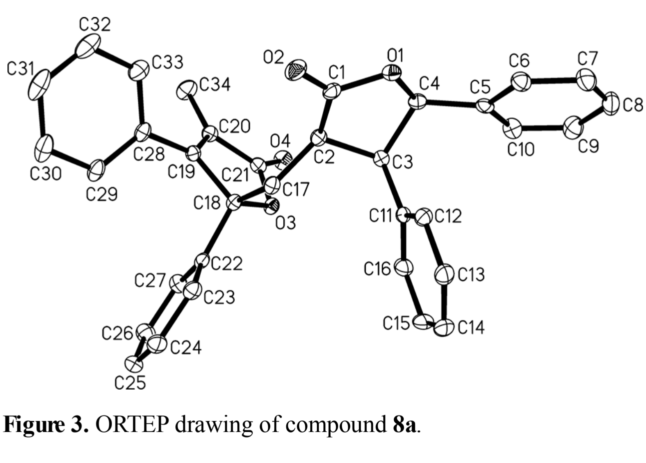
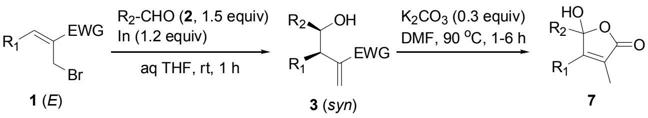


Figure 3. ORTEP drawing of compound **8a**.

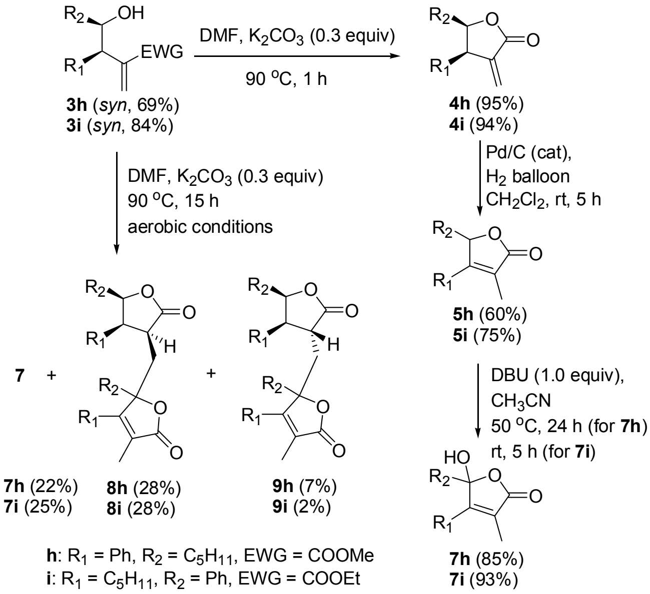
Table 1. Synthesis of γ-hydroxybutenolides



a: R_1 = Ph, R_2 = Ph, EWG = COOMe
b: R_1 = Ph, R_2 = Ph, EWG = COOEt
c: R_1 = 4-ClC_6H_4, R_2 = Ph, EWG = COOMe
d: R_1 = Ph, R_2 = 2-BrC_6H_4, EWG = COOMe
e: R_1 = Ph, R_2 = 4-ClC_6H_4, EWG = COOMe
f: R_1 = Ph, R_2 = 4-$MeOC_6H_4$, EWG = COOMe
g: R_1 = Ph, R_2 = 2-naphthyl, EWG = COOMe
h: R_1 = Ph, R_2 = C_5H_{11}, EWG = COOMe
i: R_1 = C_5H_{11}, R_2 = Ph, EWG = COOEt

Entry	**3** (%)	Time (h)	**7** (%)
1	**3a** (98)	6	**7a** (69)
2	**3b** (97)	3	**7a** (62)
3	**3c** (92)	3	**7c** (66)
4	**3d** (86)	2	**7d** (62)
5	**3e** (87)	2	**7e** (65)
6	**3f** (88)	2	**7f** (64)
7	**3g** (90)	3	**7g** (53)
8	**3h** (69)	1	**4h** (95)[a,b]
9	**3i** (84)	1	**4i** (94)[a,b]

[a]Compounds **4h** and **4i** were isolated in high yields instead of **7h** and **7i**. [b]Compounds **7h** and **7i** were synthesized from **4h** and **4i** (Scheme 2).

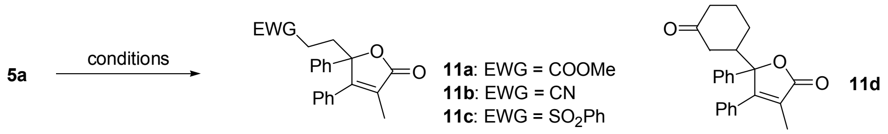


Scheme 2. Synthesis of **7h** and **7i** from **3h** and **3i** *via* three-step method.

When we subjected the reaction mixture of **3h** for a long time (15 h), as an example, we could isolate **7h** in low yield (22%), together with dimeric compounds **8h** (28%) and **9h** (7%). The reactivity of **3i** was similar and we obtained **7i** (25%), **8i** (28%) and **9i** (2%) under the same conditions (Scheme 2). Thus, we applied three-step conditions (*vide supra*) to **3h** and **3i** as in Scheme 2, namely lactonization, isomerization and aerobic oxidation. During double-bond isomerization process of **4h** and **4i**, fully reduced side products were formed a little and contaminated in about 20% (based on ^{1}H NMR) thus make the separation of pure **5h** and **5i** very difficult. Thus we carried out the isomerization under small size H_2 balloon and stopped the reaction after 5 h (starting material was remained in appreciable amounts). By using this protocol pure **5h** and **5i** were obtained in 60 and 75%, respectively. The next hydroxylation was carried out with DBU in CH_3CN. Compound **7i** was obtained at room temperature in high yield (93%), while the oxidation of compound **5h** to **7h** required elevated temperature (50 °C) and long reaction time (24 h). By using the three-step protocol, compounds **7h** and **7i** were synthesized elegantly from **3h** and **3i** in 49-65% overall yields.

