

# Stereoselective synthesis of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles from Morita–Baylis–Hillman adducts of isatin

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## Abstract

A concise stereoselective synthesis of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles from Morita–Baylis–Hillman adducts of isatin in excellent yield has been achieved following a three-step reaction sequences viz. (1) Isomerisation of the Morita–Baylis–Hillman adducts of isatin with trimethyl orthoformate and montmorillonite K10 clay catalyst, (2) a second Morita–Baylis–Hillman reaction with formaldehyde, and (3) an acid catalysed lactonization. The structure and stereochemistry of the products were assigned by X-ray crystallographic and NMR spectroscopic studies. Formation and mechanism of the minor product spirofuran oxindoles and a one-pot base promoted second Morita–Baylis–Hillman adduct formation–lactonization reaction have also been achieved.

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**Keywords:** Baylis–Hillman adduct; Spirolactone; Spirooxindole; Isatin; Lactonization

## 1. Introduction

Oxindoles functionalised at C3 as spirolactones,<sup>1–4</sup> spirocyclic ethers and spirocarbo- and heterocyclics are elegant targets in organic synthesis due to their significant biological activities.<sup>5–7</sup> These derivatives have been served as potential intermediates for the synthesis of alkaloids, drug intermediates and clinical pharmaceuticals.<sup>5–7</sup> A few examples of natural products having spirooxindole core structure are shown in Figure 1. Hence, a number of synthetic methods have been developed for expedition of these structural frameworks.<sup>8–26</sup> The synthetic versatility of isatin and its derivatives has led to the extensive use of this compound in synthetic organic chemistry.<sup>27</sup> Among various carbon–carbon bond forming reactions, the Morita–Baylis–Hillman reaction is an important reaction giving rise to densely functionalized molecules and is considered to be atom economic.<sup>28–30</sup> The synthesis of title compounds

exploiting Morita–Baylis–Hillman adducts of isatin is unknown. Thus, as part of our research in the area of novel synthetic applications of Morita–Baylis–Hillman adducts, in particular with Morita–Baylis–Hillman adduct of isatin,<sup>31–36</sup> herein we report a short and efficient stereoselective synthesis

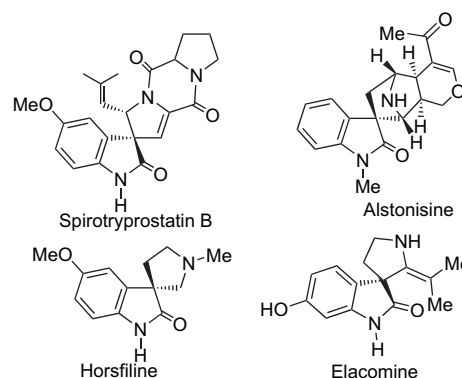


Figure 1. Spirooxindole alkaloid natural products.

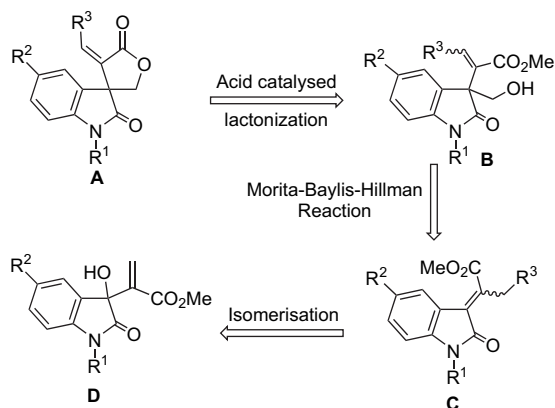
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of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles from Morita–Baylis–Hillman adduct of isatin.

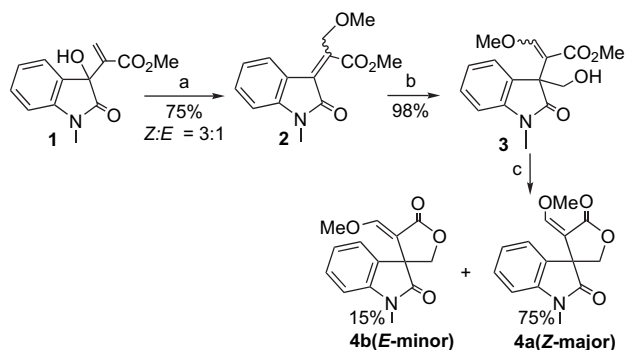
## 2. Results and discussion

The target compounds were synthesized according to retrosynthetic analysis shown in **Scheme 1**. 3-Spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles **A** could be obtained from Morita–Baylis–Hillman adduct derivative **B** by an acid catalysed lactonization reaction. The Morita–Baylis–Hillman adduct derivative **B** could be obtained through a second Morita–Baylis–Hillman reaction with isomerised adducts of Morita–Baylis–Hillman adduct of isatin **C** and formaldehyde. The isomerised adduct **C** could be prepared by isomerisation reaction of Morita–Baylis–Hillman adducts of isatin **D** with trimethyl orthoformate/Ar–H and a solid acid clay catalyst.



Scheme 1. Retrosynthetic analysis.

The preliminary study is depicted in **Scheme 2**. Initially, the reaction of Morita–Baylis–Hillman adduct of *N*-methylisatin **1** with excess of trimethyl orthoformate and montmorillonite K10 clay<sup>37–40</sup> catalyst at 110 °C for 0.5 h afforded a 1:3 mixture of *E*- and *Z*-isomer **2** in excellent overall yield (75%).



Scheme 2. Synthesis of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-methyl oxindoles **4a** and **4b**. (a)  $\text{CH}(\text{OMe})_3/\text{Mont. K10}$ , neat, 110 °C, 30 min; (b) aq  $\text{HCHO}$ , DABCO, rt, acetone, 1.5 h; (c) PTSA/benzene, 30 min.

