

## PAPER

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View Journal | View IssueCite this: *RSC Adv.*, 2019, 9, 12255

# Protecting group-directed annulations of tetra-substituted oxindole olefins and sulfur ylides: regio- and chemoselective synthesis of cyclopropane- and dihydrofuran-fused spirooxindoles†

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Protecting group-controlled annulations of tetra-substituted oxindole olefins and sulfur ylides have been achieved for the synthesis of multifunctional cyclopropane- and dihydrofuran-fused spirooxindoles. Under precise annulation regulation, a variety of cyclopropane- and dihydrofuran-fused spirooxindoles containing vicinal quaternary carbon centers were produced in up to 90% yield with up to 20 : 1 dr. This reaction demonstrates high regio-, chemo- and diastereoselectivity, broad functional group tolerance and gram-scale capacity.

Received 21st March 2019

Accepted 10th April 2019

DOI: 10.1039/c9ra02192b

rsc.li/rsc-advances

## Introduction

The important scaffold spirooxindole exists in numerous natural products, biologically active molecules and lead compounds.<sup>1</sup> In particular, three- and five-membered spirooxindoles have attracted substantial interest because of their unique skeletal diversity and biological importance (Fig. 1a).<sup>2</sup> Various powerful strategies have been developed to construct these two skeletons, which can diversify molecular libraries in spirooxindole-related medicinal chemistry.<sup>3</sup> One of the greatest challenges to diversifying libraries is building vicinal quaternary carbon centers on the ring with multiple functional groups; such carbon centers are important for biological activity (Fig. 1b).<sup>4</sup> These centers are difficult to build and modify with functional groups because steric hindrance and substrate reactivity strongly affect formation of continuous quaternary carbon centers.<sup>5</sup>

We used sulfur ylide chemistry to construct structurally complex three- and five-membered spirooxindoles containing vicinal quaternary carbon centers. As a versatile and efficient synthetic tool, sulfur ylide can facilitate formation of cyclic fragments.<sup>6</sup> Mono- or di-substituted double bond substrates tend to generate small ring compounds *via* the [2 + 1] pathway, such as cyclopropane, epoxy and aziridine (Scheme 1a, left column).<sup>7</sup> Tri- or tetra-substituted double bond substrates can generate five-membered heterocyclic compounds *via* the [4 + 1] pathway, such as dihydrofuran, dihydropyrrole and indolin (Scheme 1a, right column).<sup>8</sup> Tri- or tetra-substituted double bond substrates can also

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† Electronic supplementary information (ESI) available: Detailed experimental procedures and full spectroscopic data of all the compounds. CCDC 1895883 and 1895884. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9ra02192b

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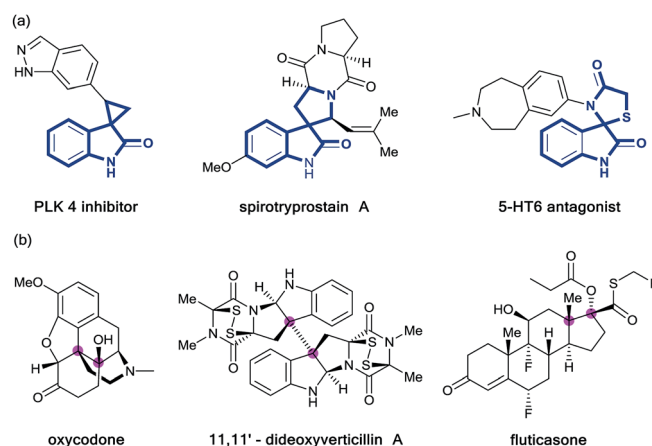
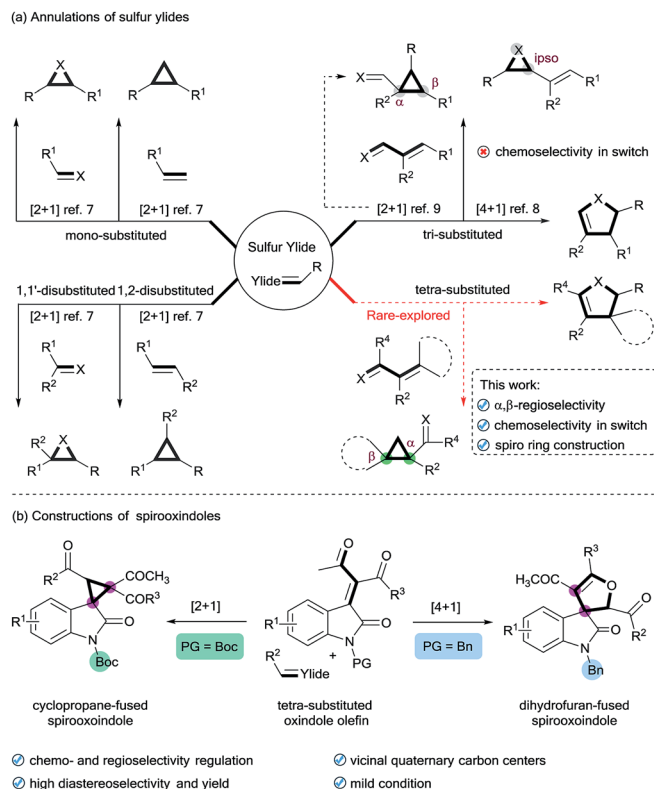


Fig. 1 (a) Natural products and drugs contain a three- and five-membered spirooxindole scaffold and (b) drug molecules contain vicinal quaternary carbon centers.



**Scheme 1** (a) Annulations between various substrates and sulfur ylides and (b) construction of cyclopropane- and dihydrofuran-fused spirooxindoles containing vicinal quaternary stereocenters.

undergo the [2 + 1] pathway to construct a three-membered ring, albeit with different regioselectivity: the tri-substituted substrate participates in the [2 + 1] pathway with *ipso* or  $\alpha,\beta$  selectivity;<sup>9</sup> the tetra-substituted substrate, with  $\alpha,\beta$ -selectivity (Scheme 1a, right column, lower panel).<sup>10</sup> The tetra-substituted substrate can directly establish quaternary carbon centers in one step, as well as control the chemoselectivity between [2 + 1] and [4 + 1] pathways. In addition, tetra-substituted double bond substrates can be used to construct the spiro ring. Nevertheless, their low reactivity and steric hindrance have limited their synthetic use.

Despite the advances in using sulfur ylide as a synthetic tool, few reports have focused on using it to form rings of desired size in a chemo- and regioselective manner.<sup>11</sup> This reflects, at least in part, uncertainty in how to control the cycloaddition pathway in a one-step reaction. Achieving chemo- and regioselective ring formation would enrich molecular libraries and accelerate new drug development. Therefore, we chose a tetra-substituted oxindole olefin as substrate to synthesize multi-substituted, three- and five-membered spirooxindoles containing vicinal quaternary carbon centers *via* sulfur ylide, as part of our continuing interest in synthesis of drug-like scaffolds.<sup>12</sup> Installing different protecting groups on the tetra-substituted substrate makes the synthesis chemoselective (Scheme 1b). This reaction allows the production of desirable cyclopropane- or dihydrofuran-fused spiro-oxindoles in high yield with high chemo-, regio- and diastereoselectivities.

**Table 1** Optimization of the reaction conditions<sup>a</sup>

Entry	PG	Solvent	Temperature (°C)	Yield <sup>b</sup> (%) (6a/9a)	Yield <sup>c</sup> (%) (7a/10a)
1	H	MeCN	25	45 (5a)	48 (8a)
2	Boc	MeCN	25	48/21	—
3	Boc	THF	25	Trace	—
4	Boc	Tol	25	68/17	—
5	Boc	DCM	25	82/9	—
6	Boc	DCM	50	63/—	—
7	Bn	MeCN	25	—	19/48
8	Bn	THF	25	—	Trace
9	Bn	Tol	25	—	14/58
10	Bn	DCM	25	—	11/67
11	Bn	DCM	50	—	15/74
12	Bn	DCM	70	—	9/61

<sup>a</sup> All reactions were carried out with 0.15 mmol of the substrate 1a/2a/3a, 0.165 mmol of 4a in 2.0 mL of solvent, unless otherwise stated; d.r. was determined to be > 8 : 1 by <sup>1</sup>H-NMR analysis of the crude reaction mixture. <sup>b</sup> Yields of the isolated products 6a and 9a. <sup>c</sup> Yields of the isolated products 7a and 10a.



