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Synthesis of heterocycle-tethered acylbenzofurans and benzodifurans from odorless and recyclable organoseleno polystyrene resin†

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Organoseleno polystyrene resin-supported synthesis provided 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 scope, 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.

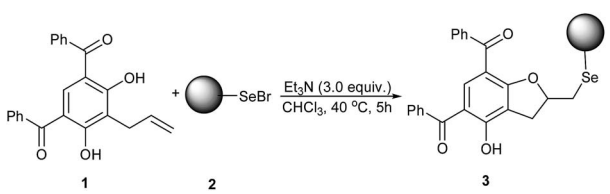
Introduction

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 the pharmaceutical industry.[1] Due to the high reactivity of selenium moieties and the removable properties through clean *syn*-selenoxide elimination[2] after preparations, the safe, odorless, stable, and recyclable organoseleno polystyrene resin is a good carrier for solid-phase synthesis.[3,4] 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.[3] Besides, organoseleno resin-supported solid-phase synthesis is also a reliable and practical methodology that has already been widely applied in natural product synthesis.[4]

On the other hand, benzofuran skeletons are often found in natural products with antimicrobial, antioxidant, anticancer and anti-inflammatory activities.[5] They are also important intermediates in organic synthesis.[6] Among these analogues, acylbenzofurans and heterocycle-tethered benzofurans are very common moieties in many drug molecules such as *Vilazodone*, *Dronedarone*, *Amiodarone*, *Benzbromarone* and others.[7] In addition, they are also widely employed in material science due to their high photoelectric activity.[8] 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.[9] 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,[10] we chose compound **1** as the starting material. After attachment with organoseleno resin **2** (Br 1.25 mmol g^{-1}), the mother heterocycle 5,7-dibenzoyl-2,3-dihydrobenzofuran-4-ol was constructed and uploaded to generate the functionalized resin **3** (eqn (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^{-1} on the resin. The reaction was terminated in 5 h, after which the carbonyl absorption did not increase any further.



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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.[11]

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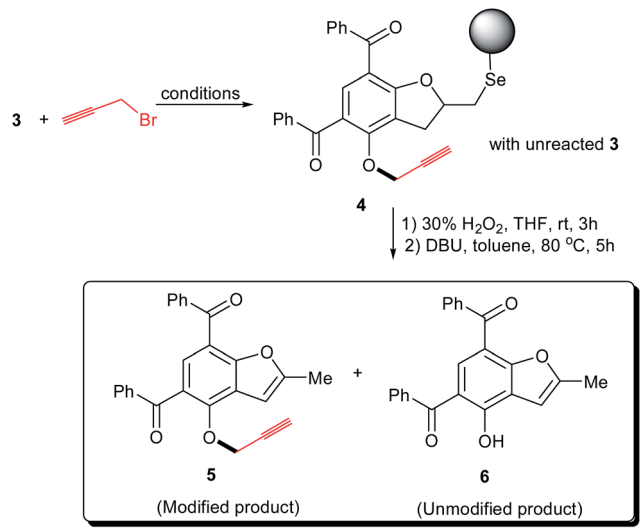
However, after heating **3** with propargyl bromide and K_2CO_3 in acetone at 60 °C for 5 h (Table 1, run 1), the IR spectra of resin showed a weak peak of C≡C absorption at 2130 cm^{-1} but a very broad and strong absorption peak of O–H, revealing that only a few of resin **3** was modified. The modified product **5** and unmodified product **6** were then cut down from resin by *syn*-selenoxide elimination.[12,13] 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, 10 h was the best reaction time (run 2), after which the reaction could not be improved any more (Table 1, run 3). Replacing K_2CO_3 with the organic base Et_3N slightly improved the yield and purity of **5** (Table 1, run 4) and further solvent screening demonstrated that DMF–$CHCl_3$ (1 : 1) was a better solvent, affording **5** in the highest yield and purity in Table 1 (Table 1, run 8 *vs.* 4–7).