The *E* and *Z* isomers were inseparable by column chromatography. However, the ratio and distinction of *E* and *Z* isomers were found based on  $^1\text{H}$  NMR study. Thus, the

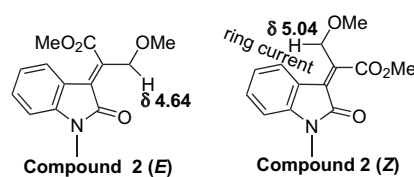


Figure 2. Distinction of *E* and *Z* isomers of **2**.

methylene protons of *E*-isomer appeared as a singlet at  $\delta$  4.64 whereas *Z*-isomer showed the methylene peak at  $\delta$  5.04 due to ring current of aryl ring (deshielding zone) as shown in **Figure 2**.

The column purified *E/Z* mixture **2** in acetone was subjected to a second Morita–Baylis–Hillman adduct formation with 40% aqueous formaldehyde and 1.5 equiv DABCO at room temperature for 2 h to afford adduct **3** in excellent yield (98%). To our surprise, attempts to form the second Morita–Baylis–Hillman adduct from the isomerised compound **2** with benzaldehyde, *p*-chloro benzaldehyde, *p*-nitrobenzaldehyde, acetaldehyde, heptanaldehyde and *E*-crotonaldehyde under optimised condition failed. Thus, we preceded further investigation with formaldehyde derived second Morita–Baylis–Hillman adduct **3**. Exposure of the compound **3** in benzene with *p*-toluenesulfonic acid (PTSA) for 30 min furnished excellent combined yield of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles **4a** (*Z*-isomer major, 75%) and **4b** (*E*-isomer minor, 15%) and the compounds were separated by column chromatography. The structure of the lactones **4a** and **4b** was confirmed by a single crystal X-ray analysis (**Fig. 3**).<sup>41</sup> The assigned geometry of compounds **4a** and **4b** was further supported by the analysis of chemical shifts of vinylic olefin protons in  $^1\text{H}$  NMR spectra. Accordingly, the *Z*-vinyl proton of major isomer **4a** was observed as a singlet at  $\delta$  7.27 whereas *E*-vinyl proton of minor isomer **4b** observed at  $\delta$  6.14 as a singlet.

Encouraged by preliminary results, we then turned our attention to investigate and to generalize the synthesis of spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles with a number of Morita–Baylis–Hillman adducts of isatin substituted at aryl and *N*-alkyl positions as shown in **Scheme 3**.

Hence, we first prepared isomerised Morita–Baylis–Hillman derivatives from various Morita–Baylis–Hillman adducts. The Morita–Baylis–Hillman adducts of isatin substituted at aryl and *N*-alkyl positions **5–10** with trimethyl

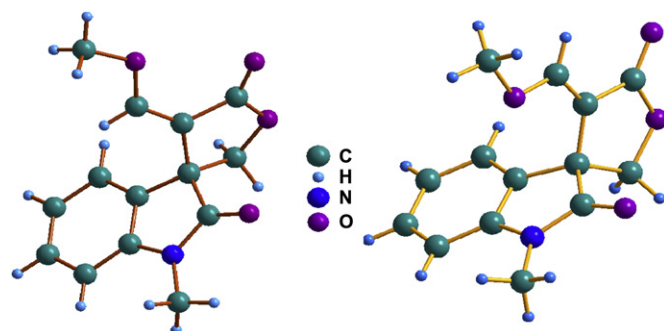
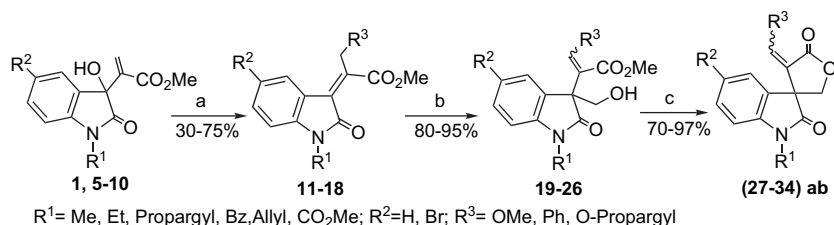


Figure 3. X-ray crystal structure of compounds **4a** and **4b**.



Scheme 3. Synthesis of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-alkyl oxindoles (**27a/b**–**34a/b**). (a)  $\text{CH(OMe)}_3$  (or)  $\text{Ar-H}$  (or) propargyl alcohol/Mont. K10, neat, 110 °C, 30 min; (b) aq HCHO, DABCO, acetone, rt, 2 h; (c) PTSA/benzene, 80 °C, 30 min.

orthoformate, and montmorillonite K10 clay catalyst at 110 °C for 1.5 h afforded the corresponding isomerised compounds **11–16** in moderate to good yields (Table 1 entries 1–6). The isomerisation of Morita–Baylis–Hillman adduct **1** with propargyl alcohol and benzene afforded the corresponding isomerised compounds **17** and **18**. It should be noted that the isomerisation reaction with benzene provided poor yield (30%) of compound **18** (Table 1, entry 8). However, the isomerisation

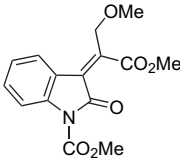
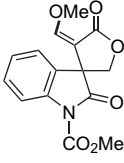
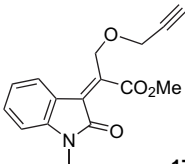
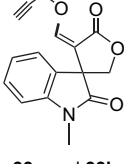
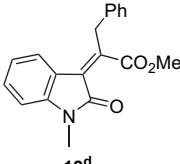
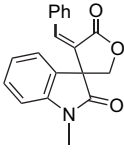
with propargyl alcohol furnished very good yield of **17** (68%, Table 1, entry 7).

