

# RSC Advances



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

*Accepted Manuscripts* are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This *Accepted Manuscript* will be replaced by the edited, formatted and paginated article as soon as this is available.

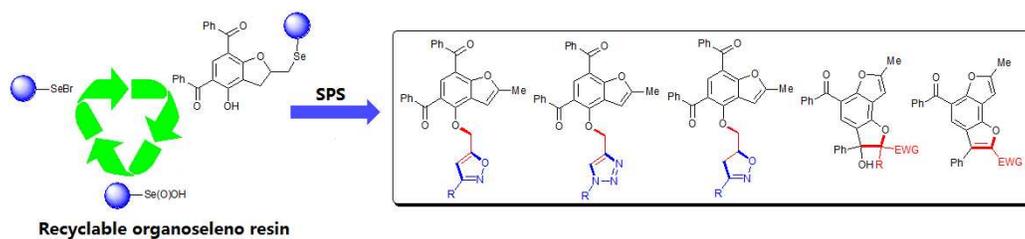
You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

## Table of Contents

### Synthesis of Heterocycle-Tethered Acylbenzofurans and Benzodifurans from Odorless and Recyclable Seleno Polystyrene Resin

Yuguang Wang, Bingchun Zhu, Qing Xu, Qing Zhu\* and Lei Yu\*



Recyclable organoseleno resin-supported solid-phase synthesis (SPS) provided a quick access to heterocycle-tethered acylbenzofurans and benzodifurans in satisfactory overall yields and purities after multiple step reactions.

## ARTICLE

# Synthesis of Heterocycle-Tethered Acylbenzofurans and Benzodifurans from Odorless and Recyclable Organoseleno Polystyrene Resin†

Cite this: DOI: 10.1039/x0xx00000x

Yuguang Wang,<sup>a</sup> Bingchun Zhu,<sup>a,b</sup> Qing Xu,<sup>c</sup> Qing Zhu<sup>\*a</sup> and Lei Yu<sup>\*c</sup>

Received 00th January 2012,

Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Organoseleno polystyrene resin-supported synthesis provided a quick access to a series of acylbenzofuran derivatives tethered to isoxazoles, triazoles and isoxazolines as well as benzodifurans. Although this methodology proceeded through multiple steps such as the seleno-induced attachment, nucleophilic substitutions, 1,3-dipolar cycloadditions, and *syn*-selenoxide eliminations from organoseleno resin, the overall product yields were generally good. The concise and safe procedures, wide application scopes, the lack of odor, stability and recyclability of the organoseleno resin, and the good yields and high purity of products are the advantages of this work over the more traditional solution-based chemistry.

## Introduction

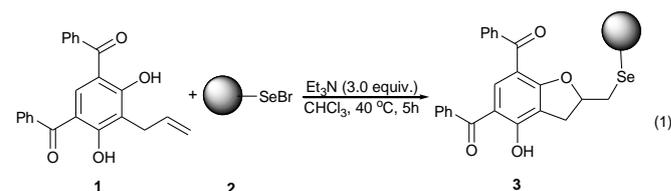
Solid-phase synthesis (SPS) is a powerful tool for the rapid generation of small, drug-like organic molecular libraries for the purpose of medicinal chemistry programs in pharmaceutical industry.<sup>1</sup> Due to the high reactivity of selenium moieties and the removable properties through clean *syn*-selenoxide elimination<sup>2</sup> after preparations, the safe, odorless, stable, and recyclable organoseleno polystyrene resin is a good carrier for solid-phase synthesis.<sup>3,4</sup> Among reported works, a series of useful bioactive heterocycles have been synthesized from organoseleno resins, such as isoxazoles, oxadiazoles, triazoles, uracils, pyrrolines, indulines and others.<sup>3</sup> Besides, organoseleno resin-supported solid-phase synthesis is also a reliable and practical methodology that has already been widely applied in natural product synthesis.<sup>4</sup>

On the other hand, benzofuran skeletons are often found in natural products with antimicrobial, antioxidant, anticancer and anti-inflammatory activities.<sup>5</sup> They are also important intermediates in organic synthesis.<sup>6</sup> Among these analogues, acylbenzofurans and heterocycle-tethered benzofurans are very common moieties in many drug molecules such as *Vilazodone*, *Dronedarone*, *Amiodarone*, *Benzbromarone* and others.<sup>7</sup> In addition, they are also widely employed in material science due to their high photoelectric activity.<sup>8</sup> Thus, building these organic skeletons rapidly affords powerful tools for both drug discovery and new material development. Our group aimed to develop concise and green methodologies with high efficiency that might be applicable in organic synthesis, pharmaceutical chemistry, agriculture chemistry and chemical industry.<sup>9</sup> Recently, we developed a quick access to heterocycle-tethered acylbenzofurans and benzodifurans through organoseleno resin-

supported solid-phase synthesis. Herein, we wish to report our findings.

## Results and discussion

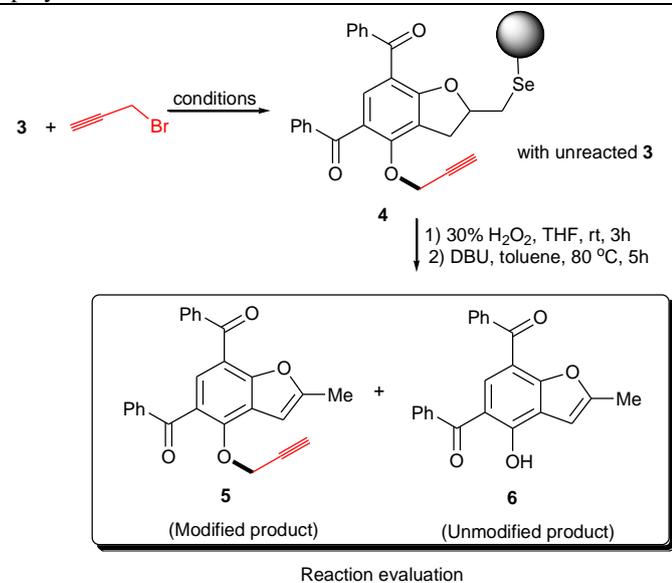
Based on our previous cooperation research project with certain companies,<sup>10</sup> we chose compound **1** as the starting material. After attachment with organoseleno resin **2** (Br 1.25 mmol/g), the mother heterocycle 5,7-dibenzoyl-2,3-dihydrobenzofuran-4-ol was constructed and uploaded to generate the functionalized resin **3** (eq. 1). This procedure was monitored by Fourier transform infrared (FT-IR) spectroscopy, which showed a strong peak of the carbonyl absorptions at 1654-1658 cm<sup>-1</sup> on the resin. The reaction was terminated in 5h, after which the carbonyl absorption did not increase any further.



With the uploaded mother heterocycle resin **3** in hand, we then tried to modify its hydroxyl group on aromatic ring with propargyl bromide according to known methodologies.<sup>11</sup> However, after heating **3** with propargyl bromide and K<sub>2</sub>CO<sub>3</sub> in acetone at 60 °C for 5h (Table 1, run 1), the IR spectra of resin showed a weak peak of C≡C absorption at 2130 cm<sup>-1</sup> but a very broad and strong absorption peak of O-H, revealing that only a few of resin **3** was modified. The modified product **5** and unmodified product **6** were then cut down from resin by *syn*-

selenoxide elimination.<sup>12, 13</sup> and the modification efficiencies were quantitatively evaluated according to the yield and purity of **5**. It was shown that the reported methodologies afforded crude **5** at a very low yield and purity (Table 1, run 1). Obviously, 10h was the best reaction time (run 2), after which the reaction could not be improved any more (Table 1, run 3). Replacing K<sub>2</sub>CO<sub>3</sub> with the organic base Et<sub>3</sub>N slightly improved the yield and purity of **5** (Table 1, run 4) and further solvent screening demonstrated that DMF/CHCl<sub>3</sub> (1:1) was a better solvent, affording **5** in the highest yield and purity in table 1 (Table 1, run 8 VS 4-7).

**Table 1** Reaction condition evaluation for the modification of polymer resin **3** to **4**<sup>a</sup>



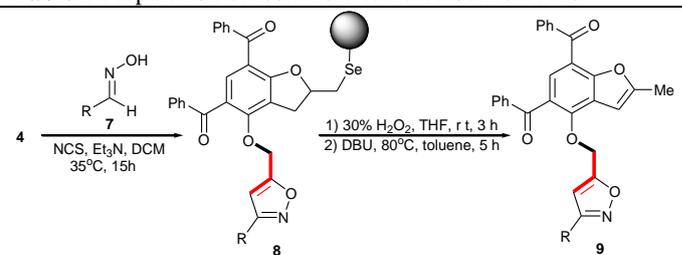
Run	Solvent	Base	t/h	yield/% <sup>b</sup>	purity/% <sup>c</sup>
1	Acetone	K <sub>2</sub> CO <sub>3</sub>	5	59	64
2	Acetone	K <sub>2</sub> CO <sub>3</sub>	10	70	72
3	Acetone	K <sub>2</sub> CO <sub>3</sub>	15	70	71
4	Acetone	Et <sub>3</sub> N	10	72	74
5	THF	Et <sub>3</sub> N	10	76	80
6	DMF	Et <sub>3</sub> N	10	85	90
7	CHCl <sub>3</sub>	Et <sub>3</sub> N	10	86	91
8	DMF/CHCl <sub>3</sub> (1:1)	Et <sub>3</sub> N	10	88	94

<sup>a</sup> Resin **3** (prepared from 0.8 g resin **2**), base (5 mmol) and propargyl bromide (5 mmol) were heated in 15 mL of solvent at 60 °C under N<sub>2</sub>. <sup>b</sup> Isolated yields of crude product **5** based on Br loading of resin **2**. <sup>c</sup> Purities of product **5** were determined by HPLC analysis.

Obtaining optimized conditions for the modification of resin **3** with propargyl bromide, it was then convenient to synthesize heterocycle-tethered benzofurans via the cyclizations of its alkyne group. Isoxazole-tethered benzofurans **9** were first synthesized through the cycloaddition of aldoximes with resin **4** and the following *syn*-selenoxide elimination.<sup>13</sup> Results summarized in table 2 showed that this methodology could produce isoxazole-tethered benzofurans **9** comprehensively and the overall product yields and purities were satisfactory. Generally, there is no appreciable difference between electron-

with drawing group (EWG) and electron-donation group (EDG) in product yields (Table 2, runs 1-3 VS 4-9). Bulky aldoximes afforded worse results than normal ones (Table 2, runs 8-9 VS 4-5; runs 12 VS 10-11). The crude product purities for most examples (Table 2, runs 1-11) were high, providing a concise synthetic methodology especially in product separation.