As we observed in the case of **4a** (*vide supra,* Scheme 1), the formation of dimeric compounds **8a** and **9a** can be regarded as the results of competition between air oxidation to **7a** and conjugate addition reaction to **8a** and **9a**.[10,13] Air oxidation was the principal pathway with K_2CO_3 at elevated temperature (90 °C) while conjugate addition was the major reaction with DBU at room temperature. Thus, for the next examination, we tried conjugate additions of **5a** with some external Michael acceptors, methyl acrylate (**10a**), acrylonitrile (**10b**), phenyl vinyl sulfone (**10c**) and 2-cyclohexen-1-one (**10d**), and the results are summarized in Table 2. As a comparison experiment, the reaction of **5a** and **10a** was carried out under aerobic conditions (entry 1), and we observed the formation of **7a** and **11a**. In order to reduce the formation of aerobic oxidation product **7a** the next reactions were carried out under the strictly controlled nitrogen atmosphere (entries 2-5). The corresponding conjugate addition products **11a-d** were obtained in good to excellent yields (66-96%) and

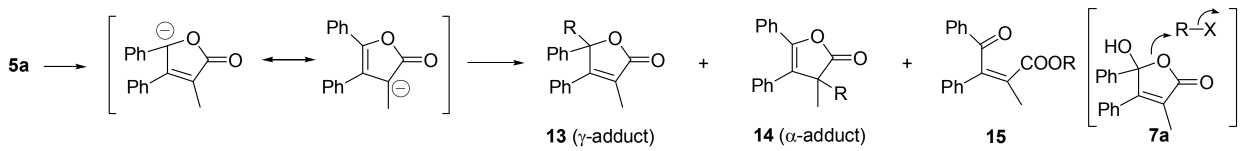
Table 2. Michael addition reaction of butenolide **5a**



Entry	Michael acceptor (**10**)	Conditions[a]	Products (%)
1	methyl acrylate (**10a**)	DBU (0.3 equiv), **10a** (3.0 equiv), CH_3CN, rt, 1 h	**7a** (35), **11a** (42)
2	**10a**	DBU (0.3 equiv), **10a** (3.0 equiv), CH_3CN, N_2, rt, 1 h	**11a** (90)
3	acrylonitrile (**10b**)	DBU (0.3 equiv), **10b** (3.0 equiv), CH_3CN, N_2, rt, 1 h	**11b** (70)
4	phenyl vinyl sulfone (**10c**)	DBU (0.3 equiv), **10c** (3.0 equiv), CH_3CN, N_2, rt, 1 h	**11c** (96)
5	2-cyclohexen-1-one (**10d**)	DBU (0.3 equiv), **10d** (3.0 equiv), CH_3CN, N_2, rt, 1 h	**11d** (66)

[a]Entry 1 was run under aerobic conditions and entries 2-5 under N_2 atmosphere.

Table 3. Alkylation of butenolide **5a**



Entry	Alkyl halide	Conditions	Products (%)
1	allyl bromide (**12a**)	DBU (0.3 equiv), **12a** (3.0 equiv), CH_3CN, N_2, rt, 1 h	**13a** (14), **14a** (67)
2	benzyl bromide (**12b**)	DBU (0.3 equiv), **12b** (3.0 equiv), CH_3CN, N_2, rt, 1 h	**13b** (4), **14b** (70)
3	iodomethane (**12c**)[a]	K_2CO_3 (1.5 equiv), **12c** (3.0 equiv), CH_3CN, rt, 5 h	**13c** (5),[b] **14c** (52), **15c** (25)[b]

[a]No reaction under DBU conditions. [b]R_f values of **13c** and **15c** were very similar and the yields of **13c**/**15c** were calculated based on ^{1}H NMR spectrum of the mixture.

we did not observe the formation of **7a** nor the dimeric compounds **8a** and **9a** in these cases.

Alkylation reaction of **5a** with allyl bromide (**12a**), benzyl bromide (**12b**) and iodomethane (**12c**) was also examined.[14] Due to the possible resonance structures of the anion of **5a**, alkylation occurred at either α- and γ-positions (Table 3).[15] The reaction of **5a** and allyl bromide under DBU conditions (entry 1) produced γ-adduct **13a** (14%) and α-adduct **14a** (67%). The trend was same in the reaction of benzyl bromide (entry 2), and α-adduct **14b** (70%) was the major product. The reaction of **5a** and iodomethane with DBU failed completely presumably due to the salt formation between CH_3I and DBU.[16] Thus we carried out the reaction under the influence of K_2CO_3 and obtained **13c** (5%), **14c** (52%) and **15c** (25%) as in entry 3 (*vide infra*). In all cases α-adduct was the major product irrespective of the kinds of alkyl halide and base. When we run the reaction with K_2CO_3 (entry 3) complete removal of molecular oxygen was very difficult due to the presence of volatile CH_3I. Thus appreciable amounts of γ-hydroxybutenolide **7a** was formed and reacted with CH_3I to produce finally γ-ketoester **15c**. Authentic compound **15c** was prepared from the reaction of **7a** and CH_3I (3.0 equiv) in the presence of K_2CO_3 (1.2 equiv) in DMF (rt, 2 h) in 93% yield.

In summary, we developed an efficient three-step synthetic protocol of γ-hydroxybutenolides starting from the Baylis-Hillman adducts: (i) bromination, (ii) Barbier reaction and (iii) one-pot K_2CO_3-mediated synthesis of γ-hydroxybutenolides. In addition, we showed the synthetic applicability of butenolides including the self-dimerization, conjugate addition reaction, and alkylations.

Experimental

General procedure. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$. The signal positions are reported in parts per million relative to TMS (δ scale) used as an internal standard. IR spectra are reported in cm^{-1}. Mass spectra were obtained from the Korea Basic Science Institute (Gwangju branch). Melting points are uncorrected. The elemental analyses were carried out at Korea Research Institute of Chemical Technology, Daejeon, Korea. All reagents were purchased from commercial sources and used without further treatment. The separations were carried out by flash column chromatography over silica gel (230-400 mesh ASTM). Organic extracts were dried over anhydrous $MgSO_4$ and the solvents were evaporated on a rotary evaporator under water aspirator pressure.