In continuation of the target compound synthesis, the second Morita–Baylis–Hillman adduct formation from isomerised derivatives **11–18** with aqueous formaldehyde and DABCO in acetone was performed and the reactions underwent smoothly to afford the corresponding second Morita–Baylis–Hillman adducts **19–26** in very good to excellent yields.

Table 1  
Generality for the synthesis of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-alkyl oxindoles

| Entry | Substrate | Products               |                                  | Yield <sup>b</sup> % |                        |
|-------|-----------|------------------------|----------------------------------|----------------------|------------------------|
|       |           | Isomerised product (A) | Lactone product <sup>a</sup> (B) | (A)                  | (B) (Z/E) <sup>c</sup> |
| 1     | 5         |                        |                                  | 63                   | 90 (2:1)               |
| 2     | 6         |                        |                                  | 65                   | 80 (1:0.2)             |
| 3     | 7         |                        |                                  | 75                   | 95                     |
| 4     | 8         |                        |                                  | 60                   | 70 (1:0.3)             |
| 5     | 9         |                        |                                  | 67                   | 77 (1:0.7)             |

Table 1 (continued)

| Entry | Substrate | Products                                                                          |                                                                                    | Yield <sup>b</sup> % |                        |
|-------|-----------|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|----------------------|------------------------|
|       |           | Isomerised product (A)                                                            | Lactone product <sup>a</sup> (B)                                                   | (A)                  | (B) (Z/E) <sup>c</sup> |
| 6     | 10        |  |  | 57                   | 67 (2:1)               |
|       |           | 16                                                                                | 32a and 32b                                                                        |                      |                        |
| 7     | 1         |  |  | 68                   | 84 (2:1)               |
|       |           | 17                                                                                | 33a and 33b                                                                        |                      |                        |
| 8     | 1         |  |  | 30                   | 97 (1:0.6)             |
|       |           | 18 <sup>d</sup>                                                                   | 34a and 34b <sup>e</sup>                                                           |                      |                        |

<sup>a</sup> Separable by column chromatography.<sup>b</sup> Yield/ratio were determined after column purification.<sup>c</sup> Stereochemistry was assigned based on <sup>1</sup>H NMR and single crystal X-ray studies.<sup>d</sup> The combined yield of the mixture **18** from **1** for 12 h was only 30%.<sup>e</sup> Inseparable by column chromatography.

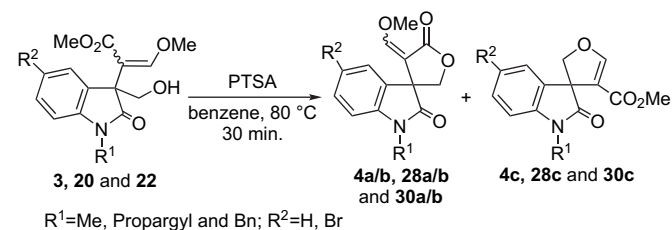
Subsequent to the second Morita–Baylis–Hillman adduct formation, reactions for the lactonization of the silica gel column purified compounds **19**–**26** using PTSA were performed and the results are collected in Table 1. In consequence, the second Morita–Baylis–Hillman adduct **19** upon lactonization using PTSA afforded *Z*- and *E*-isomer of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-ethyl oxindoles **27a/b**, separable by column chromatography, in excellent combined yield (Table 1, entry 1). Similarly, under optimised conditions, highly functionalised second Morita–Baylis–Hillman adducts of *N*-propargyl and *N*-benzyl isatin derivatives **20** and **21** afforded 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-propargyl and benzyl oxindoles **28a/b** and **29a**, respectively, in excellent yield (Table 1, entries 2 and 3). The bromo derivative **22** under lactonization reaction condition furnished spirolactones **30a/b** in very good yield (Table 1, entry 4). Likewise, the *N*-allyl compound **23** furnished the corresponding lactone derivatives **31a/b** in good yield (Table 1, entry 5). The Morita–Baylis–Hillman adducts bearing carbo methoxy functional group at *N*-H position **24** also furnished the desired spirolactones **32a/b** in 67% combined yield (Table 2, entry 6). The second Morita–Baylis–Hillman adducts **25** and **26** upon lactonization using PTSA furnished the corresponding spirooxindole lactone derivatives **33a/b** and **34a/b** in excellent combined yield (Table 1, entries 7 and 8). All the *Z/E* isomers of spirolactone compounds **27a/b**–**33a/b** were separable by column chromatography and thoroughly characterized by spectroscopic methods (IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and HRMS).

During the course of lactonization of second Morita–Baylis–Hillman adducts **3**, **20** and **22** in benzene with PTSA, in addition to the desired lactone products **4a/b**, **28a/b** and **30a/b**, a minor amount of spirofuran oxindole derivatives (<10%) **4c**, **28c** and **30c** were also isolated. The synthetic transformation and results are shown in Table 2.