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.[13] 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.

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).

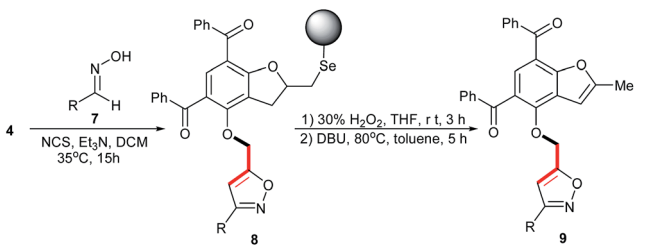
Table 1 Reaction condition evaluation for the modification of polymer resin **3** to **4**[a]



Run	Solvent	Base	*t*/h	yield[b]/%	purity[c]/%
1	Acetone	K_2CO_3	5	59	64
2	Acetone	K_2CO_3	10	70	72
3	Acetone	K_2CO_3	15	70	71
4	Acetone	Et_3N	10	72	74
5	THF	Et_3N	10	76	80
6	DMF	Et_3N	10	85	90
7	$CHCl_3$	Et_3N	10	86	91
8	DMF–$CHCl_3$ (1 : 1)	Et_3N	10	88	94

[a] 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_2. [b] Isolated yields of crude product **5** based on Br loading of resin **2**. [c] Purities of product **5** were determined by HPLC analysis.

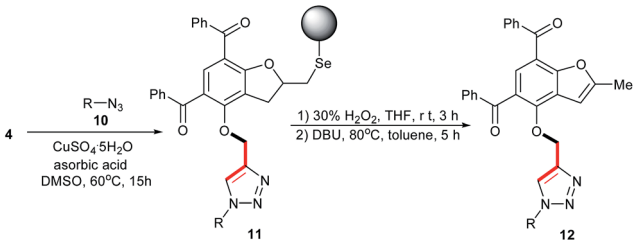
Table 2 Preparation of isoxazole-tethered benzofurans[a]



Run	R (**7**)	**9**: Yield[b]/%	Purity[c]/%
1	C_6H_5 (**7a**)	**9a**: 73	92
2	4-MeC_6H_4 (**7b**)	**9b**: 72	91
3	4-MeOC_6H_4 (**7c**)	**9c**: 71	91
4	4-BrC_6H_4 (**7d**)	**9d**: 68	90
5	4-ClC_6H_4 (**7e**)	**9e**: 69	90
6	4-FC_6H_4 (**7f**)	**9f**: 66	89
7	4-$NO_2C_6H_4$ (**7g**)	**9g**: 62	86
8	3-BrC_6H_4 (**7h**)	**9h**: 65	88
9	2-ClC_6H_4 (**7i**)	**9i**: 63	86
10	*c*-C_6H_{11} (**7j**)	**9j**: 69	90
11	*n*-C_4H_9 (**7k**)	**9k**: 70	90
12	*t*-C_4H_9 (**7l**)	**9l**: 56	76

[a] Resin **4** (prepared from 0.8 g resin **2**), aldoxime **7** (5 mmol), *N*-chlorosuccinimide (NCS, 5 mmol) and Et_3N (6 mmol) were heated in 35 mL of CH_2Cl_2 at 35 °C under N_2. [b] Isolated yields of crude product **9** based on Br loading of resin **2**. [c] Purities of product **9** were determined by HPLC analysis.

