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α-Regioselective construction of *gem*-bisprenyl structures via zinc-mediated prenylation of esters in THF

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ABSTRACT

The in situ generated prenylzinc reagent from the reaction of zinc with prenyl bromide has been shown to undergo a new type of α-regioselective addition reaction with a wide range of esters that affords *gem*-bisprenyl structures. The reaction proceeds under mild conditions to provide α,α′-adducts with complete α-regioselectivity. A mechanism with the consideration of the steric factors is proposed to account for the regioselective results.

1. Introduction

The prenyl unit occurs widely in a variety of natural products and biologically important molecules.[1] Natural products possessing a *gem*-bisprenyl fragment are very common in nature.[2] Furthermore, the *gem*-bisprenyl fragment is also an important building block and versatile synthon, frequently employed for the synthesis of polycyclic polyprenylated acylphloroglucinols (PPAPs)[3] and cyclohexane derivatives.[4] As a result, a reliable method for the construction of such a structure is therefore potentially valuable in organic and medicinal chemistry. In principle, the introduction of highly relevant *gem*-bisprenyl fragments can be easily achieved by metal-mediated bisprenylation reaction of carboxylates using prenyl halide as the prenyl source. Unfortunately, to the best of our knowledge, no report has been made on the direct bisprenylation of esters using prenylic metal reagents. One reason is that carboxylic esters are generally considered poor electrophiles in such a reaction. Another is that there is considerable difficulty in controlling the α-regioselectivity of the prenylation.[5]

Recently our group reported the direct prenylation reaction of aldehydes and ketones in a highly α-regioselective manner for the preparation of α-prenylated alcohols.[6] More recently, we described a direct synthesis of linear homoallylic amines via a highly α-regioselective prenylation of imines.[7] With these successful reports on the synthesis of biologically important molecules via α-prenylation, we became interested in exploring the α-regioselective prenylation of the relatively little explored carboxylic esters to broaden the scope of the reaction. We describe here a straightforward and practical zinc-mediated method for the prenylation of esters with high α-regioselectivity using commercially available prenyl bromide to afford bisprenyl alkyl carbinols in good to excellent yields. Although zinc as a mediator has proved to be very effective for the allylation of carboxylic acid derivatives,[8] zinc as a mediator used in prenylmetal-ester α-regioselective reaction has not been demonstrated so far. As a related reaction, Ishino's group reported the zinc-promoted *gem*-bisallylation of acid chlorides with substituted allyl chlorides, such as crotyl chloride and cinnamyl chloride in the presence of chlorotrimethylsilane to afford a mixture of α and γ products. However, when using the prenyl chloride as the allyl source, the reaction gave only a monoallylation product, phenyl prenyl ketone, as a γ product.[9]

2. Results and discussion

Conditions for the zinc-mediated approach to *gem*-bisprenylated products were explored by the reaction of methyl 4-chlorobenzoate **1a** with prenyl bromide (Table 1). To our delight, the utilization of same reaction conditions previously applied in the prenylation of aldehydes and ketones led to the desired *gem*-bisprenylated product with perfect α-regioselectivity.[6] Treating **1a** with prenylzinc bromide in hexamethylphosphoramide (HMPA) at

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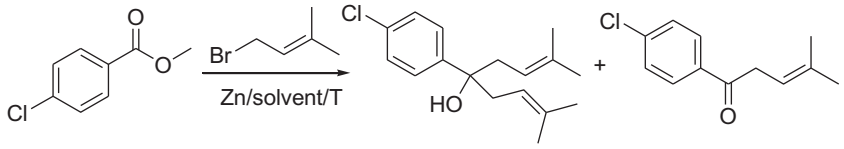
Table 1
Optimization of reaction conditions[a]



1a **2a** **3a**

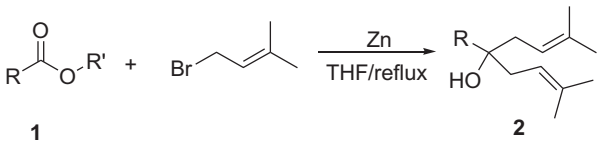
Entry	Solvent	T (°C)	t (h)	**2a**[b] (%)	**3a**[b] (%)
1	HMPA	130	12	76	—
2	DMPU	120	14	75	—
3	THF/DMPU[c]	100	14	73	7
4	THF	Reflux	15	79	13
5	THF	Reflux	20	84	Trace
6	THF	50	20	—	—

[a] Reactions were performed with ester (1.0 mmol), prenyl bromide (2.4 mmol), and zinc (3.0 mmol).
[b] Isolated yields.
[c] The ratio is 1.5/1.