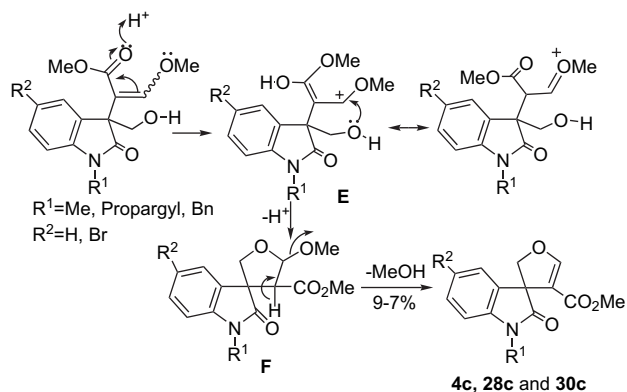
The structures of 3-spiro dihydrofuran compounds were established unambiguously using FTIR and <sup>1</sup>H NMR spectroscopic studies. Thus, in the FTIR spectrum of compounds **4a/b**, the lactone and amide carbonyl absorptions were observed at 1753, 1714 and 1755, 1704 cm<sup>−1</sup>, respectively. However, the IR spectrum of compound **4c** showed the only a merged amide and ester carbonyl absorption at 1714 cm<sup>−1</sup>. Due to the absence of lactone carbonyl absorption at ~1755 cm<sup>−1</sup> for compound **4c**, the structure was assigned as 3-spiro dihydrofuran **4c**. Further structural evidence was arrived from the <sup>1</sup>H NMR spectrum of compound **4c**. Accordingly, the olefinic proton in the spiro dihydrofuran ring appeared as a singlet at  $\delta$  7.58, the ester –OMe appeared as a singlet at  $\delta$  3.53 whereas in the spirolactones **4a/b**, the olefinic proton appeared at  $\delta$  7.27/6.14 and –OMe substituent in exocyclic double bond appeared at  $\delta$  3.67 and 3.82, respectively.

A plausible mechanism for the formation of minor amounts of dihydro spirofuran oxindole derivatives is depicted in Scheme 4. It is assumed that the protonation of second Morita–Baylis–Hillman adduct forms a methoxy-stabilised carbocation **E**. The hydroxyl group of the intermediate **E** undergoes cyclisation with stabilised carbocation by loss of a proton to

Table 2  
Synthesis of 3-spirolactone and 3-spiro dihydrofuran-*N*-alkyl oxindoles



| Entry | Adduct    | Product          |                | Yield (%) |          |
|-------|-----------|------------------|----------------|-----------|----------|
|       |           | Lactone <b>A</b> | Furan <b>B</b> | <b>A</b>  | <b>B</b> |
| 1     | <b>3</b>  | <b>4a/b</b>      |                | 90        | 8        |
| 2     | <b>20</b> | <b>28a/b</b>     |                | 80        | 7        |
| 3     | <b>22</b> | <b>30a/b</b>     |                | 70        | 9        |

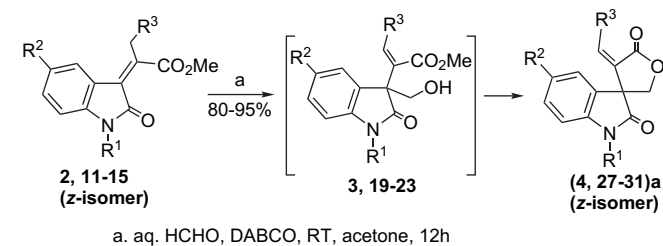


Scheme 4. A plausible mechanism for the formation of spiro dihydrofuran derivatives.

form the intermediate **F**, which upon elimination of methanol affords the spirofuran derivatives.

On further examination on the lactonization studies, we have developed a base promoted one-pot procedure for the second Morita–Baylis–Hillman adducts' formation followed by lactonization reaction. The reaction and the results are collected in Table 3. Thus, as a preliminary experiment, the isomerised *Z*-isomer of adduct **2** was treated with 1.5 equiv DABCO and aqueous formaldehyde in acetone and the

Table 3  
One-pot base promoted Morita–Baylis–Hillman adduct formation–lactonization



| Entry | Substrate | Product    | Yield % |
|-------|-----------|------------|---------|
| 1     | <b>3</b>  | <b>4a</b>  | 90      |
| 2     | <b>11</b> | <b>27a</b> | 92      |
| 3     | <b>12</b> | <b>28a</b> | 90      |
| 4     | <b>13</b> | <b>29a</b> | 95      |
| 5     | <b>14</b> | <b>30a</b> | 80      |
| 6     | <b>15</b> | <b>31a</b> | 85      |

mixture was stirred overnight (12 h). A one-pot base promoted second Morita–Baylis–Hillman adduct formation followed by lactonization occurred smoothly and provided a single *Z*-isomer of the lactone **4a** in excellent yield (90%, Table 3, entry 1).

The formation of *E*-isomer was not observed as per the analysis of crude and purified <sup>1</sup>H NMR spectra of the compounds. In order to show the generality of this observation, reactions with isomerised *Z*-isomers **11–15** with 1.5 equiv DABCO and aqueous formaldehyde in acetone for 12 h afforded the expected *Z*-isomers of 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-alkyl oxindoles **27a–31a** in excellent yields (80–95%) (Table 3, entries 2–6).

### 3. Conclusion

In conclusion, we have developed a short and efficient stereoselective synthesis of highly functionalised 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles along with minor amounts of spirofuran oxindole derivatives from Morita–Baylis–Hillman adducts of isatin for the first time. A one-pot procedure for the second Morita–Baylis–Hillman adduct formation followed by lactonization has been achieved. Further studies in this area are under way in this laboratory.

### 4. Experimental section

#### 4.1. General consideration

All the experiments were carried out in oven-dried glassware. Analytical thin layer chromatography was performed on silica gel TLC plates. Purification by gravity column chromatography was carried out using silica gel (100–200 mesh). Mixture of ethyl acetate, hexane and pure ethyl acetate were used as eluent as required. IR spectra were run on a Nicolet (impact 400D FT-IR) spectrophotometer. NMR spectra were obtained using chloroform-*d* as solvent on Bruker DPX 300 MHz NMR spectrometer. Chemical shifts are given in



$\delta$  scale with TMS as internal reference. HRMS were measured at the JMS 600 JEOL Mass Spectrometer. Yields refer to quantities obtained after chromatography. Solvents used are of reagent grade and were purified before use according to the literature procedure.<sup>42</sup>

#### 4.2. General experimental procedure for isomerisation

**Isomerisation:** A mixture of Morita–Baylis–Hillman adducts (100 mg, 0.404 mmol), excess of trimethyl orthoformate (3 mL) (or) Ar–H (3 mL) (or) propargyl alcohol (3 mL) and montmorillonite K10 clay (50% w/w) without any solvent was heated at 110 °C for 1.5 h. After the reaction (TLC), the crude mixture was purified by a silica gel column chromatography using gradient elution with hexane and hexane–EtOAc (80:20) mixture to afford isomerised products in good yields (68–75%).