**Table 2** Preparation of isoxazole-tethered benzofurans<sup>a</sup>

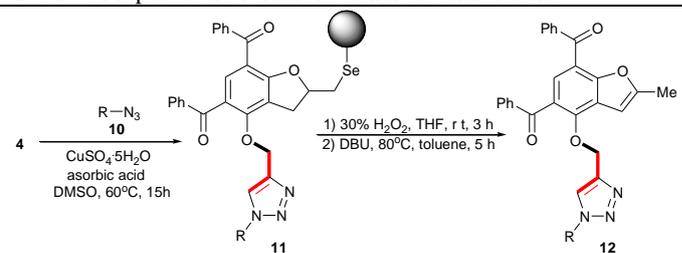


Run	R (7)	<b>9</b> : yield/% <sup>b</sup>	purity/% <sup>c</sup>
1	C <sub>6</sub> H <sub>5</sub> ( <b>7a</b> )	<b>9a</b> : 73	92
2	4-MeC <sub>6</sub> H <sub>4</sub> ( <b>7b</b> )	<b>9b</b> : 72	91
3	4-MeOC <sub>6</sub> H <sub>4</sub> ( <b>7c</b> )	<b>9c</b> : 71	91
4	4-BrC <sub>6</sub> H <sub>4</sub> ( <b>7d</b> )	<b>9d</b> : 68	90
5	4-ClC <sub>6</sub> H <sub>4</sub> ( <b>7e</b> )	<b>9e</b> : 69	90
6	4-FC <sub>6</sub> H <sub>4</sub> ( <b>7f</b> )	<b>9f</b> : 66	89
7	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> ( <b>7g</b> )	<b>9g</b> : 62	86
8	3-BrC <sub>6</sub> H <sub>4</sub> ( <b>7h</b> )	<b>9h</b> : 65	88
9	2-ClC <sub>6</sub> H <sub>4</sub> ( <b>7i</b> )	<b>9i</b> : 63	86
10	<i>c</i> -C <sub>6</sub> H <sub>11</sub> ( <b>7j</b> )	<b>9j</b> : 69	90
11	<i>n</i> -C <sub>4</sub> H <sub>9</sub> ( <b>7k</b> )	<b>9k</b> : 70	90
12	<i>t</i> -C <sub>4</sub> H <sub>9</sub> ( <b>7l</b> )	<b>9l</b> : 56	76

<sup>a</sup> Resin **4** (prepared from 0.8 g resin **2**), aldoxime **7** (5 mmol) N-Chlorosuccinimide (NCS, 5 mmol) and Et<sub>3</sub>N (6 mmol) were heated in 35 mL of CH<sub>2</sub>Cl<sub>2</sub> at 35 °C under N<sub>2</sub>. <sup>b</sup> Isolated yields of crude product **9** based on Br loading of resin **2**. <sup>c</sup> Purities of product **9** were determined by HPLC analysis.

Similarly, 1,3-dipolar cycloadditions of resin **4** with azides and the following *syn*-selenoxide elimination led to a series of triazole-tethered benzofurans **12** (Table 3). The results were even better than preparations of isoxazole-tethered **9** (Table 3 VS Table 2). This methodology had a broad application scope; both electron-rich and -deficient aryl azides afforded the corresponding triazole-tethered benzofurans in good yields with high purity (Table 3, runs 1-8). The steric hindrances of substrates did not affect the reactions much, since the bulky azides led to similar product yields and purities with normal ones (Table 3, runs 1-3 VS 4-8). Alkyl azide also gave satisfactory results in both product yield and purity (Table 3, run 9).

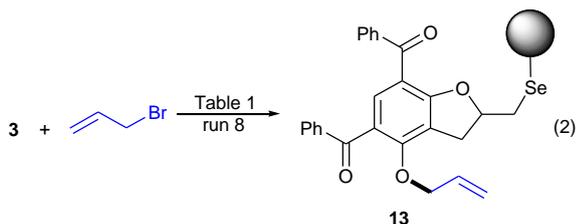
**Table 3** Preparation of triazole-tethered benzofurans<sup>a</sup>



Run	R (10)	12: yield/% <sup>b</sup>	purity/% <sup>c</sup>
1	C <sub>6</sub> H <sub>5</sub> (10a)	12a: 77	93
2	4-BrC <sub>6</sub> H <sub>4</sub> (10b)	12b: 75	92
3	4-Py (10c)	12c: 73	91
4	2-MeC <sub>6</sub> H <sub>4</sub> (10d)	12d: 72	91
5	2,5-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (10e)	12e: 72	91
6	2-Cl-4-NO <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (10f)	12f: 70	90
7	2-NO <sub>2</sub> -4-ClC <sub>6</sub> H <sub>3</sub> (10g)	12g: 69	90
8	2,4,5-Cl <sub>3</sub> C <sub>6</sub> H <sub>2</sub> (10h)	12h: 70	90
9	<i>i</i> -C <sub>3</sub> H <sub>7</sub> (10i)	12i: 62	82

<sup>a</sup> Resin 4 (prepared from 0.8 g resin 2), RN<sub>3</sub> 10 (5 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (4 mmol) and ascorbic acid (4.5 mmol) were heated in 30 mL of DMSO at 60 °C under N<sub>2</sub>. <sup>b</sup> Isolated yields of crude product 12 based on Br loading of resin 2. <sup>c</sup> Purities of product 12 were determined by HPLC analysis.

As an activated nucleophilic group, the hydroxyl on resin 3 could react with many types of electrophiles. Reactions with allylic bromide under similar conditions (Table 1, run 8), afforded allylic- modified organoseleno polystyrene resin 13 (eq. 2), which could be employed to synthesize isoxazoline-tethered benzofurans through further cycloadditions with aldoximes and the following *syn*-selenoxide eliminations (Table 4). The methodology had a wide application scope and electron-rich (Table 4, runs 1-2) and -deficient (Table 4, runs 3-7) aryl aldoximes and alkyl aldoxime (Table 4, run 8) were all applicable substrates. The product yields and purities were satisfactory in spite of multiple steps of reactions (Table 4, runs 1-8).



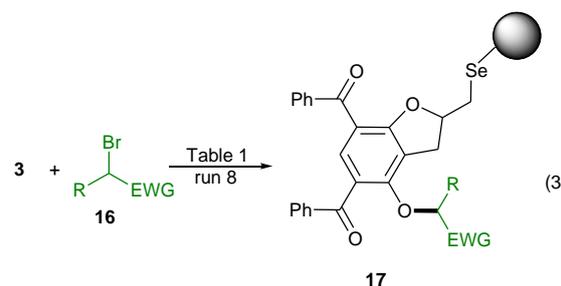
**Table 4** Preparation of isoxazoline-tethered benzofurans<sup>a</sup>

Run	R (7)	15: yield/% <sup>b</sup>	purity/% <sup>c</sup>
1	4-MeC <sub>6</sub> H <sub>4</sub> (7b)	15a: 70	91
2	4-MeOC <sub>6</sub> H <sub>4</sub> (7c)	15b: 70	91
3	4-ClC <sub>6</sub> H <sub>4</sub> (7e)	15c: 69	90
4	4-FC <sub>6</sub> H <sub>4</sub> (7f)	15d: 68	90
5	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (7g)	15e: 62	84
6	3-BrC <sub>6</sub> H <sub>4</sub> (7h)	15f: 64	88

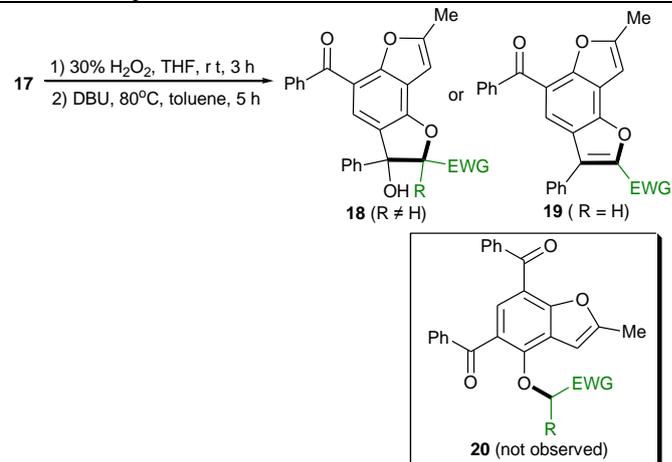
7	2-ClC <sub>6</sub> H <sub>4</sub> (7i)	15g: 63	86
8	<i>c</i> -C <sub>6</sub> H <sub>11</sub> (7j)	15h: 68	89

<sup>a</sup> Resin 13 (prepared from 0.8 g resin 2), aldoxime 7 (5 mmol) N-Chlorosuccinimide (NCS, 5 mmol) and Et<sub>3</sub>N (6 mmol) were heated in 35 mL of CH<sub>2</sub>Cl<sub>2</sub> at 35 °C under N<sub>2</sub>. <sup>b</sup> Isolated yields of crude product 15 based on Br loading of resin 2. <sup>c</sup> Purities of product 15 were determined by HPLC analysis.

In addition, nucleophilic substitutions of resin 3 with EWG and bromo *bis*-substituted hydrocarbons 16 led to modified resin 17 as expected (eq. 3). However, it was very interesting that cyclizations occurred in the *syn*-seleno elimination step of 17. The intramolecular nucleophilic substitutions generated a new fused furan ring. Instead of the originally desired product 20, these unexpected cyclizations led to benzodifuran derivatives 18 or 19 in good yields and high purities, depending on substitutes of the starting materials (Table 5, runs 1-3 VS 4-7).



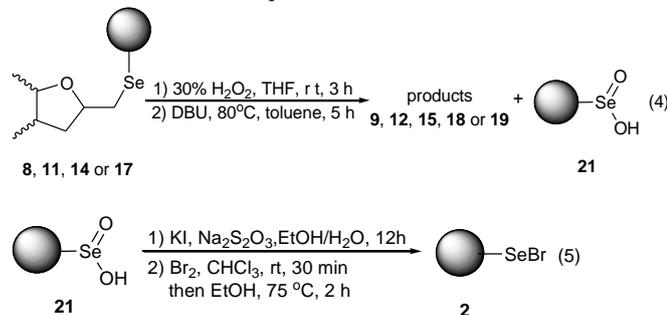
**Table 5** Preparation of benzodifurans<sup>a</sup>



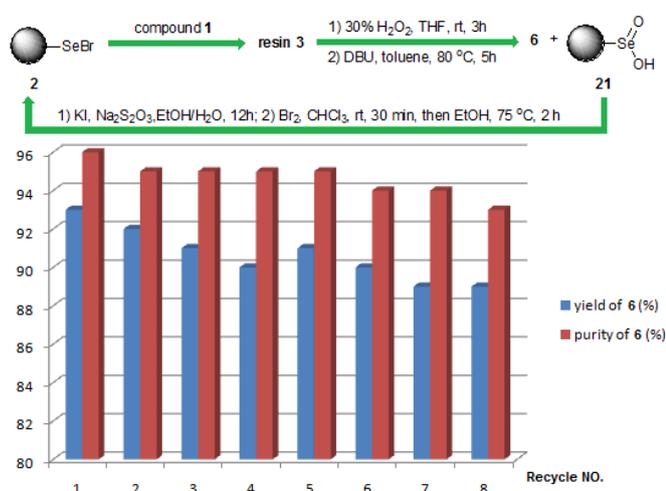
Run	EWG, R (16)	18 or 19: yield/% <sup>b</sup>	purity/% <sup>c</sup>
1	COOMe, Et (16a)	18a: 74	92
2	COOMe, <i>n</i> -Bu (16b)	18b: 72	90
3	COOMe, 2-ClC <sub>6</sub> H <sub>4</sub> (16c)	18c: 68	88
4	COOEt, H (16d)	19a: 76	92
5	Ac, H (16e)	19b: 73	91
6	PhCO, H (16f)	19c: 76	92
7	CN, H (16g)	19d: 75	92

<sup>a</sup> Resin **3** (prepared from 0.8 g resin **2**) and **16** (3 mmol) were treated as conditions in table 1, run 8. <sup>b</sup> Isolated yields of crude product **18** or **19** based on Br loading of resin **2**. <sup>c</sup> Purities of product **18** or **19** were determined by HPLC analysis.