130 °C for 12 h afforded the desired product **2a** in 76% yield (entry 1). To replace the carcinogenic HMPA by a less toxic solvent, we then examined the effect of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*) pyrimidinone (DMPU) on the bisprenylation, which is usually used as safe substitute for the carcinogenic HMPA,[10] and were pleased to observe that the alternative solvent did not affect the α-regioselective prenylation (entry 2). When the solvent was switched to the cosolvent of THF/DMPU, the reaction still proceeded efficiently to afford the desired product **2a** in 73% yield with only a small amount of the intermediate ketone **3a** (entry 3). This positive result, in which the reaction could be performed under much milder conditions, prompted us to optimize the reaction conditions further. At this point, we wondered whether THF could be used as the solvent without any additive despite the fact that THF as the sole solvent has been proven to disfavor the α-regioselective prenylation of carbonyl compounds.[6,11] Gratifyingly, the result revealed that THF alone was also an effective solvent for this α-regioselective bisprenylation (entry 4), thus making this reaction quite practical and attractive for the synthetic community. A longer reaction time was necessary to achieve good conversion of ketone **3a** (entry 5). Disappointingly, decreasing the reaction temperature to 50 °C led to complete recovery of the starting material (entry 6).

With optimized reaction conditions in hand, we next investigated the scope of the double prenylation of esters, and the results are shown in Table 2. Some esters of benzoic acid, including methyl benzoate **1b**, ethyl benzoate **1c**, and isopropyl benzoate **1d**, were investigated first. The results indicated that the alkoxy group of the esters had no obvious influence on the reaction as the same product **2b** was all obtained in similar yield (entries 1–3). Subsequently, methyl benzoate bearing different substituents in the phenyl ring was surveyed. The results showed that both electron-withdrawing and electron-donating groups on the phenyl ring, such as fluoride (entries 4–6), chloride (entries 7 and 8), bromide (entry 9), and methyl groups (entries 10 and 11), were all compatible with this reaction and gave moderate to good yields of the desired α-bisprenylation products **2e**–**l**. The phenyl group of the benzoate can be further replaced with a furyl ring, and the desired product **2m** can be obtained in moderate yield (entry 12). Moreover, the aliphatic carboxylic ester **1n** can also be applied to the method (entry 13). Notably, other substituted carboxylic esters, such as methyl 2-(2,4,5-trifluorophenyl)acetate **1o** (entry 14), methyl 2-(naphthalen-2-yl)acetate **1p** (entry 15), and methyl 3-phenylpropanoate **1q** (entry 16) could be tolerated in the process, and the corresponding α,α′-adducts **2o**–**q** could be obtained in moderate to good yields under the same condition. A noteworthy observation was that, in all entries, perfect α-regioselectivity was achieved, and no γ-prenylated products were found during the reaction.