#### 4.3. Spectral data for isomerised Baylis–Hillman adducts

##### 4.3.1. Compound (Z)-2

$R_f$  (20% EtOAc–hexanes) 0.42; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1710, 1659, 1608  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.22 (s, 3H), 3.43 (s, 3H), 3.96 (s, 3H), 5.04 (s, 2H), 6.78 (d,  $J=7.8$  Hz, 1H), 6.98 (t,  $J=7.8$  Hz, 1H), 7.22–7.31 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  25.9, 52.6, 59.1, 68.2, 108.3, 119.7, 122.4, 122.6, 124.9, 130.4, 141.6, 143.6, 166.9, 167.5; HRMS calcd for  $\text{C}_{14}\text{H}_{15}\text{NO}_4$ : 261.1001; found: 261.0988.

##### 4.3.2. Compound (E)-2

$R_f$  (20% EtOAc–hexanes) 0.42; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1710, 1659, 1608  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.20 (s, 3H), 3.48 (s, 3H), 3.95 (s, 3H), 4.64 (s, 2H), 6.82 (d,  $J=7.8$  Hz, 1H), 7.10 (t,  $J=6.9$  Hz, 1H), 7.30–7.42 (m, 2H).

##### 4.3.3. Compound (Z)-11

$R_f$  (20% EtOAc–hexanes) 0.38; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1713, 1665, 1614  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  1.26 (t,  $J=7.0$  Hz, 3H), 3.43 (s, 3H), 3.77 (q,  $J=7.0$  Hz, 2H), 3.96 (s, 3H), 5.04 (s, 2H), 6.79 (d,  $J=7.8$  Hz, 1H), 6.96 (t,  $J=7.6$  Hz, 1H), 7.22–7.30 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  12.3, 35.0, 53.2, 54.8, 63.5, 109.2, 119.5, 122.3, 123.2, 125.3, 130.2, 142.5, 143.5, 167.3, 167.8; HRMS calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_4$ : 275.1158; found: 275.1147.

##### 4.3.4. Compound (Z)-12

$R_f$  (20% EtOAc–hexanes) 0.41; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  2146, 1716, 1666, 1613  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  2.22 (t,  $J=2.4$  Hz, 1H), 3.43 (s, 3H), 3.95 (s, 3H), 4.49 (s, 2H), 5.05 (s, 2H), 7.03–7.10 (m, 2H), 7.26–7.37 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  29.6, 52.7, 57.54, 62.7, 72.2, 97.6, 111.3, 119.77, 122.51, 123.2, 125.27, 130.24, 142.06, 143.51, 166.89, 167.40; HRMS calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_4$ : 285.1001; found: 285.0992.

##### 4.3.5. Compound (Z)-13

$R_f$  (20% EtOAc–hexanes) 0.47; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1717, 1667, 1603  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.45 (s, 3H), 3.98 (s, 3H), 4.92 (s, 2H), 5.10 (s, 2H), 6.69 (d,  $J=7.8$  Hz, 1H), 6.96 (t,  $J=7.8$  Hz, 1H), 7.16–7.33 (m, 7H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  44.2, 52.8, 53.9, 62.6, 106.2, 109.3, 122.7, 123.5, 126.8 (2C), 127.6, 128.5 (2C), 129.0, 131.2, 135.4, 142.6, 143.6, 174.8, 175.7; HRMS calcd for  $\text{C}_{20}\text{H}_{19}\text{NO}_4$ : 337.1314; found: 337.1303.

##### 4.3.6. Compound (Z)-14

$R_f$  (20% EtOAc–hexanes) 0.43; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1721, 1667, 1605  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.43 (s, 3H), 3.87 (s, 3H), 4.92 (s, 2H), 5.04 (s, 2H), 6.63 (d,  $J=8.4$  Hz, 1H), 7.28–7.34 (m, 8H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  44.4, 52.9, 62.9, 73.8, 105.8, 110.5, 116.2, 126.1, 127.3 (2C), 128.2, 128.8 (2C), 131.8, 132.6, 135.1, 141.7, 143.6, 170.4, 172.8; HRMS calcd for  $\text{C}_{20}\text{H}_{18}\text{BrNO}_4$ : 415.0419; found: 415.0417.

##### 4.3.7. Compound (Z)-15

$R_f$  (20% EtOAc–hexanes) 0.47; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1715, 1664, 1612  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.54 (s, 3H), 4.08 (s, 3H), 4.45–4.52 (m, 2H), 5.18 (s, 1H), 5.29–5.35 (m, 2H), 5.5 (m, 1H), 6.91 (d,  $J=7.5$  Hz, 1H), 7.09 (t,  $J=7.4$  Hz, 1H), 7.35–7.341 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  42.6, 52.77, 52.9, 62.6, 106.20, 109.3, 117.5, 122.8, 123.2, 128.7, 130.63, 131.2, 142.5, 158.4, 173.9, 174.6; HRMS calcd for  $\text{C}_{16}\text{H}_{17}\text{NO}_4$ : 287.1158; found: 287.1150.

##### 4.3.8. Compound (Z)-16

$R_f$  (20% EtOAc–hexanes) 0.39; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1702, 1659, 1607  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.43 (s, 3H), 3.98 (s, 3H), 4.04 (s, 3H), 5.00 (s, 2H), 7.13–7.44 (m, 3H), 7.98 (t,  $J=7.8$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  52.8, 53.4, 59.3, 67.8, 105.7, 108.4, 122.3, 123.6, 129.4, 131.7, 143.3, 143.8, 167.5, 174.9, 175.3; HRMS calcd for  $\text{C}_{15}\text{H}_{15}\text{NO}_6$ : 305.0899; found: 305.0900.