Table 2 Synthesis of cyclopropane-fused spirooxindole<sup>a</sup>

Entry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Yield <sup>b</sup> (%) (6/9)	d.r. <sup>c</sup>
1	H	Ph	CH <sub>3</sub>	82/9	20 : 1 (6a)
2	H	2-FC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	74/10	18 : 1 (6b)
3	H	4-FC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	70/8	20 : 1 (6c)
4	H	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	CH <sub>3</sub>	63/10	20 : 1 (6d)
5	H	4-BrC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	75/12	18 : 1 (6e)
6	H	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	80/9	20 : 1 (6f)
7	H	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	81/7	20 : 1 (6g)
8	H	Thienyl	CH <sub>3</sub>	68/Trace	20 : 1 (6h)
9	H	Naphthyl	CH <sub>3</sub>	65/Trace	10 : 1 (6i)
10	H	OEt	CH <sub>3</sub>	79/8	20 : 1 (6j)
11	5-F	Ph	CH <sub>3</sub>	68/13	13 : 1 (6k)
12	7-F	Ph	CH <sub>3</sub>	70/10	20 : 1 (6l)
13	5-Cl	Ph	CH <sub>3</sub>	72/10	20 : 1 (6m)
14	6-Cl	Ph	CH <sub>3</sub>	79/12	20 : 1 (6n)
15	5-Br	Ph	CH <sub>3</sub>	80/5	15 : 1 (6o)
16	6-Br	Ph	CH <sub>3</sub>	81/8	9 : 1 (6p)
17	5-CH <sub>3</sub>	Ph	CH <sub>3</sub>	85/Trace	15 : 1 (6q)
18 <sup>d</sup>	H	Ph	OEt	90/Trace	18 : 1 (6r)
19 <sup>e</sup>	H	Ph	CH <sub>3</sub>	80/10	18 : 1 (6a)

<sup>a</sup> Unless otherwise noted, all reactions were performed with **2** (0.15 mmol), **4** (0.165 mmol) in 2 mL DCM at 25 °C for 2 h. <sup>b</sup> Isolated yields of the major compound **6** and minor **9**. <sup>c</sup> The diastereoselective ratio of compounds **6** were calculated based on <sup>1</sup>H-NMR analysis of the crude reaction mixture. <sup>d</sup> The relative configuration of **6r** was determined by X-ray crystallographic analysis (Fig. 2), and the relative configurations of other products **6** were tentatively assigned by analogy. <sup>e</sup> A gram scale reaction of **2a** (3.04 mmol) and **4a** (3.34 mmol) in DCM at 25 °C was carried out.

## Results and discussion

First, we took a tetra-substituted oxindole olefin without protecting group **1a** and sulfur ylide **4a** to conduct a model reaction in MeCN at ambient temperature. Two products with different ring sizes formed in one step with similar yields (**5a** : **8a** = 1.1 : 1, Table 1, entry 1). Therefore, we set out to control the chemo- and regioselectivity of the reaction and thereby influence their relative abundance. First of all, a broad type of protecting groups were tested, including methyl (-Me), allyl, acetyl (-Ac), benzyl (-Bn) and *tert*-butyloxycarbonyl (-Boc) groups (see Table S1 in ESI†). To our delight, changing the N-H (**1a**) into *N*-Boc (**2a**) generated **6a** as a major product and **9a** as a minor one (Table 1, entry 2). Using *N*-Bn (**3a**) produced **10a** as a major product and **7a** as a minor one (entry 7). Since yields were relatively low in MeCN, these initial results encouraged us to screen solvents and temperature (entries 3–6 and 8–12). The best conditions for generation of **6a** as the major product was in DCM at ambient temperature for about 2 h (entry 5). The best conditions for generation of **10a** as the major product was in DCM at 50 °C for nearly 4 h (entry 11). In other words, when the reaction with **4a** was conducted in DCM at ambient temperature generating cyclopropane-fused spirooxindole **6a** in 82% yield.

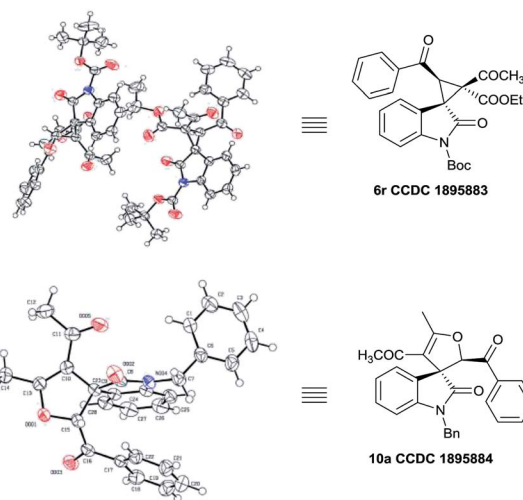


Fig. 2 Determination of relative configuration of products **6r** and **10a** by single-crystal X-ray analysis.

When the reaction was conducted with **4a** in DCM at 50 °C, **3a** preferred the [4 + 1] pathway, giving the dihydrofuran-fused spirooxindole **10a** in 74% yield.

Table 3 Synthesis of dihydrofuran-fused spirooxindole<sup>a</sup>

Entry	R <sup>1</sup>	R <sup>2</sup>	Yield <sup>b</sup> (%) (7/10)	d.r. <sup>c</sup>
1 <sup>d</sup>	H	Ph	15/74	10 : 1 (10a)
2	H	2-FC <sub>6</sub> H <sub>4</sub>	13/66	16 : 1 (10b)
3	H	4-FC <sub>6</sub> H <sub>4</sub>	11/68	16 : 1 (10c)
4	H	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	12/71	8 : 1 (10d)
5	H	4-BrC <sub>6</sub> H <sub>4</sub>	10/75	10 : 1 (10e)
6	H	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	8/78	20 : 1 (10f)
7	H	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Trace/81	18 : 1 (10g)
8	H	Thienyl	15/60	5 : 1 (10h)
9	H	Naphthyl	15/62	5 : 1 (10i)
10	H	CH <sub>3</sub>	14/74	6 : 1 (10j)
11	H	OEt	13/76	5 : 1 (10k)
12	5-F	Ph	8/70	10 : 1 (10l)
13	7-F	Ph	Trace/56	16 : 1 (10m)
14	5-Cl	Ph	14/66	5 : 1 (10n)
15	6-Cl	Ph	12/67	15 : 1 (10o)
16	5-Br	Ph	10/70	13 : 1 (10p)
17	6-Br	Ph	10/69	10 : 1 (10q)
18	5-CH <sub>3</sub>	Ph	8/80	18 : 1 (10r)
19 <sup>e</sup>	H	Ph	12/80	9 : 1 (10a)

<sup>a</sup> Unless otherwise noted, all reactions were performed with **3** (0.15 mmol), **4** (0.165 mmol) in 2 mL DCM at 50 °C for 4 h. <sup>b</sup> Isolated yields of the compound **7** and **10**. <sup>c</sup> The diastereoselective ratio of compounds **10** were determined by <sup>1</sup>H-NMR analysis of the crude reaction mixture. <sup>d</sup> The relative configuration of **10a** was determined by X-ray crystallographic analysis (Fig. 2), and the relative configurations of other products **10** were tentatively assigned by analogy. <sup>e</sup> A gram scale reaction of **3a** (3.13 mmol) and **4a** (3.44 mmol) in DCM at 50 °C was carried out.

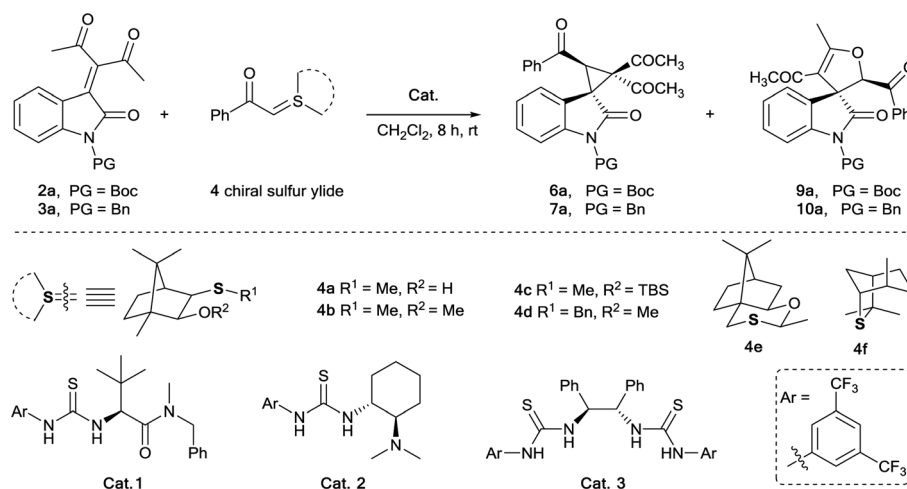


Having established optimal reaction conditions (Table 1, entry 5), we examined the scope of the reaction by varying the  $R^1$  and  $R^3$  groups of **2**, as well as the  $R^2$  moiety of **4**. Various sulfur ylides with a wide range of *ortho*-, *meta*-, and *para*-substituents with different electronic properties were explored (Table 2, entries 2–10). The compounds were well tolerated and afforded **6b–6g** in modest to high yields, and they all demonstrated good to excellent chemo- and diastereoselectivity. This indicated that the Boc protecting group favors formation of the cyclopropane-fused spirooxindole **6**. Moreover, sulfur ylide reacted well with linear and heterocycle substrates (entries 8–10). Different substituents on the aryl ring of **2** gave compound **6** in reasonable yields (entries 11–17); yield was better with an electron-donating substituent than with an electron-withdrawing one (entry 17). Replacing  $R^3$  with an OEt group led exclusively to **6r** (entry 18). The relative configuration of **6r** was determined by X-ray crystallographic analysis (Fig. 2), and the relative configurations of

other products **6** were tentatively assigned by analogy.<sup>13</sup> Finally, to evaluate the synthetic potential of this methodology, a gram scale reaction of **6a** was carried out. **2a** (3.04 mmol) and **4a** (3.34 mmol) went smoothly in DCM at ambient temperature, affording the desired product **6a** in 80% yield and 18 : 1 dr (entry 19).