To gain more environment-friendly synthetic methodologies with high resource utilization efficiency, the recycle and reuse of by-products were our next concern. Besides corresponding products **9**, **12**, **15**, **18** and **19**, all of the above reactions also generated equivalent by-product **21**, a stable organoseleno resin with a very high molecular weight that might cause waste (eq. 4). Fortunately, after successive treatments with KI, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and Br<sub>2</sub>, **21** was easy to be converted to the reusable organoseleno resin **2** again, avoiding the generation of massive amount of solid waste (eq. 5).<sup>13</sup>



The reactivities of recovered organoseleno resins were then quantitatively evaluated according to the yields and purities of compound **6**, which was cut down from resin **3**. Detailed experimental procedures and results were depicted in Figure 1. The results showed that the yields and purities of **6** were both high, proving that the organoseleno resins were very much alive even after multiple times of recovery and reuse (Figure 1).<sup>13, 14</sup>



**Figure 1** Organoseleno resin carrier recovery and reuse<sup>13,14</sup>

## Conclusions

In conclusion, we developed the practical synthesis for heterocycle-tethered acylbenzofuran derivatives and benzodifurans using safe, odorless, stable and recyclable organoseleno resin as polymer carrier. The purification procedures were concise and the overall product yields and purities were good after multiple synthetic steps. The methodology provided a comprehensive synthesis of

acylbenzofurans tethered to versatile heterocycles, such as isoxazole, triazole and isoxazoline. Besides, unexpected cyclizations in the *syn*-seleno elimination step of resin **17** generated interesting benzodifuran derivatives. All of these analogues are useful for our research projects. The further investigations on their bioactivities are ongoing in our laboratory.

## Experimental Section

### General methods

Chemicals were purchased from reagent merchant and used without further purification. Polystyrene (H 1000, 100-200 mesh, cross-linked with 1% divinylbenzene, merchant available) was treated according to reference to prepare organoseleno resin **2**.<sup>15</sup> Reactions were performed under N<sub>2</sub> unless specified. Melting points were measured using a XT-4 binocular microscope melting point instrument. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance spectrometer (400 MHz for <sup>1</sup>H NMR and 100 MHz for <sup>13</sup>C NMR spectroscopy), using CDCl<sub>3</sub> as the solvent and TMS as internal standard. Mass spectra were recorded on a Bruker Esquire 6000 mass spectrometer (ESI). Infrared spectra were recorded on a Bruker Tensor 27 spectrometer. HPLC was performed on a Waters e2695 High Performance Liquid Chromatograph (column, SunFire™ C18 5 μm 4.6 × 250 mm; mobile phase, THF/MeOH/H<sub>2</sub>O, v/v/v 50:20:30; flow rate, 1.0 mL/min; Waters 2996 Photodiode Array Detector). HRMS (ESI) were performed on an Agilent 6210 TOF LC/MS instrument. The samples were further purified by preparative TLC before NMR analysis.

### Typical procedure for the preparation of organoseleno resin **3** (eq. 1)

To a suspension of 0.8 g of organoseleno resin **2** (Br 1.25 mmol/g) in 15 mL of CHCl<sub>3</sub>, 5.0 mol of (3-allyl-5-benzoyl-2,4-dihydroxy-phenyl)-phenyl-methanone **1** was added and stirred at room temperature for 10 min. Then, 3.0 mmol of Et<sub>3</sub>N was added and the mixture was stirred at 40 °C for 5 h. The resin was collected by filtration and washed with H<sub>2</sub>O (20 mL × 2), THF (10 mL × 2), ethanol (10 mL × 2), THF/ H<sub>2</sub>O (v/v 2:1, 10 mL × 2), THF (10 mL × 2) and CH<sub>2</sub>Cl<sub>2</sub> (10 mL × 2) successively. The washed wet resin **3** was dried under vacuum overnight before use. The excess starting material **1** could be recollected by extraction.

### Typical procedure for the preparation of organoseleno resin **4** (Table 1, run 8) and compound **5**

**Preparation of resin 4.** To a suspension of resin **3** (from 0.8 g of resin **2**) in 15 mL of DMF/CHCl<sub>3</sub> (1:1), 5 mmol of Et<sub>3</sub>N and 5 mmol of propargyl bromide were added. The mixture was stirred at 60 °C for 10 h. The polymer resin was collected by filtration and washed with H<sub>2</sub>O (20 mL × 2), THF (10 mL × 2), THF/ H<sub>2</sub>O (v/v 2:1, 10 mL × 2), THF (10 mL × 2), THF/ H<sub>2</sub>O (2:1, 10 mL × 2), THF (10 mL × 2) and CH<sub>2</sub>Cl<sub>2</sub> (10 mL × 2) successively. The washed wet resin **4** was dried under vacuum overnight before use.

**Unloading of compound 5.** To a suspension of resin **4** in 15 mL of THF, 2.3 g of 30% H<sub>2</sub>O<sub>2</sub> was added and stirred at room temperature for 3 h. The resin was collected by filtration and washed with H<sub>2</sub>O (20 mL × 2), THF (10 mL × 2), THF/H<sub>2</sub>O (v/v 2:1, 20 mL × 2), THF (10 mL × 2), CH<sub>2</sub>Cl<sub>2</sub> (20 mL × 2)

and toluene (20 mL×2) successively. The washed resin was suspended in 15 mL toluene and stirred with 1.5 mmol of DBU at 80 °C for 5 h. After a filtration, the resin **21** was washed with THF (10 mL), THF/H<sub>2</sub>O (v/v 2:1, 20 mL) and THF (10 mL) subsequently and recovered. The solvent THF of the above combined filtrates was evaporated under vacuum and then dissolved in 10 mL of toluene. The solution was washed with 0.25M HCl (30 mL×2) and saturated NaHCO<sub>3</sub> (35 mL×2) and dried with anhydrous MgSO<sub>4</sub>. Evaporation of solvent under vacuum afforded the crude product **5**, the purity of which was determined by HPLC analysis.

#### Typical procedure for the preparation of isoxazole-tethered benzofurans **9** (Table 2)

5 mmol of hydroximoyl chlorides were prepared by stirring 5 mmol of aldoximes **7** and 5 mmol of NCS in 15 mL of CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 5 h. This hydroximoyl chloride solution was added to a suspension of resin **4** (from 0.8 g of resin **2**) in 10 mL of CH<sub>2</sub>Cl<sub>2</sub>. Then, a solution of 6.0 mmol of Et<sub>3</sub>N in 10 mL of CH<sub>2</sub>Cl<sub>2</sub> was added dropwisely in 4 h. After stirring at 35 °C for 15 h, resins **8** were collected by filtration and washed with H<sub>2</sub>O (10 mL×2), THF (10 mL×1), DMF (10 mL×1), THF/H<sub>2</sub>O (v/v 2:1, 10 mL×2), THF (10 mL×2), THF/H<sub>2</sub>O (v/v 2:1, 10 mL×2) and THF (10 mL×2) successively. Products **9** were then cut down from resin **8** through the similar procedures as the *unloading of compound 5*.

#### Typical procedure for the preparation of triazole-tethered benzofurans **12** (Table 3).

To a suspension of resin **4** (from 0.8 g of resin **2**) in 30 mL of DMSO, 4 mmol of CuSO<sub>4</sub>·5H<sub>2</sub>O, 4.5 mmol of ascorbic acid (in 10 mL H<sub>2</sub>O) and 5 mmol of RN<sub>3</sub> **10** were added. After stirring at 60 °C for 15 h, resins **11** were collected by filtration and washed with H<sub>2</sub>O (30 mL×2), THF (20 mL×1), hot DMF (15 mL×1), H<sub>2</sub>O (30 mL×1), THF (20 mL×1), THF/H<sub>2</sub>O (v/v 2:1, 20 mL×2), hot DMF (15 mL×1), THF (20 mL×1), THF/H<sub>2</sub>O (v/v 2:1, 20 mL×2) and THF (20 mL×2) successively. Products **12** were then cut down from resins **11** through the similar procedures as the *unloading of compound 5*.

#### Typical procedure for the preparation of isoxazoline-tethered benzofurans **15** (Table 4) and benzodifurans **18** or **19** (Table 5).

Resins **13** and **17** were prepared through similar procedures (eq. 2 and 3) as *preparation of resin 4*; Isoxazoline-tethered benzofurans **15** were prepared from resins **13** (Table 4) through the similar procedures as the *preparation of isoxazole-tethered benzofurans 9*; Benzodifurans **18** or **19** were cut down from resins **17** (Table 5) through similar procedures as the *unloading of compound 5*.

#### Procedure for the regeneration of resin **2** from **21**.

Recovered resin **21** (10 g) was first soaked in dry THF (140 mL) overnight. A solution of KI (125 mmol) and Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (125 mmol) in 140 mL of EtOH/H<sub>2</sub>O (v/v = 1:1) was added. The suspension was stirred gently at room temperature for 12 h. The resin was collected by filtration and washed with THF (50 mL×2), THF /H<sub>2</sub>O (v/v=1:1, 80 mL×2), THF (50 mL×2), MeOH (50 mL×2) and CH<sub>2</sub>Cl<sub>2</sub> (50 mL×2) subsequently and then dried at 40 °C under vacuum for 6 h. The dried yellow resin was soaked in CHCl<sub>3</sub> (100 mL) for 3 h. Bromine (12.5 mmol) was then added dropwisely over a 20 min interval under ice bath cooling. The mixture was stirred for 30 min at 0 °C and

then poured into a fritted funnel and the resin was washed thoroughly with MeOH (80 mL×2), CH<sub>2</sub>Cl<sub>2</sub> (80 mL×3) and Et<sub>2</sub>O (80 mL×2) subsequently. The washed yellow resin was then soaked in absolute ethanol (100 mL) and heated to 70 °C for 1 h. The color of the resin became dark red slowly during this procedure. After cooling, the resin was filtered and washed with EtOH (80 mL×1), (80 mL×1), CH<sub>2</sub>Cl<sub>2</sub> (80 mL×2) and Et<sub>2</sub>O (80 mL×2) subsequently. The washed resin was dried under vacuum for 8 h to regenerate the activated resin **2**.