#### 4.4. General experimental procedure for second Baylis–Hillman adduct formation and lactonisation

**Second Morita–Baylis–Hillman adduct formation:** A mixture of isomerised Morita–Baylis–Hillman adducts (100 mg, 0.382 mmol) was treated with 40% aqueous formaldehyde (0.5 mL) and DABCO (1.5 equiv) in acetone (3 mL) and stirred for 2 h at room temperature. The crude mixture was passed through a silica gel column using gradient elution with hexane and hexane–EtOAc (70:30) mixture to afford pure adducts as inseparable mixture (combined yield: 80–90%). **Lactonisation:** The mixture of second Morita–Baylis–Hillman adducts (100 mg, 0.343 mmol) in benzene (5 mL) and PTSA (cat. 0.3 equiv) was refluxed at 80 °C for 30 min. The reaction mixture in  $\text{CH}_2\text{Cl}_2$  (50 mL) was washed with saturated  $\text{NaHCO}_3$ , brine and water. The organic layer

was separated, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated under vacuum. The crude mixture was purified by a column chromatography using gradient elution with hexane and hexane–EtOAc (80:20) mixture to afford 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone-*N*-alkyl oxindoles in 70–97% isolated yields.

#### 4.5. Spectral data for 3-spiro- $\alpha$ -methylene- $\gamma$ -butyrolactone oxindoles compounds

##### 4.5.1. Compound 4a

$R_f$  (20% EtOAc–hexanes) 0.38. IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1753, 1714, 1667, 1612, 1470, 1048  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.26 (s, 3H), 3.67 (s, 3H), 4.34 (d,  $J=8.8$  Hz, 1H), 4.59 (d,  $J=8.8$  Hz, 1H), 6.86 (d,  $J=7.8$  Hz, 1H), 7.09 (t,  $J=7.5$  Hz, 1H), 7.22 (d,  $J=7.4$  Hz, 1H), 7.27 (s, 1H), 7.32 (t,  $J=7.7$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  26.6, 52.8, 62.9, 73.8, 106.2, 108.2, 122.7, 123.4, 128.9, 130.8, 143.3, 158.6, 170.8, 175.2; HRMS calcd for  $\text{C}_{14}\text{H}_{13}\text{NO}_4$ : 259.0845; found: 259.0845.

##### 4.5.2. Compound 4b

$R_f$  (20% EtOAc–hexanes) 0.28. IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1755, 1704, 1657, 1607, 1465, 1071  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.24 (s, 3H), 3.82 (s, 3H), 4.29 (d,  $J=8.8$  Hz, 1H), 4.55 (d,  $J=8.8$  Hz, 1H), 6.14 (s, 1H), 6.88 (d,  $J=7.7$  Hz, 1H), 7.12 (t,  $J=7.5$  Hz, 1H), 7.27 (d,  $J=7.4$  Hz, 1H), 7.34 (t,  $J=7.7$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  26.7, 53.1, 63.3, 73.2, 105.6, 108.7, 122.3, 123.4, 129.4, 131.6, 143.0, 158.1, 167.2, 176.5; HRMS calcd for  $\text{C}_{14}\text{H}_{13}\text{NO}_4$ : 259.0845; found: 259.0840.

##### 4.5.3. Compound 27a

$R_f$  (20% EtOAc–hexanes) 0.37. IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1750, 1715, 1667, 1611, 1486, 1051  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  1.27 (t,  $J=7.1$  Hz, 3H), 3.67 (s, 3H), 3.62–3.98 (m, 2H), 4.35 (d,  $J=8.8$  Hz, 1H), 4.59 (d,  $J=8.8$  Hz, 1H), 6.87 (d,  $J=7.8$  Hz, 1H), 7.07 (t,  $J=7.4$  Hz, 1H), 7.22–7.34 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  12.3, 35.0, 52.9, 62.5, 73.7, 106.7, 108.3, 122.9, 123.1, 128.9, 131.2, 142.4, 158.4, 170.71, 174.6; HRMS calcd for  $\text{C}_{15}\text{H}_{15}\text{NO}_4$ : 273.1001; found: 273.1006.

##### 4.5.4. Compound 27b

$R_f$  (20% EtOAc–hexanes) 0.26. IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1755, 1715, 1652, 1612, 1468, 1073  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  1.30 (t,  $J=7.1$  Hz, 3H), 3.77 (q,  $J=7.1$  Hz, 2H), 4.31 (d,  $J=8.8$  Hz, 1H), 4.56 (d,  $J=8.8$  Hz, 1H), 6.13 (s, 1H), 6.92 (d,  $J=7.8$  Hz, 1H), 7.12 (t,  $J=7.5$  Hz, 1H), 7.29 (d,  $J=6.8$  Hz, 1H), 7.35 (t,  $J=7.7$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  12.7, 35.1, 53.0, 63.3, 73.1, 105.8, 108.8, 123.6 (2C), 129.3, 131.8, 142.1, 157.9, 167.1, 176.1; HRMS calcd for  $\text{C}_{15}\text{H}_{15}\text{NO}_4$ : 273.1001; found: 273.1003.

##### 4.5.5. Compound 28a

$R_f$  (20% EtOAc–hexanes) 0.34. IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  2146, 1747, 1716, 1666, 1613, 1489, 1051  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR

( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  2.55 (t,  $J=2.5$  Hz, 1H), 3.68 (s, 3H), 4.36–4.70 (m, 4H), 7.06 (d,  $J=7.8$  Hz, 1H), 7.13 (t,  $J=7.6$  Hz, 1H), 7.25 (d,  $J=6.9$  Hz, 1H), 7.28 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  29.6, 52.7, 62.7, 72.2, 73.6, 98.0, 103.7, 109.2, 122.8, 123.8, 128.9, 130.7, 141.4, 158.7, 170.5, 174.3; HRMS calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}_4$ : 283.0845; found: 283.0837.