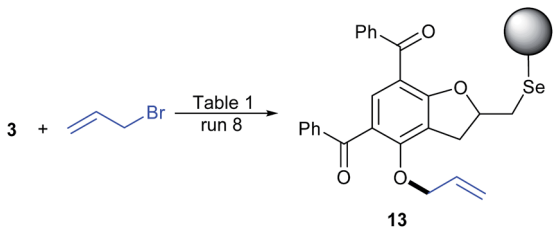
Table 3 Preparation of triazole-tethered benzofurans[a]



Run	R (**10**)	**12**: Yield[b]/%	Purity[c]/%
1	C_6H_5 (**10a**)	**12a:** 77	93
2	4-BrC_6H_4 (**10b**)	**12b:** 75	92
3	4-Py (**10c**)	**12c:** 73	91
4	2-MeC_6H_4 (**10d**)	**12d:** 72	91
5	2,5-$Cl_2C_6H_3$ (**10e**)	**12e:** 72	91
6	2-Cl-4-$NO_2C_6H_3$ (**10f**)	**12f:** 70	90
7	2-NO_2-4-ClC_6H_3 (**10g**)	**12g:** 69	90
8	2,4,5-$Cl_3C_6H_2$ (**10h**)	**12h:** 70	90
9	*i*-C_3H_7 (**10i**)	**12i:** 62	82

[a] Resin **4** (prepared from 0.8 g resin **2**), RN_3 **10** (5 mmol), $CuSO_4 \cdot 5H_2O$ (4 mmol) and ascorbic acid (4.5 mmol) were heated in 30 mL of DMSO at 60 °C under N_2. [b] Isolated yields of crude product **12** based on Br loading of resin **2**. [c] Purities of product **12** were determined by HPLC analysis.

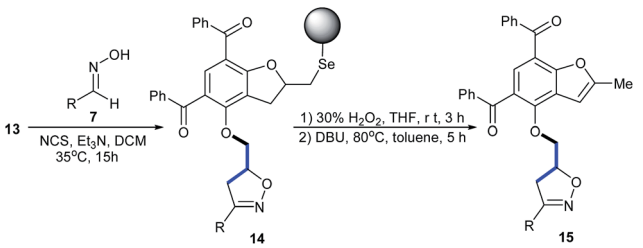
As an activated nucleophilic group, the hydroxyl on resin **3** could react with many types of electrophiles. Reactions with allylic bromide under similar conditions (Table 1, run 8), afforded allylic-modified organoseleno polystyrene resin **13** (eqn (2)), which could be employed to synthesize isoxazoline-tethered 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).



(2)

In addition, nucleophilic substitutions of resin **3** with EWG and bromo bis-substituted hydrocarbons **16** led to modified resin **17** as expected (eqn (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

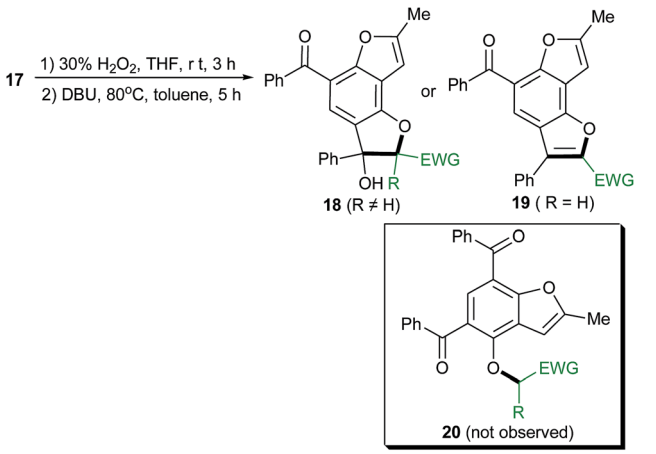
Table 4 Preparation of isoxazoline-tethered benzofurans[a]



Run	R (**7**)	**15**: Yield[b]/%	Purity[c]/%
1	4-MeC_6H_4 (**7b**)	**15a:** 70	91
2	4-$MeOC_6H_4$ (**7c**)	**15b:** 70	91
3	4-ClC_6H_4 (**7e**)	**15c:** 69	90
4	4-FC_6H_4 (**7f**)	**15d:** 68	90
5	4-$NO_2C_6H_4$ (**7g**)	**15e:** 62	84
6	3-BrC_6H_4 (**7h**)	**15f:** 64	88
7	2-ClC_6H_4 (**7i**)	**15g:** 63	86
8	*c*-C_6H_{11} (**7j**)	**15h:** 68	89

[a] Resin **13** (prepared from 0.8 g resin **2**), aldoxime **7** (5 mmol) *N*-chlorosuccinimide (NCS, 5 mmol) and Et_3N (6 mmol) were heated in 35 mL of CH_2Cl_2 at 35 °C under N_2. [b] Isolated yields of crude product **15** based on Br loading of resin **2**. [c] Purities of product **15** were determined by HPLC analysis.