Typical procedure for the synthesis of 3a.[4e] To a stirred solution of **1a** (765 mg, 3.0 mmol) and benzaldehyde (**2a**, 477 mg, 4.5 mmol) in aqueous THF (1:1, 5 mL) was added indium powder (414 mg, 3.6 mmol) and stirred at room temperature for 1 h. After extractive workup and column chromatographic purification process (hexanes/EtOAc, 8:1) *syn*-**3a** was isolated as colorless oil, 829 mg (98%). Other compounds **3b-i** were prepared similarly and the spectroscopic data of **3a-i** are as follows.

Compound **3a**[4e]: Yield 98%; colorless oil; IR (film) 3503, 1717, 1249, 1144 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.30 (d, J = 3.6 Hz, 1H), 3.45 (s, 3H), 4.26 (dd, J = 8.1 and 0.9 Hz, 1H), 5.18 (dd, J = 8.1 and 3.6 Hz, 1H), 5.74 (d, J = 0.9 Hz, 1H), 6.18 (d, J = 0.9 Hz, 1H), 7.16-7.30 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.63, 54.03, 75.41, 126.69, 126.80, 126.90, 127.48, 127.96, 128.23, 129.06, 138.56, 140.93, 142.03, 166.78; ESIMS *m/z* 283 (M$^+$+1). Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.45; H, 6.67.

Compound **3b**[4i]: Yield 97%; colorless oil; IR (film) 3498, 1714, 1454, 1250, 1144, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (t, J = 7.2 Hz, 3H), 2.11 (br s, 1H), 3.94-4.05 (m, 2H), 4.30 (dd, J = 7.8 and 0.9 Hz, 1H), 5.26 (d, J = 7.8 Hz, 1H), 5.78 (d, J = 0.9 Hz, 1H), 6.23 (d, J = 0.9 Hz, 1H), 7.20-7.33 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.92, 54.23, 60.73, 75.67, 126.53, 126.94, 127.10, 127.69, 128.16, 128.43, 129.18, 138.68, 141.29, 142.04, 166.45; ESIMS *m/z* 297 (M$^+$+1).

Compound **3c**: Yield 92%; colorless oil; IR (film) 3489, 1714, 1492, 1250, 1144 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.15 (br s, 1H), 3.57 (s, 3H), 4.23 (d, J = 4.2 Hz, 1H), 5.23 (d, J = 4.2 Hz, 1H), 5.81 (t, J = 0.9 Hz, 1H), 6.24 (d, J = 0.9 Hz, 1H), 7.19-7.31 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.87, 53.58, 75.31, 126.69, 127.09, 127.78, 128.21, 128.36, 130.66, 132.80, 137.04, 140.78, 142.03, 166.80; ESIMS *m/z* 317 (M$^+$+1). Anal. Calcd for $C_{18}H_{17}ClO_3$: C, 68.25; H, 5.41. Found: C, 68.49; H, 5.77.

Compound **3d**: Yield 86%; white solid, mp 108-110 °C; IR (KBr) 3492, 1716, 1145 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (d, J = 4.5 Hz, 1H), 3.61 (s, 3H), 4.45 (d, J = 5.7 Hz, 1H), 5.61 (dd, J = 5.7 and 4.5 Hz, 1H), 6.08 (s, 1H), 6.37 (s, 1H), 7.08-7.31 (m, 8H), 7.52-7.55 (m, 1H); ^{13}C NMR ($CDCl_3$, 75

MHz) δ 51.77, 51.99, 73.95, 122.92, 126.88, 127.28, 127.29, 128.33, 128.56, 129.12, 129.49, 132.69, 137.40, 140.68, 140.99, 167.12; ESIMS *m/z* 361 (M^++1). Anal. Calcd for $C_{18}H_{17}BrO_3$: C, 59.85; H, 4.74. Found: C, 59.48; H, 4.83.

Compound **3e**[4d]: Yield 87%; colorless oil; IR (film) 3486, 1716, 1493, 1143 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.30 (d, *J* = 3.6 Hz, 1H), 3.56 (s, 3H), 4.21 (dd, *J* = 7.8 and 0.9 Hz, 1H), 5.22 (dd, *J* = 7.8 and 3.6 Hz, 1H), 5.77 (t, *J* = 0.9 Hz, 1H), 6.22 (d, *J* = 0.9 Hz, 1H), 7.18-7.33 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.83, 54.39, 74.83, 127.00, 127.20, 128.21, 128.25, 128.46, 129.11, 133.23, 138.17, 140.61, 140.78, 166.82; ESIMS *m/z* 317 (M^++1).

Compound **3f**[4d]: Yield 88%; colorless oil; IR (film) 3504, 1718, 1514, 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.03 (br s, 1H), 3.57 (s, 3H), 3.77 (s, 3H), 4.28 (d, *J* = 8.1 Hz, 1H), 5.21 (d, *J* = 8.1 Hz, 1H), 5.77 (s, 1H), 6.21 (s, 1H), 6.80-6.85 (m, 2H), 7.20-7.36 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.82, 54.26, 55.16, 75.33, 113.57, 126.67, 127.13, 128.16, 128.49, 129.10, 134.11, 138.88, 141.09, 159.08, 166.91; ESIMS *m/z* 313 (M^++1).

Compound **3g**: Yield 90%; colorless oil; IR (film) 3463, 2925, 2854, 1716, 1464, 1259 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.27 (br s, 1H), 3.46 (s, 3H), 4.39 (d, *J* = 7.8 Hz, 1H), 5.38 (d, *J* = 7.8 Hz, 1H), 5.80 (s, 1H), 6.19 (s, 1H), 7.22-7.34 (m, 5H), 7.40-7.45 (m, 3H), 7.66 (s, 1H), 7.30-7.79 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.77, 54.22, 75.76, 124.65, 125.85, 125.97, 126.15, 126.90, 127.19, 127.57, 127.95, 128.03, 128.50, 129.19, 132.98, 133.00, 138.48, 139.45, 140.94, 166.89; ESIMS *m/z* 333 (M^++1). Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.06. Found: C, 79.43; H, 6.43.