##### 4.5.6. Compound 28b

$R_f$  (20% EtOAc–hexanes) 0.37; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  2143, 1752, 1715, 1667, 1612, 1487, 1049  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  2.28 (t,  $J=2.5$  Hz, 1H), 3.85 (s, 3H), 4.32–4.63 (m, 4H), 6.61 (s, 1H), 6.91–7.41 (m, 4H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  29.9, 53.2, 63.7, 73.1, 73.2, 77.4, 109.7, 111.3, 115.5, 116.6, 123.8, 124.5, 129.7, 158.3, 168.9, 178.3; HRMS calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}_4$ : 283.0845; found: 283.0835.

##### 4.5.7. Compound 29a

$R_f$  (20% EtOAc–hexanes) 0.35; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1747, 1714, 1667, 1607, 1486, 1050  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.62 (s, 3H), 4.38 (d,  $J=8.8$  Hz, 1H), 4.64 (d,  $J=8.8$  Hz, 1H), 4.65 (d,  $J=15.6$  Hz, 1H), 5.22 (d,  $J=15.6$  Hz, 1H), 6.75 (d,  $J=7.7$  Hz, 1H), 7.05 (t,  $J=6.9$  Hz, 1H), 7.18–7.33 (m, 8H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  44.2, 52.8, 62.6, 74.1, 106.2, 109.2, 122.8, 123.4, 127.4 (2C), 127.7, 128.7 (2C), 128.8, 130.9, 135.5, 142.4, 158.6, 170.7, 175.3; HRMS calcd for  $\text{C}_{20}\text{H}_{17}\text{NO}_4$ : 335.1158; found: 335.1153.

##### 4.5.8. Compound 30a

$R_f$  (20% EtOAc–hexanes) 0.36; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1744, 1722, 1668, 1602, 1484, 1053  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.66 (s, 3H), 4.37 (d,  $J=8.9$  Hz, 1H), 4.60 (d,  $J=15.7$  Hz, 1H), 4.63 (d,  $J=8.9$  Hz, 1H), 5.22 (d,  $J=15.7$  Hz, 1H), 6.62 (d,  $J=8.4$  Hz, 1H), 7.28–7.34 (m, 8H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  44.4, 52.9, 62.9, 73.8, 105.8, 110.8, 116.1, 126.2, 127.4 (2C), 128.0, 128.9 (2C), 131.8, 132.9, 135.1, 141.5, 159.0, 170.4, 174.9; HRMS calcd for  $\text{C}_{20}\text{H}_{16}\text{BrNO}_4$ : 413.0263; found: 413.0263.

##### 4.5.9. Compound 30b

$R_f$  (20% EtOAc–hexanes) 0.27; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1751, 1712, 1668, 1605, 1486, 1054  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.85 (s, 3H), 4.34 (d,  $J=8.9$  Hz, 1H), 4.62 (d,  $J=8.9$  Hz, 1H), 4.84 (d,  $J=15.4$  Hz, 1H), 4.94 (d,  $J=15.4$  Hz, 1H), 6.11 (s, 1H), 6.70 (d,  $J=8.2$  Hz, 1H), 7.28–7.41 (m, 7H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  44.3, 53.1, 63.6, 72.88, 105.4, 111.2, 116.4, 126.8, 127.4 (2C), 128.2 (2C), 129.1 (2C), 132.2, 135.1, 141.1, 158.3, 176.6, 178.4; HRMS calcd for  $\text{C}_{20}\text{H}_{16}\text{BrNO}_4$ : 413.0263; found: 413.0263.

##### 4.5.10. Compound 31a

$R_f$  (20% EtOAc–hexanes) 0.36; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1752, 1714, 1668, 1611, 1471, 1047  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.68 (s, 3H), 4.18 (dd,  $J=5.2$ , 16.6 Hz, 1H),

4.38 (d,  $J=8.8$  Hz, 1H), 4.54–4.62 (m, 2H), 5.22–5.28 (m, 2H), 5.79–5.85 (m, 1H), 6.84 (d,  $J=7.8$  Hz, 1H), 7.08 (t,  $J=7.5$  Hz, 1H), 7.25–7.31 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  42.6, 52.7, 62.6, 74.0, 106.3, 109.1, 117.3, 122.8, 123.3, 128.8, 130.8, 130.9, 142.4, 158.5, 170.7, 174.8; HRMS calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_4$ : 285.1001; found: 285.0992.

#### 4.5.11. Compound 31b

$R_f$  (20% EtOAc–hexanes) 0.29; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1756, 1702, 1659, 1606, 1464, 1071  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.85 (s, 3H), 4.32–4.38 (m, 3H), 4.58 (d,  $J=9.0$  Hz, 1H), 5.26–5.29 (m, 2H), 5.85 (m, 1H), 6.15 (s, 1H), 6.90 (d,  $J=7.8$  Hz, 1H), 7.13 (t,  $J=7.5$  Hz, 1H), 7.25–7.35 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  43.2, 52.8, 62.6, 74.0, 106.2, 109.2, 117.4, 122.8, 123.4, 129.3, 131.3, 131.7, 142.4, 158.6, 167.87, 175.7; HRMS calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_4$ : 285.1001; found: 285.0993.