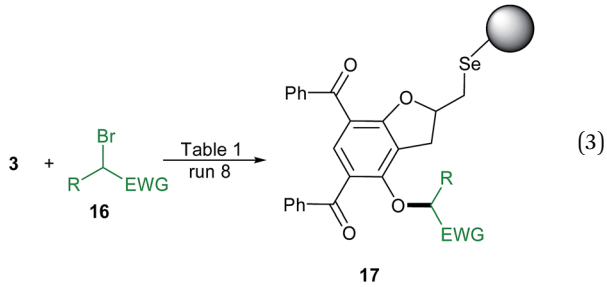
Table 5 Preparation of benzodifurans[a]



Run	EWG, R (**16**)	**18** or **19**: Yield[b]/%	Purity[c]/%
1	COOMe, Et (**16a**)	**18a:** 74	92
2	COOMe, *n*-Bu (**16b**)	**18b:** 72	90
3	COOMe, 2-ClC_6H_4 (**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

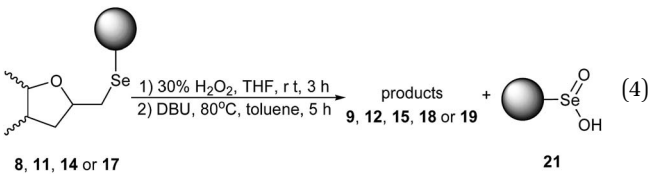
[a] Resin **3** (prepared from 0.8 g resin **2**) and **16** (3 mmol) were treated as conditions in Table 1, run 8. [b] Isolated yields of crude product **18** or **19** based on Br loading of resin **2**. [c] Purities of product **18** or **19** were determined by HPLC analysis.

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).

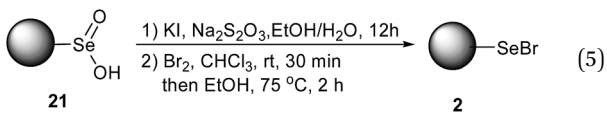


(3)

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 (eqn (4)). Fortunately, after successive treatments with KI, $Na_2S_2O_3$ and Br_2, **21** was easy to be converted to the reusable organoseleno resin **2** again, avoiding the generation of massive amount of solid waste (eqn (5)).[13]



(4)



(5)

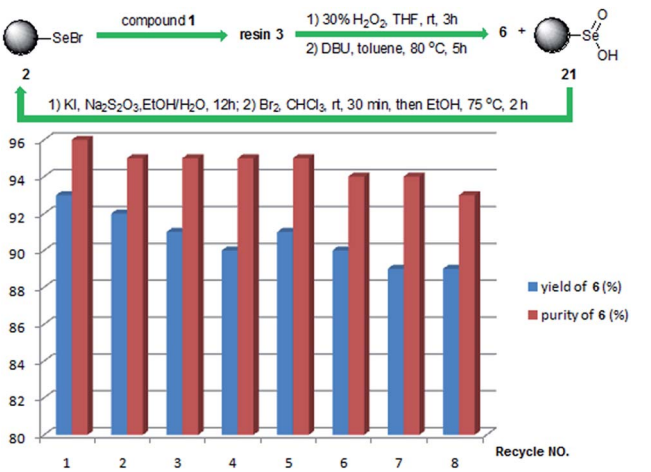


Fig. 1 Organoseleno resin carrier recovery and reuse.[13,14]