Next we studied the reaction's generality and limitations when generating product **10**. Under the optimal conditions (Table 1, entry 11), numerous sulfur ylides reacted smoothly with compounds **3** to deliver good to high yields (Table 3, entries 2–11), although a 2-F group led to slight loss of diastereoselectivity (entry 2). Sulfur ylides with linear or heterocycle substitutions performed well (entries 8–11). In all cases, the reaction showed chemo- and diastereoselectivity in forming dihydrofuran-fused spirooxindole **10**. These results support Bn as a protecting group that favors formation of compound **10**. Diverse substituents on the aryl ring of **3** led to smooth reaction with **4**, giving the corresponding compounds **10l–10r** in 56–80%

Table 4 Attempt to asymmetric catalytic synthesis of chiral products<sup>a</sup>



Entry	PG	Sulfur ylide	Cat.	Yield <sup>b</sup> (%) (6a/9a)	e.e. <sup>d</sup> (%)	Yield <sup>c</sup> (%) (7a/10a)	e.e. <sup>e</sup> (%)
1	Boc	Chiral 4a	—	61/13	18	—	—
2	Boc	Chiral 4b	—	—	—	—	—
3	Boc	Chiral 4c	—	—	—	—	—
4	Boc	Chiral 4d	—	Trace	—	—	—
5	Boc	Chiral 4e	—	35/16	—	—	—
6	Boc	Chiral 4f	—	56/12	10	—	—
7	Boc	Chiral 4a	C1	78/10	25	—	—
8	Boc	Chiral 4a	C2	68/17	20	—	—
9	Boc	Chiral 4a	C3	77/16	39	—	—
10	Bn	Chiral 4a	—	—	—	16/53	19
11	Bn	Chiral 4b	—	—	—	—	—
12	Bn	Chiral 4c	—	—	—	—	—
13	Bn	Chiral 4d	—	—	—	Trace	—
14	Bn	Chiral 4e	—	—	—	13/41	—
15	Bn	Chiral 4f	—	—	—	17/59	8
16	Bn	Chiral 4f	C1	—	—	12/76	17
17	Bn	Chiral 4f	C2	—	—	18/65	13
18	Bn	Chiral 4f	C3	—	—	13/72	32

<sup>a</sup> Reactions were performed with **2a** or **3a** (0.1 mmol), **4** (0.1 mmol), or Cat. (20 mol%) in 2 mL DCM at ambient temperature for 8 h. <sup>b</sup> Yields were calculated from the isolated compound **6a** or **9a** respectively. <sup>c</sup> Yields were calculated from the isolated compound **7a** or **10a** respectively. <sup>d</sup> ee values were calculated from chiral HPLC analysis of major isomer **6**. <sup>e</sup> ee values were calculated from chiral HPLC analysis of major isomer **10**.





yields (entries 12–18). At last, we scaled up the reaction to gram synthesis, result proved that **3a** (3.13 mmol) and **4a** (3.44 mmol) were well tolerated in DCM at 50 °C, generating the target compound **10a** in 80% yield and 9 : 1 dr (entry 19). The relative configuration of **10a** was determined by X-ray crystallographic analysis (Fig. 2), and the relative configurations of other products **10** were tentatively assigned by analogy.<sup>14</sup>

We turned to developing an asymmetric catalytic version of this reaction using chiral sulfur ylides and hydrogen bond catalysts. We screened a variety of chiral sulfur ylides for their ability to generate the chiral product **6a**, but unfortunately, the best results we obtained were 61% yield and 18% ee (Table 4). Adding hydrogen-bonding catalysts improved yield to 77% and ee to 39% (entries 7–9). Similarly, we screened chiral sulfur ylides to afford the chiral product **10a**, and obtained initial results of 53% yield and 19% ee. Screening of hydrogen-bonding catalysts identified **Cat. 3** as the best, affording product **10a** in 72% yield with 32% ee (entries 16–18).

## Conclusions

In summary, we set up a protecting group-controlled strategy to regulate ring size *via* sulfur ylide. This powerful method allows access to structurally important cyclopropane- and dihydrofuran-fused spirooxindoles containing vicinal quaternary carbon centers. This approach exhibits good functional group tolerance as well as excellent regio-, chemo- and diastereoselectivity. It can be scaled up to gram synthesis. Further studies on the bioactivity of promising spirooxindoles will be reported in due course.

## Experimental

### General method for the synthesis

NMR data were obtained for <sup>1</sup>H at 400 MHz or 600 MHz, and for <sup>13</sup>C at 100 MHz or 150 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance in CDCl<sub>3</sub> solution as the internal standard. ESI HRMS was performed on a Waters SYNAPT G2. Column chromatography was performed on silica gel (400–500 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. UV light and I<sub>2</sub> were used to visualize products.

### General procedure for the synthesis of compounds **6**

To a solution of tetra-substituted oxindole olefins **2** (0.15 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2.0 mL) was added sulfur ylides **4** (0.165 mmol) at 25 °C. The reaction mixture was stirred until the reaction completed (monitored by TLC). Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 8 : 1 to 5 : 1) to give the compounds **6** which were dried under vacuum and further analyzed by <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, HRMS, etc.

Compound **5a** was obtained according to the similar procedure. White solid, 45% yield (23.4 mg). The diastereomeric ratio was determined to be 18 : 1 by crude <sup>1</sup>H-NMR analysis. Mp 165–

166 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.37 (s, 1H), 7.89 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.58–7.52 (m, 1H), 7.48–7.39 (m, 2H), 7.22 (td, *J* = 7.6, 1.2 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.96 (td, *J* = 7.6, 1.2 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 4.26 (s, 1H), 2.36 (s, 3H), 2.26 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 198.0, 196.1, 192.0, 173.5, 141.2, 136.5, 134.1, 128.9, 128.7, 128.5, 126.7, 122.5, 121.1, 110.1, 62.5, 43.6, 42.9, 29.8, 28.4; ESI HRMS: calcd for C<sub>21</sub>H<sub>17</sub>NO<sub>4</sub>Na<sup>+</sup> 370.1055, found 370.1056.

Compound **6a** was obtained as white solid in 82% yield (55.0 mg). The diastereomeric ratio was determined to be 20 : 1 by crude <sup>1</sup>H-NMR analysis. Mp 170–171 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.90 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.59–7.55 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.30–7.27 (m, 1H), 7.09–7.02 (m, 2H), 4.28 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H), 1.64 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 197.7, 195.9, 191.7, 170.9, 148.5, 140.5, 136.4, 134.2, 128.9, 128.6, 126.0, 124.1, 119.8, 114.6, 85.3, 63.0, 44.5, 43.1, 29.8, 28.4, 28.1; ESI HRMS: calcd for C<sub>26</sub>H<sub>25</sub>NO<sub>6</sub>Na<sup>+</sup> 470.1580, found 470.1581.

Compound **6b** was obtained as white solid, 74% yield (51.7 mg). The diastereomeric ratio was determined to be 18 : 1 by crude <sup>1</sup>H-NMR analysis. Mp 143–144 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm) 7.88 (d, *J* = 7.8 Hz, 1H), 7.75 (td, *J* = 7.2, 1.8 Hz, 1H), 7.54–7.49 (m, 1H), 7.32 (dt, *J* = 7.8, 1.2 Hz, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.08–7.03 (m, 2H), 6.93 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.17 (d, *J* = 3.0 Hz, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 1.65 (s, 9H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ (ppm) 198.0, 195.9, 190.1 (d, *J*<sub>CF</sub> = 3.0 Hz), 170.9, 161.9 (d, *J*<sub>CF</sub> = 255.0 Hz), 148.7, 140.7, 135.8 (d, *J*<sub>CF</sub> = 9.0 Hz), 130.7 (d, *J*<sub>CF</sub> = 1.5 Hz), 128.9, 125.6, 124.8 (d, *J*<sub>CF</sub> = 4.5 Hz), 124.0, 119.9, 117.0, 116.9, 114.7, 85.2, 63.2, 48.6 (d, *J*<sub>CF</sub> = 7.5 Hz), 43.3 (d, *J*<sub>CF</sub> = 3.0 Hz), 29.9, 28.6, 28.2; ESI HRMS: calcd for C<sub>26</sub>H<sub>24</sub>FNO<sub>6</sub>Na<sup>+</sup> 488.1485, found 488.1487.