The reactivity evaluations of the recovered resin **2** were made according to the yield and purity of compound **6**, which was cut down from resin **3** (prepared from recovered resin **2**). The detailed procedure for the preparation of resin **3** was given in previous section; the procedure for the unloading of **6** was similar to that of compound **5**, as given in previous section.

#### Characterization of the Products

**Compound 5.** Oil; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.87 (s, 1H), 7.82-7.80 (m, 2H), 7.70-7.68 (m, 2H), 7.59-7.43 (m, 6H), 6.71(s, 1H), 4.70 (d, *J* = 2.8 Hz, 2H), 2.55 (t, *J* = 2.8 Hz, 1H), 2.47 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 201.3, 192.0, 161.3, 157.4, 156.5, 138.0, 137.7, 133.3, 132.6, 132.0, 129.7, 129.3, 128.4, 128.2, 120.3, 115.2, 113.2, 100.6, 78.2, 76.3, 60.1, 14.0; MS (ESI) *m/z* 395 (M+H)<sup>+</sup>.

**Compound 6.** White solid, mp.: 99-102 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 13.30 (s, 1H), 7.85 (s, 1H), 7.80 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 7.2 Hz, 2H), 7.58-7.52 (m, 2H), 7.47-7.42 (m, 4H), 6.70(s, 1H), 2.45 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 201.4, 192.4, 161.4, 157.5, 156.6, 138.1, 137.8, 133.2, 132.7, 132.1, 129.8, 129.2, 128.5, 128.2, 120.2, 115.3, 113.2, 100.7, 14.1; MS(ESI) *m/z* 357 (M+H)<sup>+</sup>; IR<sub>vmax</sub> (cm<sup>-1</sup>): 3425, 1634, 1596, 1397, 1289, 1195, 1114, 869, 741, 639; HRMS: *m/z* calcd for C<sub>23</sub>H<sub>17</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 357.1121, found: 357.1130.

**Compound 9a.** White solid, mp.: 91-93 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.88-7.83 (m, 4H), 7.66-7.55 (m, 5H), 7.49-7.38 (m, 7H), 6.62(s, 1H), 6.22 (s, 1H), 5.33 (s, 2H), 2.47 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.2, 192.5, 167.1, 162.2, 157.5, 155.6, 151.7, 137.8, 137.5, 133.3, 132.9, 131.2, 129.9, 129.4, 128.8, 128.3, 128.1, 127.6, 126.4, 125.4, 125.1, 122.2, 118.2, 101.5, 100.2, 66.1, 14.2; MS (ESI) *m/z* 514 (M+H)<sup>+</sup>; IR<sub>vmax</sub> (cm<sup>-1</sup>): 3083, 2982, 2870, 1658, 1594, 1447, 1241, 1109, 738, 692. HRMS (ESI): *m/z* calcd for C<sub>33</sub>H<sub>24</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 514.1649, found: 514.1660.

**Compound 9b.** White solid, mp.: 96-98 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.86-7.82 (m, 4H), 7.60-7.53 (m, 5H), 7.48-7.41 (m, 4H), 7.26-7.24 (d, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 0.8 Hz, 1H), 6.20 (s, H), 5.32 (s, 2H), 2.46 (d, *J* = 0.8 Hz, 3H), 2.40 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.2, 192.5, 167.2, 162.3, 157.6, 155.7, 151.9, 140.2, 137.8, 137.5, 133.2, 132.9, 129.9, 129.8, 129.5, 128.4, 128.3, 127.8, 126.6, 125.6, 125.0, 122.3, 118.3, 101.4, 100.5, 66.1, 21.3, 14.0; MS (ESI) *m/z* 528 (M+H)<sup>+</sup>; IR<sub>vmax</sub> (cm<sup>-1</sup>): 3085, 2920, 1771, 1657, 1595, 1446, 1241, 1106, 801, 693, 642. HRMS(ESI): *m/z* calcd for C<sub>34</sub>H<sub>26</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 528.1805, found: 528.1812.

**Compound 9c.** White solid, mp.: 102-104 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.88-7.83(m, 4H), 7.67 (d, 2H, *J* = 8.8Hz), 7.62-7.54(m, 3H), 7.50-7.43(m, 4H), 6.98 (d, 2H, *J* = 8.8Hz), 6.65(s, 1H), 6.18 (s, 1H), 5.33 (s, 2H), 3.87 (s, 3H), 2.48 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.2, 192.5, 167.1, 161.9, 161.0, 157.6, 155.7, 151.9, 137.8, 137.5, 133.2, 132.9, 129.9, 129.8, 128.4, 128.2, 128.1, 127.8, 125.0, 122.3, 121.0, 118.3, 114.2, 101.3, 100.5, 66.1, 55.3, 14.0; MS(ESI) *m/z* 544 (M+H)<sup>+</sup>; IR<sub>vmax</sub> (cm<sup>-1</sup>): 2924, 1730, 1653, 1433, 1299, 1247, 1175,

1113, 1030, 797, 699. HRMS:  $m/z$  calcd for  $C_{34}H_{26}NO_6$   $[M+H]^+$ : 544.1755, found: 544.1765.

**Compound 9d.** White solid, mp.: 116-118 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.82-7.79 (m, 4H), 7.68 (d,  $J = 8.4$  Hz, 2H), 7.60-7.55 (m, 3H), 7.50-7.43 (m, 6H), 6.64 (s, 1H), 6.21 (s, 1H), 5.33 (s, 2H), 2.46 (s, 3H);  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.1, 192.5, 167.7, 161.3, 157.8, 155.6, 151.9, 137.8, 137.5, 132.2, 133.3, 133.1, 130.0, 129.8, 128.5, 128.4, 128.3, 127.8, 127.3, 125.2, 124.8, 122.2, 118.5, 101.5, 100.3, 66.1, 14.1; MS(ESI)  $m/z$  592 (M+H) $^+$ , 594 (M+2+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3082, 2966, 2926, 2862, 1658, 1595, 1427, 1241, 1090, 1012, 851, 694; HRMS:  $m/z$  calcd for  $C_{33}H_{23}BrNO_5$   $[M+H]^+$ : 592.0754, found: 592.0759.

**Compound 9e.** White solid, mp.: 121-123 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.85-7.81 (m, 4H), 7.65-7.54 (m, 5H), 7.48-7.41 (m, 6H), 6.63(s, 1H), 6.21 (s, 1H) , 5.33 (s, 2H) , 2.47 (s, 3H) ;  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.1, 192.5, 167.8, 161.4, 157.7, 155.7, 151.8, 137.8, 137.5, 136.1, 133.2, 133.0, 129.9, 129.8, 129.1, 128.4, 128.3, 128.0, 127.8, 127.0, 125.1, 122.3, 118.4, 101.4, 100.4, 66.1, 14.0; MS(ESI)  $m/z$  548 (M+H) $^+$ , 550(M+2+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 2921, 1657, 1596, 1428, 1241, 1092, 1015, 948, 801, 694; HRMS:  $m/z$  calcd for  $C_{33}H_{23}ClNO_5$   $[M+H]^+$ : 548.1259, found: 548.1265.

**Compound 9f.** White solid, mp.: 114-116 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.88-7.83 (m, 4H), 7.73-7.69 (m, 2H), 7.60-7.55 (m, 3H), 7.50-7.44 (m, 4H), 7.17-7.13 (m, 2H), 6.65(s, 1H), 6.22 (s, 1H) , 5.35 (s, 2H) , 2.49 (d,  $J = 0.8$ Hz, 3H) ,  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.2, 192.6, 167.7, 163.9 (d,  $J=248$  Hz), 161.5, 157.7, 155.8, 151.9, 137.9, 137.6, 133.3, 133.0, 130.0, 129.9, 128.7 (d,  $J=8.3$  Hz), 128.5, 128.3, 127.8, 125.2, 124.8 (d,  $J = 2.5$  Hz), 122.5, 118.5, 116.0 (d,  $J = 22.4$  Hz), 115.9, 101.5, 100.5, 66.2, 14.1; MS(ESI)  $m/z$  532 (M+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 2922, 1658, 1526, 1433, 1237, 1105, 842, 694, 593, 522; HRMS:  $m/z$  calcd for  $C_{33}H_{23}FNO_5$   $[M+H]^+$ : 532.1555, found: 532.1558.

**Compound 9g.** Pale yellow solid, mp.: 125-127 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  8.11 (d, 2H,  $J = 8.0$ Hz), 7.83 (d, 2H,  $J = 8.0$ Hz), 7.71-7.65 (m, 4H), 7.55-7.32 (m, 7H), 6.64 (s, 1H), 6.28 (s, 1H), 5.32 (s, 2H), 2.45 (s, 3H);  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.2, 192.5, 167.20, 158.2, 156.3, 155.5, 153.0, 148.6, 137.9, 137.8, 135.3, 133.4, 132.9, 130.4, 129.9, 128.6, 128.4, 127.6, 127.6, 125.1, 123.9, 122.1, 118.0, 101.5, 100.7, 66.3, 14.1; MS(ESI)  $m/z$  559 (M+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3077, 2924, 2848, 1658, 1598, 1521, 1264, 1108, 850; HRMS:  $m/z$  calcd for  $C_{33}H_{23}N_2O_7$   $[M+H]^+$ : 559.1500, found: 559.1510.

**Compound 9h.** White solid, mp.:119-121 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.27-7.87(m, 15H), 6.65(s, H), 6.12 (s, H) , 5.36 (s, 2H) , 2.48 (s, 3H) ,  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$ 195.07, 192.49, 167.84, 161.10, 157.65, 155.73, 151.69, 137.80, 137.49, 133.26, 132.97, 132.95, 130.43, 130.38, 129.93, 129.84, 129.72, 128.45, 128.26, 127.86, 125.19, 124.96, 122.85, 122.10, 118.34, 101.32, 100.45, 66.0, 14.03; MS(ESI)  $m/z$  592 (M+H) $^+$  , 594 (M+2+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3053, 2938, 1657, 1637, 1596, 1395, 1268, 1240, 1176, 980, 790, 731, 693; HRMS:  $m/z$  calcd for  $C_{33}H_{23}BrNO_5$   $[M+H]^+$ : 592.0754, found: 592.0763.