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 Fig. 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 (Fig. 1).[13,14]

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**.[15] Reactions were performed under N_2 unless specified. Melting points were measured using a XT-4 binocular microscope melting point instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR spectroscopy), using $CDCl_3$ 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_2O, v/v/v 50 : 20 : 30; flow rate, 1.0 mL min^{-1}; 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 (eqn (1))

To a suspension of 0.8 g of organoseleno resin **2** (Br 1.25 mmol g^{-1}) in 15 mL of $CHCl_3$, 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_3N was added and the mixture was stirred at 40 °C for 5 h. The resin was collected by filtration and washed with H_2O (20 mL × 2), THF (10 mL × 2), ethanol (10 mL × 2), THF–H_2O (v/v 2 : 1, 10 mL ×

2), THF (10 mL × 2) and CH_2Cl_2 (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–$CHCl_3$ (1 : 1), 5 mmol of Et_3N 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_2O (20 mL × 2), THF (10 mL × 2), THF–H_2O (v/v 2 : 1, 10 mL × 2), THF (10 mL × 2), THF–H_2O (2 : 1, 10 mL × 2), THF (10 mL × 2) and CH_2Cl_2 (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_2O_2 was added and stirred at room temperature for 3 h. The resin was collected by filtration and washed with H_2O (20 mL × 2), THF (10 mL × 2), THF–H_2O (v/v 2 : 1, 20 mL × 2), THF (10 mL × 2), CH_2Cl_2 (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_2O (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 0.25 M HCl (30 mL × 2) and saturated $NaHCO_3$ (35 mL × 2) and dried with anhydrous $MgSO_4$. 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_2Cl_2 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_2Cl_2. Then, a solution of 6.0 mmol of Et_3N in 10 mL of CH_2Cl_2 was added dropwisely in 4 h. After stirring at 35 °C for 15 h, resins **8** were collected by filtration and washed with H_2O (10 mL × 2), THF (10 mL × 1), DMF (10 mL × 1), THF–H_2O (v/v 2 : 1, 10 mL × 2), THF (10 mL × 2), THF–H_2O (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 $CuSO_4 \cdot 5H_2O$, 4.5 mmol of ascorbic acid (in 10 mL H_2O) and 5 mmol of RN_3 **10** were added. After stirring at 60 °C for 15 h, resins **11** were collected by filtration and washed with H_2O (30 mL × 2), THF (20 mL × 1), hot DMF (15 mL × 1), H_2O (30 mL × 1), THF (20 mL × 1), THF–H_2O (v/v 2 : 1, 20 mL × 2), hot DMF (15 mL × 1), THF (20 mL × 1), THF–H_2O (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 (eqn (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 $Na_2S_2O_3$ (125 mmol) in 140 mL of EtOH–H_2O (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_2O (v/v = 1 : 1, 80 mL × 2), THF (50 mL × 2). MeOH (50 mL × 2) and CH_2Cl_2 (50 mL × 2) subsequently and then dried at 40 °C under vacuum for 6 h. The dried yellow resin was soaked in $CHCl_3$ (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_2Cl_2 (80 mL × 3) and Et_2O (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_2Cl_2 (80 mL × 2) and Et_2O (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; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$.

*Compound **6**.* White solid, mp: 99–102 °C; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3425, 1634, 1596, 1397, 1289, 1195, 1114, 869, 741, 639; HRMS: m/z calcd for $C_{23}H_{17}O_4$ $[M + H]^+$: 357.1121, found: 357.1130.

Compound ***9a***. White solid, mp: 91–93 °C; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3083, 2982, 2870, 1658, 1594, 1447, 1241, 1109, 738, 692. HRMS (ESI): *m*/*z* calcd for $C_{33}H_{24}NO_5$ $[M + H]^+$: 514.1649, found: 514.1660.