Compound **3h**[4c]: Yield 69%; colorless oil; IR (film) 3528, 2953, 2931, 2857, 1721, 1252, 1146 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, *J* = 8.0 Hz, 3H), 1.24-1.32 (m, 4H), 1.36-1.39 (m, 1H), 1.45 (d, *J* = 5.0 Hz, 1H), 1.50-1.56 (m, 2H), 3.68 (s, 3H), 3.91 (d, *J* = 6.5 Hz, 1H), 4.13-4.14 (m, 1H), 5.88 (s, 1H), 6.36 (s, 1H), 7.22-7.26 (m, 1H), 7.29-7.33 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.99, 22.58, 25.57, 31.71, 35.35, 51.94, 52.46, 72.74, 126.04, 127.03, 128.50, 129.27, 138.86, 141.71, 167.25; ESIMS *m/z* 277 (M^++1).

Compound **3i**: Yield 84%; colorless oil; IR (film) 3461, 2956, 2931, 2859, 1713, 1151 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.82 (t, *J* = 6.9 Hz, 3H), 1.05-1.26 (m, 6H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.50-1.66 (m, 2H), 2.83 (d, *J* = 3.0 Hz, 1H), 2.92-2.99 (m, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 4.84 (dd, *J* = 5.1 and 3.0 Hz, 1H), 5.42 (dd, *J* = 1.2 and 0.9 Hz, 1H), 6.22 (d, *J* = 1.2 Hz, 1H), 7.19-7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.97, 14.12, 22.45, 27.03, 27.34, 31.75, 49.37, 60.94, 76.44, 126.47, 126.76, 127.15, 127.91, 140.89, 142.65, 168.03; ESIMS *m/z* 291 (M^++1). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.77; H, 9.34.

Typical procedure for the synthesis of compound 7a. A mixture of **3a** (564 mg, 2.0 mmol) and K_2CO_3 (83 mg, 0.6 mmol) in DMF (1.5 mL) was heated to 90 °C for 6 h. After extractive workup and column chromatographic purification process (hexanes/EtOAc, 7:1) **7a** was isolated as colorless oil, 367 mg (69%). Other γ-hydroxybutenolides **7c-g** and butyrolactones **4h** and **4i** were prepared similarly and the spectroscopic data of **7a**, **7c-g**, **4h** and **4i** are as follows.

Compound **7a**[2b]: Yield 69%; pale yellow solid, mp 169-171 °C; IR (KBr) 3253, 2924, 1734, 1448, 1340, 1238, 1138 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.05 (s, 3H), 4.23 (br s, 1H), 7.29-7.33 (m, 8H), 7.40-7.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) 10.04, 106.05, 125.37, 125.83, 128.47 (2C), 128.61, 129.28, 129.60, 130.53, 137.14, 158.62, 172.58; ESIMS *m/z* 267 (M^++1). Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.46; H, 5.12.

Compound **7c**: Yield 66%; pale yellow solid, mp 152-153 °C; IR (KBr) 3357, 1741, cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.00 (s, 3H), 5.55 (br s, 1H), 7.25-7.33 (m, 7H), 7.36-7.41 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.96, 106.52, 125.53, 125.76, 128.47, 128.73, 128.94, 129.27, 129.97, 135.67, 136.70, 157.76, 173.27; ESIMS *m/z* 301 (M^++1). Anal. Calcd for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36. Found: C, 68.04; H, 4.34.

Compound **7d**: Yield 62%; pale yellow solid, mp 166-168 °C; IR (KBr) 3329, 2924, 1745 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.02 (s, 3H), 7.21-7.26 (m, 1H), 7.32-7.44 (m, 6H), 7.54 (dd, *J* = 7.8 and 1.8 Hz, 1H), 8.04 (dd, *J* = 7.8 and 1.8 Hz, 1H), 8.58 (br s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 10.02, 104.57, 120.11, 127.11, 127.66, 128.04, 128.52, 129.46, 130.27, 130.61, 131.05, 134.73, 135.38, 155.17, 172.59; ESIMS *m/z* 345 (M^++1). Anal. Calcd for $C_{17}H_{13}BrO_3$: C, 59.15; H, 3.80. Found: C, 59.46; H, 3.93.

Compound **7e**: Yield 65%; pale yellow solid, mp 129-131 °C; IR (KBr) 3315, 1743 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.01 (s, 3H), 5.55 (br s, 1H), 7.20-7.25 (m, 2H), 7.31-7.35 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.97, 106.18, 125.26, 127.40, 128.50, 128.55, 128.57, 129.71, 130.29, 135.12, 135.62, 158.76, 173.34; ESIMS *m/z* 301 (M^++1). Anal. Calcd for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36. Found: C, 67.88; H, 4.73.

Compound **7f**: Yield 64%; pale yellow oil; IR (film) 3350, 1736, 1514, 1253, cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.03 (s, 3H), 3.77 (s, 3H), 4.36 (br s, 1H), 6.79-6.82 (m, 2H), 7.31-7.34 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.99, 55.23, 106.23, 113.77, 125.08, 127.29, 128.44, 128.63, 129.19, 129.53, 130.68, 158.70, 160.16, 172.73; ESIMS *m/z* 297 (M^++1). Anal. Calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44. Found: C, 73.12; H, 5.67.

Compound **7g**: Yield 53%; pale yellow solid, mp 157-159 °C; IR (KBr) 3356, 1741 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.08 (s, 3H), 4.60 (br s, 1H), 7.25-7.39 (m, 6H), 7.44-7.52 (m, 2H), 7.74-7.80 (m, 3H), 8.02 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.10, 106.29, 123.05, 125.52, 125.60, 126.42, 126.86, 127.57, 128.42, 128.47, 128.54, 128.61, 129.62, 130.50, 132.78, 133.43, 134.41, 158.67, 172.81; ESIMS *m/z* 317 (M^++1). Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.46; H, 5.13.