Table 2
Reaction of prenyl bromide with various esters



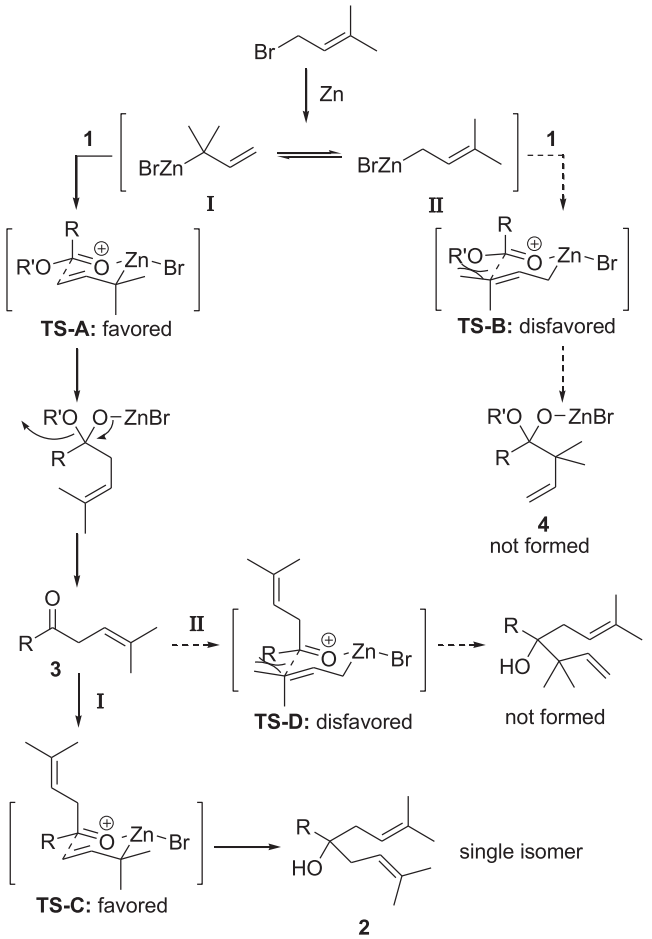
1 **2**

Entry	Substrate	Product	Yield[a] (%)
1	Methyl benzoate **1b**	**2b**	53
2	Ethyl benzoate **1c**	**2b**	56
3	Isopropyl benzoate **1d**	**2b**	54
4	Methyl 2-fluorobenzoate **1e**	**2e**	77
5	Methyl 3-fluorobenzoate **1f**	**2f**	85
6	Methyl 4-fluorobenzoate **1g**	**2g**	86
7	Methyl 2,4-dichlorobenzoate **1h**	**2h**	85
8	Methyl 3,4-dichlorobenzoate **1i**	**2i**	80
9	Methyl 4-bromobenzoate **1j**	**2j**	88
10	Methyl 3-methyl benzoate **1k**	**2k**	55
11	Methyl 4-methyl benzoate **1l**	**2l**	52
12	Methyl furan-2-carboxylate **1m**	**2m**	61
13	Methyl cyclohexanecarboxylate **1n**	**2n**	56
14	Methyl 2-(2,4,5-trifluorophenyl)acetate **1o**	**2o**	86
15	Methyl 2-(naphthalen-2-yl)acetate **1p**	**2p**	71
16	Methyl 3-phenylpropanoate **1q**	**2q**	61

[a] Isolated yields.

Polar aprotic solvents, such as HMPA and DMPU are known to play a key role in the α-prenylation of carbonyls and imines. When there is no polar aprotic solvent present, the α-regioselectivity is very poor.[6,7] In contrast, the α-adduct was obtained exclusively in the absence of HMPA or DMPU in the α-bisprenylation of esters, illustrating that a polar aprotic solvent did not play an important role in the reaction. This leads us to propose a new mechanism that is different from the previously reported [3,5]-sigmatropic rearrangement mechanism in the α-prenylation of carbonyls and imines,[6,7] as shown in Scheme 1. The first step involves the in situ formation of the prenylzinc reagent, which interconverts between primary prenylzinc species **I** and tertiary prenylzinc species **II**.[12] Consequently, two possible pathways forming the transition state **A** (TS-A) and transition state **B** (TS-B) should be considered.[13] Of the two possible transition states **A** and **B**, TS-A would be more favorable because of the absence of steric interactions between the alkoxyl group and hydrogen atom of the terminal olefin. Conversely, the presence of bulkier substituent in which the hydrogen atom is replaced by a methyl group leads to the increase of steric

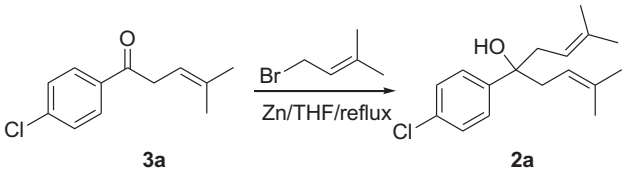
repulsion in TS-B shown in the graphic, and so the formation of **4** is prevented. The TS-A thus formed would undergo the elimination of alkyloxy zinc bromide to deliver the ketone **3** as an α product, which is subsequently attacked by the prenyl species. For this to be the case with the intermediate **3**, the reaction with prenyl species might produce two isomers: α-adduct and γ-adduct via transition state **C** (TS-C) and transition state **D** (TS-D), respectively. However, the reaction cleanly produced the α-adduct **2** as single isomer. The above rationale of the different steric repulsion between TS-A and TS-B can also be used to account for the regioselectivity in the addition of ketone **3** with prenyl species. The exclusive α-adduct **2** rather than γ-addition of ketone **3** can be rationalized by the minimization of steric repulsion between the hydrogen atom of the terminal olefin and the substituents on the carbonyl group of the substrate in TS-C, in a manner analogous to the TS-A. In the case of TS-D, the steric interaction between the terminal substituents of the olefin and the groups attached to the carbonyl group is highly unfavorable; therefore, the addition proceeds exclusively via TS-C, which results in the exclusive formation of α,α′-adduct **2**.