Compound ***9b***. White solid, mp: 96–98 °C; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3085, 2920, 1771, 1657, 1595, 1446, 1241, 1106, 801, 693, 642. HRMS (ESI): *m*/*z* calcd for $C_{34}H_{26}NO_5$ $[M + H]^+$: 528.1805, found: 528.1812.

Compound ***9c***. White solid, mp: 102–104 °C; ^{1}H-NMR ($CDCl_3$): δ 7.88–7.83 (m, 4H), 7.67 (d, 2H, J = 8.8 Hz), 7.62–7.54 (m, 3H), 7.50–7.43 (m, 4H), 6.98 (d, 2H, J = 8.8 Hz), 6.65 (s, 1H), 6.18 (s, 1H), 5.33 (s, 2H), 3.87 (s, 3H), 2.48 (s, 3H); ^{13}C-NMR ($CDCl_3$): δ195.2, 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + 2 + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + 2 + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ195.07, 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 $(M + 2 + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ195.1, 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 $(M + 2 + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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 $(M + 2 + H)^+$; IRν_{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; ^{1}H-NMR ($CDCl_3$): δ 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 ($CDCl_3$): δ 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; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$;IRν_{max} (cm^{-1}): 3058, 1656, 1595, 1446, 1238, 1105, 1043, 985, 872, 762, 694; HRMS: *m*/*z* calcd for $C_{33}H_{26}N_3O_4$ $[M + H]^+$: 528.1918, found: 528.1925.

Compound ***12e***. Solid, mp: 116–118 °C; ^{1}H-NMR ($CDCl_3$): δ 7.86–7.80 (m, 4H), 7.58–7.55 (m, 4H), 7.51–7.34 (m, 7H), 6.76 (d, 1H, J = 0.4 Hz), 5.50 (s, 2H), 2.48 (d, 3H, J = 1.2 Hz); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2922, 1657, 1595, 1446, 1241, 1100, 1041, 879, 811, 604; HRMS: *m*/*z* calcd for $C_{32}H_{22}Cl_2N_3O_4$ $[M + H]^+$: 582.0982, found: 582.0980.

Compound ***12f***. Solid, mp: 120–122 °C; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3057, 2925, 1651, 1600, 1527, 1446, 1348, 1267, 1235, 1107, 1041, 886, 808, 739, 694; HRMS: *m*/*z* calcd for $C_{32}H_{22}ClN_4O_6$ $[M + H]^+$: 593.1222, found: 593.1231.

Compound ***12g***. Solid, mp: 123–125 °C;^{1}H-NMR ($CDCl_3$): 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 = 1.2 Hz), 5.48 (s, 2H), 2.46 (s, 3H); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3065, 1657, 1596, 1543, 1447, 1351, 1242, 1177, 1109, 1041, 881, 695; HRMS: *m*/*z* calcd for $C_{32}H_{22}ClN_4O_6$ $[M + H]^+$: 593.1222, found: 593.1225.

Compound ***12h***. Solid, mp: 118–120 °C; ^{1}H-NMR ($CDCl_3$): δ 7.84–7.78 (m, 4H), 7.66 (d, 2H, J = 5.6 Hz), 7.56–7.38 (m, 8H), 6.74 (d, 1H, J = 1.2 Hz), 5.48 (s, 2H), 2.46 (s, 3H); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3059, 1657, 1595, 1482, 1241, 1176, 1105, 1042, 882, 798, 695; HRMS: *m*/*z* calcd for $C_{32}H_{21}Cl_3N_3O_4$ $[M + H]^+$: 616.0592, found: 616.0601.

Compound ***12i***. Oil; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3081, 2967, 2923, 2876, 2851, 1656, 1596, 1449, 1380, 1370, 1109, 768, 691; HRMS (ESI): *m*/*z* calcd for $C_{29}H_{26}N_3O_4$ $[M + H]^+$: 480.1918, found: 480.1912.