Compound **4h**[4c]: Yield 95%; colorless oil; IR (film) 2928, 1751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.80 (t, *J* = 7.0 Hz, 3H), 1.06-1.31 (m, 7H), 1.42-1.46 (m, 1H), 4.35 (dt, *J* = 8.0 and 2.5 Hz, 1H), 4.86-4.73 (m, 1H), 5.60 (d, *J* = 3.0 Hz, 1H), 6.44 (d, *J* = 3.0 Hz, 1H), 7.14-7.15 (m, 2H), 7.28-7.36 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.85, 22.36, 25.36, 31.32, 32.39, 49.48, 81.76, 124.07, 127.65, 128.67, 129.03, 137.58, 139.13, 170.44; ESIMS *m/z* 245 (M^++1).

Compound **4i**: Yield 94%; colorless oil; IR (film) 2955, 2931, 2859, 1769, 1147 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ

0.78 (t, J = 7.0 Hz, 3H), 0.95-1.00 (m, 1H), 1.06-1.28 (m, 7H), 3.21-3.25 (m, 1H), 5.59 (d, J = 7.5 Hz, 1H), 5.60 (d, J = 2.5 Hz, 1H), 6.32 (d, J = 2.5 Hz, 1H), 7.21-7.22 (m, 2H), 7.32-7.37 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.76, 22.14, 25.77, 28.70, 31.30, 44.43, 82.06, 121.70, 126.16, 128.28, 128.32, 135.91, 139.15, 170.51; ESIMS *m/z* 245 (M^++1). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.54; H, 8.06.

Compounds 4a, 5a and 6a were synthesized as in Scheme 1, and the spectroscopic data of these compounds are as follows.

Compound **4a**[4c,e]: Yield 95%; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.67 (dt, J = 8.4 and 3.0 Hz, 1H), 5.78 (d, J = 3.0 Hz, 1H), 5.84 (d, J = 8.4 Hz, 1H), 6.52 (d, J = 3.0 Hz, 1H), 6.73-6.77 (m, 2H), 6.82-6.86 (m, 2H), 7.03-7.13 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 51.91, 82.53, 124.82, 125.82, 127.34, 127.86, 127.91, 128.13, 129.23, 136.10, 136.28, 137.91, 170.71; ESIMS *m/z* 251 (M^++1).

Compound **5a**[7b-d]: Yield 71%; colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.16 (d, J = 2.1 Hz, 3H), 6.18 (dd, J = 3.6 and 1.5 Hz, 1H), 7.20-7.31 (m, 7H), 7.32-7.38 (m, 3H); ESIMS *m/z* 251 (M^++1).

Compound **6a**: Yield 14%; white solid, mp 155-157 °C; IR (film) 3246, 2923, 1751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.04 (s, 3H), 7.28-7.33 (m, 4H), 7.40 (s, 6H), 8.95 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.90, 111.88, 126.33, 127.43, 128.40, 128.63, 128.66, 129.69, 129.86, 130.43, 133.28, 156.29, 171.76; ESIMS *m/z* 283 (M^++1). Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.48; H, 4.84.

Typical procedure for the synthesis of compound 5h. A mixture of **4h** (244 mg, 1.0 mmol) and Pd/C (15 mg) in CH_2Cl_2 (3 mL) was stirred to room temperature for 5 h under hydrogen balloon. After removal of solvent and column chromatographic purification process (CH_2Cl_2/$CHCl_3$, 1:1) **5h** was isolated as colorless oil, 147 mg (60%). When we used different solvent system for the purification of **5h** the separation from the remaining **4h** was very difficult. Compound **5i** was prepared similarly and the spectroscopic data of **5h** and **5i** are as follows.

Compound **5h**: Yield 60%; colorless oil; IR (film) 2928, 1751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.83 (t, J = 7.0 Hz, 3H), 1.17-1.25 (m, 4H), 1.35-1.46 (m, 3H), 1.77-1.83 (m, 1H), 2.04 (s, 3H), 5.32-5.34 (m, 1H), 7.33-7.35 (m, 2H), 7.43-7.51 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.95, 13.88, 22.36, 24.15, 31.34, 32.93, 81.82, 123.67, 127.73, 129.01, 129.68, 131.71, 159.50, 174.62; ESIMS *m/z* 245 (M^++1). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.37; H, 8.02.

Compound **5i**: Yield 75%; colorless oil; IR (film) 2930, 1757 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (t, J = 6.9 Hz, 3H), 1.15-1.47 (m, 6H), 1.91 (s, 3H), 1.95-2.04 (m, 1H), 2.28-2.38 (m, 1H), 5.68 (d, J = 1.5 Hz, 1H), 7.17-7.23 (m, 2H), 7.34-7.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.02, 14.08, 22.46, 26.86, 27.48, 31.75, 84.37, 123.25, 127.20, 129.16, 129.50, 135.30, 163.52, 175.25; ESIMS *m/z* 245 (M^++1). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.96; H, 8.54.

Typical procedure for the synthesis of compound 7h. A mixture of **5h** (122 mg, 0.5 mmol) and DBU (76 mg, 0.5 mmol) in CH_3CN (1 mL) was heated to 50 °C for 24 h. After aqueous workup and column chromatographic purification process (hexanes/EtOAc, 10:1) **7h** was isolated as colorless oil, 111 mg (85%). Compound **7i** was prepared similarly and the spectroscopic data of **7h** and **7i** are as follows.

Compound **7h**: Yield 85%; colorless oil; IR (film) 3359, 2925, 1739 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.79 (t, J = 6.6 Hz, 3H), 1.16-1.23 (m, 4H), 1.28-1.35 (m, 2H), 1.73-1.83 (m, 1H), 1.93-1.99 (m, 1H), 2.04 (s, 3H), 3.48 (br s, 1H), 7.43-7.50 (m, 3H), 7.59-7.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.01, 13.79, 22.27, 22.53, 31.31, 36.94, 107.41, 125.86, 128.44, 128.76, 129.80, 130.86, 156.96, 172.01; ESIMS *m/z* 261 (M^++1). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.59; H, 7.57.