Scheme 1. Proposed reaction mechanism.

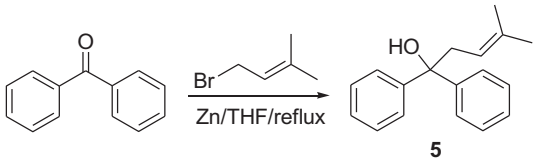
Although the proposed reaction mechanism in Scheme 1 differs from the previously reported mechanisms of the allylation of aldehyde,[14] at least the following facts support such a mechanism. First, it should be noted that the argument of TS-B being disfavored by steric reasons is chemically reasonable due to the poor electrophilicity and steric hindrance of ester despite the fact that such a transition state is possible in the case of the allylation of aldehyde. On the other hand, organozinc reagents show moderate reactivity toward many organic electrophiles and have higher functional group compatibility in comparison with organolithium and Grignard reagents. These facts imply that there might be weak complexation of ester carbonyl group with prenylzinc bromide. Consequently, TS-B is unstable compared with TS-A due to the overpowering steric repulsion of the methyl group of the terminal olefin with alkyloxy group of ester in TS-B.

To demonstrate the proposed mechanism, we performed the following experiment. First, ketone **3a** was synthesized and then treated with prenylzinc bromide at reflux in THF for 14 h (Scheme 2). During the reaction course, only α-adduct was observed. The formation of γ-adduct was not observed by TLC and GC–MS. This result showed that the proposed mechanism seemed to be a reasonable assumption.



Scheme 2. Reaction of ketone **3a** and prenylzinc bromide.

To confirm the role of steric bulk around carbonyls, we next performed a reaction by using hindered ketone benzophenone as the substrate under the aforementioned conditions (Scheme 3). The reaction afforded α-adduct **5** exclusively in 60% yield and no γ-adduct was observed by TLC and GC–MS. The result clearly demonstrates the contribution of steric repulsion in determining the regioselectivity of prenylation. This behavior is also similar to that observed in earlier work by Miginiac and Barbot,[15] thus confirming the validity of the proposed mechanism.



Scheme 3. Reaction of benzophenone and prenylzinc bromide.

3. Conclusion

In conclusion, this study introduces a highly efficient procedure for the construction of *gem*-bisprenyl building blocks by using an in situ generated prenylzinc reagent under mild conditions, enabling quick access to *gem*-bisprenyl structures found in a wide variety of natural products. The reaction is very convenient due to the use of commercially available and cheap reagents, such as prenyl bromide, zinc, and THF, and the procedure is simple. More importantly, the α-regioselectivity could be achieved in the absence of a polar aprotic solvent, thus making this protocol all the more attractive. With these advantages, we believe that this reaction will become a useful and practical method to synthesize the natural products and natural product analogues with a *gem*-bisprenyl fragment.

4. Experimental section

4.1. General procedure for the synthesis of α,α′-adduct 2

Prenyl bromide (2.4 mmol) was added into a suspension of activated zinc powder (3.0 mmol) in dry THF (15 ml); the reaction mixture was stirred for 1 h at room temperature. Filtered the solution through an Schlenk filter and kept under N_2 for the following reaction. A solution of ester **1** (1.0 mmol) in dry THF (3 ml) was

added the solution of prenylzinc bromide prepared above. The mixture was heated to reflux under N_2 atmosphere for 20 h. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate, 20/1, v/v) to afford the α,α′-adduct **2**.

4.1.1. Characterization of ***2a****.* Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (d, *J*=8.4 Hz, 2H), 7.28 (d, *J*=8.4 Hz, 2H), 4.97 (t, *J*=8.0 Hz, 2H), 2.55–2.48 (m, 4H), 2.09 (s, 1H), 1.66 (s, 6H), 1.56 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 136.2, 132.1, 128.0, 127.1, 118.4, 76.4, 40.7, 26.0, 18.1. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{23}OClNa$ $[M+Na]^+$: 301.1335; Found: 301.1358.