Compound **6c** was obtained as white solid, 70% yield (48.9 mg). The diastereomeric ratio was determined to be 20 : 1 by crude <sup>1</sup>H-NMR analysis. Mp 145–146 °C; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm) 7.96–7.93 (m, 2H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.31 (dt, *J* = 9.0, 1.8 Hz, 1H), 7.12–7.09 (m, 2H), 7.07 (td, *J* = 7.8, 1.2 Hz, 1H), 7.01 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.22 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H), 1.65 (s, 9H); <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ (ppm) 197.7, 195.9, 190.1, 171.0, 166.4 (d, *J*<sub>CF</sub> = 255.0 Hz), 148.6, 140.5, 132.9 (d, *J*<sub>CF</sub> = 4.5 Hz), 131.4 (d, *J*<sub>CF</sub> = 10.5 Hz), 129.1, 126.0, 124.2, 119.7, 116.2 (d, *J*<sub>CF</sub> = 22.5 Hz), 114.7, 85.4, 63.1, 44.3, 43.1, 29.9, 28.5, 28.1; ESI HRMS: calcd for C<sub>26</sub>H<sub>24</sub>FNO<sub>6</sub>Na<sup>+</sup> 488.1485, found 488.1487.

Compound **6d** was obtained as yellow solid, 63% yield (48.8 mg). The diastereomeric ratio was determined to be 20 : 1 by crude <sup>1</sup>H-NMR analysis. Mp 144–145 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.01 (d, *J* = 2.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.75 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.33 (td, *J* = 8.8, 1.6 Hz, 1H), 7.08 (td, *J* = 8.0, 1.2 Hz, 1H), 6.98 (dd, *J* = 8.0, 1.2 Hz, 1H), 4.13 (s, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 1.65 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 197.5, 195.6, 189.7, 170.7, 148.4, 140.5, 139.0, 135.9, 133.8, 131.0, 130.3, 129.2, 127.5, 125.8, 124.2, 119.4, 114.8, 85.4, 63.3, 43.8, 43.3, 29.8, 28.5, 28.1; ESI HRMS: calcd for C<sub>26</sub>H<sub>23</sub>Cl<sub>2</sub>NO<sub>6</sub>Na<sup>+</sup> 538.0800, found 538.0802.

Compound **6e** was obtained as yellow solid, 75% yield (59.2 mg). The diastereomeric ratio was determined to be 18 : 1 by



crude  $^1\text{H}$ -NMR analysis. Mp 147–148 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.86 (d,  $J$  = 8.0 Hz, 1H), 7.77 (d,  $J$  = 8.4 Hz, 2H), 7.57 (d,  $J$  = 8.4 Hz, 2H), 7.31 (t,  $J$  = 7.6 Hz, 1H), 7.07 (t,  $J$  = 8.0 Hz, 1H), 6.98 (d,  $J$  = 8.0 Hz, 1H), 4.20 (s, 1H), 2.34 (s, 3H), 2.26 (s, 3H), 1.65 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.5, 195.7, 190.7, 170.8, 148.4, 140.4, 135.0, 132.2, 129.9, 129.0, 125.8, 124.0, 119.5, 114.7, 85.32, 63.0, 44.1, 43.0, 29.8, 28.4, 28.0; ESI HRMS: calcd for  $\text{C}_{26}\text{H}_{24}\text{BrNO}_6\text{Na}^+$  548.0685, found 548.0686.

Compound **6f** was obtained as white solid, 80% yield (55.4 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 142–143 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.88 (d,  $J$  = 7.8 Hz, 1H), 7.56 (d,  $J$  = 7.2 Hz, 1H), 7.38 (td,  $J$  = 7.8, 1.2 Hz, 1H), 7.34–7.31 (m, 1H), 7.22 (dd,  $J$  = 15.6, 9.0 Hz, 2H), 7.09 (dd,  $J$  = 6.0, 2.4 Hz, 2H), 4.12 (s, 1H), 2.42 (s, 3H), 2.36 (s, 3H), 2.25 (s, 3H), 1.64 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 195.9, 194.7, 170.9, 148.5, 140.5, 132.6, 132.1, 129.5, 128.9, 126.2, 126.1, 124.0, 119.8, 114.6, 85.3, 63.2, 47.3, 43.5, 29.8, 28.4, 28.1, 21.2; ESI HRMS: calcd for  $\text{C}_{27}\text{H}_{27}\text{NO}_6\text{Na}^+$  484.1736, found 484.1734.

Compound **6g** was obtained as white solid, 81% yield (58.0 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 145–146 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.88 (d,  $J$  = 8.8 Hz, 2H), 7.84 (d,  $J$  = 8.4 Hz, 1H), 7.30–7.26 (m, 1H), 7.06–7.04 (m, 2H), 6.88 (d,  $J$  = 8.8 Hz, 2H), 4.25 (s, 1H), 3.83 (s, 3H), 2.36 (s, 3H), 2.25 (s, 3H), 1.64 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.9, 196.0, 189.7, 171.1, 164.5, 148.6, 140.4, 131.1, 129.5, 128.7, 126.1, 124.0, 120.0, 114.5, 114.1, 85.2, 62.8, 55.6, 44.6, 42.8, 29.9, 28.3, 28.1; ESI HRMS: calcd for  $\text{C}_{27}\text{H}_{27}\text{NO}_7\text{H}^+$  500.1685, found 500.1688.

Compound **6h** was obtained as white solid, 68% yield (46.3 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 137–138 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.86 (d,  $J$  = 7.8 Hz, 1H), 7.81 (d,  $J$  = 3.0 Hz, 1H), 7.69 (d,  $J$  = 4.8 Hz, 1H), 7.34–7.31 (m, 1H), 7.14–7.10 (m, 3H), 4.15 (s, 1H), 2.35 (s, 3H), 2.25 (s, 3H), 1.64 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.5, 195.6, 183.9, 170.9, 148.6, 143.7, 140.6, 135.9, 134.1, 129.0, 128.9, 126.5, 124.2, 119.8, 114.7, 85.4, 62.9, 60.5, 45.0, 43.2, 29.8, 28.1; ESI HRMS: calcd for  $\text{C}_{24}\text{H}_{23}\text{NO}_6\text{Na}^+$  476.1144, found 476.1145.

Compound **6i** was obtained as white solid, 65% yield (48.5 mg). The diastereomeric ratio was determined to be 10 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 153–154 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.47 (s, 1H), 7.97–7.92 (m, 2H), 7.85–7.82 (m, 3H), 7.60–7.55 (m, 2H), 7.30–7.26 (m, 1H), 7.13–7.05 (m, 2H), 4.46 (s, 1H), 2.38 (s, 3H), 2.30 (s, 3H), 1.65 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.8, 195.9, 191.4, 171.1, 148.5, 140.5, 135.9, 133.8, 132.3, 130.9, 129.9, 129.3, 128.9, 128.8, 127.8, 127.2, 126.2, 124.1, 123.5, 119.8, 114.6, 85.3, 63.1, 44.6, 43.3, 29.9, 28.4, 28.1; ESI HRMS: calcd for  $\text{C}_{30}\text{H}_{27}\text{NO}_6\text{Na}^+$  520.1736, found 520.1738.

Compound **6j** was obtained as white solid, 79% yield (49.2 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 149–150 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.91 (d,  $J$  = 8.4 Hz, 1H), 7.36 (dt,  $J$  = 8.4, 2.4 Hz, 1H), 7.14–7.12 (m, 2H), 4.21–4.18 (m, 1H), 4.14–4.11 (m, 1H), 3.33 (s, 1H), 2.30 (s, 3H), 2.27 (s, 3H), 1.63 (s, 9H), 1.22 (t,  $J$  =

7.2 Hz, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.4, 195.5, 170.6, 166.0, 148.6, 140.8, 129.1, 125.9, 124.0, 119.9, 114.8, 85.3, 62.2, 62.1, 41.6, 40.5, 29.6, 28.6, 28.1, 14.13; ESI HRMS: calcd for  $\text{C}_{22}\text{H}_{25}\text{NO}_7\text{Na}^+$  438.1529, found 438.1531.