**Compound 9i.** Solid, mp.: 101-103 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.88-7.83(m, 4H), 7.68-7.67(m, 1H), 7.61-7.54(m, 3H), 7.49-7.39(m, 5H), 7.38-7.34 (m, 2H), 6.64(s, 1H), 6.49 (s, 1H) , 5.34 (s, 2H) , 2.47 (s, 3H) ;  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$ 195.1, 192.5, 166.7, 161.0, 157.7, 155.6, 151.9, 137.8, 137.6, 133.3, 133.0, 132.8, 131.0, 130.9, 130.4, 130.0, 129.9, 128.4, 128.3, 127.9, 127.8, 127.1, 125.4, 122.9, 118.5,

105.1, 100.5, 66.2, 14.1; MS(ESI)  $m/z$  548 (M+H) $^+$  , 550 (M+2+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3040, 2925, 1655 1638, 1594, 1390, 1253, 1158, 987, 794, 740.; HRMS:  $m/z$  calcd for  $C_{33}H_{23}ClNO_5$   $[M+H]^+$ : 548.1259, found: 548.1269.

**Compound 9j.** Solid, mp.:70-72 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.87 (s, 1H), 7.82 (d,  $J = 7.6$  Hz, 2H), 7.70 (d,  $J = 7.2$  Hz, 2H), 7.59-7.54 (m, 2H), 7.49-7.44 (m, 4H), 6.64 (s, 1H), 6.22 (s, 1H), 5.34 (s, 2H) , 2.85-2.79 (m, 1H), 2.47(s, 3H), 2.12-1.30 (m, 10H);  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.2, 192.4, 167.9, 162.4, 157.7, 155.8, 151.9, 137.8, 137.5, 133.1, 132.9, 130.0, 129.8, 128.4, 128.2, 127.8, 125.1, 122.3, 118.2, 101.4, 100.4, 66.1, 35.3, 31.4, 25.5, 25.3, 14.1; MS (ESI)  $m/z$  520 (M+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3075, 2933, 2851, 1771, 1657, 1595, 1440, 1241, 1112, 799,733, 692. HRMS (ESI):  $m/z$  calcd for  $C_{33}H_{30}NO_5$   $[M+H]^+$ : 520.2118, found: 520.2125.

**Compound 9k.** Oil;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.86 (s, 1H), 7.78-7.64 (m, 4H), 7.56-7.51 (m, 2H), 7.50-7.45 (m, 4H), 6.36 (s, 1H), 6.21 (s, 1H), 5.28 (s, 2H), 2.68 (t,  $J = 7.2$  Hz, 2H), 2.45(s, 3H), 1.68-1.66 (m, 2H), 1.44-1.40 (m, 2H), 0.90 (t,  $J = 7.2$  Hz, 3H);  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.2, 192.3, 168.1, 162.6, 157.8, 155.8, 152.0, 138.0, 137.6, 133.3, 133.0, 130.1, 129.7, 128.5, 128.4, 127.7, 125.0, 122.1, 118.3, 101.5, 100.2, 66.0, 30.5, 25.8, 22.3, 14.2, 13.7; MS (ESI)  $m/z$  494 (M+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3081, 2973, 2969, 2956, 2930, 2880, 1660, 1595, 1239, 1110, 763, 692. HRMS(ESI):  $m/z$  calcd for  $C_{31}H_{28}NO_5$   $[M+H]^+$ : 494.1962, found: 494.1970.

**Compound 9l.** Oil;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.86 (s, 1H), 7.76-7.65 (m, 4H), 7.54-7.50 (m, 2H), 7.48-7.44 (m, 4H), 6.41 (s, 1H), 6.22 (s, 1H), 5.29 (s, 2H), 2.46(s, 3H), 1.34 (s, 9H);  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.1, 192.5, 168.2, 162.5, 157.7, 155.8, 152.1, 137.9, 137.5, 133.0, 132.8, 130.0, 129.8, 128.5, 128.3, 127.6, 125.2, 122.2, 118.1, 101.4, 100.1, 66.1, 32.1, 29.5, 14.1; MS (ESI)  $m/z$  494 (M+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3086, 3026, 2962, 2943, 2922, 2878, 1660, 1591, 1451, 1390, 1370, 1239, 765, 690. HRMS (ESI):  $m/z$  calcd for  $C_{31}H_{28}NO_5$   $[M+H]^+$ : 494.1962, found: 494.1973.

**Compound 12a.** White solid, mp: 100-102 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.86-7.81 (m, 4H), 7.62-7.39 (m, 13H), 6.79 (d, 1H,  $J = 0.4$ Hz), 5.50 (s, 2H) , 2.47 (s, 3H) ;  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.7, 192.9, 157.6, 156.3, 152.7, 144.5, 138.4, 138.0, 137.1, 133.3, 133.1, 130.2, 130.1, 129.9, 129.1, 128.7, 128.6, 128.2, 125.0, 122.0, 121.1, 120.7, 118.2, 101.4, 67.3, 14.3; MS(ESI)  $m/z$  514 (M+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 3058, 1656, 1596, 1446, 1240, 1106, 1044, 873, 760, 691; HRMS:  $m/z$  calcd for  $C_{32}H_{24}N_3O_4$   $[M+H]^+$ : 514.1761, found: 514.1755.

**Compound 12b.** Solid, mp: 112-114 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  7.86-7.81 (m, 4H), 7.67-7.63 (m, 2H), 7.58-7.40 (m, 10H), 6.77 (s, 1H), 5.50 (s, 2H) , 2.48 (s, 3H) ;  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.3, 192.6, 157.3, 152.3, 151.8, 144.5, 138.0, 137.6, 133.0, 132.8(3),132.7(7), 132.6, 129.9, 129.8, 129.7, 128.4, 128.2, 127.90, 124.7, 122.4, 121.7, 121.2, 120.6, 100.9, 66.9, 14.0; MS(ESI)  $m/z$  592 (M+H) $^+$  , 594 (M+2+H) $^+$ ; IR $_{\max}$  ( $cm^{-1}$ ): 2921, 1656, 1595, 1498, 1446, 1241, 1176, 1107, 987, 827, 695; HRMS:  $m/z$  calcd for  $C_{32}H_{23}BrN_3O_4$   $[M+H]^+$ : 592.0866, found: 592.0868.

**Compound 12c.** Solid, mp: 102-104 °C;  $^1H$ -NMR ( $CDCl_3$ ):  $\delta$  8.78-8.76 (d, 2H,  $J = 5.6$ Hz), 7.85-7.81 (m, 4H), 7.64-7.40 (m, 10H), 6.77 (d, 1H,  $J = 0.8$ Hz), 5.52 (s, 2H), 2.47 (s, 3H);  $^{13}C$ -NMR ( $CDCl_3$ ):  $\delta$  195.6, 192.8, 157.7, 156.2, 152.5, 151.9, 145.4, 143.1, 138.4, 137.9, 133.4, 133.2, 130.3, 130.2, 128.7, 128.6, 128.1, 125.0, 122.1, 120.5, 118.3, 113.9, 101.2, 67.1, 14.3; MS(ESI)  $m/z$  515 (M+H) $^+$ ; HRMS:  $m/z$  calcd for  $C_{31}H_{23}N_4O_4$   $[M+H]^+$ : 515.1714, found: 515.1723.

**Compound 12d.** Solid, mp: 105-107 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.84-7.79 (m, 4H), 7.57-7.53 (m, 2H), 7.47-7.28 (m, 9H), 7.19-7.16 (m, 1H), 6.77 (s, 1H), 5.48 (s, 2H), 2.44 (s, 3H), 2.10 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.7, 192.9, 157.5, 156.2, 152.8, 143.6, 138.4, 138.0, 136.5, 133.8, 133.3, 133.2, 131.7, 130.2, 130.14, 130.10, 128.7, 128.6, 128.2, 127.0, 126.1, 125.2, 124.7, 122.4, 118.2, 101.4, 67.4, 18.0, 14.3; MS(ESI) *m/z* 528 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 3058, 1656, 1595, 1446, 1238, 1105, 1043, 985, 872, 762, 694; HRMS: *m/z* calcd for C<sub>33</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 528.1918, found: 528.1925.

**Compound 12e.** Solid, mp: 116-118 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.86-7.80 (m, 4H), 7.58-7.55 (m, 4H), 7.51-7.34 (m, 7H), 6.76(d, 1H, *J* = 0.4Hz), 5.50 (s, 2H), 2.48 (d, 3H, *J* = 1.2Hz); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.6, 192.9, 157.6, 156.2, 152.6, 143.9, 138.3, 138.0, 135.5, 133.9, 133.4, 133.2, 131.9, 131.1, 130.3, 130.2, 128.7, 128.6, 128.2, 127.9, 127.0, 125.2, 125.1, 122.4, 118.3, 101.3, 67.2, 14.4; MS(ESI) *m/z* 582 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 2922, 1657, 1595, 1446, 1241, 1100, 1041, 879, 811, 604; HRMS: *m/z* calcd for C<sub>32</sub>H<sub>22</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 582.0982, found: 582.0980.

**Compound 12f.** Solid, mp: 120-122 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 8.47 (s, 1H), 8.467-8.30 (m, 1H), 7.86-7.80 (m, 5H), 7.77 (s, 1H), 7.58-7.39 (m, 7H), 6.76(s, 1H), 5.51 (s, 2H), 2.48 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.3, 192.5, 157.4, 155.8, 152.1, 148.0, 144.0, 139.2, 137.8, 137.6, 133.1, 132.9, 129.9, 129.86, 128.9, 128.3, 128.2, 128.1, 127.7, 126.3, 124.9, 124.6, 123.0, 122.2, 118.0, 100.8, 66.8, 14.0; MS(ESI) *m/z* 593 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 3057, 2925, 1651, 1600, 1527, 1446, 1348, 1267, 1235, 1107, 1041, 886, 808, 739, 694; HRMS: *m/z* calcd for C<sub>32</sub>H<sub>22</sub>ClN<sub>4</sub>O<sub>6</sub> [M+H]<sup>+</sup>: 593.1222, found: 593.1231.

**Compound 12g.** Solid, mp: 123-125 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 8.06 (s, 1H), 8.05-7.73 (m, 5H), 7.57-7.55 (m, 2H), 7.51-7.39 (m, 7H), 6.74 (d, 1H, *J* = 1.2Hz), 5.48 (s, 2H), 2.46 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.7, 192.9, 157.8, 156.2, 152.5, 144.7, 144.6, 138.3, 138.0, 137.2, 134.1, 133.4, 133.2, 130.3, 130.2, 129.2, 128.8, 128.7, 128.6, 128.1, 126.1, 125.2, 124.7, 122.4, 118.3, 101.2, 67.1, 14.3; MS (ESI) *m/z* 593 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 3065, 1657, 1596, 1543, 1447, 1351, 1242, 1177, 1109, 1041, 881, 695; HRMS: *m/z* calcd for C<sub>32</sub>H<sub>22</sub>ClN<sub>4</sub>O<sub>6</sub> [M+H]<sup>+</sup>: 593.1222, found: 593.1225.