4.1.2. Characterization of ***2b****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, *J*=8.0 Hz, 2H), 7.32 (t, *J*=7.2 Hz, 2H), 7.25–7.20 (m, 1H), 5.0 (t, *J*=4.0 Hz, 2H), 2.60–2.50 (m, 4H), 2.09 (s, 1H), 1.65 (s, 6H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.7, 135.7, 127.9, 126.3, 125.5, 118.9, 76.6, 40.7, 26.0, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{24}ONa$ $[M+Na]^+$: 267.1725; Found: 267.1725.

4.1.3. Characterization of ***2e****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (t, *J*=8.0 Hz, 1H), 7.25–7.19 (m, 1H), 7.11 (t, *J*=7.6 Hz, 1H), 6.98 (dd, *J*=12.0, 8.4 Hz, 1H), 4.98 (t, *J*=7.2 Hz, 2H), 2.75–2.59 (m, 4H), 2.24 (s, 1H), 1.64 (s, 6H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.2 (*J*=244.0 Hz), 135.8, 133.2 (*J*=12.0 Hz), 128.7 (*J*=5.0 Hz), 128.4 (*J*=8.0 Hz), 123.7 (*J*=3.0 Hz), 118.8, 115.7 (*J*=24.0 Hz), 75.8 (*J*=6.0 Hz), 39.1 (*J*=4.0 Hz), 26.0, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{23}OFNa$ $[M+Na]^+$: 285.1631; Found: 285.1640.

4.1.4. Characterization of ***2f****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30–7.25 (m, 1H), 7.16–7.13 (m, 2H), 6.93–6.89 (m, 1H), 4.99 (t, *J*=5.6 Hz, 2H), 2.58–2.47 (m, 4H), 2.12 (s, 1H), 1.66 (s, 6H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9 (*J*=243.0 Hz), 149.7 (*J*=6.0 Hz), 136.2, 129.3 (*J*=8.0 Hz), 121.1, 118.4, 113.0 (*J*=44.0 Hz), 76.4, 40.7, 26.0, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{23}OFNa$ $[M+Na]^+$: 285.1631; Found: 285.1642.

4.1.5. Characterization of ***2g****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38–7.34 (m, 2H), 7.02–6.97 (m, 2H), 4.99 (t, *J*=6.8 Hz, 2H), 2.52 (s, 4H), 2.09 (s, 1H), 1.66 (s, 6H), 1.55 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.5 (*J*=243.0 Hz), 142.2 (*J*=12.0 Hz), 136.1, 127.2 (*J*=8.0 Hz), 118.6, 114.6 (*J*=20.0 Hz), 76.4, 40.8, 26.0, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{23}OFNa$ $[M+Na]^+$: 285.1631; Found: 285.1640.

4.1.6. Characterization of ***2h****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J*=8.0 Hz, 1H), 7.34 (s, 1H), 7.22 (d, *J*=8.0 Hz, 1H), 4.91 (t, *J*=6.8 Hz, 2H), 3.02–2.63 (m, 4H), 2.32 (s, 1H), 1.64 (s, 6H), 1.61 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.8, 136.1, 132.9, 131.2, 130.7, 130.4, 126.7, 118.5, 77.1, 37.7, 25.9, 18.1. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{22}OCl_2Na$ $[M+Na]^+$: 335.0945; Found: 335.0945.

4.1.7. Characterization of ***2i****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, *J*=2.0 Hz, 1H), 7.37 (d, *J*=8.4 Hz, 1H), 7.22 (dd, *J*=8.4 Hz, *J*=2.0 Hz, 1H), 4.97 (t, *J*=6.8 Hz, 2H), 2.56–2.44 (m, 4H), 2.12 (s, 1H), 1.67 (s, 6H), 1.56 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.2, 136.6, 132.1, 130.2, 129.8, 128.0, 125.1, 118.0, 76.2, 40.6, 26.0, 18.1. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{22}OCl_2Na$ $[M+Na]^+$: 335.0945; Found: 335.0923.

4.1.8. Characterization of ***2j****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (d, *J*=8.8 Hz, 2H), 7.28 (d, *J*=8.4 Hz, 2H), 4.97 (t, *J*=6.8 Hz, 2H), 2.56–2.46 (m, 4H), 2.09 (s, 1H), 1.66 (s, 6H), 1.56 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 136.2, 130.9, 127.5, 120.3, 118.4, 76.5, 40.6, 26.0, 18.1. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{23}OBrNa$ $[M+Na]^+$: 345.0830; Found: 345.0830.