Compound **6k** was obtained as white solid, 68% yield (47.5 mg). The diastereomeric ratio was determined to be 13 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 172–173 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.92 (dd,  $J$  = 8.4, 1.2 Hz, 2H), 7.84 (dd,  $J$  = 9.0, 4.8 Hz, 1H), 7.61–7.58 (m, 1H), 7.46 (dd,  $J$  = 7.8, 1.8 Hz, 2H), 7.00 (td,  $J$  = 9.0, 3.0 Hz, 1H), 6.82 (dd,  $J$  = 9.6, 3.0 Hz, 1H), 4.30 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H), 1.64 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.4, 195.8, 191.5, 170.7, 159.3 (d,  $J_{\text{CF}}$  = 240 Hz), 148.5, 136.4 (d,  $J_{\text{CF}}$  = 36 Hz), 134.5, 129.1, 128.7, 121.7 (d,  $J_{\text{CF}}$  = 10.5 Hz), 115.7 (d,  $J_{\text{CF}}$  = 9.0 Hz), 115.6, 114.1, 113.9, 85.6, 63.2, 44.7, 43.0, 29.8, 28.4, 28.1; ESI HRMS: calcd for  $\text{C}_{26}\text{H}_{24}\text{FNO}_6\text{Na}^+$  488.1485, found 488.1483.

Compound **6l** was obtained as white solid, 70% yield (48.9 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 157–158 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.90 (d,  $J$  = 7.2 Hz, 2H), 7.60–7.58 (m, 1H), 7.45 (t,  $J$  = 7.8 Hz, 2H), 7.07–7.01 (m, 2H), 6.84 (dd,  $J$  = 7.8, 1.2 Hz, 1H), 4.30 (s, 1H), 2.35 (s, 3H), 2.27 (s, 3H), 1.61 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.2, 195.8, 191.5, 170.4, 148.4 (d,  $J_{\text{CF}}$  = 249.1 Hz), 147.0, 136.3, 134.5, 129.1, 128.7, 127.6 (d,  $J_{\text{CF}}$  = 10.4 Hz), 124.9 (d,  $J_{\text{CF}}$  = 7.4 Hz), 122.9 (d,  $J_{\text{CF}}$  = 2.2 Hz), 122.1 (d,  $J_{\text{CF}}$  = 4.0 Hz), 117.1 (d,  $J_{\text{CF}}$  = 20.0 Hz), 86.0, 63.2, 44.5, 43.0, 29.9, 28.4, 27.7; ESI HRMS: calcd for  $\text{C}_{26}\text{H}_{24}\text{FNO}_6\text{Na}^+$  488.1485, found 488.1483.

Compound **6m** was obtained as yellow solid, 72% yield (41.9 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 136–137 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.93 (d,  $J$  = 7.6 Hz, 2H), 7.82 (d,  $J$  = 8.8 Hz, 1H), 7.60 (t,  $J$  = 7.2 Hz, 1H), 7.46 (t,  $J$  = 7.6 Hz, 2H), 7.29 (d,  $J$  = 1.2 Hz, 1H), 7.05 (s, 1H), 4.29 (s, 1H), 2.34 (s, 3H), 2.26 (s, 3H), 1.64 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.2, 195.2, 191.3, 170.3, 148.3, 138.9, 136.2, 134.4, 129.7, 128.9, 128.8, 128.6, 126.2, 121.5, 115.6, 85.6, 63.1, 44.6, 42.7, 29.6, 28.3, 28.0; ESI HRMS: calcd for  $\text{C}_{26}\text{H}_{24}\text{ClNO}_6\text{Na}^+$  504.1190, found 504.1189.

Compound **6n** was obtained as yellow solid, 79% yield (57.1 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 145–146 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.93 (d,  $J$  = 2.0 Hz, 1H), 7.90 (d,  $J$  = 7.6 Hz, 2H), 7.59 (t,  $J$  = 7.6 Hz, 1H), 7.45 (t,  $J$  = 8.0 Hz, 2H), 7.05 (dd,  $J$  = 8.4, 1.6 Hz, 1H), 6.96 (d,  $J$  = 8.8 Hz, 1H), 4.28 (s, 1H), 2.34 (s, 3H), 2.25 (s, 3H), 1.64 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.3, 195.8, 191.6, 170.5, 148.3, 141.3, 136.3, 135.0, 134.4, 129.0, 128.6, 127.0, 124.2, 118.2, 115.4, 85.8, 62.9, 44.6, 42.8, 29.8, 28.3, 28.0; ESI HRMS: calcd for  $\text{C}_{26}\text{H}_{24}\text{ClNO}_6\text{Na}^+$  504.1190, found 504.1191.

Compound **6o** was obtained as yellow solid, 80% yield (63.2 mg). The diastereomeric ratio was determined to be 15 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 142–143 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.93 (d,  $J$  = 7.2 Hz, 2H), 7.76 (d,  $J$  = 9.0 Hz, 1H), 7.60 (t,  $J$  = 7.8 Hz, 1H), 7.446 (t,  $J$  = 7.8 Hz, 2H), 7.43 (dd,  $J$  = 9.0, 1.8 Hz, 1H), 7.19 (d,  $J$  = 1.8 Hz, 1H), 4.28 (s, 1H), 2.34 (s, 3H), 2.26 (s, 3H), 1.63 (s, 9H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 197.2, 195.5, 191.3, 170.1, 148.2, 139.4, 136.2, 134.4, 131.8,



129.0, 128.9, 128.6, 121.8, 117.3, 115.9, 85.6, 63.2, 44.6, 42.6, 29.6, 28.3, 27.9; ESI HRMS: calcd for  $C_{26}H_{24}BrNO_6Na^+$  548.0685, found 548.0687.

Compound **6p** was obtained as yellow solid, 81% yield (63.9 mg). The diastereomeric ratio was determined to be 9 : 1 by crude  $^1H$ -NMR analysis. Mp 149–150 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  (ppm) 8.09 (d,  $J$  = 0.8 Hz, 1H), 7.90 (d,  $J$  = 4.8 Hz, 2H), 7.61–7.58 (m, 1H), 7.45 (t,  $J$  = 5.2 Hz, 2H), 7.20 (dd,  $J$  = 5.6, 0.8 Hz, 1H), 6.90 (d,  $J$  = 5.6 Hz, 1H), 4.29 (s, 1H), 2.34 (s, 3H), 2.25 (s, 3H), 1.64 (s, 9H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  (ppm) 197.3, 195.9, 191.6, 170.5, 148.3, 141.4, 136.3, 134.5, 129.1, 128.7, 127.3, 127.2, 123.1, 118.8, 118.3, 85.9, 63.0, 44.6, 29.9, 28.4, 28.1, 28.0; ESI HRMS: calcd for  $C_{26}H_{24}BrNO_6Na^+$  548.0685, found 548.0683.

Compound **6q** was obtained as white solid, 85% yield (58.8 mg). The diastereomeric ratio was determined to be 15 : 1 by crude  $^1H$ -NMR analysis. Mp 168–169 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.90 (d,  $J$  = 7.2 Hz, 2H), 7.72 (d,  $J$  = 8.4 Hz, 1H), 7.59–7.55 (m, 1H), 7.44 (t,  $J$  = 8.0 Hz, 2H), 7.10 (dd,  $J$  = 8.4, 0.8 Hz, 1H), 6.84 (s, 1H), 4.25 (s, 1H), 2.35 (s, 3H), 2.29 (s, 3H), 2.26 (s, 3H), 1.64 (s, 9H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  (ppm) 197.8, 195.9, 191.7, 171.1, 148.6, 138.2, 136.5, 134.2, 133.7, 129.5, 128.9, 128.6, 126.5, 119.7, 114.4, 85.1, 63.0, 44.5, 43.2, 29.8, 28.4, 28.1, 21.0; ESI HRMS: calcd for  $C_{27}H_{27}NO_6Na^+$  484.1736, found 484.1740.

Compound **6r** was obtained as white solid, 90% yield (64.5 mg). The diastereomeric ratio was determined to be 18 : 1 by crude  $^1H$ -NMR analysis. Mp 147–148 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm) 8.10 (dd,  $J$  = 8.4, 1.2 Hz, 2H), 7.90 (d,  $J$  = 7.8 Hz, 1H), 7.59–7.56 (m, 1H), 7.47 (dt,  $J$  = 7.2, 1.2 Hz, 2H), 7.34–7.31 (m, 1H), 7.08 (dt,  $J$  = 7.8, 1.8 Hz, 1H), 7.01 (dd,  $J$  = 7.8, 1.2 Hz, 1H), 4.43–4.39 (m, 1H), 4.32–4.29 (m, 1H), 4.10 (s, 1H), 2.29 (s, 3H), 1.65 (s, 9H), 1.35 (t,  $J$  = 7.2 Hz, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm) 195.3, 191.0, 170.8, 165.5, 148.7, 140.7, 136.6, 133.9, 129.1, 128.9, 128.5, 125.7, 124.1, 119.7, 114.8, 85.0, 63.2, 56.7, 42.1, 42.0, 29.7, 28.2, 14.1; ESI HRMS: calcd for  $C_{27}H_{27}NO_7Na^+$  500.1685, found 500.1687.