**Compound 12h.** Solid, mp: 118-120 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.84-7.78 (m, 4H), 7.66 (d, 2H, *J* = 5.6Hz), 7.56-7.38 (m, 8H), 6.74(d, 1H, *J* = 1.2Hz), 5.48 (s, 2H), 2.46 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.6, 192.9, 157.7, 156.1, 152.5, 144.0, 138.3, 138.0, 135.1, 133.9, 133.4, 133.2, 132.6, 132.0, 130.2, 130.2, 129.0, 128.7, 128.6, 128.1, 127.3, 125.2, 125.0, 122.4, 118.3, 101.2, 67.1, 14.4; MS (ESI) *m/z* 616 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 3059, 1657, 1595, 1482, 1241, 1176, 1105, 1042, 882, 798, 695; HRMS: *m/z* calcd for C<sub>32</sub>H<sub>21</sub>Cl<sub>3</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 616.0592, found: 616.0601.

**Compound 12i.** Oil; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.87-7.80 (m, 4H), 7.70-7.66 (m, 2H), 7.60-7.48 (m, 6H), 6.76 (s, 1H), 5.52 (s, 2H), 4.98 (m, 1H), 2.46 (s, 3H), 1.30 (d, *J* = 4.0 Hz, 6H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.5, 192.6, 157.0, 152.2, 144.3, 138.0, 133.3, 132.6, 132.2, 130.0, 129.6, 129.1, 128.7, 128.5, 128.1, 126.9, 125.3, 122.4, 118.8, 101.1, 66.7, 58.7, 21.6, 21.5, 14.1; MS(ESI) *m/z* 480 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 3081, 2967, 2923, 2876, 2851, 1656, 1596, 1449, 1380, 1370, 1109, 768, 691; HRMS(ESI): *m/z* calcd for C<sub>29</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 480.1918, found: 480.1912.

**Compound 15a.** Solid, mp: 98-100 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.86 (d, 2H, *J* = 7.2Hz), 7.80 (d, 2H, *J* = 8.0Hz), 7.60-7.51 (m, 3H), 7.48-7.40 (m, 6H), 7.21 (d, 2H, *J* = 8.0Hz), 6.70 (s, 1H), 4.79-4.75(m,

1H), 4.37-4.26(m, 2H), 3.20-3.13 (m, 1H), 2.99-2.93 (m, 1H), 2.45 (s, 3H), 2.39 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.5, 192.7, 157.1, 156.3, 155.9, 152.8, 140.4, 138.0, 137.7, 133.1, 132.8, 130.0, 129.7, 129.3, 128.4, 128.3, 128.0, 126.70, 126.68, 124.4, 121.9, 117.7, 101.0, 78.4, 73.3, 36.8, 21.4, 14.1. MS(ESI) *m/z* 529 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 2924, 1658, 1597, 1447, 1247, 1109, 897, 695; HRMS: *m/z* calcd for C<sub>34</sub>H<sub>28</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 530.1962, found: 530.1969.

**Compound 15b.** Solid, mp: 107-109 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.85 (d, 2H, *J* = 7.6Hz), 7.79 (d, 2H, *J* = 7.2Hz), 7.57-7.38 (m, 9H), 6.92 (d, 2H, *J* = 8.8Hz), 6.70 (s, 1H), 4.80-4.72 (m, 1H), 4.37-4.26 (m, 2H), 3.85 (s, 3H), 3.19-3.08 (m, 1H), 2.98-2.88 (m, 1H), 2.45 (s, 3H); <sup>13</sup>C-NMR(CDCl<sub>3</sub>): δ 195.5, 192.7, 161.1, 157.1, 155.9, 152.8, 138.0, 137.7, 133.1, 132.8, 129.9, 129.8, 129.7, 128.33, 128.27, 128.24, 128.0, 124.4, 121.8, 121.6, 117.7, 114.0, 101.0, 78.3, 73.3, 55.3, 37.0, 14.1. MS(ESI) *m/z* 545 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 2962, 2924, 1658, 1260, 1100, 1024, 803, 696; HRMS: *m/z* calcd for C<sub>34</sub>H<sub>28</sub>NO<sub>6</sub> [M+H]<sup>+</sup>: 546.1911, found: 546.1903.

**Compound 15c.** Solid, mp: 109-111 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.80 (d, 2H, *J* = 7.2Hz), 7.73 (d, 2H, *J* = 7.2Hz), 7.55-7.30 (m, 11H), 6.65 (s, 1H), 4.80-4.76(m, 1H), 4.31 (d, 2H, *J* = 4.4Hz), 3.16-3.09 (m, 1H), 2.97-2.92 (m, 1H), 2.40 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.3, 192.6, 157.1, 155.8, 155.4, 152.6, 137.9, 137.6, 136.0, 133.0, 132.8, 129.9, 129.7, 128.8, 128.3, 128.2, 127.91, 127.87, 127.6, 124.4, 121.8, 117.7, 100.9, 78.9, 73.3, 36.3, 14.0; MS(ESI) *m/z* 549 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 2923, 1658, 1597, 1474, 1260, 1093, 827, 660; HRMS: *m/z* calcd for C<sub>33</sub>H<sub>25</sub>ClNO<sub>5</sub> [M+H]<sup>+</sup>: 550.1416, found: 550.1420.

**Compound 15d.** Solid, mp: 108-110 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.83 (d, 2H, *J* = 7.2Hz), 7.77 (d, 2H, *J* = 7.2Hz), 7.58-7.35 (m, 9H), 7.08-7.04 (m, 2H), 6.68 (s, 1H), 4.82-4.78(m, 1H), 4.34-4.32 (d, 2H), 3.19-3.12 (m, 1H), 3.01-2.95 (m, 1H), 2.43 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.3, 192.6, 163.7 (d, *J* = 248.9Hz), 157.1, 155.9, 155.4, 152.7, 137.9, 137.6, 133.1, 132.8, 129.9, 129.7, 128.6 (d, *J* = 8.4Hz), 128.3, 128.2, 127.9, 125.3 (d, *J* = 3.4Hz), 124.4, 121.8, 117.7, 115.7 (d, *J* = 21.5Hz), 100.9, 78.7, 73.2, 36.6, 14.0; MS(ESI) *m/z* 533 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 3059, 2920, 1658, 1596, 1446, 1259, 875, 759, 695; HRMS: *m/z* calcd for C<sub>33</sub>H<sub>25</sub>FNO<sub>5</sub> [M+H]<sup>+</sup>: 534.1711, found: 534.1722.

**Compound 15e.** Solid, mp: 112-114 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 8.21 (d, 2H, *J* = 8.8Hz), 7.81 (d, 2H, *J* = 8.0Hz), 7.72-7.67 (m, 4H), 7.56-7.32 (m, 7H), 6.65 (s, 1H), 4.93-4.89(m, 1H), 4.42-4.33 (d, 2H), 3.25-3.08 (m, 2H), 2.43 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.2, 192.6, 157.4, 155.9, 155.0, 152.5, 148.5, 137.8, 137.7, 135.2, 133.2, 132.9, 130.0, 129.9, 128.4, 128.3, 127.8, 127.5, 124.6, 123.8, 122.0, 117.9, 100.8, 79.9, 73.3, 35.9, 14.1; MS(ESI) *m/z* 561 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 2962, 1658, 1598, 1519, 1261, 1104, 1028, 802; HRMS: *m/z* calcd for C<sub>33</sub>H<sub>25</sub>N<sub>2</sub>O<sub>7</sub> [M+H]<sup>+</sup>: 561.1656, found: 561.1649.

**Compound 15f.** Solid, mp: 101-103 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 7.81-7.79 (m, 2H), 7.74-7.72 (m, 2H), 7.59-7.34 (m, 10H), 7.32-7.19 (m, 1H), 6.67 (s, 1H), 4.82-4.77(m, 1H), 4.32 (d, 2H, *J* = 4.4Hz), 3.12-3.05 (m, 1H), 2.88-2.82 (m, 1H), 2.40 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 195.3, 192.5, 157.1, 155.8, 155.2, 152.6, 137.8, 137.6, 133.1, 132.8, 131.1, 130.1, 129.9, 129.7, 129.6, 128.3, 128.2, 128.1, 127.9, 125.2, 124.4, 122.6, 121.7, 117.7, 100.9, 79.0, 73.1, 36.0, 14.0; MS(ESI) *m/z* 593 (M+H)<sup>+</sup>; IR<sub>v</sub><sub>max</sub> (cm<sup>-1</sup>): 2921, 1658, 1596, 1244, 910, 873, 786, 690; HRMS: *m/z* calcd for C<sub>33</sub>H<sub>25</sub>BrNO<sub>5</sub> [M+H]<sup>+</sup>: 594.0911, found: 594.0906.

**Compound 15g.** Solid, mp: 94-96 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.82 (d, 2H,  $J = 7.6\text{Hz}$ ), 7.74 (d, 2H,  $J = 7.2\text{Hz}$ ), 7.56-7.21 (m, 11H), 6.71 (s, 1H), 4.80-4.76(m, 1H), 4.30 (d, 2H,  $J = 4.8\text{Hz}$ ), 3.37-3.30 (m, 1H), 3.04-2.98 (m, 1H), 2.39 (s, 3H);  $\delta^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  195.3, 192.6, 157.1, 156.2, 155.8, 152.8, 137.9, 137.6, 133.2, 133.1, 132.8, 132.6, 130.8, 130.5, 130.4, 129.9, 129.6, 128.5, 128.4, 128.3, 128.2, 127.9, 126.8, 124.5, 121.9, 177.7, 101.0, 79.1, 73.3, 38.9, 14.0; MS(EI)  $m/z$  549 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 2926, 1654, 1599, 1232, 1112, 837, 736, 682; HRMS:  $m/z$  calcd for  $\text{C}_{33}\text{H}_{25}\text{ClNO}_5$ : 550.1416, found: 550.1425.

**Compound 15h.** Oil;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.86 (s, 1H), 7.79-7.72 (m, 4H), 7.60-7.45 (m, 6H), 6.72 (s, 1H), 4.78-4.74(m, 1H), 4.36-4.25(m, 2H), 3.19-3.12 (m, 1H), 2.98-2.92 (m, 1H), 2.84-2.77 (m, 1H), 2.44 (s, 3H), 2.13-1.31 (m, 10H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  195.4, 192.6, 157.1, 156.3, 155.9, 152.8, 137.8, 137.5, 133.0, 132.5, 130.2, 129.2, 128.5, 127.9, 126.7, 124.8, 122.1, 118.1, 101.7, 78.6, 73.3, 37.2, 35.4, 31.5, 25.5, 25.4, 14.1. MS (ESI)  $m/z$  522 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3075, 2928, 2852, 1659, 1596, 1446, 1375, 1247, 1110, 768, 690; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{33}\text{H}_{32}\text{NO}_5$  [M+H] $^+$ : 522.2275, found: 522.2281.