4.1.9. Characterization of ***2k****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.18–7.12 (m, 3H), 6.96 (d, *J*=6.8 Hz, 1H), 4.94 (t, *J*=7.2 Hz, 2H), 2.51–2.41 (m, 4H), 2.29 (s, 3H), 1.99 (s, 1H), 1.59 (s, 6H), 1.50 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.6, 136.4, 134.6, 126.7, 126.0, 125.2, 121.5, 117.9, 75.6, 39.6, 25.0, 20.6, 17.0. HRMS (ESI): *m*/*z* calcd for $C_{18}H_{26}ONa$ $[M+Na]^+$: 281.1881; Found: 281.1881.

4.1.10. Characterization of ***2l****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 (d, *J*=7.6 Hz, 2H), 7.13 (d, *J*=7.6 Hz, 2H), 5.02 (t, *J*=6.4 Hz, 2H), 2.54–2.51 (m, 4H), 2.34 (s, 3H), 2.05 (s, 1H), 1.66 (s, 6H), 1.58 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.7, 135.7, 135.6, 128.6, 125.4, 118.9, 76.5, 40.6, 26.0, 21.0, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{18}H_{26}ONa$ $[M+Na]^+$: 281.1881; Found: 281.1888.

4.1.11. Characterization of ***2m****.* Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (s, 1H), 6.30 (s, 1H), 6.17 (s, 1H), 5.05 (s, 2H), 2.55–2.53 (m, 4H), 2.22 (s, 1H), 1.69 (s, 6H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.8, 141.3, 135.8, 118.4, 110.1, 105.5, 74.2, 38.3, 26.0, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{15}H_{22}O_2Na$ $[M+Na]^+$: 257.1517; Found: 257.1527.

4.1.12. Characterization of ***2n****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.22 (t, *J*=7.2 Hz, 2H), 2.20–2.09 (m, 4H), 1.80–1.74 (m, 4H), 1.74 (s, 6H), 1.62 (s, 6H), 1.41 (s, 1H), 1.25–0.85 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.6, 119.6, 76.6, 45.5, 35.0, 27.1, 26.9, 26.7, 26.2, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{30}ONa$ $[M+Na]^+$: 273.2194; Found: 273.2207.

4.1.13. Characterization of ***2o****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22–7.15 (m, 1H), 6.91–6.84 (m, 1H), 5.21 (t, *J*=7.2 Hz, 2H), 2.74 (s, 2H), 2.20–2.01 (m, 4H), 1.75 (s, 6H), 1.63 (s, 1H), 1.58 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 135.7, 129.5, 126.0, 120.4 (*J*=5.0 Hz), 120.2 (*J*=7.2 Hz), 118.7, 105.0 (*J*=19.7 Hz), 104.6 (*J*=21.1 Hz), 75.2, 37.6, 37.0, 26.1, 18.0. HRMS (ESI): *m*/*z* calcd for $C_{18}H_{23}OF_3Na$ $[M+Na]^+$: 335.1599; Found: 335.1599.

4.1.14. Characterization of ***2p****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (d, *J*=8.0 Hz, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 7.76–7.74 (m, 1H), 7.51–7.41 (m, 4H), 5.28 (s, 2H), 3.27 (s, 2H), 2.30–2.16 (m, 4H), 1.75 (s, 6H), 1.56 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 134.8, 134.2, 134.0, 133.5, 129.2, 128.6, 127.2, 125.6, 125.4, 125.2, 125.1, 119.5, 76.1, 41.2, 38.0, 26.2, 18.1. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{28}ONa$ $[M+Na]^+$: 331.2038; Found: 331.2036.

4.1.15. Characterization of ***2q****.* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30–7.25 (m, 2H), 7.20–7.16 (m, 3H), 5.23 (t, *J*=7.6 Hz, 2H), 2.70–2.65 (m, 2H), 2.24 (d, *J*=7.6 Hz, 4H), 1.78–1.73 (m, 2H), 1.76 (s, 6H), 1.66 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.9, 135.1, 128.4, 125.7, 119.1, 75.0, 41.2, 37.8, 30.1, 26.2, 18.1. HRMS (ESI): *m*/*z* calcd for $C_{19}H_{28}ONa$ $[M+Na]^+$: 295.2038; Found: 295.2032.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.07.008.

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