Compound **7i**: Yield 93%; colorless oil; IR (film) 3367, 2956, 2930, 2862, 1742, 1451 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.79 (t, J = 7.0 Hz, 3H), 1.12-1.22 (m, 5H), 1.26-1.36 (m, 1H), 1.84 (s, 3H), 2.13-2.22 (m, 2H), 4.40 (br s, 1H), 7.35-7.38 (m, 3H), 7.43-7.46 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 8.60, 13.77, 22.07, 25.79, 26.98, 31.73, 106.28, 124.12, 125.64, 128.49, 129.19, 136.98, 163.27, 173.66; ESIMS *m/z* 261 (M^++1). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.67; H, 7.92.

Typical procedure for the synthesis of compound 8a and 9a. A mixture of **4a** (250 mg, 1.0 mmol) and DBU (46 mg, 0.3 mmol) in CH_3CN (3 mL) was stirred at room temperature for 5 h. After aqueous workup and column chromatographic purification process (hexanes/ether, 5:1) **8a** (156 mg, 62%) and **9a** (31 mg, 12%) were isolated as colorless oils together with small amounts of **6a** and **7a**. Compounds **8h**, **8i**, **9h** and **9i** were prepared similarly under the conditions of K_2CO_3/DMF at 90 °C from **3h** and **3i** (Scheme 2), and the spectroscopic data of **8a**, **9a**, **8h**, **9h**, **8i** and **9i** are as follows.

Compound **8a**: Yield 62%; white solid, mp 174-176 °C; IR (KBr) 1759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.93 (s, 3H), 2.33 (dd, J = 15.0 and 9.6 Hz, 1H), 2.99 (dd, J = 15.0 and 1.5 Hz, 1H), 3.22 (ddd, J = 9.6, 7.5 and 1.5 Hz, 1H), 3.84 (dd, J = 7.5 and 5.1 Hz, 1H), 5.81 (d, J = 5.1 Hz, 1H), 6.78-6.80 (m, 2H), 6.86-6.90 (m, 2H), 6.94-7.25 (m, 13H), 7.30-7.40 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.75, 31.55, 43.10, 52.64, 83.41, 90.27, 125.24, 125.34, 125.77, 127.24, 127.38, 127.83, 127.92, 128.18, 128.32, 128.39, 128.71 (2C), 129.39, 131.01, 133.84, 135.34, 137.52, 163.79, 173.46, 177.75; ESIMS *m/z* 501 (M^++1). Anal. Calcd for $C_{34}H_{28}O_4$: C, 81.58; H, 5.64. Found: C, 81.26; H, 5.48.

Compound **9a**: Yield 12%; white solid, mp 209-211 °C; IR (KBr) 1759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.74 (s, 3H), 2.31 (dd, J = 14.7 and 9.0 Hz, 1H), 3.01-3.14 (m, 2H), 4.10 (t, J = 7.2 Hz, 1H), 5.77 (d, J = 7.8 Hz, 1H), 6.53-6.55 (m, 2H), 6.70-6.73 (m, 2H), 6.77-6.80 (m, 2H), 6.92-6.99 (m, 5H), 7.05-7.07 (m, 3H), 7.16-7.20 (m, 3H), 7.32-7.38 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.44, 37.52, 42.61, 52.09, 82.90, 89.72, 124.34, 125.54, 125.81, 126.81, 127.58, 127.79, 127.82, 128.08, 128.32, 128.37, 128.49, 128.56, 129.23, 131.09, 135.28, 135.75, 136.20, 165.49, 173.02, 178.99; ESIMS *m/z* 501 (M^++1). Anal. Calcd for $C_{34}H_{28}O_4$: C, 81.58; H, 5.64. Found: C, 81.23; H, 5.92.

Compound **8h**: Yield 28%; white solid, mp 94-96 °C; IR

(KBr) 2929, 1751 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.73-0.82 (m, 6H), 0.98-1.29 (m, 12H), 1.37-1.52 (m, 4H), 1.79 (dd, J = 15.6 and 9.9 Hz, 1H), 1.93 (s, 3H), 2.43 (d, J = 15.6 Hz, 1H), 2.74-2.80 (m, 1H), 3.59 (dd, J = 7.8 and 2.1 Hz, 1H), 4.56-4.62 (m, 1H), 7.08-7.14 (m, 2H), 7.22-7.36 (m, 5H), 7.39-7.49 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.89, 13.80, 13.81, 22.23, 22.27, 22.29, 25.29, 30.68, 30.93, 31.33, 31.38, 37.15, 42.68, 50.64, 83.53, 91.17, 127.42, 127.58, 127.63, 128.60, 129.11 (2C), 129.49, 131.42, 134.78, 162.06, 173.38, 178.16; ESIMS *m/z* 489 (M^++1). Anal. Calcd for $C_{32}H_{40}O_4$: C, 78.65; H, 8.25. Found: C, 78.34; H, 8.03.

Compound **9h**: Yield 7%; white solid, mp 99-101 °C; IR (KBr) 2954, 2928, 1755 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.78-0.92 (m, 6H), 0.99-1.43 (m, 16H), 1.78 (d, J = 14.7 Hz, 1H), 1.81 (s, 3H), 2.32 (dd, J = 14.7 and 6.6 Hz, 1H), 3.19-3.26 (m, 1H), 3.66 (t, J = 7.5 Hz, 1H), 4.57-4.64 (m, 1H), 7.15-7.23 (m, 4H), 7.27-7.48 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.84, 13.86, 13.94, 22.39, 22.52, 25.52, 29.69, 30.80, 31.33, 31.48, 34.20, 38.10, 41.48, 50.72, 82.36, 89.95, 126.00, 127.60, 127.67, 128.28, 128.90, 129.07, 129.47, 131.59, 136.56, 162.73, 172.96, 178.69; ESIMS *m/z* 489 (M^++1). Anal. Calcd for $C_{32}H_{40}O_4$: C, 78.65; H, 8.25. Found: C, 78.77; H, 8.50.