Compound ***15a***. Solid, mp: 98–100 °C; ^{1}H-NMR ($CDCl_3$): δ 7.86 (d, 2H, J = 7.2 Hz), 7.80 (d, 2H, J = 8.0 Hz), 7.60–7.51 (m, 3H), 7.48–7.40 (m, 6H), 7.21 (d, 2H, J = 8.0 Hz), 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2924, 1658, 1597, 1447, 1247, 1109, 897, 695; HRMS: *m*/*z* calcd for $C_{34}H_{28}NO_5$ $[M + H]^+$: 530.1962, found: 530.1969.

Compound ***15b***. Solid, mp: 107–109 °C; ^{1}H-NMR ($CDCl_3$): δ 7.85 (d, 2H, J = 7.6 Hz), 7.79 (d, 2H, J = 7.2 Hz), 7.57–7.38 (m, 9H), 6.92 (d, 2H, J = 8.8 Hz), 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2962, 2924, 1658, 1260, 1100, 1024, 803, 696; HRMS: *m*/*z* calcd for $C_{34}H_{28}NO_6$ $[M + H]^+$: 546.1911, found: 546.1903.

Compound ***15c***. Solid, mp: 109–111 °C; ^{1}H-NMR ($CDCl_3$): δ 7.80 (d, 2H, J = 7.2 Hz), 7.73 (d, 2H, J = 7.2 Hz), 7.55–7.30 (m, 11H), 6.65 (s, 1H), 4.80–4.76 (m, 1H), 4.31 (d, 2H, J = 4.4 Hz), 3.16–3.09 (m, 1H), 2.97–2.92 (m, 1H), 2.40 (s, 3H); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2923, 1658, 1597, 1474, 1260, 1093, 827, 660.; HRMS: *m/z* calcd for $C_{33}H_{25}ClNO_5$ $[M + H]^+$: 550.1416, found: 550.1420.

Compound ***15d***. Solid, mp: 108–110 °C; ^{1}H-NMR ($CDCl_3$): δ 7.83 (d, 2H, $J = 7.2$ Hz), 7.77 (d, 2H, $J = 7.2$ Hz), 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); ^{13}C-NMR ($CDCl_3$): δ 195.3, 192.6, 163.7 (d, J = 248.9 Hz), 157.1, 155.9, 155.4, 152.7, 137.9, 137.6, 133.1, 132.8, 129.9, 129.7, 128.6 (d, $J = 8.4$ Hz), 128.3, 128.2, 127.9, 125.3 (d, $J = 3.4$ Hz), 124.4, 121.8, 117.7, 115.7 (d, $J = 21.5$ Hz), 100.9, 78.7, 73.2, 36.6, 14.0; MS (ESI) *m/z* 533 $(M + H)^+$; IRν_{max} (cm^{-1}): 3059, 2920, 1658, 1596, 1446, 1259, 875, 759, 695; HRMS: *m/z* calcd for $C_{33}H_{25}FNO_5$ $[M + H]^+$: 534.1711, found: 534.1722.

Compound ***15e***. Solid, mp: 112–114 °C; ^{1}H-NMR ($CDCl_3$): δ 8.21 (d, 2H, $J = 8.8$ Hz), 7.81 (d, 2H, $J = 8.0$ Hz), 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); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2962, 1658, 1598, 1519, 1261, 1104, 1028, 802; HRMS: *m/z* calcd for $C_{33}H_{25}N_2O_7$ $[M + H]^+$: 561.1656, found: 561.1649.

Compound ***15f***. Solid, mp: 101–103 °C; ^{1}H-NMR ($CDCl_3$): 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, $J = 4.4$ Hz), 3.12–3.05 (m, 1H), 2.88–2.82 (m, 1H), 2.40 (s, 3H); ^{13}C-NMR ($CDCl_3$): 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2921, 1658, 1596, 1244, 910, 873, 786, 690; HRMS: *m/z* calcd for $C_{33}H_{25}BrNO_5$ $[M + H]^+$: 594.0911, found: 594.0906.