**Compound 18a.** Solid, mp: 140-141 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.86-7.84 (m, 4H), 7.60-7.53 (m, 3H), 7.47-7.41 (m, 4H), 6.53 (s, 1H), 4.88 (t,  $J = 5.2\text{ Hz}$ , 1H), 3.62 (s, 3H), 2.45 (s, 3H), 1.77-1.68 (m, 2H), 0.69 (t,  $J = 7.6\text{Hz}$ , 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  195.0, 192.0, 170.3, 156.5, 155.4, 151.4, 137.7, 137.4, 132.5, 132.3, 129.4, 127.9, 127.8, 127.7, 124.3, 120.6, 120.5, 117.2, 100.4, 80.5, 51.6, 25.7, 13.5, 8.1. MS (ESI)  $m/z$  457 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3444, 3058, 2971, 2949, 2879, 1755, 1664, 1600, 1355, 1262, 1214, 1180, 1102, 1084, 956, 933, 792, 737, 708, 637, 551; HRMS:  $m/z$  calcd for  $\text{C}_{28}\text{H}_{25}\text{O}_6$  [M+H] $^+$ : 457.1646, found: 457.1642.

**Compound 18b.** Solid, mp: 124-126 °C;  $^1\text{H-NMR}$ ( $\text{CDCl}_3$ ):  $\delta$  7.85-7.84 (m, 4H), 7.60 (s, 1H), 7.57-7.53 (m, 2H), 7.47-7.42 (m, 4H), 6.51 (s, 1H), 4.91 (d,  $J = 4.0\text{Hz}$ , 1H), 3.62 (s, 3H), 2.45 (s, 3H), 1.71-1.63 (m, 2H), 1.14-1.11 (m, 2H), 1.04-1.01 (m, 2H), 0.76 (t,  $J = 6.9\text{ Hz}$ , 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  195.6, 192.7, 171.1, 156.9, 155.9, 151.8, 138.1, 137.8, 132.9, 132.8, 129.98, 129.92, 128.4, 128.3, 128.2, 124.6, 120.98, 117.7, 100.7, 80.2, 52.1, 32.6, 26.3, 22.2, 14.1, 13.7; MS (ESI)  $m/z$  485 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3452, 3056, 2953, 2921, 2861, 1754, 1667, 1598, 1448, 1329, 1264, 1209, 1099, 1046, 950, 792, 763, 737, 706, 639, 529. HRMS:  $m/z$  calcd for  $\text{C}_{30}\text{H}_{29}\text{O}_6$  [M+H] $^+$ : 485.1959, found: 485.1966.

**Compound 18c.** Solid, mp: 65-67 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.84-7.79 (m, 4H), 7.64 (s, 1H), 7.56-7.48 (m, 2H), 7.44-7.36 (m, 4H), 7.29-7.27 (m, 1H), 7.20-7.15 (m, 1H), 7.06-7.03 (m, 1H), 6.91-6.89 (m, 1H), 6.50 (d,  $J = 1.2\text{Hz}$ , 1H), 6.30 (s, 1H), 3.57 (s, 3H), 2.41 (s, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  195.1, 192.6, 168.6, 157.4, 155.8, 150.9, 138.1, 137.5, 132.84, 132.76, 132.68, 130.13, 129.91, 129.84, 129.34, 128.74, 128.31, 128.22, 128.10, 127.1, 125.4, 121.8, 118.4, 100.3, 78.6, 52.6, 14.0. MS (ESI)  $m/z$  539 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3441, 3056, 2963, 2246, 1652, 1598, 1473, 1427, 1191, 1087, 1021 942, 907, 860, 844, 804, 763, 690, 583, 531. HRMS:  $m/z$  calcd for  $\text{C}_{32}\text{H}_{24}\text{ClO}_6$  [M+H] $^+$ : 539.1256, found: 539.1249.

**Compound 19a.** Solid, mp: 111-114 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.85-7.83 (m, 2H), 7.64 (s, 1H), 7.58-7.56 (m, 3H), 7.48-7.45 (m, 5H), 6.86(s, 1H), 4.38-4.33(q,  $J = 6.8\text{ Hz}$ , 2H), 2.48 (s, 3H), 1.28 (t,  $J = 6.8\text{ Hz}$ , 3H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  193.7, 159.7, 157.2, 153.4, 148.8, 140.4, 137.8, 132.9, 130.47, 130.31, 130.14, 130.0, 128.58, 128.24, 128.17, 122.8, 120.8, 118.9, 115.7, 99.6, 61.3, 29.7, 14.1; MS (ESI)  $m/z$  425 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3058, 2971, 2949, 2879, 1755, 1664,

1600, 1355, 1262, 1214, 1180, 1102, 1084, 956, 933, 792, 737, 708, 637, 551; HRMS:  $m/z$  calcd for  $\text{C}_{27}\text{H}_{21}\text{O}_5$  [M+H] $^+$ : 425.1384, found: 425.1391.

**Compound 19b.** Solid, mp: 119-122 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.85-7.83 (m, 2H), 7.62-7.56 (m, 4H), 7.50-7.44 (m, 5H), 6.85 (s, 1H), 2.49 (s, 6H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  193.5, 188.8, 157.3, 153.7, 148.4, 147.6, 137.6, 133.0, 130.31, 130.06, 129.8, 129.0, 128.9, 128.6, 128.2, 123.1, 120.8, 119.3, 115.5, 99.4, 28.3, 14.2.; MS (ESI)  $m/z$  395 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3060, 1665, 1632, 1447, 1358, 1293, 1257, 1214, 1096, 935, 871, 802, 762, 738, 693, 607; HRMS:  $m/z$  calcd for  $\text{C}_{26}\text{H}_{19}\text{O}_4$  [M+H] $^+$ : 395.1278, found: 395.1273.

**Compound 19c.** Solid, mp: 123-125 °C;  $^1\text{H-NMR}$ ( $\text{CDCl}_3$ ):  $\delta$  7.88-7.84 (m, 4H), 7.76 (s, 1H), 7.62-7.59 (m, 1H), 7.49-7.44 (m, 5H), 7.35-7.31 (m, 5H), 6.85 (s, 1H), 2.50 (s, 3H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  193.58, 185.31, 157.32, 153.69, 148.97, 147.51, 137.87, 137.20, 133.00, 132.58, 130.81, 130.54, 130.13, 130.00, 129.76, 128.50, 128.42, 128.26, 128.04, 122.62, 121.02, 119.13, 115.75, 99.54, 14.20; MS (ESI)  $m/z$  457 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 2921, 1634, 1596, 1470, 1445, 1398, 1362, 1290, 1195, 1178, 1115, 1068, 1027, 927, 755, 743, 699; HRMS:  $m/z$  calcd for  $\text{C}_{31}\text{H}_{21}\text{O}_4$  [M+H] $^+$ : 457.1434, found: 457.1441.

**Compound 19d.** Solid, mp: 127-130 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  7.88-7.87 (m, 2H), 7.86-7.81 (m, 2H), 7.77-7.71 (m, 1H), 7.60-7.54 (m, 3H), 7.50-7.46 (m, 3H), 6.80 (s, 1H), 2.51 (s, 3H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  193.3, 157.9, 153.6, 149.8, 137.9, 137.5, 133.2, 130.1, 129.7, 129.4, 129.0, 128.4, 128.3, 128.1, 123.6, 121.4, 118.2, 115.2, 113.0, 100.6, 14.2; MS (ESI)  $m/z$  378 (M+H) $^+$ ; IR $_{\text{vmax}}$  ( $\text{cm}^{-1}$ ): 3028, 2920, 2222, 1658, 1598, 1445, 1394, 1288, 1257, 1177, 1112, 1076, 762, 732, 696; HRMS:  $m/z$  calcd for  $\text{C}_{25}\text{H}_{16}\text{NO}_3$  [M+H] $^+$ : 378.1125, found: 378.1120.

## Acknowledgements

This work was supported by NNSFC (21202141, 21202151 and 20902070), ZJNSF for Distinguished Young Scholars (R14B020009), ZJNSF (Y4090410), Science and Technology Department of Zhejiang Province Foundation of China (2010C32022), and 580 Oversea Talents Program of Wenzhou City. We also thank Jiangsu Yangnong Chemical Group Co. Ltd. for financial support, analysis centre of Yangzhou University for assistances and Dr. Lei Zhu (associate professor in the department of chemistry and biochemistry at Florida State University, US) for advises.

## Notes and references

<sup>a</sup> College of Biological and Environmental Engineering, Zhejiang University of Technology, Hangzhou, Zhejiang, 310014, P. R. of China. E-mail: [zhuq@zjut.edu.cn](mailto:zhuq@zjut.edu.cn); Fax: (+)-86-0571-88320781; Tel: (+)-86-18329193166.

<sup>b</sup> Zhejiang Research Institute of Chemical Industry, Hangzhou, Zhejiang, 310023, P. R. of China.

<sup>c</sup> School of Chemistry and Chemical Engineering, Yangzhou University, Yangzhou, Jiangsu 225002, China. E-mail: [yulei@yzu.edu.cn](mailto:yulei@yzu.edu.cn); Home page: <http://blog.sciencenet.cn/u/YuLei82>; Fax: (+)-86-514-87975244; Tel: (+)-86-136-65295901.