### General procedure for the synthesis of compounds 10

To a solution of Bn-protected tetra-substituted oxindole olefins **3** (0.15 mmol) in  $CH_2Cl_2$  (2.0 mL) was added sulfur ylides **4** (0.165 mmol) at 50 °C. The reaction mixture was stirred until the reaction completed (monitored by TLC). Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to give the compounds **10** which were dried under vacuum and further analyzed by  $^1H$ -NMR,  $^{13}C$ -NMR, HRMS, etc.

Compound **8a** was obtained according to the similar procedure. White solid, 48% yield (25.0 mg). The diastereomeric ratio was determined to be 10 : 1 by crude  $^1H$ -NMR analysis. Mp 164–165 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.84 (s, 1H), 7.43–7.38 (m, 1H), 7.35 (dd,  $J$  = 8.4, 1.2 Hz, 2H), 7.22 (td,  $J$  = 7.6, 1.6 Hz, 2H), 6.99–6.95 (m, 1H), 6.91–6.86 (m, 2H), 6.40 (d,  $J$  = 7.6 Hz, 1H), 6.27 (s, 1H), 2.55 (s, 3H), 2.15 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  (ppm) 192.8, 191.3, 178.8, 170.2, 139.9, 134.8, 133.6, 129.0, 128.4, 127.5, 127.4, 124.9, 122.8, 118.3, 109.3, 88.8, 62.2, 28.9, 15.8; ESI HRMS: calcd for  $C_{21}H_{17}NO_4Na^+$  370.1055, found 370.1054.

Compound **10a** was obtained as white solid in 74% yield (48.6 mg). The diastereomeric ratio was determined to be 10 : 1 by crude  $^1H$ -NMR analysis. Mp 168–169 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.42 (t,  $J$  = 7.2 Hz, 1H), 7.30 (d,  $J$  = 4.4 Hz, 4H), 7.25 (d,  $J$  = 4.8 Hz, 3H), 7.16 (t,  $J$  = 7.6 Hz, 2H), 6.93–6.89 (m, 2H), 6.86 (t,  $J$  = 7.2 Hz, 1H), 6.30 (s, 1H), 6.17 (d,  $J$  = 7.6 Hz, 1H), 5.08 (d,  $J$  = 15.6 Hz, 1H), 4.20 (d,  $J$  = 16.0 Hz, 1H), 2.56 (s, 3H), 2.15 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  (ppm) 192.9, 191.0, 177.3, 169.9, 142.2, 135.3, 135.0, 133.4, 128.9, 128.7, 128.3, 127.5, 127.3, 126.9, 124.7, 122.8, 118.4, 108.8, 89.0, 62.0, 44.6, 29.0, 15.9; ESI HRMS: calcd for  $C_{28}H_{23}NO_4Na^+$  460.1525, found 460.1526.

Compound **10b** was obtained as white solid, 66% yield (45.1 mg). The diastereomeric ratio was determined to be 16 : 1 by crude  $^1H$ -NMR analysis. Mp 154–155 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.35–7.31 (m, 4H), 7.31–7.24 (m, 3H), 6.95 (tt,  $J$  = 7.2, 1.8 Hz, 2H), 6.90 (t,  $J$  = 6.6 Hz, 2H), 6.86 (t,  $J$  = 7.8 Hz, 1H), 6.83–6.79 (m, 1H), 6.26 (s, 1H), 5.02 (d,  $J$  = 15.6 Hz, 1H), 4.33 (d,  $J$  = 15.6 Hz, 1H), 2.55 (s, 3H), 2.13 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm) 191.3 (d,  $J_{CF}$  = 4.5 Hz), 191.0, 177.1, 169.9, 160.4 (d,  $J_{CF}$  = 253.5 Hz), 142.8, 135.5, 134.7 (d,  $J_{CF}$  = 9.0 Hz), 130.3 (d,  $J_{CF}$  = 3.0 Hz), 129.0, 128.8, 127.6, 127.5, 127.1, 124.6, 124.3 (d,  $J_{CF}$  = 3.0 Hz), 122.8, 115.9, 115.8, 108.9, 90.9 (d,  $J_{CF}$  = 4.5 Hz), 61.6, 44.6, 29.1, 15.9; ESI HRMS: calcd for  $C_{28}H_{22}FNO_4Na^+$  478.1431, found 478.1430.

Compound **10c** was obtained as white solid, 68% yield (46.5 mg). The diastereomeric ratio was determined to be 16 : 1 by crude  $^1H$ -NMR analysis. Mp 151–152 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.33–7.32 (m, 4H), 7.31–7.28 (m, 3H), 6.94 (td,  $J$  = 7.8, 1.2 Hz, 1H), 6.91 (dd,  $J$  = 7.2, 1.2 Hz, 1H), 6.86 (td,  $J$  = 7.2, 0.6 Hz, 1H), 6.81–6.76 (m, 1H), 6.28 (d,  $J$  = 7.8 Hz, 1H), 6.25 (s, 1H), 5.04 (d,  $J$  = 15.6 Hz, 1H), 4.38 (d,  $J$  = 15.6 Hz, 1H), 2.56 (s, 3H), 2.16 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm) 191.4, 191.0, 177.3, 169.9, 165.8 (d,  $J_{CF}$  = 255.0 Hz), 142.3, 135.3, 131.4 (d,  $J_{CF}$  = 3.0 Hz), 130.2 (d,  $J_{CF}$  = 9.0 Hz), 129.1, 128.9, 127.7, 127.5, 126.9, 124.8, 122.9, 118.6, 115.6 (d,  $J_{CF}$  = 22.5 Hz), 108.9, 88.7, 62.1, 44.7, 29.1, 15.9; ESI HRMS: calcd for  $C_{28}H_{22}FNO_4Na^+$  478.1431, found 478.1429.

Compound **10d** was obtained as yellow solid, 71% yield (53.9 mg). The diastereomeric ratio was determined to be 8 : 1 by crude  $^1H$ -NMR analysis. Mp 196–197 °C;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.37–7.34 (m, 3H), 7.33 (d,  $J$  = 1.8 Hz, 2H), 7.28 (dt,  $J$  = 6.0, 1.2 Hz, 1H), 7.12 (d,  $J$  = 8.4 Hz, 1H), 7.08 (dd,  $J$  = 8.4, 1.8 Hz, 1H), 6.98 (dt,  $J$  = 9.0, 4.8 Hz, 1H), 6.88 (d,  $J$  = 4.2 Hz, 2H), 6.31 (d,  $J$  = 7.8 Hz, 1H), 6.18 (s, 1H), 5.12 (d,  $J$  = 15.6 Hz, 1H), 4.36 (d,  $J$  = 15.6 Hz, 1H), 2.55 (s, 3H), 2.16 (s, 3H);  $^{13}C$  NMR (150 MHz,  $CDCl_3$ )  $\delta$  (ppm) 191.0, 190.9, 177.1, 169.7, 142.3, 138.2, 135.2, 134.4, 133.3, 130.4, 129.5, 129.3, 128.9, 127.8, 127.5, 126.7, 126.3, 124.7, 123.0, 118.5, 109.0, 88.8, 62.0, 44.8, 29.1, 15.9; ESI HRMS: calcd for  $C_{28}H_{21}Cl_2NO_4Na^+$  528.0745, found 528.0748.

Compound **10e** was obtained as white solid, 75% yield (58.1 mg). The diastereomeric ratio was determined to be 10 : 1 by crude  $^1H$ -NMR analysis. Mp 152–153 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  (ppm) 7.35–7.31 (m, 4H), 7.25 (t,  $J$  = 4.0 Hz, 3H), 7.12 (d,  $J$  = 8.4 Hz, 2H), 6.96 (td,  $J$  = 7.6, 2.0 Hz, 1H), 6.90 (dd,  $J$  = 7.2, 1.4 Hz, 1H), 6.86 (t,  $J$  = 7.6 Hz, 1H), 6.30 (d,  $J$  = 8.0 Hz, 1H), 6.23 (s, 1H), 5.00 (d,  $J$  = 15.6 Hz, 1H), 4.41 (d,  $J$  = 15.6 Hz, 1H), 2.55 (s,





3H), 2.15 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 191.9, 190.9, 177.2, 169.7, 142.3, 135.2, 133.6, 131.6, 129.1, 128.9, 128.8, 128.7, 127.7, 127.5, 127.4, 126.8, 124.7, 122.8, 118.5, 108.9, 88.7, 61.9, 44.8, 29.0, 15.8; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{BrNO}_4\text{Na}^+$  538.0630, found 538.0632.