Compound **8i**: Yield 28%; white solid, mp 98-100 °C; IR (KBr) 2955, 2930, 1759 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.68 (t, J = 7.0 Hz, 3H), 0.80 (t, J = 7.0 Hz, 3H), 0.83-0.91 (m, 3H), 0.93-0.99 (m, 4H), 1.14-1.27 (m, 7H), 1.86 (s, 3H), 1.99 (dd, J = 15.0 and 10.5 Hz, 1H), 2.17-2.23 (m, 1H), 2.28-2.34 (m, 1H), 2.70 (dt, J = 10.5 and 2.5 Hz, 1H), 2.82-2.87 (m, 1H), 3.05 (dd, J = 15.0 and 2.5 Hz, 1H), 5.63 (d, J = 6.0 Hz, 1H), 7.19 (d, J = 7.5 Hz, 2H), 7.27-7.29 (m, 4H), 7.41 (d, J = 4.0 Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.99, 13.76, 13.77, 22.04, 22.27, 26.07, 26.25, 27.48, 28.56, 31.48, 31.87, 36.44, 43.54, 44.97, 83.06, 90.27, 122.04, 125.54, 125.60, 127.96, 128.38, 128.51, 129.07, 135.91 (2C), 167.90, 173.91, 179.64; ESIMS *m/z* 489 (M^++1). Anal. Calcd for $C_{32}H_{40}O_4$: C, 78.65; H, 8.25. Found: C, 78.44; H, 8.47.

Compound **9i**: Yield 2%; white solid, mp 113-115 °C; IR (KBr) 2955, 2930, 2860, 1760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.77-0.82 (m, 6H), 0.86-1.01 (m, 7H), 1.08-1.32 (m, 7H), 1.89 (s, 3H), 2.22-2.78 (m, 1H), 2.33-2.36 (m, 1H), 2.40-2.46 (m, 1H), 2.55-2.58 (m, 1H), 2.61 (dd, J = 15.0 and 8.5 Hz, 1H), 2.88 (dd, J = 15.0 and 3.5 Hz, 1H), 5.62 (d, J = 6.5 Hz, 1H), 7.17 (d, J = 7.5 Hz, 2H), 7.30-7.40 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.03, 13.76, 13.87, 22.01, 22.36, 26.63, 26.71, 27.03, 28.45, 31.79, 31.90, 34.60, 42.15, 46.47, 82.88, 89.48, 123.88, 124.91, 125.65, 128.18, 128.50, 128.63, 128.82, 135.67, 138.50, 166.28, 173.94, 179.29; ESIMS *m/z* 489 (M^++1). Anal. Calcd for $C_{32}H_{40}O_4$: C, 78.65; H, 8.25. Found: C, 78.32; H, 8.23.

Typical procedure for the synthesis of compound 11a. To a stirred mixture of **5a** (250 mg, 1.0 mmol) and methyl acrylate (258 mg, 3.0 mmol) in CH_3CN (2 mL) was added DBU (46 mg, 0.3 mmol) and stirred at room temperature for 1 h under nitrogen atmosphere. After aqueous workup and column chromatographic purification process (hexanes/ EtOAc, 9:1) **11a** (302 mg, 90%) was isolated as colorless oil. Other compounds **11b-d** were synthesized similarly and the spectroscopic data of **11a-d** are as follows.

Compound **11a**: Yield 90%; white solid, mp 99-101 °C; IR (KBr) 1755 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.87 (s, 3H), 2.32-2.48 (m, 3H), 2.67-2.80 (m, 1H), 3.64 (s, 3H), 6.80-6.83 (m, 2H), 7.17-7.20 (m, 2H), 7.30-7.38 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.62, 28.53, 31.19, 51.81, 89.75, 124.79, 125.78, 127.95, 128.51, 128.62 (2C), 129.30, 131.31, 136.79, 163.91, 173.09, 173.60; ESIMS *m/z* 337 (M^++1). Anal. Calcd for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 74.77; H, 6.23.

Compound **11b**: Yield 70%; white solid, mp 151-153 °C; IR (KBr) 1760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.87 (s, 3H), 2.26-2.53 (m, 3H), 2.72-2.82 (m, 1H), 6.79-6.83 (m, 2H), 7.10-7.17 (m, 2H), 7.31-7.44 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.61, 12.23, 32.46, 88.73, 118.69, 125.12, 125.53, 127.86, 128.78, 128.87, 128.94, 129.60, 130.66, 135.46, 163.31, 172.97; ESIMS *m/z* 304 (M^++1). Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.02; H, 5.86; N, 4.36.

Compound **11c**: Yield 96%; white solid, mp 133-135 °C; IR (KBr) 1759, 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.83 (s, 3H), 2.43-2.53 (m, 1H), 2.79-2.89 (m, 1H), 3.03-3.13 (m, 1H), 3.18-3.28 (m, 1H), 6.75-6.79 (m, 2H), 7.08-7.13 (m, 2H), 7.20-7.42 (m, 6H), 7.53-7.58 (m 2H), 7.63-7.69 (m, 1H), 7.85-7.89 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.51, 29.14, 51.39, 88.81, 124.83, 125.50, 127.77, 127.85, 128.73, 128.76, 128.79, 129.38, 129.49, 130.64, 133.95, 135.68, 138.74, 163.88, 173.01; ESIMS *m/z* 419 (M^++1). Anal. Calcd for $C_{25}H_{22}O_4S$: C, 71.75; H, 5.30. Found: C, 71.54; H, 5.21.

Compound **11d**: Yield 66%; white solid, mp 141-143 °C; IR (KBr) 1759, 1714 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.50-1.61 (m, 1H), 1.65-1.72 (m, 2H), 1.77 (s, 3H), 2.00-2.07 (m, 1H), 2.26-2.55 (m, 4H), 2.68-2.77 (m, 1H), 6.82-6.85 (m, 2H), 7.04-7.07 (m, 2H), 7.24-7.29 (m, 3H), 7.33-7.41 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.38, 24.69, 25.83, 41.01, 42.06, 42.88, 92.40, 125.31, 125.41, 127.89, 128.09, 128.41, 128.71, 129.25, 131.29, 136.89, 163.45, 173.63, 210.45; ESIMS *m/z* 347 (M^++1). Anal. Calcd for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.98; H, 6.37.