<sup>†</sup> Electronic supplementary information (ESI) available: Detailed table for Figure 1 and NMR spectra copies of the products. See DOI: 10.1039/b000000x/

- 1 (a) C. S. Bennett, *Org. Biomol. Chem.*, 2014, **12**, 1686; (b) J. P. Nandy, M. Prakesch, S. Khadem, P. T. Reddy, U. Sharma and P. Arya, *Chem. Rev.*, 2009, **109**, 1999; (c) Y.-D. Gong and T. Lee, *J. Comb. Chem.*, 2010, **12**, 393; (d) R. E. Dolle, B. Le Bourdonnec, A. J. Goodman, G. A. Morales, C. J. Thomas and W. Zhang, *J. Comb. Chem.*, 2009, **11**, 739. (e) C. Gil and S. Bräse, *J. Comb. Chem.*, 2009, **11**, 175; (f) N. E. Robinson and A. B. Robinson, *Pept. Sci.*, 2008, **90**, 297; (g) R. E. Ziegert, J. Tor äng, K. Knepper and S. Bräse, *J. Comb. Chem.*, 2005, **7**, 147; (h) S. Brase, *Acc. Chem. Res.*, 2004, **37**, 805; (i) V. Krchnak and M. W. Holladay, *Chem. Rev.*, 2002, **102**, 61.
- 2 For reviews: (a) H. J. Reich, *Acc. Chem. Res.*, 1979, **12**, 22; (b) D. Liotta, *Acc. Chem. Res.*, 1984, **17**, 28. For reports, see: (c) Z. S. Zhou, N. Jiang and D. Hilvert, *J. Am. Chem. Soc.*, 1997, **119**, 3623; (d) H. J. Reich, C. A. Hoeger and W. W., Jr. Willis, *J. Am. Chem. Soc.*, 1982, **104**, 2936; (e) H. J. Reich and W. W., Jr. Willis, *J. Am. Chem. Soc.*, 1980, **104**, 5967; (f) H. J. Reich, L. L. Reich and S. Wollowitz, *J. Am. Chem. Soc.*, 1978, **100**, 5981; (g) K. B. Sharpless and M. W. Young, *J. Org. Chem.*, 1975, **40**, 947.
- 3 (a) K. C. Nicolaou, J. A. Pfefferkorn and G.-Q. Cao, *Angew. Chem. Int. Ed.*, 2000, **39**, 734; (b) K. C. Nicolaou, J. A. Pfefferkorn, A. J. Roecker, G.-Q. Cao, S. Barluenga and H. J. Mitchell, *J. Am. Chem. Soc.*, 2000, **122**, 9939; (c) K. C. Nicolaou, G.-Q. Cao and J. A. Pfefferkorn, *Angew. Chem. Int. Ed.*, 2000, **39**, 739; (d) K. C. Nicolaou, J. A. Pfefferkorn, H. J. Mitchell, A. J. Roecker, S. Barluenga, G.-Q. Cao, R. L. Affleck, and J. E. Lillig, *J. Am. Chem. Soc.*, 2000, **122**, 9954; (e) K. C. Nicolaou, A. J. Roecker and G.-Q. Cao, *J. Am. Chem. Soc.*, 2000, **122**, 2966; (f) X. Huang and W.-M. Xu, *Org. Lett.*, 2003, **24**, 4649; (g) E. Tang, X. Huang and W.-M. Xu, *Tetrahedron* 2004, **60**, 9963; (h) W.-M. Xu, X. Huang and E. Tang, *J. Comb. Chem.*, 2005, **7**, 726; (i) Y.-G. Wang, W.-M. Xu and X. Huang, *J. Comb. Chem.*, 2007, **9**, 513; (j) X. Huang and Y.-G. Wang, *J. Comb. Chem.*, 2007, **9**, 121; (k) X. Huang and J. Cao, *Synthesis* 2007, 2947; (l) J. Cao and X. Huang, *J. Comb. Chem.*, 2008, **10**, 526; (m) J. Cao and X. Huang, *J. Comb. Chem.*, 2010, **12**, 1; (n) X. Huang and J.-F. Xu, *J. Comb. Chem.*, 2009, **11**, 350; (o) Y.-J. Zhang and Y.-G. Wang, *Appl. Organometal. Chem.*, 2012, **26**, 212; (p) R.-J. He, B.-C. Zhu and Y.-G. Wang, *Appl. Organometal. Chem.*, 2014, **28**, 523.
- 4 (a) K. C. Nicolaou, J. A. Pfefferkorn, G.-Q. Cao, S. Kim and J. Kessabi, *Org. Lett.*, 1999, **1**, 807; (b) K. C. Nicolaou, S. Y. Cho, R. Hughes, N. Winssinger, C. Smethurst, H. Labischinski and R. Endermann, *Chem. Eur. J.* 2001, **7**, 3798.
- 5 (a) O. M. Abdelhafez, K. M. Amin, H. I. Ali, M. M. Abdalla and E. Y. Ahmed, *RSC Adv.*, 2014, **4**, 11569; (b) G. S. Hassan, S. M. Abou-Seri, G. Kamel and M. M. Ali, *Eur. J. Med. Chem.*, 2014, **76**, 482; (c) C. Salome, V. Narbonne, N. Ribeiro, F. Thuaud, M. Serova, A. de Gramont, S. Faivre, E. Raymond and L. Desaubry, *Eur. J. Med. Chem.*, 2014, **74**, 41; (d) T. S. Chundawat, N. Sharma and S. Bhagat, *Med. Chem. Res.*, 2014, **23**, 1350; (e) R. Kenchappa, Y. D. Bodke, B. Asha, S. Telkar and M. A. Sindhe, *Med. Chem. Res.*, 2014, **23**, 3065; (f) Z.-B. Zhou, J.-G. Luo, K. Pan, S.-M. Shan, W. Zhang and L.-Y. Kong, *Planta Med.*, 2013, **79**, 1730;
- 6 (a) W. M. Yuan and S. Ma, *Org. Lett.*, 2014, **16**, 193; (b) P. Lan, M. G. Banwell and A. C. Willis, *J. Org. Chem.*, 2014, **79**, 2829; (c) G.-H. Ma, X.-J. Tu, Y. Ning, B. Jiang and S.-J. Tu, *ACS Comb. Sci.*, 2014, **16**, 281; (d) B. Li, Z.-Z. Yue, H.-Y. Xiang, L.-L. Lv, S.-S. Song, Z.-H. Miao and C.-H. Yang, *RSC Adv.*, 2014, **4**, 358; (e) Z. Wang, Q. Yao, T.-F. Kang, J.-H. Feng, X.-H. Liu, L.-L. Lin and X.-M. Feng, *Chem. Commun.*, 2014, **50**, 4918; (f) P. Das, B. Srivastava, S. Joseph, H. Nizar and M. Prasad, *Org. Process. Res. Dev.*, 2014, **18**, 665.
- 7 (a) B.-C. Zhao and C. Zhao, *Chinese Pat.*, 103,467,422, Shanxi Buchang Hi-Tech. Pharm. Co. Ltd., China, 2014; (b) W. Zhu, Y. Chen and L. Yuan, *Chinese Pat.*, 103,145,664, Shanghai Aobo Bio-Pharm. Technology Co. Ltd., China, 2013; (c) A. Friesz and C. Huszar, *US Pat.*, 20,130,131,358, France, 2013; (d) T. W. Loo, M. C. Bartlett and D. M. Clarke, *Biochemistry-US*, 2011, **50**, 4393; (e) M. G. McDonald and A. E. Rettie, *Chem. Res. Toxicol.*, 2007, **20**, 1833; (f) T. S. Han, G. R. Williams and M. P. J. Vanderpump, *Clin. Endocrinol.*, 2009, **70**, 2.
- 8 (a) M. Mazloum-Ardakani and A. Khoshroo, *Electrochim. Acta*, 2014, **130**, 634; (b) X.-T. Li, S.-Z. Pu, H. Li and G. Liu, *Dyes Pigments*, 2014, **105**, 47; (c) H. Li, G. Liu, S.-Z. Pu and B. Chen, *Dyes Pigments*, 2013, **99**, 812; (d) M. Mazloum-Ardakani and A. Khoshroo, *Electrochim. Acta*, 2013, **103**, 77; (e) C. W. Lee, K. S. Yook and J. Y. Lee, *Org. Electron.*, 2013, **14**, 1009; (f) S.-Z. Pu, R.-J. Wang, G. Liu, W.-J. Liu, S.-Q. Cui and P.-J. Yan, *Dyes Pigments*, 2012, **94**, 195; (g) A. P. Chafin, M. C. Davis, W. W. Lai, G. A. Lindsay, D. H. Park and W. N. Herman, *Opt. Mater.*, 2011, **33**, 1307.
- 9 (a) Q. Xu, J.-H. Chen, H.-W. Tian, X.-Q. Yuan, S.-Y. Li, C.-K. Zhou and J.-P. Liu, *Angew. Chem. Int. Ed.*, 2014, **53**, 225; (b) X. J. Jia, L. Yu, J.-P. Liu, Q. Xu, M. Sickert, L.-H. Chen and M. Lautens, *Green Chem.*, 2014, **16**, 3444; (c) L. Yu, J. Wang, T. Chen, Y.-G. Wang, Q. Xu, *Appl. Organometal. Chem.*, 2014, ASAP, DOI: 10.1002/aoc.3175; (d) L. Yu, H.-Y. Li, X. Zhang, J.-Q. Ye, J.-P. Liu, Q. Xu, M. Lautens, *Org. Lett.*, 2014, **16**, 1346; (e) L. Yu, Y.-L. Wu, H.-E. Cao, X. Zhang, X.-K. Shi, J. Luan, T. Chen, Y. Pan and Q. Xu, *Green Chem.*, 2014, **16**, 287; (f) H.-N. Chen, W.-J. Dai, Y. Chen, Q. Xu, J.-H. Chen, L. Yu, Y.-J. Zhao, M.-D. Ye, Y.-J. Pan, *Green Chem.*, 2014, **16**, 2136; (g) L. Yu, J. Wang, X. Zhang, H.-E. Cao, G.-L. Wang, K.-H. Ding, Q. Xu, M. Lautens, *RSC Adv.*, 2014, **4**, 19122; (h) L. Yu, J. Wang, H.-E. Cao, K.-H. Ding, Q. Xu, *Chin. J. Org. Chem.*, 2014, ASAP, DOI: 10.6023/cjoc201405004; (i) L. Yu, Y.-L. Wu, T. Chen, Y. Pan, Q. Xu, *Org. Lett.*, 2013, **15**, 144; (j) L. Yu, *Mini-Rev. Med. Chem.*, 2013, **13**, 783; (k) L. Yu, J. Wang, T. Chen, K.-H. Ding, Y. Pan, *Chin. J. Org. Chem.*, 2013, **33**, 1096; (l) L. Fan, R. Yi, L. Yu, Y.-L. Wu, T. Chen, R. Guo, *Catal. Sci. Technol.*, 2012, **2**, 1136.
- 10 With Jiangsu Yangnong Chem. Group Co. Ltd. and Zhejiang Research Institute of Chemical Industry (both of them are subsidiaries of Sinochem Group).
- 11 D. Stokmaier, O. Khorev, B. Cutting, R. Born, D. Ricklin, T. O. G. Ernst, F. B öni, K. Schwingruber, M. Gentner, M. Wittwer, M. Spreafico, A. Vedani, S. Rabbani, O. Schwardt and B. Ernst, *Bioorgan. Med. Chem.*, 2009, **17**, 7254.
- 12 After treating with H<sub>2</sub>O<sub>2</sub> and heating in toluene (see figure in Table 1), the resin was filtered and recycled. Filtrate containing compound **5** was evaporated under vacuum and the residue was weighted directly to calculate the yield of crude **5**. The purity of **5** was determined by HPLC.
- 13 For details please see experimental section.
- 14 For detailed table please see ESI.
- 15 K. C. Nicolaou, J. Pastor, S. Barluenga, N. Winssinger, *Chem. Commun.*, 1998, 1947.