Compound ***15g***. Solid, mp: 94–96 °C; ^{1}H-NMR ($CDCl_3$): δ 7.82 (d, 2H, $J = 7.6$ Hz), 7.74 (d, 2H, $J = 7.2$ Hz), 7.56–7.21 (m, 11H), 6.71 (s, 1H), 4.80–4.76 (m, 1H), 4.30 (d, 2H, $J = 4.8$ Hz), 3.37–3.30 (m, 1H), 3.04–2.98 (m, 1H), 2.39 (s, 3H); δ^{13}C-NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2926, 1654, 1599, 1232, 1112, 837, 736, 682; HRMS: *m/z* calcd for $C_{33}H_{25}ClNO_5$: 550.1416, found: 550.1425.

Compound ***15h***. Oil; ^{1}H-NMR ($CDCl_3$): δ 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}C-NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3075, 2928, 2852, 1659, 1596, 1446, 1375, 1247, 1110, 768, 690; HRMS (ESI): *m/z* calcd for $C_{33}H_{32}NO_5$ $[M + H]^+$: 522.2275, found: 522.2281.

Compound ***18a***. Solid, mp: 140–141 °C; ^{1}H-NMR ($CDCl_3$): δ 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, $J = 5.2$ Hz, 1H), 3.62 (s, 3H), 2.45 (s, 3H), 1.77–1.68 (m, 2H), 0.69 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (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 $C_{28}H_{25}O_6$ $[M + H]^+$: 457.1646, found: 457.1642.

Compound ***18b***. Solid, mp: 124–126 °C; ^{1}H-NMR ($CDCl_3$): δ 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, $J = 4.0$ 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, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (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 $C_{30}H_{29}O_6$ $[M + H]^+$: 485.1959, found: 485.1966.

Compound ***18c***. Solid, mp: 65–67 °C; ^{1}H-NMR ($CDCl_3$): δ7.84–7.79 (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, $J = 1.2$ Hz, 1H), 6.30 (s, 1H), 3.57 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (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 $C_{32}H_{24}ClO_6$ $[M + H]^+$: 539.1256, found: 539.1249.

Compound ***19a***. Solid, mp: 111–114 °C; ^{1}H-NMR ($CDCl_3$): δ 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, $J = 6.8$ Hz, 2H), 2.48 (s, 3H), 1.28 (t, $J = 6.8$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (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 $C_{27}H_{21}O_5$ $[M + H]^+$: 425.1384, found: 425.1391.

Compound ***19b***. Solid, mp: 119–122 °C; ^{1}H-NMR ($CDCl_3$): δ 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}C-NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3060, 1665, 1632, 1447, 1358, 1293, 1257, 1214, 1096, 935, 871, 802, 762, 738, 693, 607; HRMS: *m/z* calcd for $C_{26}H_{19}O_4$ $[M + H]^+$: 395.1278, found: 395.1273.

Compound ***19c***. Solid, mp: 123–125 °C; ^{1}H-NMR ($CDCl_3$): δ 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}C-NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 2921, 1634, 1596, 1470, 1445, 1398, 1362, 1290, 1195, 1178, 1115, 1068, 1027, 927, 755, 743, 699; HRMS: *m*/*z* calcd for $C_{31}H_{21}O_4$ $[M + H]^+$: 457.1434, found: 457.1441.

Compound ***19d***. Solid, mp: 127–130 °C; ^{1}H-NMR ($CDCl_3$): δ 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}C-NMR ($CDCl_3$): δ 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 $(M + H)^+$; IRν_{max} (cm^{-1}): 3028, 2920, 2222, 1658, 1598, 1445, 1394, 1288, 1257, 1177, 1112, 1076, 762, 732, 696; HRMS: *m*/*z* calcd for $C_{25}H_{16}NO_3$ $[M + H]^+$: 378.1125, found: 378.1120.

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12 After treating with H_2O_2 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.

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