Typical procedure for the allylation of compound 5a. To a stirred mixture of **5a** (250 mg, 1.0 mmol) and allyl bromide (**12a**, 363 mg, 3.0 mmol) in CH_3CN (2 mL) was added DBU (46 mg, 0.3 mmol) and stirred at room temperature for 1 h under nitrogen atmosphere. After aqueous workup and column chromatographic purification process (hexanes/ EtOAc, 20:1) **13a** (41 mg, 14%) and **14a** (194 mg, 67%) were isolated as colorless oil. Other compounds were synthesized similarly and the spectroscopic data of **13a**, **13b**, **14a-c** and **15c** are as follows.

Compound **13a**: Yield 14%; colorless oil; IR (film) 1757 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.90 (s, 3H), 2.82-2.90 (m, 1H), 3.07-3.15 (m, 1H), 5.07-5.17 (m, 2H), 5.64-5.78 (m, 1H), 6.77-6.83 (m, 2H), 7.21-7.29 (m, 3H), 7.30-7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.67, 39.61, 89.61, 120.29, 125.22, 126.02, 128.10, 128.47, 128.50, 128.54, 129.18, 130.50, 131.66, 137.57, 163.15, 173.96; ESIMS *m/z* 291 (M^++1). Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.55; H, 6.48.

Compound **13b**: Yield 4%; colorless oil; IR (film) 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.77 (s, 3H), 3.41 (d, *J* = 13.8 Hz, 1H), 3.75 (d, *J* = 13.8 Hz, 1H), 6.80-6.84 (m, 2H), 7.01-7.04 (m, 2H), 7.10-7.41 (m, 11H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.91, 41.22, 89.67, 125.73, 126.36, 127.07, 127.91, 128.45, 128.68, 128.70 (2C), 129.37, 130.69, 131.68, 133.98, 138.02, 161.51, 173.71; ESIMS *m/z* 341 (M^++1). Anal. Calcd for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92. Found: C, 84.71; H, 6.17.

Compound **14a**: Yield 67%; white solid, mp 81-82 °C; IR (film) 1797 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.42 (s, 3H), 2.34-2.42 (m, 1H), 2.47-2.55 (m, 1H), 5.10-5.19 (m, 2H), 5.68-5.82 (m, 1H), 7.17-7.35 (m, 7H), 7.37-7.46 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.48, 40.90, 52.85, 119.54, 121.44, 126.92, 128.21, 128.31, 128.46, 129.02, 129.08, 129.64, 132.07, 132.35, 146.15, 179.90; ESIMS *m/z* 291 (M^++1). Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.63; H, 5.97.

Compound **14b**: Yield 70%; colorless oil; IR (film) 1793 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.62 (s, 3H), 2.93 (d, *J* = 13.8 Hz, 1H), 3.17 (d, *J* = 13.8 Hz, 1H), 7.09-7.14 (m, 2H), 7.17-7.25 (m, 10H), 7.37-7.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.78, 42.97, 53.71, 121.15, 127.02, 127.23, 128.09, 128.12, 128.16, 128.55, 128.84, 129.03, 129.57, 129.74, 132.35, 135.74, 146.78, 180.18; ESIMS *m/z* 341 (M^++1). Anal. Calcd for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92. Found: C, 84.44; H, 5.65.

Compound **14c**: Yield 52%; white solid, mp 99-101 °C; IR (KBr) 1798, 1046 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38 (s, 6H), 7.18-7.28 (m, 5H), 7.30-7.34 (m, 2H), 7.40-7.45 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.38, 48.14, 123.67, 126.78, 128.24, 128.29, 128.60, 128.94, 129.07, 129.60, 132.43, 145.25, 181.25; ESIMS *m/z* 265 (M^++1). Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.86; H, 6.43.

Compound **15c**: Yield 93%; white solid, mp 61-62 °C; IR (KBr) 1716, 1668, 1268, 1134 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.06 (s, 3H), 3.56 (s, 3H), 7.26-7.52 (m, 8H), 7.92-7.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.56, 51.99, 128.10, 128.46, 128.54, 128.61, 128.68, 128.90, 132.93, 134.83, 135.76, 150.84, 167.62, 196.24; ESIMS *m/z* 281 (M^++1). Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.46; H, 5.79.

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11. Crystal data of compound **7a**: solvent of crystal growth (CH_2Cl_2); empirical formula $C_{17}H_{14}O_3$, *Fw* = 266.28, crystal dimensions 0.40 × 0.20 × 0.10 mm^3, orthorhombic, space group Fdd2, a = 18.2631(19) Å, b = 35.999(3) Å, c = 8.2668(7) Å, α = 90°, β = 90°, γ = 90°, V = 5435.0(9) $Å^3$, Z = 16, D_{calcd} = 1.302 mg/m^3. F_{000} = 2240, MoKα (λ = 0.71073 Å), R_1 = 0.0512, wR_2 = 0.1117 ($I > 2\sigma(I)$). We omitted hydrogen atoms for clarity (Figure 1). The X-ray data has been deposited in CCDC with number 684684.
12. Crystal data of compound **8a**: solvent of crystal growth (MeOH); empirical formula $C_{34}H_{28}O_4$, *Fw* = 500.56, crystal dimensions 0.30 x 0.30 x 0.10 mm^3, triclinic, space group P-1, a = 9.3062(5) Å, b = 9.7502(5) Å, c = 15.4367(8) Å, α = 82.6350(10)°, β = 83.4040(10)°, γ = 71.6410(10)°, V = 1314.29(12) $Å^3$, Z = 2, D_{calcd} = 1.265 mg/m^3. F_{000} = 528, MoKα (λ = 0.71073 Å), R_1 = 0.0590, wR_2 = 0.1188 ($I > 2\sigma(I)$). We omitted hydrogen atoms for clarity (Figure 1). The X-ray data has been deposited in CCDC with number 684685.
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