Compound **10f** was obtained as white solid, 78% yield (52.8 mg). The diastereomeric ratio was determined to be 20 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 178–179 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.31 (td,  $J = 7.8, 1.2$  Hz, 1H), 7.28–7.26 (m, 3H), 7.22 (t,  $J = 6.0$  Hz, 3H), 7.12 (t,  $J = 7.2$  Hz, 1H), 7.01 (dd,  $J = 7.2, 1.2$  Hz, 1H), 6.97 (td,  $J = 7.2, 2.4$  Hz, 2H), 6.89 (td,  $J = 7.8, 0.6$  Hz, 1H), 6.30 (s, 1H), 6.20 (d,  $J = 7.8$  Hz, 1H), 4.97 (d,  $J = 16.2$  Hz, 1H), 4.02 (d,  $J = 16.2$  Hz, 1H), 2.56 (s, 3H), 2.13 (s, 3H), 1.81 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 194.3, 190.9, 176.9, 169.6, 142.3, 140.1, 140.0, 135.2, 133.9, 132.3, 131.7, 129.1, 128.7, 128.5, 127.4, 127.0, 125.1, 124.5, 122.8, 118.9, 109.1, 89.4, 61.8, 44.5, 28.9, 20.0, 15.8; ESI HRMS: calcd for  $\text{C}_{29}\text{H}_{25}\text{NO}_4\text{Na}^+$  474.1681, found 474.1683.

Compound **10g** was obtained as white solid, 81% yield (56.8 mg). The diastereomeric ratio was determined to be 18 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 188–189 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.33 (t,  $J = 3.0$  Hz, 1H), 7.31 (t,  $J = 1.8$  Hz, 1H), 7.29–7.28 (m, 4H), 7.26–7.24 (m, 1H), 6.94 (d,  $J = 7.2$  Hz, 1H), 6.92 (dd,  $J = 7.2, 1.2$  Hz, 1H), 6.85 (td,  $J = 7.2, 0.6$  Hz, 1H), 6.63 (dt,  $J = 9.6, 3.0$  Hz, 2H), 6.26 (d,  $J = 7.2$  Hz, 2H), 5.03 (d,  $J = 15.6$  Hz, 1H), 4.46 (d,  $J = 16.2$  Hz, 1H), 3.78 (s, 3H), 2.55 (s, 3H), 2.15 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 191.1, 191.0, 177.5, 170.1, 163.9, 142.3, 135.5, 130.0, 128.9, 128.8, 128.0, 127.5, 127.4, 127.0, 124.9, 122.8, 118.6, 113.7, 108.8, 88.5, 62.2, 55.6, 44.7, 29.1, 16.0; ESI HRMS: calcd for  $\text{C}_{29}\text{H}_{25}\text{NO}_5\text{Na}^+$  490.1630, found 490.1631.

Compound **10h** was obtained as white solid, 60% yield (39.9 mg). The diastereomeric ratio was determined to be 5 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 172–173 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.51 (dd,  $J = 4.8, 1.2$  Hz, 1H), 7.36 (dd,  $J = 4.2, 1.2$  Hz, 3H), 7.34–7.31 (m, 2H), 7.28 (dd,  $J = 6.6, 1.2$  Hz, 1H), 6.98 (td,  $J = 7.8, 1.2$  Hz, 1H), 6.95 (dd,  $J = 7.2, 0.6$  Hz, 1H), 6.88 (dd,  $J = 7.2, 0.6$  Hz, 1H), 6.83–6.82 (m, 1H), 6.40 (d,  $J = 7.8$  Hz, 1H), 6.08 (s, 1H), 5.06 (d,  $J = 15.6$  Hz, 1H), 4.64 (d,  $J = 15.6$  Hz, 1H), 2.56 (s, 3H), 2.16 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 191.2, 184.9, 177.5, 169.9, 142.4, 140.9, 135.5, 135.4, 132.2, 129.1, 128.9, 128.8, 127.9, 127.7, 127.5, 124.8, 123.0, 118.6, 108.9, 89.2, 62.6, 44.7, 29.1, 15.9; ESI HRMS: calcd for  $\text{C}_{26}\text{H}_{21}\text{NO}_4\text{SNa}^+$  466.1089, found 466.1090.

Compound **10i** was obtained as white solid, 62% yield (45.3 mg). The diastereomeric ratio was determined to be 5 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 170–171 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.90–7.86 (m, 2H), 7.80 (d,  $J = 8.0$  Hz, 1H), 7.63–7.53 (m, 3H), 7.27 (d,  $J = 7.2$  Hz, 2H), 7.09–7.08 (m, 4H), 6.97 (d,  $J = 7.2$  Hz, 1H), 6.87–6.83 (m, 2H), 6.48 (s, 1H), 5.95 (d,  $J = 7.2$  Hz, 1H), 5.00 (d,  $J = 16.0$  Hz, 1H), 3.76 (d,  $J = 16.0$  Hz, 1H), 2.59 (s, 3H), 2.16 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.7, 190.9, 177.3, 169.9, 142.0, 135.4, 134.9, 132.3, 131.8, 129.5, 129.1, 128.9, 128.8, 128.5, 128.3, 127.7, 127.3, 127.0, 126.9, 124.7, 123.0, 122.7, 118.4, 108.8, 89.0, 62.1, 44.4, 29.7, 29.0, 15.9; ESI HRMS: calcd for  $\text{C}_{32}\text{H}_{25}\text{NO}_4\text{Na}^+$  510.1681, found 510.1682.

Compound **10j** was obtained as white solid, 74% yield (41.7 mg). The diastereomeric ratio was determined to be 6 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 145–146 °C;  $^1\text{H}$  NMR (600 MHz,

$\text{CDCl}_3$ )  $\delta$  (ppm) 7.48 (d,  $J = 7.2$  Hz, 2H), 7.36 (t,  $J = 7.8$  Hz, 3H), 7.29 (d,  $J = 7.2$  Hz, 1H), 7.15 (dt,  $J = 3.0, 1.2$  Hz, 1H), 6.93 (d,  $J = 2.4$  Hz, 1H), 6.71 (d,  $J = 7.8$  Hz, 1H), 5.38 (s, 1H), 5.10 (d,  $J = 16.2$  Hz, 1H), 4.99 (d,  $J = 15.6$  Hz, 1H), 2.50 (s, 3H), 2.12 (s, 3H), 1.77 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 201.4, 191.1, 176.9, 169.3, 142.6, 135.5, 129.4, 128.8, 127.7, 127.4, 123.5, 122.9, 109.6, 91.7, 61.2, 44.7, 28.9, 27.3, 15.7; ESI HRMS: calcd for  $\text{C}_{23}\text{H}_{21}\text{NO}_4\text{Na}^+$  398.1368, found 398.1368.

Compound **10k** was obtained as white solid, 76% yield (46.2 mg). The diastereomeric ratio was determined to be 5 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 168–169 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.44 (d,  $J = 7.8$  Hz, 2H), 7.34 (t,  $J = 7.2$  Hz, 2H), 7.28 (d,  $J = 7.2$  Hz, 1H), 7.14 (td,  $J = 7.8, 1.2$  Hz, 1H), 7.02 (dd,  $J = 7.8, 1.2$  Hz, 1H), 6.93 (td,  $J = 7.8, 0.6$  Hz, 1H), 6.67 (d,  $J = 7.8$  Hz, 1H), 5.43 (s, 1H), 5.17 (d,  $J = 15.6$  Hz, 1H), 4.86 (d,  $J = 15.6$  Hz, 1H), 4.20 (m, 1H), 3.72 (m, 1H), 2.50 (s, 3H), 2.13 (s, 3H), 0.50 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 191.2, 176.9, 169.5, 166.1, 143.0, 135.8, 128.3, 128.8, 128.0, 127.7, 123.7, 122.7, 109.2, 85.7, 61.5, 44.6, 34.4, 31.8, 29.0, 15.8, 13.3; ESI HRMS: calcd for  $\text{C}_{24}\text{H}_{23}\text{NO}_5\text{Na}^+$  428.1474, found 428.1476.