#### 4.5.12. Compound 32a

$R_f$  (20% EtOAc–hexanes) 0.37; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1756, 1702, 1659, 1606, 1464, 1071  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.68 (s, 3H), 4.04 (s, 3H), 4.36 (d,  $J=8.9$  Hz, 1H), 4.63 (d,  $J=8.9$  Hz, 1H), 7.23–7.40 (m, 4H), 7.93 (t,  $J=8.4$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  52.8, 59.3, 67.8, 74.0, 105.7, 108.6, 122.1, 123.5, 129.2, 132.4, 143.3, 158.5, 167.4, 174.8, 175.7; HRMS calcd for  $\text{C}_{15}\text{H}_{13}\text{NO}_6$ : 303.0743; found: 303.0732.

#### 4.5.13. Compound 32b

$R_f$  (20% EtOAc–hexanes) 0.27; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1756, 1702, 1659, 1606, 1464, 1071  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.68 (s, 3H), 4.13 (s, 3H), 4.36 (d,  $J=8.9$  Hz, 1H), 4.61 (d,  $J=8.9$  Hz, 1H), 6.19 (s, 1H), 6.89 (d,  $J=7.7$  Hz, 1H), 7.07–7.42 (m, 3H), 7.92 (t,  $J=8.3$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  53.2, 58.5, 66.9, 73.5, 105.6, 109.7, 122.5, 124.3, 129.3, 132.3, 143.6, 158.5, 168.4, 174.4, 175.8; HRMS calcd for  $\text{C}_{15}\text{H}_{13}\text{NO}_6$ : 303.0743; found: 303.0734.

#### 4.5.14. Compound 33a

$R_f$  (20% EtOAc–hexanes) 0.36; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  2120, 1747, 1715, 1668, 1048  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  2.42 (t,  $J=2.3$  Hz, 1H), 3.14 (s, 3H), 4.24–4.27 (m, 3H), 4.50 (d,  $J=8.9$  Hz, 1H), 6.75 (d,  $J=7.8$  Hz, 1H), 6.97 (t,  $J=7.5$  Hz, 1H), 7.13 (d,  $J=7.3$  Hz, 1H), 7.21 (t,  $J=7.6$  Hz, 1H), 7.35 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  26.9, 53.0, 61.9, 74.1, 76.2, 78.1, 108.5, 108.6, 123.0, 123.6, 129.2, 130.79, 143.6, 155.4, 170.5, 175.2; HRMS calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}_4$ : 283.0845; found: 283.0843.

#### 4.5.15. Compound 33b

$R_f$  (20% EtOAc–hexanes) 0.27; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  2123, 1754, 1713, 1667, 1051  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  2.52 (t,  $J=2.3$  Hz, 1H), 3.26 (s, 3H), 4.31 (d,  $J=8.7$  Hz, 1H), 4.55–4.65 (m, 3H), 6.34 (s, 1H), 6.89 (d,  $J=7.8$  Hz, 1H), 7.12 (t,  $J=7.3$  Hz, 1H), 7.25–7.37 (m, 2H);

$^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  26.8, 29.8, 53.2, 61.8, 73.2, 77.9, 106.4, 107.7, 123.5, 123.8, 129.5, 131.4, 143.2, 154.3, 166.5, 176.1.

### 4.6. Spectral data for 3-spiro dihydrofuran compounds

#### 4.6.1. Compound 4c

$R_f$  (20% EtOAc–hexanes) 0.47; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1714, 1615, 1492, 1471  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.27 (s, 3H), 3.53 (s, 3H), 4.64 (d,  $J=9.5$  Hz, 1H), 4.90 (d,  $J=9.5$  Hz, 1H), 6.86 (d,  $J=7.7$  Hz, 1H), 7.08 (t,  $J=7.5$  Hz, 1H), 7.21 (d,  $J=7.2$  Hz, 1H), 7.30 (t,  $J=7.7$  Hz, 1H), 7.58 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  26.6, 51.0, 56.7, 85.2, 108.0, 112.7, 113.1, 122.9, 129.0, 131.4, 143.4, 159.4, 162.9, 176.6; HRMS calcd for  $\text{C}_{14}\text{H}_{13}\text{NO}_4$ : 259.0845; found: 259.0842.

#### 4.6.2. Compound 28c

$R_f$  (20% EtOAc–hexanes) 0.48; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  2186, 1715, 1615, 1486  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  2.27 (t,  $J=2.5$  Hz, 1H), 3.51 (s, 3H), 4.51 (dd,  $J=17.6$ , 2.5 Hz, 1H), 4.62 (dd,  $J=17.6$ , 2.5 Hz, 1H), 4.80 (d,  $J=9.6$  Hz, 1H), 4.91 (d,  $J=9.6$  Hz, 1H), 7.07–7.26 (m, 3H), 7.32 (t,  $J=7.7$  Hz, 1H), 7.59 (s, 1H); HRMS calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}_4$ : 283.0845; found: 283.0838.

#### 4.6.3. Compound 30c

$R_f$  (20% EtOAc–hexanes) 0.48; IR ( $\text{CH}_2\text{Cl}_2$ ):  $\nu_{\text{max}}$  1717, 1621, 1485  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 300.1 MHz):  $\delta$  3.53 (s, 3H), 4.66 (d,  $J=9.6$  Hz, 1H), 4.77 (d,  $J=15.8$  Hz, 1H), 4.95 (d,  $J=9.6$  Hz, 1H), 5.11 (d,  $J=15.8$  Hz, 1H), 6.57 (d,  $J=8.2$  Hz, 1H), 7.27–7.35 (m, 7H), 7.62 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3/\text{TMS}$ , 75.3 MHz):  $\delta$  44.5, 51.4, 57.0, 82.3, 110.8, 112.4, 115.8, 126.5, 127.3 (2C), 127.8, 128.8 (2C), 131.9, 133.2, 135.0, 141.6, 160.3, 163.0, 176.8; HRMS calcd for  $\text{C}_{20}\text{H}_{16}\text{BrNO}_4$ : 413.0263; found: 413.0254.

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