Compound **10l** was obtained as white solid, 70% yield (47.8 mg). The diastereomeric ratio was determined to be 10 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 158–159 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.46 (tt,  $J = 7.8, 1.2$  Hz, 1H), 7.33 (dd,  $J = 8.4, 1.2$  Hz, 2H), 7.31–7.28 (m, 4H), 7.20 (td,  $J = 7.8, 1.8$  Hz, 2H), 6.69 (dd,  $J = 7.8, 2.4$  Hz, 1H), 6.60 (td,  $J = 8.4, 2.4$  Hz, 1H), 6.31 (s, 1H), 6.07 (dd,  $J = 8.4, 4.2$  Hz, 1H), 5.30 (s, 1H), 5.10 (d,  $J = 16.0$  Hz, 1H), 4.18 (d,  $J = 16.2$  Hz, 1H), 2.57 (s, 3H), 2.22 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.6, 190.9, 177.2, 159.2 (d,  $J_{\text{CF}} = 241.5$  Hz), 138.3, 135.0, 134.9, 128.9, 128.5, 127.7, 127.6, 127.2, 118.6, 115.3 (d,  $J_{\text{CF}} = 24.0$  Hz), 112.7 (d,  $J_{\text{CF}} = 24.0$  Hz), 109.4 (d,  $J_{\text{CF}} = 9.0$  Hz), 88.8, 62.4, 44.8, 29.1, 15.9; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{FNO}_4\text{Na}^+$  478.1431, found 478.1429.

Compound **10m** was obtained as white solid, 56% yield (38.2 mg). The diastereomeric ratio was determined to be 16 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 160–161 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.43 (tt,  $J = 7.8, 1.2$  Hz, 1H), 7.39 (d,  $J = 7.2$  Hz, 2H), 7.32 (td,  $J = 7.2, 1.8$  Hz, 2H), 7.28–7.25 (m, 1H), 7.23 (dd,  $J = 8.4, 1.2$  Hz, 2H), 7.12 (t,  $J = 7.2$  Hz, 2H), 6.82–6.79 (m, 1H), 6.72–6.68 (m, 2H), 6.27 (s, 1H), 5.09 (d,  $J = 15.6$  Hz, 1H), 4.48 (d,  $J = 15.0$  Hz, 1H), 2.56 (s, 3H), 2.16 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.7, 191.0, 177.1, 170.1, 146.9 (d,  $J_{\text{CF}} = 244.9$  Hz), 136.6, 134.8, 133.8, 128.6, 128.4, 127.6 (d,  $J_{\text{CF}} = 2.0$  Hz), 127.4, 123.5, 123.4, 120.7, 120.6, 118.6, 117.2, 117.0, 89.0, 62.2, 46.1, 29.1, 15.9; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{FNO}_4\text{Na}^+$  478.1431, found 478.1432.

Compound **10n** was obtained as white solid, 66% yield (46.7 mg). The diastereomeric ratio was determined to be 5 : 1 by crude  $^1\text{H}$ -NMR analysis. Mp 159–160 °C;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.46 (t,  $J = 7.8$  Hz, 1H), 7.31 (dd,  $J = 7.8, 1.2$  Hz, 3H), 7.28 (d,  $J = 5.4$  Hz, 3H), 7.24 (dd,  $J = 6.6, 5.4$  Hz, 1H), 7.21 (t,  $J = 7.8$  Hz, 2H), 6.91 (d,  $J = 1.8$  Hz, 1H), 6.87 (dd,  $J = 8.4, 2.4$  Hz, 1H), 6.29 (s, 1H), 6.06 (d,  $J = 8.4$  Hz, 1H), 5.08 (d,  $J = 16.2$  Hz, 1H), 4.18 (d,  $J = 16.2$  Hz, 1H), 2.57 (s, 3H), 2.24 (s, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.7, 191.0, 177.1, 170.1, 147.7, 146.1, 136.6, 134.8, 133.8, 128.6, 128.4, 127.7, 127.6, 127.5, 127.4, 123.5, 123.4, 120.6, 118.6, 117.2, 117.0, 89.0, 62.2, 46.1, 29.0, 15.9; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{ClNO}_4\text{Na}^+$  494.1135, found 494.1133.





Compound **10o** was obtained as yellow solid, 67% yield (47.4 mg). The diastereomeric ratio was determined to be 15 : 1 by crude  $^1\text{H-NMR}$  analysis. Mp 164–165 °C;  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.47 (tt,  $J = 7.2, 1.2$  Hz, 1H), 7.33–7.31 (m, 1H), 7.31–7.28 (m, 5H), 7.21 (td,  $J = 8.4, 1.8$  Hz, 2H), 6.84 (d,  $J = 1.8$  Hz, 2H), 6.28 (s, 1H), 6.16 (s, 1H), 5.05 (d,  $J = 15.6$  Hz, 1H), 4.18 (d,  $J = 16.2$  Hz, 1H), 2.56 (s, 3H), 2.20 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.7, 190.9, 177.4, 170.0, 143.5, 134.9, 134.7, 133.8, 129.0, 128.5, 128.9, 127.8, 127.5, 125.6, 125.5, 122.7, 118.6, 109.4, 88.8, 61.8, 44.7, 29.1, 15.9; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{ClNO}_4\text{Na}^+$  494.1135, found 494.1136.

Compound **10p** was obtained as white solid, 70% yield (54.2 mg). The diastereomeric ratio was determined to be 13 : 1 by crude  $^1\text{H-NMR}$  analysis. Mp 200–201 °C;  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.46 (td,  $J = 7.2, 0.6$  Hz, 1H), 7.31 (d,  $J = 7.8$  Hz, 3H), 7.29–7.27 (m, 4H), 7.21 (t,  $J = 7.2$  Hz, 2H), 7.04 (d,  $J = 1.8$  Hz, 1H), 7.02 (dt,  $J = 8.4, 2.4$  Hz, 1H), 6.29 (s, 1H), 6.02 (dd,  $J = 7.8, 0.6$  Hz, 1H), 5.08 (d,  $J = 15.6$  Hz, 1H), 4.18 (d,  $J = 16.2$  Hz, 1H), 2.57 (s, 3H), 2.24 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.6, 190.9, 176.9, 170.1, 141.4, 135.0, 134.8, 133.7, 131.8, 128.2, 128.9, 128.5, 127.7, 127.7, 127.6, 127.2, 118.6, 115.4, 110.3, 88.8, 62.0, 44.7, 29.1, 16.0; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{BrNO}_4\text{Na}^+$  538.0630, found 538.0632.

Compound **10q** was obtained as yellow solid, 69% yield (54.5 mg). The diastereomeric ratio was determined to be 10 : 1 by crude  $^1\text{H-NMR}$  analysis. Mp 184–185 °C;  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.47 (tt,  $J = 7.8, 1.2$  Hz, 1H), 7.32–7.31 (m, 2H), 7.30–7.26 (m, 5H), 7.21 (td,  $J = 7.2, 1.2$  Hz, 2H), 7.00 (dd,  $J = 7.8, 1.8$  Hz, 1H), 6.78 (d,  $J = 7.8$  Hz, 1H), 6.31 (d,  $J = 1.8$  Hz, 1H), 6.28 (s, 1H), 5.05 (d,  $J = 15.6$  Hz, 1H), 4.18 (d,  $J = 16.2$  Hz, 1H), 2.55 (s, 3H), 2.21 (s, 3H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 192.7, 190.9, 177.3, 170.0, 143.6, 134.8, 134.7, 133.8, 128.9, 128.5, 127.8, 127.5, 127.2, 126.1, 125.9, 125.7, 122.6, 118.5, 112.1, 88.7, 61.8, 44.7, 29.1, 15.9; ESI HRMS: calcd for  $\text{C}_{28}\text{H}_{22}\text{BrNO}_4\text{Na}^+$  538.0630, found 538.0633.

Compound **10r** was obtained as white solid, 80% yield (54.1 mg). The diastereomeric ratio was determined to be 18 : 1 by crude  $^1\text{H-NMR}$  analysis. Mp 162–163 °C;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.42 (t,  $J = 7.2$  Hz, 1H), 7.25 (d,  $J = 4.4$  Hz, 4H), 7.25 (d,  $J = 7.2$  Hz, 3H), 7.16 (t,  $J = 7.6$  Hz, 2H), 6.74 (s, 1H), 6.70 (d,  $J = 8.0$  Hz, 1H), 6.29 (s, 1H), 6.05 (d,  $J = 8.0$  Hz, 1H), 5.06 (d,  $J = 16.0$  Hz, 1H), 4.16 (d,  $J = 16.0$  Hz, 1H), 2.56 (s, 3H), 2.18 (s, 3H), 2.13 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 193.0, 191.1, 177.1, 169.9, 139.8, 135.4, 135.1, 133.3, 132.3, 129.2, 128.7, 128.5, 128.4, 128.3, 127.5, 127.4, 127.3, 126.9, 125.4, 118.4, 108.5, 89.1, 62.0, 44.6, 29.0, 20.9, 15.9; ESI HRMS: calcd for  $\text{C}_{29}\text{H}_{25}\text{NO}_4\text{Na}^+$  474.1681, found 474.1683.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

We are grateful for financial support from the National Natural Science Foundation of China (81573588, 81773889, 21702035), the Science & Technology Department of Sichuan Province (2017JZYD0001, 2017JY0323, 2016TD0006).

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- 13 CCDC 1895883 (for **6r**) contains the supplementary crystallographic data for this paper.†
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